JOURNAL of SCIENCE & MEDICINE

Wake Forest® School of Medicine

JOURNAL of SCIENCE & MEDICINE

Spring 2020 Volume 5, Issue 1

Letter From The Editors

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(ISSN 2380-3991)

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:

All the faculty at Wake Forest and beyond who served as peer reviewers. The time and expert knowledge they contributed is central to our mission of bringing quality scholarship to the scientific community.

Sue Kendall and Nick Weir with the Creative Communications Department for their ingenuity in producing digital illustrations.

Dr. Indra Newman with the Clinical and Translational Science Institute for her excellent advice on our editorial and publishing policies.

Allen Gottfried with Marketing for helping us achieve our long-time goal of setting up an ePub platform.

Tiffany Montgomery and Justin Farrar with the Creative Communications Department for working with us tirelessly through every challenge of the production process.

Our faculty advisors, Dr. Cynthia Burns and Dr. Timothy Peters for their support and guidance as we took the *Journal* in new directions.

Dr. Lauren Edgar, former Editor-in-Chief, who taught us everything we know about the *Journal* and continued to answer our questions long after she graduated.

We would also like to express our gratitude to the following for their generous financial support:
Department of Anesthesiology
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
Department of Neurobiology & Anatomy
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Journal of Science & Medicine

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Editorial Board

Dear Readers,

While offering guidance on this volume, one of our faculty advisors referred to this journal as a "miracle" that occurs every year. We would first and foremost like to thank those advisors, along with the peer reviewers, our publishing team, and of course, our extraordinary staff of students, who have all worked so hard to make this miracle come true once again.

This has been an exciting year for the *Wake Forest Journal of Science & Medicine*, as it continues to evolve and expand. For the first time since its inception, the *Journal* does not have any founding members on its editorial board. As such, this issue is a testament to the efforts and due diligence those founding members showed in successfully transitioning to a new leadership. We remain incredibly grateful for the groundwork laid by student leaders before us, and have been humbled to continue their legacy by taking the *Journal* in new directions.

In the Fall of 2019, we began archiving prior issues online in their entirety and in February of this year, we were able to successfully launch our "ePub" platform to showcase individual manuscripts online as they are finalized. Authors will now have their articles published electronically ahead of print, allowing our readers access to scientific discoveries, interesting cases, and thoughtful perspectives remotely, in a timely manner, and free of charge. Both of these steps are innovations consistent with our mission to expand the reach and accessibility of our content. In that manner, we have also begun exploring social media platforms to further engage with our authors and readers, particularly as our community is now growing far beyond Winston-Salem, NC.

For both of us, the *Wake Forest Journal of Science & Medicine* has been a cornerstone during medical school. This experience has taught us an enormous amount about leadership, scholarship, and teamwork. It is exciting to be at the heart of medical writing as it constantly lends insight into the topics and viewpoints most current to the scientific community. To play a role in the procurement and dissemination of scholarship has been a privilege – and continuing the "student-run" legacy of this publication has been a true joy. We are immensely grateful to have worked with authors, reviewers, publishers, editors, and readers over the last four years. To that end, we want to thank the many people who contribute to this labor of love. In particular, we appreciate our editorial board who put in their hard work on a completely voluntary basis. We hope they will continue to find new ways to keep the *Journal* as relevant as the content it holds.

Sincerely,

Elahhe and Danish
Editors-in-Chief

Perspectives

Global Health Initiatives for Obstetrical Care

Shahla Y. Namak, M.D.[1], Aleksandra Vejnovic, M.D.[2], Tihomir Vejnovic, M.D.[2], Julienne K. Kirk, Pharm.D.[1], Justin B. Moore, Ph.D., M.S.[1]

Background

Global health initiatives involve addressing the health of populations and achieving equity in health using the best evidence-based practices for patient safety and health professional education. Opportunities to aid in the improvement of global healthcare delivery are abundant. U.S. clinicians have multiple opportunities to be involved with global health initiatives.[1] Gaining familiarity with international practice and culture will aid interested clinicians in their quest to engage in global health initiatives.

One humanitarian organization is Kybele, Inc. and is dedicated to improving childbirth safety through innovative partnerships in low-resource settings.[2] Previous projects demonstrate the impact of collaborative programs to strengthen clinical practice and service through reinforcement of taught skills in the area of obstetrical care.[3] The purpose of this article is to highlight lessons learned from two global health initiatives targeting obstetrical care that demonstrate how primary care providers can engage with their colleagues in low-income countries to implement best practices.

Adding Postpartum Uterine Massage in a Rural Armenia Hospital

One outreach project conducted at Akhuryan Maternity Hospital, Gyumri, Armenia was undertaken where there are limited resources for labor and delivery. The unavailability of uterotonic medications, the inability to measure coagulation defects by blood test, and lack of access to coagulation products are a common scenario in everyday care. Unreliable access to blood bank services or blood products for management of coagulopathy in severe postpartum hemorrhages can make a complicated delivery challenging. The shortage of supplies for intravenous access and intravenous fluid for hydration is also an obstacle to care.[4] The standard of care is to use active management of the third stage of labor starting with ten units of intramuscular oxytocin given immediately after the shoulder delivery of the newborn.[5,6] Due to the risk of uterine hemorrhage in the early postpartum period, uterine massage was introduced as part of active management of third stage of labor (AMTSL) (Table 1).[4,5,7,8] As part of the AMTSL maneuver, adding uterine massage can provide close observation of women in labor to detect and prevent early postpartum bleeding. In low-resource settings, women with anemia who may be vulnerable to even small amounts of bleeding can benefit from AMTSL, which may reduce the risk of postpartum maternal hemoglobin lowering.[4,7,8]

Through a global health initiative (Table 2), the addition of uterine massage was investigated. At baseline prior to adding the uterine massage maneuver, there were 1125 total deliveries with 864 vaginal deliveries (77%), resulting in 23 cases

[1]Department of Family & Community Medicine, Wake Forest School of Medicine, Winston Salem, North Carolina

[2]Department of Gynecology and Obstetrics, University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

Address Correspondence To:
Shahla Y. Namak, MD
Department of Family & Community Medicine
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
snamak@wakehealth.edu

Table 1. Active Management of Third Stage of Labor (AMSTL)

Components of this Practice	Benefits of AMSTL
1. Administer Oxytocin (Pitocin) with or soon after the delivery of the anterior shoulder 2. Controlled cord traction to deliver the placenta 3. Uterine massage after the delivery of the placenta	• Prevention of postpartum hemorrhage • Reduced risk of bleeding when maternal hemoglobin level is lower than 9 g per dl • Reduced need for manual removal of the placenta

of postpartum hemorrhaging (2.6% of vaginal deliveries). The following year, there were 1148 total deliveries with 883 vaginal deliveries (77%), resulting in 10 cases of postpartum hemorrhaging (1% of vaginal deliveries). Chi-square tests were performed to determine changes in the incidence of postpartum complications. In the year following the implementation of the uterine massage maneuver less uterine atony was observed, with incidence decreasing from 1.7% to 0.6% (P=0.02). In addition, bleeding less than 24 hours decreased from 2.2% to 0.8% (P=0.02) and blood loss greater than 500 ml decreased from 1.9% to 0.8% (P=0.02). Uterine massage did not significantly decrease bleeding after 24 hours, blood loss greater than 1000 ml, or genital tract trauma from delivery or endometritis. Adding postpartum uterine massage as a standard of care included in the final step in the AMTSL is associated with positive outcomes. This example demonstrates that the development of a protocol to improve care can have a lasting impact on the populations served.

Serbia Electronic Fetal Monitoring

Another global health project conducted in Serbia (Table 3) aimed to improve teaching programs for medical residents caring for laboring patients, using simulation exercises and didactics. Often, medical residents are only observers during training. We developed an electronic fetal monitoring (EFM) seminar for residents with objectives to discuss basic fetal heart monitoring, interpretation, documentation of fetal heart monitor strips, and management of fetal intolerance to labor or distress.[9,10]

Thirty-three residents in training completed the educational intervention. Obstetric (n=20) and non-obstetric residents (eight from anesthesia, one from pediatrics, and four not specified) received the training. A local Institutional Review Board approved all materials and procedures. Participants answered ten multiple-choice pre-test questions regarding EFM. Training via an interactive slide presentation, case studies, and hands-on simulation practice was undertaken. We administered a post-test using the same 10 questions from the pre-test. We created a 2x2 ANOVA with residency type and time as independent variables and test score as the dependent variable. Statistically significant improvements were seen overall between pre- and post-test ($\Delta 1.7$, $P < 0.01$) and for non-OB ($\Delta 3.0$, $P < 0.01$) and OB residents ($\Delta 0.7$, $P < 0.05$). A significant interaction was observed, with non-OB residents displaying greater gains than obstetric residents ($P < 0.05$). Utilizing an interactive lecture, cases, and hands-on simulation improved the educational experience and enhanced the acquisition of knowledge in Serbian residents.

Challenges and Opportunities

There are some challenges to consider with any global health initiative. For the projects outlined, funding was an obstacle as it is expensive to travel and time is necessary to coordinate teaching and logistics. Even when a positive outcome occurs, decision makers and leaders are pivotal to allocate necessary funding. In the projects described, there was a general resistance to change observed among more senior providers and administrators. In some countries, for example, approval is necessary to use certain lifesaving obstetrics medications such as misoprostol. In a given region, policy change may require approval at the district or national level.

By working side-by-side with the local medical providers abroad to improve patient care, innovative teaching and practice models like those described can be successfully implemented. Working together and creatively within the infrastructure in resource-limited areas requires partnership and leadership willing to support the help of U.S. providers. It is also necessary to recognize that change may be a slow process.

Table 2. Adding Postpartum Uterine Massage to Active Management of Third Stage of Labor in a Rural Armenia Hospital

Country	Location	Observed Need	Intervention	Outcomes
Armenia 2014	Rural Akhurian Hospital, Gyumri	• Postpartum hemorrhage (PPH): 23 per 864 vaginal deliveries • Active Management of Third Stage of Labor (AMSTL) lacked the postpartum uterine massage maneuver recommended by most guidelines and the WHO • Lack of availability of a blood bank	• Palpating and massaging the uterus every 10-15 minutes for about 2 hours after delivery of the placenta that stimulates uterine contractions and expresses blood and blood clots • Physicians and midwives instructed on the maneuver • Uterine massage was added as a standard part of care	• Ten cases of PPH per 883 vaginal deliveries • Significant decreased blood loss > 500 ml and bleeding less than 24 hours • No blood transfusions were needed for 2015

Table 3. Electronic Fetal Monitoring During Vaginal Delivery in Serbia

Country	Location	Observed Need	Intervention	Outcomes
Serbia 2016	Novi Sad Department of Obstetrics and Gynecology, University of Novi Sad	• OB residents were not confident with fetal heart monitoring interpretation during labor • Lack of simulation and hands-on educational sessions	• Educational seminars presented with skills assessment for teaching intrapartum fetal monitoring to OB and anesthesia residents • Simulation and hands-on educational sessions assessed and competently completed for all participants	• Advanced Life Support of Obstetrics Courses presented and completed for 2017 and 2018 with Serbian, Romanian, and Bosnian participants

Conclusion

Introducing a new culture of learning or clinical practice in a low- or middle-income country requires intentional steps. Global health initiatives are part of many academic institutions and are a first step for clinicians to reach out to local resources. Models of teaching have demonstrated improved provider confidence and competence as well as patient outcomes in resource-stable countries.[11] Unique challenges within each country require different approaches and creativity to identify local healthcare needs within a system, hospital, clinic, or medical provider and staff. Finding solutions customized to specific needs in areas of education or patient care with the help and support of local partners and champions can lead to long-term results and sustainability.[12] Progress continues in reducing maternal and newborn mortality worldwide, but disparity in maternal and infant health outcomes remains evident between low- and high-income countries and much work remains to decrease this disparity.

Acknowledgements

The authors thank the individuals who supported this work including Kybele, Inc.; Medge Owen, MD, Department of Anesthesiology and founder of Kybele, Inc.; Avinash Shetty, MD, and Lynn Snyder, Office of Global Health; Richard Lord, MD, MA, Chair, Amanda Burton, and Stephen Davis, Department of Family & Community Medicine; the faculty and residents who donated their time to outreach trips and teaching at the Wake Forest School of Medicine.

We also thank anesthesiology colleagues, Gordon Yuill MBCh.B; Simon Miller, MD; Ivan Velickovic, MD; Curtis L. Baysinger, MD; Ashot Amroyan, MD; Emil Vardapetyan Victor Tregubov, MD; Akhuryan Maternity Hospital physicians and staff. Tonikyan Valdimid, MD; Mirzoyan Ashot, MD; Mirzoyan Sergey, MD; and the Department of Gynecology and Obstetrics, Department of Obstetric Anesthesia, and medical faculty at University of Novi Sad; along with Borislava Pujic, MD, and the faculty, residents, and staff.

Disclosures

A funding collaboration exists between Kybele Organization (www.kybeleworldwide.org), the Office of Global Health at the Wake Forest School of Medicine, and the Department of Family and Community Medicine. No conflict of interest to disclose.

References

1. Syed SB, Dadwal V, Rutter P, et al. Developed-developing country partnerships: benefits to developed countries? Global Health. 2012;8:17.
2. Kybele for safe childbirth worldwide. www.kybeleworldwide.org Access on October 2, 2019.
3. David M. Goodman, Rohit Ramaswamy, Marc Jeuland, et al. The cost effectiveness of a quality improvement program to reduce maternal and fetal mortality in a regional referral hospital in Accra, Ghana. PLoS ONE. 2017;12(7). doi.org/10.1371/journal.pone.0180929
4. Evensen A, Anderson JM, Fontaine P. Postpartum Hemorrhage: Prevention and treatment. Am Fam Physician. 2017;95(7):442-449.
5. Stanton C, Armbruster D, Knight R, et al. Use of active management of the third stage of labour in seven developing countries. Bull World Health Organ. 2009;87(3):207-15.
6. Begley CM1, Gyte GM, Devane D, McGuire W, Weeks A. Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev. 2015;2(3):CD007412. doi: 10.1002/14651858.CD007412.pub4.
7. FIGO / ICM Global Initiative to Prevent Post-Partum Hemorrhage. https://www.jogc.com/article/S1701-2163(16)30440-6/pdf. Accessed October 2, 2019.
8. Lalonde A; International Federation of Gynecology and Obstetrics. Prevention and treatment of postpartum hemorrhage in low-resource settings. Int J Gynaecol Obstet. 2012 May;117(2):108-18. doi: 10.1016/j.ijgo.2012.03.001.
9. Sweha A, Haker TW, Nuovo J. Interpretation of the electronic fetal heart rate during labor. Am Fam Physician. 1999;59(9):2487-506.
10. Bailey RE. Intrapartum fetal monitoring. Am Fam Physician. 2009;80(12):1388-96.
11. Walker DM, Cohen SR, Fritz J, Olvera-García M, Zelek ST, Fahey JO, et al. Impact Evaluation of PRONTO Mexico: A simulation-based program in obstetric and neonatal emergencies and team training. Simul Healthcare. 2016;11(1):1-9. doi: 10.1097/SIH.0000000000000106
12. Ramaswamy R, Kallam B, Kopic D, Pujic B, Owen MD. Global health partnerships: building multi-national collaborations to achieve lasting improvements in maternal and neonatal health. Globalization Health. 2016;12(1):22. doi: 10.1186/s12992-016-0159-7

Perspectives

The Wake Forest Health Professions Education Institute's Educator Conference: Supporting a community of educators by providing an outlet for dissemination of teaching scholarship

Roy E. Strowd, M.D., M.Ed.[1]

Introduction

Faculty development is vital to the success of academic physicians. Continuing professional development (CPD) brings together continuing medical education and faculty development to prepare faculty to fulfill the academic missions including patient care, education, research, and health advocacy. CPD for clinician educators is critical yet often under-resourced.[1–3] In particular, opportunities for educators to generate, disseminate, and critique teaching scholarship have been identified as a major career development gap.[4,5]

Over the last 30 years, definitions of scholarship have evolved. In 1988, the World Federation for Medical Education identified a need to "train teachers as educators, not content experts alone, and reward excellence in this field as fully as excellence in biomedical research or clinical practice."[6] Despite significant advances to change our understanding of scholarship in medical education, major gaps remain for faculty. Scholarship in medical education may include any of the four categories defined by Boyer: scholarship of discovery, integration, application, and teaching.[7] Scholarship in any of these areas as defined by Glassick should have clear goals, be adequately prepared, use appropriate methods, achieve outstanding results, be communicated effectively, and allow for reflective critique.[8] Most recently, a consensus conference statement by the Association of American Medical Colleges identified five educational activities commonly identified as scholarship by health educators including: teaching, curriculum development, advising and mentoring, education leadership and administration, and learner assessment.[9] In short, scholarly work spans the many roles of a health educator and must be made public, be available for peer review and critique, and allow scholars to build upon the work of other educators. Infrastructure to support medical educators is critical to facilitate public dissemination. This may occur through grand rounds, conferences, meetings, television or radio media, newspapers or interviews, blogs, podcasts, e-Learning platforms, and others.[10–12] Online methods include both traditional peer-reviewed publications such as MedEdPORTAL which uses citation metrics or non-periodical methods for web resources or videos that may incorporate alternative metrics including number of downloads, "clicks", or views.[11,13] Academic institutions recommend use of educator portfolios for tracking the quantity and quality of teaching efforts for purposes of promotion.[14] However, these resources often do not sufficiently protect and support teachers to produce scholarly work. Salary support principally protects time to design, deliver, and ensure certification of training programs for program directors, clerkship directors, or core teaching faculty.[15,16] There has been a proliferation of education academies and societies but often limited local infrastructure.[17]
Structured programs that build communities of educators can address these

[1]Departments of Neurology and Internal Medicine, Section on Hematology and Oncology, Wake Forest School of Medicine, Comprehensive Cancer Center of Wake Forest University, Winston Salem, NC

Address Correspondence To:
Roy Strowd, M.D., M.Ed.
Director, Health Professions Education Institute
Department of Neurology
Wake Forest School of Medicine
Winston Salem, NC 27104
rstrowd@wakehealth.edu

gaps by providing a forum for dissemination of evidence-based teaching, facilitating interprofessional collaboration, and generating mechanisms for dissemination and peer review of education scholarship.[18,19] This paper describes the development and implementation of an institutional Educator Conference as a space to publicize works, generate peer review, and facilitate reflective critique.

Design of the Educator Conference

In 2015, Wake Forest School of Medicine's Faculty Forward Survey identified faculty development as a major institutional need. A 2016 survey of departments conducted by the institution's Faculty Development Committee identified teaching techniques, assessment and feedback, student evaluation, and forums for dissemination as topics of particular interest. To address these gaps in medical education scholarship, the first annual Educator Conference was hosted on Monday, April 22nd, 2019 by the Wake Forest Health Professions Education Institute (HPEI). The meeting hosted a community of educators who shared their work and could build on other's teaching practices. The conference was convened with three primary aims: (1) to create a public forum for dissemination of teaching scholarship that has been developed at Wake Forest, (2) to facilitate peer review and critique of teaching activities, and (3) to generate an interprofessional community of educators that will exchange best-practices and build on each other's teaching practices through collaboration.

An interdisciplinary planning committee was convened with representatives from the Wake Forest Schools of Medicine, Physician Assistant Program, Nurse Anesthesia and Doctor of Nursing Practice Programs, the Graduate School of Arts and Sciences, and Pharmacy Program. A half-day conference was recommended including abstract submissions, platform and poster presentations, and skill-building workshops to address knowledge and skill gaps.

Summary of Conference Feasibility, Attendance, and Impact

Of the 91 registered participants, 79 attended the conference including 43 physicians (57%), 14 physician assistants (18%), eight healthcare education staff (11%), six students (7%), two nurses (3%), two graduate school faculty (3%), and one pharmacist (1%). Of these, 34 (42%) submitted a peer-reviewed abstract, six were selected for oral platform presentation, 17 for poster presentation, and 10 for roundtable presentation and discussion. Abstract presenters were from the School of Medicine faculty (n=13), School of Medicine students (n=6), Physician Assistant Program (n=5), School of Medicine housestaff (n=3), Pharmacy Program (n=2), Healthcare Education (n=2), CRNA Program (n=1), and Nursing (n=1). Four breakout workshops provided skill-building in evidence-based teaching. Seventeen attendees completed the post-conference survey with 88% agreeing that the content was relevant, 94% agreeing that the presentations stimulated interest in medical education, 94% agreeing that the poster presentation allowed for public dissemination of work, and 76% agreeing that they were able to identify a potential collaborator. The impact of the conference on each of the three program aims is provided with a description of how this responds to current gaps for academic educators.

Aim 1: Creating a Public Forum for Dissemination

Problem: National and regional meetings exist for medical educators, but few institutional forums are available for teachers to present their work to an interprofessional audience that includes educators from across teaching disciplines. At Wake Forest, the HPEI Education Grand Rounds began in 2016 to fill this gap and provide a quarterly forum for presentation and public dialogue. However, the grand rounds series invites only a limited number of speakers to varied audiences and may not include all interested trainees who may want to present work publically.

Solution: In response, the Educator Conference kicked off with an hour of platform presentations. These oral talks provided students, trainees, and faculty with a public forum and moderated discussion to disseminate their medical education research and curriculum innovation scholarship (Figure 1).

Medical Education Research Oral Presentations

Oral presentations opened the conference and set a high bar for scholarship presented throughout the meeting. Topics included burnout, communication skills training, and interprofessional collaborative practice. Margaux Wooster (School of Medicine, Class of 2019) identified an unintended consequence of rising burnout rates on how students learn

Figure 1. Educator Conference creating a forum for interdisciplinary collaboration and dissemination

by linking higher burnout to a loss of self-regulated learning abilities in medical students. Christine Marlow (WFU, Class of 2021) proposed the use of patient teach-back to help empower patients to be teachers and allow students to improve their communication skills in clinical clerkships. Dr. Courtney Brown (Faculty, CRNA Program) showed how interprofessional education through an inquiry-based learning method improves collaborative practice and boosts attitudes toward team-based care.

Curricular Innovations Oral Presentations

Curricular innovations were also presented and highlighted innovative technologies that are improving how students learn, how residents are mentored, and how trainees learn through patient care. Dr. Rita Poon (resident, Internal Medicine) discussed a real-time QR code tool for identifying and coaching struggling interns which has expanded its use within the medical school. Dr. Brandon Stacey (faculty, Internal Medicine - Cardiology) presented data on the impact of an interactive audience response system to improve student recognition of cardiac murmurs and boost academic achievement. Dr. Nancy Denizard-Thompson (faculty, Internal Medicine) and Sarah Martin (School of Medicine, Class of 2020) provided a discharge checklist that allowed medical students to participate in discharge planning, identify obstacles to discharge, and learn transitions of care.

Aim 2: Facilitating Peer Review and Critique of Teaching Activities through a Call for Abstracts

Problem: Effective scholarly teaching takes place in a community that generates data, critiques findings, and engages in public discourse.[20,21] Peer review is important in evaluating and improving the quality of scholarship and has been shown to provide meaningful faculty development in the area of clinical teaching.[22] However, limited opportunities exist for formative peer review in education scholarship.

Solution: The Educator Conference included structured peer review of submitted abstracts to provide opportunities for peer reviewers to engage in critical appraisal of education literature and for participants to receive reflective critique. In addition to oral and poster presentations, 10 Works in Progress were further peer reviewed at the meeting in a roundtable discussion that paired senior and junior teachers for multidisciplinary reviews of their abstracts.

Call for Abstracts

The Educator Conference Call for Abstracts requested structured submissions in three topic areas including medical education research, curricular innovations, and works in progress. In total, 33 abstracts were submitted and reviewed by 12 education experts from the School of Medicine, Nursing, PA School, Department of Medical Education, and Pharmacy Program. Abstract reviews provided an opportunity to recognize faculty reviewers and provide critique to participants. Each abstract decision included comments and suggested revisions to be considered prior to presentation at the conference.

Poster Presentations

Poster presentations highlighted the tremendous breadth and depth of medical education scholarship being conducted at Wake Forest and allowed an opportunity for educators to discuss and critique their work. Fourteen posters were presented from the School of Medicine, four from the PA program, three from Pharmacy, one from CRNA, and one from the Healthcare Education staff. A range of topics were spanned, such as high school immersion programs, longitudinal skills training, health disparities, mentoring, healthcare management and leadership, interprofessional education, and professional identity formation.

Works in Progress (WIP) Workshops

WIP are early innovative projects that have not yet been completed but have high potential to change the way we

teach, train, and educate health professionals in the future. These projects are early in development and in need of critique and debate with colleagues. This WIP roundtable workshop allowed teachers to present their work, receive constructive comments, and identify collaborators to drive these projects towards implementation and completion. Topics included a resiliency training curriculum, a workflow for student integration into ambulatory clinics, medical Spanish certificate program, and an obstetrics and gynecology bootcamp curriculum.

Aim 3: Creating an Interprofessional Community of Educators

Problem: Learning today increasingly occurs through participation and social interaction. In business, Communities of Practice (CoP) have been promoted as a mechanism for sharing knowledge efficiently, sparking innovation, reducing the learning curve for new staff, and creating social capital in employees.[23] CoP have increasingly been integrated into healthcare to guide management decisions, improve performance, and facilitate learning.[24] In medicine, many CoP exist (e.g. institutional department or division, state specialty society, national society) which often exert a stronger influence on educators than an institutional community of teachers.

Solution: The Educator Conference intentionally aimed to create an interprofessional Community of Educators (CoE). Skill-building workshops brought together educators from different health professions programs (e.g. School of Medicine, PA Program, etc). In these workshops, attendees discussed common topics and were able to network with a community of educators.

Skill-Building Workshops

Workshops included topics that would appeal to four different communities of educators: clinical educators, non-clinical educators, early career educators, and mid-career educators. For clinical CoE, a clinical breakout session focused on "How to integrate a student into ambulatory clinic," and for non-clinical CoE, a concurrent classroom breakout session focused on "How to write multiple choice questions." A skill development breakout session titled "Writing, reviewing, and critiquing the education literature" targeted a community of mid-career educators. Meanwhile, junior and senior educators engaged in the WIP workshop.

Lessons Learned and Future Directions

Several lessons were learned. Attendees requested that breakout sessions be offered in both the morning and afternoons to allow for increased flexibility required to balance clinical responsibilities. Guided poster tours were offered to create structured opportunities to network and review posters but were under-utilized by attendees who informally reviewed poster presentations. Trainees were heavily involved in the conference but desired dedicated sessions that would allow them to engage with other trainees. Future conferences will be adjusted to respond to these concerns.

Conclusion

Ultimately, the HPEI Educator Conference successfully achieved its mission. As a result, institutional investment was pledged to use this forum to recognize outstanding educators. Four top abstract awards were presented to Margaux Wooster (School of Medicine, Class of 2019), Christine Marlow (WFU, Class of 2021), Dr. Rita Poon (PGY-4, Assistant Chief of Medicine) and Dr. Brandon Stacey (Associate Professor, Internal Medicine – Cardiology). Two Excellence in Education Scholarship Awards were also presented. The Early Career Excellence in Education Scholarship award recognized two current trainees with strong future potential as educators: Dr. Rita Poon and Dr. Bita Nickkholgh (Postdoctoral Research, Instruction, and Mentoring Experience scholar). The Excellence in Education Scholarship award recognized two faculty members who have demonstrated commitment to education scholarship: Ms. Sobia Hussaini (PA Studies) and Dr. Vera Luther (Associate Professor, Internal Medicine - Infectious Disease).

In summary, institutions need infrastructure to support medical educators and foster early and sustained career development. The Wake Forest Educator Conference was successful in adding to existing infrastructure to support scholarship in medical education. A full list of peer-reviewed abstracts highlights the breadth and depth of educational scholarship that was presented (https://school.wakehealth.edu/About-the-School/Faculty-Affairs/Faculty-Development/Health-Professions-Education-Institute/2019-Education-Conference).

Disclosures

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

References

1. Chen HC, Wamsley MA, Azzam A, Julian K, Irby DM, O'Sullivan PS. The Health Professions Education Pathway: Preparing Students, Residents, and Fellows to Become Future Educators. Teach Learn Med. 2017;29(2):216-227. doi:10.1080/10401334.2016.1230500
2. Swanwick T, McKimm J. Professional development of medical educators. Br J Hosp Med. 2010;71(3):164-168. doi:10.12968/hmed.2010.71.3.46982
3. Roberts DH, Schwartzstein RM, Weinberger SE. Career Development for the Clinician–Educator. Optimizing Impact and Maximizing Success. Ann Am Thorac Soc. 2014;11(2):254-259. doi:10.1513/AnnalsATS.201309-322OT
4. Ander DS, Love JN. The evolving definition of education scholarship: What the clinician educator needs to know. West J Emerg Med. 2017;18(1):1-3. doi:10.5811/westjem.2016.12.33326
5. Darden AG, DeLeon SD. Transitioning From Medical Educator to Scholarship in Medical Education. Am J Med Sci. 2017;353(2):137-144. doi:10.1016/j.amjms.2016.11.015
6. Bauman MD, Howell LP, Villablanca AC. The Women in Medicine and Health Science Program. Acad Med. 2014;89(11):1462-1466. doi:10.1097/ACM.0000000000000403
7. Campion MW, Bhasin RM, Beaudette DJ, Benjamin EJ. Mid-career faculty development in academic medicine: How does it impact faculty and institutional vitality? J Fac Dev. 2016;30(3):49-64. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5145005/pdf/nihms-826668.pdf.
8. World Federation for Medical Education. The Edinburgh declaration. Med Educ. 1988;22(5):481–2. https://wfme.org/download/the-edinburgh-declaration/?wpdmdl=898&refresh=5d55b71f8eab51565898527. Accessed August 15, 2019.
9. Boyer EL. Scholarship Reconsidered : Priorities of the Professoriate. Carnegie Foundation for the Advancement of Teaching; 1990. https://eric.ed.gov/?id=ED326149. Accessed September 1, 2019.
10. Glassick CE. Boyer's expanded definitions of scholarship, the standards for assessing scholarship, and the elusiveness of the scholarship of teaching. Acad Med. 2000;75(9):877-880. doi:10.1097/00001888-200009000-00007
11. Simpson D, Fincher R-ME, Hafler JP, et al. Advancing educators and education by defining the components and evidence associated with educational scholarship. Med Educ. 2007;41(10):1002-1009. doi:10.1111/j.1365-2923.2007.02844.x
12. Brownson RC, Eyler AA, Harris JK, Moore JB, Tabak RG. Getting the Word Out: New Approaches for Disseminating Public Health Science. J Public Health Manag Pract. 2018;24(2):102-111. doi:10.1097/PHH.0000000000000673
13. Amath A, Ambacher K, Leddy JJ, Wood TJ, Ramnanan CJ. Comparing alternative and traditional dissemination metrics in medical education. Med Educ. 2017;51(9):935-941. doi:10.1111/medu.13359
14. Thammasitboon S, Ligon BL, Singhal G, Schutze GE, Turner TL. Creating a medical education enterprise: leveling the playing fields of medical education vs. medical science research within core missions. Med Educ Online. 2017;22(1):1377038. doi:10.1080/10872981.2017.1377038
15. Reynolds RJ, Candler CS. MedEdPORTAL: Educational scholarship for teaching. J Contin Educ Health Prof. 2008;28(2):91-94. doi:10.1002/chp.163
16. Moore JB, Maddock JE, Brownson RC. The Role of Dissemination in Promotion and Tenure for Public Health. J Public Health Manag Pract. 2018;24(1):1-3. doi:10.1097/PHH.0000000000000691
17. Gottlieb M, Dehon E, Jordan J, et al. Getting Published in Medical Education: Overcoming Barriers to Scholarly Production. West J Emerg Med. 2018;19(1):1-6. doi:10.5811/westjem.2017.11.35253
18. Schwartz A, Young R, Hicks PJ, Appd Learn FA. Medical education practice-based research networks: Facilitating collaborative research. Med Teach. 2016;38(1):64-74. doi:10.3109/0142159X.2014.970991
19. Searle NS, Thompson BM, Friedland JA, et al. The Prevalence and Practice of Academies of Medical Educators: A Survey of U.S. Medical Schools. Acad Med. 2010;85(1):48-56. doi:10.1097/ACM.0b013e3181c4846b
20. Karimbux NY. Promoting the Scholarship of Teaching and Learning Through Peer Review and Public Presentation. J Dent Educ. 2014;78(10).
21. Schimanski LA, Alperin JP. The evaluation of scholarship in academic promotion and tenure processes: Past, present, and future [version 1; referees: 2 approved]. F1000Research. 2018;7. doi:10.12688/f1000research.16493.1
22. Moon JY, Schullo-Feulner AM, Kolar C, et al. Supporting formative peer review of clinical teaching through a focus on process. Curr Pharm Teach Learn. 2018;10(6):771-778. doi:10.1016/j.cptl.2018.03.011
23. Lesser EL, Storck J. Communities of practice and organizational performance. IBM Syst J. 2001;40(4):831-841. doi:10.1147/sj.404.0831
24. Ranmuthugala G, Plumb JJ, Cunningham FC, Georgiou A, Westbrook JI, Braithwaite J. How and why are communities of practice established in the healthcare sector? A systematic review of the literature. BMC Health Serv Res. 2011;11:273. doi:10.1186/1472-6963-11-273

Perspectives

Rapid HIV Treatment Initiation in the Rural and Semi-rural U.S.: North Carolina Piloting a Model

Noah P. Manusco, B.S.[1], Christine A. Schalkoff, M.S.P.H.[1], Breana J. Uhrig Castonguay, M.P.H.[1,2], Candice J. McNeil, M.D., M.P.H.[3], Cynthia L. Gay, M.D., M.P.H.[2], Heidi Swygard, M.D., M.P.H.[2,4]

Ending the HIV epidemic in the United States has never been more possible than now. The 40,000 new infections each year are concentrated among communities of color and LGBTQ+ populations in the rural and semi-rural South and in urban centers of California and the Northeast.[1] The current administration has set forth Ending the HIV Epidemic: A Plan for America to address the public health crisis in these identified locations (Figure 1) by improving access to and retention in care in order to optimize individual health and eliminate the risk of sexual transmission.[2] To achieve the goal of a 90% reduction in new HIV infections by 2030, public health officials are encouraged to identify, learn from, and replicate successful international, state, and local interventions.[2]

An increasingly successful intervention to curb the HIV epidemic internationally is the rapid initiation of antiretroviral therapy (ART), referred to as "rapid-start" ART but with varying degrees of rapidity, for patients presenting with new HIV diagnoses. In low- and middle-income countries, evidence supports the benefits of these rapid treatment initiation (RTI) programs – which include medical, psychological, and social support – where HIV prevalence is high and access to care is limited.[3,4] RTI programs have recently been replicated in several large U.S. urban centers, too, producing high rates of viral suppression and increased retention in care compared to standard methods.[3,5,6] However, there is still a gap in the current research to support universal RTI program implementation in the U.S. because of limited evidence from rural and semi-rural settings. Further, the inconsistency on how to define "rapid-start," with definitions varying from "same day as diagnosis" to "within two weeks of diagnosis", makes proper evaluation difficult.[5,7] We believe "rapid-start" should be defined as ART initiated on the same day as HIV notification and will use this definition throughout.

Rural and semi-rural settings present different challenges for RTI compared to the RTI initiatives in urban centers. Rural-area patients have less access to public transportation, increased stigma and concerns with confidentiality, longer clinic wait times, minimal health insurance coverage, and overall lower socioeconomic status.[8-11] Addressing systematic barriers found in rural and semi-rural settings and providing more consistency to the definition of "rapid-start" ART are thus important for accurately measuring the impact of RTI. Since no model for these non-urban U.S. settings exists, we see a strong need to create and test new and innovative models specifically tailored to this setting's needs. Evidence-based results could then help pave the way for public health officials to coordinate national RTI expansion to efficiently reach the 2030 goal for HIV reduction.

[1]Department of Health Behavior, Gillings School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

[2]Department of Medicine, Division of Infectious Disease, University of North Carolina at Chapel Hill, Chapel Hill, NC

[3]Department of Internal Medicine, Section on Infectious Disease, Wake Forest School of Medicine, Winston-Salem, NC

[4]North Carolina Department of Health and Human Services, Division of Public Health, Communicable Disease Branch, Raleigh, NC

Address Correspondence To:
Heidi Swygard M.D., M.P.H.
Department of Medicine
Division of Infectious Diseases
University of North Carolina at Chapel Hill
130 Mason Farm Road, CB 7030
Chapel Hill, NC 27599
heidi_swygard@med.unc..edu

If we look at North Carolina (Figure 2), 64 of the 100 counties are considered rural by the U.S. Census making it a great testing ground for new RTI models.[12] In terms of HIV diagnosis and care, Disease Intervention Specialists from the NC Department of Health and Human Services provide notification, intervention, and counseling services within 30 days of a chronic HIV diagnosis.[13] Patients then wait anywhere from four to ten weeks to receive their first dose of ART.[13,14] This is because referral appointments to initiate treatment can take up to four weeks due to transportation barriers for patients and availability of physicians. Pretreatment labs can take an additional one to two weeks, and then under- or uninsured patients must wait an additional three to four weeks for medication approval.[13,14] This large gap between HIV diagnosis and ART initiation is not unique to North Carolina. These delays are seen across the country. With current knowledge that an undetectable viral load lowers the risk of HIV transmission to zero, a four to ten week delay creates broad public health concern. It not only delays viral suppression but also increases both the chance of loss to follow up and the potential for new HIV transmission events.[15,16]

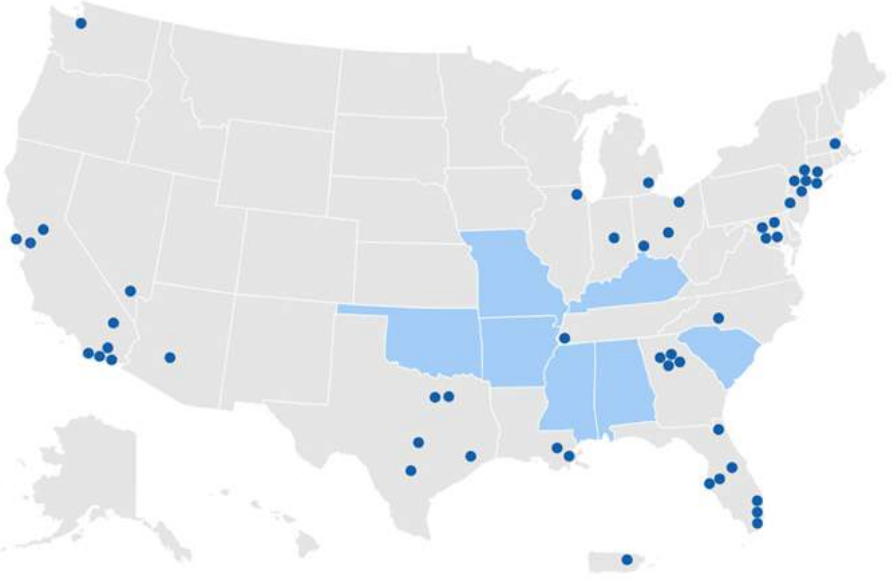


Figure 1. The 48 counties where more than 50% of new HIV diagnoses occurred in 2016 and 2017, along with seven states with a substantial HIV burden in rural areas, as reported by Ending the HIV Epidemic: A Plan for America[2]

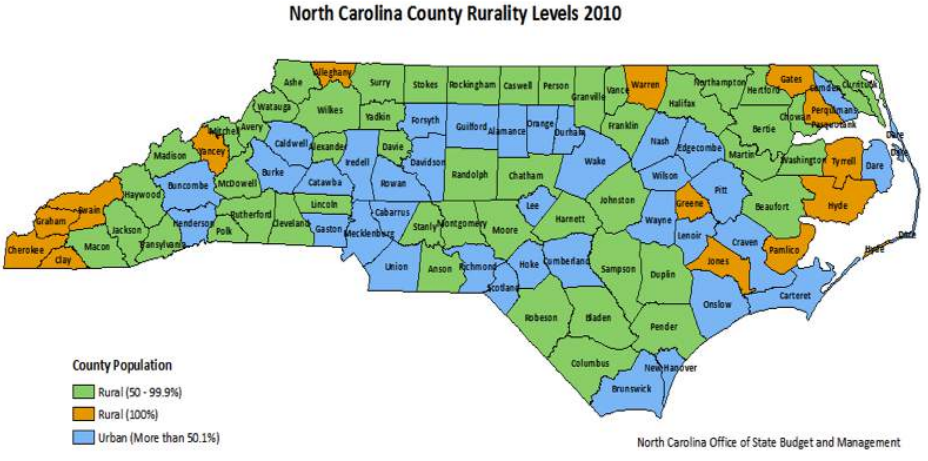


Figure 2. North Carolina Rurality Levels, 2010 Census Data[12]

To explore a potential RTI program suitable for the rural and semi-rural U.S., we will pilot the North Carolina Rapid ART Program for Individuals with an HIV Diagnosis (NC RAPID) starting in 2020. The NC RAPID program will offer newly diagnosed persons at the time of HIV notification immediate ART initiation (Biktarvy, Gilead Inc.) prior to presenting to clinic, combined with medication counseling and lab evaluation. On this same day, a clinic visit will be scheduled and a medication sustainability plan initiated to ensure continuous access to ART using existing medication assistance programs. This RTI model will be evaluated outside the metropolitan setting and is novel as it incorporates a pre-clinic definition of "rapid-start" while addressing several of the barriers to care mentioned earlier. Our outcomes of interest include time to viral suppression, linkage to care, retention in care at six and twelve months, and general acceptability of the program by both patients and local health care providers via in-depth interviews. For this pilot program, we will compare outcome data to a historical cohort in the same setting. These data will inform future implementation projects around RTI.

Health care providers and health officials are already slowly recognizing the potential of rapid HIV treatment in ending the HIV epidemic. Successful implementation and improved outcomes from NC RAPID could provide a new RTI model that specifically address the unique structural, financial, and social barriers to HIV care that exist in North Carolina and beyond. By providing evidence-based research in a non-urban setting of the U.S., supplementing the success of RTI implementation in large urban cities, North Carolina could help lay the groundwork for creating national RTI guidelines as an important tool to end the HIV epidemic in the U.S. – something never before imagined in our lifetime.

Disclosures

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

References

1. Center for Disease Control and Prevention. HIV in the United States by Region. (2019, September 26). Available at https://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html. Accessed October 27, 2019.
2. The White House, National Office of AIDS Policy. National HIV/AIDS strategy for the United States, updated to 2020. 2015. Available at: https://www.hiv.gov/sites/default/files/nhas-2020-action-plan.pdf. Accessed October 27, 2019.
3. Boyd MA, Boffito M, Castagma A, Estrada V. Rapid initiation of antiretroviral therapy at HIV diagnosis: definition, process, knowledge gaps. HIV Med 2019; 20(Suppl. 1): 3-11.
4. Rosen S, Maskew M, Fox MP et al. Initiating Antiretroviral Therapy for HIV at a Patient's First Clinic Visit: The RapIT Randomized Control Trial. PLoS Med 2016; 13(5).
5. Pilcher C, Ospina-Norvell C, Dasgupta A et al. The Effect of Same-Day Observed Initiation of Antiretroviral Therapy on HIV Viral Load and Treatment Outcomes in a US Public Health Setting. JAIDS 2017; 74: 44-51.
6. Halperin J, Butler I, Katherine C et al. Linkage and Antiretroviral Therapy Within 72 Hours at a Federally Qualified Health Center in New Orleans. AIDS Patient Care ST 2018; 32: 39-41.
7. Ford N, Migone C, Calmy A et al. Benefits and Risks of Rapid Initiation of Antiretroviral Therapy. AIDS2018; 32: 17-23.
8. Brewer RA, Chrestman S, Mukherjee S, et al. Exploring the Correlates of Linkage to HIV Medical Care Among Persons Living with HIV Infection (PLWH) in the Deep South: Results and Lessons Learned from the Louisiana Positive Charge Initiative AIDS Behav. 2018; 22: 2615.
9. Reschovsky, J, Staiti A. Access and quality: does rural America lag behind? Health Affairs. 2005; 24(4): 1128-1139.
10. Parker, K, Horowitz, JM, Brown, A, Fry, R, Cohn, D, and Igielnik, R. Views of Problems Facing Urban, Suburban and Rural Communities. Pew Research Center. 2018. Available at https://www.pewsocialtrends.org/2018/05/22/views-of-problems-facing-urban-suburban-and-rural-communities/. Accessed October 25, 2019.
11. Douthit N, Kiv S, Dwolatzky T, and Biswas S. Exposing some important barriers to health care access in the rural USA. Public health. 2015; 129(6): 611-620.
12. The US Census Bureau. The Urban and Rural Faces of North Carolina. Available at https://files.nc.gov/ncosbm/documents/files/2018ACSNC.pdf. Accessed January 15, 2020.
13. Mobley, V. Personal Communication. 2019.
14. Sena A, Donovan J, Swygard H, et al. The North Carolina HIV Bridge Counselor Program: Outcomes from a Statewide Level Intervention to Link and Reengage HIV-Infected Persons in Care in the South. J AIDS. 2017; 76(1).
15. Mateo-Urdiales A, Johnson S, Nachega JB, Eshun-Wilson I. Rapid initiation of antiretroviral therapy for people living with HIV. Cochrane Database of Syst Rev. 2019; 2.
16. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019; 393(10189).

Perspectives

"Doctor. I heard CBD might help, can I start taking it?"

Amanda Durazo, M.S.N.[1], James N. Kimball, M.D.[1]

Cannabidiol (CBD) has become more prominent in popular culture, and consequently physicians are increasingly asked by patients about the risks and benefits of CBD use. Gallup polls in August of 2019 showed that 14% of the U.S. population states they are using CBD.[1] However, here at Wake Forest Baptist Health, CBD is not included in the medication lists for patients, nor can it be added to the electronic medical record (EMR). Given that CBD is sold everywhere from CVS to Walmart[2], it is time that we as physicians start to ask our patients about CBD use. It is also time for the medical team to arm themselves with more information about CBD. Given the evidence for increasing use among the U.S. population, this article can serve as an information tool for physicians regarding CBD products and CBD use in their patients.

[1]Department of Psychiatry, Wake Forest School of Medicine, Winston-Salem, NC

Address Correspondence To:
Amanda Durazo
Department of Psychiatry
Wake Forest Baptist Health
791 Jonestown Road
Winston-Salem, NC
adurazo@wakehealth.edu

Epidiolex

The only FDA approved CBD product is Epidiolex (cannabidiol) oral solution, which obtained FDA approval in June 2018 for the treatment of seizures associated with Lennox-Gastaut syndrome and Dravet syndrome in patients two years of age or older. It is administered only as an oral solution, and dosing is weight-based. It is recommended that prescribing physicians obtain serum transaminases (ALT and AST) in addition to total bilirubin levels prior to initiating treatment. If these lab values increase to two to three times the upper limit of normal, Epidiolex should be weaned off (to prevent seizure induction) and stopped. Epidiolex can cause some side effects including dry mouth, diarrhea, reduced appetite, drowsiness, anemia, fatigue, hepatocellular injury, suicidal ideation, hypersensitivity reactions, and withdrawal reactions. Epidiolex is a moderate to strong inhibitor and strong inducer of CYP3A4 and CYP2C19. Thus, any drug that potentiates this system will have interactions, especially ones like warfarin and other anti-epileptic drugs.[3]

FDA Consumer Update

In November 2019, the FDA released a consumer update about CBD. The update noted that it is currently illegal to market CBD as a dietary supplement or to add CBD to food. Additionally, the FDA has received only limited data about CBD safety, which includes safety risks that need to be considered prior to starting CBD. The FDA also points out that CBD products are marketed with unproven claims, and that CBD products are of an unknown quality. The update highlights some of the questions that need to be answered to deem CBD safe, including: What happens with prolonged CBD use? What effect does CBD have on a developing brain? How does CBD interact with other herbs and botanicals? Does CBD cause male reproductive toxicity, as has been reported in animal studies?[4]

What Does CBD Oil Claim to Treat?

Discussion of medicinal supplements among patients is a regular occurrence, and many are using CBD for various conditions. During clinical rotations, one of the authors (AD) noted patients were using it for cancer related anorexia, nausea, pain, anxiety, arthritis, and tremor related to Parkinson and Huntington Disease. One distributor of a CBD product claims that CBD has analgesic, anti-inflammatory, antioxidant, anti-emetic, anxiolytic, anti-neoplastic, antipsychotic, anti-spasmodic, neuroprotective, anti-ischemic, and anti-epileptic properties. Additional claims include reduction of tetrahydrocannabinol (THC) psychoactivity, sleep promotion, and appetite reduction.[5] The August 2019 Gallup poll stated the top three reasons people use CBD are: pain (40%), anxiety (20%), and sleep/insomnia (11%).[1]

What Does CBD Treat According to the Evidence?

In regards to chronic pain, an overwhelming body of convincing preclinical evidence indicates that cannabinoids produce antinociceptive effects in inflammatory and neuropathic rodent pain models; however, significant human studies are lacking.[6,7] CBD represents an attractive option in chronic pain treatment, particularly in the context of opioid abuse, not only because of its potential efficacy, but also because of its limited misuse and diversion potential as well as safety profile.[8]

In regards to anxiety, studies have very small sample sizes. This means exaggerated responses or lack of significant effects could be due to a lack of statistical power. In addition, most of the studies used normal human volunteers.[9]

There are three randomized trials assessing the impact of moderate-length CBD therapy on patients with schizophrenia. They all demonstrate a reduction of schizophrenia symptomatology over time for at least some measures but differ as to the impact of CBD therapy on the disease.[9]

The only available trial of CBD in Parkinson disease did not find benefits in the movement aspect of the disorder but may impact sleep.[10] However, in an outpatient psychiatric population with insomnia without Parkinson disease, sleep scores displayed no sustained improvements during a three-month study.[11]

There are no human studies that investigated the effects of CBD in either Alzheimer disease or unipolar depression. Treatment with CBD alone was insufficient at managing choreic movements in patients with Huntington disease.[12]

Drug Interactions

CBD exhibits both pharmacodynamic and pharmacokinetic properties that could lead to adverse drug interactions and drug-drug interactions.[13] CBD has been seen in concentrations ranging from very low to potentially supratherapeutic doses that exceed FDA-approved dosing for seizure disorders.

CBD has activity at CYP450 isoforms including 3A4, 2C9, 2C19, 1A2, 2C8, 2B6, and 2E1.[13,14] However, CYP450 isoforms 3A4 and 2C19 are the most important to CBD metabolism and as such, other drugs that are either substrates, inducers, or inhibitors of 3A4 or 2C19 need to be used cautiously with CBD oil; some examples of which are: immunosuppressants, chemotherapeutics, antidepressants, antipsychotics, opioids, benzodiazepines, z-hypnotics, statins, calcium channel blockers, carbamazepine, topiramate, phenobarbital, efavirenz, pioglitazone, proton pump inhibitors, cimetidine, ketoconazole, clopidogrel, fluconazole, rifampin, phenytoin, and St. John's Wort. In addition, CBD has inhibitory effects at clinically relevant dosing on UGT1A9 and UGT2B7 medicines such as acetaminophen, canagliflozin, sorafenib, irinotecan, propofol, mycophenolate, valproic acid, dabigatran, dapagliflozin, hydromorphone, losartan, ibuprofen, naproxen, and ezetimibe.[14] These medications need to be adjusted.

Conclusion

The only certainties about CBD are that patients are using it, and more studies are needed to prove claims of efficacy as well as drug interactions. Patients using CBD should get baseline liver tests including AST, ALT, and total bilirubin. If these serum blood counts elevate to within two to three times the upper limit of normal while using CBD, CBD should be stopped. It is recommended that CBD be weaned down, versus being stopped abruptly due to the anti-epileptic properties of CBD. Care must be taken when directing patients toward CBD products because there is little regulation, and studies have found inaccurate labeling of CBD and THC quantities, even among the same manufacturers.[15] Knowing that CBD can have drug-drug interactions, it is important for prescribers to ask patients about CBD use. At Wake

Forest Baptist Health, the EMR system has been updated to include electronic cigarettes in the patient history section of their chart, but not CBD. To provide our patients with the best quality health care, it is time that CBD is added as well. Until then, prescribers need to start asking their patients about CBD use and ensure that liver function, adverse drug reactions, as well as drug-drug interactions are monitored in patients using CBD.

Acknowledgements

Special thanks to Stephen and Marian Rayburn for their significant contributions to editing.

Disclosures

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

References

1. Epidiolex [package insert]. Carlsbad, CA: Greenwhich Biosciences Inc; issued June 2018. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210365lbl.pdf
2. "What You Need to Know (And What We're Working to Find Out) About Products Containing Cannabis or Cannabis-derived Compounds, Including CBD." (2019, November 25). Retrieved From: https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis
3. "CBD Natural Health Benefits for You and the Planet" (2019, October 23). Retrieved from https://pluscbdoil.com/category/cbd-oil/
4. Donvito G, Nass SR, Wilkerson JL, et al. (2018). The endogenous cannabinoid system: a budding source of targets for treating inflammatory and neuropathic pain. Neuropsychopharmacology, 43 (1), pp. 52-79.
5. VanDolah HJ, Bauer BA, Mauck KF. (2019). Clinicians' Guide to Cannabidiol and Hemp Oils. Mayo Clin Proc, 94(9):1840-1851.
6. Hurd YL. (2017). Cannabidiol: swinging the marijuana pendulum from 'weed' to medication to treat the opioid epidemic Trends Neurosci, 40 (3), pp. 124-127.
7. White CM. (2019). A Review of Human Studies Assessing Cannabidiol's (CBD) Therapeutic Actions and Potential. J Clin Pharmacol., 59(7):923-934.
8. Chagas MH, Zuardi AW, Tumas V, et al. (2014). Effects of cannabidiol in the treatment of patients with Parkinson's disease: an exploratory double-blind trial. J Psychopharmacol., 28:1088-1098.
9. Shannon S1, Lewis N2, Lee H3, Hughes S. (2019). Cannabidiol in Anxiety and Sleep: A Large Case Series. Perm J., 23:18-041.
10. Elsaid S, Kloiber S, Le Foll B. (2019). Effects of cannabidiol (CBD) in neuropsychiatric disorders: A review of pre-clinical and clinical findings. Prog Mol Biol Transl Sci., 167:25-75.
11. Jiang R., Yamaori S., Takeda S., Yamamoto I., Watanabe K. (2011). Identification of cytochrome P450 enzymes responsible for metabolism of cannabidiol by human liver microsomes. Life Sci., 89:165–170.
12. Brown JD, Winterstein AG. (2019). Potential Adverse Drug Events and Drug-Drug Interactions with Medical and Consumer Cannabidiol (CBD) Use. J Clin Med., 8(7). pii: E989.
13. Skelley JW, Deas CM, Curren Z, Ennis J. (2013). Use of cannabidiol in anxiety and anxiety-related disorders. J Am Pharm Assoc. 2019 Dec 19. pii: S1544-3191(19)30514-X.

Perspectives

The Power of the Story

Ryan Koski-Vacirca, M.S.[1]

In October of 2017, I stepped inside a fluorescent, tiled clinic room and closed the cheap plywood door behind me. Inside, I introduced myself to John and seated myself on the stool opposite his perch on the exam table; I unfurled his paper medical chart from its manila folder. I had spent the week with a Wake Forest-affiliated clinic in Wilkesboro, North Carolina – the Western part of the state, the edge of southern Appalachia, and the heart of the opioid epidemic.[1] He quickly told me, with a chuckle, that he made the clinic appointment today for a checkup on his back pain. He said preaching helped him. He said the community in church helped him.

John's back pain started during the middle of his 20-year career on the road as a long haul trucker.

"How exactly did it start?"

He let out another good-natured laugh and pushed up his glasses. "Couldn't find something decent to eat."

In my mind's eye, I spun through memories from my own long drives on I-80 and I-70. Nebraska, Wyoming, Nevada; the desert, "Little America," Sinclair gas stations with bright lights and neon signs, "HOT SHOWERS" and plastic-wrapped pastries for $1.50. You have no choice when you're trucking, he explained to me. There are no options.

"I'm a diabetic," he said bluntly. "Couldn't find something decent to eat."

John's story – among countless others – left me voracious. What was happening to our patients – and why? I imagined myself stumbling around in the dark, reaching out; I searched everywhere with no direction. Dr. Dhruv Khullar suggests that "[the] central problem in healthcare is [that] we overestimate benefits of the status quo, and underestimate the need for change."[2] Shortly after crossing paths with that worldview, I made my decision: I would leave medical school for a public health degree, to disrupt the status quo. I would leave, and in leaving, would find answers.

I arrived at Johns Hopkins School of Public Health, wide-eyed and underqualified. In my quest for answers, I uncovered interests in health care economics and market competition, which led to internships at a nonpartisan think tank and then at the Senate's Health, Education, Labor, and Pensions Committee. Readings from inside and outside the classroom underscored the breadth and depth of experience I discovered.

The greatest insight I received this year, however, did not come from a classroom, and it did not come from an internship. It did not come from a high-powered institution,

[1]Department of Public Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Address Correspondence To:
Ryan Koski-Vacirca, M.S.
Department of Public Health
Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe St.
Baltimore, MD 21205
Email: rkoskiv1@jhmi.edu

a government agency, or from a renowned professor. It came from John. Awash in a sea of new experiences, far removed from the Wilkesboro clinic room, my time with John revealed a guiding principle – our greatest understanding is nothing without the story.

Without the story, any health care commentary is woefully incomplete; providers chart and prescribe for a present we do not understand. Without the story, policymakers legislate for a future they cannot feel. Without the story, we risk becoming unmoored from our core principles. I left Baptist Medical Center for answers, but the most important answers were right where I left them: with the patients we see.

Through the long lens of time spent away, I realized there is no greater place for these stories than "Baptist". Here, stories uniquely converge that are otherwise disparate, uncommon, and unseen. This isn't idealized, unbound conjecture. It is objective, too.

It is difficult to imagine a more diverse patient population than Wake Forest Baptist Medical Center's.[3] No single dimension or measure taken alone appropriately captures this strength. Our catchment area includes four states and three major cities.[4] Our patients live in a broad spectrum of the built environment, from urban Winston-Salem to northern Alleghany county and the edge of the Great Smoky Mountains National Park, two of the least densely populated areas in the region.[5] Our patients include some of the wealthiest in North Carolina, and also some of the poorest.[6] Our patients also represent a broad swath of cultural and ethnic backgrounds, including recently immigrated patients living in the Winston-Salem area and the largest percentage Hispanic and Latinx population in North Carolina.[7]

Pro Humanitate, the Wake Forest University motto, means just that: for humanity. But the classicist James Powell suggests that its true meaning is more complex – that our fundamental commitment is to human cultivation, to human flourishing.[8] From Cherokee County and the Appalachian foothills to Forsyth, Baptist Medical Center represents *Pro Humanitate* in motion. In no other hospital, educational environment, or city could I have converged with such a unique mixture of stories, including John's.

While we train here, we have the opportunity to learn from a diversity of perspectives afforded to few. When I think of Baptist, that is what I remember: the chance to hear powerful stories from untold voices, and the privilege to briefly orbit their corner of the world. If or when we leave, we bring that perspective along – a back-pocket gift, for use in other places that aren't so lucky.

Disclosures:

No financial support given. Author reports no conflicts of interest.

References:

1. ODPHP. Reducing Prescription Opioid Misuse in North Carolina [Internet]. News & Events | Health.gov. 2018 [cited 2019 Nov 11]. Available from: https://health.gov/news/blog/2018/01/reducing-prescription-opioid-misuse-north-carolina
2. Dhruv Khullar on Twitter: "Many folks asking if there's evidence for this. Do we really need peer-reviewed papers to treat patients more humanely? And do you have research showing HPI first is better? Central problem in healthcare is we overestimate benefits of status quo & underestimate need for change." / Twitter [Internet]. Twitter. [cited 2019 Nov 11]. Available from: https://twitter.com/dhruvkhullar/status/1070094750450098176
3. U.S. Census Bureau QuickFacts: Winston-Salem city, North Carolina [Internet]. [cited 2019 Nov 11]. Available from: https://www.census.gov/quickfacts/fact/table/winstonsalemcitynorthcarolina/RHI725218#RHI72521
4. About the Pediatric Residency Program [Internet]. [cited 2019 Nov 11]. Available from: https://www.brennerchildrens.org/Residency/About/About-the-Pediatric-Residency-Program.htm
5. Census - Map Results [Internet]. [cited 2019 Nov 11]. Available from: https://data.census.gov/cedsci6. Census - Map Results [Internet]. [cited 2019 Nov 11]. Available from: https://data.census.gov/cedsci/map?q=population%20density&hidePreview=false&table=DP05&tid=ACSDP5Y2017.
6. Census - Map Results [Internet]. [cited 2019 Nov 11]. Available from: https://data.census.gov/cedsci/map?q=population%20density&hidePreview=false&table=DP05&tid=ACSDP5Y2017.
7. Hispanics in N.C.: Big numbers in small towns | UNC Charlotte Urban Institute [Internet]. [cited 2019 Nov 11]. Available from: https://ui.uncc.edu/story/hispanic-latino-population-north-carolina-cities-census
8. Powell J, Contributor G. The Meaning of a Motto [Internet]. Wake Forest Magazine. 2012 [cited 2019 Nov 11]. Available from: https://magazine.wfu.edu/2012/01/27/the-meaning-of-a-motto/

Challenge Cases

Evolving bullous lesions in a patient with May-Thurner Syndrome

Adam M. Jorgensen, B.S.[1,2], Maria D. Avila, M.D.[3], Omar P. Sangüeza, M.D.[1,3], Christine S. Ahn, M.D.[1,3], Lindsay C. Strowd, M.D.[3]

Abstract

The diagnosis and treatment of cutaneous lesions can be challenging in cases where skin lesions undergo evolution. Here we present a complicated case in which histopathologic findings evolved over the course of the disease, reflected through different discoveries in multiple biopsy specimens. This case highlights the importance of correlating clinical history and presentation with histologic findings to obtain the correct diagnosis in dermatologic diseases.

[1] Department of Dermatology, Wake Forest School of Medicine, Winston-Salem, NC

[2] Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC

[3]Department of Pathology, Wake Forest School of Medicine, Winston-Salem, NC

Address Correspondence To:
Lindsay C. Strowd, M.D.
Department of Dermatology
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
Phone: (336) 716-2768
E-mail: lchaney@wakehealth.edu

Case Presentation

A 16-year-old male presented to the dermatology clinic with a four month history of progressively worsening pruritic blisters on bilateral lower extremities. Past medical history included a recent diagnosis of May-Thurner Syndrome with extensive deep venous thrombosis of the legs, managed with aspirin, low-molecular-weight heparin, and trimethoprim-sulfamethoxazole (TMP-SMX). Physical exam was notable for tense blisters and bullae on the plantar feet, dorsal feet, and lower legs, with some associated overlying crust and hyperpigmentation (Figure 1A). Punch biopsies of one blister edge for histologic evaluation and perilesional skin for direct immunofluorescence (DIF) were obtained. Histology showed impressive intraepidermal collections of neutrophils along with acantholysis. DIF was positive for granular deposition of IgG along the basement membrane and intercellular deposition of IgA and C3 (Figures 1B, 1C). Laboratory values were notable for mild anemia (Hgb 10.6 g/dL) and peripheral eosinophilia (11% of differential). A basic metabolic panel was within normal limits.

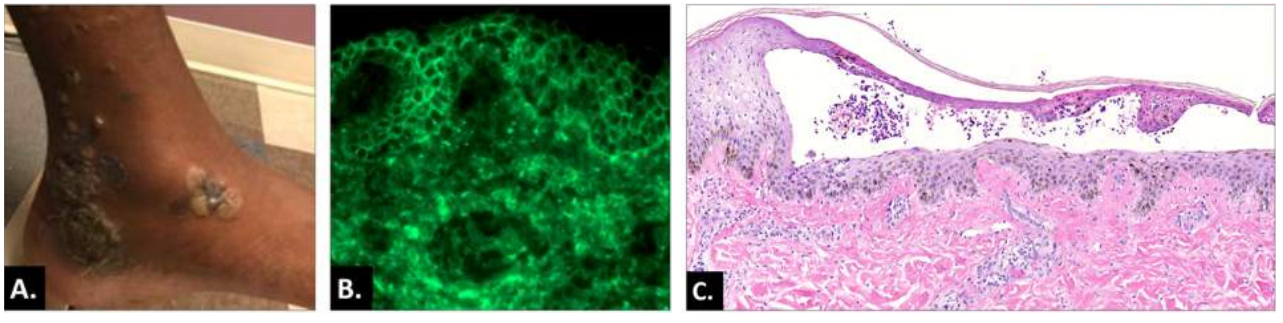


Figure 1. (A) Annular bullae with scattered pustules at the periphery on the medial ankle (B) Positive deposition of IgA in an intercellular pattern (C) Acanthosis and intraepidermal collections of neutrophils

Challenge Question 1: Based on the patient's history, clinical presentation, and histologic findings, what is the most likely diagnosis?

A. Bullous lupus erythematosus
B. Bullous drug eruption secondary to TMP-SMX
C. Epidermolysis bullous acquisita
D. Bullous pemphigoid
E. Bullous arthropod bite reaction

Based on clinical presentation and histopathologic findings, the patient was diagnosed with bullous lupus erythematosus (answer choice A) and started on methotrexate 10mg weekly. Despite therapy, lesions evolved into hypertrophic, verrucous plaques at sites of prior blisters (Figure 2A). A punch biopsy was obtained from a vegetative plaque which demonstrated acanthosis, papillomatosis, and hyperkeratosis of the epidermis with intraepidermal collections of neutrophils and eosinophils, without significant acantholysis. Within the dermis, there was an inflammatory infiltrate composed of lymphocytes, neutrophils, and eosinophils (Figure 2B). Additional serologic workup revealed negative ANA and normal complement levels. During this time, he also developed abdominal pain and diarrhea. Stool studies were negative for occult blood but notable for significantly elevated calprotectin levels. Tissue transglutaminase antibodies were negative.

Challenge Question 2: Given this additional information, what is the most likely diagnosis?

A. Bullous systemic lupus erythematosis (SLE)
B. Dermatitis herpetiformis associated with celiac disease
C. IgA pemphigus with features of pemphigus vegetans
D. Bullous drug eruption
E. Bullous pemphigoid

This patient's skin disease was ultimately diagnosed as a vegetative presentation of IgA pemphigus (answer choice C). IgA pemphigus is a rare autoimmune blistering disorder that can demonstrate variable clinical findings. This patient's clinical presentation and skin biopsies are challenging because they displayed features of three different diseases that can have overlapping findings: IgA pemphigus, pemphigus vegetans, and pyodermatitis vegetans (summarized in Table 1).

IgA pemphigus is typically characterized by the intertriginous distribution of vesicles and pustules, often in an annular configuration. The diagnosis is usually confirmed by positive

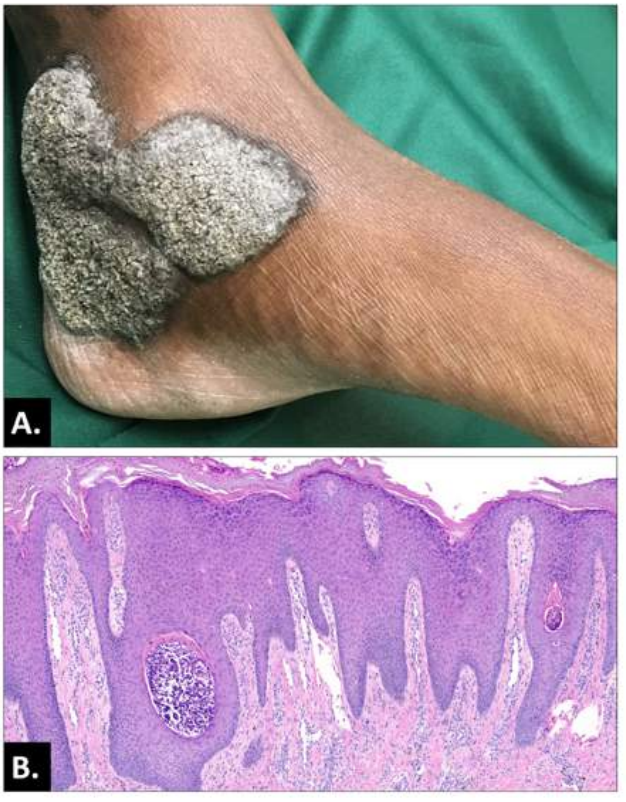


Figure 2. (A) Verrucous hyperkeratotic plaques on the medial ankle, at sites of prior bullae (B) Intraepidermal neutrophils with acanthosis and no evidence of acantholysis

IgA deposition on the cell surface of keratinocytes.[1] Pemphigus vegetans, which is a rare variant of pemphigus vulgaris, is characterized by vegetative plaques in areas of prior blisters and erosions.[2] Pemphigus vegetans most often affects the intertriginous sites, scalp, and face, but may be a response to chronic and treatment-resistant lesions of pemphigus vulgaris.[3] Direct immunofluorescence studies will show deposition of IgG and C3 in an intercellular pattern and occasionally along the epidermal basement membrane.[4] Pyodermatitis vegetans is a chronic mucocutaneous dermatosis, considered on the spectrum of neutrophilic dermatoses. It is strongly associated with inflammatory bowel disease (IBD) and manifests as papules and pustules which coalesce to form vegetating plaques. The majority of patients with pyodermatitis also have oral mucosal involvement, termed pyostomatitis. Direct immunofluorescence is usually negative, although in some cases, nonspecific positive findings have been reported, including deposition of C3, IgG, and IgA either along the basement membrane zone or at intercellular spaces of the epidermis.

Case Findings	Pyodermatitis	Pemphigus Vegetans	IgA Pemphigus
Large bullae formation		X	
Vegetative verrucous plaques	X		
Intraepidermal neutrophils	X	X	X
Epidermal acanthosis, papillomatosis with intraepidermal eosinophils	X	X	
DIF IgA intercellular			X
DIF IgG along basement membrane		X	
Association with Crohn's disease	X		X
Lack of mucosal involvement			X
Peripheral eosinophilia	X		

Table 1. Clinical presentation and histologic findings in pyodermatitis, pemphigus vegetans, and IgA pemphigus

Challenge Question 3: What additional work-up would be beneficial in this patient's case?

A. ELISA for BP180 antigen
B. Anti-neutrophil cytoplasmic antibodies
C. Colonoscopy with esophagogastroduodenoscopy
D. PET/CT scan

The patient underwent colonoscopy and esophagogastroduodenoscopy (EGD) (answer choice C), which revealed pan-colitis from the terminal ileum to the cecum. He was subsequently diagnosed with Crohn's disease and started on infliximab and prednisone, in addition to methotrexate. IBD has been associated with many different cutaneous manifestations. Some associated dermatoses are common and easily recognizable such as psoriasis, pyoderma gangrenosum, and hidradenitis suppurativa, while others are rare.

Discussion

Our patient's case was unusual and complicated in that the clinicopathologic findings did not neatly fit any single diagnosis. We hypothesize that his skin disease was likely unrelated to his medications or medical history of May-Thurner syndrome (a red herring). Rather, his inflammatory bowel disease may have triggered an immunologic response that led to the development of his cutaneous disease. Despite the initial biopsy and immunofluorescence findings, the patient's case in its entirety did not fit the diagnosis of lupus erythematosus. The patient's presentation of large vegetative plaques in areas of prior blister formation and diagnosis of Crohn's disease ultimately led to a diagnosis of IgA pemphigus with features of pemphigus vegetans (Q2, answer choice C). Treatment of this disease involves the use of immunosuppressive medications and controlling any pertinent underlying systemic illness such as Crohn's disease. At this time, the patient remains on infliximab infusions every six weeks for his Crohn's disease, along with methotrexate 12.5mg weekly. His prednisone has been slowly tapered down to 10mg daily with no recurrence of his blisters or the verrucous plaques.

Conclusion

In many specialties, pathology is relied upon to make final and definitive diagnoses. Diseases of the skin can be challenging

as similar pathologic findings can be seen in different entities, different pathologic findings can be seen within the same disease, and skin biopsies can be non-specific. Thus, focusing on both clinical and pathologic information is key to diagnosing complex cutaneous diseases. Additionally, treatment of primary diseases that drive cutaneous disease must be taken into consideration. In this case, large vegetative plaques in areas of prior blister formation with concurrent Crohn's disease led to the diagnosis of IgA pemphigus. Treating both the dermatologic disease and underlying IBD led to resolution of the verrucous plaques.

Disclosures

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

References

1. Inoue-Nishimoto T, Hanafusa T, Hirohata A, et al. IgG/IgA pemphigus representing pemphigus vegetans caused by low titers of IgG and IgA antibodies to desmoglein 3 and IgA antibodies to desmocollin 3. J Eur Acad Dermatol Venereol. 2016 Jul;30(7):1229-31.
2. Wolz MM, Camilleri MJ, McEvoy MT, Bruce AJ. Pemphigus vegetans variant of IgA pemphigus, a variant of IgA pemphigus and other autoimmune blistering disorders. Am J Dermatopathol. 2013 May;35(3):e53-6.
3. Weston WL, Friednash M, Hashimoto T, Seline P, Huff JC, Morelli JG. A novel childhood pemphigus vegetans variant of intraepidermal neutrophilic IgA dermatosis. J Am Acad Dermatol. 1998 Apr;38(4):635-8.
4. Kim TH, Kim SC. Pyodermatitis-Pyostomatitis Vegetans Associated with Crohn's Disease. Ann Dermatol. 2015;27(5):624–625. doi:10.5021/ad.2015.27.5.624

Original Science

An Airway and Anesthetic Protocol for Morbidly Obese Patients Undergoing Bariatric Surgery

Yvon F. Bryan, M.D.[1,3], Ryan Keenan, M.D.[1,4], William Morris, B.A.[1], Joseph May, D.O.[1,5], Taylor Grice, M.D.[1], Deborah M. Whelan, M.D.[1], Randy W. Calicott, M.D.[1], Kathleen N. Johnson, B.S.[1], Lauren Hoke, B.A.[1], Myron Powell, M.D.[2], Stephen S. McNatt, M.D.[2], Adolfo Z. Fernandez, M.D.[2]

Abstract

Morbidly obese (MO) patients have a high risk for difficult intubation, inadequate bag mask ventilation (BMV), and/or desaturation events. Our goal was to establish a protocol for airway and anesthetic management of MO patients to minimize complications. An IRB-approved prospective study was performed at Wake Forest Baptist Health. We recruited 406 MO patients who were scheduled for bariatric surgery. The protocol had three parts: 1) premedication, preoxygenation, and positioning; 2) rapid sequence induction-intubation using videolaryngoscopy (VL); and 3) repositioning for emergence-extubation. The primary outcome measure was the use of VL that resulted in intubation in ≤2 minutes (min), avoided the need for BMV, and did not result in SpO2 <90%. All 406 patients were intubated using VL. Of those, 391 (96.3%) took ≤2 min. BMV was avoided in 399/406 (98.3%) patients. There were 376 (92.6%) and 383 (94.3%) patients who experienced SpO2 ≥90% during induction-intubation and emergence-extubation, respectively. The mean time for visualization of vocal cords and intubation, (T(vi)), was 35.7 ± 23.6 seconds (s) for patients who maintained SpO2 ≥90%. For patients who desaturated, the mean T(vi) was 66.2 ± 31.9s. Five patients (1.2%) failed the protocol. Overall, our protocol minimized poor outcomes in patients who have a higher likelihood of complications during anesthetic and airway management.

[1]Department of Anesthesia, Wake Forest School of Medicine, Winston-Salem, NC

[2]Department of General Surgery, Wake Forest School of Medicine, Winston-Salem, NC

[3]Department of Anesthesia, Dartmouth-Hitchcock Medical Center, Lebanon, NH

[4]Department of Emergency Medicine, University of Pennsylvania, Philadelphia, PA

[5]Southern Regional AHEC Family Medicine Residency, Fayetteville, NC

Address Correspondence To:
Yvon F. Bryan, M.D.
Department of Anesthesiology
Geisel School of Medicine
at Dartmouth
Dartmouth-Hitchcock
Medical Center
1 Medical Drive
Lebanon, NH 03756
yvon.f.bryan@hitchcock.org

Introduction

Patients presenting for anesthesia and surgery are increasingly likely to be morbidly obese (MO) (body mass index [BMI] ≥35) and super morbidly obese (BMI ≥50).[1] Bariatric surgery is now commonly performed in this patient population at most medical centers[2], and these patients are more likely than leaner patients to develop hypoxemia during interventions following induction-intubation and emergence-extubation, and in the PACU following their anesthetics[3,4]. In addition, they have a higher incidence of difficulty with visualization of the glottis during intubation, inadequate rescue bag mask ventilation (BMV) during rapid sequence induction-intubation[5], and obstructive sleep apnea (OSA) predisposing to desaturation events.

Most studies in MO patients have focused their primary outcomes on only a single component of airway management[6]: intubation (I), ventilation (V), or oxygenation (O). In addition, multiple airway devices and anesthetic techniques have been described to address individual issues related to IVO in MO patients.[7]

The goal of this study was to develop a consensus-based protocol established by clinical anesthesiologists who had extensive experience in the management of MO patients undergoing bariatric surgery. An evidence-based literature review was performed. The reviewed literature focused on MO patients and the management of patients with difficult airway[8]; specifically regarding devices, techniques, and outcomes[9] with an emphasis on IVO and prevention of aspiration/desaturation events. Subsequently, the protocol was revised and amended to establish airway and anesthetic management in MO patients. Bariatric surgeons at our institution also provided valuable insight to promote the best surgical conditions for patients.

The primary outcome of the study was an evidence-based protocol for induction-intubation utilizing videolaryngoscopy that resulted in endotracheal intubation in ≤2 min, avoided the need for BMV, and did not result in a desaturation event (SpO2 <90%). The secondary outcomes measured were the length of time to visualize the vocal cords (T(v)), the length of time from visualization to successful endotracheal intubation (T(i)), the combination of these two times (T(vi)), the necessary manual maneuvers required during BMV, and levels of desaturation that occurred during intubation. Additionally, desaturations at emergence-extubation were also obtained and evaluated.

Methods

After obtaining IRB approval from Wake Forest University Health Sciences and patient written consent, obese patients (BMI ≥30 kg/m^2) scheduled for bariatric surgery (gastric banding, bypass, or sleeve gastrectomy) were recruited for an airway and anesthetic protocol study. Exclusion criteria included: ASA status of 4, BMI <30, allergies to propofol and/or succinylcholine, and a history of malignant hyperthermia.

The protocol for airway and anesthetic management consisted of three parts of the perioperative period: 1) preoperative preparation with premedication, preoxygenation, and positioning; 2) induction-intubation using video laryngoscopy (VL) and maintenance of anesthesia using isoflurane in air/O_2 along with infusion of dexmedetomidine as a narcotic sparing technique; and 3) repositioning for emergence-extubation (see appendix 1).

Midazolam 1-2mg IV was administered prior to being transported to the operating room (OR). In the OR, specific positioning was achieved prior to induction-intubation by placing the patients in the Whelan-Calicott position (reverse Trendelenburg with the head section one increment down)[10]. In order to establish a more precise placement of patients, the author modified the Whelan-Calicott position to the adapted Whelan-Calicott-Bryan (WCB18), which additionally standardized the bed position at 16-18°.

Patients were pre-oxygenated for four minutes to achieve an EtO_2 >0.8, and after the first two minutes, fentanyl (100µg IV) was administered to reduce the hyperdynamic response to VL and intubation. If an EtO_2 >0.8 was not achieved, an additional two minutes of pre-oxygenation was performed. Intravenous induction was performed with propofol and succinylcholine based on total body weight (TBW) and administered at doses of 1.5 and 1.0mg/kg, respectively. Additional fentanyl was also administered to 1.0µg/kg TBW (if weight exceeded 100kg).

Intubations were performed using different VL systems as follows: Glidescope® #3, #4, and #5, Storz® DCI #3 and #4, and CMAC® Mac 3, Mac 4, and dBlade™. Personnel performing the intubations were student nurse anesthetists (SRNAs), certified registered nurse anesthetists (CRNAs), anesthesiology residents, and the attending anesthesiologist. The VL utilized was decided by the preference of the clinician performing the intubation and/or determined by device availability. BMV was not planned nor performed unless desaturations occurred or at the discretion of the attending anesthesiologist.

After intubation, 1-2% isoflurane in air and O_2 at 1L/min each were used in addition to an infusion of dexmedetomidine (0.4µg/kg/hr). Rocuronium for neuromuscular blockade was used for maintenance and additional fentanyl was administered in increments to approximately 1.5µg/kg for the duration of the procedure. During maintenance, the ventilation mode was either pressure or volume control and additional positive end-expiratory pressure (PEEP) was used.

As the surgical procedure progressed toward removal of the ports, the patients were placed on 100% O_2 and positioned in WCB18° in preparation for emergence from anesthesia.

A size 36 French nasal airway coated with lidocaine (2% or 5%) ointment was inserted into the nare to provide access for ambulatory oxygen with continuous positive airway pressure (CPAP) support immediately following extubation, and to decrease desaturation events during transport to postanesthesia care unit (PACU).

Data were collected independent of the clinicians. Research team members were trained by the research coordinator under the supervision of the principal investigator. Proper training was achieved using video and simulation environments to provide a comprehensive understanding of airway and anesthetic management as it pertains to bariatric patients, the study design, and proper prospective data collection technique. A standardized data collection form was used (see appendix 2).

Patient desaturations were defined as SpO_2 <90% and further divided into SpO_2 80-89% and <80%. Specific times during VL and intubation were collected: the time from laryngoscope insertion in the mouth to the visualization of the vocal cords (T(v)) on the monitor screen, and the time from visualization of vocal cords on the screen to the insertion of the endotracheal tube (ETT) through the vocal cords (T(i)). Time of confirmation (T(c)) of intubation was also recorded by the presence of the $EtCO_2$ waveform using capnography. Additionally, the number of attempts to view and to intubate, aids and/or maneuvers used for intubation, as well as the number of BMV adjunct maneuvers (starting with chin lift, and additionally, jaw thrust, placement of an oral airway or two-person BMV, and the application of CPAP >20cmH_2O) were also recorded.

Statistical Analysis

We calculated the mean, standard deviation (SD), and range for age, height, weight, and BMI, and reported 95% confidence intervals (CI) for point estimates. Two-sample t-tests were performed to determine differences in T(v), T(i), and T(vi) between the non-desaturation group and those that did desaturate. A chi-squared test was performed to determine the difference between desaturation incidence in patients with BMI >50 versus those with BMI ≤50, as well as the difference between desaturation incidence for fast T(i) and slow T(i). P-values <0.05 were considered statistically significant.

Results

All 406 patients were safely intubated using videolaryngoscopy. No patients were excluded from the analysis due to protocol deviations. See Table 1 for demographics and type of procedure performed.

Table 1. Demographics (n=406)

Age* (yr)	45.0 (10.1) (23 – 68)	
Weight* (kg)	129.7 (26.0) (82 – 245)	
Height* (cm)	168 (9.4) (110 – 193)	
Body Mass Index*	45.9 (7.7) (31 – 77)	
	Number (n)	**Percentage (%)**
Gender		
Male	78	19.2
Female	328	80.8
Procedure		
Bypass	229	56.4
Banding	26	6.4
Sleeve	151	37.2
ASA Status		
1-2	101	24.9
3-4	305	75.1
Mallampati		
I/II	347	85.5
III/IV	59	14.5
Thyromental Distance		
<3 Fingerbreadths	50	12.1
3 Fingerbreadths	356	87.7
Range of Motion		
Limited	86	21.2
All	320	78.8

*Age, weight, height, and BMI are shown as the mean (SD) (range)

During induction-intubation, 376/406 patients (92.6%, 95% CI 89.6 – 95.0%) experienced SpO_2 ≥90%, while 30/406 (7.4%, 95% CI 5.0 – 10.4%) experienced SpO_2 <90%. Of the 30 patients who experienced oxygen desaturation during induction-intubation, only four had SpO_2 <80%. These four patients accounted for 1% (95% CI 0.3 – 2.5%) of the 406 patients included in the study, or 13.3% (95% CI 3.8 – 30.7%) of the 30 patients with

oxygen desaturation (Table 2). By examining the group of patients who had a BMI >50, we found a higher level of desaturation during intubation: 13.6% of the patients in this group experienced SpO_2 <90% as opposed to 5.3% for the patients with a BMI ≤50 (P = 0.0055, 95% CI 2.1-16.5%).

During emergence-extubation, 383/406 patients (94.3%, 95% CI 91.6 – 96.4%) experienced SpO_2 ≥90%, while 23/406 (5.7%, 95% CI 3.6 – 8.4%) did not. Three of the 23 patients that desaturated had SpO_2 <80%. These three patients account for 0.74% (95% CI 0.2 – 2.1%) of the total 406 patients, or 13.0% (95% CI 2.8 – 33.6%) of the 23 patients with oxygen desaturation (Table 2). During both induction-intubation and emergence-extubation, there was a similar distribution of severe desaturation (13% of the desaturation group).

Table 2. Oxygen Saturation for Induction/Intubation vs. Emergence/Extubation. Two patients desaturated at both: one had SpO2 = 80-89% at both periods and the other had SpO2 <80% at both.

Induction-Intubation		Emergence-Extubation	
SpO2 >90%	376 (92.6%)	SpO2 >90%	383 (94.3%)
SpO2 = 80-89%	26 (6.4%)	SpO2 = 80-89%	20 (4.9%)
SpO2 <80%	4 (1%)	SpO2 <80%	3 (0.7%)

We found 391/406 patients (96.3%, 95% CI 94.0 – 97.9%) required ≤2 min to intubate, while 15/406 (3.7%, 95% CI 2.1 – 6.0%) required >2 min. We also found that the group of patients who did not desaturate during intubation required a statistically significant decreased time to visualize the vocal cords and to place the ETT (Table 3a and b; Figure 1).

Table 3a. Times and Saturations

	SpO2 ≥90%	SpO2 <90%	P-value
T(v) (sec)*	14.3 (10.0)	23.6 (22.9)	0.0175
T(i) (sec)*	21.4 (19.5)	42.6 (42.6)	0.0056
T(vi) (sec)*	35.7 (23.6)	66.2 (31.9)	0.000007
T(c) (sec)	29.2 (9.4)	28.5 (10.0)	0.713

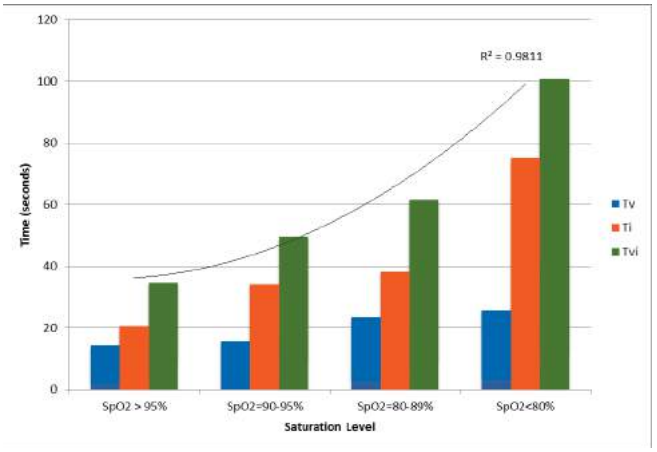
T(v) = visualization time; T(i) = ETT intubation time; T(vi) = T(v)+T(i). T(v), T(i), and T(vi) were not significantly different between level of oxygen desaturation (P = 0.385, 0.052, and 0.054, respectively)

Table 3b. Times and Saturations

	No Oxygen Desaturations		Oxygen Desaturations*	
	SpO2 >95%	SpO2 = 90-95%	SpO2 = 80-89%	SpO2 <80%
T(v) (s)	14.2 (10.1)	15.6 (9.5)	23.4 (24.2)	25.7 (11.9)
T(i) (s)	20.5 (17.8)	33.9 (32.5)	38.1 (29.3)	75.0 (32.7)
T(vi) (s)	34.7 (22.4)	49.5 (33.6)	61.5 (39.2)	100.7 (35.3)

T(v) = visualization time; T(i) = ETT intubation time; T(vi) = T(v)+T(i); T(c) = EtCO2 confirmation time; T(v), T(i), and T(vi) were statistically significantly reduced in the group of patients that did not desaturate

Figure 1. Saturation levels at intubation. Tv = visualization time; Ti = endotracheal intubation time; Tvi = Tv + Ti. Each bar represents the average times for all patients in each saturation level group (>95%, 90-95%, 80-89%, and <80%). The lower the SpO2 level, the longer each time was.



The mean visualization time (T(v)) was 15s and the mean intubation time (T(i)) was 23s. T(v) was divided into fast (<15s) and slow (>15s). Similarly, T(i) was divided into fast (<23s) and slow (>23s). When T(i) was fast, the overall incidence of desaturation was 2.9% compared to the incidence of desaturation when T(i) was slow: 13.8%. Therefore, the incidence of desaturation was significantly lower when T(i) was fast compared to when T(i) was slow (P = 0.000017, 95% CI 5.2-18.2%). Additionally, when T(i) was fast, the incidence of desaturation was not significantly different between the fast T(v) group and the slow T(v) group (P = 0.34) (Table 4). This indicated that T(i) may be more critical than T(v) when it comes to reducing desaturation events.

		T(i)	
		Fast	Slow
T(v)	Fast	190 SpO_2 <90%: 5/190 (2.6%)	61 SpO_2 <90%: 5/61 (8.2%)
	Slow	85 SpO_2 <90%: 3/85 (3.5%)	62 SpO_2 <90%: 12/62 (19.4%)

Table 4. Prevalence of Desaturation in Time Intervals for T(v) and T(i). T(v) = visualization time; T(i) = ETT intubation time. The choice of quadrant for each intubation was determined by examining the mean times for T(v) and T(i) for the whole group. Intubations with T(v) <15s and/or T(i) <23s were considered "fast," while those over that were "slow." Times were not recorded for eight patients.

During induction-intubation, 7/406 patients (1.7%, 95% CI 0.7 – 3.5%) required BMV as rescue due to either the time it took to intubate or the incidence of desaturation. These patients were either rescued with BMV due to a documented desaturation event, or the attending anesthesiologist decided to return to BMV before the desaturation started to occur.

There were 5/406 (1.2%, 95% CI 0.4 – 2.9%) who had problems with all IVO criteria: >2 min to intubate, had to be rescued with BMV, and had SpO_2 <90%. There were 8/406 (2.0%, 95% CI 0.9 – 3.8%) who took >2 min to intubate and experienced SpO_2 <90%. Eight of the 15 patients (53.3%, 95% CI 26.6 – 78.7%) who took >2 min to intubate experienced oxygen desaturations. Patients who took >2 min to intubate, required BMV, or experienced oxygen desaturation were deemed as protocol failures (Table 5).

Table 5. Protocol Failures by Category. I = intubation; V = ventilation; O = oxygenation; BMV = bag mask ventilation.

	Total #	Failed I Alone	Failed V Alone	Failed O Alone	Failed I & V	Failed I & O	Failed IVO
Intubation > 2 min	15	5	0	0	2	3	5
Required BMV	7	0	0	0	2	0	5
SpO2 <90% during intubation	30	0	0	22	0	3	5

Discussion

Our study found that by following a consensus-based protocol, the incidence of hypoxemia was decreased in MO patients undergoing elective gastric bypass, banding, and sleeve gastrectomies. All 406 patients were safely intubated using VL by clinicians with varying degrees of experience and expertise. However, 9% of patients required >2 min to intubate, BMV, and/or suffered a desaturation event (SpO_2 <90%). Five patients failed all three outcomes; thus, failed the protocol. These five patients did not have any common demographic or airway indicators to explain their challenges during intubation. The highest incidence of secondary outcome failures was comprised of the patients who desaturated. Even though those who desaturated accounted for the largest number of failures, they did not make up a large percentage of the whole study group; only 30 of our patients desaturated.

Fifteen patients required >2 min to intubate. In a fraction of these cases, the lengthy attempt at visualization and intubation led to a desaturation event with an associated need for rescue BMV. We avoided BMV as a part of our protocol based on surgical recommendations against potential gastric insufflation; however, when required as a rescue technique, no difficult ventilation encounters were recorded. The issues with intubation may have been due to variations in the clinicians' level of experience and familiarity with the VL device.[11]

The times taken to visualize the vocal cords and place the ETT were crucial in determining the other primary outcomes (BMV and desaturations). The majority of the difficult intubations were caused by clinicians having trouble maneuvering the ETT into the trachea. No study has isolated one stylet as superior to another[12], so we allowed for the use of malleable and non-malleable stylets in our study. We used three different types of VLs and found no variance in success rates between the various systems. This means the difficult intubations may have been caused by a combination of other factors, such as anatomical differences in the patients' airways (i.e., large tongue, redundant tissue, etc.), inappropriate blade size, and/or the clinician's experience level.

From our clinical experience and review of the literature, a quick intubation was vital for a successful and safe outcome. Our T(v) and T(i) differed slightly from other studies[13], but gave us the best opportunity to analyze the time throughout intubation by combining T(v) and T(i) as T(vi). We addressed the incidence of desaturation that occurred as either or both times increased. Although T(i) appeared to be a greater indicator of outcome success, it was important to examine both times together since the worst outcomes arose when both the visualization and intubation times were slow.

We compared our results to previous morbid obesity and airway device studies in patients with difficult airways. The mean BMI of our patients was 45.9. Brodsky found that MO patients were not harder to intubate, and their subject group had a median BMI of 47.5.[6] Even though their patients represented a similar group of patients undergoing elective bariatric surgery, they only used direct laryngoscopy.[6]

Our patients experienced a lower incidence of desaturation during intubation than previously stated levels.[3] Juvin[3] compared lean and obese patients and determined that there was an increased incidence of desaturation in obese patients. While we could not compare our results to a lean group, given the nature of bariatric surgery, we subdivided our patients into MO and super MO (SMO). We found a higher level of desaturation during intubation in patients with a BMI >50. Our results contradict the findings of Leykin[8] who found no significant difference in outcomes between MO and SMO patients.

While many previous studies focused on either induction-intubation or emergence-extubation[4], we examined both periods. Upon initial review, we found that there were more complications during emergence, so we improved our protocol by standardizing the patient positioning during this period to decrease oxygenation complications using the WCB18 position at both time periods. After standardizing emergence-extubation in our protocol, desaturation events were no more likely during that period of the procedure than during induction-intubation.

In addition, limiting narcotics in a high-risk group with high incidence of OSA was important for a safe intubation.[14] However, patients with chronic pain syndromes or on prescribed narcotics were allowed to receive fentanyl preoperatively. Positioning for MO patients has been studied; however, it often involved placing many blankets and pillows to obtain the ear-sternum ideal angle.[15] Boyce[15] found that a bed angle of 30°-reverse Trendelenburg led to fewer desaturations and the shortest time to return SpO_2 to 97%. However, we found 30° to be too steep and awkward for induction-intubation. By using the WCB18, we provided safe induction-intubation conditions and eliminated the use of blankets and pillows. For induction, we used succinylcholine to gain expedited intubation conditions and based our dosage on the findings of Lemmens and Brodsky[16] who used 1mg/kg using TBW.

Our findings were similar to Aziz[17] and Andersen[18] who found that the Glidescope® provided quicker views and was a better option for intubation. However, we agreed with their assertion that a quicker view did not necessarily lead to an easier intubation.[17,18] We planned the use of flexible fiberoptic bronchoscopy (FFB) and the AirQ® laryngeal mask (as a conduit) in our protocol as an emergency intubation technique. The VL was chosen as the primary technique since our subject group had a high risk of GERD and potential aspiration.[19] As noted previously, we also used a variety of malleable and non-malleable stylets to assist the placement of the ETT. This method was suggested by Cooper as a way to assist in the intubation.[20]

Boyce[15] found that using BMV for MO patients could be problematic, but that was not the case for our study. In fact, due to our limited number of BMV patients, we could not truly compare our data with that of the literature stating the difficulty to ventilate MO patients. For maintenance, we chose to use isoflurane and dexmedetomidine as a narcotic sparing technique. These recommendations came from both Feld[21] and Boyce[15]. In addition, unlike other studies that limit the level of clinician[3,6], our protocol was able to be used by all levels of clinicians with the guidance of attending anesthesiologists.

A recent national survey on the use of VL noted that the choice of device is not usually based on the literature[22]; however, we have shown that the use of VL in MO patients did result in decreased desaturations as a marker of poor outcomes. Additionally, in a systematic review, Lewis[23] stated that the use of VL was not associated with incidence of desaturation nor did it affect the time required for intubation. Our study, however, found that there was an intubation time associated

with limiting desaturation events in obese patients.

There were several limitations to our study. We were limited to collecting data at one institution; thus, we were limited to three surgeons in a variety of operating rooms. We allowed all levels of anesthesia providers to partake in the intubation of the patients. We used a combination of different blades with three different VL devices and did not randomize the use of these instruments. During ventilation and maintenance, volume and pressure control were not standardized unless the SpO_2 was <90%.

Our study focused on developing a protocol for MO patients undergoing bariatric surgery, which enhanced the success of intubation, and also avoided the need for BMV and decreased the incidence of desaturation. While the protocol was tailored to healthy MO patients undergoing bariatric procedures, it may serve as a general guideline for future MO patients undergoing other surgical procedures. In conclusion, we developed a protocol for a subset of patients that are known to be potentially difficult to intubate and/or experience an increased risk of hypoxemia events. We showed that all patients were able to be intubated successfully using VL and we associated the intubation time that prevented severe desaturation events.

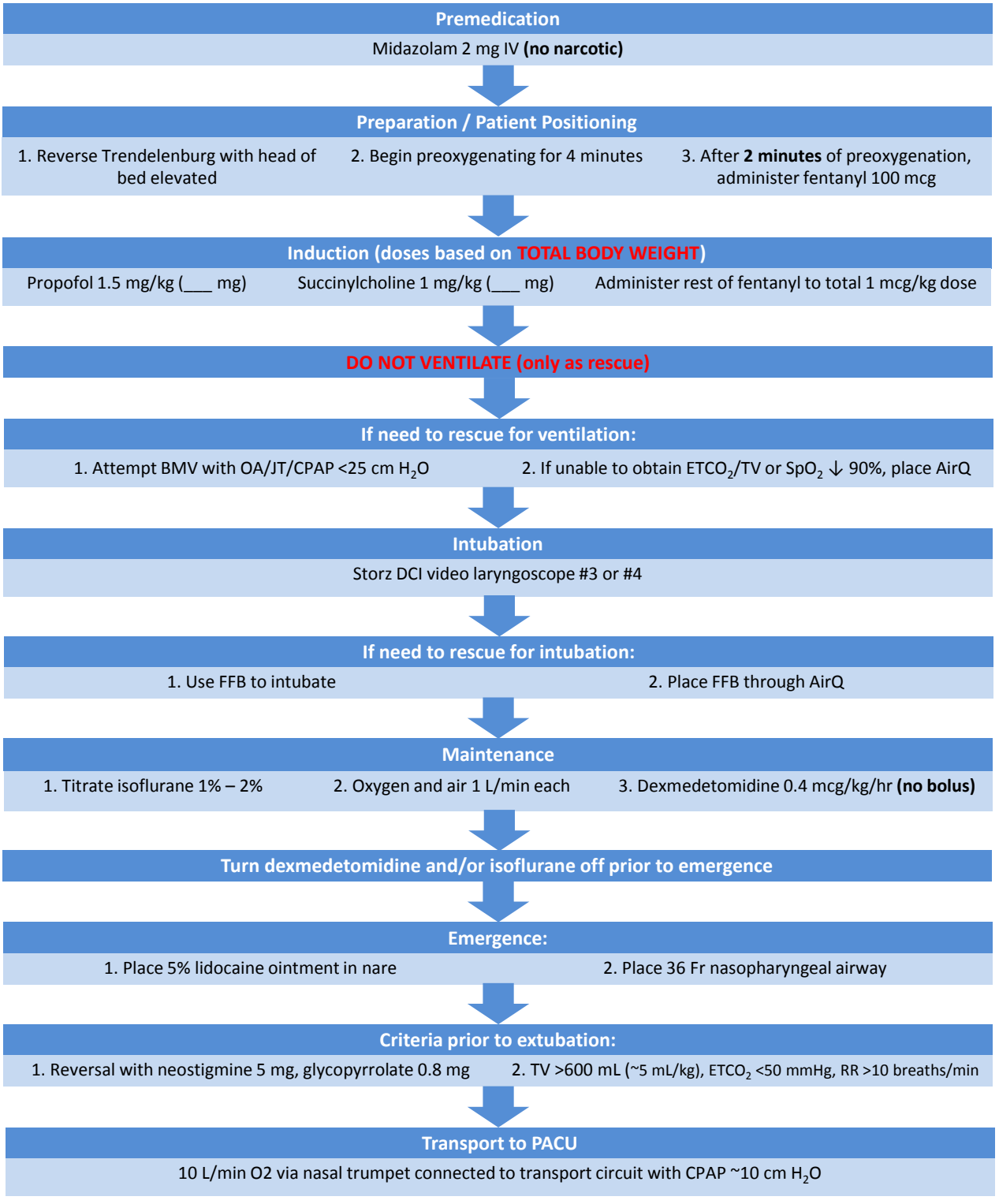
Disclosures

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

References

1. Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. Int J Obes (Lond) 2013; 37: 889-91.
2. Powell MS, Fernandez AZ Jr. Surgical treatment for morbid obesity: The laparoscopic Roux-en-Y gastric bypass. Surg Clin North Am 2011; 91: 1203-24.
3. Juvin P, Lavaut E, Dupont H, et al. Difficult tracheal intubation is more common in obese than in lean patients. Anesth Analg 2003; 97: 595-600.
4. Ahmad S, Nagle A, McCarthy RJ, et al. Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic bariatric surgery. Anesth Analg 2008; 107: 138-43.
5. Adams JP, Murphy PG. Obesity in anesthesia and intensive care. Br J Anaesth 2000; 85: 91-108.
6. Brodsky JB, Lemmens HJ, Brock-Utne JG, Vierra M, Saidman LJ. Morbid obesity and tracheal intubation. Anesth Analg 2002; 94: 732-36.
7. Kristensen MS. Airway management and morbid obesity. Eur J Anaesthesiol 2010; 27: 923-7.
8. Leykin Y, Pellis T, Del Mestro E, Marzano B, Fanti G, Brodsky JB. Anesthetic management of morbidly obese and super-morbidly obese patients undergoing bariatric operations: Hospital course and outcomes. Obes Surg 2006; 16: 1563-9.
9. Maassen R, Lee R, Hermans B, Marcus M, van Zundert A. A comparison of three videolaryngoscopes: The macintosh laryngoscope blade reduces, but does not replace, routine stylet use for intubation in morbidly obese patients. Anesth Analg 2009; 109: 1560-5.
10. Zvara DA, Calicott RW, Whelan DM. Positioning for intubation in morbidly obese patients. Anesth Analg 2006; 102: 159.
11. Cortellazzi P, Caldiroli D, Byrne A, Sommariva A, Orena EF, Tramacere I. Defining and developing expertise in tracheal intubation using a Glidescope® for anaesthetists with expertise in macintosh direct laryngoscopy: An in-vivo longitudinal study. Anesthesia 2015; 70: 290-5.
12. Jones PM, Loh FL, Youssef HN, Turkstra TP. A randomized comparison of the Gliderite® rigid stylet to a malleable stylet for orotracheal intubation by novices using the Glidescope®. Can J Anaesth 2011; 58: 256-61.
13. Cattano D, Corso RM, Altamirano AV, et al. Clinical evaluation of the C-MAC D-Blade videolaryngoscope in severely obese patients: a pilot study. Br J Anaesth 2012; 109: 647-8.
14. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: An updated report by the American Society of Anesthesiologists task force on perioperative management of patients with obstructive sleep apnea. Anesthesiology 2014; 120: 268-86.
15. Boyce JR, Ness T, Castroman P, Gleysteen JJ. A preliminary study of the optimal anesthesia positioning for the morbidly obese patient. Obes Surg 2003; 13: 4-9.
16. Lemmens HJ, Brodsky JB. The dose of succinylcholine in morbid obesity. Anesth Analg 2006; 102: 438-42.
17. Aziz MF, Healy D, Kheterpal SFu RF, Dillman D, Brambrink AM. Routine clinical practice effectiveness of the glidescope in difficult airway management: An analysis of 2,004 glidescope intubations, complications, and failures from two institutions. Anesthesiology 2011; 114: 34-41.
18. Andersen LH, Rovsing L, Olsen KS. Glidescope videolaryngoscope vs. Macintosh direct laryngoscope for intubation of morbidly obese patients: A randomized trial. Acta Anaesthesiol Scand 2011; 55: 1090-7.
19. El-Serag HB, Graham DY, Satia JA, Rabeneck L. Obesity is an independent risk factor for gerd symptoms and erosive esophagitis. Am J Gastroenterol 2005; 100: 1243-50.
20. Cooper RM, Pacey JA, Bishop MJ, McCluskey SA. Early clinical experience with a new videolaryngoscope (glidescope) in 728 patients. Can J Anaesth 2005; 52: 191-8.
21. Feld JM, Laurito CE, Beckerman M, Vincent J, Hoffman WE. Non-opioid analgesia improves pain relief and decreases sedation after gastric bypass surgery. Can J Anaesth 2003; 50: 336-41.
22. Cook TM, Kelly FE. A national survey of videolaryngoscopy in the United Kingdom. Br J Anaesth 2017; 118: 593-600.
23. Lewis SR, Butler AR, Parker J, Cook TM, Schofiel-Robinson OJ, Smith AF. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation: a Cochrane systematic review. Br J Anaesth 2017; 119: 369-83.

Appendix 1. Gastric bypass / banding (GB3) study: Anesthetic protocol



Appendix 2. Gastric Bypass/Banding (GB3) Study: Datasheet page 1

Subject #: ____

[Insert patient sticker here]

Gastric bypass/banding (GB3) study datasheet

Service date: _____ Age (yrs): _____ Weight (kg): _____ Height (cm): _____ BMI: _____
Gender: M F ASA Status: _____

Diagnosis: _____
Procedure: _____

Preparation

History of difficult airway? ❒ Yes ❒ No
If yes:
❒ By history on chart
❒ Patient/family statement
❒ Physical Exam
❒ Other: _____

Airway exam:
❒ Mallampati Class: I II III IV
❒ Mouth Opening: ___ FB
❒ Thyromental distance: ___FB
❒ Neck extension/flexion: all some none
❒ Other: _____

Midazolam (mg): _____

Time moving from stretcher to OR bed: _____
(Place in W-C position to placement of ASA monitors)

Time of beginning preoxygenation: _____
(Mask is placed on the patient's face, 100% O_2 at 10 L/min)

Induction

Initial fentanyl administration time (100 mcg):_____
(After 2 minutes of preoxygenation)

Induction time: _____
(After 4 minutes of preoxygenation)

Administration of induction agents (based on TBW):

1. Propofol (1.5 mg/kg): _____

2. Succinylcholine (1 mg/kg):_____

3. Fentanyl (mcg): _____
(Administer additional fentanyl to total 1 mcg/kg)

Intubation

VL blade size:_____
(Size 3 or 4)

Time of intubation: _____
(Time on clock)

Intubation times
(Press Silence Alarm button to read "2:00")

Recorded time on anesthesia machine monitor	Time duration (in seconds)
Placement of video laryngoscope in the mouth: 02:00	--
Visualization of vocal cords on monitor: ____	
Placement of the ETT through the vocal cords: _____	
Verification of $ETCO_2$ waveform on the monitor:_____	

Total time: _____

Appendix 2. Gastric Bypass/Banding (GB3) Study: Datasheet page 2

Problems / events during intubation: _____
_____
_____

Rescue

Bag mask ventilation required? ❒Yes ❒No
If yes: ❒ Unable to obtain $ETCO_2$
❒ SpO_2 < 90%
❒ AirQ placed (size): _____

FFB required to intubate? ❒Yes ❒No
If yes: FFB type/size**:** _____

Maintenance

1. Isoflurane titrated 1 – 2% with O_2 and air 1 L/min
2. Dexmedetomidine 0.4 mcg/kg/hr (no bolus)

Incision time: _____
(Procedure start time)

Problems/ events during maintenance: _____
_____
_____

Emergence/extubation

Surgical end time: _____ Extubation time: _____

1. Reversal- neostigmine 5 mg, glycopyrrolate 1 mg
2. Extubation criteria: TV > 600 mL, $ETCO_2$ < 50 mm Hg, RR > 10 breaths/min

Time leaving the OR: _____ Arrival to PACU: _____
(Transport with 10 L/min O_2 via nasal trumpet)

Problems/events during extubation**:** _____
_____
_____

PACU/Post-op

Pain and PONV medications administered in PACU (type/dose): _____
_____

Discharge date from the floor: _____ Discharge time from the floor: _____

Pain and PONV medications administered on the floor (type/dose): _____
_____

Protocol adjustments? ❒ Yes ❒ No
If yes, explain: _____
_____
_____

Original Science

African American Patients' Lived Experience Through Cardiac Event/Surgery, and Recovery

Aubry N. Koehler, Ph.D., L.M.F.T.[1], Jennifer L. Hodgson, Ph.D., L.M.F.T.[2], Damon L. Rappleyea, Ph.D., L.M.F.T.[2], Sharon M. Knight, Ph.D., R.N.[3], Bernice A. Dodor, Ph.D.[2]

Abstract

Introduction: Although Cardiac Rehabilitation is a Class I treatment for cardiovascular disease, only a third of eligible patients participate and rates are even lower among racial/ethnic minorities. Studies on the unique experience and recovery needs of African American patients following cardiac events and/or surgeries are limited.

Methods: African American adult patients (n=7) two months post-discharge from a Southeastern medical center were interviewed regarding their cardiac recovery experience. Semi-structured interviews were audio-recorded, transcribed, and then coded according to Coliazzi's (1978) phenomenological analysis method.

Results: Six themes were identified salient to these African American patients' lived experience: (a) Participants valued medical providers' involvement during treatment and recovery; (b) Social support and participants' need for it changed post-event/surgery; (c) Participants' pre- and post-event/surgery experiences affected health outcomes; (d) Participants' sense of agency affected their life perspectives and health behaviors; (e) Participants experienced inconsistent referral to and utilization of Cardiac Rehabilitation; and (f) Participants' investment in faith was intensified or maintained.

Discussion: This study highlighted the importance of medical provider and social support, the need for consistency and clarity in Cardiac Rehabilitation referrals and recommendations, and the role of participants' agency and spirituality as sources of strength during African American patients' recovery from cardiac events and/or surgeries.

[1]Department of Family and Community Medicine, Wake Forest School of Medicine, Winston-Salem, NC

[2]Department of Human Development and Family Science, East Carolina University, Greenville, NC

[3]Department of Health Education and Promotion, East Carolina University, Greenville, NC

Address Correspondence To:
Aubry N. Koehler, Ph.D., L.M.F.T.
Department of Family and Community Medicine
Wake Forest School of Medicine
Medical Center Blvd.
Winston-Salem, NC 27109
aubry.koehler@wakehealth.edu

Introduction

From prevention and intervention to mortality rates, African Americans have experienced significant cardiovascular health disparities. From 2006 to 2016, African Americans had a higher age-adjusted death rate from coronary heart disease than Non-Hispanic Whites (146.5 per 100,000 population for African American males and 85.4 for African American females, compared with 132.3 and 67.3 per 100,000 population for Non-Hispanic White male and females, respectively).[1] As a population, African Americans also had a higher rate of hypertension (40.3% among African Americans compared to 27.8% among Non-Hispanic Whites), but were less likely to have their hypertension controlled.[2]

Cardiac Rehabilitation (CR) is an American College of Cardiology and American Heart Association recommended program designed to treat multiple cardiovascular conditions and assist in the recovery from cardiac events/surgeries (i.e., myocardial infarction [MI], coronary artery bypass grafting [CABG], stable angina, heart valve repair or replacement, percutaneous transluminal coronary angioplasty or coronary stenting, heart/heart-lung transplant, congestive heart failure, coronary artery disease, diabetes, and peripheral artery disease).[3] CR consists of three phases, all or some of which a patient with cardiovascular disease (CVD) may participate in depending on his or her disease presentation and availability of programs: (a) Phase I—acute, inpatient treatment (one to 14 days), (b) Phase II—medically supervised outpatient treatment lasting three to six months, and (c) Phase III—minimally supervised or unsupervised maintenance.[4]

As a Class I secondary treatment and prevention program, CR has been demonstrated to improve health outcomes for patients with CVD.[3-7] However, only one third of eligible patients are referred to or participate in CR.[8-10] These rates are even lower for racial minorities and for African Americans, in particular.[10-13] Researchers studying referral rates for cardiovascular procedures and rehabilitation programs have found a relationship between race and the type of procedures and programs recommended for or received by patients.[13-18] For example, African Americans are less likely to be recommended for and receive revascularization procedures.[14-17] Researchers have also demonstrated that cardiac patients who do not receive these procedures are, in turn, less likely to be referred for CR.[10] In relation to this indicator, other researchers have shown that being scheduled for a follow-up appointment with a cardiologist or cardiac surgeon is positively associated with a CR referral.[19]

Researchers have identified a number of factors moderating poorer cardiovascular health and decreased likelihood of adopting heart healthy behaviors (e.g., recommended diet and exercise changes) among African American patients with CVD. These factors include depressive symptoms[20,21], lower socioeconomic status[22], and lower levels of social support[23-25]. Some researchers have also argued that religious fatalism is a commonly held spiritual belief in the African American community, which can reinforce a passive approach to self-care and fatalistic beliefs about cardiovascular risk factors and health.[20,26,27]

Although these differences and disparities are well documented, research on the development of interventions to address them is limited. Researchers have identified a need for interventions tailored to racial minority patients with CVD and have called for studies that measure factors specific to these groups to assist in intervention development.[9,28-30] In their systematic review of the literature, Hildebrandt, Koehler, Hodgson, Dodor, Knight, and Rappleyea found that, compared with Non-Hispanic White patients, African American patients with CVD not only had a lower likelihood of CR referral, but also had a higher likelihood of enrolling in CR with more cardiovascular risk factors, and a lower likelihood of CR participation and completion due to factors related to low socioeconomic status (e.g., lack of insurance, work conflicts, lower level of education).[12,13,31-36] In total, only seven studies addressed this topic.

Few studies have been conducted on factors impacting African American patients' CR referral and participation, and the ways in which African American patients can be best supported in their recovery from cardiac events and surgeries.[31] For this reason, a phenomenological study was conducted to explore the following research question[37]: "What is the lived experience of African American patients recovering from cardiac events and/or surgeries?"

Methods

Participants

A purposive sampling strategy was used to enroll participants from two different locations; either from (a) a Southeastern academic medical center serving a population of nearly one and a half million people and (b) a nearby, affiliated CR facility. Potential participants were identified from each facility's electronic and paper record systems. Inclusion criteria were: (a) English-speaking; (b) African American; (c) aged 18 years and older; (d) approximately two months post-discharge from a cardiac event or surgery for which CR was indicated; and (e) a resident of a city or town in the county where the academic medical center was located.

The researchers recruited five eligible patients from the academic medical center and two patients directly from the CR facility. After consenting to participate in the study prior to their discharge from the hospital, the five participants

recruited from the academic medical center were contacted by telephone six to seven weeks post-discharge to set up interviews. This timeframe was chosen because, at this point, participants were anticipated to have had at least one follow-up appointment with a primary care provider, cardiologist, or cardiac surgeon per the academic medical center protocol and had the opportunity to receive a referral to CR or to discuss recovery alternatives with their medical provider(s). The two patients recruited directly from the CR facility were contacted either by telephone or when a research assistant approached them directly at the CR facility at approximately two months post-discharge. This time point was selected to ensure that individuals recruited from the initial pool of potential participants (contacted at six to seven weeks post-discharge) would be in the same stage of recovery as those recruited directly from the facility. If patients were contacted by telephone, a time was arranged for them to complete the informed consent face-to-face at the CR facility. Once consent was obtained, interviews were scheduled.

Participants were recruited and semi-structured interviews were conducted until saturation of themes was reached. Saturation occurs when the analysis of additional data (in this case, participant interviews) yields no new themes.[38] Although the number of interviews needed to reach saturation could not be predicted[39], content analysis of qualitative studies provided some guidelines. A review of 57 phenomenology studies found that the average number of interviews associated with a phenomenology was 25, while the median number was 20, and range was seven to 89.[39] Due to the high specificity of the topic, anticipated homogeneity of the purposively selected sample, and the inclusion criteria for this phenomenological study, it was estimated that saturation would be reached within eight to ten interviews. The lead researcher planned to conduct one additional interview past the point of saturation to test comprehensiveness of themes.[40] Out of 15 eligible patients identified during the study recruitment window, seven patients participated in the study. Eight were unable to be contacted to obtain consent. Participants received an incentive ($25 gas card) mailed to them following interview completion.

Procedures

Approval for this study was obtained from a University Institutional Review Board (IRB) and privacy office. Potential participants were contacted at six to seven weeks post-discharge to set up interviews. After obtaining informed consent, the lead researcher used an interview guide (Table 1) to facilitate an audio-recorded, in-depth telephone interview with each participant.

Table 1. Interview Guide

Grand Tour Question
How would you describe your experience recovering from your cardiac event or surgery after being discharged from the hospital?
Probing Questions
• What has having a heart problem meant to you?
• What are some challenges you have faced in your recovery process? o Have you experienced any physical challenges? o Have you experienced any emotional challenges? o Have you experienced any social challenges? o Have you experienced any spiritual/religious challenges?
• What successes have you experienced?
• How have you experienced the follow-up appointments with your cardiologist or primary care provider after being discharged from the hospital? o How would you describe how you have been treated? o How were your questions/concerns addressed? o What concerns do you continue to have?
• What is your understanding about how you can best recover from your heart problem? o What messages or information have you gotten from your health care provider? o What messages or information have you gotten from others? o What messages or information have you gotten about diet? o What messages or information have you gotten about exercise?
• Did any of your health care providers discuss cardiac rehabilitation (CR) with you? Follow up probes: Which health care provider? When was it? o What do you think is the importance of CR to your recovery? o What were your intentions about participating in CR? o Did you have any concerns about CR? o Did you think about/engage in any alternatives to CR?
• What home remedies (non-medical strategies), if any, have been a part of your recovery process?
• How have you been helped or supported by others in your process of recovering? o How have health care providers, like doctors and nurses, supported you? o How have other health people supported you? o How have family members supported you? o How have friends supported you? o How has your community supported you? o How has your church/faith community supported you?
• What services (or assistance) have you needed but have not received to help you with recovery? o What could health professionals, like doctors and nurses, have offered after discharge to help you with your recovery?
• What else you would like to share?

Data Analysis

Colaizzi's phenomenological analysis method was used for this study.[41] The lead researcher transcribed all interviews verbatim and coded the transcripts successively as interviews were conducted. A triangulated researcher coded 25% of each transcript and, if the coding was not in 90% agreement with the lead researcher's coding, the triangulated researcher coded the full transcript, as well. When agreement regarding coding differences could not be reached (occurred 10% of the time), a peer debriefer assisted with reaching consensus. The peer debriefer also reviewed each step of the analysis process to ensure that it accurately reflected Colaizzi's method and was grounded in the data.[41] Researchers recorded their biases and engaged in reflexivity prior to and throughout the analysis process.[42,43] Upon completion of analysis, study findings were verified by participants using member checking which

took the form of the lead researcher calling participants and requesting verbal feedback on the exhaustive description of the study's findings.[38,44] The five study participants that the lead researcher was able to reach by phone confirmed that the exhaustive description reflected their lived experiences.

Results

Seven participants were recruited and interviewed for this study: four men and three women who ranged in age from 37 to 64 years and who had experienced MI, stent placement, CABG, or a combination thereof (see Table 2 for participant demographics). Analysis of transcripts from the seven participant interviews yielded 535 significant statements, 69 formulated meaning statements, 20 thematic clusters (TC), and six emergent themes relevant to the essence of African American patients' lived experience through cardiac event/surgery and recovery (see Table 3 for emergent themes and TC). The following section explores each emergent theme, as well as the TC categorized under it (see Table 4 for selected examples).

Table 2. Participant Demographics

Participant	Gender	Age	Event/Surgery	CR Status
1	Male	60	Stents	No referral, not enrolled
2	Male	60	MI	Referred, enrollment pending medical action
3	Male	37	MI, Stents	Referred, enrollment pending medical action
4	Female	64	Stents	Referred, enrolled, attending
5	Female	41	MI, CABG	Late referral, enrolled, attending, nearly completed
6	Male	60	MI, stents	No referral, not enrolled
7	Female	54	MI	Referred, enrolled, continued attendance pending medical action

Emergent Theme (EM) 1: Participants Valued Medical Providers' Involvement during Treatment & Recovery

All seven participants stated that medical providers' interventions impacted cardiac outcomes (TC 1a, Table 3). When participants experienced medical crises prior to cardiac events/surgeries, medical providers were the source of vital information and interventions, often revealing for participants the cause of their symptoms. Three participants noted that medical providers were often conservative in their interventions in that they observed patients first and considered less invasive treatments before proceeding to more invasive ones. There were also times when medical providers' interventions presented participants with unique challenges, for example when participants did not understand their medication regimens post-discharge.

All participants also recalled medical providers guiding them on making healthy lifestyle changes after their cardiac event or surgery (TC 1b). Guidance took the form of general messages (i.e., being encouraged to "just walk"), whereas other times guidance was specific and hands-on (i.e., medical providers referenced exercises from the same pamphlet given to the participant during hospitalization).

In addition to guidance for healthy lifestyle changes, six out of seven participants perceived that medical providers offered a combination of functional and emotional support (TC 1c). Functional support included adjusting medications, checking participants' vital signs and tolerance of treatment, putting in appropriate referrals, providing explanations of the treatment process to participants, and offering or arranging home visits. Providers' emotional support entailed offering encouragement to participants and positive feedback regarding participants' cardiac event or surgical outcome and progress during recovery. For three participants, positive feedback motivated them to adhere to treatment recommendations, whereas two others read positive feedback as meaning that they did not need additional resources such as CR, but were instead equipped to facilitate their own rehabilitation process. All participants expressed their appreciation for medical providers' level of "dedication" to participants and their health (TC 1d). Specifically, participants appreciated when medical providers seemed to invest personally in their needs. Participants frequently spoke about medical providers "really caring" for them. Connected to participants' sense of medical providers' care was the feeling that they were a part of a collaborative team with providers in which positive health outcomes were a shared goal. Participants appreciated that medical providers involved them in conversations about their care, would "sit and listen to what [the participant] got to say" and explained to them what to do and expect medically. Although participants primarily spoke about the ways in which their medical providers had been exceptionally helpful, two participants also pointed out where they would have liked additional support (TC 1e). Requests for additional

support mainly centered on post-event/surgery needs. These participants stated that it would have been helpful to have had more information about home-based recovery. For example, a 41-year-old woman who had CABG following an MI wished her provider would have recommended alternatives for sleeping comfortably the first few weeks following discharge. She suggested that renting a recliner may help patients who had difficulty sleeping vertically for the first couple of weeks.

EM 2: Social Support & Participants' Need for It Changed Post-Event/Surgery

Following cardiac events/surgeries, all participants experienced their social networks rallying to support them (TC 2a). Functional support included assistance with activities of daily living (e.g., bathing, preparing meals), financial help when/if participants were unable to work for a significant amount of time, assistance with household chores and yard maintenance, and provision of home-based accommodations for recovery and gradual transitions back into normal routines. Emotional support included check-in telephone calls or visits, words of encouragement, and advice from others who had had similar cardiac experiences.

According to five participants, a sense of isolation was often caused or compounded by lifestyle changes made post-event/surgery and participants' physical limitations during their recovery process (TC 2b). A 60-year-old man who had had an MI found that upon following his medical providers' recommendations to stop smoking and drinking, he lost contact with the friends with whom he used to engage in these activities. Although this participant recognized that these were the "wrong kind of friends" to support him in adopting a healthier lifestyle, he still expressed disappointment that they did not visit him in the hospital or post-discharge. Regarding the impact of physical limitations, one participant stated not being able to move around at social gatherings as she normally would have done left her feeling like she was "watching life go by" (41-year-old woman, MI/CABG). In contrast to feelings of isolation, five participants also reported the presence of social support that was in some way challenging for the participant (TC 2c). These participants reported that support that was "pitying", conflictual, or "humbling", was challenging to them. A 54-year-old woman who had an MI stated that she felt pitied when her family and friends looked at her "different" and spoke to her in a condescending tone. This participant stated that she made a point of "acting joyful" when she felt pitied by others. Another participant stated that needing help with activities of daily living was "humbling", especially when her husband had to help her with toileting (41-year-old woman, MI/CABG). However, she reported she did not always disclose her authentic feelings regarding her recovery experience to others. Support was conflictual when participants and supporters disagreed on treatment recommendations (e.g., amount of exercise).

EM 3: Pre- & Post-Event/Surgery Experiences Affected Health Outcomes

Four participants noted how pre-event/surgery related health problems prevented them from being able to live like they wanted to live (e.g., be more physically active) and even compounded their heart problems (e.g., obesity, musculoskeletal issues, pulmonary problems) (TC 3a). Pre-event/surgery health problems endorsed by participants included prior cardiac events, atrial fibrillation, undiagnosed cardiac problems, high blood pressure, diabetes, obesity, knee problems, prior injuries, fibromyalgia, and depression. A 37-year-old man who had an MI and stents placed stated that his obesity and knee problems made it difficult, and then impossible, to work at the physically strenuous job he had held. A 54-year-old woman who had an MI stated that injuries from a car accident (approximately 10 years prior) and fibromyalgia "kinda, like put a dent in my exercise".
Six out of seven participants experienced post-event/surgery health improvements that included successful recoveries from cardiac events/surgeries, needing fewer medications/interventions to manage health problems, and increased self-care (TC 3b). These changes led them to achieve overall improved health status.

Four participants emphasized that, following their events/surgeries, it was necessary to make adjustments to their home environments and routines to accommodate temporary and permanent limitations (TC 3c). For these participants, adjustments included different sleeping accommodations (i.e., lower beds or recliners that were easier to get in and out of for the first few weeks post-discharge), use of a walker, riding in vehicles that were easier to get in and out of (i.e., larger versus compact vehicles), and help with carrying items over

10 pounds. These participants expressed a pervasive shift in how they moved through their days and noted that social support contributed to their adaptability and resilience in not only making these accommodations but also accepting them.

Five participants reported that some post-event/surgery treatments were ineffective, inaccessible, or unaffordable and consequently not adopted by them (TC 3d). Thus, these participants experienced ongoing physical or psychological limitations. One participant reported the medications he was taking post-discharge "was messin' with me bad" (e.g., stomach aches and feeling like he was "floating") and said he felt much better after he became well enough to taper these down (60-year-old man, stents). Others described the repercussions of financial limitations, for example the sense of despair upon discovering a prescribed heart medication was unaffordable and the sense of helplessness when insurance companies denied potentially therapeutic interventions such as weight loss surgery year after year.

EM 4: Sense of Agency Affected Life Perspectives & Health Behaviors

All participants reported feeling distressed when they were faced with the unpredictability of their treatments and health outcomes (TC 4a). Their distress included anxiety about having limited control over and knowledge of their cardiac events/surgeries and outcomes; fear that engaging in exercise would trigger another cardiac event; frustration when physical limitations precluded being able to exercise as instructed by medical providers; being unsure of medications' physical and psychological effects; and feeling depressed as a result of unforeseen health-related hardships. Words participants used to describe their anxiety about limited control regarding their cardiac events/surgeries and outcomes included "scary", "frightful", "overwhelmed", and "hard to accept".

Participants also had different levels of proactivity about health and the recovery process (TC 4b). Whereas three participants stated that they researched and implemented recommended diet and lifestyle changes both pre- and post-intervention, three others stated that they passively chose not to implement these changes even though they knew that they "should" (the last participant did not comment on this theme). One participant (60-year-old man, MI/stents) stated that he opted out of certain aspects of care, such as home health care and CR, because his recovery was so successful and he had a high comfort level with exercise.

All participants reported that their cardiac events/surgeries led them to actively make some lifestyle changes (TC 4c). These changes involved shifts in both perception and behavior and included feeling inspired to get more serious about health following the wake-up calls of cardiac events/surgeries; perceiving weight changes as connected to greater health and wellbeing and engaging in behavioral modifications to manage weight; having a new appreciation for peace and quiet; and accepting and making peace with health-related limitations.

Finally, two participants stated that they not only gleaned knowledge from the experiences of their cardiac events/surgeries, they also shared this new knowledge with others (TC 4d). In particular, one of these participants (41-year-old woman, MI/CABG) gave health advice to her children regarding her children's and future grandchildren's health-related behaviors. She reported that it was very important to her that her two teenage sons internalize healthy lifestyle behaviors so they would not be faced with the same challenges she had experienced.

EM 5: Participants Experienced Inconsistent Referral to & Utilization of Cardiac Rehabilitation

Out of the seven participants, four reported receiving a referral to CR, two reported having no referral, and one reported a late referral that was made by the participant's medical provider after she directly requested a referral to CR (see Table 2). Three of the four participants who were referred to and participated in CR spoke about positive experiences with health-related successes (e.g., "get[ting] stronger," "gainin' energy back") and support from CR nurses and staff (TC 5a). One of these participants appreciated the program so much that she stated, "I would like that the program could last, you know, forever!" (64-year-old woman, stents). Functional and emotional support from CR nurses and staff was an important component of participants' positive experiences. Another participant reported that it helped motivate her "being around the people that, you know, watchin' you and pushin' you and encouragin' you" (54-year-old woman, MI). Four participants also experienced some barriers to CR participation which included perceived lack of communication from medical providers with participants about CR, perceived lack of referrals of participants to a CR program, participants

not understanding what CR was, or participants waiting on medical providers for action or clearance to begin or continue the program (TC 5b). For example, one participant was aware that one of his medical providers had submitted a CR referral for him, but he had a difficult time articulating exactly what CR was: "He [medical provider] had wanted me to do somethin'. Uh, some, uh…oh, man, I can't explain it…What is it?" (60-year-old man, MI).

One participant stated that she happened to learn about CR from a woman who had recently had cardiac surgery and attended CR. As a result of this chance conversation, this participant sought a referral from her medical providers using her online patient portal, and having been given a referral, she successfully enrolled in and completed CR. Although the participant stated that she was grateful to have learned about CR in one way or another, she also reported being disappointed that her medical providers had told her "nothing" about this resource. She stated that "they *should* let the people know. Especially right before [discharge] at the hospital would be *great*" (41-year-old woman, MI/CABG). While participants spoke positively about the support received from CR nurses and staff, two participants spoke negatively about the presence of other CR patients. A 54-year-old woman (MI) stated that the other patients were less motivated and/or less able to exercise than her and this contributed to a "gloomy" feeling. A 37-year-old man (MI/stents) reported that when he had his initial assessment at CR, he was one of the youngest patients present and this was particularly upsetting to him.

EM 6: Participants' Investment in Faith was Intensified or Maintained

All participants stated that they maintained or intensified involvement in their faith and faith communities throughout their recoveries (TC 6a). Three participants reported that their faith community members came into the hospital to visit and pray with them following cardiac events/surgeries and continued to support them after discharge.

Six out of seven participants also reported that, following their cardiac events/surgeries, involvement with their faith intensified. This included more frequent considerations about faith-based questions and seeking spiritual guidance and counsel from others. A 60-year old man (stents) reported that, during his recovery, he experienced spiritual "frustration" related to his faith in God and his worries for himself and other people. He met periodically with his pastor, and through these spiritual conversations, stated that he was able to put his worries for self and others in faith and achieve better health overall.

All participants cited faith as a source of strength and gratitude during their recovery (TC 6b). Six participants stated that they gave their troubles to God. Phrases describing this process included "God got it", and "Put it in the hands of the Lord". One participant stated faith helped her to "calm back out" following her MI and trust "He [God] was gonna take care of me" (64-year-old woman, stents).

Two participants also explicitly stated that they offered praise and gratitude to God for giving them life. One of these participants emphasized the gratitude he had for God in giving him the opportunity to see his children grow up. He stated he "thanked God every day I wake up" (37-year-old man, MI/stents). God and participants' faith in God were not only described as the primary source of participants' strength, these were also described as the very power by which their hearts were still beating.

Table 3. Emergent Themes (1-6) and Thematic Clusters (1a-6b)

1. Participants valued medical providers' involvement during treatment and recovery
1a. Medical providers' interventions impacted cardiac outcomes 1b. Medical providers offered guidance on healthy lifestyle changes 1c. Participants perceived support (functional and emotional) offered by medical providers 1d. Participants appreciated medical providers 1e. Participants needed additional support from medical providers
2. Social support and participants' need for it changed post-event/surgery
2a. Social support was increased during recovery process 2b. Participants experienced sense of social isolation/limited support during recovery 2c. Participants experienced challenges with social interactions and type of social support offered during recovery
3. Participants' pre- and post-event/surgery experiences affected health outcomes
3a. Participants had pre-event/surgery health problems 3b. Participants experienced post-event/surgery health improvements 3c. Participants' post-event/surgery limitations called for lifestyle adjustments 3d. Participants experienced some interventions as ineffective or inaccessible post-event/surgery
4. Participants' sense of agency affected their life perspectives and health behaviors
4a. Unpredictability of health challenges and outcomes affected distress level 4b. Participants had different levels of proactivity about health and recovery process 4c. Cardiac events/surgeries led to lifestyle changes 4d. Passing on new knowledge was a part of participants' recovery process
5. Participants experienced inconsistent referral to and utilization of Cardiac Rehabilitation
5a. Participants experienced health-related successes with CR 5b. Participants experienced barriers to CR participation
6. Participants' investment in faith was intensified or maintained
6a. Participants and families were involved in their faith and faith communities 6b. Participants experienced faith as a source of strength and gratitude

Discussion

The themes revealed in this phenomenological study offer important clinical considerations regarding the recovery process of African American patients who have experienced a cardiac event and/or surgery. These findings reinforced those from previous researchers who highlighted the importance of medical providers building rapport and bringing culturally-sensitive health understandings to their communication with African American patients.[45-47] However, participants took these previous findings a step further in emphasizing the importance of medical providers demonstrating a personal investment in patients' wellbeing and including patients in conversations about their recovery. The following clinical recommendations are made in consideration of previous and current study findings.

Implications for Policy & Practice

Medical providers can support patients in their recovery by:

- Using provider-patient dialogue to assess patients' social support, spiritual resources, and other psychosocial factors (e.g., insurance coverage for CR, transportation).
- Reinforcing treatment recommendations in a way that is understandable to patients and opens up discussion regarding potential barriers to implementation.
- Discussing options with patients for meeting recovery goals (e.g., exercising at home vs. exercising at CR), and involving patients in the decision-making process about their treatment and recovery.

Limitations

There are several limitations of this study. First, the sample size of this study is very small. Although sample sizes are typically smaller for qualitative studies (when compared to quantitative studies), this study's sample size is admittedly on the small end even for a qualitative phenomenological study.[39] Therefore, although the experiences of the individuals in this study may hold true for other individuals recovering from cardiac events and/or surgeries, generalization of findings is not possible, particularly across demographic lines. Participants in this study were not only racially but also regionally homogenous. Second, all the participants in this study expressed a strong affiliation with their faith. It is possible that these findings, then, are reflective of African American patients living in the Southeastern United States who self-identify as religious or spiritual and may not apply to African American patients recovering from cardiac events/surgeries who do not identify in this way. Third, the mean age of participants in this study was 53.7 years old, which is notably younger than the average age of first MI in the United States (64.7 and 72.2 for men and women, respectively)[48], which again may mean that the findings are specific to a group of people who experienced cardiac events and/or surgeries at a younger age. Fourth, in terms of cardiac event or surgery type, the group was very heterogeneous which also may have affected the themes gleaned through this study.

Finally, it is a recommended practice to conduct an additional interview past the point of saturation to confirm that all themes have been identified.[40] This confirmatory interview was unable to be secured due to availability of eligible patients for recruitment. While a triangulated researcher and peer debriefer strongly believed that saturation was achieved, it is possible that apparent saturation was reached before themes were exhausted and an additional interview would have confirmed this.

Conclusion

This qualitative study investigated the lived experience of African American patients recovering from cardiac events and/or surgeries in the context of a primarily rural and lower-income county in the Southeast. Findings from this small qualitative study underscored the importance of medical provider and social network support, the need for greater consistency and clarity in CR referrals and recommendations, and the role of participants' sense of agency and spirituality as sources of strength during recovery. In providing care for African American patients recovering from cardiac events and/or surgeries, medical providers and social network members should capitalize on patients' agency, faith, and former resilience to health challenges in order to restore—and, hopefully, improve—health and wellbeing.

Table 4. Selected Examples of Narratives and Emergent Theme Formation

Significant Statements	Formulated Meanings	Thematic Clusters	Emergent Themes
"When I went in, um, they tried to do a stent but ended up having have heart surgery [CABG] because I had, um, three blockage that were severe." –P5	Medical providers attempted smaller interventions before proceeding to larger (surgical) interventions.	Medical providers' interventions impacted cardiac outcomes	1. Participants valued medical providers' involvement during treatment and recovery
"The [physical] therapist come in. He helped me walk. I walked down the street. I did everything he asked me to do, and he said I done well with it… I had to do arm exercise, leg exercise, and then I walked down the street a block." –P4	Participants received specific, "helpful" instruction and hands-on guidance from medical providers (including doctors, nurses, and physical/occupational therapists) regarding exercises.	Medical providers offered guidance on healthy lifestyle changes	
"They, um, been thoroughly with, you know, the examination and medication and makin' sure that, you know, that, uh, that they handle the, um, monitor my symptoms and, and reactions from the medicine. I mean, they've been a help for that, you know, consider how my body is: very sensitive to things. So, they, they've been kinda supportive." –P7	Medical providers (including doctors, nurses, and physical/occupational therapists) helped participants by giving them functional support in their recovery.	Participants perceived support (functional and emotional) offered by medical providers	
"I could tell the doctors really cared. They wanted me to get well…they kept telling me, um, you gotta do this, you gotta take your medicine. You can tell when someone actually care about you." –P3	Participants' medical providers set themselves apart from other medical providers by personally investing in their needs.	Participants appreciated medical providers	
"Lettin' the family know, 'You might want to try to look into rentin' a recliner for the next couple weeks'… or something like that. You know, um, just things that they know patients will kinda struggle with for the first couple weeks." –P5	Participants wished medical providers had advised participants and family members on accommodating recovery at home.	Participants needed additional support from medical providers	
"You can't lift over 10 pounds, so, um, they would go with me… either my sons or my husband… Go to school with me and take my books into class and bring 'em outta class…." –P5	Family members increased emotional and functional support to participants through intervention and during recovery.	Social support was increased during recovery process	2. Social support and participants' need for it changed post-event/surgery
"The day after I had the heart attack…they [friends] don't come see me or nothing." – P2	Health and lifestyle changes caused participants to lose certain friends and feel more isolated.	Participants experienced sense of social isolation/limited support during recovery	
"It's like I'm being watched more, or, you know, [they say], 'How you feelin'? You feelin' alright?' [and I say], 'Yeah, I'm fine!'" –P7	Participants report others did not provide the type of support participants wanted during recovery process.	Participants experienced challenges with social interactions and type of social support offered during recovery	
"I was having so much problems breathing sometimes that if I get excited, my chest would start hurting, so I can't breathe like I wanted to because my blood pressure going up and down, up and down, I get tired quick, couldn't-couldn't hardly do nothing I wanted to." –P1	Participants experienced multiple health problems (cardiac and other) and related distress and limitations before cardiac events/surgeries.	Participants had pre-event/surgery health problems	3. Participants' pre- and post-event/surgery experiences affected health outcomes
"By my body adjustin' to certain things and gettin' stronger and stuff, I was able to get, you know them pills, off, off all the pills." –P1	As participants' conditions improved post-intervention, fewer medications, interventions, and medical providers were needed to manage their health.	Participants experienced post-event/surgery health improvements	
"When you have a recovery you have to really take your time, get around slow and stuff like that, and make sure that you got proper rest." –P6	Participants experienced a gradual recovery process during which they adjusted to temporary and permanent accommodations in home environment and routines.	Participants' post-event/surgery limitations called for lifestyle adjustments	

Significant Statements	Formulated Meanings	Thematic Clusters	Emergent Themes
"They was tellin' me in the hospital it [the medication] was like $100. They gave me a free month the first time, and then the nurse gave me like a $50 co-pay card. So, I was thinking, I got $50 from my, one of my family members and he took me up there to get the medicine, and told me $290 and my heart just dropped. I like, 'No way I can afford this.'" –P3	The combination of participants' health-related limitations, weight, medical expenses, and health insurance access have burdened participants' finances and compromised their medical compliance.	Participants experienced some interventions as ineffective or inaccessible post-event/surgery	
I thought about, you know, 'Is this gonna happen again?' That, that stays in my mind a lot [CHUCKLING], you know. Yeah, I'm, I'm concerned about it happenin' again, or, I mean, I'm anticipating – it's like every time I feel a little pain, I'm anticipatin' that, 'Okay, this may be happenin'. And um, so that's, that's the challenge that I'm facin' now as, as far as that.' –P7	Participants felt anxiety about having limited control over and knowledge of their cardiac event, intervention, and outcome.	Unpredictability of health challenges and outcomes affected distress level	4. Participants' sense of agency affected their life perspectives and health behaviors
"I know what I should be doing: get up and walk around more often." –P2	Participants did not follow through with medically-indicated recommendations pre- and post-intervention.	Participants had different levels of proactivity about health and recovery process	
"I really wouldn't have, you know, probably would've die young…This might have been a wake-up call." –P2	Participants' cardiac diagnoses/events/surgeries were wake-up calls that inspired participants to get more serious about their health and turn their lives around.	Cardiac events/surgeries led to lifestyle changes	
"You gotta kinda retrain your tastebuds, in a sense, so it ain't always, 'Okay, I want sugar, sugar, sugar.' I said [to sons], 'cause, um, 'You see people out here who don't have fingers, toes, hands, arms, legs, and they lost it to diabetes.'" –P5	Participants helped – or expressed a desire to help – others using the medical/health knowledge and life lessons they learned from their diagnoses, event/surgery, and recovery.	Passing on new knowledge was a part of participants' recovery process	
"I think it's [CR] very important to help you get, get stronger and back to, not just your own life that you had before heart surgery, but a better life." –P5	Participants received CR information and referral from medical providers, attended CR, and had a positive experience.	Participants experienced health-related successes with CR	5. Participants experienced inconsistent referral to and utilization of Cardiac Rehabilitation
"When I started the rehab thing, um, no disrespect, but when I ain't seen nothing but older people in there, like grandmoms and granddaddys, and I look at my age, I'm saying to myself, 'I shouldn't be in here.'" – P3	Participants felt that working out with others who were older, less physically able, and/or less motivated to be active than themselves threatened to negatively impact their exercise experience.	Participants experienced barriers to CR participation	
"Don't have to do, deal with too many pills, don't have to deal with a whole lotta people, and their problems and stuff. I've just been doing a whole lot, lot better… I ain't supposed to worry about nobody else's problems. All you have to do is just pray about it and just leave it alone." –P1	Participants had existing spiritual challenges that intensified and resolved post-medical intervention.	Participants and families were involved in their faith and faith communities	6. Participants' investment in faith was intensified or maintained
"Every time, you know, stuff'd go wrong, I'd think about my spiritual relationship with God, and, um, and, um, the prayer, and, uh, it's just, like, I, I had no, no fear in believing that I would be alright, you know?... I had no fear that everything would be alright." –P6	Surrendering troubles to God gave participants the strength to move forward through their recovery.	Participants experienced faith as a source of strength and gratitude	

Acknowledgements

The authors would like to acknowledge the hard work of the following individuals in supporting the data collection for this article: Stacey Greenway, Patricia Huerta, Morgan Lancaster, and Michelle Tracey. Our deepest and heartfelt thanks for everything you did to support this project.

Disclosures

No financial support given. The authors report no conflicts of interest.

References

1. American Heart Association. Heart and Stroke Statistics. Retrieved from https://www.heart.org/en/about-us/heart-and-stroke-association-statistics Accessed June 6, 2019.
2. Fryar CD, Ostchega Y, Hales CM, Zhang G, and Kruszon-Moran D. Hypertension Prevalence & Control Among Adults: United States, 2015–2016. NCHS Data Brief. 2017 Oct;(289): 1–8. Jafri, I. (2004). Cardiac Rehabilitation. In S. Cuccurullo (Ed.), Physical Medicine and Rehabilitation Board Review (pp. 670-692). New York, N.Y.: Demos Medical Publishing.
3. American Association of Cardiovascular and Pulmonary Rehabilitation. About Cardiovascular and Pulmonary Rehabilitation. 2014. Retrieved from https://www.aacvpr.org/about/aboutcardiacpulmonaryrehab/tabid/560/default.aspx
4. Jafri I. Cardiac Rehabilitation. In S. Cuccurullo (Ed.), Physical Medicine and Rehabilitation Board Review (pp. 670-692). New York, NY: Demos Medical Publishing; 2004.
5. Brown J, Clark A, Dalal H, Welch K, Taylor R. Patient education in the management of coronary heart disease. Cochrane Database of Systematic Reviews. 2011;6:CD008895.
6. Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev. 2011;7:CD001800
7. Kwan G, Balady GJ. Circulation topic review: Cardiac rehabilitation 2012. Circulation. 2012;125:e369–e373.
8. Ayala C, Xie J, McGruder HF, Valderrama AL. Receipt of outpatient cardiac rehabilitation among heart attack survivors—United States, 2005. MMWR Morb Mortal Wkly Rep. 2008;57(4):89–94
9. Cortés O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: a systematic review . Am Heart J. 2006;151(2):249–256.
10. Suaya JA, Shepard DS, Normand ST, Ades PA, Prottas J, Stason WB. Use of cardiac rehabilitation by Medicare beneficiaries after myocardial infarction or coronary bypass surgery. Circulation. 2007;116(15):1653–1662.
11. Beswick AD, Rees K, Griebsch I, et al. Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups. Health Technol Assess. 2004;8(41): iii-iv, ix-x, 1–152 .
12. Evenson KR, Johnson A, Aytur SA. Five-year changes in North Carolina outpatient cardiac rehabilitation. J Cardiopulm Rehabil. 2006;26(6):366–376.
13. Gregory PC, LaVeist TA, Simpson C. Racial disparities in access to cardiac rehabilitation. Am J Phys Med Rehabil. 2006;85(9):705–710.
14. Hannan EL, van Ryn M., Burke J, et al. Access to coronary artery bypass surgery by race/ethnicity and gender among patients who are appropriate for surgery. Med Care. 1999;37:68–77.
15. Ibrahim SA, Whittle J, Bean-Mayberry B, et al. Racial/ethnic variations in physician recommendations for cardiac revascularization. A J Public Health. 2003;93:1689–1693.
16. Peterson ED, Shaw LK, DeLong ER, et al. Racial variation in the use of coronary-revascularization procedures—Are the differences real? Do they matter? N Engl J Med. 1997;336:480–486.
17. Schneider EC, Leape LL, Weissman JS, et al. Racial differences in cardiac revascularization rates: Does 'overuse' explain higher rates among white patients? Ann Intern Med. 2001;135, 328–337.
18. van Ryn M., Burgess D, Malat, J, et al. Physicians' perceptions of patients' social and behavioral characteristics and race disparities in treatment recommendations for men with coronary artery disease. A J Public Health. 2006;96:351–357.
19. Barber K, Stommel M, Kroll J, Holmes-Rovner M., et al (2001). Cardiac rehabilitation for community-based patients with myocardial infarction: Factors predicting discharge recommendation and participation. J Clin Epidemiol. 2001;54:1025–1030.
20. Dickson VV, McCarthy MM, Howe A, et al. Sociocultural influences on heart failure self-care among an ethnic minority black population. J Cardiovasc Nurs. 2013;28(2):111–118.
21. Dickson VV, McCarthy MM, Katz SM. How do depressive symptoms influence self-care among an ethnic minority population with heart failure? Ethn Dis. 2013;23(1), 22–28.
22. Blustein J, Valentine M, Mead H, et al. Race/ethnicity and patient confidence to self-manage cardiovascular disease. Med Care. 2008;46:924–929.
23. Grewen KM, Anderson BJ, Girdler SS, et al. Warm partner contact is related to lower cardiovascular reactivity. Behav Med. 2003;29(3):123–130.
24. Liu L, Newschaffer CJ. Impact of social connections on risk of heart disease, cancer, and all-cause mortality among elderly Americans: Findings from the Second Longitudinal Study of Aging (LSOA II). Arch Gerontol Geriat. 2011;53(2):168–173.
25. Tkatch R, Artinian NT, Abrams J, et al. (2011). Social network and health outcomes among African American cardiac rehabilitation patients. Heart Lung. 2011;40:193–200.
26. Johnson KS, Elbert-Avila KI, Tulsky JA. The influence of spiritual beliefs and practices on the treatment preferences of African Americans: A review of the literature. J Am Geriatr Soc. 2005;53, 711–719.
27. Polzer RL, Miles MS. (2007). Spirituality in African Americans with diabetes: Self-management through a relationship with God. Qual Health Res. 2007;17(2): 176–188.
28. Davis AM, Vinci LM, Okwuosa TM, Chase AR, Huang ES. Cardiovascular health disparities: A systematic review of health care interventions. Med Care Res Rev. 2007;64(Suppl. 5):29S–100S.
29. Sanderson BK, Mirza S, Fry R, Allison JJ, Bittner V. Secondary prevention outcomes among black and white cardiac rehabilitation patients. Am Heart J. 2007;153:980–986.
30. Schneiderman N, Saab PG, Catellier DJ, et al. Psychosocial treatment within sex by ethnicity subgroups in the Enhancing Recovery in Coronary Heart Disease clinical trial. Psychosom Med. 2004;66:475–483.
31. Hildebrandt Koehler AN, Hodgson JL, Dodor BA, Knight SM, Rappleyea DL. Biopsychosocial-spiritual factors impacting African American patients' cardiac rehabilitation referral and participation: A systematic review. J Cardiopulm Rehabil Prev. 2016;36:320–330.
32. Allen JK, Scott LB , Stewart KJ , Young DR . Disparities in women's referral to and enrollment in outpatient cardiac rehabilitation. J Gen Intern Med. 2004;19(7):747–753.
33. Bittner V, Sanderson B, Breland J, Green D. Referral patterns to a university-based cardiac rehabilitation program. Am J Cardiol. 1999;83(2):252–255 .
34. Cannistra LB, O'Malley CJ, Balady GJ. Comparison of outcome of cardiac rehabilitation in black women and white women. Am J Cardiol. 1995;75(14):890–893.
35. Rankin SH. Women recovering from acute myocardial infarction: psychosocial and physical functioning outcomes for 12 months after acute myocardial infarction. Heart Lung. 2002;31(6):399–410 .

36. Young RF, Waller JB Jr, Kahana E. Racial and socioeconomic aspects of myocardial infarction recovery: studying confounds. Am J Prev Med. 1991;7(6):438–444 .
37. Husserl E. The crisis of European sciences and transcendental phenomenology. Evanston, IL: Northwestern University Press; 1970.
38. Creswell JW. Research design: qualitative, quantitative, and mixed methods approaches (3rd ed.). Thousand Oaks, CA: SAGE Publications, Inc; 2009.
39. Mason M. Sample size and saturation in PhD studies using qualitative interviews. Forum Qual Soc Res. 2010:11(3). Retrieved from http://www.qualitative-research.net/index.php/fqs/article/view/1428/3027
40. Morse JM, Barrett M, Mayan M, et al. Verification strategies for establishing reliability and validity in qualitative research. Int J Qual Methods. 2002:1(2):13–22.
41. Colaizzi P. Psychological research as the phenomenologist views it. In Vaile R, King M, eds. Existential phenomenological alternatives for psychology (pp. 48–71). New York, NY: Oxford University Press; 1978.
42. Bernard HR, Ryan GW. Analyzing qualitative data: Systematic approaches. Washington, DC: SAGE Publications, Inc; 2010.
43. Hennink M, Hutter I, Bailey A. Qualitative Research Methods. Washington, DC: SAGE Publications, Inc; 2011.
44. Lincoln Y, Guba E. Naturalistic inquiry. New York, NY: SAGE Publications, Inc; 1985.
45. Collins TC, Clark JA , Petersen LA, Kressin NR. Racial differences in how patients perceive physician communication regarding cardiac testing. Med Care. 2002;40(Suppl 1):I27-I34
46. Lutfiyya MN, Cumba MT, McCullough JE, Barlow EL, Lipsky MS. (2008). Disparities in adult African American women's knowledge of heart attack and stroke symptomatology: An analysis of 2003–2005 behavioral risk factor surveillance survey data. J Women's Health. 2008;17:805–813.
47. Shaw SJ, Armin J, Torres CH, Orzech KM, Vivian J. Chronic disease self-management and health literacy in four ethnic groups. J Health Commun. 2012;17(Suppl. 3),67–81.
48. American Heart Association. Statistical Fact Sheet, 2013 Update: Older Americans & Cardiovascular Disease. 2013. Retrieved from https://www.heart.org/idc/groups/heart-public/@wcm/@sop/@smddocuments/downloadable/ucm_319574.pdf

Original Science

Following in Footsteps: Children of Physicians More Likely to Attend Medical School but No More Likely to Succeed

Lindsay C. Strowd, M.D.[1], Hong Gao, Ph.D.[2], Mary Claire O'Brien, M.D.[3], Michael Cartwright, M.D.[4], Julie A. Freischlag, M.D.[5], Roy E. Strowd, M.D.[2, 4], Timothy R. Peters, M.D.[6]

Abstract

Background: Physician legacy (PL) students are over-represented in medical school compared to non-PL students. There is little published data examining how PL students perform in medical school. We sought to examine differences in medical school performance between PL students and their non-PL student peers at our own institution.

Methods: A retrospective review of three medical school classes identified students with at least one physician parent. A total of 79 PL students (24.16%) were identified out of 327 total students. Multiple medical school performance metrics were obtained for each student.

Results: There was no significant difference in Medical College Admission Test (MCAT), Step 1, Step 2, National Board of Medical Examiners (NBME) Subject exam scores, clerkship grades, or clerkship Honors. PL students were significantly more likely to be elected to Alpha Omega Alpha (AOA) Honor Medical Society.

Conclusions: PL students do not perform better on most objective or subjective assessments of performance despite higher matriculation numbers. These findings have implications for medical school admissions programs where PL applicants may be subject to positive or negative bias during the admissions process. Our recommendation is that PL status not be considered as a strength or weakness of the student's application and that admissions committees consider blinding committee members to PL status to avoid unconscious bias.

Introduction

Significant study and effort have been devoted to examining the medical school admissions process. Ideally, the admissions process should be fair, equitable, and result in selection of diverse exceptional candidates who will succeed in medical training and be representative of the communities they serve. Currently, most admission committees favor a holistic approach to the applicant, categorizing applicant attributes into three main groups: cognitive ability, non-cognitive ability, and demographics.[1] Demographic variables have been used for decades in the medical school admissions process, despite a lack of predictive validity of certain variables on medical school performance.[2] Historically, most medical school applicants come from middle- or upper-class socioeconomic backgrounds, including applicants with a physician parent. No research has established a clear performance advantage of physician legacy (PL) children though multiple studies have examined this concept.[3] Despite this lack

[1]Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, NC

[2]Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, NC

[3]Department of Emergency Medicine, Wake Forest University School of Medicine, Winston-Salem, NC

[4]Department of Neurology, Wake Forest University School of Medicine, Winston-Salem, NC

[5]Department of Vascular Surgery, Wake Forest University School of Medicine, Winston-Salem, NC

[6]Department of Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC

Address Correspondence To:
Lindsay C. Strowd, M.D.
Department of Dermatology
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
lchaney@wakehealth.edu

of evidence, applicants with physician parents are over-represented in current medical school student populations compared to the relative frequency of physician parents in the general workforce. Prior studies have shown between 13-44% of matriculating medical students have at least one physician parent, compared to physicians comprising approximately 1% of the adult workforce.[4-10] A national study in the U.S. found that 22% of the respondents had a physician relative.[11] These statistics stand in contrast to the Association of American Medical Colleges (AAMC) study which did not list parent occupation as one of the admissions variables used by admissions staff and faculty at 113 U.S. allopathic medical schools.[12]

It is possible a PL applicant may have advantages over other applicants that would enhance their medical school application. These advantages include access to prior medical experiences and parental advice on the rigors and challenges of medical school. Additionally, children of physicians may hold a socioeconomic status that allows for private tutors or preparatory courses, and a relative lack of financial burden of higher education expenses.[3] A study in Germany of medical school applicants found those with physician parents did not perform any better than non-legacy applicants in multiple mini-interviews (MMI) or in traditional admissions interviews.[13] Another explanation could be that children of physicians are more likely to apply to medical school. Legacy students in some cultures report family tradition or pressure as a motivation to choose a career in medicine independent of having a personal passion or interest for this field, which may result in lower performance in medical school or burnout.[14-16] Prior studies have shown students with high levels of extrinsic motivation, including perceived pressure from parent expectations, as opposed to intrinsic motivation, do not perform as well in medical school.[17, 18]

We aimed to address the current gap in knowledge regarding whether PL students perform better in medical school than other students.

Methods

We performed a retrospective analysis of students who matriculated to our medical school between the years of 2013-2015. We examined student admission records from the American Medical Colleges Application Service (AMCAS) and recorded each parent's occupation, which admission committee members may view under the demographics tab of each application. We identified students who had at least one parent with a primary occupation of physician and those students were included in the PL cohort. We extracted additional demographic information including age, sex, and race. Those with missing Year 3 performance data (withdrawals or dismissals) were removed from data analyses. Medical College Admission Test (MCAT) scores were obtained from admission records, and in cases of multiple MCAT scores, the highest score was used in this analysis. For MCAT scores obtained after 2015, a score converter was used to convert new scores to the former scoring system.

For performance measures during medical school, we collected (1) first attempt at United States Medical Licensing Examination (USMLE) Step 1 score, (2) first attempt at USMLE Step 2 Clinical Knowledge (CK) score, and (3) institutional Year 3 performance metrics. Due to variable methods of performance assessment in Year 3, we examined multiple different metrics. The year-end clinical clerkship score is a composite score which includes faculty and resident evaluations, National Board of Medical Examiners (NBME) Subject exam scores, and letter grades (Honors/High Pass/Pass/Low Pass/Fail) across all clerkships. For the individual clerkship clinical score, a standard form assessing eight aspects of clerkship performance (medical knowledge, history taking, physical examination, clinical data, clinical skills, communication, team rapport, and motivation and attitude) is provided to faculty and residents who worked directly with the student. Raw clerkship clinical scores were converted to Z scores to reduce variability across grading among the eight clerkships (family medicine, internal medicine, emergency medicine, obstetrics and gynecology, pediatrics, psychiatry, neurology, and surgery). NBME subject exam scores were also converted to Z scores for easier comparison between exams, using a mean of 70 and standard deviation of 8. Average number of clerkship Honors per student was calculated, as well as average Year 3 grade score (0=Fail, 1=Low Pass, 2=Pass, 3=High pass, 4=Honors). In addition, percentage of students in each cohort who achieved Alpha Omega Alpha (AOA) status and Gold Humanism Award status were determined and a Wald Chi-square test was used to determine statistical significance.

Linear regression analyses were conducted to examine the relationship between PL status and various performance outcomes during medical school (Step 1, Step 2 CK, Year 3 clinical score, Year 3 subject exam results). Regression analyses were also conducted to determine if there were differences in MCAT performance prior to medical school.

Institutional Review Board (IRB) approval was obtained for this study (IRB00043836) and students were consented for participation. Identifying information was removed from records and students were assigned a unique study number to protect individual identity. Student performance was not examined on an individual basis.

Results

The total number of participants was 327 students, with 79 PL students. Thirty-five students were excluded from analyses due to having incomplete Year 3 data. Of these 35 students, six were M.D./Ph.D. students. The 29 remaining students had missing data due to repeating portions of the curriculum, requiring additional time to pass Step 1, leave of absences, withdrawals, or transfers. Of the 29 students with missing data, three were PL students and were not included in the PL cohort. The PL students (n=79) represented 24.16% of participants. Baseline matriculation demographics of PL students versus non-PL students are shown in Table 1. There was no difference in age at matriculation or sex between the two cohorts. A higher percentage of PL students identified as White compared to the non-PL student cohort.

Comparison of objective standardized tests revealed MCAT ($p>0.49$), USMLE Step 1 ($p>0.41$), and USMLE Step 2 ($p> 0.05$) scores did not differ between the cohorts (Table 2). Multiple performance metrics relevant to Year 3 were examined. These included both objective measures such as NBME subject scores as well as subjective measures such as clinical scores from faculty evaluations. The PL cohort did not perform better on NBME subject exams ($p>0.14$), clinical scores ($p>0.66$), number of Honors clerkships ($p>0.12$), or Year 3 overall score ($p>0.15$) (Table 2). There was no difference between the two cohorts with election to the Gold Humanism society ($p>0.89$). The only assessed metric where there was a significant difference between the PL cohort and the non-PL cohort was in election to AOA ($p<0.05$).

Discussion

Our research finds medical students with a parent who is a physician do not perform better than their peers in medical school for most of the metrics we examined. This finding is true for both objective and subjective performance metrics, with the exception of AOA election. Our results generally support the null hypothesis that PL students do not outperform their peers, despite PL students being over-represented in our medical school class cohorts. The finding

	PL Students (N=79)	Non-PL Students (N=252)
Average age at matriculation (years)	23.94 (SD=2.41)	24.66 (SD=3.32)
Male	43 (54.43%)	127 (50.40%)
Female	36 (45.57%)	125 (49.60%)
White	54 (73.97%)	154 (65.25%)
Non-white	19 (26.03%)	82 (34.75%)

Table 1. Demographic data of physician legacy (PL) cohort versus their peer cohort (SD = standard deviation)
* Race is self-reported data, 22 students did not report race

	PL Students (N=79)	Non-PL Students (N=252)	p-value
MCAT score (average)	30.79 (SD=2.87)	30.52 (SD=3.09)	p=0.49
USMLE Step 1 score (initial attempt)	232.43 (SD=20.27)	230.43 (SD=18.55)	p=0.41
NBME Year 3 Subject exam (average Z scores)	1.36 (SD=0.78)	1.21 (SD=0.82)	p=0.14
Year 3 clinical scores (average Z scores)	0.12 (SD=0.61)	0.08 (SD=0.54)	p=0.66
Average number of Honors	2.90 (SD=2.22)	2.47 (SD=2.10)	p=0.12
Total score (assign 0 for F, 1 for LP, 2 for pass, 3 for HP, and 4 for Honors)	24.65 (SD=4.52)	23.82 (SD=4.44)	p=0.15
Step 2 CK score (initial attempt)	250.97 (SD=16.13)	246.89 (SD=15.67)	p=0.05
AOA status (%)	25.97%	15.66%	Wald chi-square =4.13, p <0.05
Gold Humanism Award status (%)	10.26%	10.80%	Wald chi-square =0.02, p >0.89

Table 2. Standardized exam scores, clinical clerkship performance metrics, AOA and Gold Humanism status for PL and non-PL students (SD = standard deviation, HP = high pass, F = fail, LP = low pass)

that PL students are more likely to gain admission to the AOA Honor Medical Society was unexpected, and stands in contrast to our finding that this cohort of students do not show enhanced performance in medical school. This was surprising as parental occupation is not one of the metrics included in our chapter's AOA election process. We considered several possibilities to explain this finding. Perhaps there is a bimodal distribution of PL students, with both very high performing and very low performing subgroups and the high performing group is elected to AOA. We performed further analyses to investigate this and did not find a bimodal distribution for various outcome measures. We also assessed the percentage of PL students elected to AOA for each included year, and found that in one of the three cohorts there were a high number of elected PL students compared to the other two classes, which may have potentially skewed the data and suggest perhaps this finding is truly one of chance and not a consistent yearly trend. A third possibility is perhaps PL students have additional advantages in the AOA election process, such as more research, leadership, or service experiences. Further investigation of this unexpected finding was beyond the scope of this study.

The issue of physician legacy and admissions is discussed in an ethics piece published in the American Medical Association Journal of Ethics. The authors posit that physician status likely influences admissions decisions indirectly, by consideration of PL student socioeconomic status or a focus on student academic performance. Additionally, these authors note the possibility of more direct influences on admissions, such as professional courtesy extended to legacy parents. It also suggests PL status may create negative bias towards

the applicant if admissions officers question the PL student's intrinsic motivation to attend medical school.[19]

A paper published in the 1980's sought to examine the trend in PL preference on a national level.[7] The authors examined admissions applications from all medical school applicants (n=36,141) in 1979 and extracted sixty different admissions factors from each application. These factors included sex, race, parental profession, grade point average, MCAT scores and subscores, undergraduate courses and performance, and personality characteristics, among others. Multiple regression analyses demonstrated a clear advantage for students gaining admission who had a physician as a parent. This advantage was not demonstrated for students with parents in other healthcare occupations. The authors concluded they could not find any objective reason for why children of physicians were more likely to be admitted to medical school and suggested there may be a component of nepotism.

Despite the recent campaign by the AAMC to encourage holistic admission strategies, the diversity of medical school graduates does not accurately reflect the diversity of the patient population they will be serving.[20] This is true not only in the U.S. but in other countries as well.[21] From 1987-2005, half of matriculating U.S. medical students came from the top quintile of family income. Only 5.5% of students came from the lower family income quintile. The socioeconomic status of a child's parents is a significant predictor of the child's academic achievement and correlates with higher MCAT scores.[22] In an effort to address these socioeconomic disparities, medical school admission offices should seek out structural barriers within their institutions that may prevent access to medical education for underrepresented groups.[23] Intrinsic racial bias has been shown to exist in admissions committees[24] and other types of intrinsic bias may also exist among committee members. Provided that the majority of admissions committee members are physicians, it may be prudent to blind committee members to applicant PL status to avoid both positive and negative sources of bias. Studies such as this one are important to critically appraise the admissions process and scrutinize all factors to determine their validity.

The strengths of this study include using an analytical approach to assess PL performance via multiple different medical school performance metrics. This study addresses the current gap in the literature regarding PL performance in U.S. medical schools. The pragmatic design of this study lends itself to replication at other medical schools and provides a theoretical framework for future quantitative and qualitative research on assessing correlation of admissions factors with medical school performance.

Limitations

This is a single-institution retrospective study, so it may not be generalizable to other medical school programs. Identification of parental occupation was based on student admission application information, and additional verification of employment was not obtained.

Student performance evaluations during Year 3 clerkships have subjective scoring elements. Each clerkship at our institution employs a different criteria weighing scale to calculate student final grades and the subject exam score contribution to the overall clerkship grade varies somewhat. The number of clinical evaluations varies between students and is comprised of residents, fellows, and faculty evaluators. We attempted to account for this variability by performing and presenting analysis of separate measures of clerkship performance including subject exam scores, clinical evaluation scores, Honors designation, and overall year-end performance scores.

Disclosures

No financial support given. The authors report no conflicts of interest.

References

1. Bore D, Munro D, Powis D. A comprehensive model for the selection of medical students. Med Teach, 2009; 31(12), 1066-1072
2. Benbassat J, Baumal R. Uncertainties in the selection of applicants for medical school. Advances in Health Sciences Education, 2007; 12(4): 509-521.
3. Fabbro, SK. On Choosing the "Perfect" Doctor. Virtual Mentor, Dec 2012; 14(12): 946-949.
4. Pedersen LT, Bak NH, Petersson BH. The social recruitment of medical students in year group 2006 and 2007 at the University of Copenhagen. Ugeskr Laeger. 2010 Jan 18;172(3):206-10.
5. Perez D, Belton A. Demography of medical students at the University of Otago, 2004-2008: a changing spectrum? N Z Med J. 2013 Mar 15;126(1371):63-70.
6. Heath C, Stoddart C, Green H. Parental backgrounds of Otago medical students. N Z Med J. 2002 Nov 8;115(1165):U237.
7. Lentz B, Laband D. Why So Many Children of Doctors Become Doctors: Nepotism vs. Human Capital Transfers. The Journal of Human Resources, 1989; 24(3), 396-413.
8. Hansen MN. Social background in recruitment of medical students. Tidsskr Nor Laegeforen. 2005 Aug 25;125(16):2213-5.
9. Nowacek G, Sachs L. Demographic variables in medical school admission. Acad Med. 1990 Mar;65(3):140–144.

10. Kaiser Family Foundation. (June 4, 2019). Number of active physicians in the U.S. in 2019, by specialty area [Graph]. In Statista. Retrieved November 13, 2019, from https://www.statista.com/statistics/209424/us-number-of-active-physicians-by-specialty-area/.
11. Choi KJ, Tak HJ, Bach C, Trias C, Warsi H, Abraham J, Yoon JD. Characteristics of Medical Students with Physician Relatives: A National Study. MedEdPublish 2018 Feb 2; DOI: https://doi.org/10.15694/mep.2018.0000030.1
12. Dunleavy DM, Whittaker KM. 2011. Medical School Admissions: More than Grades and Test Scores. AAMC Analysis. 11(6). 1-4.
13. Simmenroth-Nayda A, Gorlich Y. Medical school admission test: advantages for students whose parents are medical doctors? BMC Med Educ. 2015 Apr 23;15:81. doi: 10.1186/s12909-015-0354-x.
14. Goel S, Angeli F, Dhirar N et al. 2018. What motivates medical students to select medical studies: a systematic literature review. BMC Med Educ. 18;16. PMID: 29343262
15. Kunzmann, K. 2019. Parental Pressure Linked to Medical School Uncertainty, Potential Burnout. https://www.mdmag.com/medical-news/parental-pressure-linked-to-medical-school-uncertainty-potential-burnout. Accessed April 5, 2019.
16. Sulong S, McGrath D, Finucane P, Horgan M, O'Flynn S, O'Tuathaigh C. Studying medicine - a cross-sectional questionnaire-based analysis of the motivational factors which influence graduate and undergraduate entrants in Ireland. JRSM Open. 2014;5(4):204253313510157. Published 2014 Mar 12. doi:10.1177/204253331351015
17. Kusurkar RA, Ten Cate TJ, van Asperen M, Croiset G. 2011. Motivation as an independent and a dependent variable in medical education: A review of the literature. Med Teacher; 33(5): 242-262.
18. Griffin B, Hu W. Parental career expectations: effect on medical students' career attitudes over time. Med Educ. 2019 Jun;53(6):584-592. doi: 10.1111/medu.13812. Epub 2019 Feb 7.
19. Elam CL, Wagoner NE. Legacy Admissions in Medical School. Virtual Mentor. 2012;14(12):946-949. doi: 10.1001/virtualmentor.2012.14.12.ecas3-1212.
20. Thomas BR, Dockter N. Affirmative Action and Holistic Review in Medical School Admissions: Where We Have Been And Where We Are Going. Acad Med. 2018 Oct 1. doi: 10.1097/ACM.0000000000002482. [Epub ahead of print].
21. White C. Doctors from underprivileged backgrounds are poorly represented in medicine. BMJ 2013; 347 doi: https://doi.org/10.1136/bmj.f6348. Published 18 October 2013.
22. Grbic D, Jones DJ, Case ST. The Role of Socioeconomic Status in Medical School Admissions: Validation of a Socioeconomic Indicator for Use in Medical School Admissions. Acad Med; 90(7): 953-960. July 2015
23. Talamantes E, Henderson MC, Fancher TL, Mullan F. Closing the Gap - Making Medical School Admissions More Equitable. N Engl J Med. 2019 Feb 28;380(9):803-805. doi: 10.1056/NEJMp1808582.
24. Capers Q, Clinchot D, McDougle L, Greenwald AG. Implicit racial bias in medical school admissions. Acad Med. 2017;92:365-369.

Original Science

Systemic Venous versus Portal Venous Drainage in Simultaneous Pancreas-Kidney Transplantation: A Case-Control Study

David I. Harriman, M.D.[1]; Venkat Gurram, M.D.[1]; Komal Gurung, M.D.[1]; Alan C. Farney, M.D., Ph.D.[1]; Jeffrey Rogers, M.D.[1]; Giuseppe Orlando, M.D., Ph.D.[1]; Colleen Jay, M.D.[1]; Amber Reeves-Daniel, D.O.[1]; Robert J. Stratta, M.D.[1]

Abstract

Introduction: Although the standard pancreas transplant (PTx) is currently performed with exocrine enteric drainage, <20% also incorporate portal venous delivery of insulin (portal-enteric [P-E] drainage), which is our preferred technique. The purpose of this study was to analyze PTx outcomes according to surgical technique and method of venous delivery.

Methods: We retrospectively reviewed 231 simultaneous pancreas-kidney transplants (SPKTs) performed at our center between 7/2003 - 7/2019, the majority of which were performed with P-E drainage. We next identified 27 SPKTs that were performed with systemic venous (iliac vein) and enteric exocrine (systemic-enteric [S-E]) drainage in lieu of P-E drainage and compared these cases to 27 case controls with P-E drainage matched for recipient age, gender, race, and date of transplant. All patients received either r-ATG or alemtuzumab induction with tacrolimus, mycophenolate ± steroids.

Results: The two groups were well-matched for numerous donor, preservation, recipient, and immunological characteristics. Reasons for S-E drainage were central obesity/thickened mesentery (10), unfavorable vascular anatomy (11), or surgeon preference (6). The S-E drainage group was characterized by slightly more patients ≥ 80 kg (44% S-E versus 26% P-E), with C-peptide positive diabetes (30% S-E versus 18% P-E), and with diabetes onset at >20 years of age (41% S-E versus 26% P-E, all p=NS), suggesting a type 2 diabetes phenotype. Although the incidence of early pancreas thrombosis (3.7% S-E versus 0% P-E), early relaparotomy rates (30% S-E versus 22% P-E), and mean initial length of hospital stay (11 days S-E versus 8 days P-E) were numerically higher in S-E versus P-E SPKTs, none of these differences were significant. With a mean follow-up of five years in both groups, respective one- and five-year patient survival (100% and 96% S-E versus 100% and 100% P-E), kidney graft survival (100% and 93% S-E versus 100% and 85% P-E), and pancreas graft survival (96% and 96% S-E versus 100% and 85% P-E) rates were comparable.

Conclusion: The method of venous delivery of insulin following PTx does not appear to influence medium-term outcomes in SPKT with enteric exocrine drainage when S-E drainage is performed in lieu of P-E drainage.

[1]Department of General Surgery, Section of Transplantation, Wake Forest Baptist Health, Winston-Salem, NC

Address Correspondence To:
Robert J. Stratta, M.D.
Department of General Surgery
Section of Transplantation
Wake Forest Baptist Health
One Medical Center Blvd.
Winston-Salem, NC 27157
rstratta@wakehealth.edu
Phone: (336) 716-0548
Fax: (336) 713-5055

Introduction

The history of vascularized pancreas transplantation (PTx) has closely mirrored the evolution in surgical techniques. Advances in surgical techniques and clinical immunosuppression have led to improving results in vascularized PTx that are attributed to reductions both in early technical failures and immunologic graft losses over time.[1] According to the International Pancreas Transplant Registry (IPTR) data, most PTxs are performed with systemic venous delivery of insulin and enteric (systemic-enteric [S-E]) drainage of the exocrine secretions.[1] Prior to 1995, more than 90% of PTxs were performed by the standard technique of systemic-bladder drainage, usually using an allograft duodenal segment conduit for exocrine drainage into the bladder. Enteric drainage usually refers to jejunal or ileal diversion of the exocrine secretions either with or without a diverting Roux limb. Since 1995, the number of PTxs performed with primary enteric exocrine drainage has increased dramatically and currently accounts for 95% of simultaneous pancreas-kidney transplants (SPKTs) performed in the United States (U.S.). At present, nearly 90% of enteric drained SPKTs are performed with systemic (iliac or vena cava) venous delivery of insulin, resulting in peripheral hyperinsulinemia.[1] In the non-transplant setting, systemic hyperinsulinemia has been associated with insulin resistance, dyslipidemia, accelerated atherosclerosis, and macroangiopathy.

To improve the physiology of PTx, an innovative surgical technique of intraperitoneal portal venous drainage using an anterior approach to the superior mesenteric vein (SMV) was developed by Gaber et al.[2] and subsequently refined to a "retroperitoneal" or lateral approach by Boggi et al.[3] combining portal venous delivery of insulin with enteric drainage of the exocrine secretions (portal-enteric [P-E] technique). However, the potential of P-E drainage has never been fully realized as it is performed in only 12% of SPKTs in the U.S.[1] A number of studies have demonstrated no major or consistent differences in outcomes for bladder-drained or enteric-drained PTxs with either portal or systemic venous drainage.[4-8] Although nearly all PTxs are performed with one of the three above techniques, current philosophy dictates that the most appropriate technique is the one with which the surgical team has the most experience and confidence.[9,10] At our center, we have extensive experience with each technique but currently perform P-E drainage preferentially using the anterior approach to the SMV.[11,12] In this study, we chose to focus on technical considerations and analyzed our experience with S-E drainage as a "rescue" or secondary technique of PTx when P-E drainage was not deemed appropriate using a case-control design.

Methods

Study Design

The PTx program at Wake Forest originally started in 1995 (one SPKT with systemic-bladder drainage was performed in the 1990s). However, the program was resumed in November 2001 and 283 PTxs have been performed as of October 2019. For purposes of this study, we retrospectively reviewed 231 SPKTs performed at our center between 7/2003 - 7/2019 and identified 27 that were performed with S-E drainage whereas the remainder were performed with P-E drainage, which is our preferred surgical technique. These 27 patients were compared to 27 SPKT case controls with P-E drainage matched for recipient age, gender, race, and date of transplant. All patients received similar management strategies.[11-15]

Recipient Selection

General indications for PTx were insulin-requiring diabetes with complications and the predicted ability to tolerate the operative procedure, manage the requisite immunosuppression, and deal with the need for close follow-up post-SPKT irrespective of C-peptide production.[12-14] Specific indications for SPKT included stage 4/5 chronic kidney disease or end stage renal disease and the absence of any contraindications. Contraindications included age >65 years; insufficient cardiovascular reserve; current substance abuse; active infection or recent malignancy; major ongoing psychiatric illness, recent noncompliance, or lack of adequate social support; significant obesity or unfavorable anatomy; severe vascular disease; or inability to either understand or commit to the more intense follow-up associated with SPKT compared to kidney transplantation alone. Selection criteria for SPKT in "type 2" diabetes included patients <55 years of age with a body mass index (BMI) <30 mg/kg^2, requiring insulin for a minimum of three years with a total daily insulin requirement <1 units/kg/day, a fasting C-peptide level <12 ng/ml, absence of severe vascular disease or tobacco abuse, adequate cardiac function, and presence of "complicated" or hyperlabile diabetes.[12-16]

Technical Aspects

All patients were T- and B-cell negative by flow cytometry crossmatch. Nearly all PTxs were initially approached as intent-to-treat with P-E drainage using an anterior approach to the SMV and enteric exocrine drainage to the proximal ileum in the recipient (side-to-side duodeno-enterostomy, usually without a diverting Roux limb, Figure 1).[11-14] Diverting Roux limbs were used rarely and only if the donor duodenum did not reperfuse well. Arterial inflow was usually based on the recipient's right common iliac artery after the pancreas dual artery blood supply was reconstructed with a donor common iliac bifurcation "Y" graft (Figure 2).[17,18] Relative "contraindications" to portal venous drainage were a small SMV (<6mm in diameter); a deep, buried, or inaccessible SMV (usually associated with central obesity, particularly in recipients with a BMI >30 kg/m^2); a sclerotic or partially thrombosed SMV or history of venous thrombosis from a previous PTx with portal venous outflow; portal hypertension; or an arterial "Y" graft that would not reach a soft target either on the iliac artery or aorta.[11-14] In patients (particularly male) with a high BMI, the SMV can be quite deep in the mesentery and the donor common iliac artery bifurcation "Y" graft might not be long enough to reach the recipient's iliac artery through a window in the distal ileal mesentery, even with the liberal use of a donor artery "extension" graft. In these cases, S-E drainage was performed to simplify the procedure (Figure 3). In both groups, the majority of SPKTs were performed with ipsilateral placement of the kidney and pancreas to the right iliac vessels through a midline intraperitoneal approach in order to reduce operating time and to preserve the left iliac vessels for future transplantation.

Anti-coagulation

In selected SPKT recipients, 2000-3000 units of intravenous heparin (30-50 units/kg) were administered as a single dose during surgery prior to implantation of the pancreas and a heparin infusion was continued post-transplant (continuous infusion of 300 units/hour for 24 hours, then 400 units/hour for 24 hours, and then 500 units/hour until post-operative day 5) in the absence of bleeding.[18] Indications for intravenous heparin included preemptive SPKT, history of thrombophilia or clotting disorder in the recipient, small or diseased donor or recipient vessels, prolonged pancreas cold ischemia (>15 hours), extended donor criteria, or history of prior pancreas graft thrombosis.[11-13,19] Anti-platelet therapy, consisting of oral aspirin (81 mg/day), was administered to all patients.

Immunosuppression

Patients received depleting antibody induction with either alemtuzumab or alternate day rabbit anti-thymocyte globulin (1.5 mg/kg/dose, total 3-5 doses) in combination with tacrolimus, mycophenolate mofetil or mycophenolic acid, and tapered steroids or early steroid withdrawal.[12-15,20] The majority of SPKT recipients received single dose alemtuzumab induction (30 mg intravenous administered intra-operatively) in combination with tacrolimus (target 12 hour trough levels 8-10 ng/ml), full dose mycophenolate (720 mg bid), and either early steroid elimination or rapid prednisone taper (dose reduction to 5 mg/day by one month following SPKT).[15,20] All patients received anti-infective prophylaxis with peri-operative cefazolin for surgical site prophylaxis, fluconazole, valganciclovir, and trimethoprim-sulfamethoxazole. Anti-platelet therapy, consisting of oral aspirin (81 mg/day), was administered to all patients. Treatment of hypertension, hyperlipidemia, anemia, and other medical conditions was initiated as indicated, aiming to maintain the blood pressure <140/90 mmHg, fasting serum cholesterol <200 mg/dl, and hemoglobin >7-8 gm/dl.

Statistical Analysis

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. For categorical variables, the chi-square test was applied, and Fisher's exact test was used when data were sparse. Categorical data were summarized as proportions and percentages and continuous data were summarized as means and standard deviations. A two-tailed p-value of <0.05 was considered to be significant.

Results

From 7/1/03 through 7/1/19, we performed 231 SPKTs at our center and identified 27 that were performed with S-E drainage. These 27 patients were compared to 27 case-matched SPKT controls with P-E drainage. Reasons for S-E drainage were central obesity/thickened mesentery (n=10), unfavorable vascular anatomy/small SMV (n=11), and surgeon preference (n=6). The decision to abort portal venous drainage and switch to systemic venous drainage was made intra-operatively in all cases. Demographic and clinical features

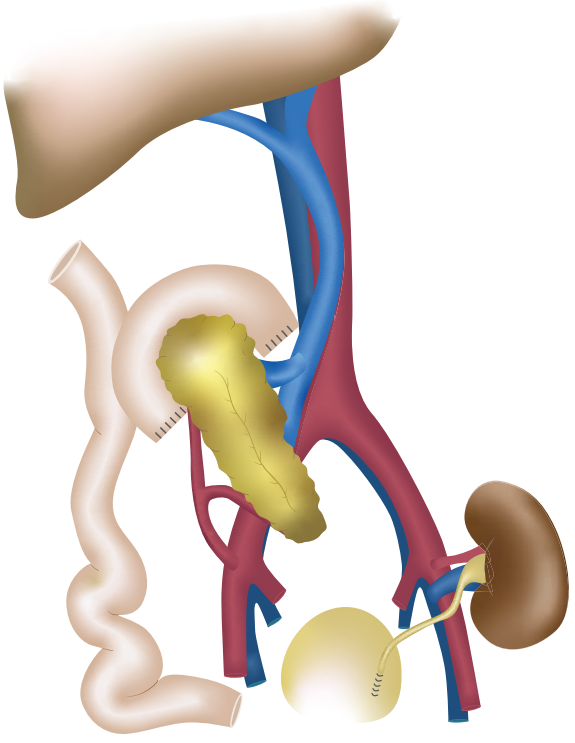


Figure 1. Technique of portal-enteric pancreas transplantation with donor portal vein anastomosis to recipient SMV followed by donor duodenal drainage to recipient small bowel.

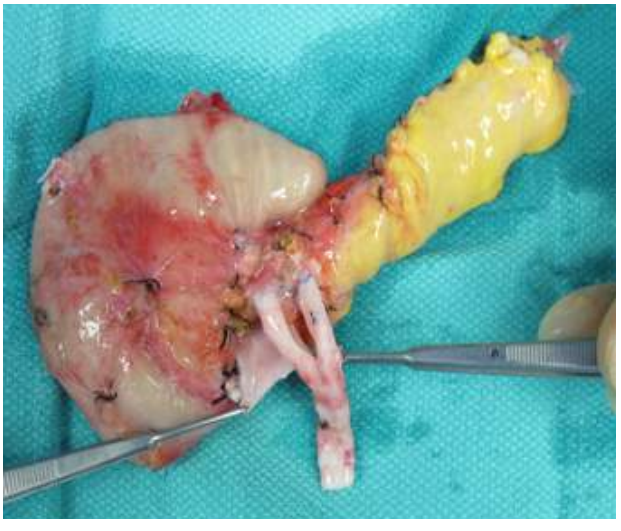


Figure 2. Back bench reconstruction of pancreas transplant with donor common iliac artery bifurcation "Y"-graft.

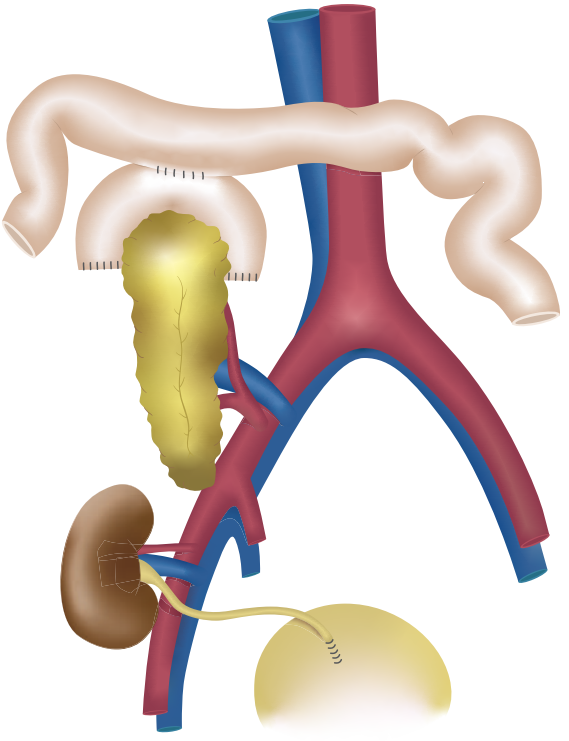


Figure 3. Technique of systemic-enteric pancreas transplantation with donor portal vein anastomosis to recipient right common iliac vein followed by donor duodenal drainage to recipient small bowel.

of the two groups according to surgical technique of SPKT are listed in Table 1. The two groups were well-matched for numerous donor, preservation, recipient, and immunological characteristics. The S-E drainage group was characterized by slightly more patients ≥ 80 kg (44% S-E versus 26% P-E), with C-peptide positive diabetes (30% S-E versus 18% P-E), and with diabetes onset at >20 years of age (41% S-E versus 26% P-E, all p=NS), suggesting a type 2 diabetes phenotype. Although the incidence of early pancreas thrombosis (3.7% S-E versus 0% P-E), early relaparotomy rates (30% S-E versus 22% P-E), and mean initial length of hospital stay (11 days S-E versus eight days P-E) were numerically higher in S-E

Table 1. Donor and Recipient Characteristics According to Surgical Technique

Characteristics	Systemic-enteric N = 27	Portal-enteric N = 27	p-value
Donor age (years)	23.3 ± 8.2	22.3 ± 8.6	NS
Donor weight (kg)	74.5 ± 15.2	67.5 ± 18.3	NS
Donor BMI (kg/m²)	24.3 ± 4.8	23.3 ± 4.2	NS
Pancreas cold ischemia (hours)	13.5 ± 4.6	13.7 ± 3.9	NS
HLA-mismatch	4.7 ± 1.0	4.5 ± 1.2	NS
PRA >10%	2 (7.4%)	4 (14.8%)	NS
CMV D+/R-	5 (18.5%)	8 (29.6%)	NS
Retransplant	1 (3.7%)	2 (7.4%)	NS
Kidney Donor Profile Index (%)	15.2 ± 17.5	19 ± 15.7	NS
Organ import	3 (11.1%)	7 (26%)	NS
Recipient age (years)	44.9 ± 10	45.1 ± 9	NS
Recipient gender: Male	19 (70.4%)	19 (70.4%)	NS
Recipient: African American	11 (40.7%)	11 (40.7%)	NS
Recipient weight (kg)	77.2 ± 10.3	71.8 ± 12.8	NS
Recipient weight ≥ 80 kg	12 (44.4%)	7 (26.0%)	NS
Recipient BMI (kg/m²)	25.6 ± 3.2	23.7 ± 3.1	NS
Hemodialysis Peritoneal Dialysis None (preemptive)	16 (59%) 5 (19%) 6 (22%)	15 (56%) 9 (33%) 3 (11%)	NS
Duration of dialysis (months)	32.5 ± 64	25 ± 27	NS
Duration of diabetes (years)	25.5 ± 10.8	28 ± 9.7	NS
Age of diabetes onset >20 years	11 (40.7%)	7 (26%)	NS
Pretransplant HbA1c level (%)	8.5 ± 1.5	8.75 ± 2.1	NS
Daily insulin dose (units)	41 ± 20	36 ± 14.5	NS
C-peptide positive pretransplant	8 (29.6%)	5 (18.5%)	NS
Time on waiting list (months)	8.1 ± 8	9.8 ± 10	NS

versus P-E SPKTs, none of these differences were significant (Table 2). Indications for early relaparotomy were unexplained fever, bleeding, or pancreatitis (three each); thrombosis (two); and one case each of enteric leak, partial small bowel obstruction, and ureteral revision. With a mean follow-up of five years in both groups, respective one- and five-year patient survival (100% and 96% S-E versus 100% and 100% P-E), kidney graft survival (100% and 93% S-E versus 100% and 85% P-E), and pancreas graft survival (96% and 96% S-E versus 100% and 85% P-E) rates were comparable (Table 2).

Discussion

With improvements in organ retrieval and preservation technology, refinements in diagnostic and therapeutic technologies, advances in clinical immunosuppression and antimicrobial prophylaxis, and increased experience in donor and recipient selection, success rates for PTx have steadily improved.[1,21] For primary, deceased donor SPKTs performed in the U.S. between 2014 and 2018, one-year patient, kidney, and pancreas graft survival (insulin-free) rates are 97%, 94%, and 89.6%, respectively, according to IPTR data.[1,22] The unadjusted five-year patient, kidney, and pancreas graft survival rates are 88%, 82%, and 76%, respectively. For patients with functioning grafts at one year, the conditional kidney and pancreas graft half-lives exceed 13 years following SPKT in the most recent era.[1,22,23] According to IPTR data, PTx outcomes are comparable regardless of surgical technique. In contrast to other treatments for diabetes, pancreas graft survival is largely defined as complete insulin independence concomitant with the absence of abnormal glycemic excursions.

The optimal surgical technique in PTx remains controversial. All surgical techniques of PTx share common ground with respect to organ donor selection and management, organ assessment and procurement, organ preservation, and back bench preparation of the pancreas.[9-18] Being familiar with multiple surgical techniques of PTx is helpful because the optimal technique may need to be individualized based on anatomic issues. Purported benefits of PTx with portal venous outflow include technical, metabolic, and immunologic "advantages".[2-12] However, these benefits have not been confirmed by either prospective cohort studies,

Table 2. Outcomes According to Surgical Technique

Outcomes	Systemic-enteric N = 27	Portal-enteric N = 27	p-value
Patient survival	24 (88.9%)	25 (92.6%)	NS
Death with functioning grafts	2 (7.4%)	1 (3.7%)	NS
Kidney graft survival	23 (85.2%)	18 (67%)	NS
Pancreas graft survival	22 (81.5%)	19 (70.4%)	NS
One year kidney graft survival	27 (100%)	27 (100%)	NS
One year pancreas graft survival	26 (96.3%)	27 (100%)	NS
Five year kidney graft survival	25 (92.6%)	23 (85.2%)	NS
Five year pancreas graft survival	26 (96.3%)	23 (85.2%)	NS
Follow-up (months)	58 ± 50	68 ± 57	NS
Early relaparotomy (<3 months)	8 (29.6%)	6 (22.2%)	NS
Early thrombosis (<1 month)	1 (3.7%)	0	NS
Days of initial hospital stay	10.8 ± 6.8	8 ± 2.9	NS

randomized controlled trials, or large analyses based on registry databases.[1-12,24] Alternatively, there are likewise no well controlled studies to suggest any major disadvantages or unique risks associated with portal venous outflow other than technical considerations. In this study, we chose to focus on technical considerations and analyzed our experience with S-E drainage as a "rescue" or secondary technique of PTx when P-E drainage was not deemed appropriate.

An advantage of portal venous outflow is that the PTx is primarily a mid-abdominal rather than a pelvic procedure, which is beneficial in patients who have had previous pelvic transplants or other lower abdominal procedures. However, a potential disadvantage of the mid-abdominal or anterior approach to the SMV is that the arterial anastomosis may be difficult and require a long interposition "Y" graft (especially in patients with central, omental, or mesenteric obesity or in patients with severe proximal iliac vascular disease). In addition, the SMV may be small, deep, or difficult to access in patients with this type of body habitus. Consequently, it is not surprising that our S-E group was characterized by more patients with either a larger body habitus or type 2 diabetes phenotype (C-peptide positive, higher body weight, older age of onset of diabetes) even though we controlled for recipient age, gender, and race. In addition to the lateral or retroperitoneal approach introduced by Boggi[3], a number of other variations of P-E drainage have evolved over the years to minimize technical challenges including the use of diverting Roux-en-Y limbs for the enteric anastomosis (either with or without a venting jejunostomy), duodeno-gastric drainage, and, more recently, duodeno-duodenal drainage.[10,11,25-32]

Based on this experience, we conclude that comparable overall technical results can be achieved in SPKT with either technique when S-E drainage is performed in lieu of P-E drainage. Strengths of this study are the case-control design and standardized management algorithms applied to all patients. However, limitations are the retrospective nature with relatively small sample sizes and nonrandomized design. Although numerous variations exist in the basic surgical techniques of PTx and nuances continue to be described, we believe that the most appropriate technique to be performed should be determined by donor and recipient anatomy as well as the comfort level and experience of the surgical team with each technique.

Disclosures

No financial support given. Authors report no conflits of interest

References

1. Gruessner AC, Gruessner RWG. Pancreas Transplantation for Patients with Type 1 and Type 2 Diabetes Mellitus in the US – A Registry Report. Gastroenterol Clin N Am 2018; 47: 417-441. doi: 10.1016/j.gtc.2018.01.009.
2. Shokouh-Amiri MH, Gaber AO, Gaber LW, Jensen SL, Britt LG. Pancreas Transplantation with Portal Venous and Exocrine Enteric Drainage. Transplant Proc 1992; 24 (3): 776-777.
3. Boggi U, Vistoli F, Signori S, et al. A Technique for Retroperitoneal Pancreas Transplantation with Portal-Enteric Drainage. Transplantation 2005; 79: 1137-1142.
4. Newell KA, Bruce DS, Cronin DC, et al. Comparison of Pancreas Transplantation with Portal Venous and Enteric Exocrine Drainage to the Standard Technique Utilizing Bladder Drainage of Exocrine Secretions. Transplantation 1996; 62: 1353-1356.
5. Petruzzo P, Da Silva M, Feitosa LC, et al. Simultaneous Pancreas-Kidney Transplantation: Portal versus Systemic Venous Drainage of the Pancreas Allografts. Clin Transplant 2000; 14: 287-291.
6. Cattral MS, Bigam DL, Hemming AW, et al. Portal Venous and Enteric Exocrine Drainage versus Systemic Venous and Bladder Exocrine Drainage of Pancreas Grafts: Clinical Outcome of 40 Consecutive Transplant Recipients. Ann Surg 2000; 232: 688-695.
7. Stratta RJ, Shokouh-Amiri MH, Egidi MF, et al. A Prospective Comparison of Simultaneous Kidney-Pancreas Transplantation with Systemic-Enteric versus Portal-Enteric Drainage. Ann Surg 2001; 233: 740-751.
8. Philosophe B, Farney AC, Schweitzer EJ, et al. Superiority of Portal Venous Drainage over Systemic Venous Drainage in Pancreas Transplantation: A Retrospective Study. Ann Surg 2001; 234: 689-696.
9. Boggi U, Amorese G, Marchetti P. Surgical techniques for pancreas transplantation. Curr Opin Organ Transplant 2010; 15: 102-11. PMID: 20010103
10. El Hennawy H, Stratta RJ, Smith F. Exocrine Drainage in Vascularized Pancreas Transplantation in the New Millennium. World J Transplant 2016; 6 (2): 255-71. doi: 10.5500/wjt.v6.i2.255.
11. Rogers J, Farney AC, Orlando G, Farooq U, Al-Shraideh Y, Stratta RJ. Pancreas transplantation with portal venous drainage with an emphasis on technical aspects. Clin Transplant 2014; 28: 16-26. doi: 10.1111/ctr.12275.
12. Rogers J, Farney AC, Al-Geizawi S, et al. Pancreas transplantation: Lessons Learned from a Decade of Experience at Wake Forest Baptist Medical Center. Rev Diabet Stud 2011; 8: 17-27.
13. Rogers J, Farney AC, Orlando G, et al. Pancreas transplantation: The Wake Forest experience in the new millennium. World J Diabetes 2014; 15; 5(6): 951-61. doi: 10.4239/wjd.v5.i6.951.
14. Stratta RJ, Rogers J, Farney AC, et al. Pancreas transplantation in C-peptide positive patients: Does "type" of diabetes really matter? J Am Coll Surg 2015; 220: 716-27. doi: 10.1016/j.jamcollsurg.2014.12.020.
15. Stratta RJ, Farney AC, Rogers J, Orlando G. Immunosuppression for Pancreas Transplantation with an Emphasis on Antibody Induction Strategies: Review and Perspective. Exp Rev Clin Immunol 2014; 10 (1): 117-132.
16. Orlando G, Stratta RJ, Light J. Pancreas Transplantation for Type 2 Diabetes Mellitus. Curr Opin Organ Transplant; 16 (1): 110-115.
17. Fridell J, Rogers J, Stratta RJ. The Pancreas Allograft Donor: Current Status, Controversies, and Challenges for the Future. Clin Transplantation 2010; 24: 433-449.
18. Fridell JA, Powelson JA, Sanders CE, et al. Preparation of the Pancreas

Allograft for Transplantation. Clin Transplant 2011; 25: E103-E112.
19. Farney AC, Rogers J, Stratta RJ. Pancreas Graft Thrombosis: Causes, Prevention, Diagnosis, and Intervention. Curr Opin in Organ Transplant 2012; 17 (1): 87-92.
20. Farney AC, Doares W, Rogers J, Singh R, Hartmann E, Hart L, et al. A Randomized Trial of Alemtuzumab versus Antithymocyte Globulin Induction in Renal and Pancreas Transplantation. Transplantation 2009; 88 (6): 810-819.
21. Kandaswamy R, Stock PG, Gustafson SK, Skeans MA, Curry MA, et al. OPTN/SRTR 2016 Annual Data Report: Pancreas. Am J Transplant 2018; 18 (suppl 1): 114-171. doi: 10.1111/ajt.14558
22. Updated International Pancreas Transplant Registry (IPTR) data, Angelika Gruessner (personal communication); United Network for Organ Sharing (UNOS) data available at: https://optn.transplant.hrsa.gov/data, Accessed on August 1, 2019
23. Gruessner AC, Gruessner RWG: Long-term Outcome after Pancreas Transplantation – A Registry Analysis. Curr Opin Organ Transplant 2016; 21 (4): 377-85. doi: 10.1097/MOT.0000000000000331.
24. Bazerbachi F, Selzner M, Marques MA, et al. Portal Venous Versus Systemic Venous Drainage of Pancreas Grafts: Impact on Long-Term Results. Am J Transplant 2012; 12: 226-232.
25. Zibari GB, Aultman DF, Abreo KD, et al. Roux-en-y Venting Jejunostomy in Pancreatic Transplantation: A Novel Approach to Monitor Rejection and Prevent Anastomotic Leak. Clin Transplant 2000; 14: 380-385.
26. Losanoff JE, Harland RC, Thistlethwaite JR, et al. Omega Jejunoduodenal Anastomosis for Pancreas Transplant. J Am Coll Surg 2006; 202: 1021-1024.
27. De Roover A, Detry O, Coimbra C, Squifflet JP, Honore P, Meurisse M. Exocrine Pancreas Graft Drainage in Recipient Duodenum through Side-to-Side Duodeno-Duodenostomy. Transplant Int 2008; 21: 707.
28. Hummel R, Langer M, Wolters HH, Senninger N, Brockmann JG. Exocrine Drainage into the Duodenum: A Novel Technique for Pancreas Transplantation. Transplant Int 2008; 21: 178-181.
29. Schenker P, Flecken M, Vonend O, Wunsch A, Traska T, Viebahn R. En Bloc Retroperitoneal Pancreas-Kidney Transplantation with Duodenoduodenostomy Using Pediatric Organs. Transplant Proc 2009; 41: 2643-2645.
30. Shokouh-Amiri MH, Zakhary JM, Zibari GB. A Novel Technique of Portal-Endocrine and Gastric-Exocrine Drainage in Pancreatic Transplantation. J Am Coll Surg 2011; 212: 730-739.
31. Gunasekaran G, Wee A, Rabets J, Winans C, Krishnamurthi V. Duodenoduodenostomy in Pancreas Transplantation. Clin Transplant 2012; 26: 550-557.
32. Linhares MM, Beron RJ, Gonzales AM, et al. Duodenum-Stomach Anastomosis: A New Technique for Exocrine Drainage in Pancreas Transplantation. J Gastroint Surg 2012; 16: 1072-1075.
33. Perosa M, Noujaim H, Ianhez LE, et al. Experience with 53 Portal-Duodenal Drained Solitary Pancreas Transplants. Clin Transplant 2014; 28 (2): 198-204.
34. Walter M, Jazra M, Kykalos S, et al. 125 Cases of duodenoduodenostomy in Pancreas Transplantation: A Single-Centre Experience of an Alternative Enteric Drainage. Transplant Int 2014; 27: 805-815.

Original Science

Openness as a Predictor for Cognitive Functioning

Gina Giorgio, B.S.[1] and Kimberly Wear, Ph.D.[2]

Abstract

Human behavior is often associated with personality, but there are emergent findings suggesting that certain personality traits are correlated with levels of cognitive functioning. Researchers have discovered that being open can serve as a buffer against cognitive decline, because people who are more open may engage in more cognitively demanding thinking and tasks. Additional studies have found that openness may be positively correlated with cognitive flexibility and verbal, fluid, and crystallized intelligence. The current study examined the correlation between openness, cognitive flexibility, and fluid intelligence in 66 undergraduate college students. Participants completed a self-reported measure of openness and cognitive flexibility and Raven's Standard Progressive Matrices. As predicted, the results indicated a positive correlation between fluid intelligence and cognitive flexibility ($r=0.29$, $p=0.02$, $n=64$) and openness and cognitive flexibility ($r=0.34$, $p=0.01$, $n=63$). A trend toward a positive correlation was found between openness and fluid intelligence ($r=0.22$, $p=0.07$, $n=65$). Results may suggest that people with more open personalities may possess the ability for more advanced, abstract, and adaptable thinking.

[1]Department of Internal Medicine, Section of Molecular Medicine, Wake Forest School of Medicine, Winston-Salem, NC

[2]Department of Psychology, High Point University, High Point, NC

Address Correspondence To:
Gina Giorgio, B.S.
Department of Internal Medicine
Section of Molecular Medicine
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157
E-mail: ggiorgio@wakehealth.edu

Introduction

Personality is a dynamic phenomenon and plays an interdisciplinary role in being human, which contributes to our behaviors, thoughts, and emotional patterns.[1] There is an increasing amount of research suggesting that certain personality traits, such as openness (commonly referred to as "openness to experience"), are related to more advanced cognitive processes.[2] Openness is one of the Big Five personality traits and is characterized as a receptivity to new ideas and new experiences.[3] The Big Five Personality Model proposes that personality can be evaluated across five major dimensions: Openness, Conscientiousness, Neuroticism, Agreeableness, and Extraversion.[2] Open people often have an intrinsic desire for knowledge and are capable of assimilating novel ideas.[3] Studies have found open personalities to be correlated with cognitive aptitude and a receptivity to intellectual involvement.[3] As such, openness may represent a behavioral pathway where cognitive engagement is associated with a lower risk for general cognitive decline.[4] In order to expand upon these findings, this study investigated the relationships between openness, cognitive flexibility, and fluid intelligence in undergraduate college students.

A substantial body of research has found openness to be positively associated with IQ test performance, leading some researchers to propose that it signifies the expression of intelligence in personality.[2] However, solely assessing intelligence is not sufficient for analyzing cognitive capabilities. It is important to consider a third variable: cognitive flexibility. Cognitive flexibility is the ability to selectively switch one's thoughts and behaviors in response to changing environments and ideas.[5] Increased cognitive flexibility is linked to favorable qualities, such as better reading abilities during childhood, higher resilience to stress and greater levels of creativity in adulthood, and enhanced quality of life in older adulthood.[5] In this regard, Deyoung et al. theorized that openness signifies a type of motivated cognitive flexibility.[6]

Given the interest in understanding the links between personality and cognition, studies have begun examining the relationship between open personalities and various types of intelligence in young adults. Multiple studies have examined the correlations between openness and/or verbal, fluid, and crystallized intelligence in young adults.[2,6,7] Fluid intelligence is the ability to reason and solve problems in novel situations, without relying on previously acquired knowledge and skills.[10] This is the opposite of crystallized intelligence, which is the ability to use existing knowledge to solve a current issue.[10] Intelligence was either examined with the Wechsler Adult Intelligence Scale–III or Raven's Advanced Progressive Matrices, which are both well-established measures of intelligence. Deyoung et al. (2005) observed that fluid and crystallized intelligence were positively related to openness.[6] However, Deyoung et al. (2014) found a stronger correlation with verbal intelligence and Schretlen et al. found a stronger relationship with verbal/crystallized intelligence.[2,7] Due to the variability in findings, it may be advantageous to consider a different method for measuring cognitive aptitude.

Although cognitive flexibility is a unique aspect of cognition, there is a limited amount of research that investigates the relationship between openness, cognitive flexibility, and fluid intelligence in young adults. Often, research in this field has analyzed adult and older adult populations and has focused on general intelligence, such as the longitudinal study by Ziegler et al.[9] Researchers assessed intelligence in 516 participants from ages 70-103 to see if people with open personalities experience less cognitive decline. The results indicated that trait openness may be a buffer against cognitive decline, because the participants that scored higher on openness performed better on the intelligence tests as they aged. Although cognitive decline and dementia are typically associated with individuals over the age of 65, Salthouse has stated that some features of age-related cognitive impairment can begin in healthy educated adults that are in their 20's and 30's.[8] This may indicate the importance of testing cognitive capabilities in younger populations.

In addition to these findings in older adults and in the general younger adult population, similar findings have been reported in college students. College students are a unique population since they engage in high amounts of social interaction, new experiences, and cognitively demanding tasks. Lin utilized undergraduate participants in order to test how their openness to change and cognitive flexibility impacted their academic performance.[11] Along with gathering data on class grades, the researchers tested variables using the Cognitive Flexibility Scale and the Openness to Change Inventory. The results indicated a positive correlation between cognitive flexibility and openness to change and between cognitive flexibility and academic performance.[11] These same findings were discovered by Murdock et al. who found that openness in college students (aged 18-29), was positively associated with cognitive flexibility, among other executive function capabilities.[12]

Associations between intelligence and cognitive flexibility have also received attention. Colzato et al. and Shi et al. both utilized Raven's Standard Progressive Matrices to explore the correlation between fluid intelligence and flexible thinking.[13,14] Researchers concluded that the participants with higher intelligence possessed a higher degree of flexible thinking.[13,14] Even further, Shi et al. determined that openness had a moderating effect on these factors when intelligence was average and below average.[14] In sum, evidence suggests that intelligence and cognitive flexibility are positively related and, at times, may only be related when openness is involved.

Although most studies have focused on existing relationships between intelligence and cognitive flexibility, Brem et al. expanded on this relationship by training participants' executive functions.[15] Researchers reported that the participants who underwent cognitive training of their executive functions, namely cognitive flexibility, also scored

higher on fluid intelligence tests. These findings suggest that cognitive flexibility may be improved with experience and practice.

Correlations between openness and cognitive functioning are well documented, but we are not aware of additional studies that directly compared these three variables. Given the evidence outlined above, the purpose of this study was to determine if there are positive relationships between openness, cognitive flexibility, and fluid intelligence in undergraduate college students. Three hypotheses were tested: (1) that openness will be positively correlated with cognitive flexibility, (2) that openness will be positively correlated with fluid intelligence, and (3) that fluid intelligence will be positively correlated with cognitive flexibility. Hypotheses were tested by measuring the variables via self-reported questionnaires and Raven's Standard Progressive Matrices intelligence test, then by assessing the data. The proposed study predicted that the personality facets associated with openness may be positively associated with higher levels of cognitive functioning through a tendency to ponder ideas, think creatively, and actively engage in or pursue cognitively stimulating activities.

Methods

Participants

Sixty-six undergraduate students enrolled in Introduction to Psychology at High Point University were recruited during research study sessions (Table 1). Participants included 55 women and 11 men ranging in age from 18-23 (mean (M)=10.20, standard deviation (SD)=1.17). Among participants, 83.4% identified as Caucasian, 6.1% as Hispanic, 4.5% as African American, 3% as Asian, 1.5% as mixed heritage, and 1.5% as other. The mean overall GPA was 3.24 (SD=0.50) and the mean major GPA was 3.35 (SD=0.44). All of the participants received credit for Introduction to Psychology.

Materials

Participants received a packet to report their demographic information, along with two questionnaires and Raven's Standard Progressive Matrices. Openness was measured with the Openness to Experience Scale, which is a reliable and valid measure for assessing openness[16]. This 90-item scale includes questions that are divided into six subscales: Curiosity, Aesthetics, Tolerance, Intellectual Efficiency, Ingenuity, and Depth. All items were rated using a 4-point Likert-type scale (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree). Some example statements are "I don't like trying new things and would rather stick with what I know", "I like to hear different people's views on political issues", and "I like coming up with imaginative plans". The higher the score the more open someone is.

Cognitive flexibility was assessed with the Cognitive Flexibility Inventory-Revised, which is a valid and consistent measure for evaluating cognitive flexibility[17]. This measure is comprised of 14 pairs of statements (each on a 1 to 6 scale; ranging from "Strongly agree with Statement A" to "Strongly agree with Statement B"). Examples include "I enjoy encountering difficult, conflicting, and disorderly concepts and find them challenging" or "I prefer simplicity, consistency, and orderliness. Whenever possible, I prefer not to encounter complex problems in school (although I deal with complexity when I have to)". Higher scores on this inventory indicate more complex epistemic beliefs.

Table 1. Descriptive statistics for gender, race, and age of sample

Gender	Frequency	Percent
Male	11	16.7
Female	55	83.3
Total	66	100.0
Race	**Frequency**	**Percent**
African American	3	4.5
Asian	2	3.0
Caucasian/White	55	83.3
Hispanic	4	6.1
Mixed Heritage	1	1.5
Other	1	1.5
Total	66	100.0

Table 2. Average scores and standard deviations for Raven's Standard Progressive Matrices, Openness to Experience Scale, and Cognitive Flexibility Inventory- Revised

	Raven's	Openness	Cognitive Flexibility
N	66	65	64
Mean	39.1818	254.0000	48.2199
SD	8.18612	30.88891	6.47783

Fluid intelligence was evaluated with Raven's Standard Progressive Matrices, which is a well-established measure for non-verbal fluid intelligence[18]. This scale includes 60 puzzles where participants find the 'missing piece' in an increasingly complex visual display of abstract shapes. The score was calculated by how many problems the participants got correct out of 60. For 19-year-olds, a score between 55-60 indicates 'intellectually superior' intelligence. An 'above average' intelligence score is between 49-54 correct, 'average' intelligence is between 38-48, and 'below average' intelligence is a score of 37 or less.

Procedure

Participants provided informed consent and were given the packet containing demographic questions, two self-reported questionnaires, and Raven's Standard Progressive Matrices. Participants could stop at any time. They were thanked, debriefed, and given an opportunity to ask questions.

Analysis

Hypothesis testing was performed using Pearson's correlation coefficient and separate two-tailed t-tests without correction of alpha for multiple comparisons. Statistical significance was established at alpha <0.05. Effect size and observed power are reported for each correlation. Statistical analyses were conducted using IBM SPSS Statistics 25.

Results

The average scores for each assessment are listed in Table 2. Participants mainly scored in the average intelligence range on Raven's Standard Progressive Matrices (M=39.18, SD=8.19). However, individual scores on this test ranged from 16/60 correct to 58/60 correct. The mean openness to experience score was 254 (SD=30.88) out of 360 and the mean cognitive flexibility score was 48.21 (SD=6.48) out of 84. These frequencies indicate a sample that is of average intelligence, slightly above average in cognitive flexibility, and above average in openness to experience.

Pearson product-moment correlation coefficients were calculated to evaluate each hypothesized relationship (Table 3). A significant direct correlation was observed between openness and cognitive flexibility (r=0.34, p=0.01, n=63; Figure 1). The effect size was 0.12. The power of the test was 0.55. A significant direct correlation was observed between cognitive flexibility and intelligence (r=0.29, p=0.02, n=64; Figure 2). The effect size was 0.08. The power was 0.56. There was a trend towards a positive correlation between openness and intelligence (r=0.22, p=0.07, n=65). The effect size was less than 0.05. The power of the test was 0.39.

Table 3. Pearson Correlations for Openness, Cognitive Flexibility, and Fluid Intelligence

Correlations		Raven's	Openness	Cognitive Flexibility
Raven's	Pearson Correlation	1	.223	.294*
	Sig. (2-tailed)		.074	.019
	N	66	65	64
Openness	Pearson Correlation	.223	1	.337**
	Sig. (2-tailed)	.074		.007
	N	65	65	63
Cognitive Flexibility	Pearson Correlation	.294*	.337**	1
	Sig. (2-tailed)	.019	.007	
	N	64	63	64

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

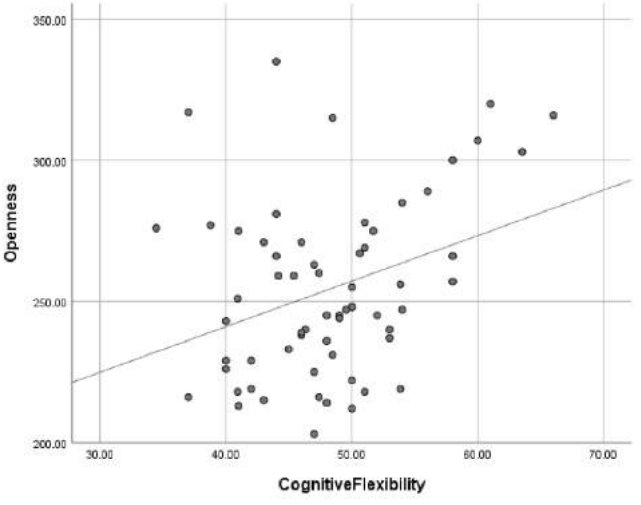


Figure 1. Individual Openness and Cognitive Flexibility scores

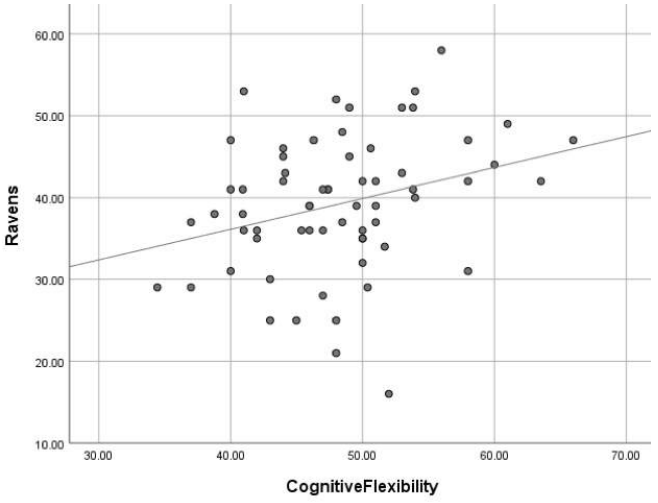


Figure 2. Individual Raven's Standard Progressive Matrices and Cognitive Flexibility scores

Discussion

The present study examined the connections between openness and elements of cognition: cognitive flexibility and fluid intelligence. Positive correlations found between openness and cognitive flexibility as well as fluid intelligence and cognitive flexibility were consistent with previous literature.[2,7,11,12] This provides further evidence for Murdock's conclusions that there may be an underlying cognitive characteristic linked with openness.[12] Furthermore, results suggested that openness is more closely associated with cognitive flexibility than intelligence. This may indicate that people who are more open may be more inclined to have flexible mental processes, but not necessarily better reasoning. Contrary to our hypothesis, there was a trend toward a positive correlation for openness and intelligence, rather than a significant positive correlation. This may reflect the findings of Schretlen et al. and Deyoung et al., who found openness to be more positively correlated with verbal/crystallized intelligence, than with spatial/fluid intelligence.[2,7]

A potential implication of these results is that openness reflects a propensity towards cognitive activities that ensure a greater cognitive reserve and reduced risk of cognitive decline and dementia later in life. If people continuously engage in more cognitively demanding tasks and/or continually seek new experiences and ideas, the cognitive aging process may be delayed. Approximately 5-8% of the world's older adult population has been diagnosed with dementia.[19] Dementia is not an inevitable consequence of aging. Rather, it is a result of lifestyle, biology, environment, and other factors.[20] Referring back to the Salthouse study, if cases of cognitive degeneration occur in early adulthood, then it would be advisable to make healthy lifestyle adjustments whenever possible.[8] Changes should promote optimal mental functioning by remaining receptive to cognitively demanding thinking and tasks.

The current study had some limitations that should be addressed in future work. A small sample of college students that are comprised mostly of the same age, race, and gender are not representative of the entire population. Participants were chosen only out of those enrolled in Introduction to Psychology, which narrows the participant pool. Lastly, Raven's Standard Progressive Matrices was not timed per participant, which may have created variability in test results.

Despite these limitations, the current investigation extended existing work between openness and intelligence by considering cognitive flexibility as a third variable. Future exploration should include additional measures of openness, cognitive flexibility, and intelligence, to see if results are consistent with other scales, as well as a larger and more diverse sample that can be better generalized to the larger population. Similar to the Brem et al. study [15], future research could be conducted utilizing cognitive enhancement tasks, in order to investigate its effects on the cognitive aging process.

Disclosures

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

References

1. Wilt, J., & Revelle, W. (2015). Affect, Behaviour, Cognition and Desire in the Big Five: An Analysis of Item Content and Structure. European Journal of Personality, 29(4), 478–497. doi: 10.1002/per.2002
2. Schretlen, D. J., Hulst, E. V., Pearlson, G. D., & Gordon, B. (2010). A neuropsychological study of personality: Trait openness in relation to intelligence, fluency, and executive functioning. Journal of Clinical and Experimental Neuropsychology, 32(10), 1068-1073. doi:10.1080/13803391003689770
3. Sharp, E. S., Reynolds, C. A., Pedersen, N. L., & Gatz, M. (2010). Cognitive engagement and cognitive aging: Is openness protective? Psychology and Aging, 25(1), 60-73. http://dx.doi.org/10.1037/a0018748 Reynolds, Pedersen, and Gatz, 2010)
4. Hertzog, C., Kramer, A. F., Wilson, R. S., & Lindenberger, U. (2008). Enrichment Effects on Adult Cognitive Development. Psychological Science in the Public Interest, 9(1), 1–65. doi: 10.1111/j.1539-6053.2009.01034.x
5. Dajani, D. R., & Uddin, L. Q. (2015). Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience. Trends in Neurosciences, 38(9), 571–578. doi: 10.1016/j.tins.2015.07.003

6. Deyoung, C. G., Peterson, J. B., & Higgins, D. M. (2005). Sources of Openness/Intellect: Cognitive and Neuropsychological Correlates of the Fifth Factor of Personality. Journal of Personality, 73(4), 825-858. doi:10.1111/j.1467-6494.2005.00330.x
7. Deyoung, C. G., Quilty, L. C., Peterson, J. B., & Gray, J. R. (2014). Openness to Experience, Intellect, and Cognitive Ability. Journal of Personality Assessment, 96(1), 46-52. doi:10.1080/00223891.2013.806327
8. Salthouse, T. A. (2009). When does age-related cognitive decline begin? Neurobiology of Aging, 30(4), 507–514. doi: 10.1016/j.neurobiolaging.2008.09.023
9. Ziegler, M., Cengia, A., Mussel, P., & Gerstorf, D. (2015). Openness as a buffer against cognitive decline: The Openness-Fluid-Crystallized-Intelligence (OFCI) model applied to late adulthood. Psychology and Aging, 30(3), 573-588. doi:10.1037/a0039493
10. Hülür, G., Gasimova, F., Robitzsch, A., & Wilhelm, O. (2017). Change in Fluid and Crystallized Intelligence and Student Achievement: The Role of Intellectual Engagement. Child Development, 89(4), 1074–1087. doi: 10.1111/cdev.12791
11. Lin, Y. (2014). The effects of cognitive flexibility and openness to change on college students' academic performance. Dissertation Abstracts International, 74(12).
12. Murdock, K. W., Oddi, K. B., & Bridgett, D. J. (2013). Cognitive Correlates of Personality: Links between executive functioning and the big five personality traits. Journal of Individual Differences, 34(2), 97-104. doi:10.1027/1614-0001/a000104
13. Colzato, L. S., Wouwe, N. C., Lavender, T. J., & Hommel, B. (2006). Intelligence and cognitive flexibility: Fluid intelligence correlates with feature "unbinding" across perception and action. Psychonomic Bulletin & Review, 13(6), 1043-1048. doi:10.3758/bf03213923
14. Shi, B., Wang, L., Yang, J., Zhang, M., & Xu, L. (2017). Relationship between Divergent Thinking and Intelligence: An Empirical Study of the Threshold Hypothesis with Chinese Children. Frontiers in Psychology, 8. doi:10.3389/fpsyg.2017.00254
15. Brem, A., Almquist, J. N., Mansfield, K., Plessow, F., Sella, F., Santarnecchi, E., & Myers, E. (2018). Modulating fluid intelligence performance through combined cognitive training and brain stimulation. Neuropsychologia, 118, 107-114. doi:10.1016/j.neuropsychologia.2018.04.008
16. Woo, S. E., Chernyshenko, O. S., Longley, A., Zhang, Z.-X., Chiu, C.-Y., & Stark, S. E. (2014). Openness to Experience Scale [Database record]. Retrieved from PsycTESTS. doi:http://dx.doi.org/10.1037/t60625-000
17. Zhang Ulyshen, T., Koehler, M. J., & Gao, F. (2015). Cognitive Flexibility Inventory—Revised [Database record]. Retrieved from PsycTESTS. doi: http://dx.doi.org/10.1037/t54991-000
18. Raven, J. C., (1938). Raven's Progressive Matrices and Vocabulary Scales. New York: Psychological Corporation.
19. Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S. G., Huntley, J., Ames, D., et al. (2017). Dementia prevention, intervention, and care. The Lancet, 390(10113), 2673–2734. doi: 10.1016/s0140-6736(17)31363-6
20. Maiese, K. (2019). Impacting dementia and cognitive loss with innovative strategies: mechanistic target of rapamycin, clock genes, circular non-coding ribonucleic acids, and Rho/Rock. Neural Regeneration Research, 14(5), 773. doi: 10.4103/1673-5374.249224

Case Reports

Severe Coagulopathy Associated with Synthetic Cannabinoid Use: A Case Report

Ronak V. Shah, M.D.[1], Charles Randall Clinch, D.O.[1], Keli Lynne Beck, M.D.[1]

Abstract

Background: The Center for Disease Control and Prevention has declared a national health advisory due to the emerging association of brodifacoum with numerous case reports of life-threatening coagulopathy in synthetic cannabinoid users since March 2018. The link between synthetic cannabinoids and brodifacoum remains unclear.

Methods: This case report describes the presentation, workup, and treatment of an individual who experienced severe hemorrhage due to brodifacoum poisoning secondary to synthetic cannabinoid use. We obtained permission to use his medical records for this report.

Results: The male patient was found to have a deficiency in vitamin K-dependent clotting factors and fifteen times the reporting limit of brodifacoum in his blood. He was started on high-dose vitamin K therapy, which gradually resolved his hemorrhage and improved his coagulation profile. He may require high-dose vitamin K for up to six months.

Limitations: In North Carolina, serum testing for brodifacoum is performed at a designated poison center and can take up to four weeks to result. This creates a delay in confirming the diagnosis.

Conclusion: Clinicians should suspect brodifacoum poisoning in synthetic cannabinoid users that present with bleeding and coagulopathy. This case serves to emphasize the importance of seeking a thorough social history in patients and promptly obtaining coagulation profiles to initiate high-dose vitamin K therapy, if indicated, and treat brodifacoum poisoning.

[1] Department of Family and Community Medicine, Wake Forest School of Medicine, Winston Salem, NC

Address Correspondence To:
Ronak V. Shah, M.D.
Department of Family and Community Medicine
Wake Forest School of Medicine
1920 W. 1st Street
Winston Salem, NC 27104
rvshah@wakehealth.edu

Introduction

Adverse effects of synthetic cannabinoids have been reported globally and in every U.S. state. These compounds are created in laboratories, targeting cannabinoid receptors to produce a "high" similar to that which users experience from marijuana. Unfortunately, these compounds are commonly linked to neurologic, cardiac, gastrointestinal, and psychiatric effects.[1] Since early 2018, synthetic cannabinoids have been linked to life-threating hemorrhage by way of a compound called brodifacoum. Brodifacoum is a highly lipophilic agent that became commercially available in 1975 as a novel poison against warfarin-resistant rodents. It is known as a "super-

warfarin" drug due to its longer half-life and greater potency than warfarin. The primary mechanism of action is by inhibiting vitamin K epoxide reductase, an enzyme required to reduce vitamin K to its active form. Several case reports as early as 1993 have linked toxic brodifacoum ingestion with hemorrhage and coagulopathy in humans.[2] Diagnoses have been confirmed by detecting elevated serum brodifacoum levels and high-dose vitamin K replacement has been the primary therapy.

Case Report

Our patient is a 57-year-old male with a past medical history of hypertension, chronic hepatitis C, and prior alcohol abuse who presented to the emergency department with gross hematuria. He reported one day of progressively worsening hematuria without associated dysuria, incontinence, fevers, or chills. He also reported having mild, intermittent, left-sided flank pain for the last three months, which was progressively worsening over the last few days. He denied recent alcohol or tobacco use.

The patient was afebrile, normotensive, had a pulse of 88 beats per minute, and a respiratory rate of 18 breaths per minute. On physical exam, he appeared well, had no ecchymoses or petechiae on the skin, and his abdominal exam was benign. He had mild left-sided costovertebral angle tenderness, but no other abnormalities. Genitourinary exam was normal and digital rectal exam revealed a small, firm prostate with no nodularity or tenderness.

Investigations

Workup in the emergency department consisted of a complete blood count (CBC) that showed a mild leukocytosis to 10,800 cells/μL, with absolute neutrophil count of 8,500 cells/μL, platelet count of 201,000 cells/μL, and hemoglobin of 13.0 g/dL. Basic metabolic panel showed a sodium of 131 mmol/L, BUN of 36 mg/dL, and creatinine of 3.09 mg/dL (baseline 1.0 mg/dL). Urinalysis was positive for nitrites, leukocyte esterase, large blood, glucose, ketones, and protein. Computerized tomographic (CT) scan of his abdomen/pelvis without contrast demonstrated bilateral hydronephrosis, as well as bilateral renal enlargement and likely parenchymal edema. There was extensive perinephric stranding of the ureters. Two 3mm calcifications were identified over the expected course of the bilateral ureters, which were not present on a prior exam from March 2015, but were deemed unlikely to account for the degree of hydronephrosis.

Treatment

The patient was given 1g of ceftriaxone intravenously (IV), one liter of normal saline IV, and subsequently admitted to the family medicine service, where urology was consulted. Urology placed bilateral ureteral stents and noted that the patient's efflux of dark red urine before and after stenting seemed to suggest alternate pathology, perhaps glomerular, as it seemed out-of-proportion to that typically seen with ureteral stones. Retrograde pyelogram confirmed that the patient's hydronephrosis was insignificant.

The next morning, he developed oral bleeding that was believed to be from trauma secondary to intubation during the ureteral stenting procedure. Otolaryngology (ENT) was consulted, where a transnasal fiberoptic laryngoscopy (TNFL) was performed and showed an actively bleeding right buccal ulceration and vocal fold ecchymosis. The patient was placed on strict voice rest and was transferred to the intensive care unit for airway protection. A coagulation panel showed prothrombin time (PT) >100 seconds, partial thromboplastin time (PTT) >122 seconds, and international normalized ratio (INR) too high to calculate. Repeat CBCs over the day showed a drop in the patient's hemoglobin from 13.0 to 9.8, then 7.1, and he required transfusion of 2 units of packed red blood cells. The patient's platelets remained within normal limits. Extrinsic and intrinsic factor panels showed significant reductions in factors II, VII, IX, and X, suggesting a vitamin K deficiency or antagonistic process.

Hematology/Oncology was consulted and recommended supplementing vitamin K and transfusing fresh plasma. Over a one week period, vitamin K was started at 5mg orally daily, but given persistent elevations in his PT/PTT/INR, the dose was titrated up to 25mg every six hours until his coagulation studies normalized. His coagulation studies did not normalize until the larger dosing of vitamin K was administered. For reference, an adult dietary supplement dose of vitamin K is 5-10mg per day. Hemoglobin levels stabilized once frozen plasma and high-dose vitamin K therapy were initiated, and his urine gradually began to clear.

As his condition stabilized, the patient was transferred back to the family medicine service. Late during this admission, the patient ultimately admitted to a history of smoking K2, a synthetic cannabinoid, approximately one month prior to his admission. A serum brodifacoum level of 155ng/mL was measured, which was elevated compared to the reporting limit (10ng/mL).

Differential Diagnosis

In addition to brodifacoum poisoning, the etiology of the coagulopathy in this case, the following should be considered based upon this patient's presentation with gross hematuria: nephrolithiasis, coagulopathy secondary to liver pathology (cirrhosis, hepatitis C, etc.), intrinsic glomerular disease, vitamin K deficiency or antagonism, platelet dysfunction, renal cell carcinoma or other malignant renal mass, disseminated intravascular coagulopathy (DIC), and hemophilia.

Discussion

The patient presented with gross hematuria and subsequently developed laryngeal hemorrhage with no prior or familial history of hemophilia or coagulopathy. Ureteral stones were cleared by stenting, and neoplastic processes were ruled out by imaging. Glomerulonephritis was ruled out as the patient remained normotensive, had normal urine production, and had a normalization of his creatinine within 48 hours. With our patient's elevated PT, PTT, and INR in the setting of a normal platelet count and elevated fibrinogen, DIC was unlikely. The patient had normal liver function tests and prior CT showed no evidence of cirrhosis, making a coagulopathy associated with liver disease from chronic hepatitis C unlikely.

The significantly low levels of factors II, VII, IX, and X from the patient's extrinsic and intrinsic factor panels confirmed a vitamin K deficiency or antagonistic process, which led to treatment with high-dose vitamin K. The diagnosis of acute brodifacoum poisoning was confirmed when serum levels returned significantly elevated. The high doses of vitamin K were required to overcome the inhibition of vitamin K reductase and vitamin K epoxide reductase by brodifacoum, as shown in **Figure 1**.

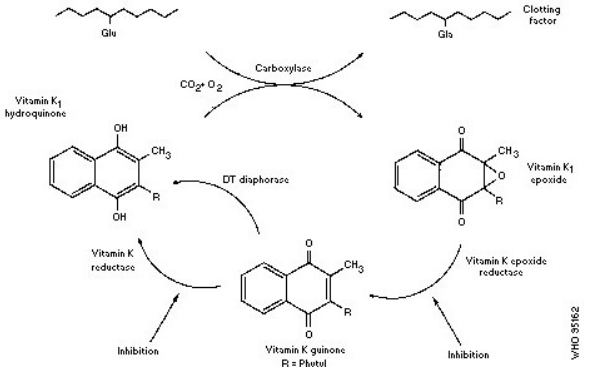


Figure 1. Inhibition of vitamin K reductase and epoxide reductase by warfarin.[3] *Reprinted with permission.*

Synthetic cannabinoid use has significantly increased in the past decade. Regulation has been difficult due to the numerous synthetic varieties, making classification of the compounds difficult. Formulations colloquially known as "K2" or "Spice," which often do not correspond to a single cannabinoid, commonly sell at convenience stores and paraphernalia shops, despite federal regulatory efforts.[4] Currently, marijuana and many identified synthetic cannabinoids are classified as Schedule I Controlled Substances, along with heroin and other opioids. However, the numerous varieties of cannabinoids and ease by which to create new cannabinoids in the laboratory make for difficult regulation.

Several case reports have identified an association with brodifacoum and synthetic cannabinoids, but a causality has not been proven. K2 and Spice are produced by spraying synthetic cannabinoids, often created in a laboratory, over non-psychoactive plants, with the drug effects attained by smoking and inhaling the mixture by pipe or cigarettes. The authors of this case report speculate that brodifacoum is used as an additive to prolong the effects of the cannabinoids, though this link remains unclear. As of July 13, 2018, over 250 cases of brodifacoum poisoning by synthetic cannabinoid use have been reported to the CDC, and its incidence is increasing.[5] Similar cases have been reported in Illinois (n=164), Maryland (n=20), and other states.[6] This marks the fourth documented case in North Carolina (Michael C. Beuhler, MD, email communication, September 2018).

Conclusion

Our patient eventually was titrated to a high-dose vitamin K regimen at 25mg orally twice daily and was discharged from the hospital. This is a costly medication: ten 5mg tablets cost approximately $223 in the United States—the dose the patient was receiving daily. He received regular PT/PTT/INR checks, which stabilized in the normal range after one month, but he required high-dose vitamin K for six months. The patient's brodifacoum level dropped significantly after one month of treatment from 155ng/mL to 50ng/mL. Two months later, it further decreased to 18ng/mL, but it remained at this level for another two months before then becoming undetectable. As with our patient, treatment courses of high-dose vitamin K may continue for approximately six months or until the patient has two consecutive brodifacoum levels under 10ng/mL.[7] This illustrates the toxin's lipophilicity.

This case highlights the importance of asking detailed social (i.e. illicit substance use) histories, specifically asking about synthetic cannabinoid use, in patients presenting with unexplained significant bleeding. It is also important to consider vitamin K-dependent antagonist coagulopathy (e.g., brodifacoum poisoning) after reported synthetic cannabinoid use within the last three months.

Acknowledgements

We would like to thank our patient for allowing us to use his information for this report.

Disclosures

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

References

1. Castaneto MS, Gorelick DA, Desrosiers NA, Hartman RL, Pirard S, Huestis MA. Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. Drug Alcohol Depend 2014;144:12-41.
2. National Library of Medicine. Brodifacoum. https://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+3916. Accessed August 30, 2018.
3. Reprinted from Internationally Peer Reviewed Chemical Safety Information, Tasheva, M., Environmental Health Criteria for Anticoagulant Rodenticides, Figure 2, Copyright (1995). http://www.inchem.org/documents/ehc/ehc/ehc175.htm [inchem.org]; ISBN 92 4 157175 1. Accessed September 2, 2019.
4. Tai S, Fantegrossi WE. Pharmacological and toxicological effects of synthetic cannabinoids and their metabolites. Curr Top Behav Neurosci 2017;32:249-262.
5. Moore, Zack. Vitamin K-Dependent Coagulopathy Associated with Synthetic Cannabinoids Use. NC Med Board, NC Dept of Health and Human Services. 30 Aug 2018.
6. Center for Disease Control and Prevention. Outbreak of Life-threatening Coagulopathy Associated with Synthetic Cannabinoids Use. https://emergency.cdc.gov/han/han00410.asp. Accessed August 30, 2018.
7. King N, Tran MH. Long acting anticoagulant rodenticide (superwarfarin) poisoning: A review of its historical development, epidemiology, and clinical management. Transfus Med Rev 2015;29:250-258.

Case Reports

NSTEMI in a 28-year-old female with recent myocarditis

Rachel Barkley, B.S.[1] & Logan Kinney, M.D.[2]

Introduction

Myocarditis and acute coronary syndrome (ACS) have similar clinical presentations and can be hard to differentiate.[1] Myocarditis is an inflammatory disease of cardiac muscle and has a variety of noninfectious and infectious etiologies. The cause of acute coronary syndrome is a mismatch between the myocardial oxygen demand and myocardial oxygen consumption. While the source of this mismatch in ST-segment elevation myocardial infarction (STEMI) is almost always coronary plaque rupture, there are several potential causes of this mismatch in non-ST-segment elevation myocardial infarction (NSTEMI). Non-coronary injury to the heart such as cardiac contusion, presence of cardiotoxic substances, and even myocarditis can produce NSTEMI.[2] Also, conditions such as hypotension, hypertension, tachycardia, aortic stenosis, and pulmonary embolism, though seemingly unrelated to the coronary arteries or myocardium, can lead to NSTEMI because the increased oxygen demand of the heart cannot be met.[3,4] Unsurprisingly, acute myocarditis is more common than ACS in younger patients aged 18–29 years, but the risk of myocardial infarction (MI) subsequently increases.[2] Additionally, risk factors such as hypercholesterolemia, diabetes, and hypertension predict MI regardless of age and gender. Although many factors go into diagnosing myocarditis and MI, distinguishing between the two is crucial because the short and long term management and prognosis is largely different.

Case Report

A 28-year-old female with history of type 1 von Willebrand disease (VWD) and recent hysterectomy presented with chest pain. Nine days earlier, she was diagnosed with viral myocarditis at an outside hospital after presenting with chest pain and left hand and foot numbness in the setting of a urinary tract infection. At that time, her troponin was elevated to 1ng/mL and a trans-thoracic echocardiogram (TTE) demonstrated mild global systolic dysfunction with an ejection fraction (EF) of 40-45%. She was subsequently discharged on a beta blocker and ACE inhibitor. However, due to low blood pressures, the medications were discontinued. The patient presented again to the ED with 8/10 chest pain, palpitations, diaphoresis, nausea, and dizziness. The patient described her chest pain as sternal with radiation to her back and neck that increased with exertion. However, her symptoms were the same as when she was first suspected to have myocarditis. She denied infectious symptoms including vomiting, fever, and cough.

Despite minor bleeding complications from the VWD, which prompted the patient

[1]Wake Forest School of Medicine, Winston-Salem, NC

[2]Department of Anesthesiology, Wake Forest School of Medicine, Winston-Salem, NC

Address Correspondence To:
Rachel Barkley, B.S.
Department of Anesthesiology
Wake Forest School of Medicine
Medical Center Boulevard
Winston-Salem, NC, 27157
rbarkley@wakehealth.edu

to get a hysterectomy the month prior, the patient had not had any serious medical problems or hospitalizations. The patient's mother, father, and sister also have VWD. The patient denied alcohol, drug, or tobacco use since 2017. Of note, the patient had an extensive family history of cardiac problems all starting around age 30 (Figure 1).

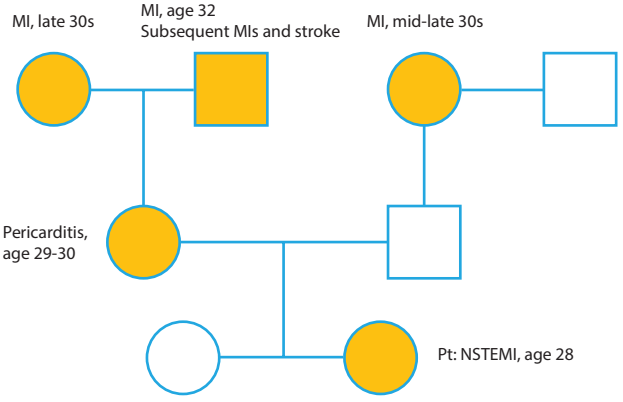


Figure 1. Patient's family history of heart conditions

The second time the patient presented to the ED, she was afebrile and hemodynamically stable. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were within normal limits. Initial troponin was 0.03ng/mL and EKG showed T wave inversions in leads III and aVF (Figure 2). The patient continued to have mild non-pleuritic chest pain with movement, which she described as pressure. On cardiovascular exam, there were no murmurs or pericardial rub appreciated and all other components of the physical exam were unremarkable.

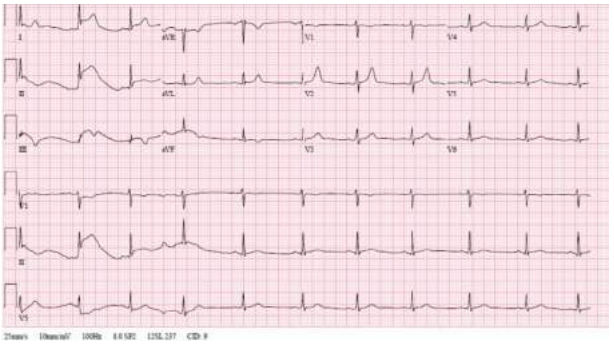


Figure 2. Patient's EKG changes demonstrating T wave inversions in III and aVF

The patient's troponins peaked at 0.052ng/mL and she was placed on aspirin and low dose captopril 6.25mg BID. Based upon the patient's age, presentation, and initial diagnosis of viral myocarditis, there was low suspicion for ACS and the patient was started on colchicine for suspected viral myocarditis. Repeat TTE was within normal limits and bubble study showed no evidence of a right-to-left shunt. Autoimmune panel (ANA, RF, C3, C4, quant immunoglobulins) and D-dimer were negative. The patient's lipid profile (LDL 54, Tot 117, TG 158, HDL 44), TSH, and BNP were also unremarkable. The patient's chest pressure completely resolved after initiating the colchicine and, with no abnormal lab results, the plan was to send her home after cardiac MRI the next day.

Cardiac MRI demonstrated normal biventricular function but, interestingly, a localized abnormal T2 signal and mild subendocardial late gadolinium enhancement, a scar pattern, and presence of edema suggestive of an acute MI in the distal left anterior descending artery territory. This favored a diagnosis of NSTEMI over myocarditis because of the distribution of injury, and the decision was made to take the patient for left heart catheterization. Cardiac catheterization revealed no evidence of coronary disease that would require stenting and normal left ventricular end-diastolic pressure with hypokinesis on the infero-apical wall. With her VWD and no evidence for stent placement, the patient was not treated with anti-platelet therapy on discharge. She went home on metoprolol tartrate 12.5mg BID and lisinopril 5mg daily with no residual symptoms or deficits from her NSTEMI. Although the patient had hypotension when discharged on a beta blocker and ACE inhibitor the first time, she was tolerating them well in the hospital so they were continued as part of her home regimen.

Discussion

The differential diagnosis of chest pain in a young female includes a wide variety of cardiac, pulmonary, and musculoskeletal etiologies. While ACS should always be a consideration even in a young healthy patient, it is usually not high on the differential. Although the etiology of our patient's NSTEMI is idiopathic, spontaneous coronary artery dissection (SCAD), a non-traumatic and non-iatrogenic separation of the coronary arterial wall, is at the top of our differential. A patient this young should not have any appreciable plaque buildup yet, so a plaque rupture, although plausible, would be less likely. Additionally, distal SCAD would appear completely normal on coronary angiography. While

uncommon, SCAD should be considered in any young patient, especially a young woman, without coronary heart disease or risk factors who presents with an acute myocardial infarction or cardiac arrest. Given this patient's demographics and her family history, SCAD seems most likely for this patient.

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is the term used to describe patients presenting with clinical features of an acute MI, but without evidence of obstructive coronary artery disease on angiography.[5] A review of the MINOCA literature reported a prevalence of 1-14% (mean=6%, 95% confidence interval: 5%, 7%) in patients with acute MI.[6] Presentation of myocarditis may mimic an acute MI, resulting in a diagnosis of MINOCA. Routine cardiac MRI in patients with MINOCA has demonstrated that as many as one-third have evidence of myocarditis, making it the most common non-coronary cause of MINOCA.[7]

Furthermore, even in patients in whom ACS is unlikely, it is important not to discount the role family history plays in the pathogenesis of ACS. There are several inherited disorders with coronary artery disease or myocardial infarction as part of the phenotypic expression. These include, but are not limited to, autosomal dominant and recessive familial hypercholesterolemia, antiphospholipid antibody syndrome, partial lipodystrophy, fibromuscular dysplasia, and homocystinuria. Additionally, family history is an independent risk factor for coronary heart disease, particularly among young individuals with a family history of premature disease. Using data from the 2011 to 2014 NHANES survey, the 2017 American Heart Association heart disease and stroke statistics report that 12.2% of adults have a parent or sibling with heart attack or angina before age 50.[8]

Conclusion

This patient's objective data (negative ESR/CRP, absence of a pericardial rub, EKG with isolated T wave inversions) pointed more to an ACS than myocarditis. Given her age, however, it seems the physicians prematurely closed on the myocarditis diagnosis. It is imperative to consider ACS in younger patients and complete a thorough work-up if their symptoms point toward ACS. Also, physicians should take a detailed family history and determine whether their patients have significant family history of heart disease. A careful review of objective data and physical exam findings will help avoid cognitive bias so a more guided approach to diagnosis and treatment can be initiated.

Disclosures

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

References

1. 1. Kindermann I, Barth C, Mahfoud F, et al. Update on myocarditis. J Am Coll Cardiol 2012;59:779–92. 10.1016/j.jacc.2011.09.074
2. Kytö V, Sipilä, J, & Rautava, P. Acute myocardial infarction or acute myocarditis? Discharge registry-based study of likelihood and associated features in hospitalised patients. BMJ open. 2015:5(5), e007555. doi:10.1136/bmjopen-2014-007555
3. Rupprecht HJ, Geeren M, Geeren M, Weilemann S, Schuster HP. Acute coronary syndrome without ST-elevation (NSTE-ACS). Herz. 2019;44:10.
4. Kamińska J, Koper OM, Siedlecka-Czykier E, Matowicka-Karna J, Bychowski J, Kemona H. The utility of inflammation and platelet biomarkers in patients with acute coronary syndromes. Saudi J Biol Sci. 2018 Nov;25(7):1263-1271.
5. Agewall S, Beltrame JF, Reynolds HR, et al. ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. Eur Heart J. 2016;38:143-53.
6. Pasupathy S, Air T, Dreyer RP, Tavella R, Beltrame JF. Systematic review of patients presenting with suspected myocardial infarction and nonobstructive coronary arteries. Circulation. 2015;131:861-70.
7. Tornvall P, Gerbaud E, Behaghel A, et al. Myocarditis or "true" infarction by cardiac magnetic resonanee ce in patients with a clinical diagnosis of myocardial infarction without obstructive coronary disease: A metaanalysis of individual patient data. Atherosclerosis. 2015;241:87-91.
8. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics—2017 Update: A Report From the American Heart Association. Circulation. 2017;135:e146-e603.

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(ISSN 2380-3991)