SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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SCANEWS

President's Message

JUNE 2021

Andrew Shaw
MB, FCCM, FFICM, FRCA
President, Society of Cardiovascular Anesthesiologists

Greetings to all SCA members and other anesthesia providers everywhere who take care of patients undergoing cardiac, vascular, and thoracic surgery. My name is Andrew Shaw, and I am the new President of the Society of Cardiovascular Anesthesiologists. It is my distinct pleasure to write this first President's message, and I would like to start by extending my congratulations and thanks to Dr. Sasha Shillcutt, Dr. Mary-Beth Brady, Dr. Jonathan Ho, and the rest of the Scientific Program Planning Committee, who did such an amazing job putting this year's virtual meeting program together.

There have been many challenges thrown at us as a Society over the past couple of years, and the way the SCA has met these challenges has meant that we are in an extremely strong position to tackle those of the coming years. However, it also provides us some opportunities to grow and to use the new skills we have all been required to learn. I would like to take a few minutes to review some of those challenges and opportunities in the paragraphs that follow.

First, I would like to thank Drs. Shernan, Troianos and Taylor as they transition out of their respective roles on the SCA Board Executive Committee. Dr. Shernan will stay on in his new position as Immediate Past President; and it is largely due to his and Dr. Troianos' and Dr. Taylor's skilled leadership that we are in the strong position that we are in. In a similar vein I would like to welcome Drs. Kathy Glas and Amanda Fox as our new President-Elect and Secretary-Treasurer, respectively. I am sure they will continue to bring the same experience, skilled judgment, and sensitive leadership with which they have served the Society and its membership in the past, to these new positions.

One of the major challenges of the past two years (other than the COVID-19 pandemic), is that as a society we have changed management companies. We changed from AMC to Veritas. We have been together now for a little over ten months and the transition has been amazingly smooth; I think the way that we have managed to conduct our educational meetings — first Echo Week and more recently the annual scientific meeting — shows how quickly our new management partners have understood us, have worked with and for us and have contributed to this success. I would like to thank Jim Pavletich, Denise Herdrich, Mary Lunn, Sue O'Sullivan, Donna Kelly, and everybody else behind the scenes at Veritas, who have helped make the SCA the "go to society" for cardiovascular and thoracic anesthesiologists around the world. We have had to deal with a COVID-19 pandemic that meant we had to cancel our annual meeting last year and transition to a virtual format for our echo week and for this year's Annual Meeting. It is

continued...

President's Message

Veritas's experience and skill with technology and their ability to grasp our needs that has made the transition so smooth. In fact, this year's ASM was our most highly attended meeting ever — including 2015 when we hosted the ICCVA in Washington DC.

In June 2021, the State of our Society is strong. From a financial perspective we are in the best position we have ever been in. We have excellent administration, we are funding new and significant grants, we have a new Diversity Equity and Inclusivity Committee, and we have great plans to use our new experience in web-based learning that we have acquired as part of the COVID-19 pandemic. In the future we plan to transition to a hybrid model of in person meetings for those that can and want to attend themselves, and a live stream for our colleagues around the world who are unable to attend in-person. When life gives us lemons, the SCA makes lemonade.

In terms of my priorities as President for the next two years I have three themes that I am going to encourage our board and our committee members (there are over 650 SCA members involved in our committee infrastructure) to focus on for the next few years.

1

Professional and Leadership Development

This year we held our first Professional Development workshop — it was amazing, and I am going to ask our program committee, our board, and our members to focus on professional and leadership development to bring opportunities for personal and professional growth for our members.

2

Perioperative Medicine

I am an anesthesiologist — I am also an intensive care physician. I think our role outside the operating room is critical as we define our specialty's future. SCA members can, should, and will play a large role in the perioperative medical care of patients undergoing cardiovascular and thoracic procedures. I am going to ask our committees to develop new educational programming and new research programs focused — in intensive care units and perioperative medicine clinics around the world.

3

International Collaboration

I am a British and American citizen and I have also worked in Canada. I have understood and seen firsthand the power of collaboration across international borders. The SCA has no geography in our name, and I am keen for us to develop and take our place in leadership in the world of cardiovascular and thoracic anesthesiology. I will be asking Dr. Alex Mittnacht and our International Committee to reach out to our partners around the world and develop new innovative collaborations, so that we can help expand and develop both professional development and perioperative medicine opportunities and programs, not just in North America, but all around the world.

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As I write these words, I am aware that I have been a personal beneficiary of our society's commitment to mentorship, sponsorship, and faculty development. It is my pledge to use our society's resources to develop programs that will allow our members to enjoy similar opportunities to the ones I have had, and in turn to give back to help develop the next generation so they can discover and disseminate new knowledge, and to train the cardiovascular anesthesiologists of the future. To that end I would like to encourage all our members to donate to our Society's Endowment, and to support Drs. Oakes and Faloye, and everyone involved in WICTA, who are doing such great work for the women of the SCA.

I look forward to serving the Society as your president for the next two years. Please reach out to me at **president@scahq.org** and let me know what you would like to see the SCA start doing, what you would like to see us stop doing, and what you would like to see us keep on doing. I am always happy to talk to any of our members at any time, day, or night, so please do not hesitate to get in touch.

Andrew Shaw

GET READY

Don't miss out on these 2022 events

Hands-On PoCUS Training is Back for 2022

Save the date for the upcoming Perioperative Ultrasound Course Hands-On Workshop — **February 17, 2022**! Participants will gain practical knowledge on how to perform safe ultrasound-guided procedures.

More information coming soon!

Save the Date for Echo Week 2022

The 2022 Echo Week will take place **February 18-20** in Atlanta, Georgia. This meeting is designed for anesthesiologists, cardiologists, cardiac surgeons, intensivists, sonographers, radiologists, and other medical professionals with an interest in perioperative echocardiography. You will have personal access to internationally recognized experts in the fields of echocardiography and cardiovascular ultrasound.

More information coming soon!

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SAVE THE DATES

Join us under the palm trees in Palm Springs, California for 2022

2022 SCA Annual Meeting and Workshops

SCA and the Scientific Program Planning Committee invite you to join us in Palm Springs, California for the 2022 Annual Meeting and Workshops, **May 14-17, 2022**. The 2022 meeting offers the latest education in anesthesiology research and advancements.

Mark your calendar NOW to join us for the 2022 Annual Meeting and Workshops in Palm Springs, CA.

More information coming soon!

Mark Your Calendars for 2022 TAS

On **May 13, 2022**, SCA will hold its 10th Annual Thoracic Anesthesia Symposium in Palm Springs, California. This is a 1-day event focused entirely on thoracic anesthesia for academics and private practitioners.

We hope to see you in May 2022 for a day full of Thoracic Anesthesia. More information coming soon!

The Thoracic Anesthesia Symposium Planning Committee is enthusiastically inviting the world of non-cardiac anesthesiologists to join us for an excellent opportunity to learn what is new in the profession!

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Meet SCA's 2021-2022 Leadership Team

SCA 2021-2022 EXECUTIVE COMMITTEE

PRESIDENT
Andrew D. Shaw
MB FCCM FFICM FRCA

PRESIDENT-ELECT
Kathryn E. Glas
MD MBA FASE

SECRETARY/ TREASURER
Amanda A. Fox
MD MPH

IMMEDIATE PAST PRESIDENT
Stanton K. Shernan
MD FAHA FASE

SCA BOARD OF DIRECTORS

DIRECTORS-AT-LARGE

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MD

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EARLY CAREER DIRECTORS

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Chair
Sasha K. Shillcutt
MD MS FASE

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Mary Beth Brady
MD

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Ludmil Mitrev, MD

EACTAIC LIAISON

Gianluca Paternoster, MD

FUND BOARD REPRESENTATIVE

David L. Reich, MD

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Announcing the 2021 grant and award winners

2021 Award Recipients

SCA MICoR Research Grant

$200,000 per year for 3 years

MICoR Grant Title: *The Effect of Continuous Low Tidal Volume Ventilation and Hyperoxia Avoidance During Cardiopulmonary Bypass*

Primary Investigators:

Marta Kelava MD MS
Clinical Assistant Professor CCLCM/CWRU
Cleveland Clinic

Kimberly Howard-Quijano MD MS FASE
Director of Translational Research
University of Pittsburgh Medical Center

Co-Investigators:

Michael K. Essandoh
MD FASE
Associate Director of Anesthesiology Clinical Research
The Ohio State University Wexner Medical Center

Andra E. Duncan
MD MS
Associate Professor of Anesthesiology
Cleveland Clinic

Edward G. Soltesz
MD MPH
Staff Cardiothoracic Surgeon; Assistant Professor of Surgery, CCLCM *Cleveland Clinic*

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2021 grant and award winners

SCA/IARS Mid-Career Research Grant

$50,000 per year for 2 years

Grant Title: *Right Ventricle Adaptive Changes in Patients Undergoing Left Ventricular Assist Device Implantation*

Alina Nicoara MD
Associate Professor
Duke University

SCA/IARS Starter Research Grants

$25,000 per year for 2 years

Grant Title: *Combined Clinical-epidemiological Risk Score for Postoperative Atrial Fibrillation After Cardiac Surgery: A Multi-institutional Study*

Sergey Karamnov MD
Instructor
Brigham and Women's Hospital,
Harvard Medical School

2021 grant and award winners

SCA/IARS Starter/Diversity Research Grants

$25,000 per year for 2 years

Grant Title: *Activated Prothrombin Complex Concentrate FEIBA to Optimize Postcardiopulmonary Bypass. Hemostasis in Pediatric Cardiac Patients*

Elena Ashikhmina MD PhD
Assistant Professor, Director of Congenital Cardiac Anesthesia
Mayo Clinic

SCA Kaplan Leadership Development Award Winner

Leadership Project Title: *Harvard Leadership Development Course for Physicians in Academic Health Centers*

Karsten Bartels MD PhD
Associate Professor
University of Nebraska Medical Center

2021 grant and award winners

SCA Early Career Investigator Award Winners

Stephanie L. Bradley MD MPH
Brigham and Women's Hospital, Harvard Medical Center

Abstract Title: *Sex Differences in Postoperative Mortality after Open Cardiac Valve Surgery*

Luis Gonzalez-Ciccarelli MD
Tufts Medical Center

Abstract Title: *Impact of Pressure Recovery Adjustment to Aortic Valve Area for Classification of Disease Severity in Transcatheter Aortic Valve Replacement Patients*

Andre Gosling MD
Duke University Medical Center

Abstract Title: *The Role of Recipient Thyroid Hormone Supplementation in Heart Transplantation Outcomes*

Asad Usman MD MPH
University of Pennsylvania

Abstract Title: *Pre-Trial Logistical Run-Up to the Rescue Transesophageal Echocardiography for In-Hospital Cardiac Arrest (ReTEECA) Trial*

Jakob Wollborn MD
Brigham and Women's Hospital, Harvard Medical Center

Abstract Title: *Elevated Angiopoietin-2 Predicts Microcirculatory Dysfunction after Cardiac Surgery*

2021 grant and award winners

2021 Distinguished Service Award Winner

The Distinguished Service Award is given to an individual who has made significant contributions to the specialty of cardiovascular anesthesiology through research, education, service, or any combination of these activities.

Scott T. Reeves MD MBA FACC FASE
Medical University of South Carolina

2021 Presidential Lifetime Outstanding Service Award Winner

The Presidential Lifetime Outstanding Service Award is given to an anesthesiologist who has made outstanding long-term contributions to the Society.

Robert M. Savage MD FACC
McLeod Healthcare System

AWEsome Woman Interview

Dalia Banks, MD FASE

University of California San Diego

Brief introduction about yourself:

Dr. Dalia Banks is a Professor at the University of California San Diego and has been an active member of the SCA since 1998. She finished her anesthesia training at Yale-New Haven Hospital and Cardiac Anesthesiology Fellowship at Beth Israel Deaconess in Boston. In October 2005, she joined UCSD where she has served as the Cardiothoracic Anesthesiology Fellowship director for the past 11 years as well as division chief for the past 9 years. She is currently serving as the Vice-Chair of Cardiovascular Anesthesia Academic Affairs. Dr. Banks serves on the editorial board as section editor for the Journal of Cardiothoracic and Vascular Anesthesia. She is nationally known for her expertise in Pulmonary Thromboendarterectomy.

1. What led you to become a Cardiovascular/Thoracic Anesthesiologist?

My first exposure to the heart room happened during my first month of residency at Yale. I was fascinated with the heart room, the team spirit, the comradery between cardiac surgeons, cardiac anesthesiologists, perfusionists and nurses. I was fortunate enough to have several role models during my residency that left a great impression on me. Drs. Jane Fitch, Roberta Hines and Susan Garwood were great female role models in the cardiac ORs. In addition, Dr. Paul Barash and Dr. Terrance Raftery are valued mentors and supported my decision to pursue cardiac anesthesiology. To this day, I remember my fascination with echocardiography and still incorporate Dr. Paul Barash's approach to teaching echo. I couldn't get enough of the heart room and elected to spend an additional 6 months in advanced clinical tract doing cardiac anesthesia, before pursuing my formal 1 year of cardiac anesthesiology fellowship at Beth Israel Deaconess in Boston.

2. How did you hear about the SCA?

I heard about the society during my residency at Yale New Haven, I was surrounded with well renowned cardiac anesthesiologists that encouraged me to get with the society. That was re-enforced during my cardiac fellowship at Beth Israel Deaconess in Boston. Attending my first SCA meeting in 2001 was such a great experience, and I have attended every year since.

3. What roles have you held for the society?

In 2010 I joined the newsletter subcommittee as a member. I truly enjoyed my contribution to the committee and was fortunate enough to serve as the chair for the Newsletter since 2016. I had the opportunity to revamp the newsletter subcommittee with additions of new sections. I am also very fortunate to have been elected this year to serve on the CME committee and looking forward to new challenges to incorporate new CME opportunities for our members.

4. What is one of your greatest achievements as a cardiovascular anesthesiologist?

I am very proud of many things that I was able to accomplish in the past 16 years of my career at the University of California San Diego.
1) Building an outstanding Cardiac Anesthesiology Fellowship program and acquiring accreditation.

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2) Putting together a fantastic team of Cardiac Anesthesiologists
3) Founding and directing a Transesophageal Echocardiography review course for the past 8 years. But one of the greatest achievements is standardizing the cardiac anesthetic management and protocol for chronic thromboembolic pulmonary hypertension (CTEPH) patients undergoing Pulmonary Thromboendarterectomy (PTE) surgery. UCSD is the leading center for the management of CTEPH and has revolutionized the treatment with PTE surgery for thousands of patients. In addition, I developed clinical pathways to deal with unique situations like the management of patients with Cold Agglutinin in PTE, management of heparin induced thrombocytopenia in patients undergoing PTE, management protocol for post PTE bleeding, which I helped develop to help saves lives from this devastating complication. I have also written several chapters in various textbooks regarding the diagnosis of CTEPH and the role of PTE. I have had the unique privilege to train several anesthesiologists from all over the world on the anesthetic management of this procedure.

5. Do you have any advice for Fellows and Residents?

1) Hard work with a smile always pays off at the end. Don't always expect praise from everyone, but you will find the people who will appreciate what you do. It will not go unnoticed.

2) Never say no, don't give your answer right away, think about it and you will see it's always in your best interest. Especially, if you are starting your career.

3) Be humble, forget your ego at home, you will win everyone around you.

4) If you need help, please ask for it, don't feel bad asking for help, you are dealing with patient lives and that's what matters.

5) On a personal level, take care of yourself first so you can take care of everyone else later.

6. Have you experienced any difficulties as a woman in the field?

I was fortunate enough to have joined the University of California San Diego where my career as a cardiac anesthesiologist took off. This was due to the leadership and mentoring of two mentors, Dr. Gerry Manecke, my chairmen who gave me all the opportunities to grow and succeed in my career and Dr. Joel Kaplan who opened many doors to pursue my academic career.

I started as the program director, shortly became division chief of cardiac anesthesia, associate chief of anesthesia at Thornton hospital and associate clinical director for the department. I came to the right place, at the right time and was surrounded with the right people. Everyone needs an opportunity and when it comes you should embrace it.

7. Do you have any advice for other women in the field?

Certainly, I am always honored when I am approached by female residents, fellows and junior faculty at the society for advice. My advice is always, think highly of yourself, stand your ground and take care of yourself. If you feel good about yourself, it will reflect in your behavior and how you interact with everyone. I have noticed that in the cardiac room, if you are too quiet and intimidated by the surgeons, they will not trust you. Stand Strong with a smile!! Always be positive and never give up. I have always said my middle name is "tenacity."

8. How do you balance work and personal life?

That's tough, it is always a struggle with feeling of guilt that you are not doing your best towards your family. The best advice I have is from a well accomplished chief operating officer at the VA. She said never neglect your family. If time is an issue, hire the help if needed, but never leave an open hole from your absence. Communication is key and a family strong in faith and love supports whatever endeavor the other pursues. There is no shame asking for help and a good nanny to help you organize things at home so you can truly just spend time with your family can truly go a long way.

9. What is something you enjoy doing outside of work?

I enjoy being around people, my church friends and family. My home is always open, I entertain quite a bit. I love traveling and recently I started going back to Egypt to teach.

10. Would you change anything about the path you took to get to where you are now?

I would not change a thing. I am very proud of what I have accomplished and thankful I had the support of my family and my mentors that helped me to live the life I have always wanted to live. As long as I am healthy and alive, there is still more to do and accomplish but at my own pace.

11. What was the best piece of advice you received?

Always be positive and never give up on your dreams. "If there is a will, there is a way."

The Next WICTA Professional Development Mentoring Program Webinars Feature:

Simon Body
MBChB, MPH, FAHA
Boston University

Hilary Grocott
MD, FRCPC
University of Manitoba

Jochen (Danny) Muehlschlegel
MD, MMSC, FAHA
Brigham and Women's Hospital, Harvard Medical School

How to Get the Very Best Out of Your Statistician and Your Study

- Most commonly used analytical statistics

Date: July 14, 2021

Time: 4:00 PM PT
6:00 PM CT
7:00 PM ET

Publishing in Medical Journals

- Explore common pitfalls
- What the Editor wants to see

Date: August 4, 2021

Time: 4:00 PM PT
6:00 PM CT
7:00 PM ET

Grant Writing

- Explore commonalities shared by successful grants
- Explore how to search for grants

Date: September 22, 2021

Time: 4:00 PM PT
6:00 PM CT
7:00 PM ET

Professional Development Mentoring Program

The purpose of this program is to foster essential skills and competencies crucial to career development in early and mid-career women and underrepresented minorities in cardiothoracic anesthesiology. This includes essential knowledge in clinical research (such as medical statistics, manuscript drafting, and grant writing), public speaking, leadership, networking, and mentorship.

At the end of this program, participants will be able to:

- Assess and recognize their personal opportunities for professional skill growth.
- Apply leadership fundamentals to their personal careers and advance their professional development.

To register for these FREE webinars, click here.

MEMBER CORNER

Message from the SCA President Andrew Shaw

MB, FCCM, FFICM, FRCA

Please **click here** to listen to Dr. Shaw's message to the SCA membership on the home page of the SCA website.

Lectures still available for CME!

2021 TAS and Annual Meeting Content — Still Available

The Thoracic Anesthesia Symposium and SCA 2021 Annual Meeting and Workshop lectures are still available for CME until June 26, 2021, and September 30, 2021, for on-demand. If you have not already purchased the content, **click here** to start your process.

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MEMBER CORNER

SCA Website — Introducing a NEW FEATURE

Committe Updates on the Website!

The Committees and Task Force page on the SCA website has been updated with the 2021-2022 rosters. Visit the page to learn about each committee's charge, who their members are, and where each falls within the committee structure diagram. And while you are there, check out the "Committee News" feature – a prime source to learn about what the committees are working on or recently accomplished.

Click here for committe updates.

Support Your Society Through the SCA Endowment

SCA is the preeminent international educational organization for this sub-specialty, leading the way in treatment innovations through care, investigation, and knowledge. By donating to the SCA Endowment, the funds help support SCA professionals to further their education, research, and professional development and to achieve their goals.

The SCA Endowment Fund online donation page is available. Making an online donation is quick, easy, and secure. To complete the online donation form, visit **www.SCA Endowment**.

Vision of the SCA Endowment

> We will be world leaders in enhancing patient care and safety and in developing excellence in the next generation of clinicians and physician-scholars through research and education in the field of cardiothoracic and vascular anesthesia.

For more details on the endowment, please email donation@scahq.org.

THORACIC CORNER

Evaluating the Impact of Pulmonary Artery Obstruction after Lung Transplant Surgery: A Systematic Review and Meta-analysis

Kumar N, Hussain N, Kumar J, et al. *Transplantation*. 2021 Apr 1;105(4):711-722.

Reviewers:

Ashley Virginia Fritz, DO
Division of Cardiovascular and Thoracic Anesthesiology
Mayo Clinic School of Medicine, Rochester, Minnesota

Archer Kilbourne Martin, MD
Division of Cardiovascular and Thoracic Anesthesiology
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Background

The role of anesthesiologists as members of cardiothoracic transplantation teams has been the focus of literature in recent years.[1] Beyond intraoperative management, literature has described the integration of anesthesiologists into the entire perioperative course, from membership on transplant selection committees, development of preoperative rehabilitation protocols, and postoperative critical care.[2] One of the key areas of where anesthesiologists have contributed to the practice of cardiothoracic surgical literature and practice is within the perioperative use of transesophageal echocardiography (TEE).[3] The first major publication describing intraoperative TEE during lung transplantation came from authors at Foch Hospital in Paris in 1997, when the researchers described assessment of vascular anastomoses in 18 lung transplantation patients.[4] This current study represents the most comprehensive evaluation of lung transplantation pulmonary arterial anastomoses in the literature to date. The authors, predominately anesthesiologists at The Ohio State University, aimed to perform a systematic review and meta-analysis of pulmonary arterial obstruction – a rare, yet highly impactful complication during lung transplantation.[5]

Methods

The authors conducted a systematic review of both quantitative and observational studies reporting on pulmonary artery obstruction in adults who have undergone single or bilateral lung transplantation. Studies were included for consideration without regard to etiology of obstruction, timing of diagnosis, or diagnostic modality. Studies reporting on exclusively pulmonary vein obstruction were excluded. Two independent reviewers assessed over 1245 studies for inclusion to the systematic review and after extensive review included 34 manuscripts. The final manuscripts where were included for review included 24 case reports, 8 retrospective studies, and 2 prospective studies with a total of 1696 patients who underwent lung transplantation. Investigators focused on a primary outcome of prevalence of pulmonary artery (PA) obstruction post-lung transplantation. The authors defined pulmonary artery obstruction as greater than a 25% reduction in the luminal PA diameter that is distal to the recipient anastomosis. Secondary outcomes included etiology of PA obstruction, diagnostic modality and timing, patient presentation, patient mortality and reintervention rates, and key hemodynamic values.

Results

The authors found that across all lung transplantations reviewed (n=1696) 62 cases of PA obstruction were reported, of which the etiology was reported for 61 cases. Pulmonary artery narrowing was the determined cause of obstruction in 63.9% of these cases (39 of 61), 24.5% were due to PA distortion secondary to donor-recipient size mismatch, 4.92% (5 of 61) were secondary to PA thrombosis, and 3.28% (2 of 61) were due to external compression.[5] The time of diagnosis was also assessed and revealed 7 patients who were diagnosed in the intraoperative period, 17 in the early postoperative and 39 in the late postoperative period. Notably, PA obstruction due to vessel distortion was more likely to be diagnosed in the early postoperative period and vessel narrowing was more likely to be discovered in the late postoperative period with a diagnostic timing ranging from 0 minutes to 6 years.[5] The method of diagnosis included pulmonary angiography, transesophageal echocardiography (TEE), and chest computed tomography (CT). Turbulent flow, increased PA pressures (40-70mmHg), and increased pressure gradients (10-46mmHg) across the obstruction were also noted. The clinical presentation of patients with PA obstruction included dyspnea, hypoxemia, pulmonary artery hypertension, systemic hypotension, and pulmonary edema. Upon evaluating further outcomes, 75.81% (47 of 62) of patients required reintervention with either surgical revision or endovascular stenting. The mortality rate was significant, with 22.58% expiring during their hospital stay.

Discussion

Although a rare occurrence, pulmonary artery obstruction is a significant complication with an alarming mortality rate of nearly 25% or 1 in 4 patients with PA obstruction.[5] The authors identified that mean peak pulmonary artery velocities above 2.6m/s or a PA luminal diameter less than 0.8cm are indictive of clinically significant patient symptoms which could lead to primary graft failure and increased mortality.[5] This paper highlights the need for further exploration into early diagnosis and intervention, as currently the diagnosis is primarily made in the postoperative period through the use of TEE and angiography. The use of intraoperative TEE or epipulmonary artery echocardiography to monitor patency of the pulmonary artery during lung transplantation is worthy of further investigation. At a minimum, the cardiothoracic anesthesiologist should possess a greater cognizance of the sequelae associated with PA obstruction.

References

1) Martin AK, Yalamuri SM, Wilkey BJ, et al. The Impact of Anesthetic Management on Perioperative Outcomes in Lung Transplantation. *J Cardiothorac Vasc Anesth.* 2020;34(6):1669-1680.

2) Wilkey BJ, Abrams BA, Mauricio Del Rio J, et al. Statement From the Society for the Advancement of Transplant Anesthesia: White Paper Advocating Desirable Milestones and Competencies for Anesthesiology Fellowship Training in the Field of Lung Transplantation. *Semin Cardiothorac Vasc Anesth.* 2020 Mar;24(1):104-114.

3) Yu S, Peffley S, Fabbro M et al. A Narrative Review of the 2020 Guidelines for Use of Transesophageal Echocardiography to Assist with Surgical Decision-Making by the Cardiac Anesthesiologist in the Operating Room. *J Cardiothorac Vasc Anesth.* 2021 Feb 8;S1053-0770(21)00106-3.

4) Michel-Cherqui M, Brusset A, Liu N et al. Intraoperative Transesophageal Echocardiographic Assessment of Vascular Anastomoses in Lung Transplantation. A report on 18 cases. *Chest*. 1997 May;111(5):1229-35.

5) Kumar N, Hussain N, Kumar J, et al. Evaluating the Impact of Pulmonary Artery Obstruction After Lung Transplant Surgery: A Systematic Review and Meta-analysis. *Transplantation*. 2021 Apr 1;105(4):711-722.

6) Martin AK, Fritz AV, Wilkey BJ. Anesthetic Management of Lung Transplantation: Impact of Presenting Disease. *Curr Opin Anaesthesiol*. 2020 Feb;33(1):43-49.

LITERATURE REVIEWS

Differences in Long-term Outcomes After Coronary Artery Bypass Grafting Using Single vs Multiple Arterial Grafts and the Association with Sex

Mario Gaudino, MD, MSCE; Zaza Samadashvili, MD; Irbaz Hameed, MD; Joanna Chikwe, MD; Leonard N. Girardi, MD; Edward L. Hannan, PhD

Reviewers:
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Medical Center

Antonio Hernandez Conte, MD, MBA, FASA
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Medical Center

Background

Generally speaking, clinical cardiologic research has focused heavily on male subjects and largely ignored female subjects. While women tend to constitute a smaller percentage of cardiac patients who undergo surgery, they remain relatively understudied. To further complicate the scenario, women who undergo CABG possess a different risk profile and clinical characteristics compared to men. This study sought to evaluate outcomes between male and female patient who underwent single versus multiple coronary arterial bypass graft (CABG) surgery.

Study Design

This study utilized study cohorts with data derived from New York's Cardiac Surgery Reporting System (CSRS) and New York Vital Statistics for patients undergoing CABG from January 1,2005 to December 31, 2014. Database demographics are extremely robust, and accuracy is audited by a utilization review agent with matching in the Statewide Planning and Research Cooperative System. The study population was limited to New York state residents. Inclusion criteria included patients who underwent nonemergent CABG with at least 1 arterial conduit and could be followed up for two years.

The incidence rates of mortality, AMI, stroke, repeated revascularization, a major adverse cardiac and cerebrovascular event (MACCE; composite of mortality, AMI, or stroke), and a major adverse cardiac event (MACE; composite of mortality, AMI, or repeated revascularization) were compared separately for male and female patients between single CABG and multiple CABG procedures at 1 year and 7 years after the index procedure.

Study Results

The final study sample comprised 63 402 patients (48 155 men [76.0%] and 15 247 women [24.0%]; mean [SD] age, 69.9 [10.5] years. Overall, women had worse baseline risk profiles compared to men for both single or multiple CABG surgery. Among 13,146 female patients, 86.2% received a single arterial graft, and 13.8% received multiple arterial grafts. Female patients undergoing multiple CBAG were younger than those undergoing single CABG and had lower a prevalence of diabetes, cerebrovascular disease, congestive heart failure, chronic obstructive

pulmonary disease, and/or kidney dialysis. For high-risk males and females, the 7-year mortality was similar for multiple CABG and single CABG. However, when different low-risk cutoffs were studied MAG was associated with lower mortality for all low-risk men, but for women no difference between multiple CABG and single CABG was observed with this same cutoff. Surgeons with low (<75 cases), moderate (75-150 cases), or high (>150 cases) annual CABG volumes were all more likely to perform single CABG versus multiple CABG for female patients.

Discussion

This is a cross sectional study that ultimately suggests that there may be a correlation between sex of patient and post CABG outcomes. The results focused on how there exist a point at which having MAG was not associated with better outcomes and this point is different between the male and female sex. However, several limitations and confounding factors exist in the data that was collected. For example, a significantly lower number of female subjects than male subjects were studied, there was no data on surgical specifics (severity of stenosis, location of target vessel, quality of target vessel, etc.) between subjects, and no data on postoperative medical therapy adherence was taken into consideration.

Another limitation of the study was the small percentage of patients in the "high-risk" group, thus a low power to be able to identify treatment differences in the groups. Furthermore, the risk stratifying system used in the study was arbitrary and not a universally accepted method for risk stratifying patients going for CABG.

While the study supports its hypothesis that the female sex presents a different outcome variable than male sex, it does not offer strong suggestions as to why this difference exists. It is suggested that research incorporating a female sex focused approach in the area of cardiac surgery is in need.

Risk Assessment of Acute Kidney Injury Following Cardiopulmonary Bypass

Wittlinger T, Maus M, Kutschka I, Baraki H, Friedrich MG. *J Cardiothorac Surg*. 2021 Jan 6;16(1):4. doi: 10.1186/s13019-020-01382-x.

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Background

Despite advancements in the field of cardiothoracic surgery acute kidney injury (AKI) remains a common complication with reported incidence ranging from 20%-40% with up to 5% of patients requiring renal replacement therapy (RRT) during postoperative period.[1,2] Furthermore, AKI is associated with increased mortality, ranging from 15%-30%.[2,3] Certain risk factors have been implicated in increasing the risk of AKI after cardiac surgery, including age, sex, and presence of preoperative kidney dysfunction.[4] Several predictive models have also been developed in order to identify patients at high risk of developing cardiac surgery-associated acute kidney injury or need for postoperative RRT.[5,6] However, there is a lack of consistency in AKI definition among those models, since most were developed before Kidney Disease: Improving Global Outcomes (KDIGO) AKI criteria was established. Furthermore, intraoperative and postoperative factors, which can be modifiable, are not always accounted for in the currently published models and biomarkers such as serum creatinine (Cr) and urine output may not provide timely diagnosis of AKI. Therefore, Wittlinger and colleagues aimed to evaluate their institutional predictive tool for diagnosis of cardiac surgery-associated AKI compared to RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) criteria.[7]

Study Design

This study was a single center retrospective observational study of patients who underwent open heart surgery requiring extracorporeal circulation between January 2000 and December 2005. The authors aimed to assess the efficiency of new AKI prediction tool in identifying incidence of postoperative AKI compared to RIFLE criteria. The study included 3574 patients (mean age 64.9 years) undergoing isolated coronary artery bypass grafting (CABG), isolated aortic/mitral valve surgery, combined valve and bypass grafting surgery, and other (neither CABG, valve surgery, or extracorporeal circulation). The authors used two different criteria for assessment of renal function: "Standard Operating Procedure" (SOP) and RIFLE classification. SOP is the authors' institutional own criteria which includes: (1) pulmonary edema or impending RV decompensation due to fluid overload that cannot be treated with diuretics, (2) uremic complications (encephalopathy, neuropathy, pericarditis, acidosis), and (3) Hyperkalemia defined as K > 6.5 mmol/l. RIFLE classification variables used to diagnose AKI included threefold elevation in serum Cr or maximum Cr of 4.0 mg/dl or decrease in GFR by 75% from baseline (consistent with R, I, F stages of RIFLE AKI). Patients were divided into two groups: cohort 1 with normal postoperative renal function, and cohort 2 with postoperative AKI requiring renal replacement therapy (RRT) with continuous veno-venous hemodialysis. The authors aimed to assess whether SOP criteria has improved efficacy compared to RIFLE criteria in identifying predictors of post-operative AKI requiring RRT.

Results

A total of 3574 patients were included in the study. Majority of patients were male (71%) with median age of 68 years. Sixty one percent of patients underwent CABG, 20% underwent isolated valve surgery, and 15% of patients underwent aortic valve replacement with CABG. Overall mortality was 6.4%. Post-operative increase in serum Cr was associated with female sex, CABG, valve surgery, reoperation, intra-aortic balloon plump (IABP) use, centrifugal pump use, and crystalloid cardioplegia use. Using SOP criteria 10% of patients were diagnosed with postoperative AKI requiring RRT with 48% mortality in this group. Older age, female sex, pervious coronary interventions, post-operative IABP use, and post-operative blood transfusion were associated with increased incidence of AKI according to SOP criteria. Intraoperative factors influencing the need for postoperative RRT included longer surgery duration, longer ischemia time, isolated valve surgery, CABG and valve surgery, and deep hypothermia. Using RIFLE criteria 7% of patients were diagnosed with postoperative AKI with 22% mortality. Only normothermia and CABG were associated with increased incidence of postoperative AKI according to RIFLE criteria. Both criteria identified an association between IABP use and reoperation and postoperative AKI requiring RRT.

Discussion

This study identified several risk factors associated with development of AKI. Specifically, using SOP criteria, long surgery duration time, prolonged ischemia time, hypothermia, and blood loss were associated with increased AKI incidence. Further SOP identified independent risk factors included previous coronary intervention, cross clamp and surgery duration. On the other hand, RIFLE criteria only identified normothermia and CABG as being associated with postoperative AKI. The authors concluded that they were able to identify modifiable AKI risk factors and suggest that limiting ischemia duration, blood loss, and maintaining normothermia may reduce the risk of postoperative AKI requiring RRT.

The overall incidence of AKI in this study was lower than previously reported. The incidence using SOP criteria was 10%, and 7% using RIFLE criteria. The authors do not specify at which time points mortality was assessed and report higher overall mortality than previously reported.8 Even higher mortality in SOP group was likely related to the overall poor prognosis in patients requiring continuous RRT. SOP criteria also identified additional variables associated with AKI, including older age, female sex and aortic valve surgery, which have been previously reported to predict increased risk of AKI. Interestingly, in this study RIFLE classification showed an association between AKI and CABG vs valve surgery or CABG-valve surgery, which is contradictory to previously published studies.

In addition to being performed at a single center, the study's limitations include retrospective design, the use of patient data that is 20 years old, and the choice of AKI definition criteria. The authors chose RIFLE AKI criteria as a comparison for SOP criteria. Recent modifications to RIFLE criteria have been established, including acute kidney injury network classification (AKIN) and KDIGO. Perhaps, the application of more contemporary criteria as a comparison to SOP would allow for identification of additional factors associated with AKI. Furthermore, SOP criteria relies on clinical judgement in interpretation of patient's hemodynamics, as well as signs and symptoms when evaluating the patient postoperatively. For instance, uremic pericarditis or impeding right ventricular decompensation are broad diagnostic criteria that require further guideline to account for wide range of clinical presentation. On the other hand, SOP criteria does not rely on kidney

function parameters, such as serum creatinine and urine output, which are dynamic parameters and may not accurately reflect renal function in real time during perioperative period.

Despite these limitations, this study is a valuable contribution to the literature evaluating the incidence and factors associated with cardiac surgery-associated AKI. SOP criteria allows for AKI diagnosis that does not rely on serum creatinine, glomerular filtration rate, or urine output which can be unreliable in perioperative setting. Although, the applicability and validity of SOP criteria as a predictive tool remains unclear, the identification of modifiable intraoperative and postoperative factors associated with increased risk of AKI can potentially impact perioperative treatment protocols. Additional research is needed to develop and validate sensitive and specific AKI risk stratification tools incorporating current AKI diagnostic criteria.

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LITERATURE REVIEWS

Association of Global Longitudinal Strain with Clinical Status and Mortality in Patients with Chronic Heart Failure

Tröbs SO, Prochaska JH, Schwuchow-Thonke S, Schulz A, Müller F, Heidorn MW, Göbel S, Diestelmeier S, Lerma Monteverde J, Lackner KJ, Gori T, Münzel T, Wild PS. JAMA Cardiol. 2021 Apr 1;6(4):448-456. doi: 10.1001/jamacardio.2020.7184

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Background

Multiple echocardiographic and laboratory biomarkers are currently used in the evaluation and prognostication of patients with chronic heart failure (HF). Left ventricular ejection fraction (LVEF) is one major echocardiographic finding that is commonly utilized in the medical decision-making process for HF patients. However, the utility of LVEF faces limitations in its prognostic utility, such as with diastolic HF patients[1] and intraobserver and interobserver variability.[2]

Myocardial strain imaging has emerged as a powerful modality that can measure subtle left ventricular myocardial deformations in longitudinal, circumferential, and radial spatial dimensions. Specifically, left ventricular global longitudinal strain (GLS) has been found to be predictive of long-term outcomes in patients with HF. However, most of the current evidence on GLS is still limited to small studies.

This large cohort study focuses on the investigation of clinical factors associated with GLS in HF patients, the relationship of GLS with established echocardiographic measures of cardiac function and N-terminal-pro hormone BNP (NT-proBNP), and the association between GLS with cardiac and all-cause mortality.

Study Design

The investigators of this study recruited patients from the MyoVasc study, which is an observational, prospective cohort study in Germany that explores the development and progression of HF.[3] MyoVasc enrolled 3,289 participants between ages 35 and 84 years with and without HF from January 17, 2013 to April 27, 2018, with a median follow-up of 3.2 years. Ultimately, 2,186 individuals from the MyoVasc cohort with American Heart Association (AHA) stages A to D HF were included in the analysis. Exclusion criteria for this study included cardiac arrhythmias, AHA stage 0 HF, and poor echocardiographic imaging quality.

All individuals participated in an extensive, standardized, 5-hour examination, which included documentation of history, laboratory work, and echocardiography. Left ventricular ejection fraction was calculated using Simpson's method in the apical four-chamber view, left ventricular mass indexed

to body height (LVMi) was calculated using the cube formula in the parasternal long-axis, and E/E′ ratio was measured during a complete cardiac cycle. The GLS was measured in all apical views, with two points at the LV base and one point in the LV apex manually selected for automatic tracking. Segments with persistently poor tracking were excluded from the analysis. All measurements were carried out by nine observers. Clinical outcomes for all-cause mortality and cardiac death were assessed by annual follow up through telephone interviews and quarterly checks of the vital status via national registration offices.

Results

Of the 2,186 participants, 1,418 participants were men (64.9%) and 768 were women (35.1%), with a mean age was 65 years. For analysis, study participants were separated into four quartiles of 546 or 547 individuals by increasing GLS impairment: first (GLS ≤-20.0), second (GLS >-20.0 to ≤-17.5), third (GLS >-17.5 to ≤-14.4), and fourth (GLS >-14.4). Multivariate regression analysis revealed that male sex, obesity, hemoglobin A1c, atrial fibrillation, coronary artery disease, and a history of myocardial infarction were clinical factors associated with higher GLS in individuals with HF. Univariate analysis revealed that GLS was associated with all established echocardiographic measures of cardiac function, including LVEF, LVMi, and E/E′, with the strongest association detected with LVEF. Multivariate analysis revealed that higher GLS was associated with higher NT-proBNP levels. In Cox proportional hazards regression analysis, there was a 1.55-times increase in all-cause mortality (95% CI 1.19-2.01; P<0.001) and 2.32-times increase in cardiac death (95% CI 1.57-3.42; P<0.001) per 1-SD higher GLS, after adjusting for image quality, observer variability, clinical profile, HF medications, NYHA class, and cardiac structure and function. However, after adjusting for NT-proBNP level, GLS remained associated with a 1.60-times increase in cardiac death (95% CI 1.07-2.41; P = .02), but not all-cause mortality (HR 1.26; 95% CI 0.95-1.66; P = .11).

Discussion

The main conclusion from this paper is that GLS may be a helpful clinical tool to improve risk stratification in individuals with chronic HF. The clinical factors associated with higher GLS scores were as expected. Specifically, sex was identified as one of the strongest clinical factors associated with GLS, and the authors postulate on a possible estrogen-mediated protective effect seen in females. The use of GLS for risk stratification also shows a superior benefit to LVEF in identifying patients with subclinical cardiac injury from hypertensive left ventricular hypertrophy with preserved LVEF. The association between GLS and establish biomarkers such as NT-proBNP validates the utility of GLS in grading the severity of HF.

While there were many strengths of the study (large sample size, standardization of cardiac workup), there were also limitations including assumptions made from a single-center study, missing GLS data, and the use of single-plane measurements of LVEF. This study amongst others reveals how GLS continues to gain value in the outpatient management of HF, but more studies are necessary to explore its utility in the perioperative setting. The perioperative use of GLS in cardiac surgery has been shown in a limited number of studies to be predictive of postoperative mortality and hospital length of stay[4,5]. Strain imaging technology will only continue to improve, and we may one day find the value of its routine use in the perioperative setting with our cardiac patients.

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PRO/CON DEBATE

At the end of the Pro/Con section, please take a moment to complete a brief questionnaire regarding inhaled pulmonary vasodilator.

Introduction

In this issue of the SCA Newsletter, inhaled pulmonary vasodilator therapy for pulmonary hypertension is discussed and debated. Specifically, three therapies are considered; Inhaled Nitric Oxide, Inhaled Epoprostenol, and Inhaled Milrinone. Pulmonary hypertension has multiple causes and results in significant morbidity and mortality. Management includes multiple considerations and therapeutic options including reversing the process of pulmonary hypertension with the administration of vasodilator therapy. Vasodilator therapy can be accomplished using the intravenous or inhaled route, both of which can relax the pulmonary arterial vessels **(FIGURE 1)**. The advantage of intravenous therapies are their lower cost, availability, and ease of application. However, non-specific intravenous vasodilators can reduce systemic blood pressure as well as increase intra-pulmonary shunt **(FIGURE 1)**. Inhaled vasodilator therapy has emerged as a viable option and, in some cases, a first line therapy for the management of pulmonary hypertension.

Once thought to be too expensive and/or require excess resource utilization, they are now readily available for perioperative application. Compared to intravenous medications, they are associated with improved matching of ventilation and perfusion resulting in improved pulmonary gas exchange and less shunting **(FIGURE 1)**. In addition, there may be fewer systemic effects such as hypotension. In this issue of the SCA Newsletter, three inhaled pulmonary vasodilator options are discussed and debated.

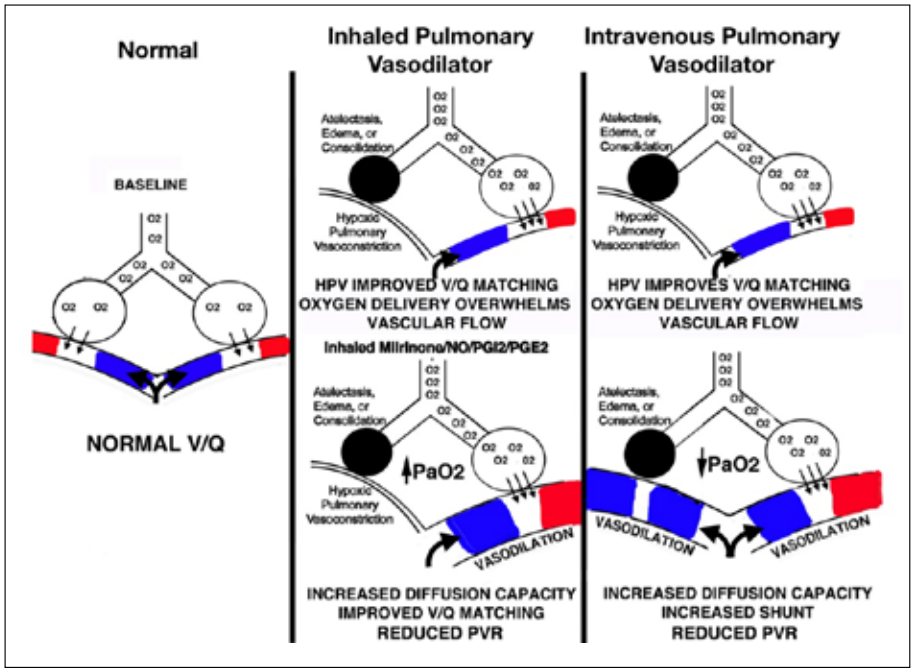

FIGURE 1: Schematic demonstrating the effects of inhaled and intravenous pulmonary vasodilators. While both are effective in reducing pulmonary vascular resistance (PVR), inhaled pulmonary vasodilators may improve matching of ventilation (V) and perfusion (Q) and increase gas exchange (O2). Although intravenous pulmonary vasodilators also reduce PVR, they may also impair V/Q matching and increase shunt. The larger curved arrows show the direction of pulmonary blood flow. The smaller arrows represent oxygen transport from alveoli to the pulmonary vasculature. CO2 = carbon dioxide; O2 = oxygen; V/Q = Ventilation/Perfusion ratio.

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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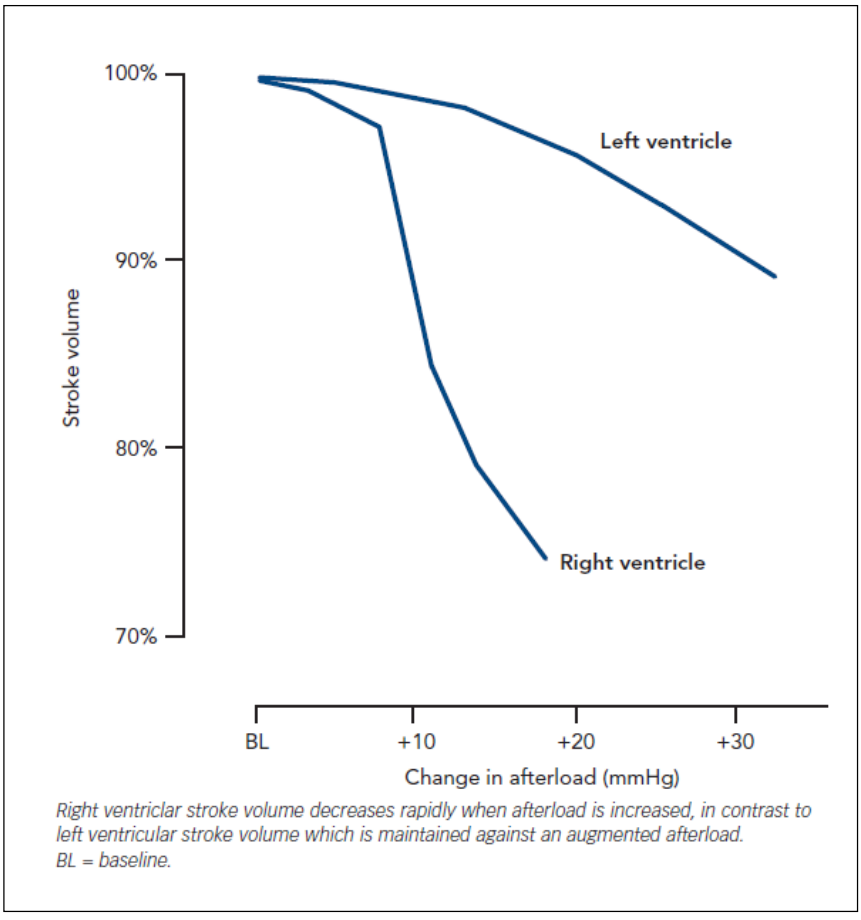
PRO: Inhaled Nitric Oxide in Cardiac Surgery

INTRODUCTION

Acute right ventricular (RV) failure represents a challenging problem in cardiac surgery. It is defined as the inability of the RV to pump adequate blood to the pulmonary circulation after separation from cardiopulmonary bypass machine. Normal RV function is depended on sufficient venous return, low-resistance right ventricular afterload, pericardial compliance, and the adequate contractility of both its free wall and the interventricular septum [1].

ETIOLOGIES AND PATHOPHYSIOLOGY OF ACUTE RIGHT VENTRICULAR FAILURE

There are many causes for this complex clinical syndrome. Any condition that leads to pressure overload, volume overload or insufficient myocardial contractility will distort right ventricular mechanics and function. The most common causes of acute right ventricular failure are summarized in table 1 [2].



Right ventricular stroke volume decreases rapidly when afterload is increased, in contrast to left ventricular stroke volume which is maintained against an augmented afterload.
BL = baseline.

FIGURE 1: Effect of increasing after load and stroke volume of the right and left ventricles. Cardiace Failure Review 2019;5(3):140–6. DOI: https://doi.org/10.15420/cfr.2019.15.2

Mechanism of acute right ventricular failure	Etiologies
Right ventricular ischemia	• Right coronary artery air embolism • Bypass graft failure: occlusion, kinked, or thrombosed
Preexisting reduced right ventricular myocardial contractility	• Chronic pulmonary hypertension • Preoperative right ventricular cardiomyopathy
Dynamic obstruction of the right ventricular outflow track [3]	• Hypovolemia • High dose inotropes •
Post-surgical reduction in right ventricular myocardial contractility	• long cardiopulmonary bypass and cross-clamp time • Inadequate myocardial protection
Development of acute pulmonary hypertension	• Protamine induced pulmonary hypertension. • Hypoventilation and hypercarbia leading to increase PVR. • Post-surgical compression of the pulmonary artery • Acute left ventricular failure
Arrhythmia	• Supraventricular tachycardia or high-grade atrioventricular block that lead to ventricular dyssynchrony and decrease myocardial contractility

TABLE 1: Causes of acute RV failure in the setting of cardiac surgery.

CONSEQUENCES OF ACUTE RIGHT VENTRICULAR FAILURE IN THE SETTING OF CARDIAC SURGERY

The consequences of developing acute RV failure are disastrous. The right ventricular chamber becomes more and more distended with development of severe tricuspid regurgitation, rapidly leading to increase venous congestion from stagnant and backward blood flow. Meanwhile, the lack of forward blood flow from the RV will impair filling of the left ventricular, leading to a decrease in the left ventricular stroke volume. Reduction in the left ventricle filling combined with the distortion of the ventricular septum subsequently lead to the development of low cardiac output syndrome.

Significant acute pulmonary hypertension is a serious cause of morbidity and mortality in patients undergoing valvular cardiac surgery or in surgery involving correction of congenital cardiac defects. Also, in the setting of heart transplantation and after institution of left ventricular assist support.

DETECTION AND DIAGNOSTIC MODALITIES

Intra operative transesophageal echocardiography is the primary diagnostic modality used to assess right ventricular size and function post cardiopulmonary bypass however, if pulmonary artery catheter is present, thermodilution technique can measure cardiac output and pressure.

Various echocardiographic techniques are used for assessment of RV size and function as described by American Society of echocardiography guidelines and British Society of echocardiography recommendation. [4].

1) Tricuspid annular plane systolic excursion (TAPSE) using M-mode to assess longitudinal ventricular measuring the excursion of the outer part of the tricuspid annulus between end-diastole and end-systole however, TEE M-mode TAPSE results are not accurate compared with transthoracic echocardiography because it is difficult alignment in midesophageal four chamber view "angle dependent" and only represent the longitudinal function of the basal portion [5]

2) Tissue Doppler imaging for tricuspid annular plane systolic velocity utilizes pulsed wave Doppler signals (S') to assess myocardial deformation at the tricuspid annulus.

3) Subjective morphological assessment:
    a. A flattened interventricular septum and D-shaped left ventricular cavity in diastole implies volume overload while D shaped during systole implies pressure overload.
    b. RV size enlargement
    c. RV free wall motion

4) Strain imaging by 2D using Transesophageal Speckle-Tracking Echocardiography. Impaired RV global longitudinal strain longitudinal and strain rate significantly predicts acute intraoperative RV dysfunction [6].

MANAGEMENT OF ACUTE RV FAILURE IN THE SETTING OF CARDIAC SURGERY

Rapid diagnosis of acute right ventricular failure with early identification of the underlying cause is required to the initiation of treatment. Management of RV has been directed towards optimization of RV preload, decreasing RV afterload, improving RV contractility, adjusting mechanical ventilation through the control of hypoxemia and hypercapnia all while restoring perfusion pressure.

Significant acute pulmonary hypertension is a serious cause of morbidity and mortality in patients undergoing valvular cardiac surgery or in surgery involving correction of congenital cardiac defects. Also, in the setting of heart transplantation and after institution of left ventricular assist support.

Pulmonary Vasodilators

These drugs act directly on the smooth muscle in the pulmonary vascular beds causing vasodilation and hence they reduce pulmonary arterial pressure. Vasodilators either administered intravenously or by inhalation and are effective in treating pulmonary hypertension.

Intravenous vasodilators

Intravenous vasodilators such as sodium nitroprusside, nitroglycerin prostaglandin I2, and prostaglandin E1 are potent pulmonary vasodilators and produce significant reduction in pulmonary vascular resistance (PVR). Mechanism of action is either through the release of NO, phosphodiesterase inhibitors, or activation of prostaglandin receptors thru adenylate cyclase stimulators. These agents are nonselective and, as a consequence, can lead to systemic hypotension and impair RV coronary perfusion and cause ischemia [7, 8].

Inhaled vasodilators

Inhaled vasodilators (e.g., nitric oxide, prostacyclin, milrinone) selectively produce vasodilatation of pulmonary vasculature thus, reducing PVR without significant systemic vasodilatation. Inhaled vasodilators are delivered primarily to ventilated lung. Every agent has its advantages and limitations.

Main limitation of these inhaled agents is in the setting of left heart failure as they can increase mortality.

We are presenting iNO benefits and advantages over other available Inhaled vasodilators.

NITRIC OXIDE AND MECHANISM OF VASODILATION IN VASCULAR SMOOTH MUSCLE

Endothelium-derived Nitric oxide or endothelium-derived relaxing factor is a naturally occurring vasodilator that is continuously generated and released from the vascular endothelial cells to regulate vascular smooth muscle tone. NO is synthesized by NO synthase enzyme. it binds to and activates guanylate cyclase, which increases cGMP level in the smooth muscle cells, and results in increasing calcium influx into the cell. This causes muscle relaxation and vasodilation. iNO is rapidly inactivated by hemoglobin [9].

PRO FOR INHALED NITRIC OXIDE

iNO is a powerful, rapid onset, rapid offset, and selective pulmonary vasodilator. iNO is given via a specialized delivery system of 10 to 80 parts per million (ppm) with typical initial dose of 20 ppm into the ventilator circuit to the ventilated lung. After it reaches the alveoli, iNO traverses the pulmonary vascular endothelium and reaches into pulmonary vascular smooth muscle cells, where it produces vascular smooth muscle vasodilation. Apart from the Cost of Nitric Oxide ($2760 per day) which remain significantly higher than both epoprostenol ($125 per day) and milrinone ($90 per day), inhaled nitric oxide (iNO) been extensively studied and has the greatest amount of evidence exists. iNO been used successfully in the treatment of right ventricular failure associated with pulmonary hypertension, mitral valve replacement, cardiac transplantation, and placement of LVADS. Review of the available literature suggests that iNO may be efficacious in managing patients undergoing lung transplant as it significantly reduces the rate of allograft dysfunction and ischemia-reperfusion injury. Also, iNO is better in the management of refractory hypoxemia after lung transplant compared with Epoprostenol. iNO setup and incorporation into the ventilation system is illustrated in figure 2.

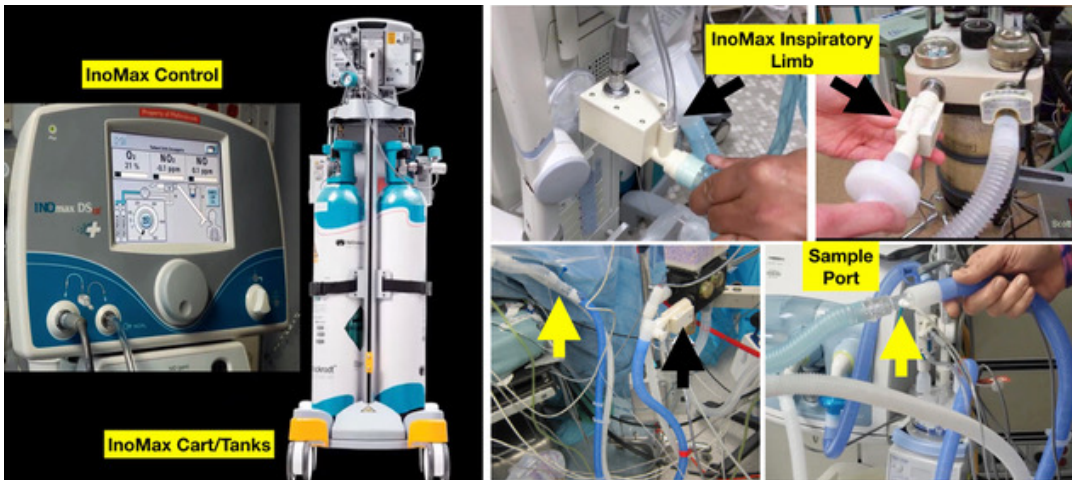


FIGURE 2: Inhaled Nitric Oxide (iNO) using the InoMax system (inomax.com; Mallinckrodt Pharmaceuticals): Administration of iNO includes a specifically designed control panel, and cart, the latter carrying iNO tanks. The drug inspiratory component (black arrow) is placed in the most proximal part of the inspiratory limb. The drug level is monitored using a sample port at a distal site of the inspiratory limb (yellow arrow).

Compared to nebulized milrinone (iMil), iNO pharmacokinetics has been determined for this route of administration and has developed delivery systems to achieve titratability to a hemodynamic goal on the other hand iMil has limitation for it is inability to determine the exact dosages when given thru nebulization and inability to titrate to a hemodynamic goal [10, 11]. iMil has a longer duration of action which makes it more difficult to titrate to effect. More research of iMil is needed to determine acceptable inclusion criteria, long-term outcomes, and management strategies including time, dose, and duration [12].

Although aerosol delivery of inhaled prostacyclins (Flolan, Veletri) is very simple and is achieved by simple nebulizer attached to the ventilator circuit, it is very inefficient, because only 2- 3% of the medication that is administered reaches the alveoli [13]. Also, inhaled prostacyclins has the potential for the ventilator valves

to become stuck from the glycine buffering agent.

Inhaled epoprostenol has been associated with impaired in vitro measures of ADP-induced platelet aggregation, providing evidence that the drug has at least some systemic absorption. Inhaled epoprostenol has the potential to be associated with increases in bleeding time or chest tube drainage after cardiac surgery [ref 14]. Another study in CF-LVAD patients found earlier administration of

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PRO: Inhaled Milrinone is the Best Pulmonary Vasodilator

Milrinone has a long and tested record of decreasing PVR when administered intravenously.[1] Milrinone increases levels of cyclic AMP through inhibition of phosphodiesterase-3 decreasing its breakdown. This results in vascular smooth muscle relaxation in both the systemic and pulmonary arterial systems. Because of these properties, milrinone can exacerbate the low SVR state (vasoplegia) which can occur in the post-cardiotomy period.[2,3] It is widely accepted that inhaled NO, PGI2, and prostaglandin analogs are effective as pulmonary vasodilators and generally devoid of systemic vasodilatory effects.[4,5] However, whether inhaled milrinone is efficacious in this manner remains controversial. Some small RCTs and observational trials have shown that inhaled milrinone can produce pulmonary vasodilatation without changes in CO/CI, MAP and SVR.[6,7] One small study of ten patients undergoing permanent LVAD implantation showed no significant increase in systemic hypotension and reduced pulmonary artery pressures with inhaled milrinone when compared to institutional controls who received inhaled NO.[8]

A 2019 meta-analysis of 36 studies and 1438 patients by Rong et al. comparing IV and inhaled milrinone to placebo failed to show a significant association between inhaled milrinone and decreased MPAP. In the IV milrinone group, only a trend toward decreased MPAP was observed. The standard mean difference between the IV milrinone group and placebo was -0.22 (95% CI -0.48 - 0.05) which brings into question power and methodological limitations of the study since this association is widely accepted to exist.[1,9] In an editorial to follow, Nguyen et al. allude to the significant underpowering of the study (194 subjects in the inhaled milrinone group), as well as other limitations including lack of standardization in dose, delivery, and timing relative to surgery.[10]

In a randomized controlled study of 150 sequential patients having mitral valve surgery with primary pulmonary hypertension, Kundra et al compared a single dose administration of inhaled milrinone (50 ng/kg); inhaled levosimendan (24 ng/kg); and inhaled normal saline administered postoperatively on arrival to the recovery room. The results demonstrated a reduction in MPAP in both the milrinone and levosimendan groups. This study demonstrates in a relatively controlled manner the association of decreased pulmonary artery pressures with administration of inhaled milrinone. The duration of effect however was short lasting about 30 minutes. Interestingly, inhaled levosimendan resulted in similar reductions in MPAP but the duration was significantly longer lasting nearly three hours.[11] If inhaled milrinone's apparent short duration of action is not accounted for in study methodologies, a clinical effect may not be apparent even when present. The short duration of action with inhaled milrinone is consistent with the pharmacodynamics observed with bolus dose IV milrinone as well.[12]

In a study by Theodoraki et al, 36 patients from 2011-2014 were retrospectively split into groups of 18 with each group having received either inhaled milrinone or inhaled iloprost. The study was powered to find a 30% reduction in MPAP. The surgeries performed included mitral valve replacement, mitral and aortic valve replacement, and mitral valve replacement with coronary artery bypass. MPAP were statistically reduced in both the iloprost and milrinone groups at all time points, including the last time point-40 minutes post-administration. PVR, TPG, MPAP/MAP and PVR/SVR ratios were reduced in both groups as well. However, the effect was only significant in the milrinone group

up to 30 minutes. In the iloprost group, these changes continued beyond the 40-minute mark, again demonstrating the limited duration of action for single dose inhaled milrinone. Echocardiographic parameters including TAPSE and TAVel were also improved in both the iloprost and milrinone group. Interestingly, PVR, MPAP, MPAP/MAP, PVR/SVR differed between the milrinone and iloprost groups only the 40-minute time interval as the milrinone group parameters had largely returned to baseline.[13] Taken collectively, these studies suggest inhaled milrinone does produce statistically and clinically significant reduction in MPAP though duration of action is limited to about 30 minutes.

Given this relatively short effect from a single 50 ng/kg dose of inhaled milrinone, why then should this medication be pursued when there are other alternatives that have well established efficacy and longer durations of action? Taking into account that value is defined as the ratio of benefit /cost, one must consider the "costs" of inhaled NO, prostacyclin (PGI2, epoprostenol), and prostacyclin analogs such as iloprost. NO is associated with toxic metabolites including N02 and requires an expensive and cumbersome delivery system. Its use is also associated with the formation of methemoglobin.[14] In the authors institution, the cost to the patient for one tank of NO can be in excess of $3000.00. Concerns for inhaled prostacyclin include susceptibility to light induced degradation thus requiring shielding, use of glycine diluent/vehicle that can spill in the breathing circuit and can cause obstruction of ventilator filters.[15] While inhaled Isoprost is devoid of many of these hazards, it remains considerably more expensive than milrinone.

Application of milrinone is relatively simple **[Figure 1]** and can be accomplished in the operating room using an available nebulizer. Milrinone comes in two different concentrations, 1mg/ml or 1mg/5ml. Either can be administered.

In conclusion, the use of inhaled milrinone for pulmonary arterial vasodilatation is in its infancy. Studies do show efficacy, but more research is needed on dose, frequency (continuous?), types of nebulization, adjustability or titratability, and pharmacodynamics. In the world if inhaled vasodilators, NO was the pioneer, prostaglandins represented a safer and less expensive alternative, and milrinone may be the next refinement, being potent, having very fewer side effects and being cost friendly. Time and will tell.

FIGURE 1: Inhaled Milrinone: Two concentrations are available; 1mg/ml or 1mg/5ml. 1-5 mg of Milrinone is injected into the drug chamber, which is nebulized using, in this picture, the Aerogen product (Aerogen.com, Ireland). A vibrator attached into the nebulizer piece, which is, in turn, connected to a T-piece. The Aerogen controller provides the vibration to nebulize the medication for either 30 minutes or continuously. The T-piece is placed in-line in the distal inspiratory limb (Red arrow), just prior to the endotracheal tube.

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PRO: Inhaled Epoprostenol is the Ideal Pulmonary Vasodilator

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Outcomes of chronic and acute pulmonary hypertension are well-described and related to both its primary etiology and its effect on right heart function.[1,2,3] Most of the right heart failure is due to left heart failure and pulmonary hypertension, the former being classified as post-capillary pulmonary hypertension.[1,3,4,5] If heart failure was solely due to post-capillary pulmonary hypertension (i.e., left heart failure) then application of selective pulmonary vasodilators, alone, may be relatively contraindicated.[1,3] Although post-capillary pulmonary hypertension can further decompensate to include capillary and pre-capillary pulmonary hypertension, for the sake of simplicity the following discussion regarding inhaled pulmonary vasodilators applies to post-capillary pulmonary hypertension.

The use of inhaled vasodilating agents for pulmonary hypertension provides selective pulmonary vasodilation, improves right heart function, oxygenation[6,7,8,9], and has minimal effect on systemic blood pressures.[10] The ideal pulmonary vasodilator agent should reduce pulmonary artery pressures (pulmonary vascular resistance), have rapid onset, be titratable, and have no side effects/adverse reactions.[10] Epoprostenol, a synthetic prostacyclin, was the first medication approved for treatment of neonatal pulmonary hypertension (PAH) in 1995; however, this was via intravenous injection.[6,7] In 1999, nitric oxide was the first inhaled medication approved for such use.[6,7] Since then, inhaled prostacyclin medications have also received approval for management for not only neonatal PAH, but for PAH due to other causes and adults in addition to the pediatric population.[6]

iNO is an effective pulmonary vasodilator, has a short biologic half-life due to rapid inactivation after binding to hemoglobin in the pulmonary capillaries, and consequently, has minimal or no reductions in systemic blood pressure.[11] Despite multiple studies involving other patient populations, iNO is FDA-approved only for the treatment of hypoxic respiratory failure associated with PAH in newborns.[12,13] Application of iNO for the adult population with PAH caused by congenital heart defects, Acute Respiratory Distress Syndrome (ARDS), and chronic obstructive pulmonary disease (COPD) has been met with disappointing results without significant outcome benefit.[13] Side effects include methemoglobinemia during administration and rebound PAH after discontinuation.[13] Inhaled administration is not an FDA-approved route for Milrinone. Its use as an inhaled agent has been reported as early as 2001 and has gained support based on cost and ease of application.[14,15] Despite an increase in popularity, the pharmacokinetics of inhaled Milrinone (iMil) have not been fully elucidated (effect duration approximately 20-60 minutes), there is no established dosing schedule, and there is very little data regarding continuous infusion.[6,7] At best, inhaled Milrinone is a useful preliminary medication to be followed by more established continuous therapies.

iEPO

Epoprostenol, a synthetic prostacyclin, is a lipid with vasodilatory, anti-inflammatory, antiproliferative, and antithrombotic properties normally produced by the pulmonary vascular endothelium.[8] Patients with pulmonary hypertension (PAH) have a decreased expression of prostacyclin synthase within the vascular endothelium, resulting in a deficiency of endogenous prostacyclin production,

and reduction in pulmonary vasodilation.[16] Exogenous administration can overcome this deficiency and induce pulmonary vasodilation.

Intravenous Epoprostenol was the first FDA-approved therapy for the intravenous treatment of pulmonary arterial hypertension (PAH) in 1995.[8] Intravenous pulmonary vasodilating agents like Epoprostenol can be problematic due to systemic vasodilation, which may decrease right coronary perfusion, and worsen right ventricular contractility.[6,7,9,17,18] In addition, non-selective pulmonary arterial dilation due to intravenous administration of vasodilators impairs intrapulmonary ventilation-perfusion matching and gas exchange, therefore increasing shunt.[9,17,18]

Inhaled Epoprostenol have been studied as early as 1996, when two studies reported favorable comparisons to iNO.[9,19,20] Since then, there is an abundant amount of data supporting its clinical benefits in patients of all ages and multiple etiologies of PAH.[6,7] In addition to its clinical benefits, inhaled Epoprostenol can be administered inexpensively and continuously using common perioperative equipment [FIGURE 1 and 2].

FIGURE 1: INFUSION RATES OF CONTINUOUS INHALED EPOPROSTENOL

Inhaled Epoprosterenol

Inhaled Epoprostenol Infusion Rate

Weight	40kg	50kg	60gk	70kg	80kg	90kg	100kg
10 ng/kg/min	1.0 ml/hr	1.0 ml/hr	1.2 ml/hr	1.4 ml/hr	1.5 ml/hr	1.8 ml/hr	2.0 ml/hr
20 ng/kg/min	1.6 ml/hr	2.0 ml/hr	2.4 ml/hr	2.8 ml/hr	3.2 ml/hr	3.6 ml/hr	4.0 ml/hr
30 ng/kg/min	2.4 ml/hr	3.0 ml/hr	3.6 ml/hr	4.2 ml/hr	4.8 ml/hr	5.4 ml/hr	6.0 ml/hr
40 ng/kg/min	3.2 ml/hr	4.0 ml/hr	4.8 ml/hr	5.6 ml/hr	6.4 ml/hr	7.2 ml/hr	8.0 ml/hr
50 ng/kg/min	4.0 ml/hr	5.0 ml/hr	6.0 ml/hr	7.0 ml/hr	8.0 ml/hr	9.0 ml/hr	10.0 ml/hr

FIGURE 1: Using the dilution as recommended (0.5mg Epoprostenol in 50 ml diluent) the above table are the infusion rates for patients ranging from 40-100 kg and infusion rates ranging from 10-50 ng/kg/min.

FIGURE 2: SET UP FOR ADMINISTRATION OF INHALED EPOPROSTENOL

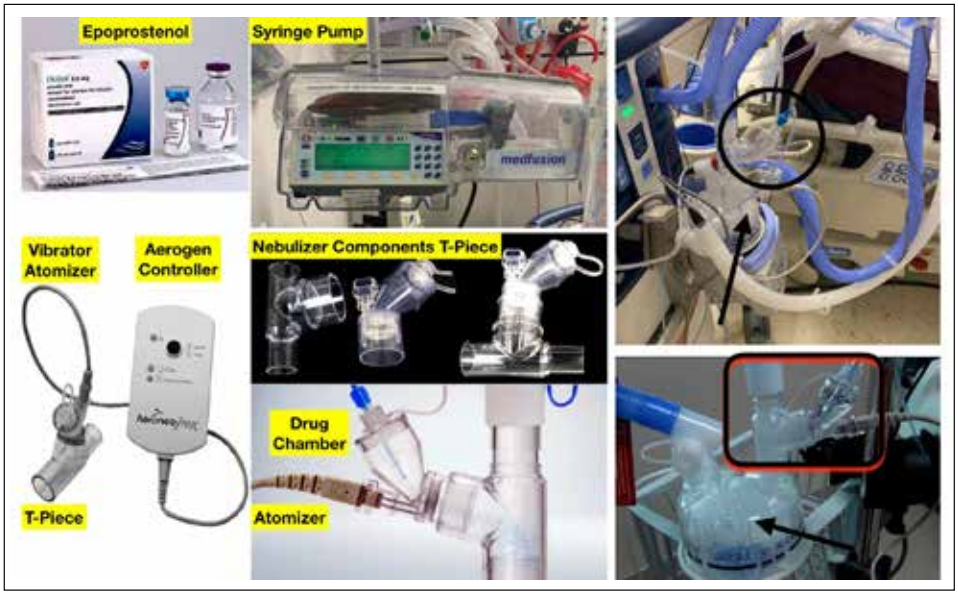

FIGURE 2: Inhaled Epoprostenol (Flolan): 0.5 mg of Epoprostenol is diluted into 50 ml of diluent and held in a 50 ml syringe to be infused using a syringe pump. The medication is infused into a drug chamber (black rectangle and circle), which is nebulized using a vibrator attached into the nebulizer piece (black rectangle and circle), which is, in turn connected to a T-piece. The Aerogen controller provides the vibration to nebulize the medication. The T-piece is placed in-line in the inspiratory limb immediately proximal to a humidifier (black arrow).

In a retrospective cohort study, a direct comparison was made between iNO and inhaled Epoprostenol (iEPO) in patients with acute PAH following cardiac surgery.[21] The primary outcome was reduction of mean pulmonary artery pressure (mPAP) to < 30 mm Hg six hours after ICU admission from the operating room.[21] There was no difference in the primary outcome of reduction of mPAP to < 30 mm Hg 6 hours after ICU admission (iNO, 33 [67%] vs. iEPO, 35 [71%]; P = 0.83) (9). However, based on cost estimates, the median cost of iEPO per patient was $363.53 versus $2562.50 for iNO (P < 0.01).[21]

A single-center prospective quality improvement study examined 729 patients within 7 adult ICUs, ORs, and PACUs, and compared the cost-effectiveness of iEPO vs. iNO. The study showed an overall increase in inhaled pulmonary vasodilators during this time, yet the hospital decreased inhaled pulmonary vasodilator costs by 47% with the addition and substitution of iNO for iEPO.[22]

In 126 patients undergoing cardiac surgery with PAH (mPAP > 30mmHg or SPAP >40mmHg), hypoxemia (PaO2/FiO2 < 150mmHg), or right heart dysfunction (CVP > 16mmHg and cardiac index < 2.2L/min/m2) were administered iEPO (20ug/ml) and assessed.[23] iEPO was administered on average for 45.6 hours without adverse events. Mean PAP and mPAP/mBP decreased by 10-20% and was associated with an increase in cardiac index. There was no significant change in mean arterial pressure.[23] The total hours of iEPO administration were 5740 hours yielding a total cost equal to $35,878. By comparison, the same duration of iNO would cost $717,564.[23]

The effects of iEPO and iMil were compared individually and in combination in twenty patients undergoing coronary artery bypass grafting and/

or cardiac valvular surgery who met inclusion criteria of right ventricular systolic pressure greater than 60mmHg and/or a recorded pulmonary vascular resistance > 200 dynes/s x cm-5 (14). Low dose iEPO (10µg/mL) showed decreases in mPAP of 6%, in pulmonary vascular resistance (PVR) of 20%, and in the transpulmonary pressure gradient (TPG) by 21%. Patients who exclusively used iEPO had a statistically significant increase in PaO2 and SvO2 when compared to iMil alone (1mg/ml).[14] While the combined iEPO (10 µg/mL) and iMil (1 mg/mL) group had a 28% decrease in PVR, reductions in mPAP and TPG were not different than iEPO alone.[14]

The efficacy of iEPO is equivalent to that of iNO in reducing PAP and PVR, and both are supported by extensive data involving continuous administration.[9,24,25] However, the administration of iEPO is simpler and at a fraction of the cost.[9,24,25] Although iMil has favorable a pharmacodynamic profile as an inhaled pulmonary vasodilator, it is not FDA approved and its application is still being established with regards to dosing and continuous administration. Currently, iEPO is the ideal inhaled medication for management of PAH, based on data, an established continuous infusion protocol, FDA approval, cost, and ease of administration.

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