

JOURNAL of SCIENCE & MEDICINE

Spring 2019

Volume 4, Issue 1

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Thank You

The all-volunteer student and faculty staff of the *Wake Forest Journal of Science and Medicine* would like to extend our deepest appreciation to the following individuals for their guidance and assistance:

Julie Freischlag, M.D.
Cynthia Burns, M.D.
Timothy Peters, M.D.
Sheila Lambert
Justin Lamont Farrar
Cinnamon Pritchard
Mark McKone
Leslie Messick

We would also like to express our gratitude to the following for their generous financial support:

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Department of Biomedical Engineering
Department of Emergency Medicine
Department of Family Medicine
Department of General Surgery
Department of Internal Medicine
Department of Internal Medicine, Section on Gastroenterology
Department of Internal Medicine, Section on Nephrology
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Dear Readers,

We present to you Volume 4 of the Wake Forest Journal of Science and Medicine. We thank each author, reviewer, faculty mentor, and administrator who has assisted us in this tremendous effort. Most of all, we thank our student staff, who have shown unwavering commitment and curiosity throughout the process.

All of us involved in the Journal stand on the shoulders of those students who established the Journal, nurtured it in its infancy, and established its reputation within our institution. We hope that our legacy will comprise continuing publication of high-quality research and expanding readership across institutions.

For the three of us, senior medical students, this is a bittersweet accomplishment as we reflect on the past several years of the Journal. We have helped it grow from a fledgling project in its first issue to an endeavor involving medical students of all levels. The journal has impacted us each individually. We will take these experiences with us as we embark upon residency training programs across the country.

We have encouraged the younger editors to dedicate themselves to the task of filling the Journal with quality research. Indeed, the variety of disciplines represented herein speak volumes of the skill of younger students to learn quickly and take ownership of their work.

We thank you for your support of the Journal. We leave it in the capable hands of the medical students who have worked assiduously alongside us in our effort. We mark the end of our medical school careers in a way that will continue, we hope, long after we leave.

We hope that you find in this issue the inquisitive spirit that drew us to medicine and continues to inspire us.

Sincerely,

Lauren Edgar, Revathy Sampath-Kumar, and Emily Gall
Editors-in-Chief

Minding the Mirror: The Real Value of Simulation to Medical Education

Jennifer Jackson, M.D.¹

“One and two and three and four; five and six, seven and eight. Again...”

Miss Christine counts out the rhythm as we attempt the new dance steps she demonstrated to our class. She paces around us, patiently watching and redirecting us when we deviate from the intended sequence. All the while, we face forward, focusing intently on the image of ourselves in the wall-sized mirror lining the studio. It gave us the visual feedback we needed to get it right.

Reflection, iterative rehearsal, and feedback on one’s skills are crucial to the development of professional expertise.¹ These elements are central to deliberate practice (DP), an expert performance principle involving highly motivated learners focused on well-defined learning objectives at an appropriate level of difficulty; with ample opportunities for focused, repetitive practice; yielding informative, immediate feedback to promote a learner’s monitoring, error correction, and more practice toward a mastery standard.² This expert performance perspective originated from domains other than medicine—sports, chess, performing arts, and the military—in which experts have long appreciated the importance of DP to expertise development.

It has only been in more recent decades that medical educators have begun applying DP to their own curricula.^{1,3} One such instructional method is simulation-based medical education (SBME), a category of instruction that offers learners opportunities to rehearse skills and achieve competence in a learning laboratory before performing those skills in the workplace. Multiple studies have demonstrated meaningful improvements in patient outcomes as a result of SBME, making it a uniquely powerful educational tool.⁴

Misconceptions regarding SBME exist, which have limited its adoption by some educators. A common perception is that SBME equates to learners interacting with a high-tech mannequin operated by an elaborate software system. While technology-enhanced instruction is certainly one form of SBME, it simply represents one subset. Simulation, broadly speaking, is an experience during which learners interact with people and/or other learning tools in order “to experience a representation of a real event for the purpose of practice, learning, evaluation, testing, or to gain understanding of systems or human actions.”⁵ SBME need not involve high-tech tools but may instead take the form of standardized patient encounters, role-plays with peers or instructors, or basic skills practice with simple props. Indeed, successful performance gains have been demonstrated even with these low-fidelity forms of SBME.

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Another common misconception is that SBME is an instructional method intended solely for procedure or resuscitation training. This is likely due in part to the context in which many clinicians have encountered SBME as learners, and also due to the plethora of SBME literature in these contexts. SBME can be applied well beyond psychomotor skills training, however, to areas such as basic science knowledge application, diagnostic reasoning, communication skills, quality improvement, patient safety, and bioethics. Within these newer educational contexts, SBME has recently gained traction, opening doors to innovative applications with evidence of more effective learning outcomes compared to traditional training methods.⁶⁻⁸

Related to the above assumptions, some educators also assume that SBME can be applied effectively only with the most advanced trainees, resulting in reluctance to apply it with more novice learner groups. However, SBME has been applied successfully across the healthcare educational spectrum, from novices to practicing professionals.

Simply using SBME does not guarantee successful learning. Certain instructional design elements are crucial—namely, the use of DP principles with special attention to establishing clear performance goals, maintaining a safe learning environment, and providing effective performance feedback.^{9,10}

In SBME settings, learners receive feedback both during a simulation exercise from the simulation environment as well as afterward, during the debriefing—a critical period during which the instructor facilitates a task analysis with learners, reflecting on their performance to identify and understand performance gaps. It is through this debriefing ‘mirror’ that the most meaningful learning in SBME takes place. This reflection step is essential to learners’ ability to meaningfully transfer learning from their simulation experience to other contexts.¹¹ For this reason, it is imperative that instructors pursue training in debriefing techniques, so that key learning objectives can be achieved effectively.¹²⁻¹⁶ Unfortunately, it is not uncommon for educators to focus primarily on the simulation exercise itself such that the debriefing becomes an afterthought rather than a deliberately planned event, which can result in sub-optimal learning.

As one of SBME’s greatest strengths is its ability to provide

learners with an engaging, active learning experience, great care should be taken to avoid learner disengagement. The importance of a safe learning environment cannot be overemphasized in this context.^{17,18} Once a learner experiences embarrassment or humiliation, s/he is thereafter disengaged, and meaningful learning is halted. Disengagement can also occur if the level of difficulty (intrinsic cognitive load) of a simulation activity is too high for learners’ stage of training. Extraneous cognitive load (cognitive load due to suboptimal instructional design) can also disengage learners during SBME and is unfortunately a common challenge in technology-enhanced SBME training environments, in which learners may struggle to interact with the technology at the expense of the intended learning objectives.¹⁹⁻²⁰ It is important, therefore, to note that technology is a tool that can either enhance or detract from successful learning and should be implemented thoughtfully.

The beauty of simulation is both its versatility and its potential to engage us, as educators, in deliberate practice of educational quality improvement. Learners’ level of engagement, their subjective experience, and their observed performance during SBME activities provide a rich dataset from which we can enhance our curricula and our teaching skills, thereby advancing our learners’ development. In this way, simulation is not simply a mirror for our learners: it is also a reflection of our own performance as their instructors.

Miss Christine understood the importance of the mirror, and so did we, even at the age of four. It’s why she insisted we always face it in her class. Let us challenge ourselves to provide learners with more opportunities to take advantage of the performance feedback mirror. And may we also seek our own reflection with open-mindedness and humility. Our students—and their future patients—deserve it.

*This work is dedicated in loving memory to
Ms. Christine Goodman.*

Disclosures

No funding was given. Author declares no conflicts of interest

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Transitioning to Adult Care for Children and Youth with Special Healthcare Needs: Patient and Caregiver Perspectives

Cara Haberman, M.D.¹, Shannon Golden, M.A.², Donna Ashford², Anna Miller-Fitzwater, M.D., M.P.H.¹

Abstract

Introduction: Transitioning from a pediatric to an adult model of care is a high-risk time for Children and Youth with Special Health Care Needs (CYSHCN). While national standards and tools have been developed for transition care, uptake remains suboptimal. Understanding the specific difficulties patients face during transition within a medical community may help identify areas of highest need for transition care services.

Methods: CYSHCN and caregivers of CYSHCN who were nearing or recently completed transition participated in focus groups which assessed various aspects of their experience with the transition process. Thematic analysis was performed with inductive coding derived from transcripts. Content of codes was reviewed through an iterative process to identify themes.

Results: Two focus groups were held consisting of five patient-caregiver units. Major themes that emerged from analysis were: age does not indicate transition readiness; patients feel prepared for their outpatient transition but not their emergency department transition; pediatric care differs from adult care in both the social and physical environment; and patients desire more transition resources.

Discussion: Transition to adult care remains difficult, and patient perspective can inform development of local transition resources. The emergency department experience is an unexpected area which may benefit from targeted transition tools.

Introduction

Transitioning from pediatric care to the adult model of health care is a stressful and potentially dangerous time for Children and Youth with Special Health Care Needs (CYSHCN).¹ It has been associated with poor outcomes and complications in a wide variety of diseases, including worsened glycemic control in patients with type 1 diabetes,² increased risk of urgent cardiac intervention in patients with congenital heart disease,³ increased emergency department visits in patients with sickle cell disease,⁴ and higher rate of graft loss in patients with kidney transplants.⁵ A 2002 consensus statement from multiple national organizations set the gold standard for transition care,⁶ yet over a decade later much of the country has failed to develop practices that meet those standards.¹ Many studies have identified barriers to successful transition within specific populations, including poor communication between providers, inadequate preparation, difficulty accessing adult care, excessive parental involvement, and reluctance of pediatric providers to relinquish care.⁷⁻¹⁰

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Proposed solutions to address these barriers also abound in the literature, with varying degrees of success. Most solutions fall into two main categories. The first consists of disease-specific clinics adopting coordinated transition programs for their specific patient population. This method has demonstrated success in specific populations, with the most prevalent literature related to improved outcomes for patients with type 1 diabetes.¹¹⁻¹³ This model requires significant resources to staff each individual clinic with knowledgeable personnel.

The second category of interventions involves the creation of transition clinics i.e., medical homes that are designed purposefully for older adolescents and young adults to shepherd them through the transition years. These clinics are typically based in large academic centers and are staffed with Internal Medicine/Pediatric trained physicians or transition-knowledgeable physicians. They generally have more services dedicated to transition needs than most pediatric clinics do.¹⁴ This model may only be practical at large institutions or those that have a combined Internal Medicine-Pediatrics residency program, and could be difficult to implement at institutions without such resources.

While there is some debate as to how transition initiatives should be assessed for success, there is a growing body of evidence that these interventions do have a positive impact on patient experience, population health and healthcare utilization.^{15,16} Despite this, many institutions still struggle to implement improvements to transition care.¹⁷ The primary aim of this study is to understand the current experience of transition to the adult care model in our community through the lens of patients and caregivers preparing for or recently completing transition. We hypothesize that an in-depth assessment of their experiences may identify transition needs that could be met through additional services. A secondary aim of the study is to identify strategies and tools that patients and caregivers would find helpful when navigating the transition process.

Methods

Setting: This was an IRB-approved, single-site study conducted at Brenner Children's Hospital, an academic children's hospital within the Wake Forest Baptist Medical Center with over 21,000 pediatric subspecialty visits per year.

Study Design: A qualitative approach using joint patient and caregiver focus groups was selected as the methodology to allow in-depth exploration of themes related to the experience of transition.

Subject Selection: Subjects were eligible if they were age 16-25 years old and had a chronic medical condition requiring a pediatric subspecialist or they were the caregiver of an eligible patient. Patients with cognitive disabilities or limited ability to communicate were eligible and in those cases parental guardians were allowed to decide to what extent their children would participate. English- and Spanish-speaking patients and caregivers were eligible, although ultimately only English-speaking patients and caregivers participated in focus groups. Patients and caregivers were recruited in person or via phone by their pediatric subspecialist on the basis of recently preparing for or recently undergoing transition to adult care. This was followed by a recruitment phone call from the study staff.

Data Collection: Focus groups were held in the evening hours to maximize participation. Child care, dinner, and gas cards were provided, and participants received an additional incentive gift card for their time. A semi-structured focus group guide with open-ended questions was designed by the research team to direct discussion (Table 1). Questions assessed the experience of both the caregiver and the patient with their pediatric health care, the transition process itself, and their adult health care. An experienced moderator conducted the focus groups and adapted questions as needed if unexpected content emerged during the course of the discussion. Focus groups were audio recorded and transcribed verbatim for analysis.

Analytic method: Transcripts were reviewed against original recordings for accuracy, then de-identified and imported into Atlas.ti (v.8). Principles of thematic analysis guided the team.¹⁸ Initial coding was inductive; codes were derived from the text to capture concepts of importance. Codes were added and applied across transcripts as additional concepts emerged from the data. Segments of text were abstracted by single codes or combinations of codes and reviewed iteratively for patterns and themes. Themes were derived by their prevalence and salience in the data.

Table 1. Focus Group Discussion Guide

Focus Group Discussion Guide
1. Let's start by sharing where you are in the process of transitioning from pediatric care to adult care (moderator establishes "complete," "not started," or "mid-transition")
2. How prepared do you or did you feel to deal with the adult health care system?
3. What did your pediatric providers do or what are they doing to help prepare you?
4. What do you wish your pediatric providers had done or would do to prepare you?
5. Finding an adult provider who is right for you or your child – tell me what this experience has been like for you.
6. For those of you who have seen an adult provider – how was that experience different from your experience with pediatric providers?
7. If you've seen adult providers, what did they do to help you adjust to a new type of health care?
8. What do you wish your adult providers had done to help you adjust?
9. What things did you think made the transition difficult?
10. What things did you think made the transition easier?
11. Tell me about any discussions you may have had about how your or your child's health insurance may change. (Discussion with whom? Was the information you were told correct?)
12. Has anyone had to deal with the question of guardianship? By guardianship, I mean your child is about to turn 18 but because he is not able to make medical decisions for himself, parents complete paperwork do you make those decisions on his behalf? If yes: How was this discussed in healthcare visits? If no: Does the parent still attend/plan to attend doctor's appointments with the patient? For how long?
13. What medical self-care skills did your pediatric provider discuss with you before you or your child went to an adult provider?
14. What, if any, community resources have helped your family make the transition to adult healthcare?
15. Is there anything else you would like to share about transitioning that we didn't ask about or may have overlooked?

Results

Two focus groups were conducted with five patient-caregiver units composed of seven individuals in total. Patient ages ranged from 18-22 years and all carried different diagnoses. Four of the five patients were considered “mid-transition” in that they had begun to see some adult providers, and one patient was pre-transition in that he had his last visit with his pediatric provider but had not yet seen his adult provider. Two parents of children with cognitive disabilities chose to participate without their child present. One young adult patient participated without a parent present. Four major themes emerged from the analysis. Each theme is followed by supporting quotations from participants in italics.

Theme 1: Age alone is not necessarily an indicator for transition readiness.

This theme was further divided into two sub-themes based on whether the patient had a cognitive disability or not. Caregivers of patients without cognitive disability focused on maturity and personal responsibility and how these are not necessarily at adult levels by age 18. Caregivers of patients

with cognitive disability focused on how the pediatric, family-centered model of care seems more appropriate for patients who are unable to make their own medical decisions.

“With millennials...they just don't understand it like when we were younger. When we were 18, we were out the door. We knew how to take care of ourselves. They don't know how to charge into things like we used to. When they have medical problems, when we, the parents, have taken care of everything and have been their voice for 18 years or 21 years, they can't just take over being their own voice all of a sudden...age does not make them an adult.”
(Caregiver, ID7)

“...the thing with special needs children, is they may be chronologically an adult, but their bodies are not always. Their bodies are still in a lot of ways pediatric...we really need to start taking a look at what do we do with special needs kids...you gotta think more than just chronologically. You gotta think how their bodies are, look at their overall medical thing to see whether or not they're ready for going to adult care.”
(Caregiver, ID1)

Theme 2: Patients and caregivers feel prepared for their first experience with their adult clinic, but not their first experience with the adult emergency department.

All patients and caregivers stated that they felt prepared for their first visit with the adult provider in a subspecialty clinic. This was generally attributed to the involvement of their pediatric subspecialist in the transition process. Being able to ask their pediatric provider questions about their condition, their future provider and the transition process are all elements that patients and caregivers associated with more successful transitioning.

“I think I'm prepared...She was really good at explaining how would things work and what I need to know to inform my new rheumatologist. Now, I'm not so worried about it.”
(Patient, ID2)

“I’m prepared... I feel confident that I trust Dr (Specialist)’s decision about transitioning him over to an adult doctor, cuz she seems to know what she’s doing... she was a really caring doctor and I’m really glad he had her.” (Caregiver, ID4)

Four out of five patients had been to the adult emergency department (ED) since transitioning and all four felt unprepared for the experience. Some patients were not yet established with exclusively adult providers and were worried their pediatric provider would not be able to care for them in the adult ED. Patients and caregivers reported being overwhelmed by the physical environment of the ED. One caregiver was concerned that the ED staff did not seem to realize her child was under guardianship.

“When I went to the emergency room, they were like, ‘You’re 18. Why are you down here? You’re supposed to be in adult.’ But I was still seeing my pediatric doctor...I told them that I wasn’t sure if I’m ready to go there because I still had a doctor at pediatrics. They were still kind of hesitant. They had to call all these other people and ask them if it’s okay, if I could still come this time. Then after like 20 minutes, they were like, ‘Yeah, you can just sign in now,’ and I’m like, ‘I could be dying right now.’ They still wanna make sure.” (Patient, ID2)

“I was totally unprepared...They treated him like he was an adult. They asked him adult questions...he’s 21, but he has a mental condition, and he does not know those things.” (Caregiver, ID5)

“We had to get permission for this, to be able to go on that (pediatric) side...I don’t want you to ask for permission. I want you to respond to what we’re comfortable with and we’ll deal with it later.” (Caregiver, ID6)

Theme 3: Pediatric care is viewed as more desirable than adult care mainly due to social and physical environment.

Overall, patients and caregivers described pediatric care as comforting and family-oriented, while characterizing internal medicine as “all business,” “abrupt...coldhearted” and lacking in comfort and bedside manner. This was not only in reference to the attitudes of providers but also to the actual physical patient environment.

“(In pediatric care)...family has a lounge chair. There’s a sofa there. There’s all these things. Then when you go to adult...it is very spartan as far as what they have to sit in and everything. It’s almost like they’re trying to tell you, ‘Hurry up and get your family member outta here.’” (Caregiver, ID1)

“In the hospital, the adult units are very sterile, very clean, very plain. The pediatric units, they have the decorations, more of a comfortable feeling...There is such a stark contrast between pediatric and adult care...it feels like there is no transition. It’s a pediatric comfort and care to, ‘You’re an adult.’ There’s no toys here to keep you comforted. There’s no characters to help you transition...It’s night and day when you’re on the pediatric and the adult units, especially the ER...It didn’t seem like the personal care was there (in the adult ER)...there is kind of a mentality of ‘Well, you’re 18 now. You’re adult so we’re gonna treat you differently.’ You can’t go from one day being 17, we’re treating you with pediatric care, to 18, you’re an adult, now you have to act like it.” (Caregiver, ID7)

“When we go to the Peds side, there’s more attention. It’s more personable... You’re trained to treat children differently. You get to the adult side, we’re serious. It’s firm, and we’re all grown up now...on the Peds side, too, the attentiveness to the family and to the child is much different...it was startling to him the first time that he went to the adult side as well, because they were more grown up. They treated him differently.” (Caregiver, ID6)

Theme 4: Patients and caregivers expressed a desire for more resources and systemic changes in transition care within the community.

Patients and caregivers suggested many potential tools and areas for improvement regarding transition care, shown in Table 2.

“It’s almost like I wish there was almost like a middle unit...When you’re seeing doctors all the time, it’s quite a shock just to go immediately from one unit to the next.” (Caregiver, ID7)

Table 2. Patient and Caregivers Suggestions for Transition Care Resources

Patient and Caregivers Suggestions for Transition Care Resources
Improved publicity and awareness of the transition process
Public education on diseases of childhood to increase peer support
Transition support groups
Support for parental and patient education via disease-specific conferences
Better insurance coverage for complex health needs
Improved delivery of existing support services, such as decreased waiting lists for state services
An intermediate-age inpatient unit for patients during the transition years
Allowing pediatric providers to care for patients past age 18
Better communication and familiarity between pediatric and adult providers
A system to alert providers that patients are under guardianship when on adult units

“...have a couple of adult physicians, they may not be your physicians, try to come and tell you about how the adult situation is different. Maybe even a field trip to the emergency room, just to share what’s different about the adult side and get you prepared to do somethin’.” (Caregiver, ID1)

“It sounds like sometimes...that the pediatric doctors don’t know anybody who’s a doctor over on the other side. I think y’all need to kinda get to know each other a little.” (Caregiver, ID1)

“They should read the chart and see that he is special needs, and he has a mother that is always there...they should read the chart and know that this kid is on a six, seven-year-old level. He’s 21, but you can’t ask him ‘cuz he doesn’t understand. I’m always there. When he gets sick, I’m there. I’m always there.” (Caregiver, ID5)

Discussion

Our study demonstrates that even though our sample of patients and caregivers felt prepared for transition, there are aspects that they were not truly prepared for, such as emergency department care. These patients and caregivers desire additional resources to help them navigate the transition period. It is reassuring that these patients and caregivers cited their pediatric providers as their main transition resource. However, having the entirety of the support for transitioning come from the pediatric side may reinforce the already-strong perception shown here that pediatrics is “nurturing” and adult medicine is “all business.”

Patient experience with the ED transition has not garnered much focus in the literature. While some studies of transition care use increased ED utilization as a marker for unsuccessful transition,^{14,19} little is known about the difficulties patients actually face during those ED visits. One study of recently transitioned young adult patients with sickle cell disease found that their adult ED experience was overall viewed negatively and that patients expressed a desire to meet ED staff prior to transitioning.²⁰ Our results support this perspective, with patients and caregivers reporting feeling overwhelmed by the many differences in the adult ED ranging from the physical space to the assumption that a patient has independent decision-making capacity. More research should be done to determine if this experience is as common as our limited sample size suggests and to identify tools that could be utilized to better prepare patients for the adult ED.

Suggestions from patients and caregivers on how to improve transition care ranged from systemic issues beyond the scope of one institution (improved insurance coverage for special needs, long waiting lists for community-based services) to practical and feasible ideas (transition support groups, flagging charts of adult patients under guardianship). The simple request that pediatric and adult providers get to know each other better within a medical community underscores the idea that transition care cannot be housed solely in the pediatric medical home. Transition resources managed by adult providers, such as educational sessions or separate transition units, might help build bridges between pediatric and adult providers as well as between adult providers and their newly transitioned patients.

Our study was limited in reliability and applicability by a small sample size of two focus groups and five diagnostically diverse patient-caregiver units. Despite all efforts to make the focus groups convenient and easily accessible, recruitment was still a challenge. Future studies could address this by incorporating individual semi-structured interviews into a day when the patient is already traveling to the medical center for an appointment.

Conclusions

Transition care is a rapidly evolving field in which the need for advancement is clear, but effective solutions are difficult to implement. The emergency department is a potentially

overlooked area that patients and caregivers struggle with during transition. Patient and caregiver perspectives continue to be vital in developing our understanding of what constitutes good transition care and what patients truly need from us as providers guiding them through this process.

Disclosures

Research supported by “Barriers to Successful Transition for CYSHCN” American Academy of Pediatrics 2016 CATCH Planning Grant and by the Qualitative and Patient-Reported Outcomes Developing Shared Resource of the Wake Forest Baptist Comprehensive Cancer Center’s NCI Cancer Center Support Grant P30CA012197.

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An Evaluation of Empathy within a Psychiatry Residency Training Program

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“No one cares how much you know until they know how much you care.” –Theodore Roosevelt

Despite evidence for the centrality of doctor–patient relationships in effective psychiatric treatment, the current research paradigm of psychiatry has paid limited attention to creating methods for working empathetically with patients.¹⁻¹⁰ Psychiatry has faced significant criticism in the lay media and psychiatric literature for excessive dependence upon the Diagnostic and Statistical Manual of Mental Disorders (DSM) and medications while disregarding empathetic, humanistic interventions.^{1,5-8} The lack of a working model for understanding empathy in psychiatric practice poses significant challenges for psychiatric education and the future of psychiatry.⁸ Without an understanding of how empathy is used in psychiatry, it remains an abstract concept, rather than a skill to be discussed, improved and taught effectively.

Empathy is comprised of imagining others’ perspectives, as well as feeling care and concern for them.¹¹ It is important to differentiate empathy from sympathy. Sympathy involves agreeing with the personal interpretations associated with stressful emotions of others.¹² It is akin to “feeling sorry” for someone. Empathy, however, means understanding a person’s emotional state without necessarily accepting their perception of these feelings.¹² “It seems this came as a surprise to you, and I can tell you are still feeling sad today.” Empathy is especially important in promoting prosocial behaviors, such as helping, cooperating, and sharing.¹³ For physicians, empathy is more useful than sympathy, as sympathy can potentially interfere with objectivity in diagnoses and treatment.¹²

Increased levels of empathy have been strongly linked to improved health outcomes, treatment compliance, increased patient satisfaction and fewer malpractice complaints.¹⁴⁻¹⁶ One study found that diabetic patients of physicians with high empathy scores were significantly more likely to have good control of hemoglobin A1c than patients of physicians with low empathy scores.¹⁶ In a randomized study, student clinicians who were given a perspective-taking intervention received significantly better patient satisfaction scores from standardized patients than did controls.¹⁶

Empathic communication also affects physicians. Interestingly, though, the relationship between empathy and burnout remains unclear. Higher levels of empathy have been associated with increased professional satisfaction, as well as improved physician health and lower risk for burnout.^{14,15,17} Physicians who experience burnout, however, are often depersonalized in social interactions and less capable of demonstrating empathy.^{13,14} “Compassion fatigue” is an example of how over-relating to a patient’s suffering may lead to emotional exhaustion among physicians.¹⁸

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Empathy typically decreases during medical training.¹⁹ A steep decline was found during the third year of medical school when students transition from the preclinical to clinical years.²⁰ This decrease was attributed to a variety of reasons including: highly demanding patients, a challenging curriculum, and stressful training.¹⁹ The American Psychological Association Task Force on Evidence-Based Therapy Relationships has designated empathy as an evidence-based element of the therapeutic relationship and recommended that training programs implement competence-based criteria for educating practitioners in relationship elements.²¹ Interestingly, though, there is very little information in the medical literature about teaching empathy to medical students and residents, especially psychiatry residents.

Psychologists and psychiatrists require highly empathic communication to understand and address their patients' suffering. Such a skill constitutes a cornerstone of all psychotherapeutic approaches, including psychodynamic, cognitive-behavioral, and group psychotherapy approaches.²²⁻²⁵ Karl Jaspers introduced empathy as a tool for psychopathological assessment more than a century ago.²⁶ A more recent article noted that brief intervention grounded in the neurobiology of empathy significantly improved physician empathy as rated by patients, suggesting that the quality of care in medicine could be improved by integrating the neuroscience of empathy into medical education.¹⁴

Much of the more recent general medical literature on physician empathy has attempted to measure empathy using scales. The Jefferson Scale of Physician Empathy, for example, was specifically designed to test empathy in physicians and is one of the scales most frequently used for this purpose.²⁷ The Jefferson scale is one of the best empirically supported measures, but its self-report questions are mostly about attitudes outside of any true clinical context, and the questions are fairly transparent, thus making it is easy for practitioners to "cheat the test." Furthermore, as Pedersen also argues, in line with poststructuralist cultural criticism, those aspects of a clinical encounter that can be reified into measurable variables do not always capture the most important elements of an interpersonal encounter.²⁸

While other empathy questionnaires exist, the Helpful Responses Questionnaire (HRQ) is unique in that the

respondent is required to provide freeform answers, as opposed to answering on a Likert scale. The HRQ is designed to measure the development of reflective listening and empathy skills. These skills are central to the implementation of motivational interviewing in mental health, addiction and social service settings.²⁹ Use of the HRQ has been limited in educational research with exceptions being studies involving undergraduate medical education, family medicine residents and pediatric residents.²⁹⁻³¹

To further evaluate the use of the HRQ, a pilot project was undertaken to measure empathy scores using the HRQ in psychiatric residents at Wake Forest Baptist Medical Center. The results showed empathy scores were lower than expected, even amongst those who had received a didactic lecture series based on listening and empathy.

Empathy affects both patient and physician wellness, thus heavily warranting further research.^{14,15,32} In lieu of the written patient vignette and subject response structure of the original HRQ studies, future research which is being planned at Wake Forest Baptist Medical Center includes the use of standardized patients in video vignettes with subjects providing a verbal response. This type of virtual study would allow for further assessment of subjects' speaking style and vocal intonation as they relate to empathy, as well as a more accurate and standardized depiction of the patient encounter. After an assessment of baseline empathy scores, methods for empathy improvement would be tested. Brief, targeted intervention techniques, such as a grand rounds, have shown to improve empathy skills.³³ This could later be translated into an empathy educational tool for all healthcare specialties.

Disclosures

No financial support given. Authors report no conflict of interest.

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CLINICAL REVIEW

The Medical Management of Intracranial Hemorrhage: A Review Article

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Abstract

Purpose: There are four broad types of intracranial hemorrhage (ICH): intraparenchymal hemorrhage, subarachnoid hemorrhage, subdural hematoma, and epidural hematoma. The bulk of this review will focus on the four types of ICH, with directed information regarding surgical indications, ICU specifics, antiepileptic use, reimaging, and prognosis for each subgroup.

Given the increasing incidence and shift toward medical management, this review will serve as a tool for neurologists, hospitalists, intensivists, and others involved in the medical management of ICH.

Recent findings: The incidence of ICH has increased four-fold over the past decade with the increased use of anticoagulant medications. There has been a general shift towards medical management as opposed to surgical intervention, though surgical intervention is still critically important for certain types of ICH and in certain settings.

Search Strategy and Selection Criteria: Data for this review were identified by searches of PubMed, Guidelines.gov, Cochrane Database, and references from relevant articles using the search terms "intracranial hemorrhage," "intracerebral hemorrhage," "intraparenchymal hemorrhage," "subdural hematoma," "epidural hematoma," "extradural hematoma," and "subarachnoid hemorrhage." Abstracts and reports from meetings were included only when they related directly to previously published work. There were no language restrictions.

Summary: This review covers general diagnostic and management principles for all types of ICH in adults, and then discusses the epidemiology, risk factors, presentation, and management of each specific type of ICH.

Introduction

There are four broad types of intracranial hemorrhage (ICH): intraparenchymal hemorrhage (IPH), subarachnoid hemorrhage (SAH), subdural hematoma (SDH), and epidural hematoma (EDH). The incidence of ICH has increased four-fold in the last decade with the increased use of anticoagulants.¹ While some patients with ICH require neurosurgical intervention, it is now recognized that medical management alone can sufficiently reduce morbidity and mortality for many.² Given the increasing incidence and shift toward medical management, this review will serve as a tool for neurologists, hospitalists, intensivists, and others involved in the medical management of ICH.

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Following a discussion of diagnostic principles that guide the detection of ICH, this review will outline the general management approaches that apply to all adult patients with ICH. The bulk of this review will focus on the four broad types of ICH, with directed information regarding epidemiology, risk factors, diagnosis, acute management, and long-term management for each subgroup.

General Diagnostic Principles for ICH

An efficient history (including anticoagulant use, illicit drug use, recent head trauma, presence of hypertension, tobacco use, and prior ischemic or hemorrhagic stroke) and neurologic exam are required in those with possible ICH. A non-contrasted head computed tomography (CT) is sensitive and specific for ICH, with hemorrhage appearing as a hyperdensity within minutes of symptom onset.³ Over 1 to 3 weeks this will become isodense, with transition to hypodense around 4 to 6 weeks.³ Immediate laboratory evaluation should include prothrombin time, partial thromboplastin time, international normalized ratio (INR), complete blood count, and urine drug screen.⁴ These laboratory studies are useful because they assess for the presence of coagulopathies that may complicate management, and they assist in the initial investigation into the underlying etiology of the hemorrhage (including possible illicit drug use).

Additional tests should be considered in the setting of a traumatic brain injury (TBI). In addition to a multisystem trauma evaluation, CT of the head should be obtained in those with decreased level of consciousness or focal neurologic deficits. To assess for vascular injury, CT angiogram (CTA) is the preferred study after penetrating injury or a skull base fracture that traverses the carotid canal or venous sinus. Conventional angiography can confirm CT findings and allow for endovascular intervention as needed.⁵ Magnetic resonance imaging (MRI) is helpful in identifying the etiology of the hemorrhage in some cases, as it may reveal underlying structural causes of the hemorrhage, such as tumors.⁵ Epidemiology, risk factors, common presenting signs and symptoms are highlighted in Table 1.

General Management Principles for ICH

The goals of ICH management are to stabilize the patient and limit hemorrhage expansion, hydrocephalus, cerebral

vasospasm, seizures, hyperglycemia, hypertension, fever, and infection.⁶ Immediate surgical consultation should be obtained if there is concern for herniation, mass effect, or obstructive hydrocephalus.⁴ More specific surgical indications are discussed in each subsequent section, but in many instances these indications are complex and beyond the scope of this paper. Critical care management is immediately indicated to stabilize patients by addressing airway, breathing, and circulation.⁷ Trauma guidelines specify that a Glasgow Coma Scale (GCS) < 8 is an indication for mechanical ventilation.⁸ Once the airway is secured, blood pressure should be lowered, with specific goals dependent on the type of ICH (see subsequent sections).⁹ Intravenous antihypertensives with short half-lives such as labetalol, nicardipine, enalapril, hydralazine, or nitroglycerin are preferred.¹⁰ If present, hypotension should be rapidly corrected, as it is an independent predictor of increased mortality.¹¹

Care in a neurologic intensive care unit (ICU) or neurology inpatient service is associated with improved outcomes in patients with ICH.¹² This includes frequent neurologic examinations dictated by the severity of the condition. Intermittent pneumatic compression stockings are recommended for prevention of venous thromboembolism, given that anticoagulants cannot be administered.¹³ Clinically evident seizures should be treated, but there is little evidence to support the use of prophylactic anticonvulsive medications after spontaneous ICH.^{2,14} Phenytoin or valproic acid is recommended to reduce the incidence of early posttraumatic seizures (within 7 days of TBI), but prolonged use is not recommended for primary prevention.¹¹ Tight glucose control with insulin is recommended, though an exact target is not yet defined.^{2,12} Maintaining normothermia with antipyretics or cooling is also recommended.²

Elevated intracranial pressure (ICP) is a common complication of ICH. The goal of treating elevated ICP and maintaining cerebral perfusion pressure (which is the difference between mean arterial pressure and ICP) is to decrease nonessential intracranial volume (such as edema). Conservative measures include elevation of the head to 30 degrees, maintenance of a neutral neck position to allow for venous drainage, pain control, antipyretics, and mild sedation.^{2,6} Hyperventilation is effective in treating acute elevation in ICP by causing vascular constriction and decreasing intracerebral volume; however,

it carries the risk of cerebral ischemia, and therefore is not recommended for prolonged ICP management. Hyperosmolar therapy with mannitol or hypertonic saline should be instituted early for cerebral edema. For refractory edema, deep sedation and neuromuscular blockade can reduce ICP. Finally, a barbiturate coma with continuous electroencephalogram (EEG) monitoring (to follow the degree of cortical activity suppression) can be used if all other therapies have failed, though cardiac depression may occur.¹⁵

In all ICH, urgent correction of coagulopathy is required.^{1,7} The Neurocritical Care Society and Society of Critical Care Medicine recently composed guidelines for the reversal of anticoagulants in ICH (Table 2). The use of vitamin K antagonists (VKA), most commonly warfarin, more than doubles the risk of spontaneous IPH (from 0.15% baseline risk per year to 0.3% to 1.1% risk) and is associated with 12% to 14% of all IPH deaths. The majority of VKA-associated IPH cases occur in the setting of a therapeutic INR.1 With an increased INR, correction alone does not reduce mortality.⁷ In the neurologically intact patient with only mild elevation in INR and a small hematoma, reversal may not be required.⁷ The risk of ICH is approximately 50% lower with the use of the direct oral anticoagulants [FXa inhibitors (rivaroxaban, apixaban, edoxaban) and FIIa inhibitor (dabigatran)] than with VKAs.¹⁶ A major concern, specifically with the increased use of FXa inhibitors, is the lack of reversal agents in the setting of a life-threatening hemorrhage. Though VKAs increase the risk of ICH, recent multi-level analyses revealed no difference in 90-day mortality, baseline ICH volume, hematoma expansion, and functional outcome between VKA-associated-ICH and direct oral anticoagulant-associated-ICH.¹⁷

There is uncertainty regarding the impact of antiplatelet medications on ICH incidence, hematoma expansion, morbidity, and mortality.¹ Transfusion of platelets is not without risk, including a 14% to 16% risk of hypotension, fever, cardiac and respiratory events, and decline in neurologic status. Recent recommendations for platelet transfusion are dependent mainly on whether a neurosurgical procedure is indicated, along with the type of antiplatelet being used (Table 2).¹

No randomized trials have been conducted to determine the appropriate time to restart anticoagulation after ICH, and the

decision depends largely on the indication for anticoagulation and comorbidities.¹⁸ In patients without prosthetic heart valves, American Heart Association/American Stroke Association guidelines recommend avoiding anticoagulants for at least 4 weeks. They suggest aspirin monotherapy is an appropriate alternative that may be restarted in the days after ICH (though optimal timing remains uncertain). Patients with prosthetic heart valves may require earlier initiation of anticoagulation after ICH.¹⁹ A summary of management strategies for all types of ICH is presented in Table 3.

Acute Intraparenchymal Hemorrhage (IPH)

Surgical Indications: Most patients will not need surgical evacuation after IPH.²⁰ There is not clear benefit of early hematoma evacuation compared to evacuation once clinical deterioration occurs. However, hematoma removal is indicated for cerebellar hemorrhage greater than 3 cm or the presence of brainstem compression, with or without hydrocephalus.²¹ Supratentorial hematoma evacuation, either through craniotomy or craniectomy, may be indicated as a life-saving measure in a deteriorating patient.^{2,20}

ICU Specifics: A protocol has been developed by the Neurocritical Care Society for acute management of IPH.¹² The most recent guidelines recommend acute lowering of systolic blood pressure to 140 mm Hg for those with systolic pressure between 150 and 220 mm Hg without contraindications. For those with systolic pressure greater than 220 mm Hg, aggressive reduction with intravenous antihypertensive medication should be considered, but target systolic blood pressure should be individualized.²²

Antiepileptic Use: The management of seizures after IPH remains controversial. Lobar location is the strongest predictor of post-IPH seizure.^{5,23,24} The majority of post-IPH seizures occur at IPH onset, and they have not been found to be associated with worse outcome.^{23,24} There is no evidence for the use of prophylactic antiepileptic treatment after IPH. Continuous EEG monitoring is recommended in IPH patients with depressed mental status out of proportion to degree of brain injury.²

Reimaging: If no etiology is determined, it is recommended to repeat vessel examination with CTA, contrasted MRI brain, or MRA 3 to 6 months after initial presentation.⁵ Often, the

same imaging modality as was initially used is repeated, to facilitate direct comparisons.

Prognosis: The “ICH Score”, a strong predictor of 30-day mortality, factors in age, IPH volume, the presence of IVH, GCS, and infratentorial origin of hemorrhage. Mortality increases with increasing ICH score, from 0% with a score of 0, to 100% with scores of 5-6.²⁵ In traumatic IPH, predictors of poor outcomes include advanced age, lower GCS at time of admission and follow-up CT, cranial fracture, absence of pupillary response and other brainstem reflexes, increased ICP, obstruction of the basal cisterns or third ventricle, certain lesion location, increased ICH volume, severity of cerebral edema, delay of surgery, preoperative neurologic deterioration, and acute hemispheric swelling or concomitant SDH.²⁶

Acute Subarachnoid Hemorrhage (SAH)

Surgical Indications: There are several potential causes of SAH, but the most common are trauma and aneurysmal rupture. In the cases of aneurysmal rupture, obliteration of the aneurysm, through endovascular coiling or surgical clipping, is a mainstay of treatment and should be performed as early as possible after presentation to avoid the risk of rebleeding.¹⁴

ICU specifics: The main goals of ICU treatment of SAH are initially to control blood pressure and prevent re-bleeding, treat cerebral edema, prevent delayed cerebral ischemia from vasospasm, and treat hyponatremia from cerebral salt wasting. Systolic blood pressure < 160 mm Hg (or mean arterial pressure < 110 mm Hg) is a “strong recommendation” per Neurocritical Care Society’s multidisciplinary Consensus Conference. Antihypertensives should be discontinued as soon as the aneurysm is secured and systolic pressure allowed to rise to 180 to 200 mm Hg to prevent ischemia from vasospasm. Antifibrinolytics may also be used to prevent re-bleeding, but carry a higher risk of vasospasm and hydrocephalus.²⁸

Treating concomitant cerebral edema is important, as this is often the cause of depressed level of consciousness. In SAH, this is usually done with hypertonic saline over mannitol, given the propensity for salt wasting and desire to maintain euvolemia to prevent vasospasm and delayed cerebral ischemia. Approximately 70% of patients have vasospasm on imaging, which may lead to delayed cerebral ischemia. Occurring in 40% of patients, this presents as neurologic deterioration

days after SAH or new infarcts that appear 72 hours post-rupture. Prophylaxis against delayed cerebral ischemia involves maintaining euvolemia, systolic blood pressure between 180 and 200 mm Hg, and use of nimodipine.^{29,30} While oral nimodipine has not been proven to prevent vasospasm, dosing 60 mg by mouth every 4 hours results in a reduction in poor outcomes when administered for 21 days.³¹

Hydrocephalus after SAH can either present immediately or delayed,³² and acute hydrocephalus is the most common early neurologic complication after SAH.¹⁴ While many patients display radiographic hydrocephalus, only 20% will develop symptomatic hydrocephalus, and these patients should be managed by surgical cerebrospinal fluid diversion.²⁹

Hyponatremia is another common complication of aneurysmal SAH, which can occur anytime through the first 3 weeks after hemorrhage due to cerebral salt wasting. Treatment is to maintain euvolemia. Sodium repletion in the form of salt tablets can be helpful for sodium > 130 mEq/L, or the use of 3% saline for sodium < 130 mEq/L.

Pharmacologic prophylaxis against deep vein thrombosis with unfractionated or low molecular weight heparin can usually be safely restarted 24 hours after aneurysm obliteration.³³

Antiepileptic Use: Seizure-like activity occurs in as many as 26% of people at the time of SAH, though it is unknown whether these events represent seizures or posturing from increased ICP. There is no evidence for the use of prophylactic antiepileptic treatment after SAH.¹⁴ The use of phenytoin as a prophylactic antiepileptic results in worse neurologic and cognitive outcomes in SAH. Continuous EEG monitoring is recommended in comatose patients after SAH since non-convulsive seizures can occur in 10 to 20% of these patients.^{28,29}

Reimaging: For patients younger than 40, repeat imaging in 3 to 5 years is recommended, especially in females, those with greater than one aneurysm, and those with a family history of SAH or polycystic kidney disease.³⁴

Prognosis: The strongest predictors of outcome in aneurysmal SAH include the severity of clinical presentation (using such scales as the Hunt and Hess or the World Federation of Neurological Surgeons) and rebleeding.³⁵ Additional factors that suggest a poor prognosis in spontaneous SAH

include older age, preexisting severe illness, global cerebral edema, IVH and IPH, symptomatic vasospasm, delayed cerebral infarction, hyperglycemia, fever, anemia, and other systemic complications.³⁵ Poor outcome in traumatic SAH is associated with low GCS score on admission, advanced age, amount of subarachnoid blood, presence of associated parenchymal damage, and progression of SAH.^{36,37}

Acute Subdural Hematoma (SDH)

Surgical Indications: Guidelines exist only for the surgical management of acute traumatic SDH.^{38,39} If an acute SDH is > 10 mm or if there is a midline shift > 5 mm, then surgical evacuation is indicated. For comatose patients who do not meet the former criteria, surgical evacuation is recommended with any of the following: GCS score decreased by 2 or more points from the time of injury, asymmetric or dilated pupils, or ICP > 20 mm Hg.³⁸

ICU specifics: Similar to IPH, a target systolic blood pressure < 140 mm Hg is recommended. ICP management is of key importance in management of SDH. As a hematoma expands the ability of cerebrospinal fluid to reabsorb and blood flow to auto-regulate becomes disrupted, causing increased ICP. While trauma guidelines recommend the use of fiberoptic ICP devices or external ventricular drains in the setting of GCS < 8 and abnormal CT scan, use of these techniques initially can release CSF, and paradoxically increase the size of SDH. Similarly, mannitol and hypertonic saline should be avoided in the setting of SDH, except on the way to the operating room for lifesaving measures.⁹ Medical management of cerebral edema and increased ICP remain vitally important after surgical evacuation of SDH for acute, traumatic SDH, however in those with chronic SDH, this should be avoided to allow for brain reexpansion.⁹

Antiepileptic Use: Up to 24% of traumatic SDH present with early seizure.⁹ In acute traumatic SDH, antiepileptics are recommended if a patient presents initially with seizures, GCS < 10, or an abnormal CT scan. While phenytoin is recommended in TBI guidelines, levetiracetam is more commonly used, given its lower side effect profile and similar efficacy.^{9,40} No guidelines exist regarding use of antiepileptic medication in nontraumatic SDH.⁴⁰

Reimaging: Follow-up CT with frequent neurologic exams

is critical, as hematomas frequently enlarge.⁴ Close interval follow-up CT should be obtained (4 to 6 hours) in the presence of anticoagulation, otherwise a 24 hour repeat CT is sufficient.

Prognosis: Fewer than 25% of patients with an acute SDH will have full neurologic recovery.⁹ In acute SDH, such factors as pupillary abnormalities, low GCS score, additional intracranial lesions, and advanced age are associated with worse prognosis. Unreactive pupils are associated with an increased mortality rate of 81% with one unreactive pupil and 97% for bilateral.⁹

Chronic SDH

Surgical Indications: Surgery is the primary mode of treatment for symptomatic chronic SDH and results in favorable outcomes in 80% of patients. Recurrence rate requiring reoperation ranges from 10 to 25%, with risk factors including bilateral presentation, use of anticoagulant or antiplatelet medications, older age, persistence of midline shift, poor brain re-expansion during surgery, thick membranes, large original hematoma size, septate or mixed-density lesions, intracranial air, and presence of post-operative seizures.⁹

Antiepileptic Use: No randomized clinical trials have assessed the utility of antiepileptic prophylaxis in this patient population. Three retrospective case-control studies on patients with chronic SDH treated surgically have offered variable results and recommendations, with the majority recommending against prophylactic antiepileptic use.⁹

Reimaging: As with acute SDH, a post-operative CT is recommended to assess the patient's new baseline and follow-up imaging is recommended within 1 to 2 weeks.⁹

Prognosis: Few studies have examined prognosis in patients with chronic SDH. Important postoperative prognostic factors may include GCS score, coagulopathy, presence of medical comorbidities, and modified Rankin Scale at admission.⁹

Acute Epidural Hematoma (EDH)

Surgical Indications: Surgery is the mainstay of treatment for acute EDH, with the main determinants including GCS score, pupillary exam, comorbidities, CT findings, age, and ICP in delayed cases. Per the Brain Trauma Foundation Guidelines, surgery is indicated for an EDH greater than 30 cm³, regardless of a patient's GCS score. For patients with a

GCS > 8 who do not display focal deficits and with an EDH that is < 30 cm³, < 15 mm thickness, and < 5 mm midline shift, surgery is not indicated. Such patients can be managed with serial CT scans and close neurologic observation. Those with a temporal EDH more commonly fail non-operative treatment due to a higher risk of hematoma growth.⁴¹

ICU specifics: The majority of hematoma enlargement occurs in the first 36 hours after initial injury. In patients for which conservative management is suitable, it is vital to perform frequent neurologic checks and serial CT scans in a neurosurgical center to monitor for decompensation. Delayed deterioration is possible as a result of cerebral edema, ischemia, re-hemorrhage, or continued hemorrhage.⁴² Given the vast majority occur in the setting of TBI, general ICU management for severe TBI should guide treatment.¹¹

Antiepileptic Use: No specific guidelines exist for the use of anti-seizure prophylaxis in EDH. General recommendations for use of anti-seizure prophylaxis in TBI should be considered, with the majority of studies not supporting use of anti-seizure prophylaxis unless there is an early post-traumatic seizure (within 7 days of injury).¹¹

Reimaging: Patients who are managed non-operatively should have a follow-up CT scan at 4 to 6 hours after initial trauma, with repeat serial CT scans thereafter due to the high risk of hematoma expansion in the first 36 hours after injury.⁴²

Prognosis: The most important variable in predicting morbidity and mortality those with EDH undergoing surgery is GCS score. Additional prognostic factors include age, bilateral mydriasis, additional associated intracranial lesions, and elevated ICP above 35 mm Hg. Conflicting evidence exists, but it is likely that EDH size, mixed density, midline shift, and associated traumatic SAH are related to poor outcome in EDH.⁴¹

Conclusion

The increased use of anticoagulant and antiplatelet medications has resulted in an increase in individuals with ICH. This increase, along with the shift toward the medical management of ICH, has resulted in more patients under the care hospitalists, general neurologists, and other providers that may not have specific training in the management of ICH. This review of

IPH, SAH, SDH, and EDH emphasizes the importance of considering hypertension, anticoagulant/antiplatelet reversal, antiepileptic use, and re-imaging strategies as key aspects of the medical management of ICH. While these considerations are important during hospitalization, it is also important during the first hours following an ICH to address surgical intervention and intensive care management strategies, which should involve collaboration with neurosurgeons and neuro-intensivists.

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Table 1. Overview of ICH Epidemiology, Risk Factors, and Presentation

	Epidemiology	Risk Factors	Characteristic Symptoms	Imaging	Risk of Expansion
IPH	Incidence: 16 to 33 cases per 100,000 person years. ^{47–49} Occurs in 8.2% of all TBI and 13% to 25% of severe TBI. ²⁶ Mortality: 1-month mortality is 40%, 1-year mortality is over 50%, and 5-year mortality is 70%. ^{50,51}	Modifiable: HTN, anticoagulant use, tobacco use, ETOH, lower LDL, lower triglycerides, trauma. Non-modifiable: Older age, CAA, underlying lesions (eg, arteriovenous malformation, aneurysm, and tumor), male sex, black ethnicity. ^{1,52–54}	Dependent on location. Often present with focal neurologic deficits along with severe headache. May also see nausea, vomiting, decreased level of consciousness, and seizures. ^{5,23,24}	“Spot sign” on CTA: 69% positive predictive value for hematoma expansion. ^{3,54}	~ 40% of IPH expand in size after initial presentation, 75% in the first 6 hours and 25% within the first 24 hours. ^{6,54}
SAH	Incidence: 2 to 16 cases per 100,000 person years. ⁵⁵ 40% in moderate and severe TBI cases. ³⁶ Mortality: 32% in aneurysmal SAH. ⁵⁶ 43% to 47% in traumatic SAH. ³⁷ Isolated SAH carries low mortality.	Modifiable: HTN, ETOH, low BMI, tobacco use, cocaine use within the past 3 days in young patients (18 - 49 years), high daily coffee consumption (> 5 cups/day), and trauma. ^{35,57,58} Non-modifiable: Increasing age, female sex, non-Caucasian ethnicity, family history, genetic syndromes (eg, ADPKD and type IV Ehlers-Danlos), vasculitis, septic emboli, aneurysm size, location, and morphology. ⁵⁷	Sudden and severe “thunderclap” headache, peaking over an hour. May also have sentinel headache, loss of consciousness, nausea, vomiting, meningismus, focal neurologic deficits, cerebral edema, hydrocephalus, death. ^{14,29}	CT: 100% sensitivity in first 3 days after SAH. LP: may be necessary after 5-7 days as rate of false-negative CT increases. ¹⁴ CTA: identify aneurysm (may need conventional angiography if < 3 mm). ¹⁴	Aneurysm re-bleeding occurs in 4% to 13.6% of patients within the first 24 hours, with the majority occurring in the first 6 to 12 hours. ¹⁴ Risk of progression of traumatic SAH is low.
SDH	Incidence: The incidence of acute SDH is 11% in TBI (21% in severe TBI), and rarely occurs spontaneously. ³⁸ The incidence of chronic SDH ranges from 0.001 to 0.002% per year. ⁹ Mortality: In acute traumatic SDH, 1-month mortality ranges from 40 to 60% (50 to 90% in patients presenting with GCS < 8). ⁴⁰ For chronic SDH, mortality is 1–5%. ⁵⁹	Modifiable: Oral anticoagulation therapy, ETOH or cocaine use, and antithrombotics. ^{9,40,60} Non-modifiable: Cerebral atrophy secondary to elderly age or trauma, male sex, coagulopathy, or neoplasm. ⁶⁰	Acute: history of trauma most commonly, often with lucid interval initially; may see non-convulsive seizures. Chronic: gait disturbance, contralateral weakness, cognitive decline, acute confusion, headache. ⁶¹	Crescentic mass overlying cerebral convexity, falx cerebri, tentorium cerebelli, crossing suture lines but not midline. ⁹	Risk of radiographic expansion varies from 11% to 22%, while clinically significant risk of expansion is 10.7 to 11.6%, similar in both anticoagulated and non-anticoagulated patients. ⁶²
EDH	Incidence: Incidence of EDH among TBI ranges from 2.7 to 4%, with mean age between 20 and 30. EDH is rare in patients over age 50 and is rare in very young children and neonates. ⁴¹ Mortality: Mortality in patients undergoing surgery for EDH is 10% in adults and 5% in children. ⁴¹	Modifiable: The vast majority of EDH are secondary to trauma, with most common causes including traffic-related accidents (53%), falls (30%), and assaults (8%). ⁴¹ Non-modifiable: None	Lucid interval, coma, pupillary abnormalities, focal deficits, seizures. 3–27% present neurologically intact. ⁴¹	Hyper-dense lens-shaped biconvexity that does not cross suture lines but may cross the midline. ⁴¹	Frequency of expansion ranges from 5.5 to 6.5%. Mean time to enlargement is 8 hours after injury and 5.3 hours after initial CT, with mean enlargement of 7 mm. ^{42,63}

HTN: hypertension, ETOH: heavy alcohol use, CAA: cerebral amyloid angiopathy, BMI: body mass index, LDL: low-density lipoprotein cholesterol, CTA: computed tomographic angiography, ADPKD: autosomal dominant polycystic kidney disease, CT: computed tomography, LP: lumbar puncture

Table 2. Anticoagulant (A) and Antiplatelet (B) Medication Reversal^{1,2,7,43-45}

Table 2A. Anticoagulants

Anticoagulant Agent	Mechanism of Action	Elimination Half-Life	Reversal in ICH	Monitoring Parameters
Unfractionated heparin	Activates antithrombin III, which in turn inactivates coagulation factors (eg, thrombin [factor IIa], factor Xa)	45-90 minutes	Discontinue unfractionated heparin Urgent reversal of anticoagulation in patients receiving full dose heparin infusion; not necessary to reverse for prophylactic subcutaneous heparin if aPTT is not significantly prolonged Protamine sulfate 1 mg IV per 100 U of heparin given in prior 2-3 hours, slower than 5 mg/min to avoid allergic reaction (max dose of 50 mg is usually sufficient); may pre-treat with corticosteroids and antihistamines If aPPT remains elevated, repeat dose protamine at 0.5 mg IV per 100 U heparin	aPTT
Low molecular weight heparin (enoxaparin, dalteparin, nadroparin, tinzaparin)	Inactivates factor Xa via antithrombin III	4 hours	Discontinue low molecular weight heparin Urgent reversal of anticoagulation in patients receiving therapeutic dose; not necessary to reverse for prophylactic dosing Enoxaparin: If present < 8 hours after administration: protamine sulfate 1 mg per 1 mg enoxaparin(max single dose of 50 mg); If present > 8 hours after administration: 0.5 mg protamine per 1 mg enoxaparin; minimal utility in reversal if >12 hours from dosing Dalteparin, nadroparin, tinzaparin: Protamine sulfate 1 mg per 100 anti-Xa U If ineffective, may give additional protamine sulfate 0.5 mg per 100 anti-Xa U or per 1 mg enoxaparin After 3-5 half-lives have elapsed, protamine not needed If protamine is contraindicated, administer rFVIIa at 90 mcg/kg IV Not recommended to use FFP, PCC or aPCC No recommendation for or against use of hemodialysis	Anti-Xa assay
Danaparoid sodium	Inactivates factors Xa and IIa at a ratio 20:1 via antithrombin III	24 hours	Discontinue danaparoid Administer a one-time dose of rFVIIa at 90 mcg/kg IV Plasmapheresis may be considered for a critical bleed	Anti-Xa assay
Fondaparinux (Penta-saccharide)	Indirectly inactivates factor Xa via antithrombin III	17-20 hours (and up to 72 hours with renal dysfunction)	Discontinue fondaparinux Urgent reversal of anticoagulation in patients receiving therapeutic dose fondaparinux; not necessary to reverse for prophylactic dosing (unless evidence of drug accumulation) Administer aPCC at 20 IU/kg IV If aPCC contraindicated or not available, administer rFVIIa at 90 mcg/kg IV Protamine is not recommended	Anti-Xa assay
Warfarin	Vitamin K antagonist	4-5 days	Discontinue warfarin* Administer vitamin K (10 mg IV over 30 minutes); redose with vitamin K 10 mg IV if repeat INR remains elevated > 1.4 within 24-48 hours after initial dosing Initiate four-factor PCC** or three-factor PCC (four-factor is preferred) – dosing is weight-based and dependent on INR and type of PCC used FFP (10-15 ml/kg IV over 3-6 hours) plus vitamin K 10 mg IV may be administered if PCC is unavailable	PT/INR (goal INR < 1.4) Repeat INR testing 15-60 minutes after PCC administration, and every 6-8 hours for the next 24-48 hours, then daily until anti-coagulation is reversed

Table 2A. Anticoagulants (Cont.)

Anticoagulant Agent	Mechanism of Action	Elimination Half-Life	Reversal in ICH	Monitoring Parameters
Dabigatran	Direct oral factor IIa (thrombin) inhibitor	13 hours (22-35 hours in renal impairment)	<p>Discontinue dabigatran</p> <p>Determine degree of anticoagulation exposure: time and quantity of last dose, renal function, medication interactions</p> <p>Activated charcoal (50 g) can be used if most recent dose taken < 2 hours prior (if patient is intubated with enteral access and/or alert with low aspiration risk)</p> <p>If ICH occurred within 3-5 terminal half-lives of exposure: administer idarucizumab (5 g IV in two doses of 2.5 g/50 mL); if idarucizumab is not available or in the case of an alternative direct thrombin inhibitor: administer aPCC (50 U/kg) or four-factor PCC (50 U/kg)</p> <p>If idarucizumab, PCC, or aPCC are not effective, consider redosing idarucizumab or hemodialysis</p> <p>Hemodialysis can be used if rapidly deployable and if hemodynamically stable in the patient with renal insufficiency or dabigatran overdose, if idarucizumab is not available or not effective</p> <p>rFVIIa, FFP, and vitamin K are not recommended</p>	<p>aPTT, TCT reversal should be guided by bleeding (major or intracranial)</p> <p>Normal TT and aPTT imply that high level of dabigatran is unlikely</p>
Bivalirudin	Direct thrombin inhibitor (DTI)	Bivalirudin 25 minutes (1 hour in severe renal impairment, 3-5 hours in dialysis-dependent patients)	<p>Discontinue DTI</p> <p>If ICH occurred within 3-5 terminal half-lives of exposure: administer aPCC (50 U/kg) or four-factor PCC (50 U/kg)</p> <p>Hemodialysis, hemofiltration, or plasmapheresis may be considered for critical bleed</p>	<p>ACT or aPTT INR will be falsely elevated in most cases</p>
Argatroban		Argatroban ~45 minutes hepatic impairment < 181 minutes		
Rivaroxaban	Direct oral factor Xa inhibitors	7-9 hrs	<p>Discontinue rivaroxaban/apixaban/edoxaban</p> <p>Activated charcoal (50 g) can be used if most recent dose taken < 2 hours prior (if patient is intubated with enteral access and/or alert with low aspiration risk)</p> <p>If ICH occurred within 3-5 terminal half-lives of exposure or in a patient with liver failure: administer four-factor PCC (50 U/kg) or aPCC (50 U/kg)</p> <p>rFVIIa is not recommended due to higher risk of adverse thrombotic event; hemodialysis does not reverse drug effects since they are highly protein bound</p> <p>Specific antidotes to reverse oral factor Xa inhibitors are under investigation</p>	<p>No laboratory monitoring – reversal should be guided by bleeding. PT may be elevated (rivaroxaban >apixaban)</p> <p>PT/INR</p> <p>Anti-Xa chromogenic assay may be helpful to assay presence of drug if curve is calibrated to specific drug</p>
Apixaban		9-14 hours		

Table 2B. Antiplatelets

Antiplatelet Agent	Mechanism of Action	Elimination Half-Life	Time to Normal Platelet Function	Reversal in ICH	Monitoring Parameters
Aspirin	Irreversibly inhibits platelet activation by inactivating platelet cyclooxygenase	20 min	5-7 days	Conflicting views – decision should be made after careful assessment of risks and benefits Discontinue antiplatelet If neurosurgical procedure is not indicated: do not transfuse platelets	Platelet light aggregation (gold standard) or platelet function assay
Clopidogrel	P2Y ₁₂ (ADP) antagonists (anti-platelet)	Parent Compound ~6 hrs Active metabolite ~30 min	5-7 days	If neurosurgical procedure is indicated: -Aspirin- or ADP inhibitor-associated ICH: transfuse platelets -NSAID or GP IIb/IIIa inhibitor-related ICH: do not transfuse platelets (not effective) If transfusion is indicated: begin with 1 dose of single-donor apheresis unit of platelets, repeat only if abnormal platelet function tests and/or bleeding persists In aspirin/COX-1 inhibitor, ADP receptor inhibitor-associated ICH, or in those undergoing neurosurgical procedure, consider adjunctive one-time dose of desmopressin (DDAVP) 0.4 mcg/kg IV	Platelet light aggregation (gold standard) or platelet function assay
Prasugrel		7 hrs	5-7 days		
Ticagralor		Parent compound ~7hrs Active metabolite~9 hrs	3-5 days		
Abciximab	Glycoprotein IIb/IIIa inhibitors (inhibit platelet aggregation)	30 min	12-36 hrs	In GP IIb/IIIa inhibitor-associated ICH, rFIIa and fibrinogen may be considered, though there is little literature to support this	Platelet light aggregation (gold standard) or platelet function assay
Tirofiban		1.5 hrs	4-8 hrs		
Eptifibatide		2.5 hrs	4-8 hrs		

PCC: prothrombin complex concentrates, APCC: activated PCC (eg, factor VIII inhibitor bypass activity (FEIBA), rFVIIa: recombinant factor VIIa, FFP: fresh frozen plasma, TT: thrombin time, aPTT: activated partial thromboplastin time, PRBC: packed red blood cells

*Do not discontinue anticoagulation in the setting of cerebral venous thrombosis. Assess risks and benefits in patients that also have symptomatic thrombosis, ischemia, heparin-induced thrombocytopenia, or DIC.¹

**Current recommendations suggest the use of four-factor PCC rather than FFP, since FFP poses the risk of allergic reaction or infection, requires a longer preparation time and cross-matching, and a higher volume must be administered compared to PCC.^{1,44,46} PCC and rFVIIa are faster acting than FFP (normalize the INR within minutes for PCC versus hours for FFP) and have a lower infection risk, though no randomized controlled studies currently exist to demonstrate improved clinical outcomes with use of PCC.^{2,44}

Table 3. An Overview of Acute ICH Treatment

Hemorrhage Type	Surgical Indications	BP Goals	Role of Antiepileptic Medications
IPH	Cerebellar hemorrhage > 3 cm with neurologic deterioration or brainstem compression and/or hydrocephalus should undergo surgical evacuation of hematoma Supratentorial hematoma in deteriorating patients should have decompressive craniectomy with or without hematoma evacuation as a life-saving measure	< 140 mm Hg systolic	Prophylactic antiepileptic is not recommended Clinical seizures should be treated with antiepileptic Those with change in mental status and electrographic seizures should be treated with antiepileptics
SAH Aneurysmal	Surgical clipping or endovascular coiling within 24 hours of presentation if aneurysm present	< 140 mm Hg until aneurysm is secured, then 100-200 mm Hg systolic	Avoid phenytoin Short course (3-7 days) in immediate post-hemorrhagic period may be considered (no consensus)
Traumatic		< 160 mm Hg systolic	Long-term (3-6 months) if clinical seizure or with increased risk of delayed seizure (prior seizure, intracerebral hematoma, or infarction)
SDH	If SDH > 10 mm diameter or midline shift > 5 mm, then surgical evacuation using craniotomy +/- bone flap removal and duraplasty is indicated For comatose patients (GCS < 9) who do not meet the above criteria, surgical evacuation is recommended if any of the following occurs: GCS score change \geq 2 from the time of injury to hospital admission; asymmetric or fixed/dilated pupils; and/or ICP > 20 mm Hg	< 140 mm Hg	Acute traumatic SDH: antiepileptics recommended if patient presents with seizures or decreased level of consciousness with GCS < 10 (phenytoin is medication of choice) No guidelines exist regarding use of antiepileptics in nontraumatic SDH
EDH	Surgery is indicated for EDH > 30 cm ³ , regardless of a patient's GCS score. Additionally, patients in a coma (with GCS < 9) with anisocoria should have surgical evacuation of EDH urgently.	> 90 mm Hg	Antiepileptic prophylaxis not indicated unless there is an early post-traumatic seizure (within 7 days of injury)

CHALLENGE CASES

Intra-Arterial Calcium Stimulation for Pancreatogenous Hypoglycemia after Bypass Surgery

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Abstract

The case presents how interventional radiology can contribute to the evaluation of hypoglycemia after gastric bypass. A middle-aged woman status post Roux-en-Y gastric bypass presented for a second opinion after being diagnosed with nesidioblastosis and failing medical management for symptomatic hypoglycemia. After failed clinical management, she was recommended to revise her gastric bypass to a sleeve gastrectomy. During her evaluation, cross-sectional imaging with CT and MRI was interpreted as negative. However, with supplemental angiography and an intra-arterial calcium stimulation test the correct diagnosis of an insulinoma was definitively achieved. Her hypoglycemia immediately resolved after surgical removal of the insulinoma which could not have been completed without the diagnosis and localization by interventional radiology.

Case Presentation

A middle-aged female with remote history of Roux-en-Y gastric bypass (RYGB) presented for a second opinion following failed medical management of symptomatic hypoglycemia with blood sugars as low as 30 mg/dL. She was previously diagnosed by her endocrinologist with noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS), or nesidioblastosis, attributed to insulin resistance from prior surgery. She had trials of diazoxide, verapamil, and acarbose without benefit. Her endocrinologist recommended surgical consultation for RYGB reversal to sleeve gastrectomy revision.

Our patient had no history of multiple endocrine neoplasia syndromes. Initial laboratory analysis demonstrated a negative sulfonyleurea screen and elevated proinsulin, C-peptide, and beta-hydroxybutyrate, favoring an endogenous insulin-mediated process. Subsequent laboratory analysis demonstrated elevated proinsulin and insulin with associated hypoglycemia of 40 mg/dL, and elevated chromogranin A. The elevated chromogranin A prompted imaging studies with a multiphase contrast enhanced CT and MRI protocol for the evaluation of neuroendocrine cell tumors (NETs); both which were reported negative on initial imaging.

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Challenge Questions

Q1: Based on the patient's history, diagnostic testing and refractory hypoglycemia, what is the most likely diagnosis?

- A. Nesidioblastosis
- B. Late Dumping Syndrome
- C. Insulinoma
- D. Surreptitious use of insulin or sulfonylurea

Q2: In light of the presumed diagnosis, what is the best subsequent step in management?

- A. Repeat MRI and CT
- B. Psychiatric Consultation
- C. Sleeve Gastrectomy Revision
- D. Calcium-Stimulation Test

Challenge questions: answers and explanations

The correct answer to Q1 is C.

While CT and MRI were negative for insulinoma, these screening modalities can be unreliable in the setting of small functional primary NETs. Furthermore, lab findings including elevated proinsulin, insulin and C-peptide that are refractory to medical management are suggestive of an insulinoma (C). Nesidioblastosis (A) has been documented as a rare complication of RYGB; however, most patients respond to nutritional or medical treatment, whereas this patient's hypoglycemia was refractory to hyperglycemic agents. Late dumping syndrome (B) is associated with an abnormally high post-prandial insulin level. Insulin levels are expected to be in normal ranges outside of the post-prandial interval. This patient's insulin levels are more likely due to constitutive insulin release secondary to NETs. Surreptitious use of insulin (C) is unlikely as C-peptide levels were also elevated. Additionally, the negative

sulfonylurea screen ruled out the use of sulfonylurea as a causative agent.

The correct answer to Q2 is D.

Calcium-stimulation testing (D) has been shown to identify insulinomas more effectively compared to CT and MRI. Repeat MRI and CT (A) are not likely to yield a true positive screen for insulinoma as initial imaging findings were negative. Psychiatric consultation (B) may be beneficial in

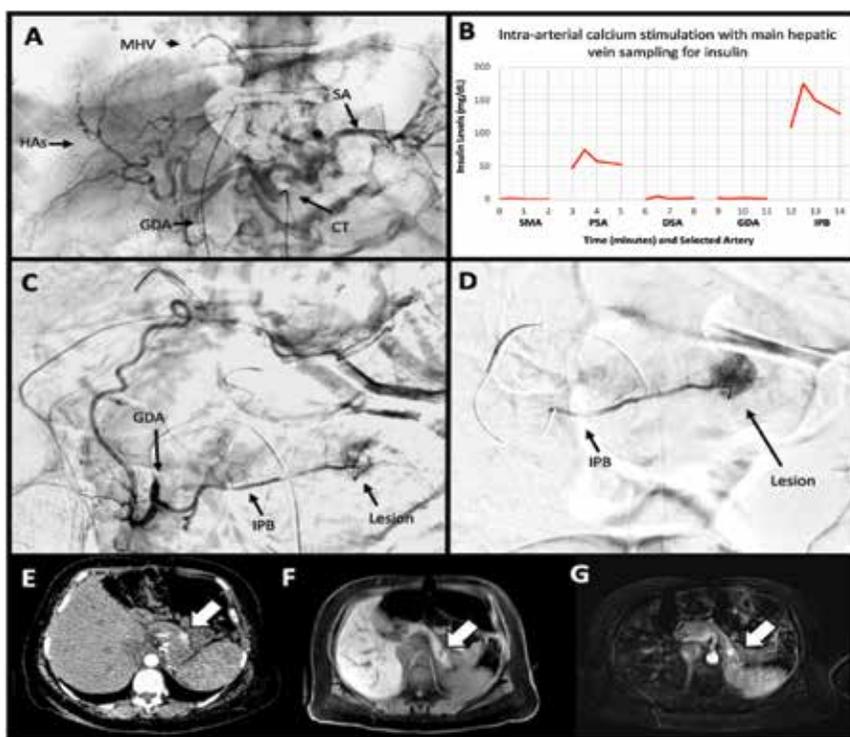


Figure 1. Radiologic evaluation for pancreatogenous hypoglycemia demonstrating [A] selective angiography of the celiac artery via a right common femoral artery approach infusion catheter at the ostium of the celiac trunk (CT) and opacification of the major branches including splenic (SA), hepatic (HAs), and gastroduodenal (GDA) arteries. There is an additional right femoral vein approach catheter terminating in the main hepatic vein (MHV) for blood sampling. [B] Insulin levels from the main hepatic venous blood sampling after calcium infusion demonstrates elevated levels with interrogation of the proximal splenic artery (PSA) and inferior pancreatic branch (IPB), whereas there are baseline levels after interrogation of the superior mesenteric (SMA), distal splenic (DSA), gastroduodenal (GDA) arteries. [C] Selective angiography of the GDA with a 2 cm hypervascular lesion identified from the inferior pancreatic branch (IPB) territory. [D] Selective angiography of the IPB with better delineation of the hypervascular lesion consistent with a primary neuroendocrine tumor and elevated insulin levels with calcium infusion. [E] Axial arterial-phase contrast enhanced CAT scan, [F] axial T1-weighted fat saturated nonenhanced MRI, and [G] axial arterial-phase contrast enhanced subtraction MRI of the distal pancreas, which when interpretation was supplemented with the results from the calcium infusion, was able to identify a small arterially-enhancing lesion allowing for surgical planning.

the setting of factitious disorder or surreptitious drug use, but these diagnoses were ruled out. Sleeve revision (C) may be indicated in some cases of nesidioblastosis but would not treat the underlying NETs.

Discussion

Hypoglycemia after RYGB is becoming increasingly recognized as a complication in the post-operative course with a differential of nesidioblastosis, late dumping syndrome, and insulinoma.¹ Neuroglycopenia, a hyperinsulinemic hypoglycemia state deprives the central nervous system of glucose and could become life threatening. It can occur up to one or more years post-operatively.² Nesidioblastosis was first described in 1938 as a pediatric congenital neof ormation of pancreatic islets from duct epithelium leading to abnormal β -cell hypertrophy; it has since also been documented in adults as a contributing cause of NIPHS and post-operative neuroglycopenia.^{3,4}

CT and MRI can be unreliable modalities for the evaluation of small functional primary NETs. Comparison of imaging modalities for the identification of a primary NETs demonstrated a sensitivity of 95.2% for MR, 78.5% for CT, and 49.3% for octreotide nuclear imaging scans.⁵ An additional, commonly forgotten technique for evaluation is angiography with intra-arterial calcification stimulation (IACS).⁶ This technique has been demonstrated to have better regional localization compared to MRI and CT.^{7,8} IACS has been shown to identify 93.5% of insulinomas compared to 90% by Gallium-68 DOTATATE PET/CT, 55% by CT, 61% by MRI, 21% by transabdominal ultrasound, 93.5% by intra-operative ultrasound, and 83% by intra-operative manual palpation.⁹

After negative cross-sectional imaging, she was referred to interventional radiology for IACS. This technique consists of selective-catheterization of the major pancreatic arteries, infusion of 50 mcg of calcium gluconate, and obtaining blood samples via a second catheter from the main hepatic vein

at 0, 30, 60, and 120 seconds after infusion. The calcium gluconate infusion stimulates an influx of calcium into the neoplastic beta cells of the insulinoma resulting in the release of insulin. In contrast to the neoplastic cells, normal beta cells maintain their regulatory mechanisms preventing insulin release.

Initial angiography demonstrated a 2 cm hypervascular lesion arising from the inferior pancreatic branch of the gastroduodenal artery, suspicious for

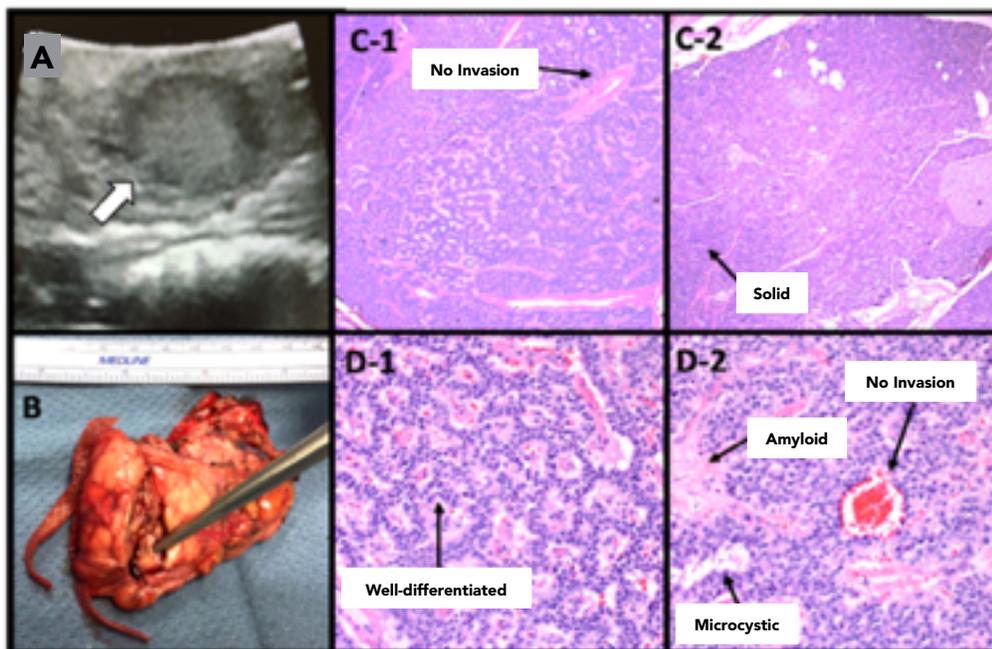


Figure 2. [A] Intra-operative ultrasound in the region of interest of the distal pancreas demonstrating a 2 cm solid lesion. [B] Distal pancreatectomy specimen with demonstration of the 2 cm solid lesion. Histology of the lesion stained with hematoxylin-eosin (H-E) and original magnification [C-1 & C-2] to x40 [D-1 & D-2] demonstrates a predominately solid growth pattern, with some areas of microcystic growth, and no vascular invasion. Furthermore, the cells have a uniform polygonal appearance with round and oval nuclei and eosinophilic granular cytoplasm, resembling that of a normal islet cell, compatible with a well-differentiated neuroendocrine tumor. Lastly, there is acellular eosinophilic amyloid which is seen only with insulinomas.¹⁰

a primary NET (Figure 1). Angiographic findings concurred with subsequent IACS which demonstrated the highest insulin levels after infusion into the inferior pancreatic branch of the gastroduodenal artery consistent with an insulinoma. Subsequent retrospective review of the patient's cross-sectional CT and MR images revealed a small, circumscribed lesion with faint arterial-phase contrast enhancement in the same location as the corresponding angiogram.

The patient proceeded to distal pancreatectomy, at which time a 2 cm lesion was discovered by manual palpation and intraoperative ultrasound within the body/tail of the pancreas (Figure 2). Pathology confirmed the diagnosis of insulinoma. The surgery was well tolerated without complications and the patient experienced immediate resolution of her hypoglycemic episodes.

Conclusion

This case demonstrates a growing awareness of delayed hypoglycemia after RYGB and the pitfalls with diagnostic imaging. Well-differentiated primary NETs, including insulinomas, are prone to false-negative cross-sectional imaging as their hypervascularity is difficult to capture and requires precise imaging timing. Furthermore, false-negative imaging can lead to misdiagnosis and occult progression to neuroglycopenia. We demonstrate an additional imaging technique that addresses and supplements the pitfalls of cross-sectional imaging for primary NETs. We believe IACS plays a valuable adjunctive role in the diagnostic algorithm for the evaluation of pancreatogenous hypoglycemia after bypass surgery.

Disclosures

No financial support given. Authors report no conflict of interest.

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CHALLENGE CASES

Transient Arm Pain Followed by Orthopnea in a 62-year-old Male

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Case Presentation

A 62-year-old Caucasian male with history of hypertension and hyperlipidemia presented with shortness of breath for the past month. At symptom onset, he had severe right shoulder pain that lasted two days. This pain kept him from participating in his new disc golf hobby and made working as a painter more difficult. He endorsed numbness and paresthesias in the right arm but denied weakness. Three weeks later, he developed shortness of breath. The shortness of breath was worse at night and required him to sleep in his recliner. The patient denied fever, chills, productive cough, and leg swelling. No signs or symptoms of recent gastrointestinal or respiratory infections, and had not received vaccinations recently. He had no history of heart failure, and never smoked. He had no family history of lung disease or neuromuscular disease. The patient denied any new physical activity or injuries. He denied any recent upper respiratory symptoms upon the current presentation. He had not traveled or associated with ill contacts.

On exam, the patient was sitting up, using accessory muscles to breathe, and tachypneic to 28 breaths per minute. Cranial nerves were intact and he displayed normal muscular bulk and tone. The patient exhibited 5/5 strength in deltoids, biceps, triceps, wrist flexion and extension, dorsal interosseous, abductor digiti minimi, and abductor pollicis brevis. Neck flexion/extension and lower extremity strength testing also revealed full strength throughout. Upon visual inspection, he had no scapular winging and no fasciculations. Reflexes and sensation to light touch, pinprick, and temperature were intact. There was no Babinski or Hoffman's sign. He had no rigidity or spasticity and no resting or intention tremor. Coordination testing revealed no dysmetria and normal rapid alternating movements. Gait and arm swing were normal. He had no bradykinesia. There was full range of motion in legs with no ataxia.

He was well-nourished and in no apparent respiratory distress. He had no dysarthria or hypophonia, but exhibited conversational dyspnea. On lung auscultation, he had decreased breath sounds throughout, without rhonchi, wheezes, or rales. No pain could be elicited with palpation of arms and shoulders, nor with passive or active range of motion.

The patient developed orthopnea during the first night of his admission, requiring oxygen via nasal cannula to maintain oxygen saturation overnight. However, his oxygenation improved upon ambulation and standing. In addition, EKG showed normal sinus rhythm and a prior myocardial perfusion study showed a left ventricular ejection fraction of 50%, normal ventricular function, and no wall motion abnormalities.

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Investigation and Work-up

Pulmonary function studies were initially performed to characterize the severity of the patient's presentation. Percent predicted values were significantly diminished from sitting upright to lying supine: FVC and FEV1 were 49% and 51% while upright, versus 23% and 21% while supine. Chest X-ray showed evidence of an elevated right hemidiaphragm. In addition, chest x-ray with fluoroscopy showed paradoxical motion on the right with sniff testing and diminished right diaphragmatic motion. Left diaphragm was unremarkable.

Extensive serum laboratory studies were completed to investigate causes of neuromuscular dysfunction. Serum lead, Lyme disease antibody panel, GM-1 Antibodies (IgG, IgM), Acetylcholine (Ach) receptor blocking antibodies, Ach receptor antibody, Ach modulating antibody, MUSK antibody, and SEPT9 mutation were negative. Urine screen for heavy metals was negative.

Nerve conduction studies done with surface electrodes, about three weeks after initial chest x-ray with fluoroscopy, showed absent phrenic nerve activity bilaterally. Due to the patient's increased dyspnea while lying flat, we were unable to obtain an MRI of the brachial plexus or cervical spine, which would have been helpful to exclude pathologies such as spondylosis/stenosis, spinal tumor, or syrinx. Thus, we relied on nerve conduction studies and ultrasonography to confirm neuromuscular dysfunction.

EMG and nerve conduction studies were also done on C3-C4 paraspinal muscles to rule out possible pathology of the cervical spine, specifically C3-C5 radiculopathy. The lateral antebrachial cutaneous nerve response was normal, and all muscles studied (deltoid, sternocleidomastoid, rhomboid major, trapezius, and infraspinatus) were normal on EMG. US of the bilateral brachial plexus was also normal. US of the diaphragm revealed minimal change in thickness from inhalation to exhalation (2.3 to 1.8 mm on the right and 2.3 to 1 mm on the left). In addition, there was marked intercostal muscle thickening and excursion, suggesting use of the accessory muscles. The right lung did not enter the axillary region; the left lung entered the 3rd intercostal space. The combination of EMG, nerve conduction, and US studies confirmed isolated impairment of the phrenic nerves resulting in weakened diaphragms, explaining the patient's shortness of breath.

Diagnosis

Our patient's rapid onset of severe musculoskeletal pain followed by weakness in a discrete nerve distribution is characteristic of an inflammatory acquired brachial plexopathy or Parsonage Turner Syndrome (PTS).^{1,2} PTS is a painful form of plexopathy, which may be hereditary, associated with a SEPT9 gene mutation, or acquired.³ Diagnosis of this already rare syndrome is further complicated when patients present with less variants involving single nerves (mononeuropathies) and/or distributions outside of the brachial plexus such as the cervical plexus. As discussed above, diagnosis involves localizing the neurologic lesion, then ruling out specific etiologies of disease in that level of the nervous system. If careful history is not taken, a physician could miss the initial painful part of the syndrome and only address the weakness. Thus, PTS is often misdiagnosed as an entrapment or muscle strain. A patient with pain followed by weakness in a separate nerve distribution should raise high suspicion for PTS, and timely diagnosis with EMG/NCS is important to help facilitate treatment.

Treatment

Treatment for PTS is mostly symptomatic and most patients have functional motor recovery after three years.^{4,5} Early treatments during the first few weeks target pain management and include opiates, NSAIDs, and neuropathic pain modulating agents such as tricyclics, and antiepileptic agents.^{6,7} Long-acting opioids in combination with an NSAID are currently the best option for managing severe nerve pain in these patients in the acute phase.^{8,9} Immunomodulators such as prednisone are commonly administered as immune-mediated processes may be involved in the etiology of PTS. There is anecdotal evidence for use of corticosteroids in the literature and some evidence that early treatment with prednisone may shorten duration of pain and recovery, but other studies have been inconclusive.³ Intravenous immunoglobulin (IVIg) has also been suggested by case studies but has no definitive support in the literature.^{9,10} In a retrospective case studies report comparing patients who received IVIg + Methylprednisolone Pulse Therapy (MPPT) versus MPPT alone, no clear difference in clinical improvement was observed.¹¹

Unilateral diaphragm paralysis can be treated with diaphragm plication, diaphragm pacing, or neurotization of the phrenic nerve.^{12,13,14} Diaphragmatic plication is a surgical procedure

that can decrease lung compression and improve quality of life by moving the paralyzed diaphragm to a position of maximal inhalation.^{12,15} Diaphragm pacing allows for phrenic nerve stimulation via electrodes placed on the neck or chest. Electrodes can also be directly placed on the diaphragm if needed. In this case, two electrodes are implanted in each diaphragm and are connected to an external stimulator.¹³ Neurotization of the phrenic nerve could restore diaphragm function in the case of complete or nearly complete phrenic nerve injury.¹⁴

Bilateral diaphragmatic paralysis management depends on severity and etiology. Generally, ventilatory support such as non-invasive positive pressure ventilation (NPPV) or continuous positive airway pressure (CPAP) can prevent ventilatory failure that commonly occurs with bilateral diaphragmatic paralysis.¹⁶

Our patient was started on IV solumedrol, CPAP at night, and monitored with daily NIF testing. After seven days of solumedrol, his dyspnea while flat improved so that he no longer used supplemental oxygen. NIF improved from -19 to -30. Pulmonology recommended that CPAP be used at night to help facilitate expansion of diaphragm via positive inspiratory pressure. Surgical treatment options were explored. Cardiothoracic surgery determined that diaphragm plication would not be an option as both sides of the patient's diaphragms were now compromised. Nerve transfer was considered but not attempted due to the chronicity of the presentation.

Challenge Questions

Q1: How would you localize the patient's neurologic lesion based on history and physical exam?

- A. Diaphragm Muscle
- B. Neuromuscular Junction
- C. Phrenic Nerve
- D. Cervical Spine
- E. Cardiovascular disease

Q2: What is the most affected anatomical area in PTS?

- A. Long Thoracic n.
- B. Phrenic n.
- C. Radial n.
- D. Brachial Plexus
- E. Lumbosacral Plexus

Q3: Have any associations been identified as potential risk factors for acquiring PTS, if so, what are they?

- A. Environmental toxins
- B. Viral infections
- C. Mechanical stress
- D. B and C
- E. No associations are postulated; PTS is sporadic and inherited

Challenge questions: answers and explanations

The correct answer to Q1 is C.

The patient complained of transient right-sided shoulder pain with numbness and paresthesias, followed by acute onset of dyspnea that worsened by lying flat. Initially, a cardiopulmonary etiology such as congestive heart failure was considered. However, his negative CAD history coupled with an absence of chest pain and pedal edema made this less likely. This information in conjunction with the associated upper extremity symptoms heightened the suspicion for a neuromuscular etiology of the patient's shortness of breath.

Cervical spine nerve roots C3-C5 compose the phrenic nerve, which innervates the diaphragm. Thus, an insult to the cervical spine at this level may present with a change in respiratory status. In addition, the upper extremity is innervated by C5-C8 as well as T1, so pathology at these levels could explain the patient's pain and paresthesias. Cervical spine lesions considered included cervical spine trauma, spondylosis, and initial presentation of multiple sclerosis (MS). The patient did not report any neck trauma, though working as a painter could have lead to chronic structural changes. Cervical spondylosis is a degenerative condition of the spine where hypertrophy of the posterior longitudinal ligament, ligamentum flavum, or facet joints causes impingement of the cervical spine and nerve roots. Patients present with neck and shoulder pain along with headache in up to one-third of patients¹, with or without radiation and weakness of the arms, which did not resemble our patient's complaints. The patient's history and presentation was also not suspicious for MS, which would classically present as a "relapsing" disease in middle-age, with a history of pain, numbness, or weakness. MS requires two separate lesions of the nervous system, separated by time for diagnosis. Other intramedullary lesions in the differential

aside from MS would include sarcoid, lupus, Behcet's myelitis, infectious myelitis (Lyme disease, syphilis, HIV, hepatitis C, HTLV1-2), nutritional deficiencies such as B12 or copper, neoplasms, or congenital such as syrinx. However, due to the patient's normal reflexes, a spinal cord localization was less likely. Infectious etiology was also not likely due to lack of infectious symptoms and exposures. Nutritional deficiency did not fit due to lack of lower extremity involvement and limitation to one limb. Syrinx was felt unlikely given his onset history.

Neuromuscular junction disorders such as myasthenia gravis and Lambert-Eaton myasthenic syndrome affect the bulbar, respiratory, and proximal limb muscles with fluctuating weakness and/or eventual paralysis during exacerbations. The timeline of our patient's presentation made these diseases less likely. In acute exacerbations, myasthenic patients' symptoms are worse later in the day, and they progressively worsen sometimes until ventilatory support is necessary. In addition, our patient's pain with lack of weakness and lack of bulbar involvement made these less likely.

Conditions that can potentially affect the phrenic nerve include Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Parsonage-Turner Syndrome (PTS), Amyotrophic Lateral Sclerosis (ALS), and Spinal Muscular Atrophy (SMA). ALS classically presents with both upper and lower motor neuron signs, and is confirmed with EMG testing. Our patient did not present with childhood or young adult onset, progressive weakness as seen in SMA or chronic course of weakness as seen in CIDP. PTS, however, was a possible diagnosis as it could present with subacute weakness and atrophy involving one arm.

Insults to the diaphragmatic muscle and phrenic nerve can be chronic, subacute, or acute. Patients with muscular dystrophies such as Limb-Girdle Muscular Dystrophy would have an insidious, chronic presentation that could lead to severe respiratory issues. Depending on the disease, patients also can present with an impaired gait, scapular winging, lordosis and cardiomyopathy. Inflammatory pathology or diseases of abnormal deposition such as dermatomyositis, systemic sclerosis and amyloid infiltration can cause weakening of the diaphragm but would have other systemic involvement.

Acute insults would include trauma or thoracic surgery. The most common cause of acquired diaphragmatic palsy is cardiovascular surgery, which can account for almost 64% of phrenic nerve injuries.² Blunt trauma can also potentially cause diaphragmatic rupture, which would present with acute shortness of breath, decreased lung sounds, and pain in the upper chest and abdomen. The patient's history enabled us to rule out these potential etiologies.

The answer to Q2 is D

The most common phenotype is shoulder pain followed by paresis in a nerve of the brachial plexus. The classic phenotype presents with abrupt, excruciating shoulder pain followed by unilateral arm weakness in the muscles supplied by the long thoracic and/or suprascapular nerve in about 71% of cases. Less often, musculocutaneous or axillary nerve involvement is observed.⁸ PTS is unique in that the pain and motor symptoms are "patchy", and can follow different myotomes. Diagnosis of this already rare syndrome is further complicated when patients present with uncommon variants, such as mononeuropathies, lumbosacral plexus involvement, or a recurrence.

The phrenic nerve mononeuropathy variant of PTS in this patient is uncommon, found in only about 6.6% of cases (Figure 1).⁸ A high level of clinical suspicion is necessary for diagnosis of PTS. However, this patient was more difficult to diagnose due to the isolated phrenic nerve involvement, and even more uncommon, bilateral presentation. More common phenotypes of PTS manifest with pain followed by, for example, atrophy of deltoid or scapular winging. This patient's weakness, however, presented as shortness of breath. The connection with the shoulder pain history and thorough neuromuscular exam were crucial in arriving at his diagnosis.

The answer to Q3 is D

As stated above, PTS may be either hereditary or acquired. Our patient's genetic testing for SEPT9, the only gene thus far associated with PTS, was negative. Therefore, we assume that he acquired his disease. Pathophysiology of acquired PTS is unknown; however, cohorts have been associated with higher percentages of biomechanical factors (i.e. strenuous exercise of the upper extremities) and autoimmunity (i.e. infection or surgery).⁸ In van Alfen and van Engelen's review of 246

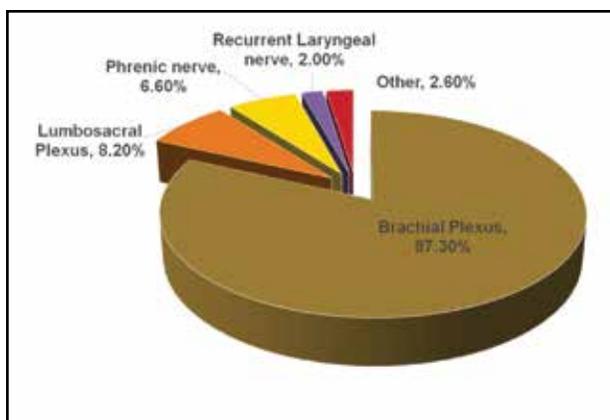


Figure 1. PTS Manifestations: Frequency of Paresis Location in Reported Cases⁸

cases of PTS, over one-half of the cases were associated with antecedent events. The most common event was infection, followed by exercise, surgery, and peripartum (either during pregnancy or puerperium period).⁸ The majority of the events occurred in the week prior to onset of pain.

A multitude of case reports exist supporting these associations. An early case involved an epidemic of PTS that occurred in 1949: workers in a knitting factory whose village was also infected with Coxsackie A2 virus.¹⁷ Another, more recent case was reported with two surfers who had contracted HEV and bilateral PTS.¹⁸ Both of these cases are interesting in that they involved both immunological (infection) and biomechanical (knitting and surfing) stressors.

Antecedent Event	Percentage	Cases
Infection	43.5	50
Exercise	17.4	20
Surgery	13.9	16
Peripartal	8.7	10
Vaccination	4.3	5
Stress (Psychological)	4.3	5
Trauma	4.3	5

Figure 2. Antecedent events prior to PTS onset (from comprehensive review of 246 cases⁸)

Upon further questioning, our patient stated that he had begun playing competitive disc golf several times per week in the month prior to onset of shoulder pain. He is right-handed, which correlates with his right-sided shoulder pain and right-phrenic nerve weakness. Thus, we suspect this new mechanical stress could have contributed to the onset of his PTS.

Discussion

Parsonage-Turner Syndrome, or neuralgic amyotrophy, is an uncommon, idiopathic brachial plexopathy that sometimes manifests as other peripheral neuropathies (see Figure 1). Its presentation can be variable, but typically begins with shoulder pain followed by progressive unilateral weakness. Although uncommon, Parsonage-Turner syndrome should be included in the differential for cases involving the described pain and weakness, as the diagnosis is often unrecognized and results in delay of diagnosis.³

The diaphragmatic involvement in our case also highlights the importance to consider other causes of phrenic neuropathy, such as cervical spine dysfunction. Specific bilateral phrenic neuropathy can also be a manifestation of either motor neuron disease or neuromuscular junction disorders.

Serum antibody testing can be utilized and is helpful in ruling out other etiologies, but often seronegativity is seen in most cases. SEPT9 is a genetic test that can be obtained to assess for hereditary forms of this disorder. The most important diagnostic procedure is the EMG/NCV of the diaphragm.

However, this can be technically difficult to perform and there is variability in styles. Another important diagnostic study is MRI of the cervical spine but is often difficult to perform in these patients given the degree of respiratory distress and inability to lie flat. Thus, it is important to look for specific denervation patterns to clarify plexus vs. cervical nerve root involvement via electrodiagnostic testing.

Our patient's case demonstrates a rare case of bilateral PTS, which can be considered as two instances of phrenic neuropathy separated in time with incomplete recovery following initial insult. Literature review revealed two other similar published cases of bilateral phrenic nerve palsy with PTS as etiology,

however both presented as a single occurrence, not a recurrent syndrome with one side, then the other effected.^{19,20} Most insight into treatment options come from cases with etiologies of trauma, ALS, or other chronic or degenerative diseases. This case highlights the lack of treatment options available for this subset of patients, as the available treatments are mostly symptomatic. Surgical options are available for unilateral cases but are limited in bilateral cases given the irreversibility of procedures in a possibly reversible disorder. Future research could be aimed at working towards more effective diagnostic testing such as biomarkers and other genetic testing. Additionally, with the varied techniques within EMG/NCV of the diaphragm, it would be helpful to develop a standardized approach. It may also be beneficial to investigate alternative treatment options for symptomatic management to improve quality of life.

Disclosures

No financial support given. All authors report no conflict of interest.

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Eversion Endarterectomy of the Deceased Donor Renal Artery to Prevent Kidney Discard

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Abstract:

Introduction: Deceased donor (DD) kidneys exhibiting severe atherosclerosis involving the renal artery (RA) may represent a contraindication to kidney transplantation (KT).

Methods: Eversion endarterectomy (EE) was performed as a salvage procedure to permit KT.

Results: We identified 17 cases (1.2% of all DD KTs during the study period) involving EE of the DD RA. Thirteen (76.5%) kidneys were imported and mean Kidney Donor Profile Index (KDPI) was 81%. Mean DD age was 59 years, mean RA plaque length was 1.7 cm, and mean glomerulosclerosis on biopsy was 10%. Mean recipient age was 64 years and dialysis vintage was 32 months. With a mean follow-up of 36 months, actual patient and graft survival rates were both 76.5%. One patient died early without a technical problem. Of the remaining 16 patients, 2-year patient and graft survival rates were both 100%. There were no early or late vascular complications. The incidence of delayed graft function was 35%. Mean serum creatinine and GFR levels in patients with functioning grafts at latest follow-up were 1.8 mg/dl and 40 ml/min, respectively.

Conclusions: EE appears to be a safe and under-utilized procedure that may prevent discard of marginal donor kidneys and is associated with acceptable short-term outcomes.

Introduction

For patients with end stage renal disease (ESRD), kidney transplantation (KT) offers both additional life-years, improved quality of life, and is cost-effective compared to dialysis.¹⁻⁵ In 2017, the United Network for Organ Sharing (UNOS) national waiting list for solid organ transplantation had nearly 100,000 patients awaiting KT.⁶ Depending on blood type and Donor Service Area (DSA), KT waiting times in the United States (US) range from a median of 850 to 1935 days.⁶ In 2017, there were more than 4500 deaths in patients awaiting KT and up to 10,000 patients were removed from the waiting list for reasons other than receiving a KT or death. Coincidentally, there were approximately 35,000 additions to the kidney waiting list.⁶ Unfortunately, only 19,848 KTs were performed in 2017, of which 14,037 (71%) were from deceased donors.⁶ Moreover, in the past decade, the annual number of KTs in the US has been relatively static whereas the waiting list continues to grow. Consequently, more patients are dying instead of receiving a potentially life-extending KT.⁷

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One of the major challenges in organ transplantation today is the disparity between kidney supply and demand, which has been described as an insurmountable problem. To increase the size of the pool of donors, initiatives such as the Organ Donor Breakthrough Collaborative and other national initiatives were implemented.^{8,9} As a result of these endeavors, an upturn in the number of “marginal” donors such as expanded criteria donors (ECD),¹⁰⁻¹² donation after cardiocirculatory death (DCD) donors,^{13,14} donors with prolonged warm or cold ischemia time (CIT),¹⁵⁻¹⁹ dual kidneys from donors at the extremes of age,^{20,21} or donors with acute kidney injury (AKI) occurred.²²⁻²⁴ Commensurate with efforts to enlarge the donor pool and with changes in the Kidney Allocation System (KAS) including implementation of the Kidney Donor Profile Index (KDPI), the kidney discard rate increased from 10% in 1998 to 20% in 2017.^{6, 25-32}

At present, more than 3000 kidneys that are recovered from deceased donors (DD) with the intent to use them for KT are discarded annually in the US.^{6,32} The increasing number of discarded DD kidneys has become a national crisis, particularly since it is believed by many that a substantial proportion of these kidneys may be usable for transplantation in the “right” recipient. With kidneys recovered from older donors, high KDPI donors, or ECDs, >50% are discarded.²⁷⁻³² Anatomic considerations are one of the primary reasons for kidney discard.

DD kidneys exhibiting severe aortic atherosclerosis with hard ulcerative occlusive plaque extending into the renal artery (RA) may represent a contraindication to organ utilization because of a lack of acceptance by multiple centers. Limited data are available on eversion endarterectomy (EE) as a salvage procedure to permit successful KT in this setting.³³ The purpose of this study was to analyze our single center experience with EE of the DD RA as a method of graft salvage to prevent kidney discard.

Methods

Study Design: We conducted a retrospective chart review of all DD KT performed in adult recipients at Wake Forest Baptist Medical Center from 1/1/08 to 1/1/18. Specific exclusions included pediatric recipients (younger than age 19 years), simultaneous kidney-pancreas transplant recipients, and living donor KT recipients. During this 10-year study

period, a total of 1467 DD KT were performed in adult recipients. Standardized donor and recipient selection and management algorithms were followed during the period of study.^{12,14,21,24,34,35}

Definitions: ECDs were defined by UNOS criteria as all DDs age 60 and older or donors age 50-59 years with any two of the following three specific co-morbid conditions: Brain death from cerebrovascular accident, history of hypertension, or a terminal serum creatinine (SCr) level >1.5 mg/dl.¹⁰⁻¹² All DDs were considered standard criteria donors (SCD) unless they met the above ECD definition. DCD donor was defined as organ recovery after withdrawal of life support in the absence of brain death. Delayed graft function (DGF) was defined as the need for dialysis for any reason in the first week following KT. Renal allograft loss was defined as death with a functioning graft, allograft nephrectomy, resumption of dialysis, retransplantation, or return to the pretransplant SCr level in patients transplanted preemptively. The KDPI is a numerical scoring system that explicitly compiles 10 donor factors to rank order the quality of kidneys as defined by an aggregate population relative risk (recovered and transplanted deceased donor kidneys from the previous calendar year) to project all-cause allograft survival associated with the use of that particular organ.^{25,26,30} The KDPI is based on the Kidney Donor Risk Index (which uses a Cox proportional hazards regression model) and became the basis for the new KAS that was implemented in December 2014.^{25,26,30,36}

Technique of EE: EE was performed by subintimal dissection of the Carrel aortic patch surrounding the RA (Figures 1 and 2) followed by complete eversion and removal of the RA cast (Figures 3 and 4). Debris was then washed from the arterial lumen using heparinized saline, as the RA was carefully flushed antegrade to check for vascular patency, integrity, and any leaks or disruption (Figure 5). Indications for EE were hard occlusive plaque involving the ostium with extension into the RA such that resecting the area of involvement would result in an extremely short RA that would be difficult to implant. Patients received localized heparin intra-operatively and aspirin post-operatively. KT duplex ultrasonography was performed on post-operative day one and whenever clinically indicated.

Donor Selection: No specific DD age limits were excluded from consideration; the oldest DD in this study was 78 years.

The Cockcroft-Gault formula was employed to estimate adult DD creatinine clearance (CrCl), using both the admission and terminal donor SCr level and adjusted body weight to calculate a range of DD kidney function in order to determine optimal kidney utilization.^{12,14,21,24,34} If the estimated DD CrCl was >65 ml/min, then a single KT was usually performed. If the estimated DD CrCl was 40-65 ml/min, then an adult dual KT was performed, preferably into an older recipient with a body mass index (BMI) <30 kg/m².^{12,21} If the estimated DD CrCl was <40 ml/min, then the kidney(s) were not transplanted at our center.

Kidney Assessment: Donor kidney biopsy was used to assist in the evaluation of preexisting and terminal renal parenchymal



Figure 1. The atheroma is identified in the main renal artery distal to the Carrel aortic patch.

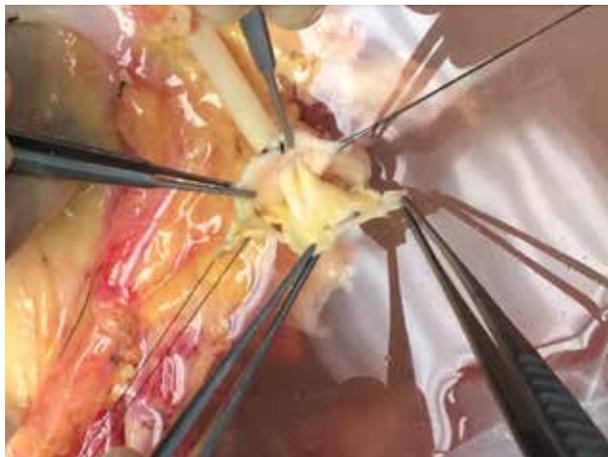


Figure 2. A plane is developed for subintimal dissection.



Figure 3. The artery is everted. Dissection is continued circumferentially until the plaque is freed.



Figure 4. Specimen of intact cast that has been removed.

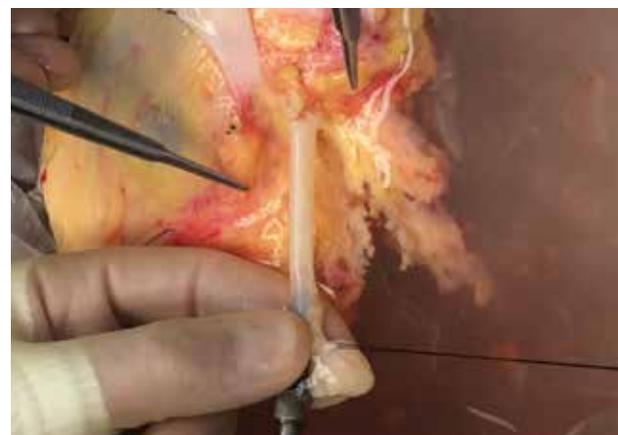


Figure 5. The vessel is carefully flushed with heparinized saline to wash out debris and check for any leaks or vessel wall disruption.

injury. Renal cortical wedge biopsies for frozen section were performed and evaluated for the presence and degree of glomerulosclerosis, interstitial fibrosis, chronic interstitial inflammation, tubular atrophy, and vascular hyalinosis or sclerosis.^{12,14,21,24,34} Moderate to severe vascular or interstitial changes, tubular atrophy, or glomerulosclerosis $\geq 35\%$ was a contraindication to kidney utilization. Whenever possible, DD kidneys were placed on hypothermic machine perfusion preservation to minimize preservation injury, maintain functional reserve and endothelial integrity, and provide another means of assessment.^{12,14,21,24,34} Although pump parameters were not exclusively used to discard kidneys, a flow rate > 80 ml/min and a resistance < 0.40 mmHg/ml/min after a minimum of 6 hours on the machine perfusion apparatus were considered thresholds for single kidney utilization.³⁴ If the kidney(s) were pumping well, CITs up to 40 hours and beyond were considered acceptable (the longest CIT in this study was 45 hours). If the pump flows were 60-80 ml/min or resistances were 0.4 -0.5 mmHg/ml/min, then the kidneys were either considered for dual KT (when possible) or discarded.³⁴ In addition, the logistics of transplanting the kidney with an acceptable (< 36 hours) CIT was a consideration, particularly if the kidney was not placed on machine preservation locally and was being imported from another service area. Whenever possible, DD kidneys were accepted by our center with a minimum of "pump and anatomic waivers" and usually full waivers. A "waiver" implies that a kidney acquisition charge does not have to be paid by the accepting center if the kidney is not transplanted on condition that documentation is provided as to why the kidney was considered unusable (for example, poor pump parameters or unexpected anatomic findings). However, with application of the above donor selection, biopsy, and pump criteria, it was unusual (probably $< 5\%$) that accepted kidneys were ultimately discarded although we do not specifically track this data.

Recipient Evaluation and Selection: At our center, no specific upper age limit was an absolute contraindication to DKT; the oldest recipient in this series was 75 years. All patients underwent a comprehensive pre-transplant medical, psychosocial, and financial evaluation, with emphasis placed on the cardiovascular system to determine operative risks and physiologic age.^{12,14,21,24} Non-contrast abdominal/pelvic

computerized tomographic imaging (to assess iliac artery calcifications) and cardiac stress testing were performed in all patients. In general, elderly patients needed to be reasonably well compensated, active and functional, not have multiple comorbidities, and have a solid social support system.³⁷⁻³⁹ All patients age 70 years and older also underwent carotid and iliac artery duplex ultrasonographic imaging, cardiology consultation, and heart catheterization. Specific exclusion criteria in the elderly included the presence of dementia, nursing home residence, poor overall functional status or frailty, lack of social support, advanced disease or organ failure in an extra-renal organ system, recent malignancy, or severe cardiac or vascular disease.³⁷⁻³⁹

With marginal donor kidneys, recipient selection was usually not by standard kidney allocation but based on older age (> 40 years) and smaller size (BMI < 30 kg/m²) matching and identifying low immunological risk patients such as primary KT, human leukocyte antigen matching, low panel reactive antibody level (usually 0%), and informed consent. In addition, age-matching between donor and recipient was a consideration as we tried to avoid age mismatches > 15 years.

Immunosuppression: KT recipients received depleting antibody induction with either multi-dose rabbit antithymocyte globulin or alemtuzumab 30 mg intravenous as a single intra-operative dose.³⁵ Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil (2 gm/day), and either rapid tapering doses of steroids or early steroid withdrawal based on immunological risk stratification. Target 12 hour tacrolimus trough levels were 6-10 ng/ml; recipients age 60 years and over received half dose mycophenolate mofetil (1 gm/day) in two divided doses.^{35,37-39} Early steroid withdrawal was performed in low-risk patients whereas steroids were continued in high immunologic risk patients such as patients receiving retransplants, patients with a current panel reactive antibody level $> 20\%$, and patients experiencing prolonged DGF.³⁵

Post-Transplant Management: All patients received surgical site prophylaxis with a first-generation cephalosporin for 24 hours, antifungal prophylaxis with nystatin or fluconazole for one to two months, and anti-Pneumocystis prophylaxis with sulfamethoxazole-trimethoprim (Dapsone® if allergic to sulfa) for at least 12 months. Antiviral prophylaxis consisted

of oral valganciclovir for three to six months, depending on donor and recipient cytomegalovirus serologic status. Specifics regarding drug dosing and duration have been published previously.^{12,14,21,24,34,35} Most patients received aspirin prophylaxis. Treatment of hypertension, hyperlipidemia, anemia, diabetes, and other medical conditions was initiated as indicated, aiming to maintain the blood pressure <140/90 mmHg, fasting serum cholesterol <200 mg/dl, hematocrit >27%, and fasting blood sugar <126 mg/dl. Post-transplant renal allograft function was evaluated by measuring SCr levels as well as calculating glomerular filtration rate (GFR) using the abbreviated Modification of Diet in Renal Disease (MDRD) formula.

Statistical Analysis: Endpoints included patient survival as well as uncensored and death-censored graft survival (DCGS). Other study endpoints included DGF and renal allograft function (based on SCr level and estimated GFR). Data were compiled from both prospective and retrospective databases, with confirmation by medical record review in accordance with local Institutional Review Board guidelines and approval.

Results

Over a 10-year period, we identified 17 cases (1.2% of all DD KTs) in which EE of the DD RA were performed on the backbench prior to KT. All cases were technically successful and resulted in KT. A total of 13 (76.5%) of the kidneys were imported from other DSAs; 11 (65%) were from ECDs, and the mean KDPI was 81% (Table 1). Kidneys were accepted on anatomic waivers and all resulted in successful KT. Mean DD age was 59 years, mean estimated creatinine clearance was 75 ml/min, and mean total cold ischemia time was 27.6 hours. Nine DDs were age 60 years or older. Other donor characteristics are shown in Table 1. All kidneys were placed on machine preservation prior to KT; mean pump time was 11.8 hours (with a mean flow of 117 ml/min and a mean resistance of 0.27 mmHg/ml/min). Mean RA plaque length was 1.7 cm and mean percent glomerulosclerosis on donor kidney biopsy was 10%.

Mean recipient age was 63.6 years with a mean dialysis vintage of 32 months (Table 2). Fourteen recipients were age 60 years or older and 6 were ≥ age 70 years. Other recipient and transplant characteristics are shown in Table 2. With a mean follow-up of 36 months (range 10-87 months), actual

patient and graft survival rates were both 76.5% (Table 3). One dual KT patient died early from a cardiovascular event without evidence of a technical problem. In this case, the DD was age 78 years and the recipient was 73 years of age. Of the remaining 16 patients who received single KTs, 2-year patient and graft survival rates were 100% and actual survival rates were 81%. Two patients died with functioning grafts (at 38 and 52 months post-transplant) and another patient experienced graft loss secondary to acute rejection at 73 months and then subsequently died of sepsis at 85 months. The DCGS rate was 92.9%. There were no early or late vascular complications. The incidence of delayed graft function was 35% and mean length of initial hospital stay was 4.8 days. Mean serum creatinine and GFR levels in patients with functioning grafts at latest follow-up were 1.8 mg/dl and 40 ml/min, respectively.

Table 1. Donor and Preservation Characteristics

Mean ± SD or n (%)	N=17
Donor age (years)	58.9 ± 10
Donor weight (kg)	82.5 ± 19
Donor BMI (kg/m ²)	28.5 ± 6
Donor gender: Male	9 (52.9%)
Donor: African American	2 (11.8%)
Donor category: SCD	3 (17.6%)
DCD	4 (23.5%)
ECD	10 (58.9%)
Cause of death: Trauma	2 (11.8%)
Cerebrovascular	10 (58.8%)
Anoxia	5 (29.4%)
Dual kidneys	1 (5.9%)
Imported kidney	13 (76.5%)
Terminal CrCl (ml/min)	75 ± 31
Terminal SCr (mg/dl)	1.1 ± 0.4
Machine preservation	17 (100%)
Pump time (hours)	11.8 ± 7.6
Pump flow (ml/min)	117 ± 30
Pump resistance (mm Hg/ml/min)	0.27 ± 0.07
Cold ischemia time (hours)	27.6 ± 8.8
Kidney Donor Profile Index (%)	81 ± 14

with liberalization of DD criteria, the number of kidneys recovered each year with the intent to transplant and then ultimately discarded has doubled in the past decade.^{6,32,40} Reasons for discard are myriad and include poor organ function, extended ischemia and anatomic considerations. Expanding the donor pool mandates an ongoing reappraisal of the limits of acceptability when accepting kidney offers from DDs.

In 1992, Nghiem et al., reported on 34 DD KT that required backbench EE prior to engraftment.³³ This study noted an acceptable graft survival of 76.4% with a mean serum creatinine of 2.3 mg/dl at a mean follow-up of four years. Utilization of these grafts expanded the center's KT volume by 18% per annum. There was no increase in the risk of hypertension and no vascular complications were noted. The procedure was shown to be safe and effective in this single center study cohort. In 2006, Sagban and colleagues reported on RA thrombo-endarterectomy in 10% (115/1134) of cases of DD KT because of intrinsic atherosclerotic plaque causing RA stenosis.⁴¹ In an additional 23 cases, the length of plaque precluded safe EE and a saphenous vein interposition bypass graft was placed after resecting the involved segment of RA. Mean donor age was 61 years and the 5-year graft survival rate was 84.3%.

Despite the implications of using EE to expand the donor pool of organs, today, more than 25 years after the Nghiem paper, few additional studies have reported on its use. Herein we describe our single center experience with RA EE as a method of graft salvage in 17 patients undergoing KT. The majority of these kidneys were imported from other DSAs, suggesting that multiple centers had refused these kidneys prior to acceptance by our center.⁴² Moreover, most of these kidneys would probably have been discarded in the absence of our rescue utilization. Many transplant programs regard severe DD aortic and RA atherosclerosis as a surrogate marker for intra-renal atherosclerosis and intrinsic renal parenchymal disease. Consequently, in this setting, centers are extremely reluctant to consider these kidneys for transplantation. However, in this study, severe RA atherosclerosis was not associated with severe glomerular disease, as confirmed by a mean of 10% glomerulosclerosis on pre-implantation biopsies. Most of these kidneys were from ECDs or DDs with a high KDPI, again suggesting a burden of atherosclerosis related

to advanced age, longstanding hypertension, or diabetes that may influence renal recovery and outcomes. In spite of severe RA atherosclerosis, we were able to successfully pump these kidneys, which may suggest a selection bias that excludes cases in which either near-occlusive or hard circumferential plaque is present. Moreover, the absence of acceptable pump parameters may exclude cases with severe intra-renal vasospasm, atherosclerosis, or other parenchymal damage.³⁴ It is also important to emphasize that for cases of ostial stenosis (without significant plaque extension into the RA), our preferred reconstruction technique is to merely cut the RA away from the aorta and perform the implantation similar to a living donor KT. We reserve EE only for those cases in which the involved segment of RA is such that amputation distal to the plaque would leave an extremely short RA, which would then be difficult to implant. It is interesting to note that our medium-term outcomes (three year survival rates of 76.5%) are near-identical to those reported by Nghiem.³³

In summary, the critical shortage of donor kidneys compounded by the increasing rate of kidney discards defines two of the major challenges in organ transplantation today. EE appears to be a safe and under-utilized procedure that may prevent discard of marginal donor kidneys and is associated with acceptable medium-term outcomes. The presence of severe atherosclerosis with partially occlusive plaque extending into the RA should not be considered an absolute contraindication to KT, particularly in the setting of acceptable biopsy findings and pump parameters. Finally, appropriate patient selection is paramount in order to optimally match the functional capacity of the kidney with the estimated demand in the recipient.

Disclosures

No financial support given. All authors report no conflict of interest. Presented at the American Society of Transplant Surgeons 16th Annual State of the Art Winter Symposium and the American Transplant Congress 2016.

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Multi-Specialty Direct Observation Testing for Extended Focused Assessment with Sonography for Trauma

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Abstract

Introduction: Point of care ultrasound (PoCUS) is an essential skill for both emergency medicine and trauma surgeons (TS) in the care of trauma patients in the emergency department. The purpose of this study was to incorporate extended focused assessment with sonography in trauma (E-FAST) training to improve image acquisition and interpretation for both emergency medicine and trauma surgery residents while improving interdepartmental collaboration.

Methods: This study describes a half-day course teaching E-FAST to trauma surgery and emergency medicine resident physicians. The educational material was standardized using core teaching objectives and ultrasound videos. The participants completed five learning stations which included an E-FAST normal station on a patient model followed by an E-FAST pathology station on a peritoneal dialysis model. The course had pre and post direct observation assessment by ultrasound faculty and participants completed web-based testing.

Results: There were statistically significant improvements overall and within each specialty. The mean pre-E-FAST score improved 46% from 7.3 to 15.7 out of a maximum 18 points ($P < .0001$). Individual lung testing improved 62% from 2.0 to 5.7 points and abdominal with cardiac testing improved 39% from 5.3 to 10.0 points ($P < .0001$). There was significant improvement in web-based testing with confidence, image acquisition and interpretation.

Conclusion: Our observational pilot study showed that a half day E-FAST training collaboration significantly improved trauma surgery and emergency medicine resident confidence and ability to acquire and interpret E-FAST images.

Introduction

Point of care ultrasound (PoCUS) is an essential skill for both emergency medicine and trauma surgeons in the care of trauma patients in the emergency department. It is regularly used for patient care in the emergency department for resuscitative, diagnostic, therapeutic and procedural purposes.¹⁻⁷ Since the 1970's physicians have utilized bedside ultrasound to rapidly detect intraperitoneal fluid early in trauma patients.¹ The extended focused assessment with sonography in trauma (E-FAST) is a specific test used to identify significant bleeding. It has been shown to decrease time to diagnosis of hemoperitoneum and help identify those patients that require timely surgery consultation and early laparotomy.¹ The American College of Surgeons utilize the Advanced Trauma Life Support (ATLS) protocol that recommends early utilization of the E-FAST exam.⁸

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An E-FAST exam incorporates lung views to the standard abdominal and cardiac views to identify hemoperitoneum, hemothorax and pneumothorax. These ultrasound views have been supported with research showing PoCUS is superior to chest x-ray for both hemothorax and pneumothorax.¹ This technology allows timely identification and intervention of life threatening diagnoses in the trauma evaluation. The nuances in performing the E-FAST exam with skill and competence takes training and experience.

Currently there is no standard for E-FAST education methods. Today, the majority of emergency physicians receive PoCUS training through an ACGME approved emergency medicine residency while others utilize the practice pathway.⁷ In 2010, a survey among surgery programs in Canada found that the majority of general surgery residents were not trained adequately nor were they comfortable performing the E-FAST exam.³ In 2014, The American Association for the Surgery of Trauma (AAST) recommended Acute Care Surgery fellows complete 25 E-FAST examinations during their curriculum.⁸ E-FAST training experiences include residency training, ultrasound courses, small group hands-on practice, conference attendance, online recorded lectures, and podcasts.

Furthermore, there is variability in educational methods and proficiency assessments from residency programs which may include tracking number of scans, scanning both normal and abnormal patients, direct observation testing, use of cadavers, simulation models and quality assurance to help meet residency standards, specialty guidelines, and hospital requirements.¹ Despite the importance of the team approach to trauma care, the majority of E-FAST training and assessments are done within one's own specialty and not in collaboration with other team members.

The care of the trauma patient is complex and requires multidisciplinary approach from trauma surgery and emergency medicine. This is the first study that we are aware of that involves collaboration between both specialties for E-FAST training.

The purpose of this study was to incorporate E-FAST training with both emergency medicine and trauma surgery residents

with assessments utilizing direct observation on both normal and live pathology models. The goal of this collaboration was to improve E-FAST PoCUS skill set and knowledge in a multidisciplinary learning opportunity.

Methods

This observational study was performed in November 2017 at a level 1 academic trauma center in North Carolina. This study describes a half-day hands-on course that taught E-FAST to 16 trauma and emergency medicine resident physicians. The primary goal of this observational study was to improve the PoCUS skill set of trauma surgery and emergency medicine residents while secondarily improving interdepartmental collaboration. The direct observation assessments were performed by ultrasound trained teaching faculty representing emergency medicine, trauma surgery, and critical care. The faculty had significant PoCUS experience ranging from fellowship training, national and international conference instruction, residency training, and ultrasound directorships.

Prior to the event, the PoCUS leaders from both departments discussed the educational goals of improving resident E-FAST PoCUS skill set along with enhancing interdepartmental collaboration. The educational material was standardized among PoCUS instructors to include standard views, means to improve difficult views, image acquisition, and image interpretation of normal and pathology images. A detailed document with standard teaching points and a PowerPoint file of normal and pathologic ultrasound videos were given to all instructors in advance. The models were live human models that included normal patients without intraperitoneal fluid as well as peritoneal dialysis patients with intraperitoneal fluid.

There were eight PGY II and III residents from the general surgery program and eight PGY I residents representing emergency medicine that completed direct observation testing. We were unable to include the entire class due to clinical obligations and scheduling conflicts. There was one trauma surgery resident unable to complete the planned direct observation testing due to clinical obligations, thus was eliminated from our statistical analysis.

Each resident first completed a pre-test online which included

survey questions for data collection, prior ultrasound experience, confidence with performing ultrasound and images focused on acquisition and interpretation. This pre-test included 14 multiple choice questions with seven focusing on image acquisition such as sensitivity, probe selection, standard views and indeterminate scans. The other seven multiple choice questions focused on image interpretation.

A Direct Observation Testing Scoring Sheet (Table 1) was developed to assess for the obtainment of appropriate views. This scoring sheet provided a range of 0 to 3 points for each core view including right upper quadrant, left upper quadrant, suprapubic, cardiac, right anterior lung, left anterior lung. The maximum points for the lung and abdominal-cardiac portions were 6 and 12 respectively for a total maximum of 18 points.

The PoCUS E-FAST course was arranged into five separate stations, each in a separate room in the ultrasound training center at the hospital. The first station had direct observation testing before any training occurred to establish an educational baseline using a standardized checklist (Direct Observation Testing Scoring Sheet). The second station focused on E-FAST education on a normal patient which reviewed the standard six views utilized. During each view the instructor demonstrated proper probe selection. Hands-on image acquisition on a normal live model and image interpretation was illustrated using normal images and videos in a standard Power-Point. The third station involved performing the E-FAST on a peritoneal dialysis patient illustrating image interpretation of pathology in multiple views. Furthermore, to reinforce pathology, abnormal ultrasound images and videos were shown using standard slides on laptop computers. During the fourth station, the learner underwent post-direct observation testing using the same standardized checklist as in the first station with a five-minute maximum time limit. The direct observation testing was performed by one of the ultrasound faculty.

The fifth station was a web-based post-test and survey sent to all participants after completion of the course to assess knowledge acquisition and course feedback.

Statistical Analysis: Results were summarized using descriptive statistics. Pretest scores were compared to posttest scores using paired t-tests. Software was Statistical Analysis Systems (SAS), Version 9.2, Cary, NC.

IRB Approval: The study was submitted to the institutional review board of Wake Forest School of Medicine and was designated as Exempt as research conducted in established or commonly accepted educational settings, involving normal educational practices, such as research on regular instructional strategies for ultrasound skills training.

Table 1. Direct Observation E-FAST Exam Scoring

View	Points				Comments
Right upper quadrant (diaphragm to inferior pole)	0	1	2	3	
Left upper quadrant (diaphragm to inferior pole)	0	1	2	3	
Bladder view (transverse AND sagittal)	0	1	2	3	
Subxiphoid (4 chambers visualized) *may use any cardiac view	0	1	2	3	
Anterior Lung Right (showing sliding)	0	1	2	3	
Anterior Lung Left (showing sliding)	0	1	2	3	

*Scoring: 0 points if view not obtained, very poor view or incorrect view, 1 point if proper view however axis is off or not all areas visualized, 2 points for complete view but minor areas of improvement, 3 points for perfect view.

Results

Pre- and post-survey data were completed by 15 residents which included eight trauma surgery and seven emergency medicine residents. The trauma surgery residents were in their third and fourth years while the emergency medicine residents were in their first year of training. 33% of participants had no clinical ultrasound training while 67% had significant dedicated ultrasound training prior to participation. A minority of participants had previously performed E-FAST during trauma activations. The pre and post analysis indicated statistically significant improvement in confidence in performing and interpreting E-FAST exams in clinical practice, improving 46% from 1.6 to 3.9 out of

5 and 30% from 2.3 to 3.8 out of 5 respectively (P<.0001). Paired t-test showed significant improvement of 0.7 out of 7 in technical and image acquisition test scores (P<.0001). In addition, a significant improvement of 1.4 points out of 7 was appreciated for image interpretation portions from pre to post multiple choice tests.

training. The standardized approach utilized within this course will allow for replication in future E-FAST training. A limitation however is that as standardization increases there is potential to limit creativity and flexibility within our instructors' approach.

Table 2. Direct Observation of E-FAST Data (P<.001)

Specialty	Number of residents	Pre Abd-Cardiac	Post Abd-Cardiac	Pre-Lung	Post-Lung	Pre-E-FAST	Post-E-FAST
Trauma Surgery	8	3.9	9.4	0.5	5.4	4.4	14.8
Emergency Medicine	8	3.5	6.0	6.8	10.6	10.1	16.6

Utilizing direct observation and knowledge based pre- and post-testing allowed a balanced approach to monitor ultrasound skill and knowledge progression. The course received positive feedback on the utility of the live peritoneal dialysis model to provide realistic abnormal intraperitoneal views.

Discussion

Our E-FAST study showed that a half day collaboration significantly improved E-FAST knowledge acquisition and direct observation skill assessment for both trauma surgery and emergency medicine resident physicians. There were statistically significant improvements overall and within each specialty from pre to post direct observation testing. Furthermore, there was significant improvement within individual lung and abdominal-cardiac components of the E-FAST. The lung and abdominal-cardiac portions were further separated for data analysis to investigate and compare possible differences in resident ability to acquire individual skills. This would provide insight into focusing training efforts if residents had more difficulty obtaining skills in one particular organ compared to another.

Although emergency medicine residents received higher mean post testing scores, trauma surgery residents showed greater mean improvement of 10.4 points compared to emergency medicine at a 6.5 point increase in overall scores. This is likely explained by the longitudinal point of care ultrasound curriculum that emergency medicine residents receive throughout intern year compared to limited exposure for trauma surgery residents.

The teaching protocol provided a standardized approach to assist the ultrasound instructors in providing consistent training while focusing on important aspects of E-FAST

There are a number of limitations to this observational study. The greatest limitation was the small number of participants that completed the direct observation testing which significantly decreases the ability to generalize the results. Furthermore, the direct observation scoring checklist is unique and has not been validated at other institutions or settings. Repeating the direct observation testing is planned at a later date to test knowledge and skill retention in a longitudinal fashion.

Conclusion

This observational E-FAST training collaboration showed significant improvement with both trauma surgery and emergency medicine resident physicians clinical ultrasound image acquisition and interpretation skills. It is imperative that both trauma surgery and emergency medicine specialties gain competence in performing and interpreting the E-FAST examination to improve the care of our trauma patients. Future studies at other institutions with a larger number of participants are required to further validate this pilot protocol.

Disclosures

No financial support given. All authors report no conflict of interest.

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A Personalized Sequential Intervention Reduces the No-Show Rate in an Academic Internal Medicine Clinic

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Abstract

Background: No-shows (patients who fail to keep a scheduled appointment without cancelling it in advance) detract from resident education and patient care in residency clinics. This quality improvement project investigated the effectiveness of a personalized sequential intervention (PSI) on reducing no-show rates at an academic internal medicine residency clinic.

Methods: Residents in the program are divided into clinic teams. We selected two similar-sized clinic teams, and assigned one to receive the intervention and the other to serve as the control. We included all patients scheduled to see these teams over a 10-week period (11/2015-1/2016). Patients in both clinic groups received an automated telephone reminder 48-72 hours pre-appointment, per the clinic's usual practice. Patients in the intervention group also received the PSI, which included a telephone call one week before their appointment. If no personal contact was made, these patients also received a reminder postcard in the mail and a repeat call three days prior to the appointment.

Results: 602 patients were included (255 control, 347 intervention). Those in the intervention group had a significantly lower no-show rate (43% control vs 26% intervention, $p < 0.0001$), increased appointment attendance (42% control vs 52% intervention, $p < 0.02$), and increased appointment cancellation (15% control vs 22% intervention, $p = 0.02$). Non-randomized quality improvement design at a single academic residency clinic with a high baseline no-show rate.

Conclusion: Implementing a PSI protocol could improve clinic efficiency by reducing no-show rates and increasing attendance and cancellation rates in other similar clinics.

Introduction

Patients who fail to keep a scheduled appointment without canceling it in advance ("no-shows") can account for up to half of scheduled outpatient appointments, significantly decreasing clinical revenue and hampering effective patient care. Not only do no-shows fail to receive care, they preclude others from receiving care by occupying a scheduled slot.¹

No-show rates are frequently higher in academic medical centers. No-shows are more likely to be patients who are younger, and of lower socioeconomic status, and less likely to have a significant ongoing relationship with a single physician.² Most medical center clinics staffed by residents serve patients of lower socioeconomic status who lack an ongoing relationship with a single physician, since residents are transitory. In such clinics,

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high no-show rates detract from education by decreasing the volume of patients seen by medical students and residents.

The most commonly cited reasons for no-shows are forgetfulness and miscommunication.³ Multiple interventions to reduce no-show rates have been explored.⁴⁻⁸ Short messaging systems (SMS) – “text messages to mobile phones,” telephone call reminders, and postal reminders can improve clinic attendance rates and chronic disease management.^{4,5} A 2013 Cochrane review found show rates in an ambulatory care clinic of 67.8% for no reminders, 78.6% for SMS, and 80.3% for phone call reminders.⁶ Automated and in-person telephone call reminder systems demonstrate variable efficacy.⁷ In one study, an in-person telephone call reminder system reduced the no-show rate by 39% versus a reduction of 29% with an automated telephone reminder system.⁷ A sequential hybrid approach incorporating SMS and telephone calls was evaluated in Sweden, where a 48-hour pre-appointment telephone call was made, and if the patient was not contacted, an SMS or letter reminder was sent. In this study, the control group had a no-show rate of 11.4%, whereas the sequential intervention group had a no-show rate of 7.8% ($p < 0.01$).

The literature supports the efficacy of in-person telephone call reminders compared to automated ones, and sequential intervention models tend to reduce no-show rates and increase the utilization of cancelled appointments.^{4,7,8} One study used telephone call reminders 2 days before appointments, which limited the ability to rebook appointments with other patients.⁸ In general, whether such strategies will be effective in residency clinics, in which patients typically have higher no-show rates and greater barriers to care, is unknown.

Methods

QI Methodology

Our project utilized the EPIS (Exploration, Preparation, Implementation, and Sustainment) quality improvement framework.⁹ In the Exploration Phase, the no-show problem was identified by the primary author’s observation of a relatively high no-show rate in his internal medicine residency clinic. Based on the literature,⁴⁻⁸ he designed a personalized sequential intervention (PSI) with the goal of studying the PSI’s effect in an academic general internal medicine clinic with a high no-show rate. The key stakeholders identified included the internal medicine resident teams, the clinic medical director,

and clinic appointment schedulers. In the Preparation Phase, the primary author met with the key stakeholders and discussed the project’s methods and goals and obtained permission to carry out the initiative. The details of the Implementation Phase can be seen below. The Sustainment Phase was beyond the scope of this project, as it requires institutional support for implementation on a broader scale.

Setting

This project was conducted in an internal medicine residency continuity clinic at Wake Forest Baptist Health. The clinic includes 39 residents who serve as primary care providers under the supervision of general internal medicine faculty. The residents are divided into clinical teams of seven to eight residents per team. In fiscal year 2016, the clinic had 5,743 office visits. Most patients had health insurance (38% Medicare, 22% Medicaid, 19% other) and 21% were uninsured.

Study Sample and Study Period

The primary author implemented the PSI for patients scheduled to see his resident team. As a control group, another resident team was chosen with an equal number of PGY-1, PGY-2, and PGY-3 residents. Each team had three PGY-1 residents, three PGY-2 residents, and two PGY-3 residents. PGY-1 residents are scheduled for an afternoon of clinic each week on the same day of the week. PGY-2 and PGY-3 residents have a full week of clinic, on average once every four weeks. We included all patients who were scheduled at least one week in advance to be seen by these two teams over a consecutive 10-week period from November 2015 through January 2016.

Intervention

The schema of the intervention is shown in Figure 1. In the PSI group, patients received an in-person telephone call reminder one week prior to the appointment. If there was no response at the patient’s primary telephone number, then the patient’s secondary contact number was called. If the patient could be reached by phone and confirmed the appointment, no further action was taken. However, if no in-person contact was made, a reminder letter was mailed and a second in-person telephone call reminder was made three days prior to the scheduled appointment. This reminder letter was in a template format and was routed to administrative assistants to send to the patient, which was a cost incurred by the medical center. For each call where the patient was not reached, a reminder voicemail was left if possible.

The in-person telephone reminder calls were made by the first author who introduced himself by name but did not indicate he was a physician (unless he was calling his own patients). The primary author volunteered his time over the course of a 10-week time period while simultaneously working as a second-year internal medicine resident. The in-person telephone call reminder was structured and consisted of an introduction, an inquiry if the patient knew of scheduled appointment, and then assessment of the patient's plans to attend.

As is usual in this clinic, all patients in the study received an automated telephone reminder 48-72 hours prior to their scheduled appointment. Those in the control group received no other interventions or reminders.

Outcome Measures

The primary outcome of interest was failing to attend or cancel an appointment in advance (no-show). Secondary outcomes included appointment cancellation lead time (defined as number of days in advance cancellations occurred), and whether a cancelled appointment slot could be rescheduled with another patient.

Statistical Analysis

We conducted bivariate analyses for our outcomes of interest using chi-square tests for proportions. We then constructed a multivariable logistic regression model where the outcome of failing to attend or cancel an appointment in advance was the dependent variable. Covariates included patient demographic factors and clinic schedule factors. Patient demographics were patient age (by quartiles), gender, insurance status (uninsured vs. some type of insurance), and prior clinic history (new patient, seen previously in urgent care only, or established patient). Clinic schedule factors included day of appointment, time of appointment (morning vs. afternoon), and training year of the resident physician to be seen. To account for clustering by physician, the SAS GLIMMIX procedure was used. All analyses were done using SAS version 9.3 (Cary, North Carolina) with an alpha of 0.05.

Results

Baseline characteristics of the intervention and control group scheduled appointments were similar, except for the day of the week and resident training level (Table 1). 610 patients were scheduled at least one week in advance to their appointment. We excluded eight patient appointments from the study due to clinic closure for inclement weather, leaving 602 eligible patient appointments (347 intervention, 255 control) in the analyses.

The PSI group had a significantly lower no-show rate (43% control vs. 26% intervention, $p < 0.01$), and a 10% higher rate of appointment attendance (42% control vs. 52% intervention, $p < 0.02$). The intervention group had a 7% increase in the number of cancelled or rescheduled appointments (15% control vs. 22% intervention, $p = 0.02$).

When appointments were cancelled, intervention group patients were more likely to do so at least 2 days in advance (60% vs. 29%, $p < 0.01$). Appointments cancelled at least 2 days in advance had an 81% chance of being rebooked compared to 34% for appointments cancelled with less than 2 days' notice ($p < 0.01$).

After adjusting for patient and appointment factors, patients who received the PSI were less than half as likely to be a no-show for a clinic appointment (odds ratio [OR] 0.44, 95% confidence intervals [CI] 0.27 – 0.70). Those who were

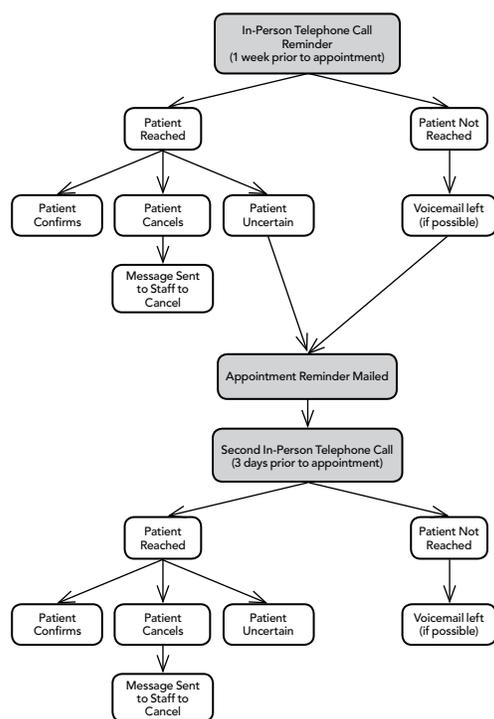


Figure 1. Schema of the Personalized Sequential Intervention

older and had health insurance were also less likely to be a no-show (Table 2).

In a post-hoc analysis of the intervention group only, we found that the inability to speak with a patient significantly increased the likelihood of being a no-show (OR 4.1, 95% CI: 2.4-7.1). Two subgroups of patients had a very high likelihood of no-showing. Those with whom no contact was made and no message could be left had an 81% chance of being a no-show (95% CI 66% - 96%). Furthermore, new patients who could not be reached by phone had a 73% chance of being a no-show (95% CI 56% - 90%).

Table 1. Baseline Characteristics of Patients and Types of Appointments (n=602)

		Intervention % (n)	Control % (n)	P-value*
Gender				
	Male	47% (164)	44% (113)	0.47
	Female	53% (183)	56% (142)	
Insurance status				
	Insured	70% (244)	71% (180)	0.94
	No insurance	30% (103)	29% (75)	
Day of the week				
	Monday	7.8% (27)	15% (38)	<0.01
	Tuesday	21% (74)	29% (73)	
	Wednesday	26% (89)	13% (33)	
	Thursday	19% (66)	18% (45)	
	Friday	26% (91)	26% (66)	
Appointment time				
	Morning	49% (171)	45% (115)	0.29
	Afternoon	51% (175)	55% (140)	
Clinic history				
	New Patient	25% (88)	25% (63)	0.98
	Urgent Care Only	4.3% (15)	4% (11)	
	Established	70% (244)	71% (181)	
Resident PGY				
	PGY-1	17% (60)	27% (68)	<0.01
	PGY-2	55% (191)	39% (99)	
	PGY-3	28% (96)	35% (88)	
Age quartile				
	Q1 > 59	26% (89)	21% (53)	0.25
	Q2: 52-59	27% (94)	25% (63)	
	Q3: 42-52	22% (78)	29% (73)	
	Q4: < 42	25% (86)	26% (66)	

*chi-square test

Discussion

The personalized sequential intervention effectively reduced the no-show rate by 17% in our academic residency clinic. Our clinic was already using an automated appointment reminder system. In-person telephone calls, while more labor intensive, were found to be superior to automated calls in other studies.¹⁰ In an academic outpatient practice, no-show rates were 13.6% and 17.3% when calls were made by staff members versus an automated system respectively.¹⁰ Of note, the reduction in no-shows we observed was considerably greater.

Longer lead times for cancellations and a higher rate of cancelled appointment utilization occurred in the intervention group in our study. Two subgroups of patients had a low likelihood of attendance - those with whom no contact was made and no message could be left, and new patients who could not be reached by phone (attendance rates of 8% and 12% respectively). While a regular double-booking strategy may not be the best approach for all appointments, due to the low likelihood of clinic attendance by patients in these two subgroups, double booking these appointment slots utilizes a clinic appointment which would often result in a no-show.

Our study has limitations. First, it was performed at a single academic outpatient internal medicine clinic with a relatively high baseline no-show rate (over 40%), which limits its generalizability. However, other academic primary-care settings may have similar no-show rates. Second, while the in-person telephone calls in our study were made by a physician, he identified himself as a physician in only a small subset of patients (his personal patients). A sensitivity analysis excluding these patients showed similar results. In a prior study in a psychiatric resident clinic, when in-person telephone call reminders from resident physicians versus technicians were compared, clinic attendance did not differ based on who made the reminder

Table 2. Appointment and Patient Factors and Likelihood of No-showing Appointments (n=602)

	Odds Ratio (95% CI)	p-value
Appointment Factors		
Sending intervention reminders (ref = control group)	0.44 (0.27 – 0.70)	<0.001
Day of appointment (ref = Friday)		0.77
Monday	0.92 (0.46 – 1.9)	
Tuesday	0.96 (0.54 – 1.7)	
Wednesday	0.83 (0.45 – 1.6)	
Thursday	0.67 (0.36 – 1.3)	
Afternoon appointment (ref = morning)	1.3 (0.84 – 2.0)	0.23
Training level of resident physician (ref = PGY-3)		0.85
PGY-1	0.81 (0.39 – 1.7)	
PGY-2	0.93 (0.53 – 1.6)	
Patient Factors		
Female gender (ref = male)	0.96 (0.66 – 1.4)	0.82
Health insurance (ref = uninsured)	0.55 (0.36 – 0.82)	<0.01
Patient's prior history with clinic (ref = regular patient)		0.30
Seen previously in acute care clinic only	1.1 (0.45 – 2.7)	
No prior visits	1.4 (0.91 – 2.2)	
Age (ref = < 42 years)		<0.001
42 – 51 years	0.63 (0.38 – 1.0)	
52 – 59 years	0.48 (0.29 – 0.80)	
> 59 years	0.30 (0.17 – 0.54)	

call.¹¹ These findings suggest that a personalized sequential intervention (with in-person telephone calls) made by non-physicians might be effective in reducing no-show rates; this strategy merits further study. Furthermore, this project did not investigate other potentially modifiable specific barriers to clinic appointment attendance such as cognitive impairment, physical frailty, transportation dependency, or literacy.

Based on our study's results, potential next steps could be to implement this PSI on a clinic-wide scale. We also could test whether double-booking appointments for those most likely not to attend is worthwhile. Furthermore, a cost-effectiveness analysis would determine financial feasibility and sustainability.

Conclusion

A personalized sequential intervention incorporating in-person telephone calls and postal reminders effectively decreased the no-show rate in an outpatient academic internal medicine

residency clinic by 17% compared to automated telephone call reminders alone. Implementing a double-booking strategy for patients who fall into a high-risk subgroup for clinic non-attendance may exert a compounding effect in realizing clinic efficiency, improve management of chronic conditions among patients, and optimize resident education.

Disclosures

No financial support given. All authors report no conflict of interest.

Prior Presentations: Wake Forest Annual Quality Improvement Showcase, Winston-Salem, North Carolina, May 2016; Internal Medicine Research Day, Winston-Salem, North Carolina, May 2016; Academic Internal Medicine Week, Baltimore, Maryland, March 2

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Feasibility and Acceptability of Group Exercise for Homeless Men who Use Cocaine

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Abstract

Objective: While exercise has demonstrated efficacy in reducing alcohol abuse, cigarette, cocaine, and marijuana use, the feasibility and acceptability of its use with homeless individuals who use cocaine is unknown. In the present study, we examined the feasibility and acceptability of recruiting men experiencing homelessness who reported cocaine use and piloted the use of an 18-session group fitness intervention. The study focused on the following aims: 1) to assess the feasibility and acceptability of our approach to recruiting homeless men; 2) to assess the feasibility and acceptability of our proposed physical assessment and other outcome measurements; and 3) to examine adherence and retention rates for the intervention, including issues of safety and perceptions about the study intervention.

Results: We enrolled seven participants in the study, five of whom were medically cleared to participate in the intervention. We found challenges to recruitment and difficulties with retention. Based on participant feedback, however, the study procedures and the intervention appeared to be well-received, and there were no safety issues.

Conclusions: Findings suggest that modifications can be made to the protocol to enhance our ability to successfully recruit and retain participants in future research, including revising our recruitment strategy, possibly changing the location to increase the population of eligible participants, and increasing the compensation paid to participants.

Introduction

In 2015, 20.8 million people in the U.S. had a substance abuse disorder within the past year; 900,000 of which were cocaine use disorders.¹ Substance abuse and addiction in the homeless population is higher than in the general population, and therefore takes a greater toll on that population.² Approximately one in five homeless individuals has a chronic substance use disorder, and drug overdose is a rising cause of death among the homeless.^{3,4} Cocaine is the second most commonly used illicit drug, after cannabis, and use of cocaine is especially problematic in the homeless population, with high rates of use and poor treatment outcomes.^{1,2}

Pharmacologic treatments exist for addiction to some substances, but not cocaine.^{5,6} Current non-pharmacologic treatments include cognitive behavioral therapy (CBT), therapeutic communities, and 12-Step facilitation programs, with some evidence for the use of alternative treatments such as yoga and acupuncture.⁷⁻¹² There

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continues to be a need for effective methods of intervention that can be used to enhance the effects of treatment or can help those not in treatment. Exercise is a relatively inexpensive intervention without the potential side effects of pharmacologic treatments and with possible secondary health benefits. Surprisingly, many homeless individuals are overweight or obese and almost half do not meet physical activity recommended guidelines.¹³

Both exercise and drugs have similar effects on the brain.¹⁴ Reward regions of the brain are activated by addictive drugs, which cause increases in the release of dopamine, triggering further craving for the drug. Exercise can also increase the brain's concentration of dopamine and can influence many of the brain's molecules and structures that mediate the positive reinforcing effects of drugs.^{15,16,17}

Promising preclinical animal research regarding exercise and cocaine use has been conducted with rats. Using models of cocaine self-administration, investigators have been able to mimic the stages of drug use through which humans typically progress: acquisition, maintenance of regular use, escalation of use, binges, and relapse/reinstatement after cessation of use.¹⁷ Positive effects of exercise on cocaine self-administration were found for each of the stages, suggesting that exercise could have beneficial effects on humans in these stages as well.¹⁸⁻²²

Despite the promise exercise seems to hold for treatment of addiction in humans, there is a paucity of human research into this topic. A 2012 review by Zschucke et al found eight studies that examined the therapeutic effects of exercise in drug-dependent individuals.²³ A 2015 review by Linke and Ussher failed to identify any new studies of exercise and illicit drug use since the Zschucke et al. 2012 review.²⁴ The work of De La Garza and colleagues (2016) stands alone as the only investigation of the effects of exercise specifically on cocaine use in humans, though they focused on concurrent cocaine and tobacco use.²⁵ There are currently no studies of group exercise as treatment for cocaine addiction in the homeless population, but this type of intervention may be a desirable option for these individuals. Research on the exercise preferences of patients in substance abuse treatment indicated that the majority of those surveyed expressed an interest in exercise, particularly during substance abuse

treatment or early (first three months) into sobriety with a preference for moderate to high intensity intervention.¹ In addition, exercise research with individuals with other health conditions has demonstrated the social benefits of exercising with others that may be of particular benefit to persons who are homeless and may lack support.^{27,28}

Research on the use of exercise among persons with cocaine use is complicated given the associated medical risks. Cocaine is a known cardiotoxin; use may increase risk of thrombosis in the setting of physical exertion and chronic use is associated with higher systolic blood pressures during exercise compared to age and race-matched control participants.^{29,30} Cocaine-induced vasospasms and tissue hypoxia is thought to be associated with increased risk of myocardial ischemia up to two weeks after last use.³¹ Although these findings may suggest a biologic plausibility to increased risk of exercise in the setting of recent or chronic cocaine use, available literature suggests more benefit of exercise than harm in the setting of substance use disorder.³² In fact, others have found that individuals with substance use disorders are able to handle high intensity exercise despite low aerobic power.³³

The purpose of this pilot study was to determine the feasibility and acceptability of a standardized six-week exercise intervention for homeless men who report use of cocaine. Cocaine use continues to be a drug of choice for many homeless adults who tend to be difficult to engage in treatment and have trouble maintaining abstinence.³⁴⁻³⁷ Considering the majority of drug abusers do not seek treatment and that homelessness represents one of the most severe environmental consequences of drug abuse, examining the effects of exercise as an intervention in non-treatment-seeking, homeless individuals, has enormous significance. As a precursor to an outcome study, this study focused on piloting our protocol and survey instruments as well as examining the success of our recruitment strategies to identify any practical challenges associated with the project.³⁸ Others have focused on the feasibility of interventions targeting substance-using populations.³⁹

Methods

Overview: This pilot study focused on the feasibility and acceptability of group exercise for men with self-reported histories of cocaine use who were currently homeless. We

attempted to recruit and enroll participants, evaluate them for medical clearance to participate in a high intensity group exercise class, engage them in an 18-session group exercise class, and follow them over time with periodic assessments including urine drug testing. The specific aims were as follows: 1) to assess the feasibility and acceptability of our approach to recruiting homeless men; 2) to assess the feasibility and acceptability of our proposed physical assessment and other outcome measurements; and 3) to examine adherence and retention rates for the intervention, including issues of safety and perceptions about the study intervention. The university's Institutional Review Board approved all procedures.

Recruitment: Study participants were recruited from a homeless shelter for men in a mid-sized Southeastern city via flyers posted at the shelter where the study was conducted, word of mouth, and announcements at shelter meetings. Interested participants spoke with the study coordinator and were provided with information about the study. Those who were interested in possible participation were scheduled for a study screening visit, and, if eligible, provided written informed consent. Next, they were scheduled for a physical exam and fitness testing to determine if they were eligible to continue with the exercise sessions, which were held less than two weeks later to minimize attrition.

Inclusion and Exclusion Criteria: Initial inclusion criteria were as follows: 1) male; 2) age 18-64 years; 3) self-reported cocaine use within the past 30 days; 4) currently homeless and living at the shelter; 5) willing to participate in a six-week exercise intervention to be held at that shelter and 6) willing to participate in a physical exam and behavioral and physical assessments. Difficulties with initial recruiting led to expansion of the inclusion criteria to use of cocaine within the past year rather than 30 days, and to homeless individuals living at any shelter in the county rather than the specific shelter where the intervention took place. Recruitment was limited to males for this pilot study because the shelter location where the intervention was conducted only provided residential services to males. In addition, investigators wanted to know whether this type of intervention could augment existing services, which precluded women from participating.

Exclusion criteria included: 1) having a legal guardian; 2) regular exercise (≥ 30 minutes three times per week); 3)

a physical impairment or condition that would preclude exercise; or 4) having been told by a physician within the past year that he should not exercise, or answering "Yes" to the question "Have you been told that you had a heart attack or stroke, or have you had eye, chest or abdominal surgery within the past three months?" We also excluded those impaired by any substance or actively psychotic at the time of the screening, or who had any cognitive impairment that would preclude giving informed consent. This determination was made based on direct observation by the study team member obtaining informed consent with one of the study investigators (a licensed mental health professional) available for consultation.

Assessments

Physical Assessments: The initial physical assessment included a brief physical exam by a physician and a graded exercise "stress" test (GXT) on a motor-driven treadmill, as well as a 6 Minute Walk (6MW) test and anthropometric measurements. The purpose of the GXT and physical exam was to screen for any cardiovascular abnormalities and to ensure that individuals were determined by a physician to be safe to participate in a vigorous-intensity exercise intervention. The 6MW for assessing submaximal exercise capacity was administered on the same 120-meter indoor track at baseline and six-week follow-up testing. Participants were instructed to walk at their own pace while trying to cover as much ground as possible in six minutes. Anthropometric measurements were taken at both baseline and six-week follow-up, including body weight and percent body fat using a calibrated scale, skinfold calipers and standard three-site skinfold techniques for men.

Urine Drug Testing: At both baseline and six-week follow-up, the iCup Drug Screening Device (Redwood Toxicology Laboratory) urine drug screening (UDS) process was used to test for the presence of cocaine and other drugs of abuse. In addition, twice per week UDSs were administered to test for presence of cocaine and other drugs prior to exercise.

Behavioral Assessments: In addition to basic demographic and background data, we piloted several assessments relevant to use in larger trials. To assess substance use severity, we used the Addiction Severity Index, and to assess the frequency of crack cocaine use and other substances (alcohol and

other drugs); we used the Timeline Follow Back (TLFB), a calendar-based method of obtaining retrospective reports of behaviors.^{40,41} Given that one of the intended secondary impacts of the intervention was to increase social support, we used the Multidimensional Scale of Perceived Social Support (MSPSS) a 12-item measure with three subscales that uses a seven point Likert scale.⁴² Lastly, to assess severity of psychiatric symptoms, we used the Modified Colorado Symptom Index, a 14-item measure that was developed for use in treatment outcome studies and has well-established psychometric properties for use with homeless adults.⁴³ We used this scoring system which produces scores from zero to 56.⁴³

Intervention

The intervention for this study was a group exercise intervention that was implemented three times per week over six weeks at a homeless shelter for men. Each session was a one-hour standardized, choreographed Body Attack or Body Combat class developed by the LesMills fitness corporation and led by two certified instructors at each class (six instructors total).⁴⁴ The routines included a five-minute warm-up and a five-minute cool-down. The sessions took place in a common area of the shelter approximately 1.5 hours before the shelter was open to other guests to allow for privacy. In addition, participation in the study allowed participants to enter the shelter earlier than the other current residents, which we believed was a possible incentive to participation. Prior to the start of each exercise session and again at the end of each session, participants' resting heart rate and blood pressure were measured and recorded. One or more study team member was present during all exercise sessions and each participant's attendance and total minutes exercised (out of 60) per session was recorded (based on direct observation of the sessions). To address the safety of the participants, a physician was on-call during all of the exercise sessions, and the study staff were trained to use an AED device if needed.

Compensation: We provided each participant with exercise attire to use during the exercise sessions, and participants were allowed to keep the clothing at the end of the study. In addition, each participant was given a pair of athletic shoes to wear for the exercise sessions. These shoes were

kept in the study office during the study period, but upon completion of study, participants were allowed to keep them. Incentives were given for completion of the study assessments, but participants were not compensated for participating in the exercise sessions. They were eligible to receive \$15 for the first assessment that included the fitness testing and \$20 for each of the other three assessments for a total of up to \$75. Compensation was in the form of a gift card to a local merchant.

Results

Description of the Sample: Five of the seven individuals enrolled cleared the medical screening to participate in the intervention. A description of the sample is presented in Table 1. While the study was open to any male, all participants were African-American. The mean age was equivalent to a high school diploma (12 years of education), however, three participants had attended some college. Three were divorced, and two had never been married. While none of the participants intentionally exercised ≥ 30 minutes three times per week (study exclusion criteria), all reported using walking as their main method of transportation. At intake, three reported that they had used cocaine within the past 30 days, and two reported cocaine use within the past year but

Table 1. Description of the Sample

Variable	Mean (SD)
Age	53.4 (3.2)
Years of Education	12.2 (0.9)
Body Mass Index	34.0 (2.2)
Multidimensional Scale of Perceived Social Support	
Significant Other Subscale	17.75 (1.67)
Family Subscale	16.25 (1.74)
Friends Subscale	20.75 (1.50)
Total Scale	18.25 (1.66)
Modified Colorado Symptom Index	13.40 (14.98)

not the past 30 days. Number of times homeless including the present time ranged from one to eight, with two participants homeless for the first time. Four participants self-reported a diagnosis of a mental health disorder. Initial urine drug screens indicated the presence of cocaine only for two participants; both cocaine and marijuana for one participant; and both cocaine and methamphetamine for one. One participant had a negative drug screen at baseline.

Aim 1: To assess the feasibility and acceptability of our approach to recruiting homeless men. For this phase of the study, we examined rates of recruitment as well as reasons participants declined consideration and/or participation. Twenty-five subjects had some type of screening through informal conversations (N=11) or formal screening with a study interviewer (N=14). Those who informally spoke with a study interviewer to get more information about the study but did not want to proceed with an official screening to assess eligibility verbally indicated the reasons for not wanting to pursue participation. The most common reason was not being interested in the study and/or not wanting to exercise (N=5) or not being able to exercise for health reasons (N=3). Others uniquely reported that they were either working, moving, or did not meet the cocaine use criteria.

For those who completed a formal study screening, the most common reason for not participating was not meeting the inclusion criteria of staying at the shelter (N=3). One person was over the age limit and another had a recent medical issue. Two declined to participate: 1) one person did not want to exercise and did not want to go to the facility where the fitness testing was taking place; and 2) one did not want to commit the time.

After some difficulties, we revised the study criteria to allow less recent cocaine use (past year) and allow people who were homeless but not staying at the shelter where the study was conducted to participate. This change allowed three people who were originally not eligible and who could be located to enroll. Seven people met the study criteria and enrolled in the study. Thus of the 25 individuals who had some level of contact with a study interviewer, seven enrolled, and five were cleared to participate in the study intervention.

Aim 2: To assess the feasibility and acceptability of our proposed physical assessment and other outcome measurements. For this

phase of the study, we piloted all of the proposed assessments and procedures. Participants were asked to get up early to be transported to the exercise lab for the baseline assessments. All seven who were screened were ready when scheduled early in the morning (before 7:00am). No participants raised any concerns about this process or about any assessments, including urine drug testing.

Aim 3: To examine adherence and retention rates for the intervention, including issues of safety and perceptions about the study intervention. We examined the rates of medical clearance for those who enrolled in the study and rates of participant retention over the study period. In addition, to further understand possible factors influencing adherence and retention, we examined the acceptability of the intervention based on participant feedback as well as safety issues.

Medical Screening: Of the seven participants who consented to participation, two did not pass the fitness test due to abnormal graded exercise “stress” test results, and thus were not eligible to proceed to the intervention phase of the study. These individuals were given information about referrals for follow-up care in the community.

Participation and Retention: Thus, five participants were eligible to exercise after medical clearance by a study physician. One of the 18 study sessions was cancelled because none of the participants were able to participate that day. Of 17 exercise sessions offered, the mean number attended was five (SD=5.73). Based on total number of sessions, attendance rate was 29.41% with one participant attending all but one session. During the intervention phase, one participant moved after the fitness testing, one attended four sessions and then moved out of the area, and one obtained housing and did not have transportation to come back for the sessions. In terms of the study assessments, two of the five participants completed the nine-week follow-up assessments and the Exit Interview survey (conducted three weeks after the exercise sessions ended). The overall results of the Exit Interview survey indicate very good acceptability of treatment. One participant gave the study location a low score, indicating that he would prefer to go to the YMCA or a location where others would not see him exercising who were not themselves exercising.

The mean number of minutes exercised per session was 49.28. Based on the total number of minutes of exercise performed

per session out of 60 possible minutes exercised per session, participants who attended a session exercised for 82.13% of possible minutes during the entire intervention.

Perceptions of the Intervention: Two participants completed the follow-up assessments, including the Exit Interview Survey. Where 1 is “Poor” and 10 is “Excellent,” one participant rated the overall exercise experience as an 8 and the other rated it as a 10, for a mean of 9. Where 1 is “Very Unlikely” and 10 is “Very Likely”, the answer for both participants to the question “How likely is it that you will continue to exercise?” was 10. One participant indicated that he noticed a decreased interest in using cocaine when exercising and the day after exercising. The other participant answered that the questions regarding those things were “Not Applicable.” Similarly, in other research on substance use and exercise, participants reported no disadvantages to participating in a 10-week group exercise intervention.¹⁶

In answer to the question, “What did you like best about the study?” one participant answered that he liked getting to know and talk to people, specifically the instructors. In terms of things liked least about the study, one participant indicated that there was nothing that he did not like, and another recommended changing the location. This finding is consistent with previous research that has documented that among persons with substance use who are engaging in exercise, there was a preference for group vs. individual exercise and encouragement from coaches (instructors) to attend.¹⁶

Safety: Another important issue that we were able to examine through this study was whether there were any significant safety issues. Individuals who were deemed by the study physicians to be at-risk for intense exercise were excluded from participation, in order to decrease the risk of any adverse medical event during the exercise portion of the study. Fortunately, no medical issues were observed or reported during or after the vigorous exercise intervention sessions. Prior to each session, heart rate and blood pressure screenings led to no participants excluded from participation.

Discussion

While we anticipated multiple challenges in this feasibility and acceptability study, we were able to learn important lessons and identify some simple changes to our protocol to

enhance our success in future studies. Two main areas for modification to the study protocol were identified: changing the location of the study and revising the recruitment and retention strategies, including compensation.

With regard to location, one of the challenges to conducting a study of this type in a medium sized city is identifying enough eligible participants. The city where this study was conducted had decreasing numbers of homeless adults, particularly chronically homeless adults who are likely to be struggling with substance abuse. The time-period when the study was implemented was at the end of the community’s Ten Year Plan to End Chronic Homelessness, which positively affected the number of homeless men accessing shelters. Future studies with this population may need to be conducted in larger urban areas or areas where there are larger number of homeless adults. Having access to a larger potential participant pool would also allow for the recruitment of more recent cocaine users. We had to change our study criteria to include a larger time frame for use which could present problems in a clinical trial if the focus was on reducing cocaine use as the primary outcome of interest.

This study involved a unique population and recruitment was found to be more challenging than expected, with fewer individuals screened than anticipated. Since we believed there was a significant proportion of the homeless population using illicit drugs, it was not anticipated that we would have difficulties getting participants to enroll. Interestingly, many of those who initially expressed an interest in participating stated that they were not interested in participating in an exercise intervention. One reason may be our initial inclusion criterion of cocaine use in the past 30-days. It is possible that participants did not want anyone to know that they had recently used substances for fear that this might be viewed negatively by others, such as the shelter staff. We subsequently changed the inclusion criterion to “within the past year,” but our initial recruitment strategy may have negatively impacted future involvement. Given that our focus was on recruiting males, a second possible reason for low enrollment was the description of “group fitness” was not a desirable type of intervention. In our future work, we plan to re-label the intervention to see if this makes a difference.

The fact that 24% of individuals screened were excluded due

to health issues indicates that investigators must contend with the fact that health issues are likely to be seen in this population. We had a higher rate of medical screen failures than reported in other recent research on the use of exercise with methamphetamine users, stimulant use and individuals on methadone.^{45,46,47} Therefore, in future studies, it will be important to screen a larger number of individuals for participation to allow for the fact that some individuals will not be cleared to exercise.

It appears that the transient nature of this population affected our retention rate. Those who left the shelter were difficult to keep engaged in the study. Perhaps offering transportation to exercise sessions might address this challenge. Burling et al. (1992) was the only study to use exercise as substance abuse treatment in homeless participants and had a much higher retention rate (67.60%).⁴⁸ However, all participants in that study were at an inpatient residential treatment center for homelessness and substance abuse, whereas participants in the current study were not in such a program. To increase retention in future studies, one approach is to use short message service (SMS) reminders and motivational messages, which have been found to be promising tools to engage vulnerable populations in exercise.¹⁶

Our session attendance rates were lower than anticipated, and these results compare to a 44% attendance rate for all sessions from a study of individuals in residential substance abuse treatment.¹⁶ Nonetheless, the low attendance rate and mean session attendance as measures of acceptability of treatment are deceiving because the calculations included the three drop-outs: one attended no exercise sessions, another attended one session, and a third attended four sessions. On the other hand, one participant's attendance rate was 94%. One option for future studies is to provide transportation to participants who leave the shelter. Moving the exercise intervention off-site from the homeless shelter would likely worsen retention due to transportation issues and would also negate our attempt to integrate exercise as treatment for cocaine use into existing homeless shelter programs.

Another area where we learned an important lesson in this study was compensation. In this study, participants were able to earn a fairly minimal amount of compensation compared to similar types of studies. In De La Garza et al's exercise

study (2016), participants were able to earn up to \$700 in compensation for fewer sessions, and others have paid higher levels of compensation as well as incentives for exercising.⁴⁹ One recent study reduced the amount of compensation that could be earned for missed sessions.⁵⁰ A concern about compensation as it relates to reproducibility is that most homeless shelters operate on tight budgets that may not allow for compensating participants outside of research settings. In terms of a positive finding, providing exercise attire and athletic shoes seemed to be an acceptable strategy.

In addition to the positive feedback received about the intervention itself, another major strength of this study is the use of a manualized fitness regimen, LesMills, which requires no special equipment and allows for replication anywhere in the world. Others can easily replicate our intervention procedures if future studies find that these classes are of benefit to homeless individuals struggling with cocaine abuse for this population. Lastly, this is a low cost intervention to replicate which is important given the limited funds available for homeless services in most communities.

In conclusion, this paper presents the results of the first known study of group exercise with homeless men. This study was not designed to assess for changes in substance use, but was focused on whether doing a larger study with the current protocol is warranted or whether additional changes to the protocol need to be made. As with any new research area, important lessons can be learned from studies that assess whether new interventions are both feasible and acceptable. While the sample size for this pilot study was small, the lessons learned from this research suggest modifications that can be made to these methods to replicate this study in a larger scale trial.

Acknowledgements

The authors thank Brianne Ferguson for her work on this project; Fleet Feet of Winston-Salem, NC, for the athletic shoe donations; and Drs. Heath Thornton, Andrew Wood, and Suzanne Lichtenstein who conducted the medical screening of participants.

Disclosures

This research was supported by the Maya Angelou Center for Health Equity at Wake Forest School of Medicine.

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Increasing Patient Technology Utilization in North Carolina Otolaryngology Clinics

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Abstract

Purpose: (1) To quantitatively characterize current otolaryngology patients' engagement with technology. (2) To quantitatively determine when, how, and which type of patients use online medical information to try to self-educate about their symptomatology. (3) To explore how healthcare professionals can use technology in ways to improve healthcare communication and patient education.

Materials and Methods: This cross-sectional study was conducted from July 2014 to January 2015 in outpatient adult and pediatric otolaryngology clinics of all subspecialties at a tertiary care hospital. The survey queried respondents on demographics, mobile phone ownership, internet utilization in their healthcare, and perspectives on electronic health records (EHR). Outcomes' frequencies were calculated and comparisons by demographics and subspecialties were performed. Fisher's Exact Test was used to analyze strength of statistical correlations.

Results: A total of 194 respondents (86 male) participated in the study. Over half (51%) of respondents searched for health information related to their primary concern prior to their clinic visit. Over three quarters of respondents (76%) owned smartphones. In general, respondents who were female, were younger, had higher incomes, and had higher levels of education had statistically greater healthcare-related technology use ($P < .05$). In general, family members of pediatric respondents had higher technology usage versus other subspecialties; conversely, otology respondents demonstrated lower utilization.

Conclusion: Internet and technology use is prevalent and continues to increase in the otolaryngology patient population. Physicians must continue to improve the quality and accuracy of online medical information. Healthcare professionals can make use of increased patient connectivity to improve healthcare outcomes.

Introduction

Patients now have unprecedented access to online health and healthcare information. Four-fifths of all United States households reported having internet access at home or through smartphones in 2015¹. Greater than two-thirds (68%) of American adults owned smartphones in the same year. It is now normal for patients to have searched on the internet for diseases and treatments prior to engaging a physician in their care. In fact, more than two-thirds of American adults (72%) looked online for health information in 2012, and more than one-third of American adults (35%) used online information to attempt to diagnose a medical condition.²

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With the advent of increased connectivity, patients can now electronically participate in their own healthcare through use of secure patient portals or personal health records (PHR). As 75% of US hospitals use at least a basic electronic health record system (EHR)³, lab results and messages are routinely relayed between physicians' offices and patients. This communication often becomes part of the EHR. With the development of mobile interfaces that enter PHRs, patients can now theoretically reach physicians in seconds.

Previous studies have investigated the ways in which otolaryngology patients have used technology in their healthcare. These studies reveal the trend that patients are increasingly searching for online information pertaining to their medical conditions⁴⁻⁹. For instance, in a study published in 2002, Rokade et al. found that only 13% of patients with internet access at their outpatient clinics used the internet to search for health information⁴. In 2006, Tassone et al. found that 18% with access had used the internet for health information prior to their initial consultation⁵. Internet access alone increased from 45% to 64% between these two studies. In 2009, Shaw et al. found that internet access had jumped to 85% of all outpatients, and that 37% of them had used the internet for health information prior to the appointment⁸.

Given how rapidly technology has evolved, study findings from over a decade ago may not necessarily be applicable to current patients' views⁴⁻⁶. Other studies have been conducted in other countries, including the United Kingdom^{4,8}, Ireland¹⁰, Germany¹¹, Brazil⁷, and Israel⁹, which may not be representative of the typical US patient population.

The purpose of this study is to characterize the current otolaryngology patient engagement with technology in the United States. This study seeks to determine when and how patients use online medical information to try to self-educate about their symptomatology, as well as the demographic factors that affect patient engagement with technology. This information can guide healthcare professionals in developing technology-based communication and education strategies, and assist in anticipating patient expectations.

Materials and Methods

Institutional review board approval was obtained at a tertiary care academic institution. This cross-sectional study was

conducted from July 2014 to January 2015 in this institution's outpatient adult and pediatric otolaryngology clinics. Survey data were collected from patients of 13 otolaryngologists' clinics in paper form, with all otolaryngology subspecialties included. The questionnaire queried adult respondents and pediatric respondents' family members on demographics, mobile phone ownership, internet utilization in their healthcare, and perspectives on EHR. Potential respondents were informed that participation was voluntary and that the data would be used for research purposes only.

Statistical analysis was performed by an independent biostatistician using SPSS 21.0 software for Windows (SPSS, Inc, Chicago, Illinois). Survey result frequencies were calculated and comparisons by demographics and subspecialties were performed. Fisher's Exact Test was used to analyze strength of statistical correlations.

Results

Survey Results: A total of 194 respondents, 55.7% female and 44.3% male, participated in the study. Table 1 outlines their demographic composition. For pediatric otolaryngology, 26 of 30 respondents (86.7%) were mothers of the pediatric patients. Age range was representative of the general medical adult population, and respondents were predominantly Caucasian (84.5%). Education level and annual household income was evenly split across categories. Respondents were predominantly from rural and suburban communities. There was a fairly even representation of patients by each otolaryngology subspecialty.

In total, 54.1% of respondents stated that they had internet access only at home, and 36.0% had access in multiple locations. Six patients (0.3%) denied having any internet access. Cell phone use was nearly ubiquitous at 95.9% of respondents. 76.2% of all respondents had smartphones, defined as having internet access via cell phone.

Four-fifths of respondents (79.9%) endorsed having looked up health-related information in general on the internet, with search engines (Google, Bing, or Yahoo) being the most commonly used resource for online searches (Table 2).

Half of respondents (49.2%) stated they had looked up health-related information using their smartphones, though

Table 1. Patient Demographics

		Number of Subjects (N)	Percentage of Total
Sex			
	Male	86	44.3
	Female	108	55.7
Age, years			
	18-30	16	9.8
	31-50	34	20.9
	51-64	65	39.9
	65+	48	29.5
Race			
	Caucasian	163	84.5
	African-American	24	12.4
	Hispanic	4	2.1
	Other	2	1
Education			
	High School or Less	44	22.8
	Some College	53	27.5
	College	53	27.5
	Graduate School	43	22.3
Household Income			
	<30K	50	27.6
	30-50K	34	18.8
	50-75K	32	17.7
	>75K+	65	35.9
Transit time to practice, hours			
	<1	138	71.1
	1-2	41	21.1
	2+	15	7.7
Community Type			
	Urban	37	19.4
	Suburban	69	36.1
	Rural	85	44.5
Subspecialty			
	Pediatric	30	15.5
	Head & Neck	29	14.9
	Rhinology	32	16.5
	Facial Plastics	22	11.3
	Otology	40	20.6
	Laryngology	29	14.9
	General	12	6.2

few (21.2%) had downloaded a cellphone app to specifically track or manage their health. Half (51.3%) of respondents had looked up information online related to the primary concern for their otolaryngology clinic visit. 59.0% and 37.0% of respondents stated they “agree” and “somewhat agree” that the online information was understandable, respectively. Only 6.4% of respondents stated they actually used treatments found from online searches for concerns related to their clinic visit. 5.3% endorsed participating in online forums or chat rooms pertaining to their primary concern.

Two-fifths (39.5%) of respondents had accessed their personal medical information using a secure patient portal or PHR, and had communicated with a healthcare professional over the internet via email or PHR. The vast majority (80.0%) stated they would be willing to receive emails or texts with information pertaining to their primary concern and were in favor of providing patients with the ability to schedule appointments via email or Internet.

Nearly all (94.2%) believed that their medical information was currently kept private and secure in their healthcare institutions. However, 62.1% believed there were increased privacy risks associated with EMR when compared to paper charts.

Table 2. Most Common Online Resources Used

Resource	Number of Subjects (N)	Percentage of Total
Search Engine (Google/Bing/Yahoo)	117	60.3
Wikipedia	9	4.6
Facebook	7	3.6
WebMD	66	34
Medscape	9	4.6
Medline	5	2.6
Mayo Clinic Website	23	11.9
Other	6	3.1

Response Analysis: Responses were then analyzed across demographic variables for statistical significance using Fisher’s Exact Test.

Compared to males, females were significantly more likely to use technology in their healthcare ($P < .048$, Figure 1). Increasing age was associated with decreased smartphone ownership ($P < 0.001$, Figure 2). However, nearly all age groups owned basic cell phones (92% and greater). Younger age (18-30 years) was correlated with searching for health-related information on cell phones ($P < 0.001$). Conversely, increasing age was associated with decreased willingness to receive emails pertaining to medical concerns ($P = 0.017$).

Race was not correlated with ownership of a cell phone, smartphone, or whether respondents had looked up health-related information on the internet.

In general, higher education and income levels were correlated with greater health-related technology usage (Figures 3-4). These statistically significant metrics include looking up health information online, searching for information related to chief complaint, and usage of smartphones, PHR, health apps, email, and text messaging ($P < 0.05$).

Though there was no significant correlation between income and cell phone ownership (92.0% to 98.5%, $P = 0.391$), higher incomes were associated with greater smartphone ownership (Figure 4). The relationship between income and looking up health information on mobile phones was bimodal; the top and lowest quartiles were more likely to search for medical information on their phones ($P = 0.004$).

Suburban respondents were more likely than urban and rural respondents to have looked up personal medical information using PHR and communicate electronically with healthcare professionals ($P < 0.14$).

Compared to all other subspecialties, pediatric otolaryngology patients' family members were statistically more likely to utilize healthcare technology ($P < 0.002$, Figure 5). Otolaryngology/Neurotology respondents were statistically less likely to have looked up health information online ($P = 0.001$), and to look up information pertaining to their primary concern ($P = 0.005$). Facial Plastics respondents were statistically more interested in securing appointments electronically ($P = 0.016$).

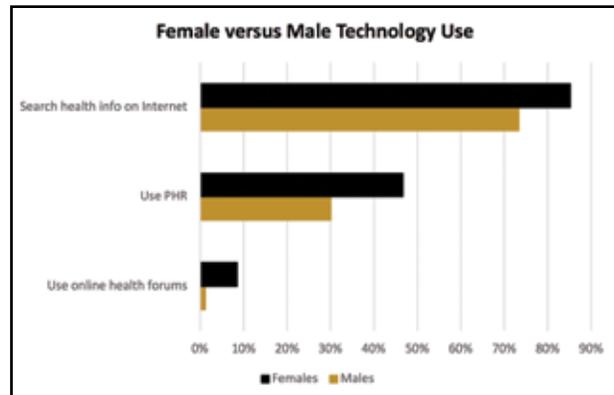


Figure 1. Females demonstrated significantly greater technology use with their health care (top to bottom respectively: $P = .048$, $.045$, $.025$).

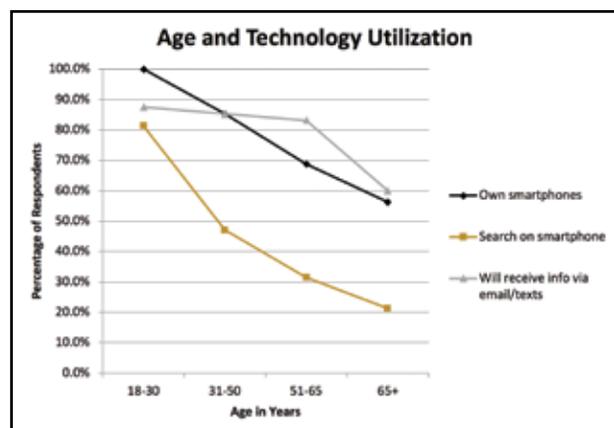


Figure 2. Decreasing technology use is observed with increasing age ($P < .05$).

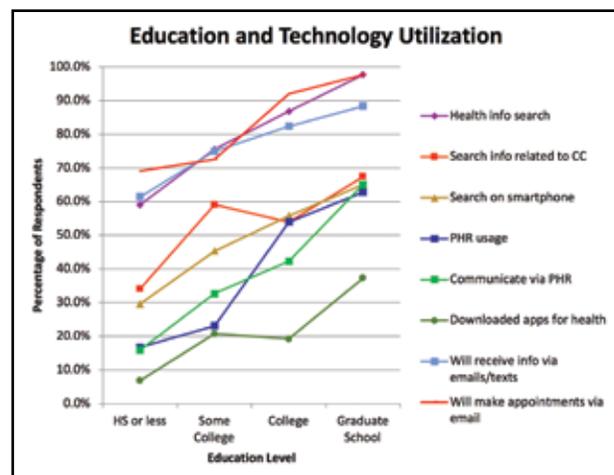


Figure 3. Increasing technology use is observed with increasing education levels ($P < .05$).

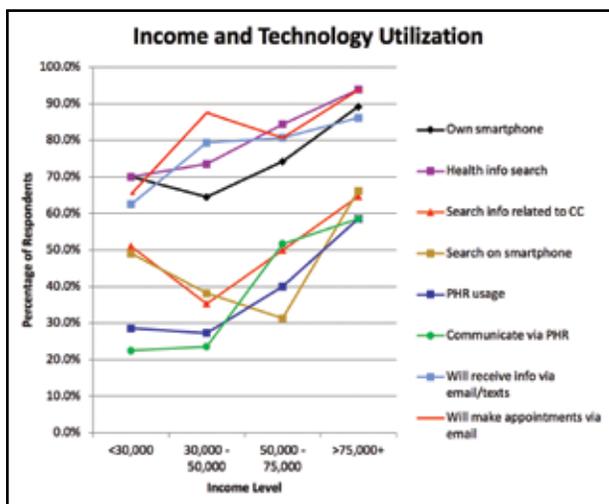


Figure 4. Increasing technology use is observed with increasing income levels ($P < .05$).

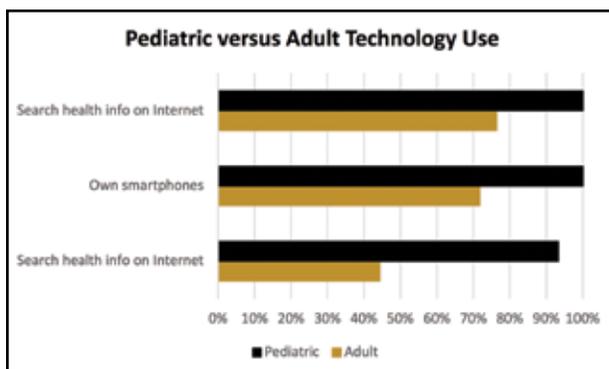


Figure 5. The pediatric respondents, 86.7% of which were their mothers, demonstrated significantly greater technology use with their health care (All $P < .0002$).

Discussion

Central to the increasing utilization of healthcare technology is internet accessibility. In our study, 90% of respondents stated they either had internet access at home, or at multiple locations including at work and the library. These figures correspond with the current survey studies¹. This increased connectivity can largely be explained by the fact that over three quarters (76%) of our respondents had smartphones, which is above the national average of 68%. In fact, home internet access is currently declining in popularity in favor of smartphone use. The most common reasons to abandon landline access were cost of broadband internet access and the smartphone's capability to perform the same functions¹.

As the streamlining of mobile sites and apps continues to improve, tasks that have become predominantly online activities including bill payment are no longer as dependent on landline access.

Remarkably, our study found that over half (51.3%) of otolaryngology patients now search for health information related to their primary concern prior to their clinic visit. Within otolaryngology, this is a greater proportion than found in older studies^{4, 5, 8} and consistent with more recent study findings⁹. In our study, almost all of these respondents either agreed or somewhat agreed that the information was understandable and helpful (96%, 93%, respectively), which reinforces similar results in past studies^{6, 10}. This type of data can have multiple interpretations, given that the quality of such resources is certainly questionable.

Studies have revealed the relative inaccuracy of online otolaryngology topics. Volsky et al. found that content accuracy of otolaryngology topics was generally poor¹²; however, eMedicine had the highest accuracy index versus Wikipedia and MedLinePlus. Additionally, two sources^{13, 14} found that YouTube videos describing pediatric otolaryngology conditions contained high levels of misinformation, with a significant percentage (66%, 28%, respectively) formatted in testimonial-type videos. With the majority (60%) of our respondents using search engines to find medical information, the quality of that information is inherently highly variable and likely poor. Additional content analysis of websites, such as those included in our questionnaire (Mayo Clinic, Medscape, WebMD), is necessary to identify which sites are most informative.

Numerous studies have investigated readability of online otolaryngology information. Unanimously, they found that websites wrote in a much higher reading level than the National Institutes of Health's recommendations of writing at a fourth- to sixth-grade level¹⁵⁻²⁰. On average, resources were written at a Flesch-Kincaid Grade Level above the tenth grade, with academic or professional websites having more difficult readability.

Despite this, patients favor physicians as the best source of information over other sources, including nurses, friends or family members, books, brochures, and websites.^{6, 10}

Thus, in an increasingly connected healthcare environment, otolaryngologists must continue to develop their online presence and to provide accurate online materials to those doing internet searches. Ideally, this information would be freely accessible and understandable to the general population.

Higher education and income levels had the highest correlation with technology utilization in our study, which is consistent with previous findings. As of 2012, 8% of all individuals had used email for these purposes⁸, compared to 39% in our study just three years later. While this may represent a broader paradigm shift in communication in society, it is important that all patients, especially those with lower education levels, are informed about the multiple options to communicate with physicians. This is especially appropriate given the universality of internet access in our study.

Our study confirmed that parents or caretakers of pediatric otolaryngology patients were significantly more likely to search online for medical information^{6,7}. Conversely, our study found that technology utilization was lower with older otolaryngology patients, which is in agreement with previous studies¹¹. Barriers to technology use in the elderly are multifactorial, and are especially relevant in an aging US population. These include familiarity, access, physical difficulties with vision, sight, or coordination, as well as cognitive deficiencies.²¹ As technology becomes increasingly fundamental in healthcare utilization, the elderly would benefit from additional training in navigation of websites or apps to improve their familiarity.

Weaknesses of the study include data from only one institution, which restricted the catchment to one geographical region. Additionally, income and racial proportions were not representative of the US population as a whole. Number of total respondents was limited as well. Cross-subspecialty analysis was limited given the number of respondents in each group. Moreover, the parents of pediatric otolaryngology patients were typically younger respondents, and thus age is identified as a confounding variable given that we did not analyze their responses against their age group.

Conclusion

Internet and technology usage continue to increase in the North Carolina patient population. Within otolaryngology patients, discrepancies in technology utilization and views on

that utilization exist. Knowing this, we consider the prevalence of smartphones in our patient population as an opportunity to facilitate communication regarding patients' appointments, surgeries, and general compliance issues. With three quarters of patients owning smart phones, automated text or smartphone app-mediated notifications can be easily utilized to remind patients to comply with a myriad of recommendations for their healthcare. To illustrate, we envision a rhinology patient being reminded of their scheduled nasal saline irrigations and intranasal corticosteroid administrations. A pre-surgical patient can be notified to stop their anti-platelet regimen and be guided through a pre-operative optimization program. Applicable to all healthcare practitioners, patients who smoke can be sent smoking cessation materials as well as reminders to quit on a more consistent basis.

Ultimately, we hope that healthcare professionals and institutions can adapt their approach in educating patients on how to use relevant technology. Physicians should continue to improve their online presence and the quality of online medical information, as the internet is now a major information resource for patients.

Disclosures

No financial support given. Authors report no conflict of interest. This article was presented as a poster at the 2016 Combined Otolaryngology Spring Meetings (COSM), The Triological Society, May 19-20, 2016; Chicago, Illinois, USA.

Acknowledgements

The authors acknowledge Dr. John Spangler, M.D., and Gregory Russell, M.S., for their contributions to the study. There are no financial disclosures.

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Micronized Oral Progesterone Compared to Placebo and Time to Resolution from Concussion in College Athletes: A Feasibility Study

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Abstract

Objectives: To determine whether study subjects treated with micronized progesterone will have improved time to resolution and/or improved daily symptom scores compared to placebo.

Methods: College athletes sustaining a concussion according to consensus guidelines at two southeastern United States universities, one public and one private, were randomized in a double-blinded and placebo-controlled trial using oral micronized progesterone (five days) versus placebo in acute phase of concussion.

Results: Eighteen athletes received the study drug and seven received a placebo. The progesterone group had a mean of 7.3 days until symptom resolution, while the placebo group had a mean of 4.5 days with a non-significant difference found ($p=0.42$). There were two athletes that received the study drug that had symptoms lasting longer than thirty days. When excluded, the mean duration of symptoms for both groups was 4.5 days ($p=0.95$). The mean symptom score decreased at a higher rate in the placebo group.

Conclusions: In this pilot trial, the use of oral micronized progesterone did not shorten the days symptomatic from concussion. The rate of improvement was slower in the intervention group. The study showed feasibility and tolerability of the medication. Additional studies in large samples evaluating progesterone are needed given the benefit seen with progesterone in other models.

Introduction

Concussions are a common injury among athletes in the United States. From 2001 to 2012, the rate of emergency room visits for sports and recreation-related injuries with a diagnosis of concussion or traumatic brain injury (TBI) has doubled.¹ The likelihood of an athlete in a contact sport experiencing a concussion is as high as 20% per season.² 30% to 80% of those diagnosed with concussion will go on to experience symptoms of post-concussion syndrome, making sports-related concussion a serious public health concern.³

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Two independent clinical trials have demonstrated promise for progesterone as a potent neuro-steroid. Wright and colleagues conducted a phase II clinical trial resulting in a 50% reduction in mortality in patients with moderate to severe brain injuries who were treated with progesterone.⁴ These data were supported by a second trial among severely brain injured subjects with a dramatic decrease in mortality (18% in the progesterone treated group versus 32% in the placebo group), as well as better functional outcomes at three and six months.⁵ Progesterone is widely available and inexpensive making it an ideal agent for mild TBI. In animal studies, acute post-injury treatment progesterone has been associated with reducing cerebral edema, neuro-inflammatory markers, neuronal loss and improved behavioral outcomes.⁶ Previous studies found good tolerability with few adverse events or side effects related to progesterone.⁴⁻⁵ Micronized progesterone has a consistent pharmacokinetic profile and an oral option for treatment. Cutler et al. reported enhanced behavioral recovery with a tapered dose.⁷ Duration of progesterone therapy has been investigated. Results indicated that five days of treatment resulted in improved outcomes when compared to three days of treatment⁸. Clinical data is needed regarding the role of progesterone as an efficacious treatment for concussions. The aim of this pilot study is to assess feasibility of implementing concussion research among college athletes using progesterone and to explore whether micronized oral progesterone given in the acute phase (<24 hours post-injury) decreases the symptomatic period following a concussion.

Materials and Methods

Study participants are members of the universities' athletic programs participating in National Collegiate Athletic Association sanctioned sports or club sports (e.g. football, soccer, field hockey, basketball, rugby). Athletes voluntarily provided informed consent at the beginning of the sports season. Exclusion criteria included pregnancy, active breast or reproductive organ cancers, allergy to peanuts, history of or current thrombophlebitis or venous thromboembolic disorder (including deep venous thrombosis and pulmonary embolism), females taking birth control, known hypersensitivity or prior adverse reaction to progesterone, or liver disease. The study protocol was approved by the Wake Forest School of Medicine Institutional Review Board.

The Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT®) was used for the study.¹¹ This test confers an objective measurement of the following composites: verbal memory, visual memory, processing speed, reaction time, and impulse control as well as a total symptom score. Baseline ImPACT™ composites were obtained prior to the diagnosis of concussion. The athlete was diagnosed with concussion by an experienced medical professional trained in concussion recognition and treated within 24 hours of the initial injury. For this study, concussion was defined as any noticeable change in mental status or consciousness or any self-reported symptoms following an impact (i.e., headache, nausea, confusion, dizziness, etc.).

The concussed athlete was randomized in a 2:1 fashion to receive either oral micronized progesterone (Prometrium®) at a dose of 400mg for three days followed by 200mg for two days or placebo (five days) within 24 hours of being diagnosed with concussion. A tapered dose was chosen based on Cutler et al.'s study that showed enhanced behavioral and molecular recovery.⁷ Participating athletes were not allowed to use NSAIDs for the first 48 hours post-concussion. Study subjects were permitted to use acetaminophen immediately following injury or ibuprofen after 48 hours, if needed.

Daily symptom scores were recorded until either the end of five days or the complete resolution of symptoms, whichever was longer. The Sport Concussion Assessment Tool V.3 (SCAT3™), a standardized tool for evaluating injured athletes for concussion, was utilized and is composed of 22 items assessed on a scale of 0 (none) to 6 (severe) regarding how they feel at the time of the survey⁹. All athletes and investigators were provided a list of common side effects associated with oral micronized progesterone (Prometrium®). Side effects were assessed daily by medical staff while the participant was taking the study drug and recorded on a daily symptom assessment log.

Once the athlete self-reported to be asymptomatic, the ImPACT® test was used to confirm the athlete did not have neurocognitive deficits that may not have been apparent by a symptom inventory alone. The concussion was not deemed to be "cleared" until both symptoms had resolved and ImPACT® testing had normalized. Both groups were prescribed a complete cessation of video games, homework

and classwork. Data was analyzed using Statistical Package for Social Sciences (SPSS) IBM Corp.¹⁰ Results were analyzed using descriptive statistics and comparisons between groups were done using chi square tests for proportions and t-tests procedures for continuous variables.

Results

Eighteen college athletes received the study drug and seven received placebo. Baseline characteristics of each group, outlined in Table 1, include the sport played and headache/migraine history of each participant. The majority of all participants (n=25) were male (n=23) and played football (n=17). Demographic characteristics between study groups were grossly similar.

The baseline sideline score assessment of concussion using the ImpACT® assessment and the SCAT3™ varied widely for each athlete with scores ranging from 5 to 54. The group receiving micronized progesterone (Prometrium®) had a mean of 7.3 days until symptom resolution, while the placebo group had a mean of 4.5 days (p=0.42), Figure 1. The range of symptom scores from the SCAT3™ in the placebo group varied from 1 to 33 while the Prometrium® ranged from 1 to 19. There were two athletes that received the study drug that had symptoms lasting longer than thirty days. When excluded, the means of both groups were 4.5 days of symptoms (p=0.95). The mean symptom score decreased at a higher rate in the placebo group. There were no serious adverse events reported from any athlete participant. Common symptoms reported on the daily symptom log included but were not limited to headache, difficulty concentrating, fatigue, and feeling slowed down.

Table 1. Baseline Characteristics of Athletes

Characteristic	N	Percent
Age at Consent	25 ± 1.08 (mean 19.59)	
Male	23	92
Female	2	8
Sport*		
Football	17	68
Soccer	4	16
Baseball	2	8
Basketball	1	4
Field Hockey	1	4
Treatment for headaches	8	32
Treatment for migraine	3	12

*Concussion is secondary to each sport played.

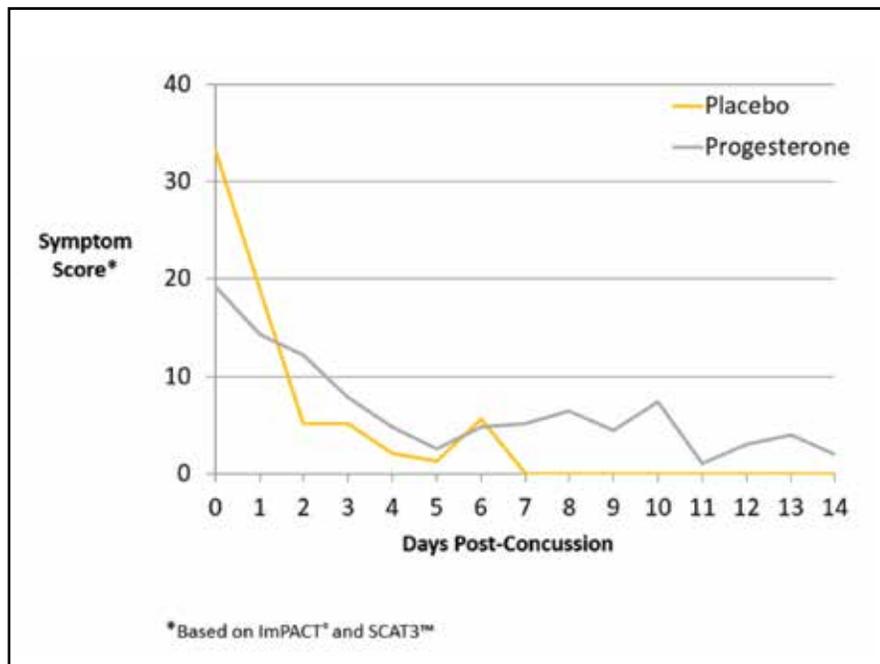


Figure 1. Symptom Scores by Group and Days Post-Concussion.

Discussion

Athletic TBI remains a common complication of sports injuries for which medical therapy has not advanced over time. Our pilot study results do not support the hypothesized benefit of oral micronized progesterone for symptom burden and/or duration after concussion. The symptom scores reported in this study represent an average time to resolution for each group which showed a wide range. Both symptom score and symptomatic days were not significantly different between treatment and placebo groups. Previous studies with progesterone have been conducted in animal models and a variety of TBI patients.^{4-6,12-15} While progesterone has been associated with neuroprotective effects, there have been differences in the pathophysiology of athletes who experienced mild versus moderate/severe TBI. Considering the inflammatory cascade associated with varying degrees of TBI, it is possible that differences among the athletes' levels of TBI may have impacted our results. It is also unclear if any of the delay in symptom recovery may have been related to medication side effects. Reported side effects of Prometrium® included headache, nausea, and fatigue. It is likely that concussion represents a spectrum of disorders, some of which may not be responsive to progesterone therapy (e.g. inner ear dysfunction, cervicogenic symptoms, sleep disturbances, as well as anxiety/depression).

The limitations to the current study include the small sample size. A 2:1 study design, in which more individuals received the study drug than placebo, provided for more accurate estimates of the effect in the intervention group. While this was ideal to show the tolerability for the medication, the placebo group had a smaller sample size (n=7) making the placebo group data less generalizable. Additional tolerability studies could be performed by randomizing non-concussed athletes to receive study drug or placebo. This pilot study did not show benefit of oral micronized progesterone in the reduction of symptom score or symptomatic days. The length of therapy and dosage of progesterone for our study was based on previous trials that may not be generalizable to the athletic concussions in this study.⁷⁻⁸ Polich and colleagues postulated that a placebo may be a therapeutic for TBI which may skew results of studies such as ours.¹⁶

At the time of this study, the role of aerobic exercise was not part of routine treatment strategies. More recently,

the initiation of aerobic exercise post-concussion has been studied in a retrospective analysis among athletes and has been associated with a quicker return to sport and school work.¹⁷ Improved cerebral blood flow with aerobic activity may play a role.¹⁸ Additionally, efforts have been directed towards concussion prevention. Strategies have promoted equipment modification with developments in helmet technology. Despite advances in helmet technology, these interventions have not been shown to decrease the likelihood of concussion.

More research is needed for the efficacious treatment of concussion. Considering the complex nature of TBI as a heterogeneous disorder that is linked to secondary injury cascades, progesterone may need to be used with other adjunctive treatments.¹⁵ The design and implementation of this study indicates that a larger trial using a similar study design is feasible. Additional data is needed to fully understand the role of progesterone treatment in the acute phase of concussion that could ultimately be combined with other treatment modalities such as aerobic exercise.

Disclosures

This research was funded by the American Medical Society for Sports Medicine Foundation. Authors report no conflict of interest.

Acknowledgements

We would like to thank Dr. Abbie Eaton for her time and efforts in executing this study and the Wake Forest School of Medicine Clinical and Translational Science Institute (CTSI) for supporting this study.

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Thirty Day Readmission Rates and Seven Day Follow Up among High Risk Patients: Interrupted Time Series Design

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Abstract

Background and Objectives: Reducing hospital readmissions continues to be a focus within health care systems in the United States. Studies indicate that timely follow up appointments with a primary care physician (PCP) decrease readmission rates. The main goal of this study was to use an electronic health record (EHR) integrated alert to improve 7-day hospital follow-up (HFU) appointment completion rates and thereby 30-day readmission rates in high-risk patients.

Methods: A prospective study of 413 high-risk hospitalized patients admitted to a suburban, academic medical center was conducted from August 2016–May 2017. High-risk patients (modified LACE Score above 18) were identified and triggered best practice advisories (BPAs). It would suggest the need for a 7-day follow up appointment with a PCP.

Results: High risk modified LACE Score patients that completed an HFU appointment in seven days did not demonstrate decreased 30-day readmission rates in the post-intervention period ($p=0.186$). In contrast, low-to-moderate risk patients (modified LACE Score less than or equal to 18) who completed seven day HFU had a significantly lower 30 day readmission rates compared to patients who did not complete seven day HFU appointments in the same risk group (12.8% versus 37.1%, $p<0.0001$).

Conclusion: The hypothesis that this intervention could improve readmission rates in high-risk patients was not supported by this study. However, data collected during the study suggest that low- to-moderate risk patients may benefit from the intervention.

Introduction

The Centers for Medicare & Medicaid Services (CMS) calls avoidable readmissions one of the leading problems facing the US healthcare system.¹ Since 2004, approximately 20% of all Medicare beneficiaries are readmitted to the hospital within 30 days of their original admission.^{2,3,4} Although some readmissions are unavoidable, many are preventable. Estimates on Potentially Preventable Readmissions (PPR) for all cause readmissions ranges widely from 9 to 90%.^{3,4} In 2004, the federal government reported the total cost of readmissions for Medicare patients alone was \$26 billion; specifically, more than \$17.4 billion of it was for avoidable admissions.¹⁻⁴ In addition to increased financial costs, readmissions are associated with decreased quality of life for patients and increased risk for healthcare related adverse events.⁴

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In 2012, CMS established the Hospital Readmissions Reduction Program (HRRP), which penalizes hospitals with higher than expected readmission rates.⁵ Reductions in Medicare reimbursement began in October 2012 for hospitals with high 30-day readmission rates for pneumonia, congestive heart failure, and acute myocardial infarction.^{6,7} In 2013, 2,217 hospitals suffered “readmission penalties”, approximately 300 of which received the highest penalty of 1% of their regular Medicare payments for the coming year.⁷ The average penalty per hospital amounted to a 0.4% reduction in total Medicare payment, or between \$125,000 and \$164,000 per hospital, and a total savings of approximately \$300 million for CMS.^{6,7} The HRRP penalty maximum increased to 2% in 2014, and then to 3% in 2014.^{6,7,8} It is estimated that total Medicare penalties assessed on hospitals for readmissions will increase to a total of \$528 million in 2017, which is \$108 million more than in 2016. The increase is due mostly to more medical conditions being measured.⁹

The HFU appointment presents a critical opportunity to address the condition that precipitated the hospitalization and to prepare the patient and family caregiver for self-care activities.^{10,11} Early HFU appointments provide the patient and provider with the opportunity to review medications, test results, and discuss symptoms of worsening conditions.^{3,10,11} Multiple studies have suggested that patients who followed up with their PCP within seven days were less likely to be readmitted to the hospital.^{3,10} Furthermore, evidence shows a direct link between the patient’s clinical complexity and the benefit of early follow-up.¹²

Methods

Study Design

The objective of this prospective, interrupted time series, interventional study was to increase the number of 7-day HFU appointments completed, with the goal of decreasing 30-day inpatient readmissions. In order for an appointment to be considered “completed”, the patient must arrive for the appointment and the physician must complete the necessary documentation within the EHR. The project utilized the Plan-Do-Study-Act (PDSA) method of quality improvement. The PDSA is a simple tool used by many healthcare institutions, including the Institute for Healthcare Improvement and CMS to accelerate process improvement. The PDSA cycle

is shorthand for testing a change—by planning it, trying it, observing the results, and acting on what is learned.¹³ The quality improvement team included the Associate Chief Medical Officer (CMO) of Lahey Hospital Burlington, Medical Director of Inpatient Informatics for Lahey Health, Vice President of Data Warehousing, Director of Patient Access, Case Management Nurse Managers, an Epic® EHR Analyst, and a Project Manager. The study consisted of two PDSA cycles that unfolded over a ten-month period (8/1/2016-5/31/2017). The interventions implemented in each PDSA were defined by the initial pilot study. The Institutional Review Board at Lahey Hospital approved the study and deemed it as a quality improvement project. Per the institutional review, no consent was required. The study was unblinded as the project team was also responsible for the data collection and analysis.

Setting

The setting for this study, Lahey Hospital & Medical Center (LHMC), is a 335 bed non-profit, academic medical center located approximately 10 miles north of Boston in Burlington, Massachusetts. LHMC admits over 20,000 patients a year to one of nine inpatient units.^{14,15} LHMC is a founding member of Lahey Health System, which provides a full continuum of integrated health services in virtually every specialty and subspecialty.

Participants

Patients eligible for the study included those admitted to the Division of Hospital Medicine directly from outpatient providers’ offices, as transfers from other hospitals, and as admissions through the emergency room. This population accounts for approximately 47% of all admissions to LHMC. Patients who were discharged to home, group homes, or assisted living facilities between January 1, 2016 and May 31, 2017 were included in the study. Patients discharged to nursing homes, skilled nursing facilities, or other acute care hospitals were excluded. Due to limitations in the ability to manage appointments and coordinate care with PCPs outside of the Lahey network, all patients with PCPs external to the Lahey Health system were excluded from the study.

Additionally, upon admission to LHMC, patients were stratified based on their risk of readmission using the Lahey derived modified LACE Score (see appendix A and below). Figure 1 provides a breakdown of the initial target population and

the criteria used to identify the study population, along with additional patient demographics for the study population based on risk category.

that the top 10% of risk was associated with a modified LACE Score of greater than 18.

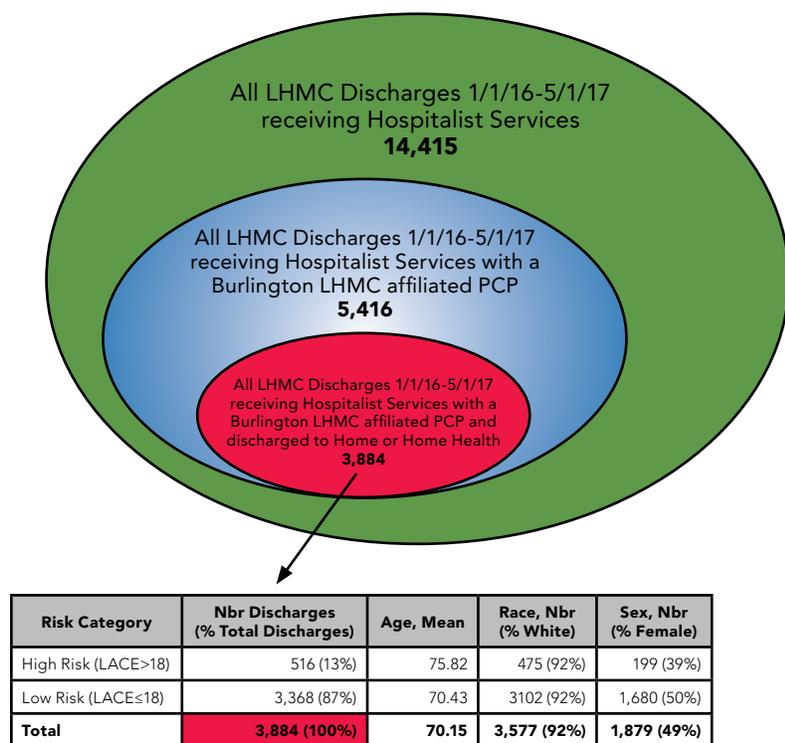


Figure 1. Characteristics of Study Sample by Risk Category

The LACE Score, a widely used, validated, risk stratification tool was used and has been shown to have a moderate to high predictive value in identifying those patients at risk for unplanned inpatient readmission within 30 days of discharge, and a high predictive value in identifying those patients at risk to return the Emergency Department. Lahey Health decided to use the “modified” LACE Score because it captures many social determinants of readmission risk that are not captured in the classic LACE Score. Based on internal review, we noted

Statistical Analysis

Readmission rates prior to the study were compared to readmission rates after the study using the Chi-square test. Process metrics were analyzed using the t-test for two independent means. For the outcome and process metrics, a p-value less than 0.05 was considered significant. Results were reported on a regular basis using SQL database tools with data exported from EPIC®. Data was exported from the Clarity data warehouse into Excel® for further analysis.

Results

Baseline Measurement: Observation and Pilot Study

Prior to the start of the quality improvement initiative, data from one nursing unit at LHMC was collected and analyzed over a 30-day period (January 11, 2016 – February 12, 2016).

The initial analysis included two steps. First, the impact of 7-day HFU appointments on readmission rates for patients at LHMC was examined. Seven-day and 30-day readmissions

for patients that completed a hospital follow-up visit within seven days and those that had not were compared. Thirty-day readmission rates dropped from 15.4% to 12.5% for patients that completed a 7-day HFU visit (n=286, p=0.68).

Only 20% (77/286) of all discharged patients completed an HFU appointment with a PCP within seven days of discharge. See figure 2 for Barriers to HFU identified prior to the main study below.

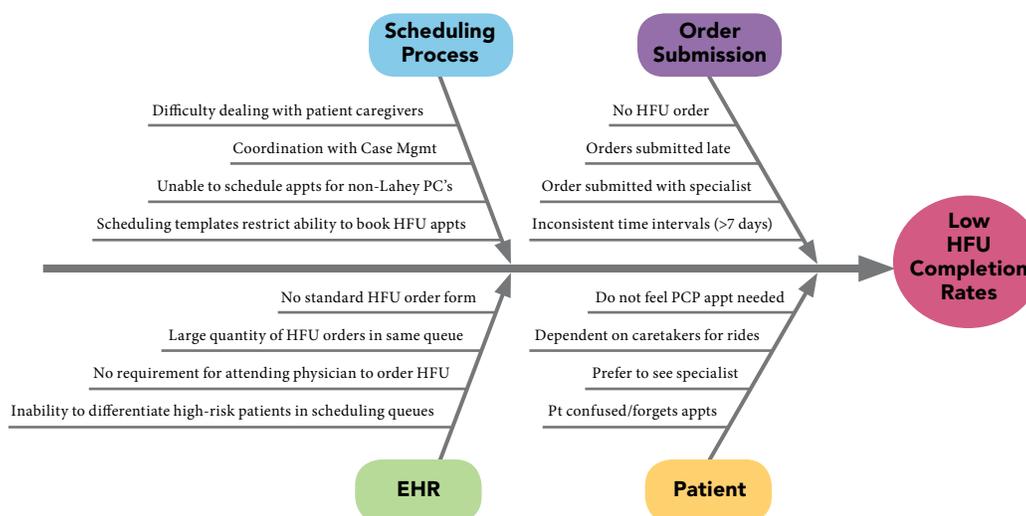


Figure 2. HFU Pilot: Ishikawa Fishbone Diagram: Causes of Low HFU Completion Rates.

PDSA Cycle 1 (August 1, 2016–January 16, 2017)

Almost 25% of readmissions were attributed to a small group of high-risk patients. Therefore, the first strategy employed in PDSA Cycle #1 was to identify and prioritize patients that had a high risk of readmission to ensure that they were scheduled an HFU appointment within seven days of discharge. Given that these follow-up appointments were a limited resource, the investigators hypothesized that they would be most impactful in the high risk cohort. The goal was to identify patients with a LACE Score within the top decile of risk and to ensure that inpatient providers were submitting follow-up orders early in each patient's admission, rather than waiting until the time of discharge. A BPA was triggered in the hospital's EHR immediately once a patient's LACE Score reached the high risk threshold of above 18.

PDSA Cycle 2 (January 17, 2017–May 31, 2017)

This cycle was aimed at improving the scheduling workflow to increase the number of seven-day HFU appointments scheduled. Despite improvements made to the ordering process for high-risk patients in PDSA Cycle #1, the percentage of HFU appointments scheduled within seven days continued to hover around 43%. In an effort to increase the percentage of high-risk patients (as determined by LACE Scores) scheduled for HFU appointments, all HFU orders for high risk patients submitted in EPIC were funneled into a special high-risk work queue monitored by the hospital scheduling team.

Process Metrics

Four process metrics aimed at measuring the impact of the interventions on the ordering and scheduling processes were calculated on a monthly basis.

1. Timing of HFU order relative to discharge
2. Timing of HFU appointment booking relative to discharge
3. Timing of HFU appointment completion relative to discharge
4. Percentage of HFU appointments booked within seven days of discharge
5. Percentage of HFU appointments completed within seven days of discharge

The high-risk group was compared pre-intervention (January 1, 2016 to July 31, 2016) and post-intervention (August 1, 2016 to May 31, 2017). There were 206 unique pre-intervention discharges as compared to 310 post-intervention discharges.

Provider Response to BPA

Among high-risk hospital medicine patients that were discharged home with HFU through the local primary care group, the order was placed at 10.72 hours prior to discharge pre-interventions. Post-intervention, the order was placed 56.9 hours prior to discharge (p=0.001).

Timing of Appointment Booking Relative to Discharge

Another goal of the project was to move the booking time of the HFU appointment as close to the discharge date and time as possible. The scheduling department and patient access services leadership were equipped with the proper EPIC® tools to differentiate the high-risk discharges from all discharges. Post-PDSA Cycle #2 appointments were booked 1.49 days after discharge ($p=.015$). This represents a 35% (0.79 day) decrease in the amount of time it takes for the scheduling team to book a seven-day HFU appointment post-discharge.

Timing of Appointment Completion Relative to Discharge

The average time from discharge to completion of HFU visit decreased by approximately one day (pre-PDSA Cycle #2 = 8.01 days, post-PDSA Cycle #2 = 6.94, $p=0.042$).

Percentage of HFU Appointments Scheduled and Completed within Seven Days

The percentage of HFU appointments scheduled pre- versus post-PDSA Cycle #2 was 64% versus 63%, respectively ($p=0.413$). The HFU appointment completion rates increased 7% total, from 29% to 36% pre- versus post-intervention ($p=0.034$).

Lastly, after PDSA Cycle #2, the number of seven day HFU appointments completed increased 32%, from an average of 8.5 HFU appointments per month to 11.2 HFU appointments per month ($p=0.030$, $t= -2.03$).

Outcome Metrics

The outcome metric targeted for the study population was the 30-day inpatient readmission rate. Readmissions were defined as a return to any Lahey Health hospital within 30 days of a previous discharge for any reason. The readmission did not need to be clinically related to the initial admission. Additionally, there was no differentiation made between planned and unplanned readmissions.

The high-risk group data was compared pre-intervention (January 1, 2016 to July 31, 2016) and post-intervention (August 1, 2016 to May 31, 2017). The 206 unique pre-intervention discharges were compared to 310 post-intervention discharges.

30-Day Readmissions Data

Thirty day readmission rates dropped from 42.0% to 33.9% in the high-risk LACE Score group ($\chi^2=5.18$, $p=0.023$), and from 17.2% pre-intervention to 16.4% post-intervention in the low-to-moderate LACE Score group over this period ($\chi^2=.276$, $p=0.599$).

Thirty-day readmission rates for high LACE Score patients discharged post-intervention that completed a HFU appointment (32.8%) were compared to those that had not (reduction by 4.7%, $\chi^2=1.75$, $p=0.186$). See Figure 3.

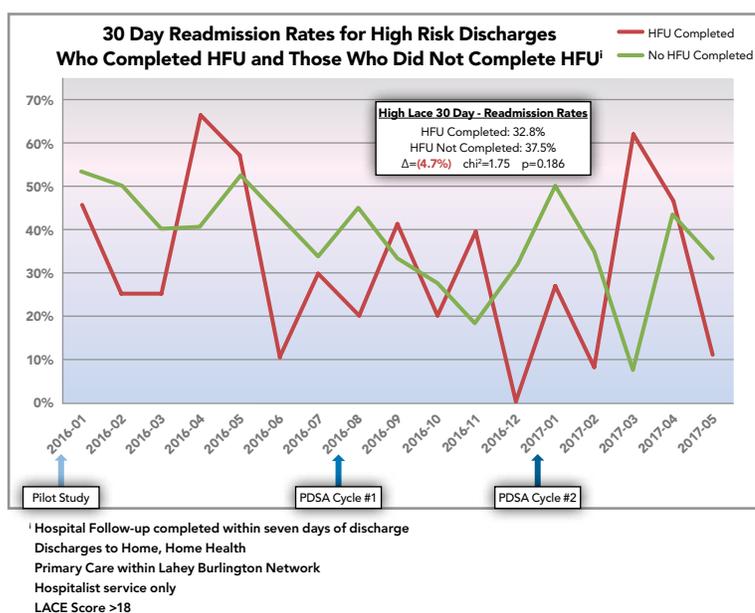
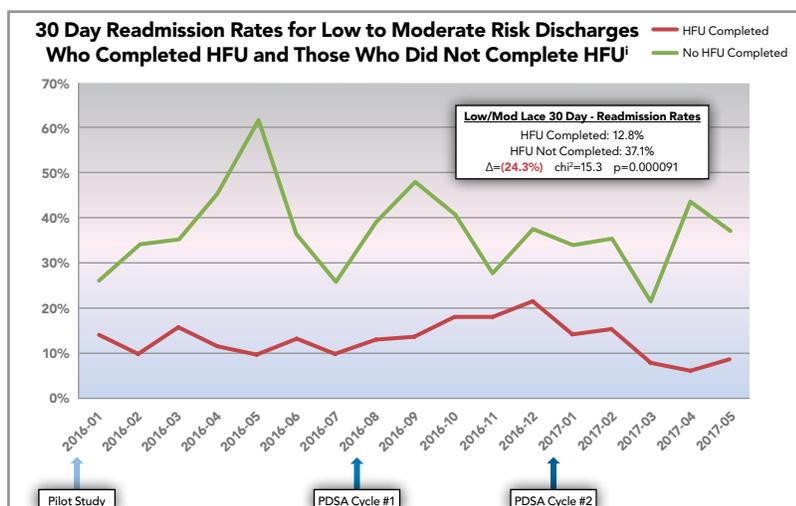


Figure 3. Thirty Day Readmission Rates for High LACE Discharges Who Completed a Hospital Follow-up and Those Who Did Not Complete a Hospital Follow-up.

Finally, 30 day readmissions for low-to-moderate LACE Score patients that completed a HFU and those that had not were compared ($p<0.001$). The 30 day readmission rate for low-to-moderate LACE Score discharges that completed a HFU was 12.8% compared to 37.1% for those that did not ($\Delta=24.3\%$, $\chi^2=15.3$, $p=0.000091$). See Figure 4.



¹ Hospital Follow-up completed within seven days of discharge
Discharges to Home, Home Health
Primary Care within Lahey Burlington Network
Hospitalist service only
LACE Score ≤18

Figure 4. Thirty Day Readmission Rates for Low to Moderate LACE Discharges Who Completed a Hospital Follow-up and Those Who Did Not Complete a Hospital Follow-up.

Discussion

The goal of this project was to deploy EHR interventions aimed at improving the scheduling of HFU appointments and therefore reduce 30-day readmissions.

Process metrics improved because of improved workflows. HFU appointment orders were placed 33.86 hours earlier post-intervention. Moreover, HFU appointments were booked by patient access services 18.96 hours earlier post-intervention. HFU appointment completion rates increased by 7%, from 29% to 36% (p=0.034).

Thirty day readmission rates demonstrated a dramatic drop, from 42% to 33.9% (chi²=5.18, p=0.023) in the high-risk group. However, when comparing those discharged patients that completed an HFU appointment versus those that did not, there was no significant difference in 30 day readmissions for high LACE Score patients (p=0.283, p=0.186). This would suggest that HFU completion was not the driver of the readmission reduction in the high-risk group. Perhaps increased awareness of high-risk status may have changed provider behavior in a different way, although this was not measured.

Retrospectively, the low-to-moderate LACE Score discharges that completed a HFU appointment showed a significant decrease in 30 day readmission rates (Δ=24%, p=0.000091). After further analysis, perhaps the LACE Score threshold of 18 or greater was too high. Discharges with a LACE Score of 18 or higher have multiple comorbidities and socioeconomic factors that may make it too difficult to complete an HFU appointment. Research shows that high risk patients may require multiple, bundled interventions in order to be successful in reducing readmissions.

There may be more success in reducing readmission rates by focusing on moderate-risk discharges with this single intervention, HFU appointments. This moderate risk group may be more likely and able to schedule and complete a HFU. Moreover, PCPs may be better able to identify and resolve issues to prevent hospitalizations for

this group. These results provide an opportunity to expand this intervention to a larger population with the goal of reducing readmissions.

There are several limitations of the study. Given the study design and lack of randomization, it is possible that other variables were in play to reduce readmissions. There were other readmission initiatives happening at the same time, although none focused on high-risk patients along a similar timeline. The study was conducted at only one site with a limited sample size. Another potential limitation in this study is the use of a Lahey specific Modified LACE Score, which includes socioeconomic factors that are not captured in the classic LACE Score employed by other hospital systems. This may result in varying patient populations being identified as “high” LACE. Additionally, the study population was limited by the number of patients that had Lahey affiliated PCPs.

Conclusion

In summary, readmission rate reductions are possible using EHR risk stratification, BPAs, and scheduling enhancements. This study did not demonstrate a significant reduction

in readmissions for high-risk discharged patients that completed an HFU appointment. The single intervention (HFU appointment) design of this study may not have been effective for high-risk patients. However, data collected over the course of the study suggests a future direction for targeting the intervention to low-to-moderate risk patients as a potentially more effective strategy.

Disclosures

Authors declare no conflict of interest. No financial support given.

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Appendix A: Original LACE versus Lahey-Derived Score

Original Score:

LACE index for the quantification of risk of death or unplanned readmission within 30 days after discharge.

Attribute	Value	Points*
Length of stay, days ("L")	<1	0
	1	1
	2	2
	3	3
	4-6	4
	7-13	5
	≥ 14	7
Acute (emergent) admission ("A")	Yes	3
Comorbidity (Charlson comorbidity index score) ("C")	0	0
	1	1
	2	2
	3	3
	≥ 4	5
Visits to emergency department during previous 6 mo ("E")	0	0
	1	1
	2	2
	3	3
	≥ 4	4

Van Walraven et al. (2010) Van Walraven C, Dhalla IA, Bell C, Etchells E, Stiell IG, Zarnke K, Austin PC, Forster AJ. Derivation and validation of an index to predict early death or unplanned readmission after discharge from hospital to the community. *CMAJ: Canadian Medical Association Journal*. 2010;182(6):551–557. doi: 10.1503/cmaj.091117

Lahey-Derived Model:

Readmission Risk		
Readmission Risk:	34	
Patient has >1 ED visit in last 6 mo:	2	
IN & OBS visits 365 days:	5	
Length of stay:	5	
Patient is >65 yrs old:	0	
Cancer:	2	
Metastatic Cancer:	6	
Hypertension:	1	
CHF:	4	
HX of Myocardial Infarction:	1	
COPD:		
Dementia:		
CAM Delirium:		
Depression:	1	
Sepsis:		
HIV/AIDS:		
Diabetes:	2	
Liver Disease:		
Chronic Renal Impairment:	2	
Added social determinants of health	Alcohol Dependence & Abuse:	
	Drug Dependencies:	1
	ADM RISK: BMI > 35:	
	Current Smoker/Tobacco:	
	Lives Alone:	
	Current Medications > 8:	2

CASE REPORTS

Congenital Sternal Cleft and Mediastinal Lung Hernia in a 76-year-old Woman

Brad Perry, M.D.,¹ and John M. Holbert, M.D.¹

Abstract

Congenital sternal cleft is a rare developmental anomaly, resulting from failure of normal ventral chest wall fusion, which produces a cleft in the sternum. Mediastinal pulmonary hernia is exceedingly rare in which all previously reported cases involved herniation of the posterior mediastinal pleura. Presented is a case of a woman with a partial congenital sternal cleft with the first reported concomitant anterior mediastinal pulmonary hernia.

Introduction

Sternal cleft and anterior mediastinal pulmonary hernia are both rare findings; simultaneous occurrence of these two conditions points to a common embryologic origin. Sternal formation is complete by the tenth week of development in which the lateral plate mesoderm migrates and the developing chest wall fuses at the sternum.¹ A sternal cleft results if this fusion fails. Sternal clefts are complete if the sternum is completely absent, or partial if sternal formation is incomplete, leaving a longitudinal defect. Sternal clefts are more commonly partial, as was seen in this patient. The incidence of sternal cleft is unknown.² Sternal cleft occurs rarely in isolation and is usually associated with various genetic syndromes including PHACES.^{2,3} PHACES syndrome includes posterior fossa abnormalities, hemangiomas, arterial lesions, cardiac abnormalities, aortic coarctation, eye abnormalities, and sternal defects.² Cases are routinely diagnosed at birth or early infancy but can be diagnosed even earlier on prenatal ultrasound.⁴ The few previously published cases of adult sternal clefts have primarily been in young adults, with the oldest reported case in a 52-year-old patient who proceeded to surgical repair.^{2,5,6}

Prompt surgical repair of sternal cleft is recommended for protection of the heart and mediastinal structures.³ Surgery is usually performed in early infancy, because the flexibility of the chest wall makes repair much easier. Surgical treatment is indicated because of the susceptibility of the patient to trauma without an intact chest wall, concern for spread of skin infection to the pericardium, and paradoxical movement of the anterior chest wall, which can lead to mediastinal displacement and right ventricular failure.⁷ Several techniques have been described, including cartilage and muscle mobilizations and periosteal flaps.⁷

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Case Report

A 76-year-old woman with a history of congestive heart failure (CHF), diabetes, and hypertension presented with a CHF exacerbation. Initial chest radiographs showed a possible retrosternal mass. Unenhanced chest computed tomography (CT) was performed to assess the anterior mediastinum. Although no retrosternal mass was present, CT showed a partial sternal cleft and an associated hernia of the right middle lobe through the anterior mediastinal pleura (Figures 1A, 1B, and 2). The patient had no history of trauma or surgery, other than prior ICD placement eight years earlier after an episode of ventricular fibrillation.



Figure 1A. Coronal noncontrast reformatted CT image with intermediate bone and lung windows in which the gold arrow shows the sternal cleft and the black arrow shows the associated hernia of the right middle lung lobe through the anterior mediastinal pleura.

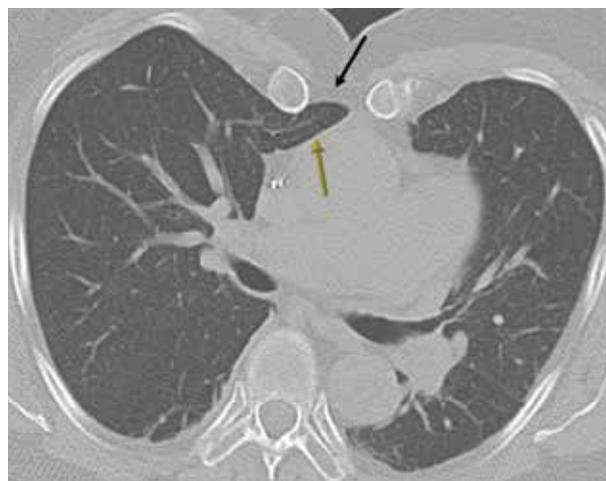


Figure 1B. Axial noncontrast CT image with intermediate bone and lung windows, in which black arrow denotes the sternal cleft with pectus excavatum and gold arrow denotes partial herniation of a right middle lobe through the anterior mediastinal pleura.

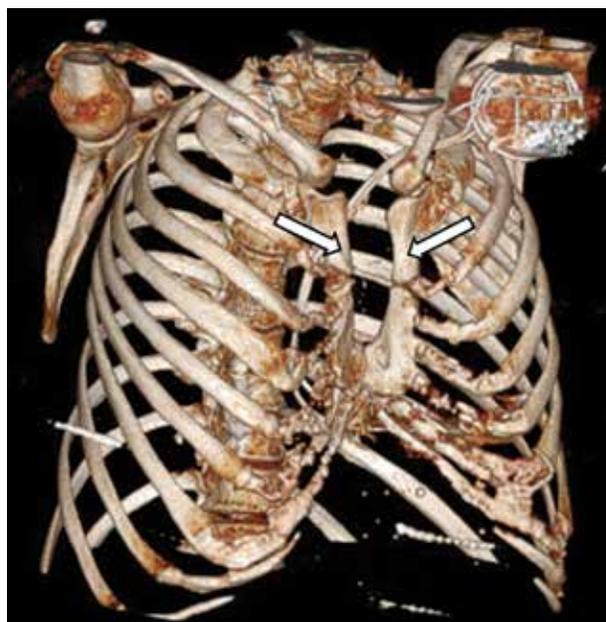


Figure 2. Right anterior oblique 3D bone reconstruction in which white arrows show the partial sternal cleft with pectus excavatum.

Discussion

The association between sternal cleft and pectus excavatum is rare, although it has been reported in the literature.⁸ Pectus excavatum results from abnormal growth of the lower costal

cartilages, leading to a depressed sternum.⁸ Repair of pectus excavatum and sternal cleft can be achieved simultaneously in young patients.⁸

This patient's right middle lobe hernia through the anterior mediastinal pleura is concordant with a midline fusion defect. To our knowledge, true anterior mediastinal pulmonary hernia through a defect in the mediastinal pleura has not been described alone or in association with sternal cleft. After lobectomy or pneumonectomy, the mediastinal pleura remains intact on both sides, so the extension of the contralateral lung across midline to fill the operative space is not a true hernia. However, the rare occurrence of posterior mediastinal lung herniation has been described with pulmonary sequestration and hypogenetic lung syndrome.^{9,10} Two additional conditions have a similarity to mediastinal pulmonary hernias but are not true mediastinal pulmonary hernias.^{11,12} The first is congenital fusion of the posterobasal portions of both lungs, which leads to formation of a continuous band of pulmonary parenchyma anterior to the descending thoracic aorta and posterior to the heart (commonly referred to as horseshoe lung).¹¹

The second is a single continuous pleural space (commonly referred to as buffalo chest).¹² Buffalo chest typically occurs after cardiothoracic surgery, although it can arise spontaneously.

The classification of lung hernias was originally described by Morel-Lavallée.¹³ He characterized hernias according to anatomic location (cervical, thoracic, or diaphragmatic) and etiology (congenital or acquired). Congenital hernias are caused by weakness of the thoracic wall musculature or increased intrathoracic pressures.¹⁴ According to Shameem et al, most lung hernias are acquired, predominantly after trauma. Trauma can lead to immediate lung herniation or delayed herniation secondary to chronic weakening of the intercostal musculature. Intercostal hernias represent approximately 70% of all lung hernias and can be seen in the setting of increased intrathoracic pressures, such as those occurring in weightlifters and wind instrument musicians.¹⁵ Common complications of both congenital and acquired lung hernias include pain, difficulty breathing, and incarceration of lung parenchyma.¹⁵ Cervical lung hernias are less common and typically occur in elderly patients with weak supraclavicular fascia.¹⁶ The lung herniates into the anterior thoracic inlet between the anterior scalene and sternocleidomastoid muscles. Diaphragmatic lung

hernias are exceedingly rare and are mostly seen in infants.¹⁵

This patient was born in 1940, before the first surgical repair of sternal cleft in 1943.¹ Sternal cleft predisposes patients to arrhythmias and could contribute to this patient's heart disease.⁷ Given the risks and difficulties associated with surgical repair, as well as this patient's relative lack of symptoms, partial sternal cleft and mediastinal lung hernia are unlikely to pose a threat to this patient's health.

Disclosures

No financial support given. Authors report no conflict of interest.

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CASE REPORTS

Perioperative Management of a Patient with An Anomalous, Retroaortic Left Circumflex Coronary Artery During Mitral Valve Replacement

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Introduction

The anomalous origin of a coronary artery can have a variable clinical significance ranging from being an incidental discovery to sudden death.^{1,2} The origin of the left circumflex coronary artery (CCA) from the right aortic sinus is a rare finding with a probably benign natural history.^{3,4} However, this anomaly has significant implications during aortic and/or mitral valve surgery. We report a case where a patient scheduled to undergo mitral valve repair/replacement was found to have anomalous origin of the CCA during cardiac catheterization and was closely monitored for complications intraoperatively using transesophageal echocardiography.

Case Report

A 61-year-old female (120.2 kg) with past medical history of hypertension, obstructive sleep apnea treated with bilevel positive airway pressure, moderate to severe pulmonary hypertension, type II diabetes, cirrhosis due to nonalcoholic steatohepatitis, and rheumatic mitral stenosis presented to the hospital with worsening dyspnea. She had previously undergone a percutaneous balloon valvuloplasty of her mitral valve three years prior. Her medications included amlodipine, carvedilol, furosemide, spironolactone, omeprazole, alprazolam, and escitalopram. Preoperative testing including a transthoracic echocardiogram which demonstrated an ejection fraction of 60-65%, diffuse thickening of the mitral valve leaflets with restricted leaflet opening, a mitral valve area of 0.94 cm² by pressure half time, and a mean gradient across the mitral valve of 9 mmHg with a heart rate of 53 beats per minute and sinus rhythm. Left heart catheterization revealed non-obstructive coronary artery disease, but was concerning for an anomalous CCA (Figure 1) that was not detected during prior cardiac catheterizations. The CCA appeared to originate from the right aortic sinus, but it was unclear whether it was a proximal branch of the right coronary artery (RCA) or if it had a separate ostium. Furthermore, the course of the CCA was not described in the report. Right heart catheterization demonstrated a pulmonary artery pressure of 61/36 mmHg, an improvement from 101/50 mmHg three years prior. The patient was treated with diuretics and referred for surgical mitral valve replacement.

On the day of surgery, her blood pressure was 176/66 mmHg with a heart rate of 52 beats per minute. Standard monitors and an arterial line were placed, and she was intubated after an uneventful induction with 2 mg midazolam, 100 mg lidocaine, 30 mcg sufentanil, 50 mg propofol, 10 mg vecuronium, and 60 mcg phenylephrine. An introducer central line and pulmonary artery catheter were subsequently placed without difficulty. The cardiac indexes provided by the pulmonary artery catheter ranged from 2.6-3.4 L/min/m² before cardiopulmonary bypass (CPB). In addition, a

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Figure 1. Coronary angiogram showing anomalous CCA (yellow arrows) with retroaortic course.

transesophageal echocardiography (TEE) probe was placed for cardiac evaluation. TEE exam demonstrated normal biventricular function, severe mitral stenosis, mild mitral regurgitation, trace aortic regurgitation, and trace tricuspid regurgitation. The right ventricular systolic pressure could not be estimated due to insufficient tricuspid regurgitation. Despite the history of pulmonary hypertension, there was no right ventricular hypertrophy or dilation. In addition, the anomalous coronary artery was visualized (Figure 2 and Figure 3). Color Doppler interrogation of the coronaries demonstrated the origins of the CCA and RCA, which appeared to arise from the same ostium. The CCA then took a retroaortic course and was found to travel along the aorto-mitral continuity. Color Doppler flow was confirmed to be in the CCA before CPB. These findings were discussed with the surgical team before valve implantation to help prevent inadvertent harm to the CCA.

After CPB was initiated, the heart was arrested using antegrade Del Nido cardioplegia. The patient underwent a mitral valve replacement with a 25 mm Epic™ bioprosthetic valve. The patient successfully separated from CPB without pharmacologic support and the mitral valve was noted to be well seated and competent without intravalvular or paravalvular regurgitation. Although the mitral valve was thought to be replaced without harm to the CCA, a comprehensive TEE exam was repeated to be thorough, including confirmation that color Doppler flow was still present in the CCA without any regional wall motion abnormalities (with close examination of the lateral wall of the left ventricle). She was subsequently transferred to the intensive care unit (ICU). Her postoperative



Figure 2. TEE mid-esophageal aortic valve long axis view using X-plane technique. The picture on the right represents the orthogonal view of the picture seen on the left. The red arrows indicate the CCA. LA = left atrium; MV = mitral valve; AV = aortic valve.

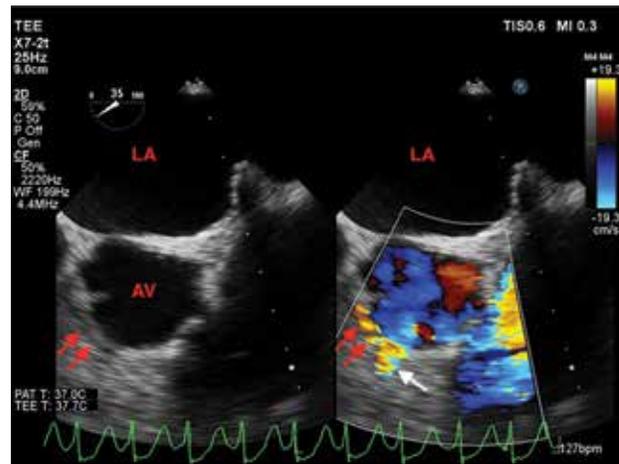


Figure 3. TEE mid-esophageal aortic valve short axis view using color compare mode. The same picture can be seen in 2D without color (left) and with color (right). The CCA originates from the right aortic sinus (course is indicated by the red arrows). The white arrow indicates right coronary artery flow. LA = left atrium; AV = aortic valve.

course was remarkable for altered mental status thought to be related to her liver dysfunction, but there were no apparent complications related to her anomalous CCA.

Discussion

Coronary artery anomalies represent a diverse subset of congenital disorders. These coronary arteries can arise from

different sinuses, or possibly other unusual areas such as cardiac chambers, the ascending aorta, and the pulmonary artery. Ultimately, the clinical implications of these anomalies are highly variable and are dependent on the origin and course of the artery.

An anomalous CCA originating from the right sinus of Valsalva is an uncommon finding. While one study found the anomaly described in this report in 13 out of 1,950 (0.67%) patients, a larger study only found it in 10 out of 12,457 (0.08%).^{5,6} Some coronary variants predispose patients to serious complications such as myocardial ischemia, volume overload, and increased risk for atherosclerosis. Fortunately, a CCA originating from the right sinus is thought to be a predominantly benign finding.⁷ However, there are some instances where patients with this anomaly are predisposed to complications. First, patients undergoing aortic or mitral valve surgery are at risk for compression from prosthetic valves or rings.⁸⁻¹⁰ After the anomalous CCA originates from the right sinus of Valsalva, it takes a retroaortic course and runs just above the aorto-mitral continuity. This results in a close anatomic relationship with the anterior mitral annulus and aortic valve. It is therefore recommended that a smaller sized prosthesis should be considered, if required, to reduce the risk of mechanical compression or distortion of the CCA. In addition, CCA ligation or laceration are also possibilities. Second, patients with dilated aortic roots may be at risk for compression of the CCA due to its retroaortic course.¹¹ Third coronary artery bypass grafting to the proximal anomalous CCA could be technically challenging due to the retroaortic course.^{12,13} Fourth, aortic root replacement with reimplantation of the CCA may require extensive mobilization of the coronary artery to prevent kinking.⁷ Finally, inadequate myocardial protection during CPB could occur in some circumstances. For example, if the CCA has a separate coronary ostium from the right and left coronary arteries, antegrade cardioplegia administered by direct cannulation of the individual coronary ostia requires the surgeon to recognize the presence of the additional ostium and perform selective cannulation.

Cardiac catheterization is able to demonstrate the anomalous CCA. One suggestive finding is the “aortic root sign.” This sign refers to appearance of the CCA coursing behind the aortic root when obtaining a left ventriculogram in the right anterior oblique projection.¹⁴ In addition, the “nonperfused

myocardium sign” is also characteristic albeit a misnomer; it is defined as absent arterial flow to a significant area of the posterolateral left ventricle when injecting dye into the left main coronary artery. Normally, the CCA originates from the left main coronary artery (LMCA). Thus, injection of dye into the LMCA would demonstrate arterial flow to the areas that are perfused by the CCA, such as the posterolateral left ventricle. However, if the CCA does not originate from the LMCA, then there is absent arterial flow and this could be misinterpreted as a perfusion defect. Echocardiographically, the anomalous CCA typically manifests as an atypical, small, and round structure that appears to be directly adjacent to the aorto-mitral continuity. Some authors have referred to this as the “bleb sign.”¹⁵

There are three variants of an anomalous CCA originating from the right sinus of Valsalva.¹⁶ Type I refers to a separate ostium for both the RCA and CCA. Type II refers to a single, common ostium for both the RCA and CCA. Type III refers to when the CCA is a proximal branch of the RCA. In this patient, the left heart catheterization was not able to definitively show which type this patient exhibited. The TEE exam suggested that this patient had a type II variant. Although direct visualization during surgery could have confirmed this, the surgical team did not attempt to distinguish which type was present.

Although the abnormal CCA was correctly recognized in this case, there are other diagnoses that could be considered based on its echocardiographic profile. For example, the appearance in the midesophageal long axis may be confused for a fistula between the aorta and the left atrium. The appearance of the CCA as it takes its retroaortic course in the midesophageal short axis view could also raise the possibility of an aortic root abscess. Color Doppler interrogation can be useful in evaluating these diagnoses. The presence or lack of vegetations and clinical suspicion based on patient history could also help assess the likelihood of these diagnoses when establishing a differential.

In this case, the diagnosis of an anomalous CCA was made based on the preoperative cardiac catheterization, so the main intraoperative challenges were identifying the CCA echocardiographically, determining its course, evaluating the CCA both pre- and post-CPB for evidence of stenosis,

and examining the left ventricle for any evidence of regional wall motion abnormalities. A comprehensive TEE exam demonstrated the course of the CCA to be retroaortic with close proximity to the aorto-mitral continuity. The CCA appeared patent by two-dimensional and color Doppler echocardiography, with demonstration of flow both before and after the mitral valve was replaced. In addition, no electrocardiogram changes or wall motion abnormalities were seen post-CPB. Had injury to the CCA occurred, coronary artery bypass grafting and percutaneous coronary intervention (PCI) are options that have been used with success.^{4,17} Although there were no apparent complications related to the anomalous CCA in this case, the ability to carefully interrogate the coronary artery and evaluate for any clinical sequelae after mitral valve replacement provided reassurance to the surgical and ICU teams.

A discussion about the abnormal variant anatomy is important postoperatively both during transition of care to the ICU team as well as after the patient is discharged from the hospital. Complications are not limited to the operating room and sudden death has been reported even five years after surgery.⁸ In this case, the details of her abnormal coronary anatomy and possible risks were included as part of the transfer of care to the ICU team. In addition, these findings were discussed with the patient to ensure she was aware. Should the patient develop problems in the future due to compression, PCI may prove a therapeutic option.¹⁷

Conclusion

This case highlights the successful management of a patient undergoing mitral valve replacement with an anomalous CCA. The role and utility of various imaging modalities was also exemplified. While cardiac catheterization played a key role in diagnosis, TEE was instrumental in intraoperative evaluation both before and after mitral valve replacement. Although this particular coronary artery variant is typically benign, clinicians should be aware of the potential complications during cardiac surgical procedures as well as methods to lower perioperative risk.

Disclosures

No financial support given. Authors report no conflict of interest.

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CASE REPORTS

Tapia Syndrome: A Rare Cause of Dysphonia and Dysphagia

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Introduction

Tapia syndrome is a rare disease described in literature fewer than seventy-five times.¹ The syndrome is often associated with airway manipulation and comprises paralysis of the hypoglossal nerve (cranial nerve [CN] XII) and the recurrent laryngeal branch of the vagus nerve (CN X).^{1,2} Patients often present with dysphonia, dysphagia, and tongue deviation towards the affected side.^{1,2} Treatment involves corticosteroids and speech therapy, and recovery from Tapia syndrome usually takes six months.^{2,3} This case illustrates the presentation of a rare complication and the full recovery process from Tapia syndrome after undergoing vocal fold (VF) injection laryngoplasty.

Case Report

A 23-year-old man presented with a three-week history of dysphagia, dysarthria, dysphonia, and tongue weakness that developed immediately following a three-day intubation for respiratory failure secondary to acute liver failure. Voice symptoms prevented him from attending his regular employment in sales.

On examination, he had leftward tongue deviation (Figure 1), and video laryngostroboscopy (VLS) revealed an immobile left VF. The remainder of the neurologic exam was normal. Computed tomography of the brain was unremarkable. Hypoglossal electromyography (EMG) did not show hypoglossal neuropathy. Laryngeal EMG did not reveal an increase in resting activity; upon activation of the left thyroarytenoid/lateral cricoarytenoid muscle complex, several motor units of normal morphology, near-normal motor recruitment configuration, appropriate recruitment, and no fibrillations were noted. Synkinesis was not observed.

These EMG results suggested that recovery of motion was likely; in the presence of acutely problematic voice changes, however, the patient elected for immediate VF injection laryngoplasty using an aqueous/glycerin/carboxymethylcellulose (Prolaryn Gel™ injectable implant, Merz, North America, Raleigh, North Carolina).

One month post-operatively, his dysphonia was much improved, and VLS revealed a recovering but still hypomobile VF (Figure 2). Bilateral tongue movement was now present, though not fully symmetric. Dysphagia was much improved. Three months post-operatively, VF function and tongue movement had fully recovered.

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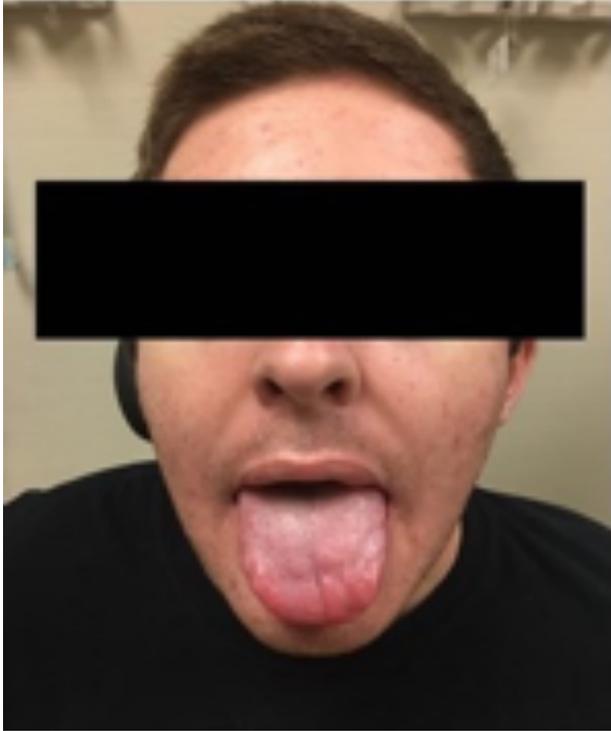


Figure 1. Patient shown with a leftward deviated tongue.



Figure 2. Laryngoscopic image shows medialization of the left vocal fold.

Discussion

Cases of Tapia syndrome have been described fewer than seventy-five times.¹ It is a condition characterized by simultaneous paralysis of the hypoglossal and recurrent

laryngeal nerves. It was first described by Spanish laryngologist Antonio Garcia Tapia in 1904 after observing the phenomena in a toreador injured posterior to the angle of the mandible by a bull.⁴ The spinal accessory nerve is spared, differentiating this syndrome from the jugular foramen syndromes, such as Vernet (affecting CN IX, X, XI), Collet-Sicard (affecting IX, X, XI, XII) and Villaret (Collet-Sicard and Horner's syndrome).^{2,4} The etiology is not entirely clear, but compression or stretching of the hypoglossal and vagus nerves where they cross at the nodose ganglion is often provided as an explanation.^{2,5,6} More specifically, causes may include neuropathy due to head extension during intubation, extreme lateral flexion of the head, endotracheal tube malposition or overinflation, translaryngeal cuff inflation, or accidental extubation.^{5,6}

Patients often present with voice changes, ipsilateral tongue deviation, and dysphagia. Brain imaging should be performed to rule out central causes. Although there is no clearly established treatment regimen, patients who receive early intervention with oral corticosteroids and voice therapy have shown earlier improvement.² Unfortunately, 37% of patients show incomplete recovery or lack of functional recovery altogether.^{2,4} The difference in outcomes may be influenced by the degree of nerve injury. Full recovery may take up to 13 months, and VF medialization can dramatically improve quality of life. Prognostic implications from laryngeal EMG may influence the choice of injection material.^{6,7}

Conclusion

This case report is presented to contribute to the literature regarding Tapia syndrome and to describe a patient who fully recovered after 3 months post-VF injection laryngoplasty. The procedure was performed to treat the patient's voice changes, but it also showed to be useful in the treatment of his dysphagia and tongue paralysis. While this condition is very rare, Tapia syndrome should be considered if there is suspicion of concurrent paralysis of the hypoglossal and recurrent laryngeal nerves. This syndrome should also be considered if imaging excludes jugular foramen syndromes, internal or external carotid artery dissection, and complications with CN X, CN XII, the brain and chest.²

Disclosures

No financial support given. All authors report no conflict of interest.

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CASE REPORTS

Lung Cancer Metastasis to the Cricoid Cartilage: A Case Report

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Introduction

Identifying metastatic sites on cancer staging imaging is a critical task of the radiologist, as it influences both the treatment and prognosis of the patient. Radiologists who routinely read these staging scans are accustomed to carefully examining common metastatic sites such as lymph node drainage basins, bones and other organs, but they may not scrutinize an area such as the laryngeal cartilages, a rare site for metastatic disease from primary tumors outside the neck. A metastasis to this region would be important to note, not only for staging purposes, but also because the patient may be symptomatic if the lesion exerts mass effect on the airway or vocal folds. We present a case of lung cancer metastatic to the cricoid cartilage in the setting of other osseous metastases.

Case Presentation

A 67 year-old woman presented to the Emergency Department with two months of worsening chest discomfort, shortness of breath and intermittent cough. Notably, the patient had no smoking history. Her chest radiograph revealed a widened mediastinum and small right pleural effusion. Chest CT subsequently revealed a right suprahilar mass with mediastinal invasion, most concerning for primary bronchogenic carcinoma, with mediastinal lymphadenopathy as well as osseous and hepatic metastases (Figure 1B). In addition, faint sclerosis of the cricoid cartilage, consistent with metastasis, was visible (Figure 1A). Staging PET/CT confirmed hypermetabolic activity throughout the skeleton as well as within the liver lesion (Figure 1C), again compatible with metastatic disease. The laryngeal region was poorly evaluated due to a small amount of physiologic uptake by the vocal cords. Bronchoscopy followed by tissue sampling of the liver and bone lesions revealed metastatic pulmonary adenocarcinoma. While on chemotherapy, the patient experienced approximately one year of stable disease by CT imaging. Thereafter, the patient had gradual progression of disease. In addition to increased number and size of osseous and hepatic lesions, a laryngeal cartilage metastasis became more sclerotic and larger (Figure 2A), mirroring the progression in other organs (Figure 2B). The patient's chemotherapy was adjusted owing to disease progression. Subsequent imaging demonstrated stable metastatic disease.

Discussion

Laryngeal cartilage metastases, especially from infraclavicular primary neoplasms, are rare and have been infrequently reported in the literature. More specifically, a

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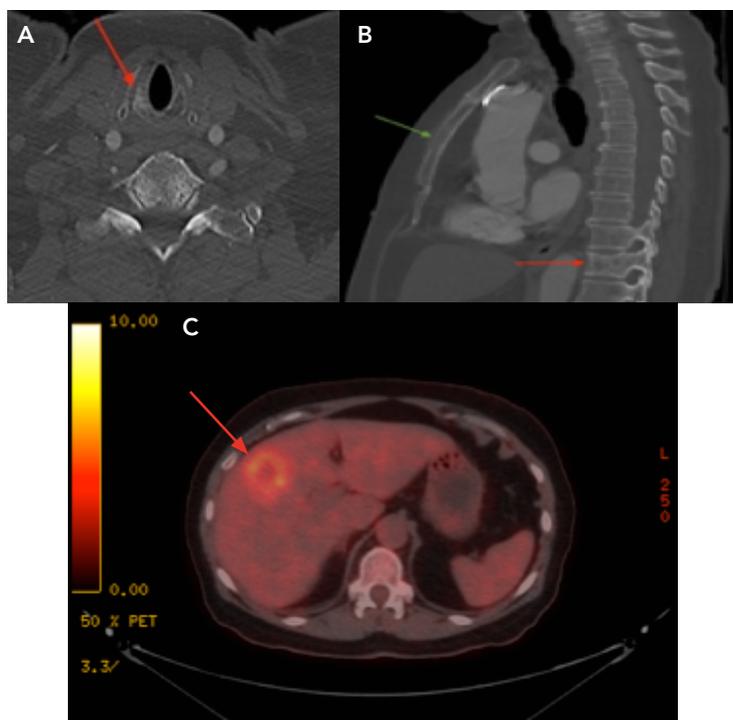


Figure 1A. Initial axial CT scan revealed a faint area of sclerosis within the right aspect of the cricoid cartilage (arrow); **1B:** Initial sagittal CT reconstruction shows metastasis to the T12 vertebral body (red arrow) as well as some cortical thinning in the mid-sternum (green arrow), suspicious for another metastatic site; **1C:** Staging PET/CT shows a hypermetabolic lesion in the right hepatic lobe (arrow). FNA of this lesion later confirmed metastatic pulmonary adenocarcinoma.

lung cancer metastasis to the laryngeal cartilage is quite rare, with less than ten cases currently documented in the literature. Lung cancer often metastasizes hematogenously, and the laryngeal cartilages are relatively avascular in comparison to bone and soft tissues.¹ For example, when lung cancer metastasizes to sites within the neck, thyroid gland and cervical chain lymph node involvement is more commonly seen due to the increased vascular supply. In an older patient, however, laryngeal metastases may occur in the setting of osseous metastatic disease due to ossification of the laryngeal cartilages.² Hematogenous spread likely occurs either via the external carotid artery to the superior thyroid artery or retrograde through the vertebral venous plexus.³ Bone, brain and liver are the most common metastatic sites of non-small cell lung cancer outside of the lung itself.⁴ When a laryngeal cartilage metastasis is seen, a head and neck primary cancer is often the culprit, as it is rare for infraclavicular primary neoplasms to present in such a fashion.⁵ If a primary neoplasm has not yet been established, it is important to consider that melanoma, renal cell, colorectal, breast and lung carcinoma are the five most common primary neoplasms to metastasize to the larynx.⁶

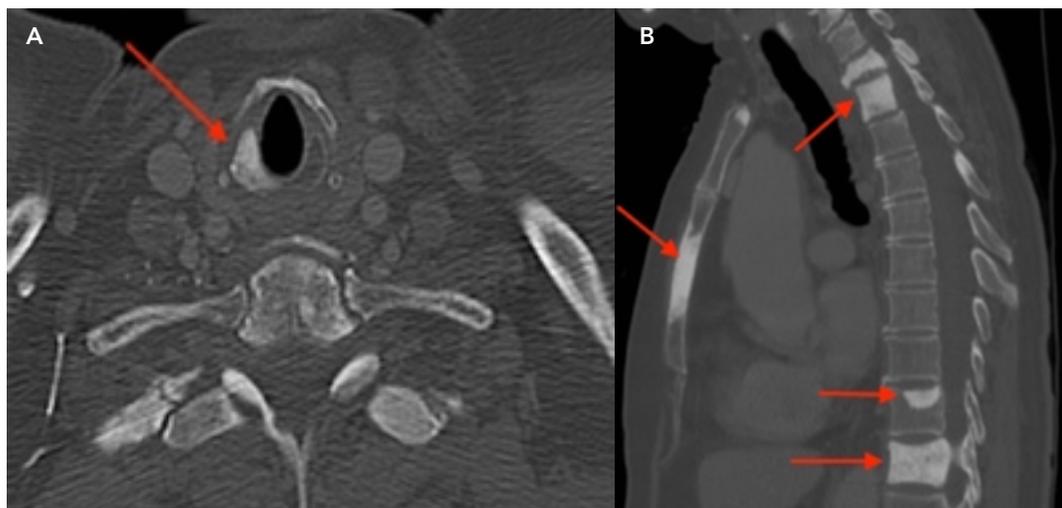


Figure 2A. Axial CT scan over one year later reveals increase in size and degree of sclerosis of the cricoid metastasis without soft tissue component (arrow); **2B:** Sagittal CT reconstruction over one year later (same date as 2A) shows marked worsening of blastic osseous metastatic disease in the thoracic spine and sternum (arrows).

The laryngeal cartilages can be a difficult area to evaluate by PET due to frequently identified physiologic uptake in the nearby vocal cords. Recognition of a metastasis to the laryngeal cartilages on anatomic imaging is important, as it may impact both prognosis and treatment options. More aggressive intervention, such as laryngectomy or radiation therapy, may be indicated in the setting of oligometastatic disease to the larynx or if the cartilaginous metastasis is associated with a soft tissue component producing hoarseness or dysphagia, unlike in our patient.

Conclusion

Metastases to the laryngeal cartilages are rare, especially from primary neoplasms outside the head and neck. It is important that the radiologist be attuned to this region on anatomic imaging, such as CT, as this area can be difficult to evaluate by PET due to confounding nearby physiological uptake. Metastasis to this region should be mentioned in reporting, as it may impact prognosis and treatment but may also necessitate otolaryngology referral if the patient is symptomatic.

Disclosures

No financial support given. All authors report no conflict of interest.

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CASE REPORTS

Radiation Induced Brachial Plexopathy Neuroimaging Findings

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Abstract

A 68-year-old woman with a history of myasthenia gravis, tonsillar cancer, and invasive ductal breast carcinoma, treated with radiotherapy in 1995 and 2017 respectively, presented with respiratory failure and upper extremity weakness. Treatment for presumed myasthenic crisis failed. Electromyography showed mixed myopathic/neuropathic units with myokymia in the right biceps. Deltoid biopsy showed neurogenic atrophy with hyperchoic brachial plexus on ultrasound. Magnetic resonance (MR) of the plexus showed bilateral smooth, enlargement and contrast enhancement within the brachial plexus, as well as right deltoid denervation and apical pleural thickening consistent with radiation induced plexopathy (RIBP). A literature review on average latency of radiation induced plexopathy and the symmetrical, bilateral nature, our patient's plexopathy supported that tonsillar radiation rather than unilateral breast radiation was the etiology of this patient's presentation. This report is significant because it details the time delayed response of radiation induced plexopathy in the setting of a clinically complex patient with two prior radiation treatments and myasthenia gravis.

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Introduction

Radiation induced brachial plexopathy (RIBP) is an important side effect of radiation-based cancer treatments. Symptoms of RIBP include paresthesias, weakness, pain, and muscle atrophy. RIBP can contribute significantly to patient morbidity after radiation treatment.¹ This report details a complicated case of RIBP with associated neuro-imaging findings in a patient who presented in respiratory failure with a history of myasthenia gravis and two prior radiation treatments in the brachial plexus area in 1995 and 2017.

Case Report

A 68-year-old woman with a past medical history of antibody-negative myasthenia gravis (MG), left tonsillar cancer (status post 1995 radiation therapy; no chemotherapy), invasive ductal breast carcinoma and DCIS (status post 2017 radiation therapy), COPD, pulmonary fibrosis, and atrial fibrillation presented to an outside hospital for respiratory failure. Respiratory failure resulted from a presumed myasthenic crisis in the setting of aspiration pneumonia and *Clostridioides difficile* infection, at which point she was intubated and received IVIG for five days with minimal improvement. She was extubated and worsened acutely, so she was transferred to the neurology intensive care unit for further management.

The patient was treated with seven sessions of plasma exchange (PLEX) without improvement and remained intubated without sedation with intact and normally

functioning cranial nerves, 3/5 neck flexion weakness, 4-/5 right deltoid and 2/5 left deltoid strength in the setting of a known left-sided rotator cuff tear. The remainder of her strength testing showed 4/5 neck extension strength, 4-/5 triceps strength bilaterally, 4/5 biceps strength bilaterally and 4+/5 grip strength bilaterally. Her lower extremities were 4/5 strength throughout bilaterally except for 5/5 plantarflexion bilaterally. Reflexes were 2+ and symmetric in all four extremities with downgoing Babinski, and sensation was intact to light touch, vibration, and pinprick in all four extremities. She had no ataxia, dysmetria, or tremor.

With her lack of clinical improvement in respiratory strength and peripheral weakness, a thorough workup was performed: AChR and Anti-MuSK antibodies were negative, EMG/NCS showed a mixture of myopathic and neuropathic units with notable myokymia in the right biceps and normal repetitive stimulation of the left ADQ and trapezius. A right deltoid biopsy was consistent with neurogenic atrophy and neuromuscular ultrasound showed atrophy and hyperechoic appearance of the brachial plexus.

In the setting of her past tonsillar and breast radiation, RIBP was suspected and an MR of the right brachial plexus with and without contrast was obtained.

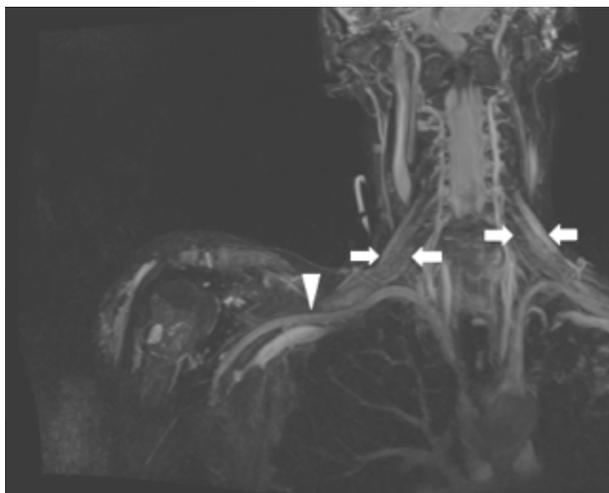


Figure 1. A thick maximum intensity projection (MIP) of STIR SPACE sequence shows bilateral enlargement (solid arrows) and enhancement of the brachial plexus, in which extent of augmentation is greater in the proximal and superior aspects. Anatomic relationship of brachial superior to the subclavian artery (arrowhead) is demonstrated.

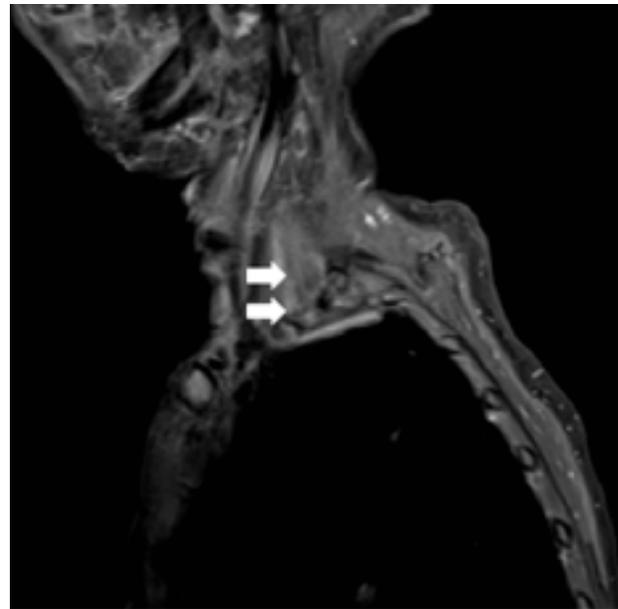


Figure 2. T1 fat saturation (Dixon method) post-contrast image shows smooth enhancement within the brachial plexus (solid arrows), consistent with radiation-induced plexopathy. There is no nodular enhancement, which would be more concerning for metastatic spread to the brachial plexus.

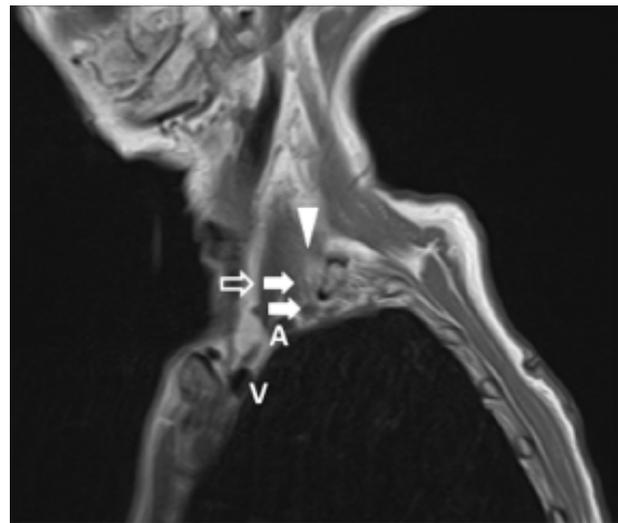


Figure 3. A T1 sagittal cut without contrast shows the relationship of the superior, middle, and inferior trunks of the brachial plexus (solid arrows) are enlarged. The plexus can be seen posterior to the anterior scalene (open arrow), the subclavian vein (V) and the subclavian artery (A), and anterior to the middle scalene (arrowhead). The MR brachial plexus showed smooth, symmetric enlargement and enhancement of the proximal superior brachial plexus (Figures 1, 2, and 3) as well as right apical pleural thickening (Figure 4), likely consistent with radiation fibrosis.

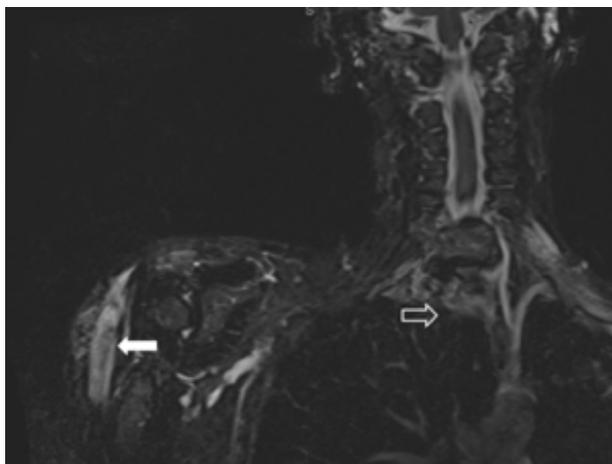


Figure 4. Coronal sequence showing significant abnormal signal within the right deltoid musculature (solid arrow), suggestive of denervation, which correlates with the patient's weakness. Apical pleural thickening can also be seen (empty arrow).

Significant deltoid and infraspinatus denervation was also identified with abnormal signals in both, correlating with the patient's significant weakness (Figure 4).

Discussion

RIBP is a known form of radiation-induced peripheral neuropathy, first described by Stoll and Andrews over fifty years ago.² They described the pathophysiology of RIBP on autopsy as fibrous replacement and thickening of the fibrils with demyelination and atrophy.² RIBP is known to affect upper and middle trunks of the brachial plexus, which is consistent with our patient's imaging and clinical findings (Figure 1).¹

The average latency of RIBP after radiation treatment is several years, cited as an average of 4.26 years in literature by Cai et al versus an average of 8.2 years, according to a cohort studied by Gu et al with nasopharyngeal carcinoma.^{1,3} The average latency of RIBP is 4-8 years based on a few small studies. Our patient had two prior radiation treatments of unknown type and dose to the brachial plexus area in 1995 and 2017, making either of them possible culprits for her fibrotic changes and clinical decompensation.

The symmetric nature of the changes makes the more remote tonsillar cancer radiation a more likely cause of the RIBP. Additionally, Powell et al followed 449 breast cancer patients

who received radiotherapy to the breast and lymph nodes and found no cases of RIBP in the first ten months following radiotherapy to the breast and nodes.⁴ Our patient's breast radiation 8 months prior is therefore an unlikely cause of the plexus enlargement.

In the setting of the MR findings, EMG-confirmed myokymia, and a history of radiation to chest and neck, the patient's progressive weakness and respiratory failure was likely due to chronic radiation-induced brachial plexopathy.

Disclosures

No financial support given. All authors report no conflict of interest.

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CASE REPORTS

A Rare Cause of Pediatric Deep Vein Thrombosis

David A. Masneri, D.O.¹ and Zachary Burroughs, M.D.²

Abstract

Pediatric deep vein thrombosis (DVT) is rare in comparison to adult DVT, but it can be associated with significant morbidity in the form of post-thrombotic syndrome consisting of persistent pain and edema. We describe a case of a previously healthy 13-year-old boy who presented to the emergency department with profound right lower extremity edema from massive from massive clot burden as a result of extensive right lower extremity deep vein thrombosis. Computerized tomography angiography revealed inferior vena cava (IVC) agenesis, a rare cause of DVT. He received intravenous anticoagulation and subsequent catheter-directed ultrasound facilitated thrombolytic therapy. He responded well to this therapy and was discharged on continued oral anticoagulation. A three month follow-up revealed significant improvement in pain and swelling. In young patients presenting with unprovoked lower extremity DVT, IVC atresia or agenesis should be included in the differential diagnosis.

Case Report

A previously healthy 13-year-old boy presented to the emergency department with leg pain and swelling. He was diagnosed with influenza three days earlier and had since been resting in bed. The pain and swelling began one day prior and continued to worsen. He denied any previous similar symptoms, family history of clotting or bleeding disorder, and recent trauma. Vital signs were within normal ranges, with blood pressure 136/78 mm Hg, pulse 85 bpm, temperature 36.7° C, respiratory rate 20 bpm, and pulse oxygen saturation of 98% on room air. Physical exam revealed benign cardiac, pulmonary, and abdominal examinations. Extremity examination revealed profound edema (3 plus and to above the knee) and mottling of the right lower extremity (Figure 1). Distal posterior tibial and dorsalis pedis pulses were normal. Pertinent laboratory results included an elevated d-dimer level of > 20 mcg/ml (normal range = 0.0-0.5mcg/ml). Complete blood count, basic metabolic panel, and prothrombin/INR were unremarkable. Ultrasound of the right lower extremity revealed extensive deep vein thrombosis involving the right common femoral, femoral, profunda femoral, popliteal, posterior tibial, and peroneal veins (Figure 2). He was diagnosed with a massive DVT extending from the iliac to the tibial veins. Computerized tomography angiography (Figure 3) demonstrated an atretic IVC with associated abnormal collateral venous drainage system. He received intravenous anticoagulation with unfractionated heparin. Vascular surgery was consulted emergently and performed catheter-directed ultrasound facilitated thrombolytic therapy. He had an uneventful hospital course and was discharged on continued

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(lifelong) oral anticoagulation. At three-month follow-up, he reported significant improvement of pain and swelling.



Figure 1. Physical examination reveals significant right lower extremity edema.



Figure 3. CT demonstrating inferior vena cava atresia.



Figure 2. Color ultrasound of right common femoral vein revealing thrombus.

Discussion

Pediatric DVT is rare in comparison to adult DVT, but this diagnosis can be associated with morbidity in the form of post-thrombotic syndrome with persistent pain and edema.¹ Greater than 90% of pediatric thrombosis is associated with

prothrombotic risks.² Central venous catheters are associated with > 50% of DVTs in children and > 80% of cases in newborns.² Pediatric thrombosis tends to occur in a bimodal distribution observed most commonly in neonates and adolescents.² IVC atresia is a rare cause of a DVT in a young patient, but it must be considered in cases of unprovoked DVT.^{3,4} IVC development occurs between the weeks four and eight of gestation.⁵ The complex process of IVC development allows for many opportunities for malformation. Many IVC anomalies are clinically silent and incidentally discovered on abdominal imaging, but some IVC anomalies can manifest clinically significant pathology including thrombosis formation, abnormal cardiac circulation and back pain.⁵ The treatment of pediatric DVTs is evolving; newer therapies including various thrombolytic techniques, surgical treatment with IVC reconstruction where IVC agenesis or atresia is present, and new oral anticoagulants are being incorporated into pediatric practice.^{1,5,6}

Conclusion

Emergency medicine and pediatric providers must develop competency in recognition, diagnosis, and treatment of pediatric DVT. In young patients presenting with unprovoked lower extremity DVT, IVC agenesis should be included in the differential diagnosis. Patients with DVT resulting from IVC agenesis require emergent consultation with hematology and vascular surgery to ensure prompt collaborative treatment.

Disclosures

No financial support given. Authors report no conflict of interest. Written consent was obtained from the parent of the patient.

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CASE REPORTS

Right-Sided Frontal Alien Limb Phenomenon (“Dr. Strangelove Syndrome”) in the Context of Left MCA Territory Infarct of Cardioembolic Etiology

Alyssa Arena M.D.¹, Aleshia Magee, M.D.¹, Dipendra Chaudhary, M.D.², Bryce Hamilton, M.D.³

Abstract

Alien limb phenomenon, also known as alien hand syndrome and Dr. Strangelove syndrome, is a rare neurologic phenomenon with autonomous movement of a limb purportedly caused by diminished parietal feedback of motor activity. It is typically seen in corticobasal degeneration, a parkinsonian disorder, and is highly uncommon following cardioembolic stroke. In this case, a 71-year-old woman with hypertension, seizures, and restless leg syndrome presented to with an NSTEMI, and severe systolic heart failure requiring a coronary artery bypass graft (CABG). Post-operative course was complicated by expressive aphasia and right-sided weakness due to a cardioembolic stroke of the left middle cerebral artery (MCA) in the M2 segment involving the left insula and parietal and posterior frontal cortex which was treated with thrombectomy. During inpatient rehabilitation, she developed a saddle pulmonary embolism and was found to have bilateral lower extremity deep vein thromboses (DVTs) and heparin-induced thrombocytopenia and thrombosis (HITT). The patient was observed to have intermittent levitating right arm movement without purpose which persisted since her stroke several days prior. In the absence of other neurologic deficits, a diagnosis of alien limb phenomenon was made. She was started on gabapentin with subsequent improvement of symptoms. This was a rare case of frontal-version alien hand syndrome because the phenomenon occurred in the context of a left-sided cardioembolic cerebrovascular accident with acute onset of motor symptoms and relative patient apathy. This patient presentation was less severe than the self-stroking and self-groping behaviors characteristically noted in literature, which likely contributed to her nonchalance over her right upper limb autonomy. We hope that by documenting this unique presentation and comparing it to existing literature, this variable phenomenon may be further elucidated and an evidence-based pathway to medical management be developed.

Introduction

Alien limb phenomena are involuntary goal-directed movements of one limb. They can manifest in the upper or lower extremity.¹ The affected limb exhibits complex movements, appears to be in constant motion, and may even grab other objects.² It is often described by patients as a sensation that the limb does not belong to the patient and has a will of its own.²

Alien limb phenomenon is most commonly observed in the context of corticobasal degeneration (CBD), an uncommon neurodegenerative atypical parkinsonian

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disorder. CBD was first described in 1967 under the term corticodentatonigral degeneration with neuronal achromasia in three patients with an asymmetric, rigid-akinetic neurodegenerative presentation with cerebral cortical dysfunction.² CBD classically presents sporadically in the sixth to eighth decades of life with akinesia, myoclonus, apraxia, rigidity, and cognitive and behavioral abnormalities. Alien-limb phenomena manifest in 30 to 50 percent of patients with CBD.² Although alien limb phenomenon is highly suggestive of CBD, it is not pathognomonic for the disease and has also been reported in unique cases of Alzheimer disease, progressive supranuclear palsy, Lewy body dementia, and frontotemporal dementia (Pick disease).² In fact, some experts use the term corticobasal syndrome (CBS) for clinical diagnoses, reserving the term CBD only for the cases confirmed by neuropathology that distinguishes it from other tauopathies.² In addition, alien-limb phenomena can be a sequela of stroke.

Early during CBD, neuroimaging is typically unremarkable. Asymmetric cortical atrophy is seen in up to half of patients as the disease progresses.² This atrophy predominantly occurs in the posterior frontal and parietal cortex and appears as dilation of the lateral ventricles and atrophy of the corpus callosum.² Some cases display minor signal hypointensity of the putamina and pallida on T2-weighted imaging, while sparing the remainder of the basal ganglia.²

Alien hand syndrome can be classified into at least four categories, based on clinical presentation: 1) intermanual conflict, in which hand actions contradict one another; 2) alien hand sign, in which a patient does not feel the hand belongs to him or her; 3) syndrome of anarchic hand, in which the affected hand performs seemingly goal-directed activity that is completely involuntary; and 4) supernumerary hand, in which the patient feels as though he has an extra limb.¹ Another possible subtype is levitating hand, in which the patient's limb levitates involuntarily. More detrimental manifestations include self-groping behavior, slapping the other hand, and even self-suffocation. There is no known treatment for this condition and it can last from days to years.¹

The literature outlines three distinct mechanisms of alien hand syndrome based on specific brain lesions.³ The frontal version results from damage to the supplementary motor area, anterior cingulate gyrus, and medial prefrontal cortex of the

dominant cerebral hemisphere and anterior corpus callosum, with involvement of the dominant limb.³ This limb presents with increased exploratory reflexes, including involuntary groping, grasping, and compulsive behaviors, secondary to inhibition of nondominant hemispheric inhibition. A second form occurs after damage to the anterior corpus callosum, with or without accompanying bilateral frontal lesions.³ This results in hemispheric disconnection with subsequent intermanual conflict, especially when performing tasks under control of the dominant hemisphere. Frontal and callosal alien hand syndromes have rarely co-existed. Finally, posterior alien hand syndrome occurs after involvement of the nondominant thalamus, basal ganglia, occipital and inferior parietal regions, and may or may not spare the corpus callosum. These patients typically deny ownership of the nondominant limb and its involuntary movements, and they may also have sensory impairment, visual field defects, and spatial neglect.³

One study examined the etiology of alien limb syndrome in 150 patients, of which 122 had isolated upper extremity sequela, while thirteen had isolated leg sequela, twelve had ipsilateral involvement, and three had bilateral involvement.⁴ Results revealed 108 patients with corticobasal syndrome, fourteen with stroke, nine with Creutzfeldt-Jakob disease, five with hereditary diffuse leukoencephalopathy with spheroids, four with a brain tumor, and the remaining ten with progressive multifocal leukoencephalopathy, demyelinating disease, progressive dementia not otherwise specified, posterior reversible encephalopathy syndrome, corpus callosotomy, intracerebral hemorrhage, or thalamic dementia.⁴ Of the fourteen stroke patients with alien limb syndrome, ten had suffered from a right hemispheric stroke and all cases involved the parietal lobe. One stroke patient documented that she “woke up in the morning and felt that there were extra hands and arms in her bed but when she looked it was her hands and arms” and felt that she could not control her left arm which was grasping parts of her.⁴

Of the forty-four patients with corticobasal syndrome from the Alzheimer's Disease Research Center cohort, twenty-two had alien limb with 73% of cases involving the left extremities. In fact, the presence of alien limb was significantly associated with left-sided corticobasal syndrome. The study concluded that these findings supported the theory that alien limb phenomenon is related to damage to the parietal cortex,

especially on the right side.⁴ In addition, other studies have localized lesions in the left mesial frontal region and corpus callosum.³

Functional MRI has been used to study this phenomenon and has revealed isolated activation of the contralateral primary motor cortex upon initiation of motor activity. This contrasts with the typical activation of extensive networks seen in normal movement. This may result from lesions in the parietal cortex that release the motor cortex from the intentional planning systems and disrupt proprioceptive feedback.¹

Case Report

A 71-year-old Caucasian female with hypertension, hyperlipidemia, mild systolic heart failure (40-45% EF), gastroesophageal reflux disease, iron deficiency anemia, hypothyroidism, pre-diabetes (HbA1c 5.8), restless leg syndrome, major depressive disorder, kyphoscoliosis, and osteoarthritis initially presented to the referring hospital with shortness of breath and chest heaviness that had progressively worsened over the course of a week. She was found to have an NSTEMI with severe multivessel disease and was transferred to cardiothoracic surgery for CABG evaluation.

EKG upon transfer showed left axis deviation with ST depression in I, aVL, V5, and V6, along with troponin peak of 60 ng/mL. Echocardiography was significant for moderate left ventricular dysfunction with an ejection fraction of 35-40% from her baseline of 40-45% and preserved right ventricular function. The patient was medically managed with a heparin drip, aspirin, and beta blockers.

CABG was performed four days after transfer. Her

postoperative course was complicated by sudden-onset aphasia and right-sided weakness. CTA revealed a left MCA territory infarct of suspected cardioembolic etiology, with left M2 occlusion involving the left insula, parietal, and posterior frontal cortex (Figure 1). MRI further confirmed a left MCA territory infarct with a small focal hemorrhage within the left parietal lobe in addition to age-advanced chronic ischemic microvascular disease. She was ineligible for tissue plasminogen activator (tPA) and she emergent left frontal M2 thrombectomy. Expressive aphasia and right-sided weakness persisted after the procedure, and she was admitted to inpatient rehabilitation four days later. The following day, she reported pain and swelling in the right lower extremity. A venous duplex Doppler exam revealed acute superficial phlebitis of the great saphenous vein without evidence of deep vein thrombosis. Phlebitis was treated symptomatically with warm compresses.

The patient participated in therapy until the fourth day of rehabilitation, when she developed acute dyspnea and tachypnea with hypoxia to 88% which corrected to 93-95% with administration of 2L of oxygen. Emergent CTA chest revealed an acute bilateral saddle pulmonary embolism extending into

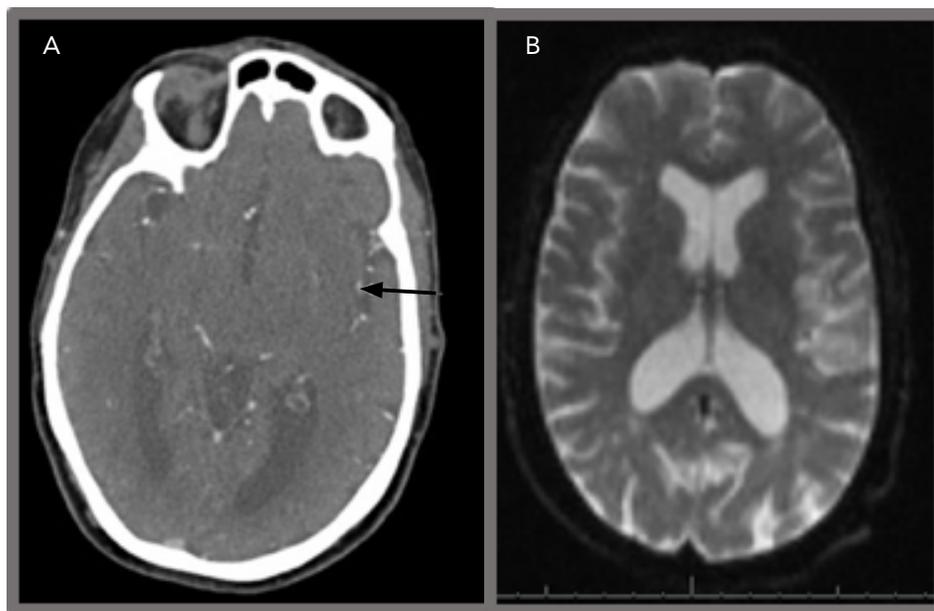


Figure 1. (A) CTA head displaying left middle cerebral artery occlusion along the insular M2 branch without evidence of aneurysm. (B) Diffusion-weighted imaging (DWI) axial MRI confirming restricted diffusion in the left insula, posterior frontal, and parietal lobes consistent with acute ischemia of the left MCA territory.

the right and left pulmonary arteries, with occlusive and non-occlusive emboli present throughout the lobar, segmental, and subsegmental bilateral panlobular pulmonary arteries (Figure 2). CBC showed acute thrombocytopenia with a platelet count of 58,000, decreased from 232,000 platelets three days prior, concerning for heparin-induced thrombocytopenia and thrombosis (HITT). HITT antibody testing confirmed a positive HIT antibody titer of 2.449, and serotonin release assay was also positive. The patient was transferred to an intermediate care unit and an argatroban drip was started with a PTT goal of 50-70. Repeated lower extremity venous duplex Doppler exam revealed acute completely occlusive deep vein thromboses of the right posterior tibial and bilateral popliteal and peroneal veins with severe reduction of venous return. The patient was observed to have intermittent right arm movement without purpose that had persisted since her stroke several days earlier.



Figure 2. CTA chest displaying saddle embolus within the main pulmonary artery draping into the right and left main pulmonary arteries with both occlusive and nonocclusive emboli present throughout the lobar, segmental, and subsegmental pulmonary arteries of all lobes of both lungs.

The patient and her husband reported that her right arm seemed to levitate, drift upwards on its own, and then move about randomly. She maintained only partial control of the limb during these intermittent episodes, which occurred five to ten times per day, but appeared unbothered by them.

Neurology evaluated the patient and started gabapentin 300 mg TID, and the patient's symptoms improved. On exam, the patient followed commands well with significant expressive aphasia in which her main speech output was "yeah." She did progress to a few other words with speech therapy assistance. She nodded and shook her head appropriately to questions. She gestured to help indicate needs and could write single words with her left hand, her dominant hand prior to the stroke. Sensation, reflexes, and CN II-XII were all normal. She moved all extremities against gravity with mild right hemibody weakness. In addition, her right upper extremity moved with and without purpose in a drifting manner. The movement was not rhythmic and did not resemble a seizure.

That patient was bridged from argatroban therapy to warfarin. Argatroban was discontinued a week before discharge to inpatient rehabilitation, where her autonomous limb movements decreased gradually on gabapentin therapy. Somatosensory evoked potentials will ideally be performed in future to evaluate whether the patient lacks right-handed cortical response.

Discussion

The case reported here is a unique presentation of right-sided frontal alien limb phenomenon, which should be juxtaposed against current literature and examined in the context of other presentations of stroke-induced alien limb phenomenon.

The same study that examined one-hundred fifty patients for etiology of alien limb phenomenon also listed examples of the presentation of the phenomenon based on etiology. As previously stated, ten of the fourteen stroke patients with alien limb phenomenon had suffered from a right hemispheric stroke, and all cases involved the parietal lobe.⁴ In addition, of the CBS affected patients, almost three-quarters of cases involved the left extremities. Overall, roughly eighty percent of cases involved an isolated upper extremity.⁴ Our patient had a left M2 stroke that affected the parietal lobe and subsequently experienced apathetic right-sided alien upper limb phenomenon. This lateralization is rare in an already exceptionally rare affliction, considering her minimal distress. Given her willing participation in physical therapy and apparent eagerness to communicate more effectively, it is unlikely that is related to post-stroke apathy alone.

Additionally, a case report described a 77-year-old woman who presented with autonomous left-hand movement while watching television.¹ She described a thirty-minute incident in which her left hand stroked her face and hair, as if controlled by someone else, and remained uncontrollable, even with assistance from the right hand. This episode was followed shortly by mild left hemiparesis, when the patient noted numbness and weakness of the left upper extremity with dragging of her left leg while walking.³ She had recently discontinued her anticoagulation for chronic atrial fibrillation due to an upcoming spinal surgery. CT and MRI revealed acute bilateral infarcts in her parietal lobes without evidence of thrombus on TTE or TEE, suggesting cardioembolic etiology.¹ She gradually recovered left-sided limb control over the next six hours, and she was discharged with advice to maintain her anticoagulation regimen at all times.² This thirty-minute episode is the shortest duration of alien limb phenomenon recorded and one of only two recorded cases secondary to cardioembolic TIA.¹ Our case followed a cerebrovascular accident, yet it was also likely a result of cardioembolic phenomenon, making it an extremely rare phenomenon. Again, it is notable that this patient had left upper limb manifestations and that right limb involvement is uncommon.

Another report described a 68-year-old right-handed man who presented with sudden onset uncontrollable left upper limb involuntary movements.³ He felt as though his right hand was being touched by someone else and noted his left hand trying to hold his right hand of its own accord. The patient was mildly hypertensive (140/80 mmHg) but had no other abnormalities. When he arrived at the hospital, he had regained some control of his left hand, but the limb still felt unfamiliar to him. His exam revealed levitation of his left upper limb with minor hypotonia despite normal strength. In addition, all sensation was absent over the left upper limb, and sensation was decreased over the left lower limb. All other exam findings were normal. He could perform bimanual tasks without difficulty. After two hours, his symptoms subsided, and the patient felt he had complete control over his left upper limb. His exam remained consistent with left sided hypotonia and sensory loss with additional mild incoordination on left-sided finger-to-nose testing. MRI showed altered signal intensity of the right frontoparietal region, with hypointensity in T1-weighted imaging and hyperintensity in T2-weighted

imaging. The right frontoparietal region also had restriction on diffusion-weighted images, suggestive of an acute right frontoparietal infarct involving the superior division of the MCA. This presentation is characteristic of frontal alien hand syndrome, comprising involuntary limb levitation, use, and unfamiliarity. Our patient, with damage to the left insula, parietal, and posterior frontal cortex secondary to M2 occlusion, also presented with a frontal version of alien hand syndrome; she initially demonstrated classic sequelae of a MCA stroke, however, and only later developed alien limb manifestations. Alien hand syndrome in the context of stroke typically persists for several months before gradually subsiding, so this gentleman's case was unusual. We again note the laterality difference in our case, with alien limb phenomenon of her right upper extremity, compared to most other reports in literature.

The final case is the first documented description of an acute onset sensory alien hand phenomenon affecting the dominant hand.⁵ Sensory alien hand phenomenon is very rare and characterized by a constantly moving semi-purposeful hand, with corresponding proprioceptive loss and a significant disturbance of self-control. Even more uncommon is the involvement of the nondominant limb. The patient was a 78-year-old healthy right-handed female who lost consciousness while playing cards. She was intubated and found to have mild left facial weakness and right hand tonic posturing without evidence of weakness with left dorsal tegmental pontine hemorrhage on CT. She developed levitation of the right arm, during which episodes the patient did not respond to commands. After extubation, she remained mildly confused with intermittent ocular bobbing. Strength was symmetric, but her right hand was hypertonic and clumsy, especially on finger-to-nose testing. When the patient closed her eyes, her right arm abducted and drifted upward with finger flexion. When her attention was diverted, both the right hand and, to a lesser extent, the right foot exhibited constant semi-purposeful movement, both limbs appearing to seek the bed cover. She complained of painful and cold sensations and had marked proprioceptive loss. As her other symptoms improved over the course of a week, she experienced an episode of her right hand grabbing her left hand, and she requested restraint of her right arm. The patient maintained bilateral control for two-handed tasks, such as donning socks and

shoes. MRI confirmed no changes from her prior imaging. A somatosensory evoked potential study of her bilateral median nerves revealed an absent cortical response from the right arm, which is consistent with findings noted in other studies.

Conclusion

Reported is a rare case of frontal-version alien hand in the unexpected context of a left-sided cardioembolic cerebrovascular accident with acute right-sided symptoms and apathy. Her presentation appears less severe than typical behaviors noted in the literature, which may contribute to her apathy. This case highlights the complexity of alien hand syndrome and the need for further research to determine more definitively the etiologies and treatments of such an infrequent disorder.

Disclosures

No financial support given. Authors report no conflict of interest.

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