SCA NEWS

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
Knowledge • Care • Investigation

Volume 32, Number 16
August 2022

PRESIDENT'S MESSAGE

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

Welcome, and this month it is my distinct pleasure to welcome back Dr. Chris Troianos, our President from 2017-2019.

Christopher A. Troianos
MD, FASA, FASE
Past President
Society of Cardiovascular Anesthesiologists

Chris has been instrumental in securing the future of our specialty through his tireless advocacy for certification, and in the sections that follow he brings us up to date on the timeline for establishment (and examination) for subspecialty certification in cardiac anesthesia, through a report of a special session held at our Annual Meeting in Palm Springs this year.

"We are grateful for the opportunity to provide the best quality educational programming we can, both in person and online."

The Annual Meeting of the Society of Cardiovascular Anesthesiologists (SCA) held this past May 2022 in Palm Springs included a well-attended and important panel that discussed the rationale and process in establishing board certification in Cardiac Anesthesiology. The panel discussion was proposed and moderated by SCA President Andy Shaw and SCA Program Committee Vice Chair Mary Beth Brady who wanted to highlight the meaning and purpose of board certification to our society and to our specialty. Chris Troianos, Past President of the SCA, was joined by Tom McLoughlin (Director for the American Board of Anesthesiologists and Chair of the ABA's Taskforce on Cardiac Anesthesiology Board certification), Immediate Past President Stan Shernan, Abimbola Faloye, and Daryl Oakes.

Dr. Troianos began the panel discussion with an overview of the history, strategy, and process to the SCA application, given his role as the Chair of the SCA's Working Group on Cardiac Anesthesiology Board Certification. He pointed out that subspecialty certification typically follows the formal establishment of a curriculum, training requirements, and accreditation of training programs. The Accreditation Council for Graduate Medical Education (ACGME) approved an SCA sponsored application for fellowship training in adult cardiothoracic anesthesiology (ACTA) in 2006 and began accrediting cardiac anesthesiology fellowship training programs shortly thereafter.

The need for specialized cardiac anesthesiology training and care was driven by the population's shifting health characteristics and accelerated technological developments. Interest in cardiac anesthesiology training has been demonstrated by the ACTA Match data between 2013 and 2020, which reported a 36% increase in fellowship applications, a 43% increase in applicants matched, a 6% decrease in unmatched applicants, a 43% increase in positions filled, and a 30% increase in participating programs.

Continued...

PRESIDENT'S MESSAGE

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"The need for specialized cardiac anesthesiology training and care was driven by the population's shifting health characteristics and accelerated technological developments."

There are now 70 accredited programs with a capacity to train over 200 fellows each year. All ten of the highest-ranked hospitals for cardiac care by US News & World Report, have ACGME accredited cardiothoracic anesthesiology fellowships. However, the only opportunity for cardiac anesthesiologists to demonstrate their specialized training and expertise in cardiac anesthesia care is through a board certification in perioperative transesophageal echocardiography (PTE).

The SCA initially prepared and submitted an application to the American Board of Anesthesiology (ABA) in August 2012, in response to a request from the ACTA Fellowship Program Directors, who wished to acknowledge the education and training obtained through the newly accredited programs. ABA reviewed that application and sent a formal decision to SCA in the spring of 2013 that it would not endorse a cardiothoracic anesthesiology subspecialty certification application to the American Board of Medical Specialties (ABMS).

The SCA submitted a second application to the ABA in January 2020 that recognized the evolution of the subspecialty over the intervening years with a distinct and unique body of knowledge within anesthesiology. The application demonstrated that clinical applicability was sufficient to support a distinct clinical practice, with contributions to the scholarly generation of new information that advanced the field.

Cardiac Anesthesiology board certification was proposed to specifically recognize clinical expertise beyond echocardiography to include the anesthetic management of complex cardiac physiology, anticoagulation, hypothermia, circulation, mechanical ventilation, cardiac arrhythmias, end-organ ischemia, bleeding, and the systemic response to extracorporeal circulation.

This second application emphasized that those practicing cardiac anesthesiology have developed expertise to prevent, treat, and rescue patients from hemodynamic perturbations that are potentially life threatening as a consequence to their cardiac disease. Mechanical circulatory assistance for the treatment of heart failure has also evolved beyond the intra-aortic balloon pump, and now includes percutaneous extracorporeal circulatory assistance, which in some centers is initiated and managed by cardiac anesthesiologists. Expertise has also developed in the perioperative management of cardiac patients beyond the operating room to the critical care unit.

Dr. Troianos pointed out key data within the ABA application that included the SCA's own bi-annual salary survey with nearly 4,000 SCA members participating. More than 50% of respondents reported spending more than 60% of their clinical time providing cardiac anesthesia services. Dr. McLoughlin had also shared data from 1,760 ABA diplomats enrolled in maintenance of certification in anesthesiology, who identified that more than 25% of their practice was spent providing cardiac anesthesia care.

A key concern of the SCA was to maintain the importance of echocardiography knowledge within the new adult cardiac anesthesiology sub-specialty. The SCA shared their desire that potential diplomates must demonstrate their knowledge of PTE by passing the National Board of Echocardiography (NBE) Advanced PTE examination (Advanced PTEeXAM®). THE NBE's Advanced PTEeXAM® has been the "gold standard" for assessment of this knowledge throughout the world for over 20 years.

Continued...

The new ACA certification process will therefore include a pre-requisite that potential ABA ACA diplomates must pass the NBE's Advanced PTEeXAM® exam in order to enter the ABA's certification process. This allows the new ACA exam to focus on other aspects of cardiac anesthesia care, and not require those who have already demonstrated mastery of PTE knowledge to be redundantly tested on this same material.

Dr. Troianos shared another key element that led to submission of a successful ABA application, which was the ABA's own policy revision to allow current ABA Directors to engage subspecialty societies to evaluate the advantages and disadvantages of establishing subspecialty certification. Although ABA Directors could now listen to the society discussion, they remained unable to assist with the preparation of the application to the ABA. They maintained the requirement that specific inquiries regarding the application must be formally communicated to the Secretary of the ABA, who would then provide an official ABA response.

Another key development that differed from SCA's 2012 application was the decision to pursue cardiac, rather than cardiothoracic anesthesiology board certification. Similarly, the SCA's certification application did not include vascular, as included in the SCA's formal name. These decisions eliminated the controversy for those who provide thoracic or vascular anesthesia care, many of which do not pursue formal ACTA fellowship training.

"There was general agreement that this will likely be one of the most significant developments to advance the subspecialty of cardiac anesthesiology during our lifetime."

Of note, the American Society of Anesthesiologists (ASA) did not oppose the 2020 SCA application as they had in 2012. In contrast, the SCA's application was formally endorsed by the American Board of Thoracic Surgery, the National Board of Echocardiography, and the American Board of Internal Medicine, having heard from their cardiology constituents regarding the importance of cardiac anesthesia expertise among their colleagues with which they work collaboratively during structural heart procedures.

The ABA endorsed this new approach to subspecialty board certification and submitted their application to ABMS in December 2020, in response to the SCA's application to the ABA. ABMS notified ABA in June 2021 that they had approved a new board certification for Adult Cardiac Anesthesiology (ACA). The ABA convenes exam and certification oversight committees consisting of members recommended by SCA and ABA. The committees met virtually to discuss content outline and certification criteria in November 2021.

Dr. Troianos concluded his introductory remarks by thanking the SCA's working group on Cardiac Anesthesiology Board Certification consisting of a diverse group of academic, employed, and private practice cardiac anesthesiologists: Stan Shernan, Mark Stafford Smith, Alina Nicoara, Mary Beth Brady, Jennifer Hargrave, Andy Weisinger, John Allyn, and Jake Abernathy.

The panel then addressed relevant and important questions from the audience both in-person and on-line. An important point was made emphasizing that the intention of subspecialty certification is to improve standardization of educational curricula and learner effort, covering the full breadth of content expertise required for consultant-level cardiac anesthesiology practice.

It is anticipated that subspecialty certification will have a more beneficial effect on patient care than inclusion of the sub-discipline into general anesthesiology training does or would. Training programs would likely continue to increase with an established route to an ABMS certification.

Continued...

PRESIDENT'S MESSAGE

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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Many audience participants expressed thanks to the panel for explaining the process and rationale, with general agreement that this will likely be one of the most significant developments to advance the subspecialty of Cardiac Anesthesiology during our lifetime.

Finally, we are a Society founded in education and service to our members and their patients. As an organization that places high value on learning, it is important for us to learn too, both from our programmatic content and, periodically, our mistakes. We are aware that some of our members found some of the other content provided during our Annual Meeting to be in questionable taste and for this I unequivocally apologize. We have listened to all the feedback we have received from members (good and not so good) and will work hard to make sure the content in all our future programs remains of the highest educational and professional standards possible.

I remain immensely proud to be your President, and understand the buck stops on my desk. We will do better as we move forward, and we are grateful for the opportunity to continue to provide the best quality educational programming we can, both in person and online. Please enjoy the rest of the summer, and hopefully we can all find time for some vacation with our loved ones.

Sincerely,

Andrew Shaw

Mark Your Calendars for PoCUS 2023!

Please join us on **Thursday, February 16, 2023, in Atlanta, Georgia** for this fantastic opportunity for any anesthesiologist who is eager to implement basic echocardiography and point-of-care ultrasound into their practice. Before this live workshop, participants in this course will have access to online modules via the iTeachU app covering basic echocardiography and point-of-care ultrasound of the lungs, abdomen, blood vessels, and nerves. Participants who complete both the online iTeachU modules and the hands-on workshop at Echo Week can later submit a case log of studies to receive a program completion certificate. The course faculty for the workshop is comprised of anesthesiologists all of whom share an enthusiasm for teaching echocardiography and point-of-care ultrasound.

The workshop focuses on the practical application of point-of-care ultrasound and can be useful to anesthesiologists in private practice or in the academic setting.

We hope to see you in Atlanta.

Location: **Loews Hotel**
1065 Peachtree Street NE
Atlanta, GA 30309

SCA website will be updated as more information becomes available.

Registration opening soon!

Make Plans to Attend 2023 Echo Week!

The 2023 Annual Echo Week will take place **February 17 - 19, 2023.** This meeting is designed for anesthesiologists, cardiologists, cardiac surgeons, intensivists, sonographers, radiologists, and other medical professionals with an interest in perioperative echocardiography.

Participate in hands-on workshops, take pre – and post-tests to provide a baseline for your education in ultrasound and perioperative transesophageal echocardiography, network with your peers and sponsors, and earn CME credits!

Location: **Loews Hotel**
1065 Peachtree Street NE
Atlanta, GA 30309

Registration opening soon!

Do not miss out on the 2023 event – mark your calendars now!

SCA website will be updated as more information becomes available.

Annual Meeting is Heading to Portland, Oregon in 2023!

The SCA Annual Meeting and Workshops takes place **May 6-9, 2023** and will update you on the latest cardiothoracic anesthesia information through fantastic plenary sessions, controversial panel discussions, pro-con debates, hands-on workshops, mentoring sessions, and problem-based learning sessions.

Come and connect with the experts in the field of cardiovascular anesthesiology. Plan to hear on hot topics such as updates in coagulation, what is new in mechanical support, and professional development topics such as leadership and mentorship.

Start making your plans today to join us in Portland!

Location: **Oregon Convention Center/Hyatt Regency Portland**
NE Corner of 2nd Avenue
Portland, OR 97232

Submit an Abstract for the Annual Meeting!

Get ready to submit your scientific abstract or complex case to be considered for presentation at the 2023 Annual Meeting & Workshops!

Call opens: September 6, 2022
Call closes: November 10, 2022

Submissions will be accepted for the following calls:

- Scientific Program
- Fellow and Resident Complex Cases
- Super Echo

SCA website will be updated as more information becomes available.

Portland in 2023 – Here We Come!

Please join us in Portland, Oregon for a day of lectures, workshops, and mentoring through both PBLDs and resident/fellow sessions. Join us for a town hall discussion on anything you may want to explore or share with our panel of experts or with your colleagues. We are excited to offer you updates, controversies, and new practices in the field of thoracic anesthesia.

We are looking forward to seeing you all in Portland.

Location: **Oregon Convention Center/Hyatt Regency Portland**
NE Corner of 2nd Avenue
Portland, OR 97232

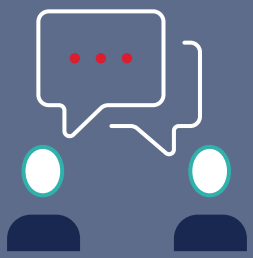
TASW Abstracts – Here's Your Chance to Present

You are invited to submit a scientific abstract or complex case for consideration for the 2022 Thoracic Anesthesia Symposium and Workshops!

Call opens: September 6, 2022
Call Closes: November 10, 2022

SCA website will be updated as more information becomes available.

Submit your abstract today!



SCA NEWS

2022 Call for Nominations is NOW Open!

Apply Today for an SCA Leadership Position
Submissions Close Monday, September 26, 2022

The opportunity is NOW if you want to play an integral role in shaping the future of the Cardiovascular Anesthesiology profession. The SCA seeks nominations for the following positions:

Eligible nominees must be an SCA "Active" Member in good standing.

President-Elect (1 opening)

- Term: 2-year term commencing in May 2023.
- Overview: The President-Elect shall assist in the performance of the President's duties, serves as Chair of the CME Committee, and is responsible for the overall goals of the Society's educational programs.
- ***Prior to assuming office, each officer shall have completed at least one full term as an elected, appointed, or ex-officio member of the Board of Directors. (Bylaws Article 5, section 5.1.2)***
- Must attend up to 4 Board meetings per year.

Secretary/Treasurer (1 opening)

- Term: 2-year term commencing in May 2023.
- Overview: The Secretary/Treasurer is charged with monitoring and reporting the financial health of the organization, in addition to assuring the proper record of all formal Society proceedings.
- ***Prior to assuming office, each officer shall have completed at least one full term as an elected, appointed, or ex-officio member of the Board of Directors. (Bylaws Article 5, section 5.1.2)***
- Must attend up to 4 Board meetings per year.

Director-at-Large (2 openings)

- Term: 3-year term commencing in May 2023.
- Overview: The Director-at-Large will bring expertise in cardiovascular anesthesiology, governance, and finance to the Board.
- **The ideal candidate will have prior SCA involvement experience.**
- Must attend up to 4 Board meetings per year.

Continuing Medical Education (CME) Committee Member (1 opening)

- Term: Up to a 4-year term commencing in May 2023.
- Overview: The CME Committee leads and facilitates the independent development of unbiased, scientifically balanced, CME activities.
- **The ideal candidate will have prior SCA involvement experience.**
- Must be able to attend up to 2 CME Committee meetings.

Nominating Committee-at-Large Member (2 openings)

- Term: 2-year term commencing in May 2023.
- Overview: The Nominating Committee assembles a list of the willing and most qualified candidates for positions in the Society leadership.
- **Nominating Committee members should have knowledge of the Society and previous involvement with SCA.**
- Must be able to participate in up to 4 meetings per year.

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All nominees for any of the positions listed on previous page must submit the following:

- A self-nomination letter or a letter of nomination from a Society member (for self-nominees, this letter cannot be combined with the statement of intent).
- Two letters from Society members seconding the nomination.
- A statement of intent from the nominee.
- The nominee's curriculum vitae.
- Biography – **150 words or less** (Those more than 150 words will be returned for revisions).
- A high-resolution, color business photo of the nominee.

If you are self-nominating or submitting your application:
Please complete the online application. Your SCA username and password is required.

CLICK HERE

to submit your application.

Submissions are due by 11:59 pm (Eastern) on Monday, September 26,2022.

If you are nominating another SCA member:
Please submit your letter of nomination to committees@scahq.org.

Newly elected leadership will be required to attend the Annual Meeting May 6 – 9, 2023.

Questions? Call us at 855.658.2828 or email committees@scahq.org.

The Society of Thoracic Surgeons

Join us for this September Conference

On behalf of The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists, we invite you to join us at the Sheraton Denver Downtown Hotel on September 8-10 for the **19th Annual Perioperative and Critical Care Conference.**

This event will include interactive presentations, hands-on demonstrations, and scientific abstracts — all dedicated to cardiovascular and thoracic critical care and enhanced recovery after surgery.

Every member of your critical care or ICU team will benefit from hearing new concepts, management protocols, and clinical experiences in their respective disciplines shared by an expert, multidisciplinary faculty. Continuing medical education, perfusion, and nursing credits will be offered.

Join us September 8-10

View Agenda | Register Now

Do not miss the opportunity to attend a conference of this caliber! To secure hotel accommodations, **reserve your room** at the Sheraton Denver.

Questions?

- **Program and Abstracts:** education@sts.org
- **Registration and Housing:** meetings@sts.org

Accreditation Information

The Society of Thoracic Surgeons is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Society of Thoracic Surgeons designates this live activity for a maximum of 14.25 *AMA PRA Category 1 Credits™.*

STS has applied for nursing and perfusion CEUs for this course. Further information is forthcoming.

The Call for Volunteers Opens in October!

The Call for Volunteers, which is the process in which SCA committees are populated, will open in October for the 2023-2024 term.

Watch your in-box and future issues of the Newsletter for more details.

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The Call for Research Grants Opens Soon!

The 2023 Research Grant applications open in October.

SCA Members are eligible to apply for 1 of 3 types of grants offered in 2023:

- **SCA/IARS Starter Grant** – up to $25,000 a year for 2 years
- **SCA/IARS Mid-Career Grant** – up to $50,000 a year for 2 years
- **Diversity and Inclusion Grant** – up to $25,000 a year for 2 years

Award recipients will be announced during the SCA 2023 Annual Meeting & Workshops. The grant period of 24 months can begin any time from July 1 to December 31 of the year granted.

Applications will close in January 2023. More information about these funding opportunities will be posted on the SCA website.

SCA Affirms Importance of Patient-Physician Relationship

The Society of Cardiovascular Anesthesiologists (SCA) is an international organization of healthcare professionals whose mission is excellence and leadership in providing cardiovascular and thoracic patient care through education and research. SCA is not an advocacy organization. However, we support safe, equitable, and unobstructed access to all healthcare. SCA strongly objects to any interference in either the medical decision-making process or the physician-patient relationship.

Still Time to Register for the ICCVA-CASSA Meeting

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SPECIAL INTEREST GROUP NEWS

Advancement in simulation education, research, and collaboration

SIM

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Simulation in Cardiothoracic Anesthesia (SIM) Special Interest Group is Making Waves

As cardiac anesthesiologists, we are often confronted with conflicting clinical challenges and a wide range of patient-specific parameters. Consequently, we are most equipped with mental algorithms, based on our clinical experiences, which allow us to find rapid solutions in complex situations. These conceptualized pathways, as essential as they are, will not be truly effective if they are remotely accessed and not put into action frequently. Medical education has significantly transformed over the last decade and simulation training has been identified as an effective venue for education. Simulation training is a safer method of learning in high-stakes scenarios, making it appealing to training programs at all levels. It is therefore not surprising that most major academic centers have incorporated this important educational tool into the medical education curriculum as well as resident and fellowship programs.

The SIMulation Special Interest Group (SIM SIG) was created to provide a platform for advancement in simulation education, research, and collaboration. We would like to encourage our national and international colleagues to join this effort which will enrich learning, enhance communication skills, and improve patient care. The SCA leadership has always been a strong advocate for advancement of education and patient care and has provided unwavering support for the creation of this group.

Our SIM SIG will begin its mission with efforts revolving around three main axes:

1) Regularly Scheduled Meetings

Why? Our bimonthly meetings will provide a space for shared ideas, updates on existing projects and the launching of new initiatives.

2) Online Education

Why? Online educational tools and webinars will help to improve access and collaboration both nationally and internationally. In addition, we will showcase the current simulation efforts by all members of the society.

3) SCA Annual Meeting

Why? The goal is to give our SIG permanent presence at the annual SCA meetings, where our members can meet in-person and create opportunities for networking and engagement within the larger SCA community. These interactions will allow our SIG to build a strong foundation and to have robust growth for years to come.

We want to take this opportunity to share with you that Healthcare Simulation Week will be celebrated around the world September 12-16. As the Society for Simulation in Healthcare has put it, we want to celebrate "professionals who use simulation to improve safety, effectiveness and efficiency of healthcare delivery." This was exemplified during the COVID pandemic where experts in simulation were in a unique position to impact the lives of many through simulation education. When COVID arrived in 2019 bringing the entire world to a standstill, the healthcare community witnessed first-hand the value, power, and impact of simulation education. To celebrate "SIM Week" we will be showcasing members of our society who are involved in simulation. The table below highlights a handful of SCA simulation educators and their respective areas of interest, who participated in our kickoff meeting.

The SIM SIG is excited to have a place in the SCA and we are looking forward to continued growth. In the upcoming weeks we will be sending out a survey to learn more about who you are and what you are currently doing in this exciting field. Please consider joining the SIM SIG!

SIM NEWS

SCA is Proud to Introduce the Simulation Cardiovascular Anesthesia (SIM) SIG Leadership:

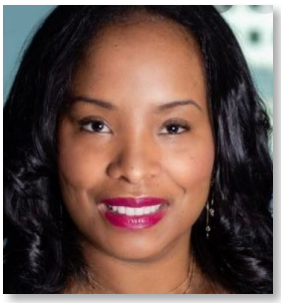
Chair

Sergio Bustamante MD, MS, CHSE
Cleveland Clinic

Vice-Chair

Sujatha Bhandary, MD
Emory School of Medicine

Secretary



Michele Sumler, MD
Emory School of Medicine

Meetings Leader

Choy R. Lewis, MD
Northwestern Medicine

Website Content & Advancement Leader

Shahriar (Charles) Shayan, MD
Northwestern Medicine

NAME	INSTITUTION
Anabelle Levine	Northwestern Memorial Hospital (IL)
Brett Wakefield	Cleveland Clinic (OH)
Farzad Ebrahimi	Advocate Illinois Masonic Medical Center (IL)
Harry Acevedo	Moffitt Cancer Center (FL)
Michele Sumler	Emory University (GA)
Neil Mohammed	University of Miami (FL)
Nikola Bradic	University Hospital Dubrava (Croatia)
Soojie Yu	Mayo Clinic (AZ)
Sushart Konar	Postgraduate Institute of Medical Education & Research
Sujatha Bhandary	Emory (GA)
Choy Lewis	Northwestern (IL)
Shahriar (Charles) Shayan	Northwestern (IL)
Sergio Bustamante	Cleveland Clinic (OH)

SIG Description: The mission of the SCA Simulation in Cardiothoracic Anesthesia Special Interest Group (SIM SIG) is to provide a platform for advancement in simulation education, research, and collaboration.

If you are interested in joining the SIM SIG, please **click here** to complete the online application.

SIM

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WICTA Fellow's Professional Development Webinar

The purpose of this webinar is to help develop the skills and confidence when searching and starting your first job as a cardiothoracic anesthesiologist.

Title:

Approaching the Job Search and Landing Your First Job as a Cardiothoracic Anesthesiologists

Date:

September 22, 2022

Time:

4:00 – 5:30 PM PT
5:00 – 6:30 PM CT
6:00 – 7:30 PM ET

FREE WEBINAR

Register Here

Moderators

Choy Lewis, MD | Northwestern Medicine
Agnieszka Trzcinka, MD, FASE | Tufts Medical Center

Panelists

Kiran Belani, MD | INOVA Fairfax
Diba Daneshrad, MD, MPH | Providence Cedar Sinai
Natalia Ivascu, MD | Weill Cornell Medicine
Linda Shore-Lesserson, MD | Northwell Health
Marie La Penta McHenry, MD | ACAMG/Stanford
Tjorvi Perry, MD | University of Minnesota
Stanton Shernan, MD, FAHA, FASE | Brigham & Womens Hospital
Richard Thalappillil, MD | Montefiore Medical Center

WICTA

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MEMBER CORNER

AWEsome Woman Interview

Sasha K. Shillcutt, MD, MS, FASE

University of Nebraska Medical Center, Omaha, Nebraska

Introduction:

Sasha K. Shillcutt, MD, MS, FASE is a tenured and endowed Professor and the Vice Chair of Strategy in the Department of Anesthesiology at the University of Nebraska Medical Center (UNMC). Sasha is CEO & Founder of Brave Enough, a well-published researcher in cardiac anesthesiology and gender equity, author, and international speaker. Sasha's greatest passion is empowering and encouraging others to achieve well-being in their professional and personal lives. She speaks frequently to executives and leaders on the topics of professional resilience and gender equity. Her TEDx talk titled ***Resilience: The Art of Failing Forward*** has been viewed by thousands of people. Her writing has been published in both the New England Journal of Medicine and JAMA. She leads conferences and retreats for professional women through her organization, Brave Enough. Her first book, ***Between Grit and Grace: How to be Feminine and Formidable,*** has sold thousands of copies and her second book, ***Brave Boundaries,*** will be released September 6, 2022.

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

I fell in love with cardiac anesthesiology during my first rotation in the cardiac ORs in residency. I was determined to learn TEE as I immediately recognized the ability of imaging to influence perioperative medicine. I knew early on that I wanted to learn echocardiography so that I could answer questions that would allow me to have the maximum amount of information possible to take care of critically ill patients in the OR.

2. How did you hear about the SCA?

I heard about the SCA from one of our cardiac faculty during residency. I remember receiving an email announcing the Super Echo Panel, a new session for junior faculty to submit an interesting case and have the opportunity to present for a few minutes at the annual meeting. I decided I would submit a case and was selected. Being invited to present at the Super Echo Panel opened many doors for me in the society that I am grateful for. It was an important first step that built my confidence to put myself out there for more roles and join different committees to get involved.

3. What roles have you held for the society?

I have served on the Scientific Program Committee for multiple terms and led workshops at the annual meeting for several years. I introduced and put on the first transthoracic echo workshop, which was the first one ever put on by the SCA and at the time was a little controversial to put forward. It was successful and has evolved to be the PoCUS workshop, which is a phenomenal workshop. After serving several years on the program committee, I became the PBLD and Workshop Chair, then the Vice Chair, and then finished my term as Chair of the Scientific Program committee this year. I have also served on the Board of Directors, in WITCA, and on the CME Committee. I've had the privilege of being on faculty for the SCA Echo Board Week meeting and also the iTEE meeting, a basic TEE meeting we used to run as well.

4. What is one of your greatest achievements as a Cardiovascular/Thoracic Anesthesiologist?

I think my biggest achievement is through my service to the specialty as a teacher of echocardiography, as I have held several CME echocardiography courses throughout my career for my institution as well as taught in SCA courses and published quite a bit in

academia on echocardiography. I would like to think that I have shown our specialty that women have a place in both education and academic leadership. I hope I have shown a light on the importance of having women leaders, and that we are richer and more innovative society when we have women physicians at every table where decisions are made.

5. Do you have any advice for fellows and residents?
My biggest piece of advice is to remember that medicine is on average a 35-year career. It is a journey, not a sprint, and the most important thing you can give yourself is the gift of well-being. Only you know what brings you joy and what will keep you engaged in the long game of medicine; so, do more of whatever that is. It is different for every person, and only you know what lights your heart up and makes you the happiest in your career. I would also tell trainees to not let small-minded people limit what you can do. Find mentors who will listen and sponsor you in your passion.

6. Have you experienced any difficulties as a woman in the field?
I have experienced many challenges and obstacles as a woman leader in anesthesiology and still do. They don't stop as you progress, if anything, they increase. Once you recognize that you will be judged harsher and that you will often be left out of spaces you belong in, albeit unintentionally, you can either decide to push the door open on your own or you can back down. Sometimes, you find yourself doing a little of both. I have found the only way I can "stay in the fight" so to speak, is to have a small group of women and men who support me and who "get it". The SCA has many of those allies, and I am grateful for them all.

7. Do you have any advice for other women in the field?
Find a group of other women who understand. And invest in your own professional development; don't wait for some leader to invest in you as we know women are often overlooked for these opportunities.

8. How do you balance work and personal life?
I am a work in progress. I do, however, have extremely strong boundaries around my personal time. I have learned that the only way for me to maintain some sort of healthy relationships in my personal life is to set boundaries – mostly for myself – of what and when I will and will not do. I now teach these principles formally to other physicians through my company, Brave Enough, as I have figured this out and am I very passionate about physicians staying well.

9. What is something you enjoy doing outside of work?
My family and I love the beach and to travel. We enjoy any sport or activity that involves water, so we try and get away 2-3 times a year and hang out near water.

10. Would you change anything about the path you took to get to where you are now?
I wish I would have had an early career mentor in the first 1-5 years of my career to tell me to focus and help me learn to say 'no, thank you' early on to opportunities that did not fit my career goals.

11. What was the best piece of advice you received?
To never let my ego, get in the way of taking care of patients. And to not let small-minded people define my goals. I say these two things to myself on a daily basis, because I need them on a daily basis.

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THORACIC CORNER

Impact of Opioid-free Anesthesia After Video-Assisted Thoracic Surgery: A Propensity Score Study

Selim J, Jarlier X, Clavier T, et al. Ann Thorac Surg 2022;114:218-24

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Background

Enhanced recovery after surgery (ERAS) has become a focus throughout perioperative care for surgery patients. The European Society of Thoracic Surgeons (ESTS) and the ERAS society released guidelines for enhanced recovery after lung surgery in 2019 which highlighted the use of multimodal analgesia during thoracic and lung surgery for pain relief and reduction of postoperative opioid use.[1] Unfortunately there continues to be a lack of data supporting the optimal anesthetic technique to minimize postoperative pain and subsequent pulmonary complications.[2]

In this study the authors aimed to compare postoperative morphine consumption and pulmonary complications in opioid free anesthesia (OFA) and opioid anesthesia (OA).

Methods

This is a single center, observational retrospective study with propensity analysis, conducted on eighty-one adult patients undergoing thoracic surgery between April 2018 and November 2018, in Rouen, France. Patients enrolled in the study were undergoing lobectomy or segmentectomy utilizing video or robotic assisted thoracic surgery. Patients with a history of chronic pain, chronic analgesia consumption, current or prior drug abuse history, and patients who underwent conversion to thoracotomy were excluded from the study.

The OFA group (n=48) received a dexmedetomidine bolus preoperatively, with boluses of lidocaine and ketamine at induction, followed by infusions of dexmedetomidine, lidocaine, and ketamine intraoperatively.

The group assigned to OA (n=33) received remifentanil intraoperatively and morphine. Both groups received nefopam, paracetamol, and ketoprofen intraoperatively. Patients in both groups received a standardized regional anesthesia block by either paravertebral block (PVB) or serratus plane block (SPB) with 40mg of ropivacaine each. Postoperatively patients' pain was assessed on a numerical scale from 0-10. Patients with a pain score 5 of 10 or less received non-opioid analgesics including paracetamol, nefopam, and ketoprofen every 6 hours. Patients with a pain score 6 of 10 or greater received 10mg of morphine sulfate orally every 6 hours.

Uncontrolled pain was treated with intravenous patient controlled-system analgesia. Cumulative postoperative opioid consumption at 48 hours was evaluated as a primary endpoint. In addition, postoperative pain scores, hemodynamic and respiratory complications were assessed.

Results

The study's primary outcomes included evaluation of morphine consumption at 48 hours. Secondary outcomes included pain at 3, 24 and 48 hours, cumulative consumption of non-opioid analgesics at 48 hours postoperatively, and pulmonary

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complications. The total median cumulative morphine consumption at 48 hours was lower in the OFA group at 28.5mg compared to the OA group at 55mg (p=0.002).[3] Interestingly, there was a significant association between active smoking and increased morphine consumption (p=0.018).

Postoperative median pain score at 48 hours was lower in the OFA group compared to the OA group, (0 vs 2.5 p=0.034) respectively although there was no significant difference in pain scores at 3 and 24 hours. There was no reported difference between the groups in utilization of vasoactive medications and there were no respiratory complications or patient deaths.

Discussion

The current literature is limited in large scale randomized control trails focusing on outcomes of anesthetic techniques in thoracic surgical patients. The authors aimed to compare the effect on postoperative morphine consumption in patients who were administered an opioid free intraoperative anesthetic. Although this retrospective analysis suggests that an opioid free anesthetic in thoracic surgery may reduce postoperative morphine requirements, it is limited by sample size and showed no statistical significance in postoperative complications or hospital stay.

Additionally, the authors did not discuss heterogenicity of regional anesthesia block, the possibility of remifentanil opioid-induced hyperalgesia, or the effect of OFA on chronic pain postoperatively. Further studies with larger patient population, a control group, and follow-up for chronic pain should be considered to determine if opioid free anesthesia for thoracic surgical procedures provides a clinical benefit.

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LITERATURE REVIEWS

Frailty and Perioperative Patient-Reported Disability in Patients Undergoing Cardiac Surgery: A Pilot Study

Benjamin Milne, Joshua Lucas de Carvalho, Salma Ayis, Sanjay Chaubey, Habib Khan and Gudrun Kunst. Frailty and Perioperative Patient-Reported Disability in Patients Undergoing Cardiac Surgery: A Pilot Study. Br J Anaesth 2022; 128 (6): 949-958

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Background

Frailty, characterized by vulnerability for the development of increased dependency and mortality when exposed to a stressor, has been strongly associated with postoperative mortality and morbidity specifically in cardiac surgery.[1,2] Disability, defined by the development of difficulty or dependency in completing activities of daily living, is a potential adverse outcome of the frail patient.[3] When selecting a cardiac surgical candidate and assessing operative risk using traditional risk scoring models, there is limited data concerning how preoperative frailty predicts patient-center outcomes such as patient-reported disability.

The authors of this study focus on the Comprehensive Assessment of Frailty (CAF) and WHO Disability Assessment Schedule 2.0 (WHODAS) to assess if frailty assessment can help inform surgical decision-making and contextualize surgical consent with a patient-centered outcome, such as disability scores. The authors propose that preoperative frailty would be associated with being free of disability and alive (disability-free survival [DFS]) at 3 months in adult patients undergoing elective cardiac surgery. Their aim was to further explore the association of preoperative frailty and perioperative disability scores.

Methods

This was a prospective, single-center cohort study of 146 patients who underwent elective cardiac surgery, such as coronary artery bypass graft, valvular replacement/repair or combination procedure surgeries at King's College Hospital from January to May 2016. Exclusion criteria included inability to provide informed consent, emergency surgery and severe concurrent CNS disease.

During preoperative assessment, all consenting participants underwent CAF evaluation which included biological marker evaluation, patient-reported levels of exhaustion and activity, physical tests of strength and stability and subjective investigator assessment using the Canadian Clinical Frailty Scale (the mean of two scores by two independent scorers, each blinded to the other's evaluation). Patients who scored ≥11 were assigned frail and <11 non-frail. Patients also filled out a 12-question self-reporting version of WHODAS to establish baseline values (in percentage of the maximum disability score, 48) and the binary outcome DFS (with disability defined as a value ≥25%).

Patients then underwent cardiac surgery according to approved institutional methods and were taken to the cardiac ICU post-operatively, following institutional protocols.

Post-operatively, operative characteristics and outcome data were collected by research members who were blinded to preoperative CAF and WHODAS values. At 1 and 3 months postoperatively, telephone interviews were conducted to establish levels of DFS using WHODAS values. Mortality data was also collected when appropriate.

Primary outcome was the association of preoperative frailty with postoperative disability-free survival (DFS) at 3 months. Secondary outcomes included patient-reported disability scores preoperatively, and 1 and 3 months after surgery.

Results

The final study sample was comprised of 146 patients who underwent preoperative frailty and disability assessment with 134 of those patients who completed follow-up at 1 month and 125 patients who completed follow-up at 3 months. When comparing the non-frail vs frail cohort, there was no statistically significant difference between the groups in age or operative characteristics. Factors that had statistically significant difference included preoperative CAF (median of 7.5 [non-frail] vs 14.5 [frail]), preoperative disability (11% [non-frail] vs 66% [frail]), frailty predicts death one year after cardiac surgery test score (mean of 5.6 [non-frail] vs 9.8 [frail]) and European system for cardiac operative risk evaluation II (1.2% [non-frail] vs 2.1% [frail]).

In investigating the primary endpoint of preoperative frailty association with postoperative DFS, preoperative frailty was associated with reduced likelihood of patients being free of disability and alive at 3 months. Frail patients had significantly higher perioperative median disability scores of 31.[3] preoperatively, 29.2 at 1 month and 14.6 at 3 months postoperatively when compared with non-frail patients, who had 10.4 preoperatively, 16.7 at 1 month and 2.1 at 3 months postoperatively. The fraction of people who were free of disability and who were alive was higher in the non-frail patient group with 64.8% and 90.7% at 1 and 3 months, respectively, when compared with frail patients, with only 39.5% and 69.2% at 1 and 3 months, respectively.

When evaluating the secondary outcome, median disability scores in frail patients were non-significantly reduced from baseline to 1 month (P=0.72) but significantly from baseline to 3 months (P=0.02), whereas non-frail patients had a significant increase in disability scores at 1 month (P<0.001), before a significant decline in disability scores at 3 months (P<0.001) when compared with preoperative disability scores. Non-frail patients had increased disability burden at 1 month, whereas frail patients had reduced disability burden (+4.2% vs -2.1%; P=0.04). Although the disability burden decreased for both groups at 3 months, this reduction was significantly greater in the frail patients (-6.3% vs -10.4%; P=0.02).

Empirical ROC analysis demonstrated that frailty and disability scores predict being free of disability and alive (DFS) at 3 months postoperatively more reliably when compared with the Euro-SCORE. CAF score shows a moderate correlation with WHODAS scores, a weak correlation with 1 month disability scores and a moderate correlation with 3-month postoperative disability scores.

Discussion

AThe result of this study demonstrated that preoperative frailty (determined by CAF score) is associated with reduced likelihood of being free of disability and alive compared with non-frail patients at 1 and 3 months postoperative. Notably, disability burden transiently increased at 1 month after surgery in non-frail patients, but continuously decreased in frail patients, demonstrating a positive trajectory of this patient-centered outcome for frail patients. Though frailty is associated with increased mortality, surviving frail patients are more likely to see continuous improvement of their disability burden after cardiac surgery when compared with non-frail patients. It may be due to the benefits from improved postoperative cardiac performance to those most seriously affected (i.e., the frail cohort).

Limitations of this study include sample size, risk of observer bias when incorporating subjective investigator's score into the CAF score, and potential recall bias for patients filling out WHODAS. Additionally, this cohort is limited to patients from a single center in Europe. Lastly, it is unclear how the authors determined the cut-off value for disability-free patients after cardiac surgery to be <25% given that the WHO guidelines continue to refine this threshold.[4]

In summary, the authors propose that although frail patients had higher disability scores postoperatively after cardiac surgery when compared to non-frail patients, within the group of frail patients, frailty may be associated with a relatively positive recovery trajectory of disability after cardiac surgery. Thus, using frailty measures like CAF in the preoperative period may help with perioperative optimization strategies and guide both patient expectation and surgical decision-making.

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Comparison of Different Metrics of Cerebral Autoregulation in Association with Major Morbidity and Mortality After Cardiac Surgery

Xiuyun Liu, Joseph Donnelly, Ken M. Brady, Kei Akiyoshi, Brian Bush, Raymond C. Koehler, Jennifer K. Lee, Charles W. Hogue, Marek Czosnyka, Peter Smielewski and Charles H. Brown IV British Journal of Anaesthesia, 129 (1): 22e32 (2022)
doi: 10.1016/j.bja.2022.03.029 Advance Access Publication Date: 18 May 2022, Cardiovascular

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Background

There is strong evidence in the literature, particularly in critically ill patients with neurological injuries that maintaining optimal mean arterial pressure (MAP) is associated with improved neurological and other patient outcomes. Optimal MAP is the MAP at which optimal brain autoregulation occurs. In cardiac surgery, it is common that optimal MAP values are not always achieved for various reasons such as cardiopulmonary bypass, non-pulsatile blood flow, need to decrease BP to avoid bleeding or to decrease aortic sheer stress or perhaps the need to decrease inotropic support.

In cardiac surgery there is not enough literature correlating outcomes such as morbidity, mortality, or acute kidney injury (AKI) with indices of cerebral autoregulation as it relates to MAP. There is evidence that optimal MAP can differ among patients as shown in differences in cerebral autoregulation, suggestive of individualized BP management. However, there is no unified method to assess hypoperfusion leading to significant variability in the literature.

Most studies in cardiac surgery use as a MAP threshold the lower limit of autoregulation (LLA), the lowest MAP at which cerebral perfusion is maintained, instead of the optimal MAP. Both optimal MAP and LLA can be estimated from cerebral autoregulation monitoring, but which is best to maintain in cardiac surgery to limit adverse outcomes? Cerebral autoregulation can be estimated with the transcranial Doppler-based mean flow index and the near-infrared spectroscopy-based cerebral oximeter index.

The transcranial Doppler-based technique is not possible in all patients and can be hard to maintain quality data through the temporal windows. The near- infrared spectroscopy technique is easier, but is it accurate or are we making assumptions? Finally, is it the duration only of hypotension leading to adverse outcomes, the magnitude or both?

Study Design

This is an observational study which took place at Johns Hopkins Hospital, Baltimore MD, between 8/4/2016 and 8/23/2019. Adult patients undergoing coronary revascularization, valvular surgery, myectomy or combined procedures were included. Patients undergoing transplants, ventricular assist devices, patients with ESRD on HD or patients without adequate transcranial Doppler window were excluded.

Data were collected continuously from induction of anesthesia till surgical closure. Invasive arterial BP, transcranial Doppler (Doppler Box; DWL, Singen, Germany) and near-infrared spectroscopy (Covidien, Boulder, CO, USA) for measurement of total hemoglobin and regional cortical oxygen saturation were used.

Calculations were performed using ICM+ software and the data collected were not used to manage the patient. Management goals were established after discussion between the Anesthesiologist and the Surgeon e.g. (MAP on CPB was >50-60 and in the ICU 65-90mmHg).

Transcranial Doppler- based mean flow index was calculated as a moving Pearson's correlation coeddicient[1] as well as the near-infrared spectroscopy based cerebral oximetry index.[2] Optimal MAP and LLA were measured from the U shape curves with both techniques.

To account for the duration of hypotension in the prediction model for adverse outcomes, the area under the curve (AUC) was calculated as the product of pressure difference or magnitude from optimal MAP or LLA multiplied by Δ time. Visual demonstration of patient outcomes at different pressure-time burdens were included in colorful graphs as described by Guiza et al.[3] The primary endpoints were to show association of AKI (AKIN criteria), major morbidity and mortality, incidence of stroke with deviation of MAP from optimal MAP or LLA. Occurrence ratios were calculated among hypotensive patients who experienced a bad outcome (e.g., NAKI/N. Outcomes comparison was performed between patients with prolonged bypass time, e.g. (>2h) vs (<2H), or cerebral oximeter saturation <50 vs >50.

Results

From the 240 patients included in the study, 205 patients had transcranial Doppler recordings. Optimal MAP could be identified in 91.3% and 94.2% using transcranial Doppler and cerebral oximeter index, respectively. Six patients had postoperative stroke, 23.3% AKI and 33.3% major morbidity and mortality.

The MAPs and AUCs calculated with both techniques were not statistically different. Mean flow index and cerebral oximeter index both identified the cerebral LLA, MAP below which was associated with increased incidence of AKI and major morbidity and mortality. MAP below LLA was found to be stronger associated with AKI and major morbidity and mortality than MAP below optimal MAP. AUC and duration of hypotension showed similar association with AKI and major morbidity and mortality.

Of all parameters examined the AUC of MAP<LLA had the strongest association with AKI and major morbidity and mortality with odds ratio of 1.05 (1.01-1.09), meaning that every 1mmHg increase in AUC (drop of MAP below LLA) is associated increased odds for AKI by 5% on average. No association was found between cerebral autoregulation metrics and stroke.

Finally, with visual demonstration of a colorful graft the authors showed that the exact demarcation of different risk thresholds may vary according to other factors. For example, patients who experience longer CPB or have lower cerebral oxygen saturation are more likely to develop AKI and adverse outcomes for the same level of low MAP.

Discussion

In this interesting observational study, the investigators show the strong association of hypotension, particularly when MAP is below the low level of cerebral

autoregulation, with postoperative AKI and severe morbidity and mortality.

The lack of association with stroke may be related to the low incidence of stroke in the study group.

The magnitude and duration of hypotension are equally significant. Near-infrared spectroscopy -based cerebral oximeter index and transcranial Doppler-based mean flow index can be used to estimate the optimal MAP and LLA for each patient.

It is the reviewer's opinion that further research is needed to clarify whether intervention using the information observed will aid in improving patient outcomes. It will be interesting to see if a randomized trial or perhaps a comparison of an individualized treatment approach with a traditional fixed protocol will help improve our knowledge and patient outcomes.

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Reassessment of Vegetation Size as a Sole Indication for Surgery in Left-Sided Infective Endocarditis

Gabezón G, López J, Vilacosta I, et al. J Am Soc Echocardiogr. 2022 Jun;35(6):570-575.

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Background

Left-sided infective endocarditis (LSIE) has a mortality rate in the range of 30% and with antibiotic therapy and surgery as only therapeutic options.[1] LSIE with symptoms like heart failure and sepsis are indications for surgery but guidelines also recommend surgery based on vegetation size in the absence of these symptoms.[2] LSIE of >10 mm size considered large and thought to be associated with increased mortality and surgery is suggested to be beneficial in this group.[3] In this retrospective study the authors studied the evidence about the benefit of surgery in patients with large vegetations when other indications are not present.

Methods

The study is a multicenter retrospective study. Patients with confirmed diagnosis of endocarditis based on the Duke criteria were recruited in the study. Vegetations were visualized and measured in all cases by two-dimensional transesophageal echocardiography within 48 hours of hospital admission.

The maximal length in at least two orthogonal views was calculated. With multiple vegetations, the largest vegetation was recorded for the statistical analysis. In the presence of a mechanical prosthesis, different views and projections were used to avoid the acoustic shadow. Right-sided IE and vegetation-free cases were excluded.

Uncontrolled infection was defined as: (1) fever for longer than 7 days without an identifiable source; (2) positive blood cultures after 72 hours of antibiotics; or (3) septic shock. Embolism was diagnosed based on clinical signs and from imaging tests. Mortality was defined as death occurring during hospitalization irrespective of its cause.

Results

A total of 726 patients studied. Patients were divided into two groups according to vegetation size: group A (vegetation >10 mm, n = 420) and group B (vegetation #10 mm, n = 306). The mean and median sizes of vegetation in group A patients were 19.4 and 16 mm, respectively. Univariate and multivariate analyses of all patients were performed and showed that age, Staphylococcus aureus, perivalvular complications, heart failure, kidney failure, and septic shock were independently related to death. It was found that the vegetation size was not independently associated with death.

Patients from group A has higher rates of mitral valve involvement (47.6% vs 38.2%; P = .012), ruptured leaflet (11.4% vs 5.6%; P = .006), and valvular regurgitation (73.6% vs 60.5%; P < .001) than group B.

Mortality rates were higher in group A (31.7% vs 24.8%; P = .045). No differences were found regarding heart failure, perivalvular complications, or embolism. Also, prosthetic valve was not found to be associated with poor prognosis. Surgery was not significantly related to survival in the 139 patients with vegetations >10 mm, who did not develop heart failure or uncontrolled infection: 18.6% mortality when surgery was undertaken (n = 70) vs 11.6% with only medical treatment (n = 69).

For patients from group A without heart failure or uncontrolled infection who had an embolism (n = 54), mortality was similar in patients who underwent surgery (n = 26; 18.8%) versus those who did not (n = 17; 13.6%).

Discussion

The study results show that vegetation size has increased mortality as shown in the previous studies.

[4]But in the study, surgery in patients with large vegetations without other indications was not associated with survival and did not show benefit from surgical intervention. In LSIE patients with heart failure or uncontrolled infection, the surgical intervention is beneficial.

In the absence of symptoms, surgery is recommended for the vegetation is larger than 15 or 10 mm by the current European and American guidelines, respectively. There is no standardized method for the echocardiographic evaluation of vegetations and maximal length is used to predict an embolic event in LSIE.

Size should not be the only parameter when assessing the embolic risk of a vegetation. Other risk factors for embolization are the microorganism, location, and morphology of the vegetation.[5] Mitral vegetations are more prone to embolism than aortic as well as vegetations caused by S. aureus. Timely initiation of antibiotic therapy is considered the most effective method to reduce embolic events.

The authors discussed some limitations of the study. The study design is retrospective, which increases the possibility of some biases in patient selection, and only in-hospital mortality was studied. The results cannot definitively conclude that surgery does not improve the prognosis in all patients with large vegetations as it has been reported that vegetation size is associated with complications like heart failure or failure to respond to antibiotics.[6]

In summary, this study supports the concept that large vegetations are associated with poor outcome, but surgical intervention may not be required in all patients with large vegetations and should be studied further.

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PRO CON

PRO/CON DEBATE

Prothrombin Complex Concentrate is Preferred to Fresh Frozen Plasma/Cryoprecipitate for Perioperative Coagulopathy

Perioperative bleeding and acquired coagulopathy increase morbidity and mortality and is directly responsible for up to 40% of trauma related mortality.[1,2,3,4] Decision making and management of bleeding and coagulopathy are guided by multiple variables ranging from baseline coagulation, mechanism of injury, cardiovascular, pulmonary, and metabolic functions, on-going bleeding, and product/factor cost, risks, and availability.[1,2,3,4] Confounding acquired or iatrogenic coagulopathy is the increased administration of anti-platelet and anti-coagulant medications used for cardiovascular pathologies and patients. More recently, societal, and institutional guidelines have been reported to improve utilization and outcome.[2,5,6] Optimally, decision making may be guided by point-of-care-tests such as activated clotting times and viscoelastic testing. However, time to perform tests may be a limiting factor. Excessive bleeding with hemodynamic instability seen in the perioperative period, especially that involving cardiac surgical patients, major liver surgery, and trauma patients may not be able to rely on on-going tests that require a relatively long time (> 10-20 minutes) to perform, and products and coagulation factors may be given despite suggested use.[7,8] For such patients an on-going discussion, debate, and research helps guide the clinician to help optimize care.[2,9,10] Information provided in this introduction and that found in the Pro-Con Debate regarding Prothrombin Complete Concentrate (PCC) and Fresh Frozen Plasma add to the knowledge base and demonstrate advancements in management of coagulation abnormalities.

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TABLE 1: DESCRIPTION OF COMMONLY USED BLOOD AND COMPONENT PRODUCTS

	Contents (per unit)	Dose	Changes	Volume	Onset	Cost	Risk/Benefit
FFP	All Coagulation Factors Fibrinogen (FactorI) 1-1.5gm Factor I/600ml	10-20 ml/kg	Raise Factor Levels 20%-30% Fibrinogen Increases 600ml increases Fibrinogen by 30-50 mg/dl 1500ml increases Fibrinogen 100 mg/dl	250ml/unit	Duration of infusion	$82/unit	Infection TRALI risk low TACO (Patients with history of CHF)
Cryo	Fibrinogen 150-250mg/20ml VIII vWF	1 unit/10kg Body Weight 1-2 pool = 5-10 units	1U/10 kg increase fibrinogen 50 mg/dl	100ml/unit	Duration of infusion	$345/5units	Infection TRALI risk low
Platelets	3-4x10^{11}Platelet/Unit 1 Unit = Pool of 4 to 6 whole blood–derived platelet concentrates	1-2 units	30,000/microliter	200-300 ml	Duration of infusion/Storage	$685/5units	Fever Allergic Reaction
Whole Blood	*Everything*	10-20 ml/kg	Hgb 1 gm/dl/70kg	450 ml	Duration of infusion	$200/Unit	All Blood Components Infection
4 Factor PCC	II 380-800 unit VII 200-500unit IX 400-620unit X 500-1020unit C 420-820unit S 240-680unit	Depends on INR 25IU/kg for INR 2-4 50IU/kg for INR >6	II 2.0units/dl VII 2units/dl IX 1.3units/dl X 2.0units/dl C 2.0units/dl S 2.2units/dl	500u/20ml 1000u/40ml	15-30 minutes	$1.27/unit or $2540 /2000unit	Purified; Low risk infection Thromboembolic Risk No Fibrinogen Need Vit K
FVII	Synthetic Factor VIIa 1200KIU/mg1.25 mg	≥ 25 ug/kg Infusion 50ug/kg/hr	Increase VII ≥ 0.5 ug/ml	Small volume	15-30 minutes	$2480/mg	Thromboembolic Risk Repeat Dosing Short Half Life < 5 hours
Fibrinogen Concentrate	Factor I	70mg/kg 1-4 gm/70 kg	Raise Fibrinogen 125mg/dl	50 ml per gram	15-30 minutes	$1000/gm	Purified; Low risk infection Thromboembolic Risk
DDAVP	Desmopressin	0.3-0.4 ug/kg	Stimulate release vWF from endothelium	4 ug/ml	30 minutes	$87/ml $870/10ml	Hypotension Headache Flushing

FFP = Fresh frozen plasma; Cryo = Cryoprecipitate; PCC = Prothrombin complex concentrate; F = Factor; DDAVP = 1-deamino-8-D-arginine vasopressin or Desmopressin; vWF = vonWillebrand Factor; ug = micrograms; kg = kilogram; ml = milliliter; dL = deciliter; mg = milligram; kg = kilogram; TRALI = Transfusion related acute lung injury; TACO = transfusion associated cardiac overload;

FIGURE 1: Simplified depiction of the coagulation cascade including Intrinsic, Extrinsic, and Common pathways. Primary hemostasis begins with platelet activation, adhesion, activation and formation of a platelet plug, providing a surface for the interaction and activation of coagulation factors (secondary hemostasis). Factors and their interactions are included as well as anti-platelet and anticoagulant therapies. Solid lines and arrows point toward activation pathways while dotted lines represent inhibition. The final hemostatic result is the cross-linked fibrin clot including platelet plug (square).

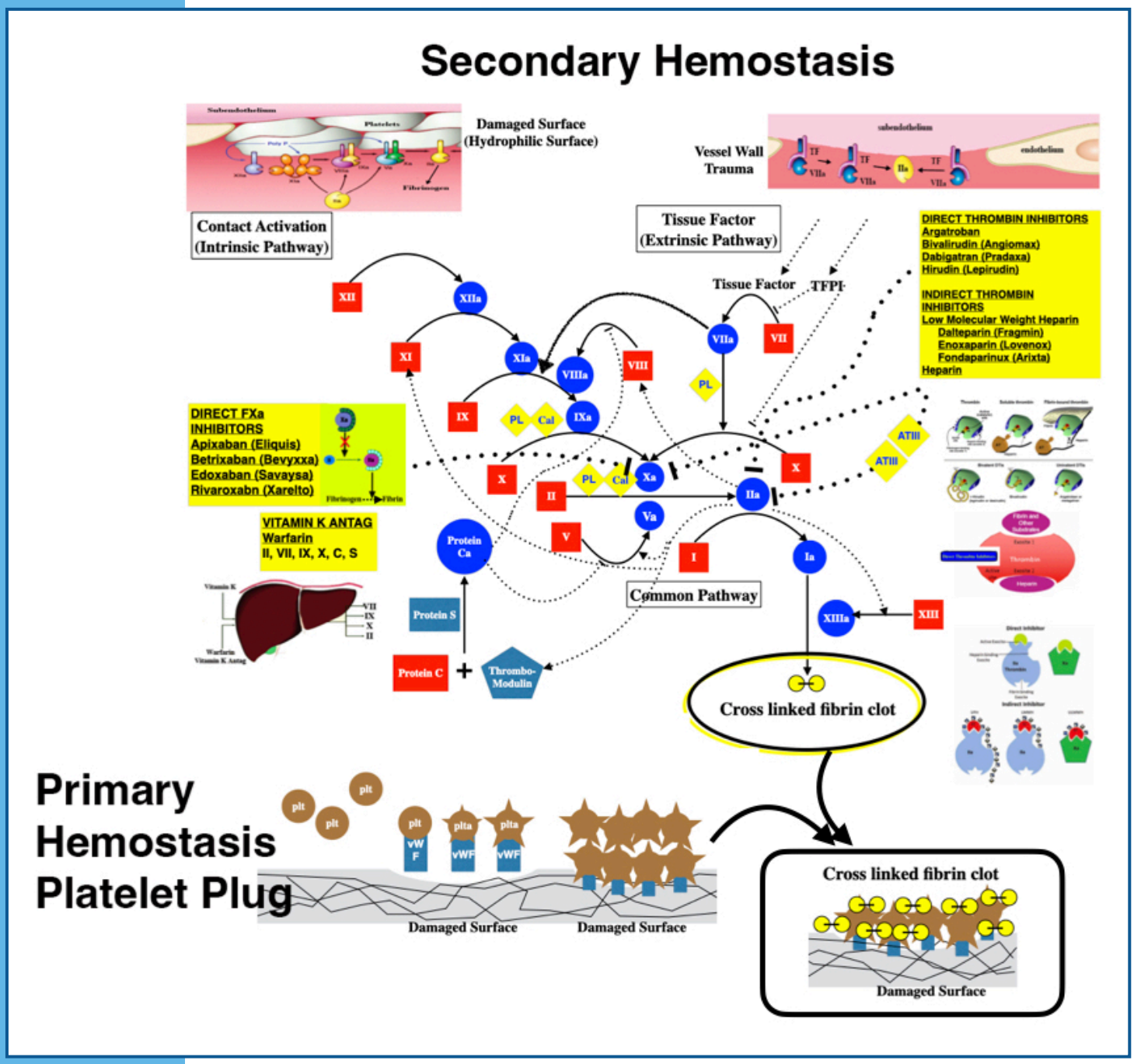


FIGURE 2: Example of a transfusion algorithm for intraoperative bleeding during cardiac surgery guided by point of care testing.

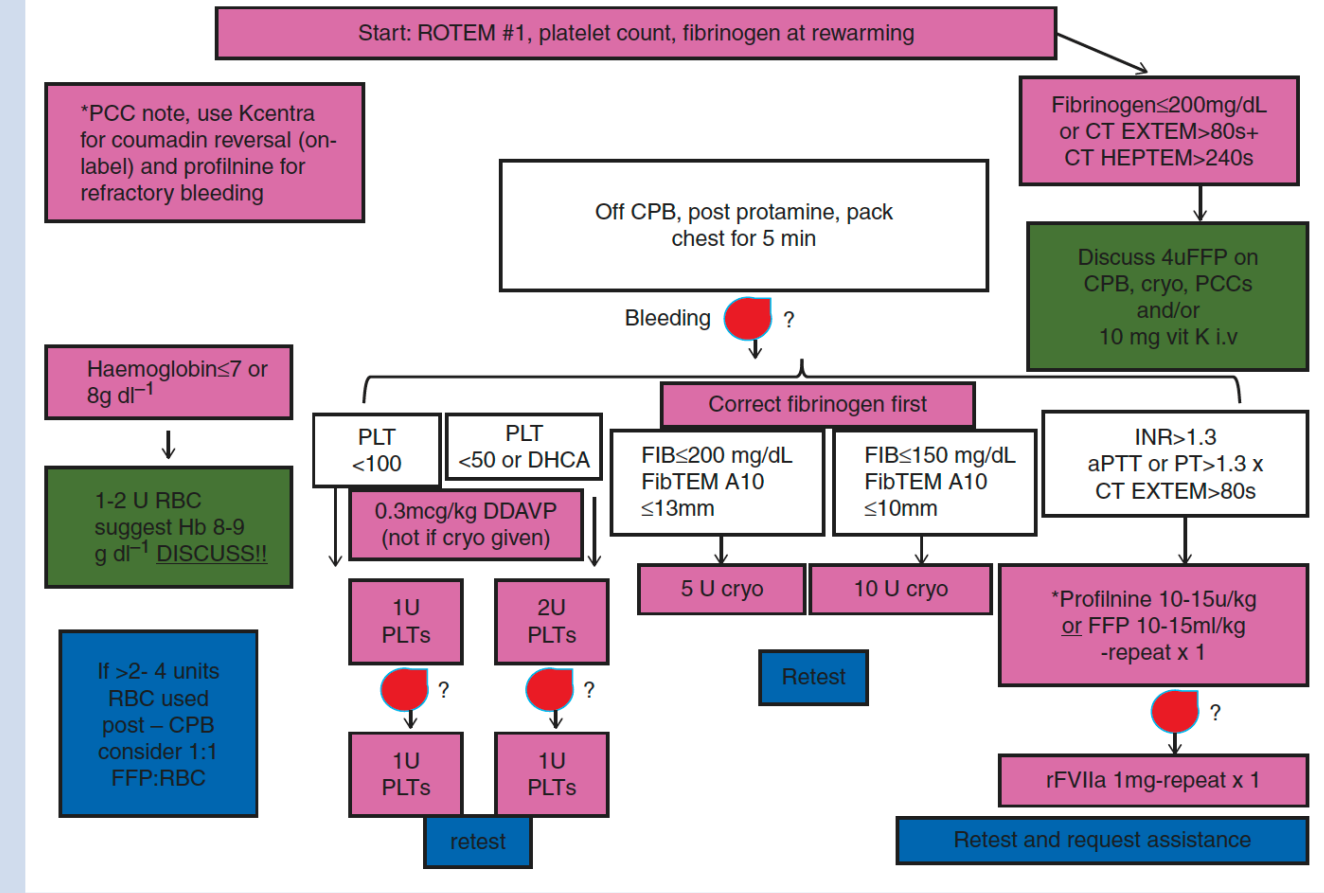


Fig 3 Transfusion Algorithm for intraoperative bleeding during cardiac surgery. In this laboratory, viscoelastic testing (ROTEM©) paradigm, samples are sent upon body temperature rewarming during CPB. Our algorithm directs the correction of hypofibrinogenaemia (using the Klaus Fibrinogen assay or FibTEM© A10 values and thrombocytopenia. Patients whom have undergone hypothermic circulatory arrest and the ensuing platelet dysfunction of hypothermia, receive platelet concentrate transfusion depending on platelet value during on-CPB rewarming values, when temperatures are >33 °C. Notably, because of established institutional practices, a first set of haemostasis blood samples are sent to the laboratory on CPB, and in order to account for heparin effect, HEPTEM© is sent in addition to EXTEM©. Thus, if HEPTEM© is >240 s, then it is presumed the added prolonged clotting time is as a result of additional factor deficiencies and requires FFP administration. A HEPTEM© CT <240 s indicates manufacture-established values after heparin antagonism. This value aids the practitioner in deciding on FFP administration while on CPB, in order to avoid delayed initiation of coagulation management after separation from CPB. Consideration is also made to post-CPB PCC administration, as PCC usage on CPB might be less useful owing to the larger volume of distribution and potential deposition of PCC factors onto CPB filters. With opportunities for clinical observation and laboratory values for deciding further clinical intervention, various deficiencies are managed through such blood, plasma, and factor concentrate administration. Antifibrinolytic therapy is standard practice for our cardiac surgical patients that require CPB. Notably, we have internally tested our 5U-pack of cryoprecipitate and have found fibrinogen concentration to range between 1.5-2.5 grams. We recommend a similar assessment locally within each hospital to help with best practice. *Figure modified from a draft version of our local cardiac surgery transfusion protocol.* AT III = Antithrombin III; CT = Clotting time; CPB = cardiopulmonary bypass; Cryo = Cryoprecipitate; FFP = fresh frozen plasma; FIB = Fibrinogen concentration; Hb = Haemoglobin; PCCs = Prothrombin complex concentrate; PLT = platelet count; RBC = Red blood cell; rFVIIa = Recombinant activated factor VIIa; U = unit.

With permission from: Ghadimi K, Levy JH, Welsby IJ: Perioperative management of the bleeding patient. Brit J Anaesthesia 2016;117:iii18-iii30. doi: 10.1093/bja/aew358.

FIGURE 3: Transfusion algorithm for intraoperative bleeding during noncardiac surgery guided by point of care testing.

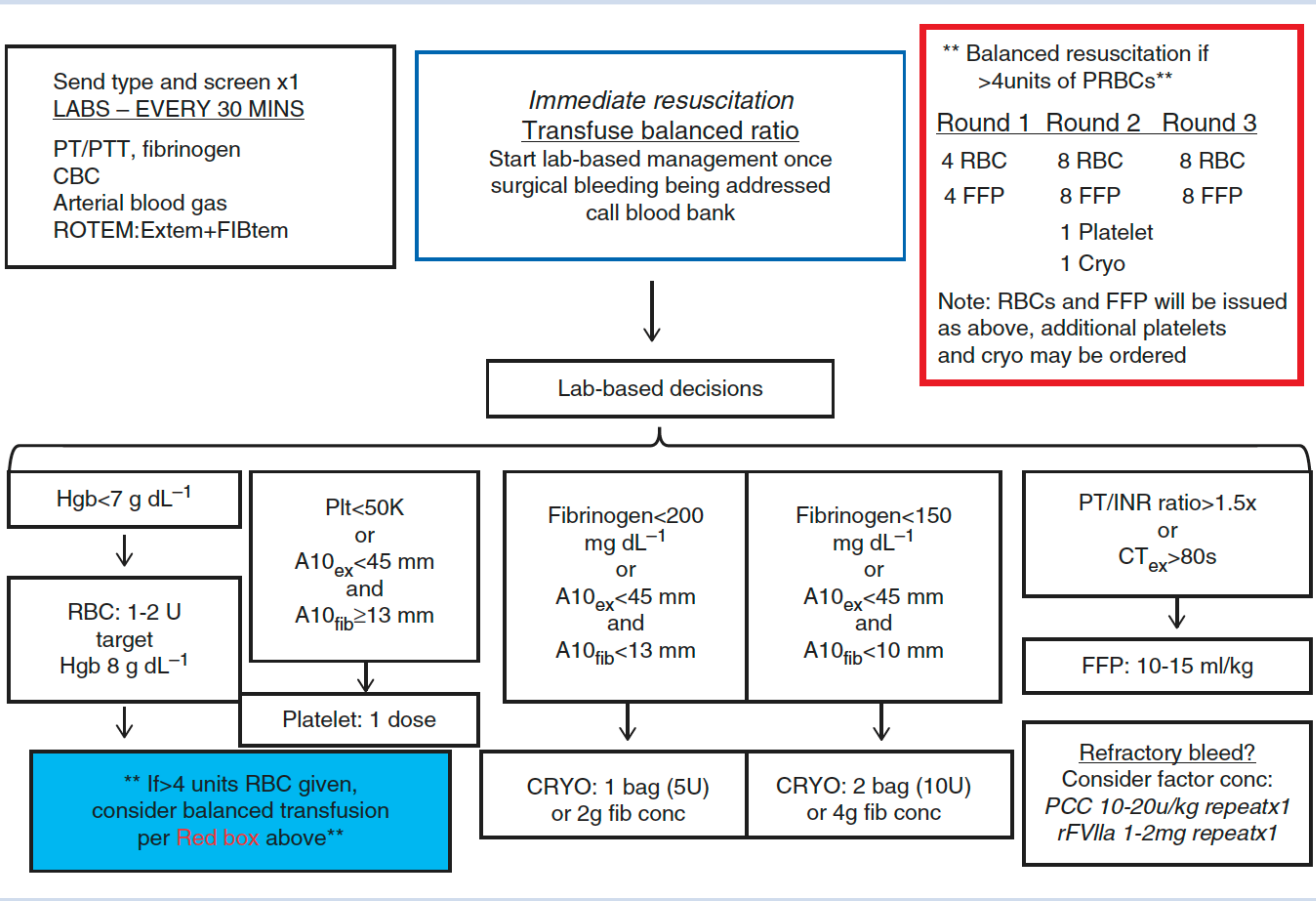


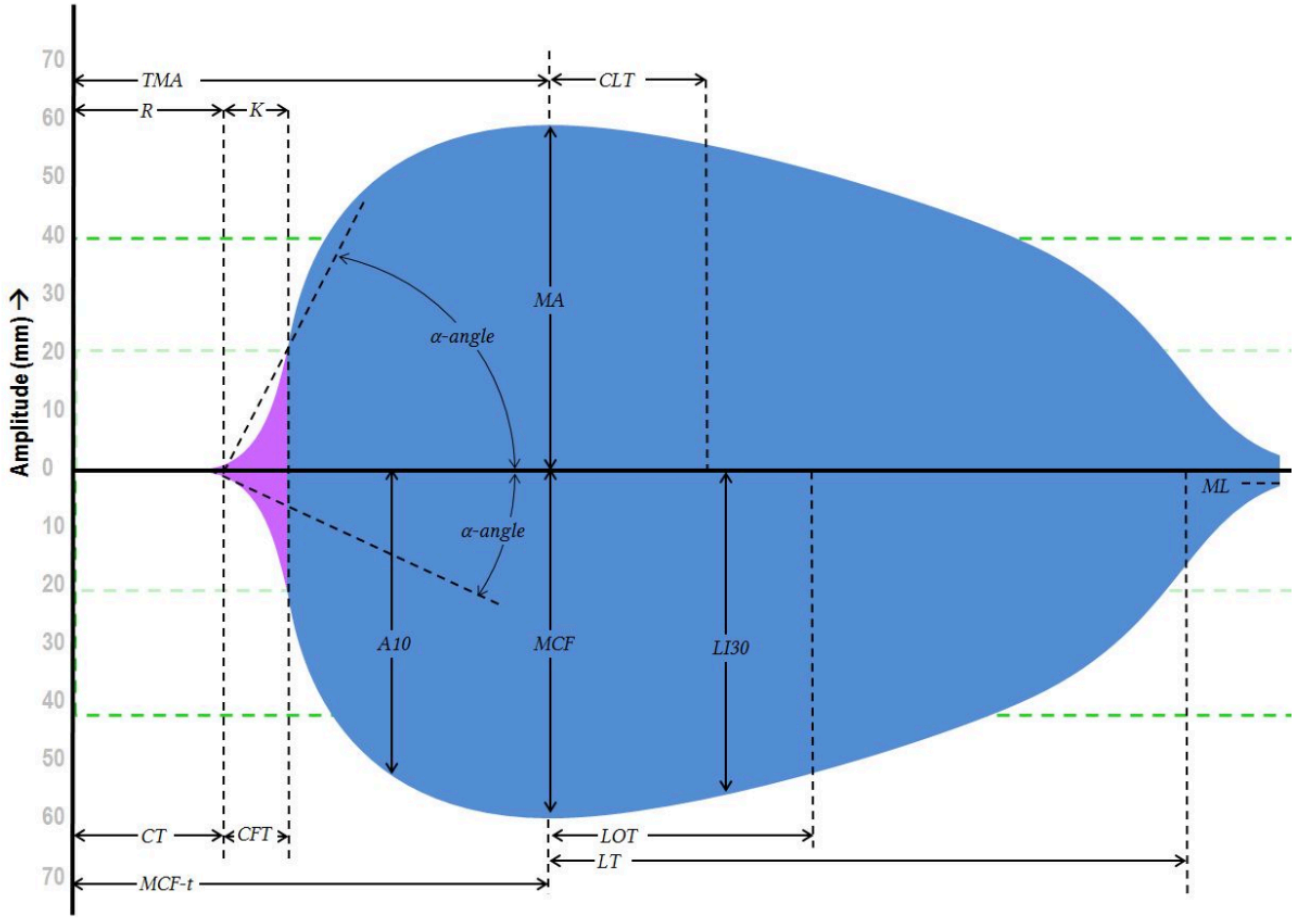
Fig 2 Transfusion algorithm for intraoperative bleeding during noncardiac surgery. Focus on a laboratory-based, viscoelastic testing paradigm, with opportunities for intervention based on clinical decision-making. Our protocol advocates antifibrinolytic therapy, correction of acidosis, and correction of acute hypocalcaemia. Inside the redbox, our balanced ratio recommendations are presented if the patient has been transfused four units of blood and intraoperative haemorrhage is ongoing. Consideration is given to low-dose factor concentrate usage (PCCs, rFVIIa) if bleeding is refractory to balanced resuscitation and algorithmic options. *Figure modified from a draft version of our local massive transfusion protocol.* CBC, complete blood count; Cryo, cryoprecipitate; FFP, fresh frozen plasma; Hgb, haemoglobin; RBC, red blood cell; PLT, platelet count; T & S, type and screen; PCC, prothrombin complex concentrates.

With permission from: Ghadimi K, Levy JH, Welsby IJ: Perioperative management of the bleeding patient. Brit J Anaesthesia 2016;117:iii18-iii30. doi: 10.1093/bja/aew358.

The TEG and ROTEM Graphs, and Differences in Nomenclature

TEG NOMENCLATURE

R = Reaction time (time from start to amplitude = 2mm)
K = Kinetics (time from amplitude = 2mm until amplitude = 20mm)
α-angle = slope from 2mm to 20mm amplitude
TMA = Time to Maximum Amplitude
MA = maximum amplitude
CLT = Clot Lysis Time (time taken for amplitude to decrease by 2mm from MA)



ROTEM NOMENCLATURE

CT = Clotting Time (time from start to amplitude = 2mm)
CFT = Clot Formation Time (time from amplitude = 2mm until amplitude = 20mm)
α-angle = slope of the line at 2mm amplitude
A10 = amplitude at 10 minutes; ...there can be any number of A(x) variables
MCF-t = Time to Maximum Clot Firmness
MCF = Maximum Clot Firmness
LOT = Lysis Onset Time (time taken for amplitude to decrease by 15% of MCF)
LT = Lysis Time (time taken for amplitude to drop to 10% of MCF)
LI30 = Lysis Index at 30 minutes (% drop in amplitude from MCF)
ML = Maximum Lysis (minimum amplitude achieved at the end of test run time)

PRO/CON DEBATE

Prothrombin Complex Concentrates (PCC) should be used as first-line agents for hemostasis in perioperative cardiac surgery instead of Fresh Frozen Plasma (FFP)

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Introduction

The unnecessary administration of allogeneic blood products leads to increased healthcare costs and has been shown to increase patient morbidity and mortality in the perioperative care of cardiac patients. Patient blood management (PBM) practices have become critical to the optimal care of the cardiac surgical patient both in striving to conserve blood products as a precious commodity and to reduce unnecessary transfusions that can lead to worse patient outcomes. Central to patient blood management is the use of hemostatic agents during cardiac surgery to help reduce or even eliminate the need for allogeneic transfusions. Bleeding diatheses in cardiac surgical patients often arise from anticoagulant therapy, dilutional coagulopathy during resuscitation, and from factor depletion during cardiopulmonary bypass.

Historically, fresh frozen plasma (along with platelets and cryoprecipitate) would be administered to treat coagulopathy by restoring depleted or inactivated blood coagulation factors. The advent of purified coagulation factor concentrates has provided a simpler and more effective method to achieve hemostasis in the bleeding cardiac surgical patient.

Prothrombin Complex Concentrates

Prothrombin complex concentrates (PCCs) are a mixture of Vitamin-K dependent coagulation factors in the nonactivated (pro-enzyme) form purified from pooled plasma. There are generally two types of PCCs: 3-factor PCC that contains factors X, IX, and II (prothrombin) or 4-factor PCC that contains X, IX, II, and VII. The relative amounts of specific factors in PCC formulations depends upon the product manufacturer. Interestingly, PCCs also contain varying amounts of blood anticoagulant proteins including Protein C, Protein S, Protein Z, and antithrombin III (ATIII), dependent on manufacturer preparations.

The presence of these anticoagulants is thought to provide a more balanced hemostatic effect and reduce the risk for adverse thrombotic events. Heparin is also added to PCC preparations to prevent factor activation. It is important to note, however, that certain formulations, such as FEIBA (Shire/Baxalta), do contain activated factor VII (fVIIa) and were originally designed to treat hemophilia patients with a fVIII inhibitor.

Prothrombin complex concentrates undergo a rigorous purification methodology to eliminate the presence of infectious agents. The purification process includes ion-exchange chromatography with ammonium sulfate precipitation to remove theoretical prion particle contamination followed by viral inactivation via heat pasteurization and nanofiltration.

PCCs were originally FDA approved for treatment of hemophilic syndromes and since 2013 have been approved for the rapid reversal of vitamin-K antagonist (VKA) induced coagulopathy in adult patients experiencing acute hemorrhage.

The American College of Cardiology recently supported the use of PCCs as first-line

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therapy over FFP for warfarin (VKA) reversal and for reversal of non-vitamin K oral anticoagulants (NOAC) if the specific antagonist or antidote was unavailable (ie, andexanet alfa, idarucizumab).

There are few contraindications for using prothrombin factor concentrates. As many formulations include heparin, PCC should not be used in patients with known heparin-induced thrombocytopenia (HIT). PCC should be avoided in patients with disseminated intravascular coagulation (DIC).

Advantages of PCC over Fresh Frozen Plasma

The main goal in treating coagulopathy during cardiac surgery is to prevent hemorrhage and check further blood loss. Restoration of balanced hemostasis requires the rapid replenishment of optimal levels of coagulation factors without excessive procoagulant activity leading to uncontrolled thrombosis.

Fresh frozen plasma administration has been the mainstay of therapy for perioperative bleeding but has several disadvantages. Transfusions of significant volumes of plasma in cases of trauma or massive hemorrhage can result in catastrophic volume overload and pulmonary edema (TACO). Furthermore, due to the presence of anti-HLA antibodies, FFP transfusion may also lead to potentially fatal acute lung injury (TRALI). Being a pooled blood product, there is still a risk for contamination with an infectious agent particularly if multiple units of FFP are given.

Plasma contains ABO hemagglutinins requiring crossmatching and is stored at ≤ -18 C necessitating thawing, creating considerable delays to transfusion. In fact, the use of FFP for reducing bleeding has not shown any efficacy or benefit across many indications including in 24-hour blood loss post-cardiac surgery based on a meta-analysis of recent RCTs.

The advantages of PCC over FFP are many. Prothrombin complex concentrates do not require cross-matching nor thawing (stored at room temperature) and have a short time to reconstitute and administer. PCCs provide faster increases in blood factors levels than FFP.

Studies by Sarode et al. (2013) and Goldstein et al. (2013) demonstrated that infusions of PCC rapidly increased coagulation factors levels and reduced INR levels to ≤1.3 for VKA (warfarin) reversal within the first 30 minutes of infusion as compared to FFP. , The lack of immunoglobulins, leukocytes, and small administration volume eliminates the risk of transfusion reactions, TACO, or TRALI.

Lastly, the protein purification process and inactivation steps provide an extremely low risk for viral contamination.

Efficacy of PCC in VKA Reversal in Cardiac Surgery

In comparison to fresh frozen plasma, there have been several studies that provide examples of improved hemostasis by PCC in several clinical situations. Several studies have demonstrated non-inferiority of PCC over FFP in reversal of VKA. In cardiac surgical patients on VKA anticoagulation undergoing urgent or semi-urgent procedures, PCC has also been shown to reduce target INR faster and more efficiently then FFP. In another study, patients undergoing pulmonary endarterectomy were randomized to FFP or 4-factor PCC for perioperative VKA reversal. The results noted increased blood loss via chest tube drainage in the patients who received FFP compared to factor concentrates over the first 12 hours.

The American College of Cardiology, Society of Thoracic Surgeons, and Society of Cardiovascular Anesthesiology have recommended the use of 4-factor prothrombin complex concentrates as first-line therapy for emergency reversal of vitamin-K inhibitor induced coagulopathy as well as alternate therapy for reversal of non-Vitamin-K oral

anticoagulants (NOACs) if first-line agents are unavailable.[7] 4-factor PCC has also been used safely to reverse warfarin induced coagulopathy in LVAD insertion and in LVAD patients presenting with acute intracranial bleeds.

PCC First-line Therapy for Post-cardiopulmonary Bypass Coagulopathy

The coagulopathy emerging from cardiopulmonary bypass arises from several considerations including contact activation and the generation of tissue factor. The consumption of coagulation factors, loss of platelets, and the triggering of the fibrinolytic cascade in part may lead to a significant hypocoaguable state after cardiopulmonary bypass and heparin reversal. Traditionally, in addition to platelets and cryoprecipitate, several units of FFP were administered as first-line therapy to correct coagulopathy directed by point-of-care testing such as thromboelastography (TEG) or laboratory tests such as an INR.

As mentioned above, there are a myriad of disadvantages using FFP transfusion to correct factor deficiency post-cardiopulmonary bypass. Depending on the extent of cardiopulmonary bypass time and surgical factors (ie, deep hypothermic circulatory arrest), post-bypass bleeding can be very significant, requiring massive resuscitation measures. Large volume blood loss, whether surgical or non-surgical, will require excessive volumes of blood products including FFP.

The preparation time to obtain FFP after crossmatching and thawing results in resuscitation fluids or packed red blood cells (PRBCs) leading to further dilutional coagulopathy. FFP administration comes with several risks including transfusion reaction, risk of viral infection, and immune-mediated inflammation leading to TRALI. Large volumes of FFP also can further cause circulatory overload resulting in TACO, particular in those cardiac patients with heart failure or chronic renal disease. PCC can be given as a single dose in a much smaller volume (~100 ml) with the same efficacy as FFP.

Ideally the restoration of coagulation factor levels to promote thrombin generation needs to occur early in cases of post-bypass coagulopathy allowing for better hemostatic control and reducing the need for further transfusion. FFP infusions can take several hours to reach adequate factor levels as seen in studies with warfarin reversal. Those same studies noted restoration of most major clotting factors within 0.5-1 hour of single administered dose of 4-factor PCC.10,11 These facts argue strongly in favor of using prothrombin concentrates as first-line therapy in post-bypass hemostasis in lieu of FFP transfusion.

Several European groups have pioneered the use of coagulation factor concentrates first-line therapy in coagulation management post-cardiopulmonary bypass. In a single center study, Görlinger et al, (2011) looked retrospectively at two cohorts of cardiac surgical patients: those who were treated by traditional blood product management compared those patients who were treated using a new transfusion algorithm guided by viscoelastic testing. The transfusion algorithm implemented the use of coagulation factor concentrates (including fibrinogen concentrates) as first-line therapy over FFP transfusion. The researchers found that implementation of this new coagulation management algorithm decreased the units of FFP transfused by 95% and decrease allogeneic PRBCs transfusions by approximately 20%. They also discovered that the incidence of massive transfusion and surgical re-exploration decreased nearly by half. Additionally, the rate of adverse thromboembolic events decreased in the factor concentrate cohort.

Another small non-randomized retrospective study by Arnékian et al (2012) studied three patient groups with post-bypass bleeding treated either with plasma, PCC alone, or PCC plus plasma. The investigators determined that those treated with PCC alone had less red

cell transfusions and a lower percent of re-exploration for bleeding. Interestingly, patients treated with both PCC and plasma had the most need for red cell transfusion.

The only adverse thrombotic event occurred in the FFP alone cohort. Similarly, Ortmann et al., (2015) compared 55 patients treated with FFP to 45 patients treated with PCC undergoing pulmonary thrombectomy and found lower post-operative blood loss in the PCC group, although red cell transfusion rates were comparable.

This study also found no adverse events associated with PCC. Cappabianca et al., (2016) conducted a single center propensity-matched observational study of cardiac surgical patients receiving 3-factor PCC as a replacement for FFP for post-bypass bleeding intraoperatively or postoperatively in the ICU.

Comparing propensity match pairs, red cell transfusion decreased by approximately 10% (84 vs 93%) with an odds-ratio 0.5 and post-operative blood loss decreased by about 11% (median blood loss of 836 vs 935 ml). Importantly, this study was the only study to report an increased risk of AKI and renal replacement therapy in the PCC-treated patient group with an odds ratio of 1.44 and 3.35, respectively. It should be noted, the PCC group had more patients with NYHA class III-IV heart failure in the propensity matched analysis.

No difference in mortality or adverse thromboembolic events were noted, however, and the investigators suggested the increased AKI may have resulted from less overall volume transfused in the PCC arm compared with the FFP group. Fitzgerald et al, (2018) also conducted a single-center retrospective observational study looking at the management of bleeding post-cardiac surgery. One group received FFP alone and the second received PCC with or without FFP.

Therapy was guided by platelet function and viscoelastic testing. Propensity matched groups demonstrated that the PCC group had reduced red cell transfusions, less episodes of massive transfusion (≥ 10 red cell transfusions), and less refractory bleeding. There were no significant differences in the risk for adverse events including risk of AKI, DVT/PE, stroke, or death.

Most recently, Karkouti et al, (2022) conducted a randomized pilot trial at two medical centers comparing either FFP or PCC as first-line therapy for post-cardiac surgical bleeding. The PCC arm demonstrated decreased median chest tube output at 12 hours (310 vs 500 ml) and 24 hours (450 vs 700 ml). Again, there was no increase in the risk of AKI or thromboembolic events in comparing the two groups.

A recent meta-analysis looked at four clinical trials and 861 patients that used PCC for treatment of perioperative bleeding in cardiac surgery. The studied concluded that PCC appeared to more effective than FFP in reducing perioperative transfusions and post-operative bleeding without increasing the risk of adverse events including mortality, stroke, or AKI.

The PROPHESY pilot trial randomized cardiac surgical patients with post-operative bleeding in the first 24 hours to receive15 IU/kg of prothrombin complex concentrate or 15 ml/kg of fresh frozen plasma. The main endpoint is to evaluate safety and efficacy of PCC as first-line therapy for cardiac surgical bleeding.

Analysis of the pilot trial continues to demonstrate no increase in adverse thromboembolic events with PCC. Even with this evidence, there is still a need for larger prospective randomized controlled trials to demonstrate non-inferiority or even superiority of prothrombin complex concentrates in treating post-cardiac surgery coagulopathy.

Remaining Barriers to Use

There are a few barriers to the use of PCC as a 1st-line agent in post-bypass coagulopathy to highlight. First, many of the studies used a point-of-care (POC) testing-based transfusion algorithm including viscoelastic and platelet function assays to guide PCC or blood product administration.

Currently comparable blood management protocols have not been widely adopted by cardiac surgical and anesthesiology practices in the United States despite recommendations by the Society of Cardiovascular Anesthesiologists and Anesthesia Quality Institute.

Secondly dosing regimens of PCC based on viscoelastic testing may differ between institutions and it remains to be determined what standard dosing regimen by viscoelastic assay or INR is appropriate for post-cardiac surgical bleeding.[4] The last barrier may be cost.

The activity-based cost for single unit of transfused FFP is approximately $410 at single U.S. medical center. Current non-discounted cost for KCentra® (CSL Behring) in the U.S. is $3.26 per unit, thus for a 70-kg patient the total cost for a 25 IU/kg dose would be about $5700. The reduction of FFP transfusion needs to exceed 14 units per patient for any cost saving from a single dose of PCC. Obviously, the true cost-benefit analysis heavily depends upon institutional discounts for factor concentrates.

Conclusion

In aggregate, the available clinical data clearly indicates that use of PCC as a 1st-line hemostatic agent as compared to FFP reduces the amount of red blood cell transfusions, post-operative bleeding, and need for re-exploration without a significant increase in perioperative adverse events. Clearly, the use of PCC for reversal of anticoagulation from vitamin-K antagonists or newer non-VKA oral anticoagulants is warranted, particularly for urgent cardiac surgery.

Recent trials continue to build support for the use of prothrombin complex concentrates as alternate therapy to FFP for post-cardiac surgery bleeding, and the risk of thromboembolic events remains low with the newer preparations. Based on this, 3- or 4- factor prothrombin complex concentrates should be considered a reasonable first-line alternative to FFP transfusion in cases of post-cardiac surgery bleeding.

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Fresh Frozen Plasma and Cryoprecipitate is Preferred Over Prothrombin Complex Concentrate

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Hemostasis is a complex process that starts with constriction of the damaged vessel and exposure of the vascular endothelial to provide a surface for the attraction and attachment of platelets and initiation of the coagulation cascade.[1,2,3] Primary hemostasis, due to platelet adhesion, activation, and aggregation, initiates a 'plug' and provides a surface for the activation and interaction of multiple clotting factors and co-factors to form a strong cross-linked fibrin clot.[1,2]

This attracts and activates inflammatory cells and inflammation to help stabilize the clot and promote healing of the damaged tissue. Once achieved, hemostasis is balanced by fibrinolysis, a normal response to the escalation of the coagulation system, to prevent pathologic thromboembolic events.

Perioperative bleeding increases morbidity and results in up to 40% mortality patients, with trauma patients being at greatest risk.[2,3,4] While surgical trauma and injury to blood vessels are the primary cause of blood loss, the continued loss, dilution, and/or consumption of coagulation components (e.g., platelets, coagulation factors) further complicates hemostasis.

General management for all patients includes avoidance of hemodilution, maintaining stable cardiovascular-pulmonary and metabolic functions, and temperature regulation. While often overlooked, the maintenance of metabolic and temperature homeostasis is important for the multiple enzymatic reactions to occur and for proteins to function normally.[2,3] In addition to preserving normal hemostatic functions, preventing, or attenuating fibrinolysis should be considered.

While routine for cardiac surgical patients, the administrations and/or infusions of anti-fibrinolytic agents such as Tranexamic acid (TXA) or Epsilon Aminocaproic Acid (EACA) for other surgical procedures has become more common (e.g., orthopedic surgeries). [2,3]

Confounders include preoperative anticoagulant medications, and/or congenital deficiencies/dysfunctions.[5,6,7] The presence and mechanisms of oral anticoagulant medications and congenital defects in coagulation are usually known prior to surgery and can be managed, according to guidelines, with either a delay in surgery to reduce serum levels, or by administering therapies to counter specific effects or defects.[5,6,7]

Therapies can either include blood components or specific factor concentrates targeting the underlying mechanism of the anticoagulant medication or defect.[1,2,3,8] Although an increasing number of patients managed with oral anticoagulants and antiplatelet medications will present to the operating room, most present with no prior history of abnormal coagulation beyond a preoperative aspirin, a drug that does not need to be discontinued except for the highest risk patients.

For those who are receiving antiplatelet, anti-Xa, and Anti-II (thrombin) medications,

guidelines emphasize discontinuation prior to surgery and delaying surgery to allow blood levels to decline to safe/minimal levels.[3]

For most surgical patients, the cause of excessive bleeding is iatrogenic (acquired; microvascular) coagulopathy due to surgical trauma to blood vessels, blood loss, hemodilution, and consumption coagulation factors. These cases present a larger more complicated hypocoagulant condition involving multiple coagulation components.[2,3,9,10] Platelet loss and/or dysfunction is associated with greater mortality and requires platelet transfusions.[9,10] Replacement or replenishment of coagulation factors can be accomplished with specific coagulation factor therapies such as Prothrombin Complex Concentrate (PCC) or a generalized approach with Fresh Frozen Plasma (FFP) and Cryoprecipitate (Cryo).

By comparison, FFP and Cryo increase the full complement of the coagulation system, while PCC are limited to the Vitamin K dependent factors. Ultimately, hemostasis requires formation of a strong platelet plug that is strengthened by Fibrin-Fibrin cross linking and Factor XIII.[1,2,3,4,11,12]

Perioperative bleeding requires a generalized approach to replenish coagulation components beyond just the Vitamin K factors. It is known that fibrinogen levels decline early in cases of major bleeding and that replenishment is critical toward hemostasis and outcome.[11,12]

Surgical repair and/or ligation of injured blood vessels is a primary management to stop blood loss and further loss of coagulation components. Thereafter, management options of the iatrogenic coagulopathy are multiple, and decisions should be based on outcome data, therapeutic efficiency, cost, and complications.

For the majority of cases who develop a perioperative coagulopathy, FFP and Cryo offer a generalized, relatively low cost, low risk solution to replenish loss of coagulation factors.[1] For patients with a known preoperative history of congenital coagulation defects or for those who were prescribed specific therapies for cardiovascular pathologies, specific therapies may be available. Although expensive, these therapies can be planned and administered prior to surgery.

Optimally, the surgical procedure can be delayed allowing a safe time period to discontinue anticoagulant medications.[13] For example, if surgery cannot be delayed allowing coumadin levels to drop until coagulation normalizes, then based on the preoperative INR either FFP or Prothrombin Complex Concentrates (PCC) can be administered.[13]

The decision to administer PCCs or FFP balances the costs and risks of either therapy, the baseline INR, the urgency of the surgical procedure, institutional preferences, and availability.[13] For a patient with severe heart failure PCCs may be preferred as it will require significantly less volume compared to FFP.[13]

The patient who develops a coagulopathy due to surgical trauma, blood loss, loss and/or consumption of coagulation factors, is further complicated by severe anemia, cardiovascular shock, and metabolic acidosis. This scenario has been well described for trauma and cardiac surgical patients.[1,2,3] For these patients, volume resuscitation is necessary including red blood cells, platelets, and coagulation factors. FFP and Cryo provide a full complement of coagulation factors necessary for hemostasis as part of a massive transfusion protocol and to address coagulation factor deficiencies.[14]

When considering the etiology of acquired coagulopathy, recognizing the

pharmacokinetics and roles of clotting components is important toward understanding therapy. Factor VII has the shortest half-life (5 hours) followed by Factor VIII, while Factor V is potentially labile. Thrombin has positive feedback by activating multiple precursor factors (XI, VIII, and V) to form Tenase (VIII-IX) and Prothrombase (V-X) to activate more Thrombin, which splits fibrinogen to form cross-linked Fibrin-Fibrin bonds and stabilize the platelet clot.[1] This is further enhanced by Factor XIII. Even within this simplified description of the clotting cascade, it is evident that adequate coagulation requires a full complement of factors ultimately leading to Fibrinogen, which is not present with PCC.[1,2]

When considering the complexity of coagulation, clotting requires normal platelet function, coagulation factors, and control of fibrinolysis the totality of which is beyond the administration of PCC.

FFP is prepared from units of whole blood or plasma collected by aphaeresis. It is frozen to -18 to -30 degrees Celsius within 8 hours of collection, stored and able to be used approximately one year from the point of collection.[15] The volume of one unit of FFP is approximately 250 ml.

In the United States, plasma is frozen within 8 hours following phlebotomy (FFP) or within 24 hours (PF24). Cryoprecipitate can be manufactured from FFP but not PF24 however both can be transfused interchangeably. Thawed plasma (either FFP or PF24) is stored up to five days before administration which helps limit the waste of plasma which is often in short supply.

FFP contains all clotting factors including and beyond the vitamin K dependent clotting factors: II, VII, IX, X, Protein C, and Protein S. Cryoprecipitate contains Fibrinogen vWF (von Willebrand Factor) and Factor XIII. The 3 and 4 factor Prothrombin Complex Concentrate (PCC) only contain the specific vitamin K derived clotting factors.

Since data shows that 4-Factor PCC are superior to 3-Factor PCC, due to the inclusion of Factor VII, the remainder of the discussion will assume 4-Factor PCC.[16] Although high levels of vitamin K dependent factors are important for hemostasis, the absence of fibrinogen, labile factor V, cofactor VIII, factor XI and XII, and stabilizing Factor XIII make PCCs an incomplete therapy for patients with perioperative coagulopathies.

Even when considering specific factor therapy for those receiving coumadin controversy exists. Guidelines from the American College of Cardiology (ACC), American Society of Hematology (ASH), and Neurocritical Care Society currently recommend 4- factor-prothrombin complex concentrate (4F-PCC) as the preferred choice for urgent reversal of vitamin K antagonists.[17] Despite these guidelines, phase 2 and 3 clinical trials comparing FFP and 4F-PCC for vitamin K antagonist reversal found no differences.[17,18] However, several studies have reported slightly higher incidences of thromboembolism in patients receiving PCC reversal of coumadin anticoagulation compared to those receiving FFP.1[7,19,20]

A retrospective analysis showed that transfusions of 300-600 mL of FFP was associated with a significant reduction in mortality (OR, 0.29; 95% confidence interval, 0.09 -0.98) in patients with warfarin anticoagulation related intracranial hemorrhage (ICH) (21). When balanced with cost and fluid volume the choice between PCC and FFP is guided by the baseline INR, perhaps choosing FFP with lower INRs requiring smaller amounts of FFP in volume.[17,18,21]

In trauma patients, or any surgical patient with large blood loss, a trauma induced coagulopathy occurs. The response to large blood loss is massive transfusion (defined as 5-10 units RBCs within 12 to 24 hours respectively), has included FFP, Platelet Concentrates (PC) and Cryo as first line therapy.[1,22,23] FFP was shown to reduce the death rate by 60%

(OR, 0.38) and reduced the risk of multi-organ failure by 60% when compared to the control group.[2,19] Roback et al found 10 observational studies that determined that transfusion of FFP:Platelet Concentrates (PC), and Red Blood Cells (RBC) ratios of 1:1:1 was associated with significant reductions in mortality (OR 0.38, 95% CI).[21,24,25] FFP contains the full spectrum of clotting factors (unlike 4F-PCC).

Depletion of factor V and factor VIII have been linked to a worsening of trauma coagulopathy.[26,27,28] FFP and Cryo contain fibrinogen, which declines quickly during trauma and is of critical importance in the correction of trauma induced coagulopathy. Preferred levels being > 80 mg/dl.[1,29] PCC lacks fibrinogen (Factor 1), Factors V, and VIII. Although FFP contains fibrinogen, Cryo therapy provides a higher concentration of Fibrinogen (150-250 mg/20 ml) along with vWF (necessary for platelet adhesion and activation) and Factor XIII, the latter helping to strengthen cross-linked Fibin clot.[30,31]

One unit of Cryo (15 ml) per 10 kg body weight has been reported to increase the Fibrinogen level 50 mg/dl, while 30 ml/kg of FFP will increase Fibrinogen by 100 mg/dl.[31,32,33] By contrast, PCC contains a 25x greater concentration per ml of clotting factor than what is found in FFP.[34] However, emphasis on PCCs is not supported by outcome data perhaps due to a limited 'arsenal' of coagulation factors (35). It is possible that a hybrid approach may result in benefits from both therapies while minimizing risks.[42,43]

The acquired coagulopathy associated with cardiac surgery and cardiopulmonary bypass is multifactorial resulting from a combination of heparin administration and factor inhibition, component loss due to bleeding and hemodilution, factor consumption, heparin administration, cellular trauma due to the cardiopulmonary bypass circuit, and fibrinolysis.[1,2,3]

EACA and TXA are administered to help counter fibrinolysis and protamine is ultimately administered to bind circulating heparin. Platelet and/or coagulation factor trauma, dysfunction and loss may become critical requiring replacement therapy. Important coagulation factors known to decline with trauma and CPB include fibrinogen, Factors II (Thrombin), V, VII, X, and XIII.[3,23] Although the literature has highlighted critical reductions in certain coagulation factors, without specific assays it can be assumed that all factor activity is reduced.

For the bleeding patient with prolonged point-of-care clotting assays (e.g., activated clotting time) a generalized and cost-effective approach includes additional protamine, antifibrinolytics, and if still necessary, 10-15 ml/kg FFP and Cryo (1 unit/10kg).[2] While the administration of PCC has been reported for cardiac surgical patients, the results vary likely reflecting the limited scope of PCC to counter the multifactorial causes of coagulation abnormalities including coagulation factors beyond the Vitamin K dependent ones such as fibrinogen.[1,2,3,36,37] Although, Fibrinogen concentrates are available, compared to Cryo, the equivalent effective dose to raise serum similar fibrinogen levels is significantly more expensive without added outcome benefit.[38,39]

The safety profile and costs of each therapy should also be taken into consideration. At our institution, the cost per unit of

FFP 1 unit	$81.37 (10-15 ml/kg would cost approx. $325)
Cryo 5 pooled units	$345
5-unit platelets	$685
4-Factor PCC	$1.27/Unit or $2540 for 2000 U.
25 U/kg for a 70kg =	$2222
Fibrinogen Concentrate	$1000/1 gram vial
Factor VII	$2480/1mg vial

Focusing on Fibrinogen replacement, comparing 15-20 units of Cryo to 3-4 gm of Fibrinogen Concentrate show a lower cost with Cryo.[39] To be cost equivalent the cost of Fibrinogen concentrate would need to be 44% less and/or reduce ICU stay.[39]

Survey results reported that 96.7% of United States medical centers did not use Fibrinogen concentrate due to 1) cost, 2) off-label use, and 3) lack of outcome data supporting its use.[39] When considering that these therapies may need to be repeated in 6 hours the cost issues become more significant.

Administration of FFP/Cryo offers a broader less expensive therapeutic approach for the patient whose perioperative period is complicated by iatrogenic, acquired coagulopathy.[2,36]

The risks of FFP/Cryo administration are low. Transfusion Associated Lung Injury (TRALI) is an immune mediated non-cardiogenic pulmonary edema which occurs following blood component administration.[40] This serious complication is rare, occurring in roughly 1 in 2,000 FFP transfusions.[41]

Transfusion Associated Circulatory Overload (TACO) occurs in vulnerable patients when the sudden increase in circulating volume associated with blood component transfusion precipitates pulmonary edema. TACO is also comparatively rare occurring in 1 in 9,000-13,000 transfusions.[42] Infectious diseases such as HIV (0.04 cases per million transfusions) and Hepatitis C (0.01 cases per million transfusions) thankfully remain very rare complications of blood transfusion in the US.[44]

By comparison, PCC are a high concentration of Factors II, VII, IX, and X that have, through preparation, been deactivated regarding infection, and are administered in low volume reducing risk of volume overload. However, specific high concentration factor concentrates are associated with a greater risk of thromboembolism being reported up to or greater than 20% being associated with high complications rates and mortality (45,46,47,48). While lower doses may lessen the risk of thromboembolic complications, the need for repeat doses may increase the risk.

FFP/Cryo and PCC are often misused despite guidelines regarding their proper administration.[49,50] The use of these agents should be monitored and used appropriately when possible as plasma and 4F-PCC are of limited supply (49,50). As approved by the FDA, specific component therapy may be best reserved for known preoperative specific factor deficiencies undergoing high risk procedures and/or complicated by refractory bleeding. As time allows, therapeutic approaches can be further guided by point of care testing, factor assays, and viscoelastric tests such as Thromboelastometry or Thromboelastography.[1,2]

Institutional protocols are defined as much by published guidelines as it is by blood component or specific factor concentrate availability. Ideally goal-directed therapy based on mechanism and point-of-care tests will guide selection of blood component therapy and/or factor concentrates.[2,16,51,52] PCC do not satisfy replacement of the many coagulation proteins lost during surgical bleeding, especially fibrinogen.

Reliance on PCC may necessitate administration of Fibrinogen concentrates to return fibrinogen levels toward a desired level.[23] Given the absence of robust supportive outcome data and the possibility of having to repeat a very expensive therapy, it is understandable why support for FFP/Cryo continues.

The comprehensive approach to replenishing coagulation components is shown in the renewed interest in whole blood administration either in total or after separation into platelet rich and platelet poor plasma.[53,54]

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