SCA NEWS

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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PRESIDENT'S MESSAGE

Volume 34, Number 18
December 2022/January 2023

At this time of year, it is traditional to look back at the past year and reflect on what went well, what went not so well and what to look forward to next year. We have had a terrific year at SCA, and I mentioned some of our successes in the article for Anesthesiology News in November. Specialty certification is of course our highlight, but so is the ongoing strength of our Society, and the dedication of our members to our mission of providing high quality education for all who serve cardiovascular and thoracic surgical patients.

One of the fun parts of representing our Society as President is the opportunity to attend the EACTAIC Annual Congress which this year was held in Naples, Italy, from December 14-16. EACTAIC were forced to relocate their meeting from Vilnius in Lithuania because of the ongoing situation in Central Europe. The program committee chairs from Vilnius were present and actively engaged in the Naples program, and they retained the theme of the meeting (Expanding Boundaries) as well. The meeting was a great success, and we (SCA) had the pleasure of sponsoring a session on Thoracic Anesthesia (see photo). We had four excellent speakers from SCA (Alessia Pedoto, Amanda Kleiman, Diana Anca and Max Meineri) who gave the audience a great two-hour long session focused on current issues in Thoracic Anesthesiology. It was my pleasure to moderate this session, and to enjoy the incredibly high-quality presentations these physicians had put together. I received several compliments on how good the session was, and Dr Pedoto is to be congratulated for her excellent stewardship in organizing it.

I will end by wishing all our members a very Happy Holiday season, and I hope everyone gets a few days to rest and spend time with friends, family and other loved ones. For those who have lost a loved one this past year, we send our condolences and thoughts and prayers. For those who are working over the Holidays we say thank you, your dedication is appreciated and we know the sacrifice you make. Take care and we will see you all in January to see what 2023 holds for us at SCA.

Andrew Shaw

Join Us for the PoCUS Hands-On Workshop

We hope to see you on **February 20, 2023, in Atlanta, Georgia** for the upcoming Perioperative Ultrasound Course: Hands-On Workshop!

The SCA Perioperative Ultrasound Course offers training in utilizing basic clinical ultrasound to assist in clinical assessment and decision making and to guide percutaneous procedures. This reverse classroom–style program gives participants the opportunity to learn ultrasound skills through an hands-on workshop.

Attendees will gain practical knowledge from subject-matter experts on how to perform safe ultrasound procedures.

Click Here to register and for hotel information.

Looking forward to seeing you in Atlanta, Georgia!

Join Us in Atlanta, Georgia!

February will be here before you know it, which means it's time to register for the 2023 Echo Week! Join us **February 17-19, 2023, in Atlanta, Georgia.**

This three-day conference will feature multidisciplinary panels on the role of echocardiography in surgical decision making in valvular disease and mechanical circulatory support, clinical dilemmas uniquely encountered in the operating room that may alter the surgical plan, and structural heart disease transcatheter procedures.

Registrants will also have access to our on-demand Echo Core Series, several lectures focused on reviewing fundamental echocardiographic concepts in physics, valvular disease, ventricular function evaluation, mechanical circulatory support, and transcatheter procedures.

Echo Week three-day conference will feature:

- 3D Symposium
- Decision Making in Aortic and Tricuspid Valve Surgery – MOCA – Case Based
- Decision Making Mitral Valve Symposium
- MCS and Transplant
- Clinical Dilemmas
- State of the Art Future Directions

Registration is NOW Open!

Registrants to this event will also have access to our on-demand Echo Core Series, several lectures focused on reviewing fundamental echocardiographic concepts in physics, valvular disease, ventricular function evaluation, mechanical circulatory support, and transcatheter procedures.

Click Here to view the agenda, registration rates and hotel information.

Introducing the 16th Annual Arthur E. Weyman, MD, Lecturer

Rebecca T. Hahn, MD

Professor of Medicine, Columbia University Irving Medical Center, Chief Scientific Officer of the Echo Core Lab at the Cardiovascular Research Foundation and Director of Interventional Echocardiography at the Columbia Structural Heart & Valve Center

The 2023 Weyman Lecturer takes place Saturday, February 18, 2023, at 12:00pm Eastern. Make sure to register for Echo Week to hear Dr. Hahn speak.

REGISTER NOW!

COR-PM is Back by Popular Demand!

The Scientific Program Committee is thrilled to announce the ***second-ever*** Cardiovascular Outcomes Research in Perioperative Medicine (COR-PM) **conference to be held in person and online on Friday, May 5th, 2023**, in conjunction with the following SCA 45th Annual Meeting and Workshops in Portland, Oregon.

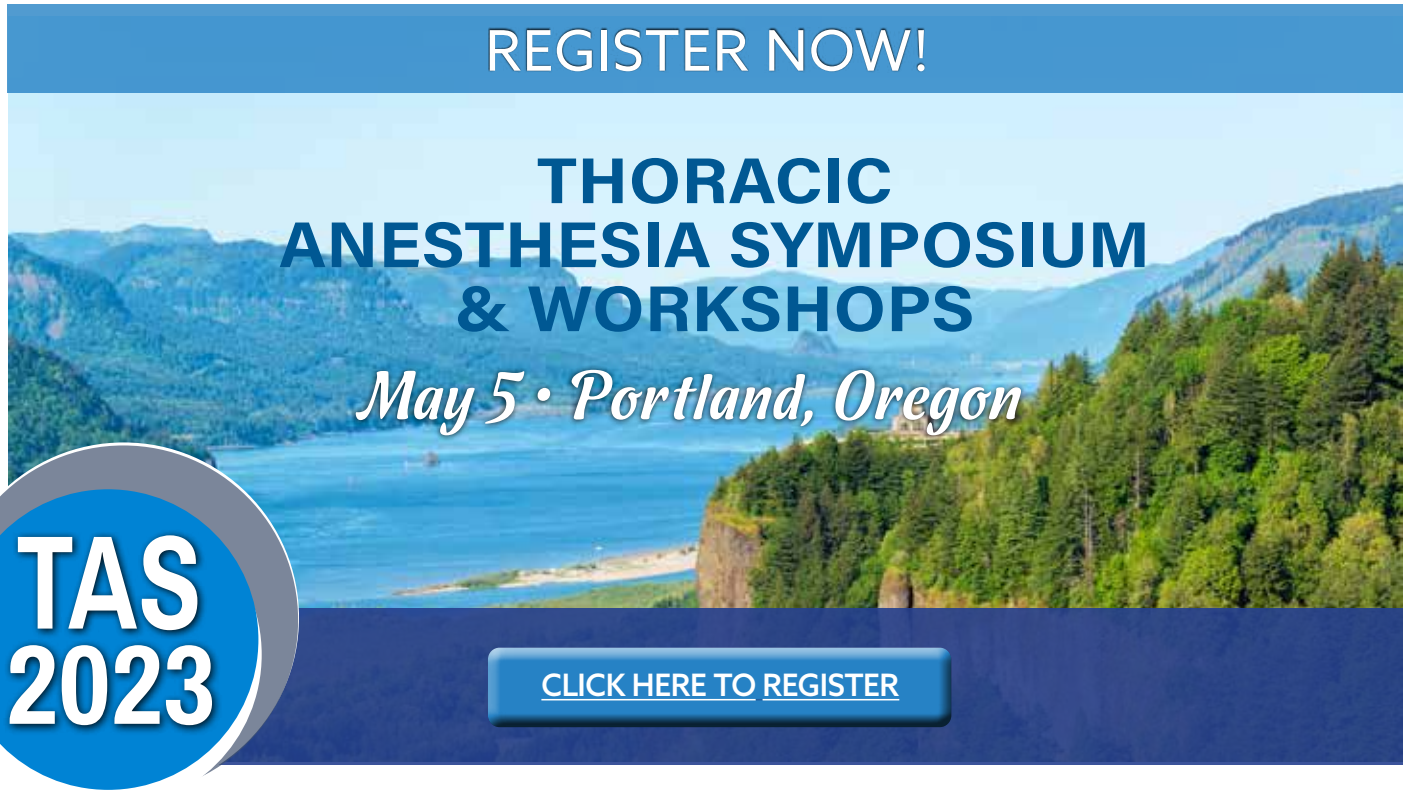
The COR-PM program was drafted by a group of diverse early- and mid-career anesthesiologists from across the U.S. to:

- Advance our understanding of high-quality clinical outcomes research within the T2-T4 translational spectrum.
- Provide mentorship capacity for early- and mid-career participants by providing a small-sized conference that permits "face time" with recognized leaders in the field, including Drs. Dan Sessler, Brittney Williams, Anthony Bonavia, Lisa Rong, Kimberly Howard-Quijano, Jochen Steppan and many more.
- Create a personal, inclusive, and welcoming conference.

We were glad to have seen so many of you in-person and virtually in 2022, we are thrilled to welcome you to Portland in 2023!

Click Here to view the preliminary agenda, registration rates and hotel information.

Registration NOW Open!



Don't Miss Out — Early Bird Discount Available NOW through February 20, 2023.

The Thoracic Anesthesia Symposium (TAS) Planning Committee invites you to join the world of non-cardiac anesthesiologists from around the world for the **2023 TAS meeting on May 5, 2023, in Portland, Oregon.**

Look forward to:

- A focus on dramas, traumas, experts, and controversies, along with everyday challenges in the chest
- Thought leaders provide a deep-dive exploration of new topics in thoracic surgery and anesthetic challenges
- Hands-on workshop format! Focus on your clinical interests and explore what is new with an interactive experience with the authorities in the field

At the SCA Thoracic Anesthesia Symposium you can:

- Choose 3 in-person workshops and register for an optional live PBLD for a conference experience tailored to YOUR educational needs
- Network with 200 other professionals in anesthesiology to help you gain insight into your practice and career
- Connect with our exhibitors to learn about new products and programs

Click Here to view the agenda, registration rates and hotel information.

Join Us and Celebrate Together!

Early Bird Discount Available NOW through February 20, 2023 – Don't Delay!

The Scientific Program Committee is thrilled to gather in person at the Society of Cardiovascular Anesthesiologists **45th Annual Meeting and Workshops in beautiful Portland, Oregon on May 6-9.** The 2023 conference will celebrate the SCA's incredible history and also marks the return of the always popular Gala Event!

Hot topics include multidisciplinary approaches to heart failure, an international panel on cardiopulmonary bypass, a mitral valve symposium, a beginner course in structural heart echocardiography and an expert panel on coagulation conundrums. And of course, we are celebrating the SCA past with a plenary session on the history of the society – learning from the past and recognizing that you are its future.

Sessions include experts from the world of cardiology, cardiothoracic surgery, perfusion, critical care medicine, regional anesthesiology, law, and finance. Specific sessions are designed for trainees as the program offers a robust choice of sessions geared toward medical students, residents, and fellows. The workshops are state of the art, hands on opportunities to learn cutting edge technology from true experts in the field.

As always, cutting edge discovery will be presented via abstract presentations, the crowd-pleasing SuperEcho returns, and the PBLDs capture a vast array of topics.

The In-Person conference will once again be the primary draw – and a virtual option to participate is also available!

We are thrilled to welcome you to Portland in 2023!

SCA ANNUAL MEETING

SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS
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Look forward to:

- Amazing content delivered by experts in cardiothoracic anesthesiology, interventional cardiology and cardiothoracic surgery
- Experts will provide didactics, small group breakout teaching, and high-yield discussions
- Problem based learning discussions, scientific abstracts, and workshops are planned to optimize attendee learning and connection on critical cardiothoracic anesthesiology topics
- Attendee networking, idea-sharing, and exhibits

This year, in-person you can:

- Attend live discussion sessions to help you discover up to date practice pathways and innovations in the field
- Register for Workshops and PBLDs tailored for YOUR educational needs
- Network with 1,200 other professionals in anesthesiology to help you gain insight into your practice and career
- Connect with industry and exhibiting companies to learn about new products and programs

Click Here to view the agenda, registration rates and hotel information.

Annual Meeting & Workshops – May 6-9

Portland, Oregon

Introducing the 2023 Annual Meeting Earl Wynands Lecturer

Philip Jones, MD

Dr. Philip Jones provides anesthesia care at the University Hospital (London Health Sciences Centre) and St. Joseph's Hospital (including the Regional Mental Health Centre). He also supervises and trains medical students, anesthesia residents, and fellows. In addition, Dr. Jones works as an intensivist in the Cardiac Surgical Recovery Unit. Dr. Jones also currently serves as the Chair for the LHSC Drugs and Therapeutics Committee, a position which presents many research opportunities. At the University Hospital, the Department of Anesthesia and Perioperative Medicine provides services for the following surgical disciplines: cardiac surgery, general surgery, neurosurgery, orthopedic surgery, urology, and plastic surgery. Dr. Jones is an active clinical leader and participant in all of these areas. Dr. Jones recently received an appointment as an ICES Adjunct Scientist with the Cardiovascular research program at ICES Western.

The 2023 Wynands Lecture takes place on Sunday, May 7, 2023, at 8:00am Pacific.

Make sure to **register** for the Annual Meeting to hear Dr. Jones speak.

Introducing the 2023 Annual Meeting Keynote Lecturer

Clyde W. Yancy, MD, MSc, FHFSA

Dr. Yancy is a cardiologist and the Magerstadt Professor at Northwestern University Feinberg School of Medicine. He has previously served as the Past President of the American Heart Association.

The 2023 Keynote Lecture takes place on Monday, May 8, 2023, at 11:00am Pacific.

Make sure to **register** for the Annual Meeting to hear Dr. Yancy speak on Diversity, Equity, and Inclusion.

2023 Research Grants – Apply Now!

SCA enthusiastically supports cardiothoracic and vascular research projects. This is the basis for the creation of the SCA/IARS Starter Grant,SCA/IARS Mid-Career Grant, SCA Diversity and Inclusion Grant, and the In-Training Grant.

Grants Information

Four types of grants will be awarded in 2023 to SCA members ONLY:

- **SCA/IARS Starter Grant** – up to $25,000 per year for two
- **SCA/IARS Mid-Career Grant** – up to $50,000 per year for two
- **SCA Diversity and Inclusion Grant** – up to $25,000 per year for two years
- **SCA In-Training Grant** – $15,000 for one year

The SCA is committed to promoting the representation of women and underrepresented minority investigators. Diversity is vitally important to advance scientific discovery. The SCA is especially encouraging individuals from all racial, ethnic or gender groups to apply.

The awards will be announced during the 2023 SCA Annual Meeting & Workshops in Portland, Oregon. The grant period of 24 months can begin any time from July 1 to December 31 of the year granted. Grant recipients are required to present their work at a subsequent SCA Annual Meeting.

Application submission period will close on January 27, 2023.

Click Here **Research Grants** for more information about these funding opportunities.

Visit **Research Grants** to review the eligibility, application requirements, and to learn more about past winners. Make sure to submit your application by 11:59 pm CST on Friday, January 27, 2023.

START YOUR APPLICATION

The Kaplan Leadership Development Award is NOW Accepting Applications!

The 2023 Kaplan Leadership Development Award application submission opened December 1, 2022. The award is designed to assist cardiothoracic and vascular anesthesiologists in their career by granting funding to further their leadership development through coursework and leadership-specific studies.

The Kaplan Leadership Award will be adjusted accordingly to offer an aggregate of $5,000 to either one recipient or divided among two

- **$5,000/$2,500 from the SCA Endowment, with a $5,000/$2,500 match from the applicant's institution to fund a leadership education strategy**

The deadline to submit your application is January 14, 2023.

Click here **Kaplan Leadership Development Award** for more information on this award and how to apply.

Questions about the grant and grant application should be emailed to operations@scahq.org, or via telephone at 855.658.2828.

WEBINAR

Anesthesiology and Critical Care Professional Community Webinar

An International Update on Perioperative Lung Transplantation Management

Tuesday, February 7, 2023

3:00 - 4:00PM EST

In the spirit of International Society for Heart and Lung Transplantation (ISHLT) collaboration, they have invited speakers from fellow cardiothoracic anesthesiology societies with representation from Society of Cardiovascular Anesthesiologists (SCA), Society for the Advancement of Transplant Anesthesia (SATA), and the European Association of Cardiothoracic Anesthesiology and Intensive Care (EACTAIC) to present an international update in lung transplantation.

We hope that this multi-societal, multidisciplinary webinar will highlight the collaborative spirit of team work and expertise within the SCA transplantation committee to anesthesiology colleagues from around the world.

Registration is free, and the link can be found here:

REGISTER HERE

Join Our February Webinar

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GRANTS

You Can Make a Difference by Supporting the SCA Endowment!

By donating to the SCA Endowment, you help SCA achieve its mission and assist cardiovascular anesthesiologists in furthering their education, research, and professional development.

Making an online donation is quick, easy, and secure. Access the SCA Endowment Fund donation page by visiting **SCA Endowment.**

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

Apply Now for a 2023 SCA Junior Resident Scholar Grant

The Society of Cardiovascular Anesthesiologists Diversity, Equity and Inclusion Committee (DEI) Junior Resident Scholar Program provides selected underrepresented minority (URM) anesthesiology residents (CA1) an opportunity to attend the SCA annual meeting.

The goals of this grant are:

- To expose URM residents to the clinical practice of cardiothoracic anesthesiology by attending the SCA annual meeting.
- To give URM resident scholars early involvement in the SCA through interactions with and mentorship by leaders of the sub-specialty and other cardiothoracic anesthesiologists.

GRANT INFORMATION

Ten grants will be awarded in 2023. Funding amount: $1,000.

Requirements:

- Nomination of URM resident by the program director.
- The nominee must be an academically promising URM CA1 resident in good standing in an ACGME-accredited residency program.
- Each nominee must submit an essay addressing the following (maximum 500 words):
  a. Diverse background of the nominee
  b. Nominee's understanding of the issues of DEI in Cardiovascular medicine
  c. Nominee's interest in CV anesthesia
- A letter of support from the program director and one additional letter of recommendation from a faculty member.
- The CV of the nominee.

APPLY FOR GRANT

Application submission period will close on January 15, 2023.

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SF MATCH

2024 SF Match Fellowship Agreements — NOW Open!

Applicant Registration Began	November 7, 2022
Central Application Service Target/ Deadline Date	March 1, 2023
Rank List Submission and SCA Exception Agreement Deadline	June 1, 2023
Results Sent to Program Directors/ Applicants and Medical Schools	June 15, 2023
Post-match Vacancies Posted	June 16, 2023
Training Position Starts	July 2024

In-order to provide more consistency and predictability to the ACTA fellowship application process, the ACTA programs participate in a common application and match process provided by SF Match for recruitment.

Applicants and programs participate by registering with SF Match and applicants applying to the programs of their choice. Both programs and applicants submit a rank list based on their preferences. Notably, only programs where an applicant has interviewed can be ranked in the match.

Critical to the match process, programs and applicants can make an Exception Agreement prior to submitting their rank list to SF Match. Exception Agreements allow an applicant and program to agree to match each other prior to submitting their respective rank lists. Importantly, all ACTA positions must be included in the match, including all Exception Agreement positions.

Exceptions to the standard match process have been agreed upon by the ACTA Fellowship Program Directors Council in the following situations:

1. Applicants who are in active military service at the time of application.
2. *Internal candidates, i.e. applicants who are currently in the anesthesiology residency program* at the same institution as the ACTA fellowship.
3. Applicants who are making a commitment to come to the institution of the ACTA fellowship for more than one year.
4. Applicants who are enrolled in an anesthesiology residency outside of the USA at the time of application.
5. Applicants who reside outside the USA at the time of application or who are not eligible for ABA certification due to non-US training.
6. Applicants whose spouse or partner is applying for a GME-approved post graduate training program in a medical specialty in the same region as the ACTA fellowship.

Please Note: *Eligible applicants and programs who wish to take advantage of an exception rule are still required to participate in the match ranking process and must complete an exception agreement found on the SCA website via the link below. Any match irregularities will be referred to the ACTA Fellowship Program Directors Council of the SCA.*

Program directors complete the first part of the match exception process.
Click here to begin.

You will need to log in with your SCA username and password. Once the program director completes this portion of the process, the applicant will receive an email with a link to the form they must complete.

Any match irregularities will be referred to the ACTA Fellowship Program Directors Council of SCA.

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2023 Nominating Slate

Get Ready to Cast Your Vote!

The SCA Nominating Committee, chaired by Immediate Past President Dr. Stan Shernan, MD FAHA FASE, is pleased to endorse the following candidates for the 2023 election cycle. Information about each candidate will be available in the February newsletter and through the online election system.

President-Elect

One position available. Among the following nominee:

- **Amanda A. Fox**, MD, MPH – University of Texas Southwestern Medical Center

Secretary/Treasurer

One position available. Among the following nominees:

- **Michael Eaton**, MD, FASA – University of Rochester School of Medicine
- **Sasha K. Shillcutt**, MD, MS, FASE – University of Nebraska Medical Center
- **Douglas C. Shook**, MD, FASE – Brigham and Women's Hospital

Director-at-Large

Two positions available. Among the following nominees:

- **Andra Duncan, MD, MS** – Cleveland Clinic
- **Jiapeng Huang, MD** – University of Louisville
- **David McIlroy**, MBBS, MD – Vanderbilt University Medical Center
- **Ludmil (Lou) Mitrev**, MD, FASA – Cooper University HealthCare/Cooper Medical School
- **Jochen (Danny) Muehlschlegel,** MD, MMSc, MBA, FAHA, FASA – Brigham and Women's Hospital
- **Jochen Steppan,** MD, DESA, FAHA, FASE – Johns Hopkins University

CME Committee Member

One position available. Among the following nominees:

- **Vaibhav Bora**, MD – Augusta University
- **Pablo Motta**, MD – Texas Children's – Baylor Medical Center
- **Prakash A. Patel**, MD, FASE – Yale University
- **Sarah Smith**, MD, MS – Westchester Medical Center / New York Medical College

Nominating Committee Members

Two positions available. Among the following nominee:

- **Peter Neuburger**, MD, FASE – NYU Grossman School of Medicine
- **Theodore J. Cios**, MD, MPH, FASA, FASE – Penn State Health Milton S. Hershey Medical Center
- **Mathew Varghese Patteril**, MD, FRCA – University Hospital of Coventry and Warwickshire

The 2023 online election for SCA leadership is scheduled to open on January 27, 2022.

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SPECIAL INTEREST GROUP NEWS

WICTA

Registration Opening Soon

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Upcoming WICTA Webinar – Join Us!

HOSTED BY:

SCA's Member Engagement Committee and the WICTA-SIG

Financial Health and Strategic Financial Planning

January 19, 2023

5PM - 6:30PM CST

PANELISTS:

James Hargrave | *Director of Financial Planning My Financial Coach*
James Hargrave brings professional experience in financial planning from his history of working in the banking, investing, and fin-tech industries. He has obtained his Master's in Business Administration, CFP®, CLU®, Series 7 & 63, and the Life & Health License. His background includes working with negative cashflow clients, physicians, executives/directors, and business owners with significant expertise in employers' benefits and personal financial decision-making.

William L. MacDonald | *CEO & Founder of My Financial Coach*
William L. MacDonald is the Founding Partner of many leading organizations in the executive compensation and benefit consulting field, notably Compensation Resources Group, LLC, Merrill Lynch Executive Compensation Group, and Retirement Capital Group, LLC. He also serves as a managing director for market leader Executive Benefit Solutions. Bill has written two bestsellers and long term is involved with a leadership/CEO group at Harvard Business School.

Nora Yousif | *Financial Advisor and Senior Vice President The Empower Wealth Group of RBC Wealth Management*
Nora Yousif, CFP®, CDFA®, CPFA®, MBA is a Financial Advisor and Senior Vice President at the Empower Wealth Group of RBC Wealth Management. In addition to educating her clients one on one, she has presented on personal finance and investments for over 300 organizations. Nora frequently contributes to TV and Radio shows like NBC Boston, Channel 5, and Yahoo! Finance Live. Nora has been published in CNBC articles, MarketWatch, and Forbes. Finally, she received her MBA from MIT Sloan, having been immersed with some of the brightest minds in the world of finance.

MODERATORS:

Choy Lewis, MD

Gina Linganna, MD

Agnieszka Trzcinka, MD

Added Benefit of SCA Membership

SCA UNIVERSITY
An Online Learning Management System

About SCA University

SCAU is a powerful new learning management system available exclusively to SCA members. This powerful platform allows you to access hours of learning tailored to your needs, accessible whenever are wherever is most convenient for you.

We developed this content library to offer more educational opportunities on the topics that are most important to our members. SCA University allows us to tap into the wealth of of knowledge and expertise in our organization, providing the latest clinical updates, innovative presentations, and relevant publications from around our community. New content on the hottest topics will continually be released throughout the year.

We've developed this powerful resource to be the go-to knowledge base for the international community of cardiac, thoracic, and vascular anesthesiologists.

Incredible Educational Content

View an ever-growing library of courses across an incredible range of topics from leading experts in cardiovascular anesthesiology!

Earn CME Anywhere

View an ever-growing library of courses across an incredible range of topics from leading experts in cardiovascular anesthesiology!

Time to Renew?

SCA would like to take this opportunity to thank you for your continued support during 2021. Your involvement is important and very much appreciated. We hope that you would take the time to renew your membership and remain part of our organization. It couldn't be easier — just **click here** to pay your dues online.

If you have any questions regarding your membership dues, please contact Karen Potempa at **karen@veritasamc.com.**

Fellow Membership Update!

Congratulations to all who have recently completed their fellowship!
When renewing your SCA membership, please be sure to renew at the active or associate rate. Should you need assistance when doing so, please contact Karen Potempa at **karen@veritasamc.com.**

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THORACIC CORNER

Effect of Propofol versus Sevoflurane Anesthesia on Acute Kidney Injury after Lung Transplantation Surgery: A Prospective Randomized Controlled Trial

Song, Y.; Paik, H.-C.; Kim, N.; Jung, H.; Lee, J.-G.; Yoo, Y.-c. Effect of Propofol versus Sevoflurane Anesthesia on Acute Kidney Injury after Lung Transplantation Surgery: A Prospective Randomized Controlled Trial. J. Clin. Med. 2022, 11, 6862. https://doi.org/10.3390/ jcm11226862.

Reviewers:

Melissa Burtoft, MD
Department of Anesthesiology and Perioperative Medicine
University of Pittsburgh Medical Center, Pittsburgh, PA

Ashley Fritz, DO
Division of Cardiovascular and Thoracic Anesthesiology
Mayo Clinic, Jacksonville, FL

Background

Respiratory failure is a predominate cause of death globally, and lung transplantation remains the only definitive treatment for end stage lung disease (ESLD).[1] Complications secondary to lung transplant (LTx) are common and the most frequent complication following LTx is acute kidney injury (AKI), occurring in up to 70% of recipients.[2] There are many nonmodifiable risk factors contributing to AKI in LTx, including ischemia reperfusion injury (IR), utilization of extracorporeal circulation, nephrotoxic medications, transfusion of blood products, and surgical stress. Recently, authors from Yonsei University in Republic of Korea investigated possible preventative strategies for AKI in LTx by comparing the organ protective effects of sevoflurane and propofol.

Methods

In this single center, prospective, randomized controlled trial, authors sought to compare the effects of sevoflurane and propofol anesthesia on AKI following lung transplant surgery.[3] Between 2014 and 2016, sixty adults were randomized to either maintenance of general anesthesia with sevoflurane or continuous propofol infusion. The primary outcome assessed was acute kidney injury as defined by the Acute Kidney Injury Network (AKIN) criteria and by the assessment of blood biomarkers of AKI. The blood biomarkers assessed were serum interleukin (IL)-1β, IL-6, tumor necrosis factor-β, and superoxide dismutase, neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C levels. Levels were assessed before surgery and within 48 hours after surgery. Secondarily, authors assessed the post-operative 30-day morbidity and long-term mortality. Notably, all patients underwent isolated double lung transplant with intraoperative veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Patients with a body mass index greater than 30kg/m2, allergy to propofol, recent self-administration of antioxidants, donor age >70 years old, and patients with moderate to severe chronic kidney disease at baseline were excluded from the trial.

Results

The number of patients who received HCV NAT+ lungs increased from 2 in 2016 to 118 in 2019. The number of lung transplants per year also increased throughout the study period. Obstructive lung disease was more common in HCV+ recipients ($p = .002$); FEV1 was lower ($p = .001$); and mean lung allocation score was also lower ($p = .009$). HCV+ donors were more likely to be younger ($p = .017$), white ($p < .001$), and were twice as likely to use drugs or alcohol. HCV+ donors were more likely to have PaO2/FiO2 ratios > 300 ($p = .029$). Lungs from HCV+ donors travelled longer distances and had longer

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ischemic times than HCV- lungs (p < .001). There was significant regional variability regarding where HCV+ lungs were transplanted. For example, 33% of HCV+ lungs were transplanted in region 1 (New Fifty-nine patients were included in the final analysis twenty-nine were randomized to the sevoflurane arm and thirty were randomized to the propofol arm (1 patient was excluded due to surgery cancellation). Authors reported that 11 patients (38%) had an incidence of post-operative AKI according to the AKIN criteria in the sevoflurane group compared with 4 patients (13%) in the propofol group (p = 0.030). Additionally, authors reported the NGAL levels were significantly lower in the propofol group immediately, and 24 and 48 hours after surgery as compared to the sevoflurane group. Notably, no patients in the propofol group developed stage II or III AKI, compared with four patients in the sevoflurane group. The authors reported no statistically significant differences in post-operative morbidity, hospital length of stay, incidence of primary graft dysfunction (PGD) grade 3, or mortality at 1, 3, and 5 years. Independent of the anesthetic choice, patients who developed AKI showed a significantly lower 5-year survival rate as compared to those recipients without AKI.[3]

Discussion

There is evidence that both sevoflurane and propofol provide some level of renal protection during surgery.[4,5] This study suggests that propofol reduces the incidence of AKI in patients undergoing LTx when compared with the utilization of sevoflurane.[3] However exciting, this manuscript presents considerable limitations that should be analyzed when considering the data posed. The study proffers a small sample size and does not delineate the duration of ECMO support, incidence of hypoxia, or perioperative hemodynamic instability, or the use of vasoactive medications. Reduction in the incidence of AKI in lung transplant recipients could improve survival rates and continued attention should be paid to methods in which AKI can be prevented.

References

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3. Song Y, Paik HC, Kim N, Jung H, Lee JG, Yoo YC. Effect of Propofol versus Sevoflurane Anesthesia on Acute Kidney Injury after Lung Transplantation Surgery: A Prospective Randomized Controlled Trial. *J Clin Med*. 2022;11(22).
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5. Yoo YC, Shim JK, Song Y, Yang SY, Kwak YL. Anesthetics influence the incidence of acute kidney injury following valvular heart surgery. *Kidney Int*. 2014;86(2):414-422.

LITERATURE REVIEWS

Mitral Annular Elasticity Determines Severity of Regurgitation in Barlow's Mitral Valve Disease

Karl-Andreas Dumont, MD, PhD, Hans Martin Dahl Aguilera, MSc, Robert Persson, MD, Victorien Prot, MSc, PhD, John-Peder Escobar Kvitting, MD, PhD, and Stig Urheim, MD, PhD, Oslo, Trondheim, and Bergen, Norway. J Am Soc Echocardiogr. 2022;35(10): 1037-1046. doi:10.1016/j.echo.2022.07.001

Reviewers:

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Background

Barlow's mitral valve disease is a clinically important form of degenerative mitral valve disease that can be challenging for most cardiac surgeons. The two most common etiologies of degenerative mitral valve disease include fibroelastic deficiency and Barlow's disease.[1] Barlow's disease is characterized by pronounced annular dilatation, bileaflet prolapse, presence of thick, spongy leaflets due to excessive myxomatous tissue proliferation, as well as abnormally thickened leaflet tissue with or without calcifications.[2] It can also involve the subvalvular apparatus and result in annular dilatation.

In a normal beating heart, conformational changes of the mitral annulus take place during late diastole and isovolumetric contraction phases, preventing flow reversal during ventricular systole.[3] The characteristic saddle-shape of the mitral annulus allows it to contract like a sphincter, enhancing leaflet coaptation. However, in Barlow's mitral valve disease, the annulus is often larger and more dynamic. This research study used a holographic display enabling in-depth visualization of 3-dimensional transthoracic echocardiographic (3D-TTE) data to determine if the onset and severity of late systolic regurgitation is determined by annular dynamics and mechanical stress on the left ventricle (LV).

Methods

The study population consisted of 10 consecutive Barlow patients with moderate to severe mitral regurgitation and 10 healthy controls without history of cardiovascular disease. Parameters such as resting blood pressure, heart rate, left atrial volumes, left ventricle dimension and volumes, and cardiac output were measured. 3D-TEE was analyzed using a holographic display which allows tracking and measurements of mitral annulus surface area (ASA) throughout the cardiac cycle. Mitral annular disjunction was determined if there was a wide separation (β5mm) between the posterior leaflet insertion into the left atrial wall and the base of the LV free wall. The disjunction index was calculated as the product of the maximal disjunction distance and the disjunction arc degree. The mitral ASA was tracked and measured throughout the cardiac cycle. A novel annulus elastance index was derived, defined as βASA/βP (cm2/mmHg), calculated between aortic valve opening and onset of mitral regurgitation.

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From the 3D echocardiographic data, the mitral apparatus was segmented and modeled using a finite element framework to obtain a measure of the relative change in annulus size during systole. Global annulus stretch rate was also calculated by differentiating the global annulus stretch with respect to time.

Results

Compared to controls, patients with Barlow's mitral valve disease had larger LV and left atrial volumes. Left ventricular ejection fraction was normal for both groups. Mitral regurgitation in Barlow patients occurred in late systole and were characterized by functional mitral valve prolapse, with an average number of regurgitant jets of 2.3 β 0.7. Hemodynamic variables differed in age, LV internal dimension diastole index, LV internal dimension systole index, LV cardiac output index, and left atrial volume index.

Measurements of the annulus geometry throughout the cardiac cycle were obtained in healthy control versus Barlow patients. Peak systolic surface area, commissure width, and septal-lateral length were increased in patients with Barlow's mitral valve disease, as well as peak systolic annulus height to commissure width ratios. Peak systolic ASAs in controls were 9.3 β 0.6 cm2 versus 21.1 β 3.1 cm2 in patients with Barlow's mitral valve disease. In addition, patients with Barlow's mitral valve disease had paradoxical annular motion during systole.

Severity of regurgitation varied in relation to annulus dynamics and blood pressure. Mean systolic annulus elastance index 0.058 β 0.03 cm2/mmHg correlated strongly with disjunction index. Regurgitation volume also showed a positive correlation with systolic blood pressure.

Discussion

TThe present study analyzed mitral annulus dynamics using high temporal resolution holographic display in Barlow's mitral disease patients. The holographic display appears to improve visualization of commissures and anatomical landmarks compared to the multiplane reconstruction method. There was a positive correlation between mitral annulus dysfunction and systemic blood pressure.

In patients with Barlow's mitral valve disease, the study confirmed paradoxical enlargement of annular dimensions during systole, as well as a characteristic late-systolic widening of commissural width with a flattened mitral annulus. The present study introduced a novel elastance index of the mitral annulus which correlated with the severity of mitral annulus disjunction in patients with Barlow's mitral valve disease. In addition, the severity of regurgitant flow across the mitral orifice area was blood pressure dependent, with an acute response to reduction in blood pressure.

Limitations include that this was a small-scale study. In addition, the LV volumes that were measured were obtained from TTE for mitral valve analysis. The volume rate is generally higher compared to other studies using transesophageal echocardiography. LV pressures were also measured non-invasively, which can affect the estimates of the annulus elastance index. In addition, the LV flow data and echocardiography was not obtained simultaneously, thus not accounting for differences in heart rate.

This study is promising because creating patient-specific finite element models may allow us to reproduce the patient's in vivo valvular behavior, which can potentially improve surgical planning and procedures, as well as enable the development of new and sophisticated surgical implants.

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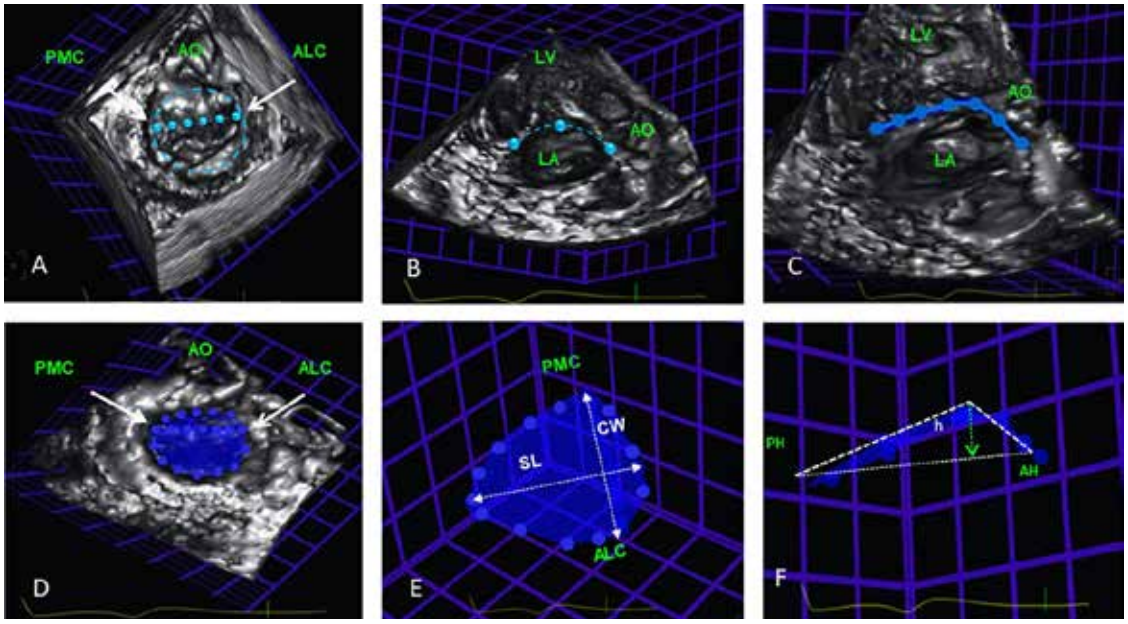

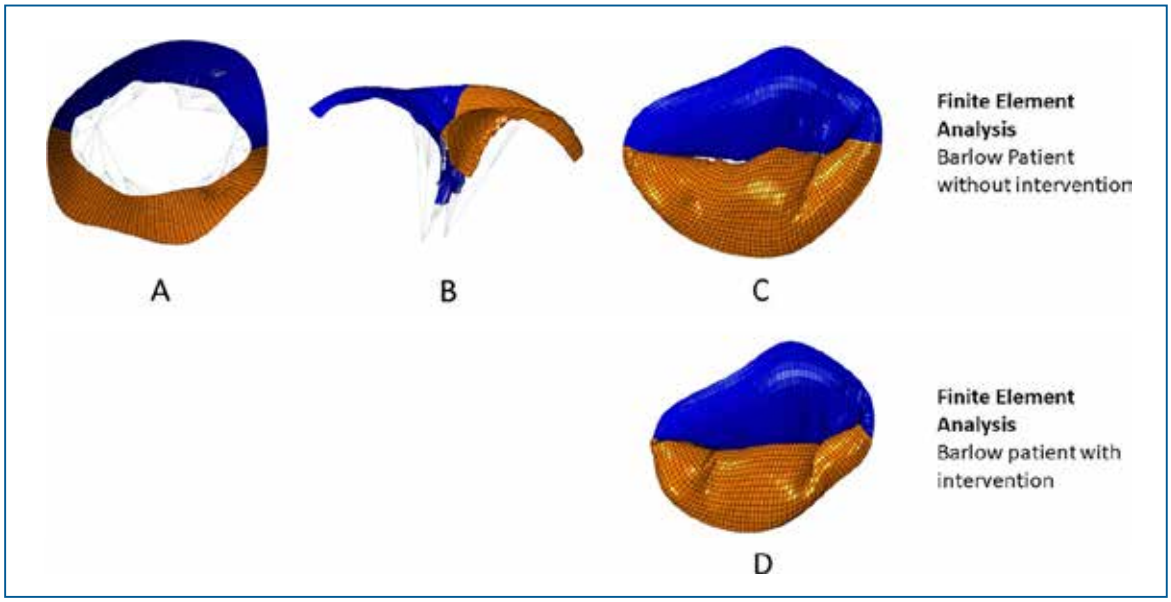

Illustration of the finite element analysis of the mitral valve, mitral annulus, and chordae of a Barlow patient.

Sex Differences in In-Hospital Mortality After Open Cardiac Valve Surgery

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Background

Patients with severe valvular heart disease, have significant morbidity and mortality, therefore are referred for corrective cardiac surgery, valve repair or replacement, open or percutaneous according to the specific valvular pathology, age and comorbidities. Are there differences in the outcomes between men and women? A few, relatively small and mostly single center studies1-5, looked at postoperative outcomes for coronary revascularization only or specific valvular procedures (e.g., mitral valve repair or percutaneous valve deployment) and showed worse outcomes in females. None of these prior studies are large or multicenter. The authors of the study used inpatient data available through the Healthcare Cost and Utilization Project (HCUP) State Inpatient Database (SID) from 2007-2018 in Washington, Maryland, Kentucky, and Florida; 2007-2011 in California; and 2007-2016 in New York. Inpatient data from 272,954 patients in 345 hospitals were analyzed. The hypothesis was that female sex is associated with increased in-hospital mortality after open cardiac valve surgery.

Study Design

The study is a retrospective cohort of patients who underwent open cardiac valve surgery from 2007-2018 utilizing data from 272,954 inpatients in 345 hospitals from the HCUP SID6 database. IRB approval was granted by Weil Cornell Medicine. Written informed consent was waived because the data in the HCUP SID database are deidentified. The database captures data from nearly 95% of inpatient hospital stays classified by state. Data for over 100 variables such as diagnosis, procedure codes, demographics, length of stay (LOS), complications, hospital course, disposition at discharge or hospital-specific data are included in the database. Patients with insufficient demographic information, under 18 years old and those who had percutaneous procedures were excluded.

Objectives of the study were: estimation of the confounder-adjusted association of sex (female vs male) with in-hospital mortality (primary outcome) and LOS (secondary objective) after open cardiac valve surgery.

The primary outcome captured mortality across the entire cohort after any open valvular repair or replacement. A separate multivariate subgroup analysis was performed for each valve including aortic valve repair, aortic valve replacement, mitral valve repair, mitral valve replacement, etc. for the pulmonic and tricuspid valves as well as for multiple valves or for combined valve /CABG procedures.

Separate analysis was done to investigate the interaction of sex with various factors included in the database such as the hospital volume or state, the category of primary insurance payer (uninsured, Medicare, Medicaid, private), age, race, zip code, income,

comorbidities, complications, year of surgery, elective, urgent or emergent surgery.

In the analysis of the secondary outcome LOS, to account for competing risk of mortality, LOS for any patient who died was calculated as the longest LOS in the group because the outcome was time of discharge alive.

The applicable guidelines from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)7 were followed. SAS version 9.4 (SAS institute) and Stata Se version 16 were used for the statistical analysis.

Results

The majority of the 272,954 patients included were men (60.27%) but the mean age between men and women was similar (66.3±13.8 and 67.6±14.3 years respectively). 76% of male patients and 71.9% of female patients were white. Medicare was the predominant insurance coverage in men and women (57.9% and 65.1% respectively). The stratification by individual valve type is as follows:

Aortic valve replacement N=75,565, repair N=4661

Mitral valve replacement N=59,392, repair N=20,461

Surgery on multiple valves N=17,377

CABG/valve combined N=89,639

Other single valve N=5859 (pulmonic or tricuspid repair or replacement cases were analyzed together because neither reached statistical significance alone due to the small number. Most commonly tricuspid or pulmonic valve surgery was done in combination with another valve or CABG).

From the 11,793 in hospital deaths (4.32%), 6282 were male (3.82% of men) and 5,511 were female (5.08% of women).

The median LOS was 9 days for women and 8 days for men.

From the multivariate logistic regression analysis of the confounder odds ratios, it was estimated that there are 41% greater odds of inpatient mortality in the females after open valvular surgery than in males.

After stratification for procedure type, higher odds ratios for in-hospital mortality had females who underwent aortic or mitral valve replacement, combined valve replacement or valve replacement and CABG. The odds for in hospital mortality in females was not higher for isolated valve repair, aortic, mitral, or other.

Also, female patients who underwent open aortic valve replacement alone were less likely to die in the hospital after surgery than male patients who underwent combined CABG/ valve surgery. In contrast, female patients who underwent multiple valve surgeries were more likely to suffer in hospital death than male patients who underwent CABG/ valve surgery.

Conclusions and Discussion

In this retrospective cohort of 272,954 patients who underwent open cardiac valve surgery females were found to have increased unadjusted and confounder- adjusted in-hospital mortality. Subgroup analysis did not find higher mortality in females after single valve repair. The result of this analysis agrees with the results of previous smaller studies which focused on specific valvular pathology. The etiology of the observed higher mortality after open cardiac valve surgery in females is neither well understood

nor studied. Further research is needed to identify parameters and factors which with optimization will improve outcomes of female patients after cardiac surgery.

Strengths of the study are the large number of patients, from different hospitals, in different states, the 12-year time span, the high level of statistical power achieved as well as the multivariate and subgroup analysis of the data.

Limitations of the study are:

1. As a retrospective cohort, the study is subject to selection bias, confounding and reliability concerns. For example, not accurate or missing values in the database such as absence of the intraoperative data (anesthetic technique, duration of CPB or complexity of the surgery). The effect of a possible low data reliability is amplified in large cohorts.

2. A small sample size and therefore low statistical power for the repair group.

3. Potentially important information which may be independently associated with increased morbidity and mortality, such as the severity or etiology (eg endocarditis) of the valvular disease, the surgical technique used, the severity of certain comorbid conditions, body size or the utilization of blood transfusions, blood loss and significant intraoperative events, were not included in the database.

4. Only the in-hospital mortality was included in the database, which may represent an underestimation of the mortality.

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Balloon- vs Self-Expanding Valve Systems for Failed Small Surgical Aortic Valve Bioprostheses

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Background

Patients with aortic stenosis (AS) and a small annulus have worse outcomes with aortic valve replacement than those with larger annulus size; attributed to higher flow gradients and severity of patient-prosthesis mismatch (PPM).1 PPM results when the valve is small for the patient's body size, leading to a decreased indexed effective orifice area (EOA), a resultant increased flow gradient, reduced left ventricular mass regression, and recurrent AS.1 Surgical aortic valve replacement (SAVR) is associated with higher rates of PPM than transcatheter aortic valve replacement (TAVR) for patients with a small annulus2 and higher valve gradients.1

In patients with surgical-valve dysfunction, valve-in-valve TAVR (ViV-TAVR) has emerged as a method of repair; however, having a smaller annulus is associated with worse survival in retrospective studies.3 Studies comparing ViV-TAVR types show self-expanding valves (SEV) may offer better hemodynamics than balloon-expanding valves (BEV) with lower post-procedural gradients3,4 and PPM.3 Given the retrospective nature of the studies, confounding variables such as an unequal distribution of mechanism for surgical valve failure (with more patents with primary stenosis treated with BEV)3 and use of multiple generations of valves4 limit definite conclusions. This study is a randomized, multicenter trial assessing the differences in echocardiographic (ECHO) flow dynamics at 30 days between BEV and SEV in patients with small annulus.

Methods

Using experienced centers in the United States, Canada, and Europe, 102 patients with small (β23 mm, β21mm inner diameter) failed stented surgical aortic valves were randomized to BEV SAPIEN (3/ULTRA, Edwards Lifesciences) or SEV Evolut (R/PRO/PRO+, Medtronic) using a centralized process that ensured equal representation of means of valve failure (primarily stenosis or regurgitation) between groups. Ultimately, 98 patients underwent ViV-TAVR, of which 49 had a BEV and 53 had a SEV; one patient in the BEV group did not undergo ECHO at 30 days. ECHO at 30 days was assessed at a central core laboratory for left ventricular ejection fraction, mean aortic gradient, maximal aortic gradient, effective valve area, and severe PPM based on Valve Academic Research Consortium (VARC)-2 (EOA β0.65 cm2/m2)5 and VARC-3 (EOA β0.65 cm2/m2 for BMI <30 kg/m2 or β0.55 cm2/m2 for BMI β30 kg/m2)6 definitions. Surgical ring fracture was at the discretion of the heart team.

A hemodynamic substudy was also performed at baseline, during the TAVR procedure, and before discharge on a subset of 55 consecutive patients.

Results

The mean age of the patients was 80 ± 6 years. The surgical value dysfunction was seen at 11.0 ± 5 and 10.7 ± 4.0 years for the BEV and SEV groups, respectively. Predominately stenosis was seen as the more common mechanism for surgical valve failure with 33 BEV and 35 SEV patients, while 16 BEV and 18 SEV patients had predominately regurgitation. Baseline patient characteristics including medical therapy, preexisting medical conditions, and ECHO gradients were similar between groups. ViV-TAVR placement was successful in all patients. There were no differences in clinical outcomes, including death, stroke, myocardial infarction, major bleeding, major vascular complication, or permanent pacemaker implantation. The only procedural complication incurred by any patient was one coronary obstruction while undergoing BEV (P = 0.47). Surgical ring fracture was performed significantly more in the BEV group (BEV n = 14 and SEV n = 7; P = 0.04), resulting in a significant reduction in mean transvalvular gradient in both the BEV (P = 0.001) and SEV (P = 0.02) groups. ECHO of 9 BEV and 9 SEV patients could not be performed at 30 days due to COVID restrictions and were thus not included in results. There were no deaths at 30 days. Compared to BEV, SEV showed better maximal (15 ± 8 and 23 ± 8 mmHg; P < 0.001) and mean (28 ± 16 and 40 ± 13 mmHg; P < 0.001) transvalvular gradients. EOA was higher for SEV (0.77 ± 0.28 cm2/m2) than BEV (0.65 ± 0.24 cm2/m2) patients (P = 0.04); however, rates of VARC-3 defined severe PPM did not reach statistical significance (39% of BEV and 20% of SEV patients; P = 0.053). No patients had moderate or severe aortic regurgitation (AR) post procedure.

The substudy demonstrated that during the cases, mean and peak gradients were similar between BEV and SEV patients on invasive hemodynamics. Similarly, ECHO during the case showed similar mean and maximal gradients between groups. Interestingly, ECHO before discharge (median of 1-day post-procedure) showed the SEV group to have significantly lower mean (P = 0.001) and maximal (P = 0.001) gradients.

Discussion

ViV-TAVR is a safe procedure with a very low rate of complications. This study group demonstrated no cases of post procedural moderate or severe AR, stroke, or death at 30 days. There were also no cases of permanent pacemaker implantation in both groups. This important finding is in accordance with other recent data suggesting a lack of difference in conduction disturbance requiring pacemaker implantation following ViV-TAVR between the newer generation BEV and SEV systems, unlike earlier generation valves which did demonstrate a significant difference with higher rates occurring in CoreValve (vs SAPIEN/XT) recipients.7

The SEV group was shown to have better flow dynamics and a trend toward lower severe PPM on ECHO at 30 days, while invasive hemodynamics at time of valve placement did not demonstrate differences between groups. However, there was discordance between invasive and ECHO hemodynamics with lower gradients on invasive measurement than ECHO; these differences tended to be larger in the BEV group. The discordance may reflect the inability of the ECHO measurements to capture pressure recovery more distally. It should also be noted that, as recommended per-protocol and valve manufacturer, the BEV group had a higher number of smaller valves placed than the SEV group. Further, while the rates of balloon predilation (<10% in both groups) and postdilation (27% and 30% in the BEV and SEV groups, respectively) were similar between groups, the BEV group used surgical ring fracture

maneuvers (35% vs 12% in the SEV group) more than the SEV group to improve flow gradients after ViV-TAVR placement. Use of the maneuver did not result in any complications and the gradients significantly improved in both groups (mean reduction in the transvalvular mean gradient of 11 mmHg in both groups), suggesting it may be a safe and effective technique in ViV-TAVR at experienced centers.

Additional limitations include small sample size and short follow up time. Future studies with a follow up period longer than 30 days will be needed to make inferences about the long-term clinical impact as well as the optimal technique for measuring valve hemodynamics in ViV-TAVR recipients.

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Early Mortality in Type A Acute Aortic Dissection: Insights From the International Registry of Acute Aortic Dissection

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Acute aortic dissection is a surgical emergency for which mortality increases with each hour. In 1996 twenty aortic centers from 9 countries formed the International Registry of Acute Aortic Dissection (IRAD). It has since grown to include 58 aortic centers in 13 countries (https://www.iradonline.org/sites). By collecting, coordinating and communicating clinical data, IRAD has significantly improved the knowledge, management, and outcome of Type A Acute Aortic Dissection (TAAAD). Harris et al present an analysis of IRAD data to assess 48-hour mortality for patients presenting with TAAAD.

Methods[1]

In a retrospective analysis using the extremely comprehensive International Registry of Acute Aortic Dissection (IRAD) database, the authors identified 5611 patients with Type A Acute Aortic Dissection (TAAAD) from 14 countries between January 1996 and November 2018. The data were split between two groups based on intended management: 1: Surgical (5131 or 91.4%) and 2: Medical (480 or 8.6%). Forty-eight-hour (from hospital arrival) mortality was compared between the two groups and within the surgical group, the latter to report a multivariate analysis of mortality predictors. A sub-analysis of the surgical group was performed for those who died before the intended surgery. Additionally, the authors compared two times periods between 1996 and 2018: 1996-2007 vs 2007-2018.

Results

Overall mortality within 48 hours of hospital arrival was 5.8% or 0.12%/hour. The 48-hour mortality for the medical group was 23.7% or 0.5%/hr. For the surgical group the 48-hour mortality was 4.4% or 0.09%/hr. Surgical outcome was improved outcome in surgical patients from 2007-2018 compared to the preceding years (5.5% vs 3.9% p = 0.01). Figure 1 suggested that mortality was a steady linear occurrence from the time of admission.

Fifty-one (1%) of surgical patients died before surgery. This group was older, presented with pulse deficits, loss of consciousness, or coma (e-table 3 supplement). This group was complicated by more major end organ injury. Cause of death included cardiac tamponade, limb ischemia, and rupture. The median time to death of these 51 patients was 8.9 hours. For those who had surgery, the median time to diagnosis was 2.5 hours and the median time to surgery was 6 hours.

Predictors of in-hospital death for surgical patients included age, mal-perfusion, hemodynamic instability, prior cardiac surgery, and timing from hospital admission to surgery.

Discussion

The authors describe the first 48 hours as a 'vulnerable time frame' for patients with TAAAD to emphasize the outcome value of facilitating care. Suspicion, assessment, and definitive care would prevent the occurrence and/or severity of end organ ischemia/dysfunction, bleeding, cardiac tamponade and/or rupture.

The differences in outcome data between surgical and medical patients support the value of surgery. However, the data presented may be skewed. The 4.4% 48-hour mortality for surgical patients does not capture those who may have died prior to arriving to the hospital. The authors present a 5x benefit of surgery over medical management, however, this was a data base retrospective analysis, and the medical group were significantly older, sicker, more comorbidities, higher risk, and presented with greater comorbidities and injury severity including but not limited to age, lung disease, prior heart surgery, prior dissection, diabetes, greater neurologic complications, mesenteric ischemia/infarction, kidney failure, and hypotension.

Delaying surgical intervention has severe consequences for patients presenting with TAAAD by increasing the chance of progression to include tamponade/rupture, visceral ischemia, and neurologic complications. Approximately 50% of TAAAD present unstable defined by hypotension/hemodynamic instability and/or severe end-organ ischemia/dysfunction. Surgery for TAAAD is emergent even for the stable as any delay increases the chance of converting a stable patient to an unstable patient.

Once diagnosed there is little benefit in delaying definitive care. The data from this study was based on the time of hospital arrival. A large percentage of patients are suspected or diagnosed with TAAAD at an outside facility requiring transfer to the tertiary center. The 'clock' would have started ticking.

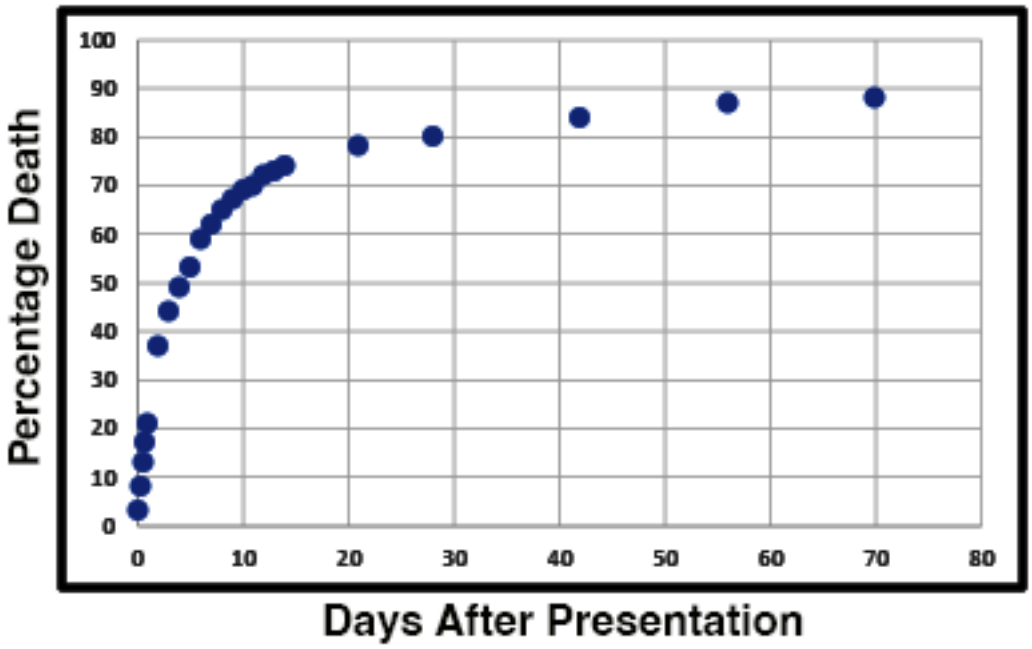
The fist described TAAAD by Frank Nicholls who performed an autopsy on King George II of England who died in October 1960.[2]

". . . the pericardium was found distended with a quantity of coagulated blood, nearly a pint . . .; the whole heart was so compressed as to prevent any blood contained in the veins from being forced into the auricles; therefore, the ventricles were found absolutely void of blood . . .; and in the trunk of the aorta we found a transverse fissure on its inner side, about an inch and a half long, through which some blood had recently passed under its external coat and formed an elevated ecchymosis."

Hirst et al presented review the clinical presentation of 505 cases between 1933 and 1954 diagnosed, at autopsy with aortic dissection.[3] Less than 20% were correctly diagnosed prior to death. More common presentations included chest, back, and/or arm pain, tachycardia, cardiovascular shock, pericardial and/or pleural effusions, and/or cyanosis.

Mortality increased with increasing time after presentation (See FIGURE 1 next page):

Figure 1: Extracted mortality data from Hirst et al (3)



In 1954 Debakey et al reported their first surgical repair of a TAAAD and by 1956 they reported a 22% 2-year survival of their first 18 patients.[4,5,6] In the 1980s the group reported a 20 year follow up of surgically treated aortic dissection. While operative mortality declined for Type 1 (27% to 20%) and II (15% to 8%) dissection, long term mortality was high at 5, 10, and 20 years, with survival rates of 57%, 32%, and 5% survivals.[5,6]

Hospital or 30-day mortality for Type A (I and II) aortic dissection is higher with medical management compared with surgery (60.2% vs 23.6%) and that outcome is dependent on reducing the time between presentation and surgery.[1,7,8] Even under optimal conditions, 30 day or hospital mortality for surgical patients ranges from 17 to 30%.[7,9,10,11,12] Predictors of death include instability on presentation and greater end-organ dysfunction.[9] Postoperative complications include cardiac dysfunction (up to 50%), respiratory failure (up to 40%), neurologic dysfunction (30-40%), renal dysfunction (25-30%), bleeding (20%) and multi-organ failure (20%).[13] Causes of death include rupture, cardiac tamponade, visceral ischemia, multi-organ failure, and/or neurologic injury.[1,7,8,13]

Suspecting an aortic dissection should prompt emergent action. More than 70% of patients have a history of hypertension, evidence of atherosclerosis in < 30%, and more than 70% present with pain either in the chest, the back, and/or arm.[7,10] Twenty to more than fifty percent present with instability, e.g. hypotension, cardiovascular shock, visceral (e.g. mesenteric) ischemia/infarction, lower extremity ischemia and/or neurologic injury.[9,10,11] Interestingly, electrocardiographic changes are non-specific in approximately 40% or may be consistent with ischemia/infarction in 15-20% perhaps contributing to delays in diagnosing AD.[10] Since 1996, the use of computed tomography, transesophageal echocardiography and magnetic resonance imaging has increased and now provide the definitive assessment and are critical to formulating a therapeutic plan for those suspected of having aortic dissection.[10]

The hourly mortality data presented by Harris et al (0.09%) is similar and slightly less than that previously presented in other data (1-2%).[10] Although management pathways

are better defined there is still a significant delay to make a diagnose and arrive to the operating room. The total median time of 6-9 hours does not include the delay for those who present to outside hospitals and transferred to an aortic center.[1,10] Kawabori M, Kaneko et presented a 'Code Aorta' to describe a coordinated process for a suspected aortic dissection including management of acute complications, diagnostic imaging, and, if necessary, facilitating transfer to an aortic center. Simultaneously the necessary care givers are alerted as to the possible cardiac surgical emergency.[14]

PRO CON

PRO/CON DEBATE

Assessing The Cause of Postoperative Bleeding in the Cardiac Surgical Patient

Andrew Maslow MD

Excessive bleeding (1-2 ml/kg/hr) occurs in 5-15% of cardiac surgical patients.[1,2,3] Post cardiopulmonary bypass sternal re-exploration is reported in 3-5% of all cases.[3,4,5,6] Bleeding, transfusion with or without re-exploration is associated with prolonged intubation, length of ICU and hospital stay, and increased morbidity and mortality.[1,2,3,4,5,6] Prevention of and/or determining the etiology of bleeding is critical to establish hemostasis.

Causes of perioperative bleeding can be divided into 'surgical' and 'non-surgical'. For cardiac surgical patients, more than 60% is related to poor surgical hemostasis.[7,8] Causes of non-surgical bleeding include a host of perioperative variables. Generally, preoperative congenital coagulation defects and anticoagulant and anti-platelet medications are known form history and standard lab tests. Congenital coagulation issues can be specifically addressed depending on the defect. Preoperative anticoagulant/antiplatelet medications are addressed with cessation and time.[1,2] For urgent or emergent cases, when timely is not possible, an alternate plan is needed to reverse the anticoagulant effects.[9]

Anti-Platelet Medications

Name	Mechanism	Action	Route	Reversible/Irreversible - Duration of Effect On Platelet or T1/2	Treatment	Cessation
Aspirin NSAIDs	Cox Inihibtors	COX inhibitor reducing prostaglandin and thromboxane Thromboxane activates the GIIb/IIIa receptors on platelets and initiates platelet aggregation. ADP binds to the $P2Y_{12}$ G-protein-coupled receptor that, in turn, increases the platelet cytosolic calcium (Ca^{2+}) level and induces platelet activation. Reduces binding of G-Protein reducing intracellular Ca^{2+} and activation of Protein Kinase C	PO	Irreversible - 10 days Reversible - 4-7 days	DDAVP Platelets TXA/AA	For high risk: 5 days
Abciximab (ReoPro) Eptifibatide (Integrilin) Tirofiban (Aggrastat)	GPIIb/IIIa Inhibitors	Inhibit PLT aggregation by preventing binding of fibrinogen, vWF, and other adhesive molecules to GPIIb/IIIa on activated platelets	IV IV IV	Irreversible - 0.5 hour (T1/2) Reversible - 2.5 hour (T1/2) Reversible - 2 hour (T1/2)	Platelet Platelet; DDAVP; Cryo Platelet; DDAVP; Cryo	
Cangrelor (Kengrexal) Clopidogrel (Plavix) Prasugrel (Effient) Ticagrelor (Brilinta) Ticlopidine (Ticlid)	P2Y12 Inhibitors Thienopyrdines	Inhibits ADP binding to platelet receptors thereby inhibiting activation of GPIIb/IIIa complex	IV PO PO PO PO	Reversible - < 10 min (T1/2) Irreversible - 6 hours (T1/2) Irreversible - 7 hours (T1/2) Reversible - 12 hours (T1/2) Irreversible - 12+ hours (T1/2)	Platelet; DDAVP; Cryo Platelet; DDAVP; Cryo Platelet; DDAVP; Cryo Bentracimab Platelet; DDAVP; Cryo	 ≥ 5 days ≥ 7 days ≥ 3 days ≥ 8 days

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Anti-Coagulant/Factor Medications

Name	Mechanism	Action	Route	Reversible/Irreversible Duration of Effect (T1/2)	Treatment	Cessation
Warfarin/Coumadin	Vitamin K Inhibition	Inhibit synthesis of vitamin K dependent coagulation factors II, VII, IX, X	PO	Reversible/40 hours Duration of action 2-4 days	Vitamin K Prothrombin Complex Concentrate FFP	> 4 days
Rivaroxaban (Xarelto) Apixaban (Eliquis) Edoxaban (Lixiana) Betrixaban (Bevyxxa)	Factor X Inhibition	Inhibits free and clot bound Factor Xa and Prothrombinase activity	PO	Reversible - 5-9 hours (T1/2) Reversible- 6-12 hours (T1/2) Reversible - 8-10 hours (T1/2) Reversible - > 24 hours (T1/2)	Andexanet/Andexxa Andexanet/Andexxa PCC PCC	> 2 days
Dabigatran (Pradaxa) Argatroban Bivalirudin (Angiomax) Hirudin (Lepirudin)	Direct Thrombin Inhibition	Binds thrombin preventing thrombin mediated activation of V, VIII, XIII, Platelet Activation	PO IV IV IV	Reversible - 12-14 hours (T1/2) Irreversible - 45 minutes (T1/2) Reversible - 25 minutes (T1/2) Reversible - 40 minutes (T1/2)	Idarucizumab (Ab) PCC/Cryo PCC/Cryo PCC/Cryo	> 2 days
Heparin (UFH) Enoxaparin (Lovenox; LMWH) Fondaparinux (Arixta)	Indirect Thrombin Inhibition	Binds and activates Antithrombin to inhibit Thrombin and Thrombin related activation of V, VIII, XIII, Platelet Activation Add Factors: Xa, IXa, XIa, XIIa	IV SC SC	Reversible - 60-90 minutes (T1/2) Not well reversed - 4-7 hours (T1/2) Reversible - 17-21 hours (T1/2)	Protamine Protamine Novo7/PCC	4-6 hours > 24 hours > 24 hours
Alteplase (Activase) Reteplase (Retevase) Tenectaplase (TNKase)	Plasminogen Activator	Forms Plasmin which lyses Fibrinogen and Fibrin Tenectaplase Binds Fibrin	IV IV IV	Reversible - 5 minutes (T1/2) Reversible - 18 minutes (T1/2) 20-24 minutes (T1/2)	No real antidote Tranexamic Acid Aminocaproic Acid	

Intraoperative non-surgical acquired causes include administration of heparin, blood loss, trauma, hemodilution and dilutional coagulopathy.[10,11,12,13,14] The thrombogenic surface of the cardiopulmonary bypass circuit activates both primary and secondary hemostatic components causing a consumptive coagulopathy. Predictors or risk factors for bleeding and reoperation are multiple including, but not limited to emergency surgery, hypocalcemia, acidosis, hypothermia, and duration of cardiopulmonary bypass.[4,6,7,15]

Despite the best preoperative preparation, the perioperative administration of antifibrinolytics (Tranexamic Acid or Aminocaproic Acid), the reversal of Heparin with Protamine, and monitoring and management of metabolic dysfunctions, bleeding still occurs. Although all coagulant components are impacted on, thrombocytopenia/platelet dysfunction, and hypofibrinogenemia are more significant postoperative bleeding.[4,15,16,17] Although data point toward more common causes of non-surgical bleeding, gaining more information regarding primary and secondary coagulation is important to decide between medical management, blood component therapy, factor replenishment, or a return to the operating room for re-exploration.[16]

The Pro-Con section in this SCA Newsletter discusses whether viscoelastic (VE) testing is preferred and necessary in the early postoperative period vs standard lab tests (SLT) to guide hemostasis management. The Pro section highlights the benefits of VET and is followed by the Con section that presents an analysis of the clinical outcome data. While none would refute the value of added information discussion continues about cost, practicality, availability and accuracy of coagulation tests.[1,2,20,21] Ultimately, it is likely that the best assessment and transfusion algorithms are a combination of the two with emphasis on assessment of platelet concentration/function and fibrinogen levels.[1,2,21,22,23,24]

Standard Lab Tests (SLT)

TEST	RANGE	ASSESSMENT
Prothrombin Time (PT/INR)	12-15sec/0.8-1.4	Extrinsic (Tissue Factor) and Common Pathways (II, VII, X)
Partial Thromboplastin Time (PTT)	30-50 sec	Intrinsic (Contact Activation) and Common Pathways (All factors except VII and X)
Activated Clotting Time (ACT)	80-130 sec	Whole Blood Clotting (Factors, Platelet Function)
Platelet Concentration	150-450 x 10^9/L	Platelet Concentration
Fibrinogen Concentration	200-400 mg/dl (2-4g/L)	Fibrinogen Concentration
Thrombin Time	12-14 sec	Factor II Activity
Anti Xa Assay	0.0	Factor Xa levels
Ecarin Clotting Time (ECT)	22-29 sec	Factor II Activity

TEG	Meaning	ROTEM
R value (reaction time)	Time of Latency from start of test until fibrin formation begins (amplitude 2mm). Reflects initiation phase and dependent on clotting factors	CT (Clot Time)
K value	Amplification Phase until a level of clot strength is achieved (20mm) reflecting fibrinogen levels and function	CFT (Clot Formation Time)
α angle	Propagation Phase speed at which fibrin cross linking occurs or a rate of clot formation (slope between R and K) reflecting fibrinogen levels and function	α angle
Maximum amplitude (MA)	Clot Strength Strongest point of fibrin/platelet clot. 80% due to platelet function; 20% due to fibrinogen. The interaction via GPIIb/IIIa	Maximum Clot Formation
LY30	Fibrinolysis Time or Clot Lysis Time Percent decrease in MA in 30+ minutes	LY30, LY60

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Assessing The Cause of Postoperative Bleeding in the Cardiac Surgical Patient

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Introduction

Coagulation is a complex interaction of many different components: platelets, coagulation factors, endothelium, regulatory proteins, and balancing this with clot lysis. Coagulopathic bleeding is anticipated post CPB. Typically, CPB-related coagulopathy is caused by multiple factors and unlikely caused by insufficient reversal of systemic heparin anticoagulation alone. The parts of the bypass circuit induce systemic inflammation and cause insults to the various elements of the coagulation and fibrinolytic systems.

Factors that Could Contribute to CPB-related Coagulopathy Include[1]:

- Hemodilution from priming the circuit with fluids leading to dilutional coagulopathy.
- Inadequate rewarming as hypothermia impairs platelet aggregation and decreases clotting enzyme activity.
- The activation of the intrinsic coagulation pathway due to direct contact of circulating blood with the synthetic surface of the CPB circuit leading to continuous thrombin production and consumptive coagulopathy.
- The activation of the extrinsic coagulation pathway by tissue factor releases in response to tissue trauma and blood vessels injury leading to continuous thrombin production and consumptive coagulopathy
- Residual systemic heparin anticoagulation or protamine overdose
- Transient platelet dysfunction and failure of platelet aggregation formation

All these variables, as well as the presence of certain patient characteristics, such as the patient's use of antiplatelet medications, can contribute to CPB-related coagulopathy.

Approximately 30% of patients with non-surgical bleed continue to bleed postoperatively. It is essential to treat the underlying cause of coagulopathy and to minimize blood loss. "Shotgun therapy" is the most common treatment strategy used for the cardiac surgery patient, which involves blindly transfusing various combinations of fresh frozen plasma, cryoprecipitate, and platelets to control bleeding. Even though this approach is effective, unnecessary transfusions incur substantial financial costs and increase patient morbidity and mortality. Recognizing the risks associated with excessive transfusion has led to the development of another strategy that employs laboratory-based testing and clinical judgment to direct post-cardiopulmonary bypass transfusion management for cardiac surgery patients. Current traditional coagulation testing with prothrombin time (PT) and by extension international normalized ratio (INR), activated partial thromboplastin time (aPTT), and fibrinogen level. However, there are limitations to this approach.[2]

Limitations of Traditional Coagulation Testing[8]

1. These tests are designed to evaluate the traditionally described extrinsic, intrinsic, and common pathways of coagulation. While useful for monitoring effects of certain medications on coagulation they do not describe coagulation in whole blood.
2. These are laboratory-based tests done under standardized conditions without any information of the current condition of the patient such as temperature.
3. Importantly when using these tests to guide transfusion and resuscitation these

tests must be sent off to the lab and can take significant amounts of time prior to receiving results. Serial measurement

4. They also do not predict the quality of the clot that is formed, nor do they predict the risk of bleeding or ability to form a clot.
5. While these tests can help identify patients who are at a higher risk of bleeding due to thrombocytopenia for example, they do not provide information on the quality of platelet function, such as that which occurs after taking antiplatelet drugs or in uremia.[9-11]

To overcome these limitations and to pinpoint exactly our resuscitation efforts Viscoelastic point of care Tests can be used in the cardiac operating room and postoperatively to identify any abnormalities throughout all phases of the clotting process and to direct the transfusions after cardiopulmonary bypass surgery. These tests evaluate the entire hemostatic process from platelet activation and coagulation cascade to clot formation and lysis. Instead of measuring a single endpoint in a conventional coagulation test such as prothrombin time (PT), activated plasma thromboplastin time (APTT), international normalized ratio (INR), platelet count, D-dimer, fibrinogen assay, and clotting time, multiple endpoints are examined.

The Various Types of Viscoelastic Function Monitoring that are Available

Viscoelastic testing is a general term used to describe a collection of commercially available point of care (POC) tests that examine the dynamic process of formation and lysis of blood clots in whole blood sample mixed with an activator in real time. They create a diagram displaying the various stages of clotting over time; The various components of the tracing represent distinct phases of the process. Currently, there are six in vitro diagnostic devices for viscoelastic assays of coagulation; these are the thromboelastogram (TEG 5000, TEG 6s), rotational thromboelastometry (ROTEM gamma, delta, sigma), Sonoclot coagulation analyzer, ClotPro, ReoRox G2 assay and the Quantra Hemostasis Analyzer. The two most widely studied viscoelastic testing devices are TEG and ROTEM which both use a pin and a cuvette with a sample of blood.[9,11]

The Measuring Principle of Viscoelastic Tests[12]

Thromboelastogram (TEG®; Haemonetics, Braintree, MA)

In 1948, Dr. Hellmut Hartert developed and first described TEG at the University of Heidelberg in Germany.13 Using a cylindrical plastic cuvette containing a whole blood sample (0.36 ml) is warmed to at 37oC (normal human body temperature) and the cuvette oscillates and rotates back and forth slowly 4.75° every 10 seconds to simulate venous blood movement. A pin is submerged into cuvette containing the blood sample and is suspended by a torsion wire allowing it to spin and create torsion. When the blood is viscous material, the pin does not move. As the blood begins to clot, the submerged pin adheres to the clot and as the cuvette oscillates the pin begins to move with it and as a result the torsion wire that is connected to a transducer that generate a signal which creates a diagram displayed in an output illustrating the progression of the clot formation and lysis over time. The amount of pin motion is directly proportional to the strength of the clot.[12,14]

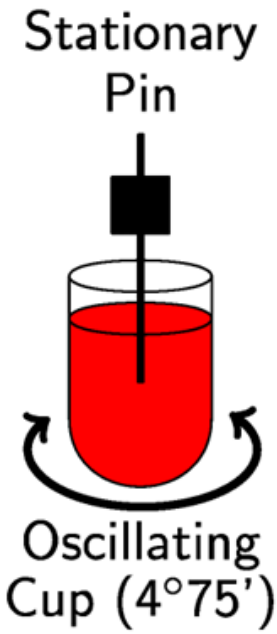
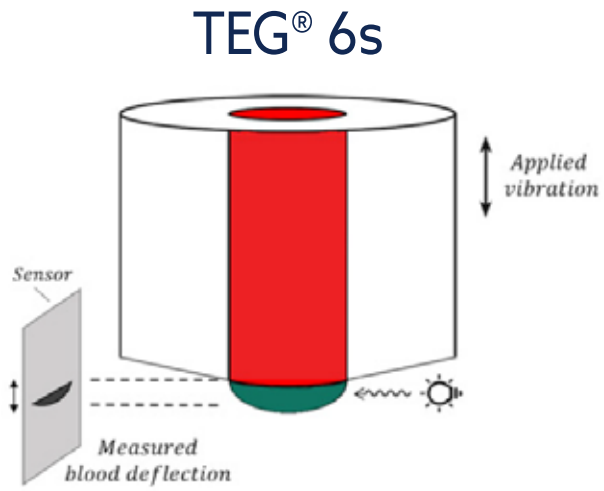


Figure 1. Illustrates, Thromboelastography a pin descends into a cup containing a sample of whole blood that is maintained at 37 °C. device.[15]

The new TEG® 6s is an automated mulz-channel cartridge containing four assays system which measures the clot viscoelaszcity using a resonance method. The mulz-channel cartridge uses a citrated blood sample that is mixed with dried reagents within each of the 4 channels. The sample is directed into the four verzcal short test tubes that are open from top and bottom. The sample blood is supported by surface tension. A convex meniscus forms naturally at bottom opening that is subjected to vibrazon at a predetermined frequency, and by using LED illuminazon, a sensor measures the verzcal mozon of the blood meniscus and idenzfy the frequency leading to blood resonance. The resulzng data is converted to a tracing represenzng clot dynamics.[16,17]
Strong clot formazon has higher resonant frequencies and higher TEG readouts.



Illustrates, Thromboelastography TEG6s resonance method.[15]

Rotational Thromboelastometry (ROTEM®, Instrumentation Laboratory, Bedford, MA, USA) ROTEM is similar to TEG in that a cuvette containing an activated whole blood sample and a pin is submerged within a cuvette; however, in ROTEM, the pin rotates while the cuvette remains still. The ROTEM device exists in three versions: ROTEM-gamma, ROTEM-delta, and ROTEM-sigma.[18] Blood samples and reagents for ROTEM-gamma and -delta are pipetted by hand into cuvettes, but the newest device, ROTEM-sigma, is an automated, closed system that uses prefilled cartridges with four parallel channels. NATEM, INTEM, EXTEM, FIBTEM, APTEM, and HEPTEM are the primary assays used with the ROTEM device, depending on what activators or inhibitors are added to the sample. INTEM, EXTEM, FIBTEM, and APTEM are the usual assays, with others being performed as extras.

- NATEM is used to investigate the intrinsic pathway via the contact phase only with no activator
- INTEM is used to investigate the intrinsic pathway via the Ellagic acid and provides information like that of the APTT
- EXTEM is used to investigate the extrinsic pathway via activation by thromboplastin (tissue factor) and provides information like the PT.
- FIBTEM is used to investigate the fibrinogen component. The same activation as in EXTEM, but with cytochalasin D to break down the platelet cytoskeleton and remove platelet contribution.
- APTEM is used to investigate hyperfibrinolysis. The activation as in EXTEM combined with aprotinin to prevent fibrinolysis.
- HEPTEM assay is used to investigate coagulopathy that is NOT due to heparin. The activation as in INTEM combined with heparinase to degrade heparin.[18,19]

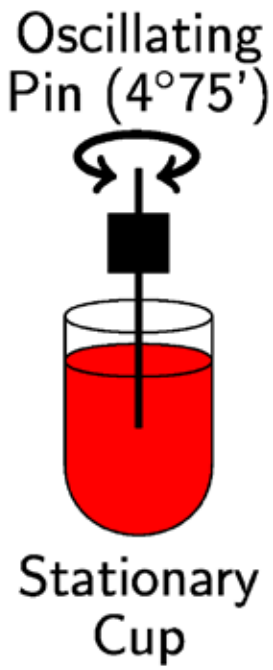


Figure 3.
Illustrates, Thromboelastometry a pin descends into a cup containing a sample of whole blood that is maintained at 37 °C. device.[15]

Sonoclot Coagulation Analyzer (Sienco Inc., Arvada, CO)
The Sonoclot Coagulation Analyzer is a POC test device that employs a mechanism different from that of the TEG and the ROTEM. The Sonoclot probe capable of oscillating vertically within a blood sample and the probe's impedance to movement is altered as a blood clot forms, creating a signature pattern graph where on the x-axis, time is marked, and on the y-axis, millimeters of the movement of the test probe are marked from which multiple coagulation cascade components can be interpreted.[20,21]

ClotPro (ClotPro® Haemonetics Corporation, Boston, MA, USA)
ClotPro is a six-channel, modified thromboelastometry system. In contrast to ROTEM Delta device, clot formation is measured using a cuvette and a pin, with the pin remaining stationary while the cuvette rotates. It is equipped with active tip technology; thus, manual Reagent handling is not necessary. The analyzer continuously detects alterations in viscoelastic properties. EX-test, IN-test, FIB-test, and HI-test are comparable to the ROTEM tests EXTEM, INTEM, FIBTEM, and HEPTEM respectively.[15,22]

ReoRox G2 Assay (Medirox AB, Nyköping, Sweden)
The ReoRox G2 assay is a viscoelastic-based system that utilizes free oscillation by a magnet to determine the viscoelastic properties of whole blood.[23]

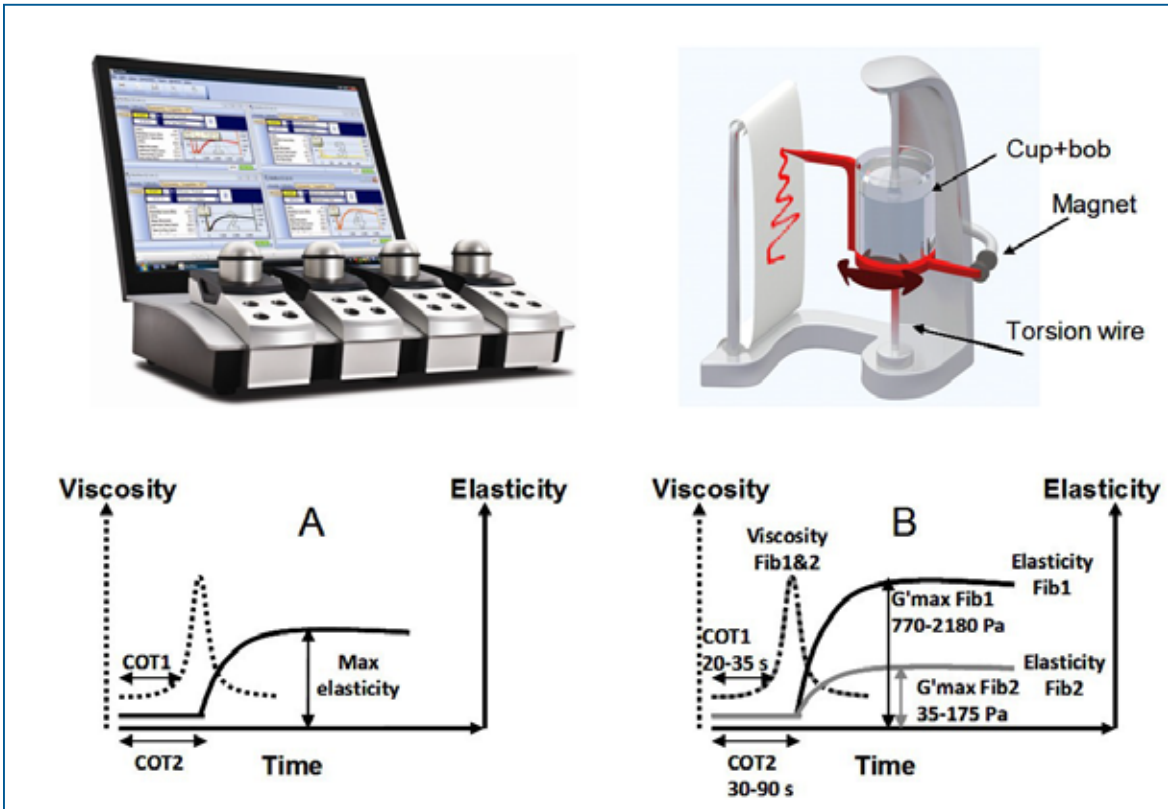


Figure 1. Illustrates, Free oscillation rheometry ReoRox G2 assay device.[23]

Quantra (HemoSonics LLC, Charlottesville, VA)
The Quantra utilizes a technology known as SEER (Sonic Estimation of Elasticity via Resonance) Sonorheometry, in which a transducer emits ultrasound pulses to cause blood sample vibrations and resonance. As blood begins to clot and stiffen over time, its resonant frequencies will increase. Measurements are made of clot stiffness and clot times. A multi-test cell plastic cartridge with embedded reagents is used for each test. Each of the cartridge's four test channels utilizes a unique combination of reagents to conduct four parallel and independent measurements.[24-26]

Figure 1. Images for various viscoelastic devices Top left: TEG6s, TOP right: ROTEM sigma, Bottom left: ClotPro, Bottom middle: ReoRox G2 assay, Bottom right: Quantra.

TEG & ROTEM Descriptive Parameters:

		TEG	ROTEM	Explanation	Interpretation
Coagulation	Clot Initiation	R time	CT	Time until initiation of fibrin formation, taken as a period to 2 mm amplitude on the tracing	Concentration of soluble clotting factors in the plasma
	Clot Propagation	K time	CFT	Time period for the amplitude of the tracing to increase from 2 to 20 mm	Indicates clot kinetics
		α angle	α angle	Angle between the tangent to the tracing at 2 mm amplitude and the horizontal midline	Rapidity of fibrin build up and cross-linking
Fibrinolysis	Clot Lysis	MA	MCF	Greatest vertical width achieved by the tracing reflecting maximum clot strength	Number and function of PLTs and fibrinogen concentration
		CL30	LY30	Percent reduction in amplitude 30 min after MA	Clot stability and fibrinolysis
		CL60	LY60	Percent reduction of clot firmness 1 h after MA	Clot stability and fibrinolysis

Table 1. R time- reaction time; CT- clotting time; CFT- clot formation time; MA- maximum amplitude; MCF- maximum clot firmness; CL 30- clot lysis at 30 min; LY30- lysis at 30 min; CL 60- clot lysis at 60 min; LY60- lysis at 60 min.

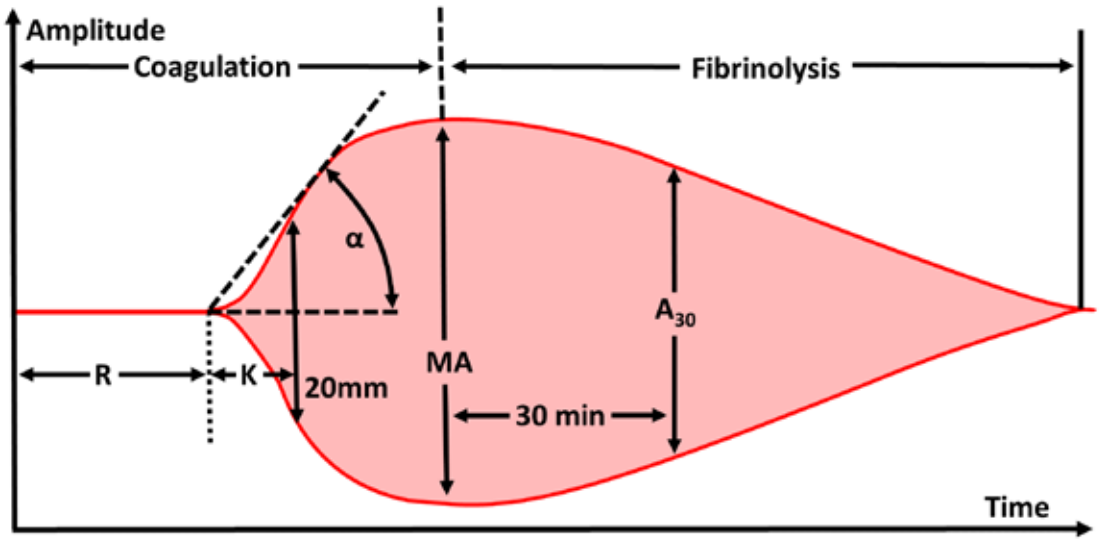
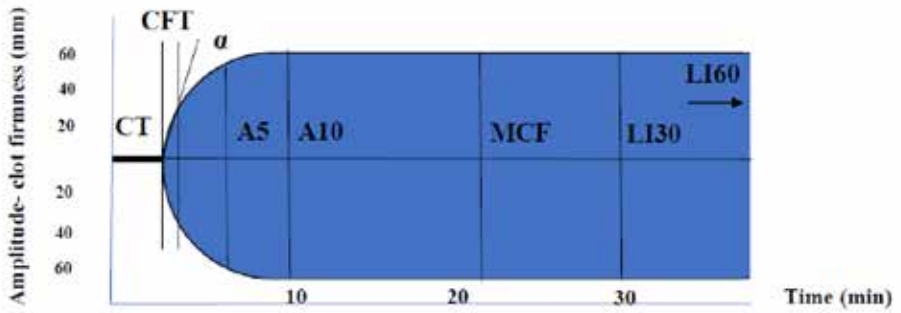


Figure 6. Thromboelastography Parameters as It Appears on TEG courtesy of Mikael Häggström, M.D.



ROTEM parameter	Parameter definition	What does it mean?
CT - clotting time (clot initiation)	Time to reach 2 mm amplitude	Period from the beginning of the clotting to the start of fibrinogen polymerization
CFT - clot formation time (clot amplification)	Time between 2 and 20 mm amplitude	Estimation of velocity of the clot formation
A - alpha angle (clot amplification)	Angle formed by tangent line from baseline to 20 mm	Same meaning as CFT
A5, A10 - early clot firmness amplitudes (clot propagation)	Amplitude at 5 and 10 minutes after CT	Estimation of clot strength at 5 and 10 minutes after CT, which correlates well with MCF
MCF - maximum clot firmness (clot propagation)	Maximum amplitude of clot firmness reached during the test run; if accompanied by an *, it is not already the final result	It reflects the mechanical strength of the clot and depends on platelet function, fibrin polymerization, and factor XIII activity
LI30, LI60, ML - lysis indices and maximum lysis (platelet-mediated clot retraction and fibrinolysis)	Lysis indices characterize the residual clot firmness in percentage of MCF at 30 or 60 minutes after CT; ML is defined as the decrease in clot firmness in percentage of MCF during run time	Estimation of platelet-mediated clot retraction and fibrinolysis

Figure 7. Illustration of thromboelastometry (ROTEM®) tracing and the accompanying parameters.[27]

Interpretation Viscoelastic Point of Care Tests and Guided Therapy

While the actual values cannot be compared between TEG and ROTEM and each measurement has a different name, the graphs are similar, and the terms can be equated to enable understanding (Table 1).

The cardiac surgery patient may have many different causes of coagulopathy and continued bleeding after surgery. In addition to inherited disorders of coagulation many of these patients are taking anti-platelet agents for another medical condition or recent bleeding may result in diffuse intravascular coagulation (DIC). Viscoelastic testing can graphically show the two different stages of DIC based on the number of consumed factors and platelets.

TEG graph patterns as a treatment guide

- IF R time is prolonged give FFP
- If alpha angle is reduced less than 65o (lack of fibrinogen) give Cryoprecipitate or Fibrinogen concentrate
- If MA is reduced less than 55mm (reflects dysfunctional platelets ± lack of fibrinogen) give Platelets ± Cryoprecipitate
- If fibrinolysis is increased LY-30 more than 5% give antifibrinolytic (aminocaproic acid or tranexamic acid)

ROTEM graph patterns as a treatment guide

- IF clotting time (CT) is prolonged (INTEM CT more than 240 seconds or EXTEM CT more than 100 seconds) give FFP
- If FIBTEM amplitude of clot firmness at 10 min (A10) is decreased less than 11 mm (lack of fibrinogen) give Cryoprecipitate or Fibrinogen concentrate
- If FIBTEM A10 more than 10 mm and EXTEM A10 less than 40 mm (reflects dysfunctional platelets) give Platelets
- If EXTEM ML more than 15% (reflects accelerated fibrinolysis) give antifibrinolytic (aminocaproic acid or tranexamic acid)[28,29]

Limitations of Viscoelastic Point of Care Tests[30]

1. Test equipment needs to be calibrated on a regular basis, and tests need to be run by a qualified individual.
2. Because the tests rely on using whole blood samples, the results may vary from lab tests in cases of in situations like hemodilution and platelet dysfunction as experienced during and post CPB.
3. Various manufacturers with different reagents can produce results with varying degrees of sensitivity.

Evidence that Viscoelastic POC Tests Reduces Transfusion Requirements after Cardiac Surgery

The most obvious benefits of viscoelastic testing include the point of care with real time analysis as well as the ability to analyze blood specimens under in whole blood conditions.

Most studies of TEG and ROTEM have been conducted in cardiac surgery patients but other groups at high risk for bleeding such as trauma, OB, orthopedic surgery, and liver transplantation have also been studied. Clear benefits have been found when using viscoelastic testing to guide transfusion medicine.[32-36]

A Cochrane review originally published in 2011 and then updated in 2016 which only included randomized controlled trials which compared transfusion strategies guided by TEG or ROTEM and those guided by clinical judgement or laboratory data found 17 studies. The majority of patients in the review were cardiac surgery patients particularly with patients on cardiopulmonary bypass (1435 patients: 96% of patients).

This review found several significant differences. Using a subset of 8 reviews covering 717 patients the review found an overall reduction in mortality [7.4% versus 3.9%, risk ratio (RR) 0.52, 95% confidence interval (CI), 0.28–0.95]. Transfusion requirements for all of the major blood products were also found to be significant: pRBC (RR 0.86, 95% CI: 0.79–0.94, 10 studies, 832 patients), plasma (0.57, 95% CI: 0.33–0.96, 8 studies, 761 patients), platelets (RR 0.73, 95% CI: 0.60–0.88, 10 studies, 832 patients).

This same review found no difference in the proportion of patients needing surgical re-intervention, massive transfusion, or patients with excessive bleeding. These variables do not depend on transfusion but rather are likely related to the surgery and complications of the surgery itself and cannot be fixed using laboratory testing. The reviewers believed that the use of Viscoelastic POC tests guided transfusion techniques may minimize the need for blood products and improve morbidity in patients with bleeding, particularly in the context of elective cardiac surgery, but warned that the quality of the evidence to support the conclusions was inadequate citing large heterogeneity, low number of events, imprecision, and indirectness in the included studies.[37]

In 2016, Deppe et al performed a meta-analysis of 8332 patients of randomized controlled trials and observational trials to determine the current evidence for or against POCT-

guided algorithm in patients with severe bleeding after cardiac surgery. The reviewers concluded that TEG/ROTEM-based coagulation management decreases the risk of allogeneic blood product exposure after cardiac surgery. Furthermore, it results in significantly lower re-exploration rate.[38]

In 2016, Karkoiti et al conducted a multicenter randomized controlled trial. The reviewers concluded that implementation of point-of-care hemostatic testing within the context of an integrated transfusion algorithm reduces red blood cell transfusions, platelet transfusions, and major bleeding following cardiac surgery. Their findings support the broader adoption of point-of-care hemostatic testing into clinical practice.[39]

In 2015, a Dutch/British health technology assessment report on cardiac surgery patient subset analysis confirmed the results of the Cochrane analysis and showed that viscoelastic testing was cost-effective and more efficient than standard laboratory testing. This subset analysis included 11 randomized control trials with 1089 patients and found a significant reduction in RBC transfusion [RR 0.88, 95% confidence interval (CI): 0.80–0.96; 6 studies], platelet transfusion (RR 0.72, 95% CI: 0.58–0.89; 6 studies) and fresh frozen plasma to transfusion (RR 0.47, 95% CI: 0.35–0.65; 5 studies). There were no significant differences between groups in terms of other blood products transfused, surgical reintervention, length of stay, and mortality but many of the studies were not designed to analyze this.[40]

In 2017, Serraino et al conducted a systematic review and meta-analysis of randomized controlled trials for fifteen trials with a total of 8737 participants were included for the analysis. The reviewers concluded that use of viscoelastic testing reduced red blood cell and platelet transfusion, but had no effect on mortality or major morbidity, except acute kidney injury. Use of TEG® or ROTEM® resulted in reductions in the frequency of red blood cell (Risk Ratio 0.88, 95% Confidence Interval 0.79-0.97; I2=43%) and platelet transfusion (Risk Ratio 0.78, 95% Confidence Interval 0.66-0.93; I2=0%). However, they concluded that the evidence for routine use in cardiac surgery is lacking.[41]

In 2019, Caie Li et al conducted a systematic review and meta-analysis for nineteen studies with a total of 15,320 participants, including 13 randomized controlled trials to evaluate the effects of TEG/ROTEM-guided transfusion algorithm compared to traditional coagulation tests in adult cardiac surgical patients with CPB. The reviewers concluded that TEG or ROTEM-guided transfusion strategies may reduce blood loss volume and the transfusion rates in adult patients undergoing cardiac surgery.[42]

In 2019 Kuiper et al conducted Observational, prospective open cohort study comparing blood management in two cohorts—one by traditional coagulation tests guided algorithm and the other by ROTEM-guided algorithm. The authors concluded that implementation of a ROTEM-guided transfusion algorithm in cardiac surgery patients significantly reduced the use of blood products RBCs (17%) and FFP (12%) in the ROTEM group.[43]

In 2019, Dias et al found that TEG-guided management reduced platelet transfusion ($P = 0.004$), FFP transfusion ($P < 0.001$), operating room length of stay ($P = 0.005$), intensive care unit length of stay ($P = 0.04$), and bleeding rate ($P = 0.002$). However, mortality remained comparable between the treatment and the control group and erythrocyte transfusion ($P = 0.14$) did not reach significance.44

Meanwhile In 2020, Meco et al found TEG/ROTEM reduced FFP transfusion (risk difference, 0.22; 95% CI, 0.11 to 0.33; $P < 0.0001$) and reduced erythrocyte transfusion (odds ratio, 0.61; 95% CI, 0.37 to 0.99; $P = 0.04$) but not platelet transfusion (odds ratio, 0.61; 95% CI, 0.32 to 1.15; $P = 0.12$). They also found a reduction in postoperative bleeding at 12 h: −178.7 (95% CI, −308.9 to 48.4; $P = 0.007$), the need for redo surgery unrelated to surgical bleeding (odds ratio, 0.51; 95% CI, 0.28 to 0.94; $P = 0.03$), and postoperative

intensive care unit stay (odds ratio, −4.03; 95% CI, −6.28 to −1.78; P = 0.005). Similarly, to other studies it did not find a reduction in mortality (odds ratio, 0.57; 95% CI, 0.18 to 1.74; P = 0.28).[45]

Society Advisory and Guidelines

The most obvious benefits of viscoelastic testing include the point of care with real time analysis as well as the ability to analyze blood specimens under in whole blood conditions.

1) Practice Guidelines for Perioperative Blood Management: An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management in 2015 recommend protocols or algorithm-Guided Therapy of Perioperative Bleeding. It suggested TEG/ROTEM-guided algorithms reduced the blood transfusion requirements in presence of coagulopathy.[46]

2) In 2019, the Society of Cardiovascular Anesthesiologists (SCA) released clinical practice improvement advisory for management of perioperative bleeding and hemostasis in cardiac surgery patients. To guide hemostatic intervention, it was recommended that transfusion algorithms with predetermined intervention triggers based on point-of-care coagulation monitoring assays be used. The SCA also stated that the introduction of transfusion and coagulation management algorithms (based on ROTEM/TEG) and goal-directed treatment with coagulation factor concentrates (fibrinogen and/or PCC) may minimize transfusion-associated adverse events. Please see figure 6 with part of the SCA Summary Statement on Blood Conservation.47

3) National Institute for Health and Care Excellence (NICE) Centre for Health Technology Evaluation United Kingdom released recommendations on viscoelastic tests. This guidance was issued in August 2014 and updated in April 2022.

Current guidance for cardiac surgery:

- Recommendation 1.1 The ROTEM system and the TEG system are recommended to help detect, manage, and monitor hemostasis during and after cardiac surgery.
- Recommendation 1.2 The Sonoclot system is only recommended for use in research to help detect, manage, and monitor hemostasis during and after cardiac surgery. Research is recommended into the clinical benefits and cost effectiveness of using the Sonoclot system during and after cardiac surgery.[48]

4) The British Society for Hematology Guideline published a guideline on the use of viscoelastic hemostatic assays in the management of major bleeding in 2018. Cardiac surgery services should use transfusion protocols based on Viscoelastic point-of-care testing to reduce use of blood components and potentially improve clinical outcomes in bleeding patients. The assays can be used to assess fibrinogen concentration to guide fibrinogen replacement.[49]

5) The EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery (2017) concludes that viscoelastic point of care testing is supported by the evidence, although it is not recommended in patients without antithrombotic treatment.5

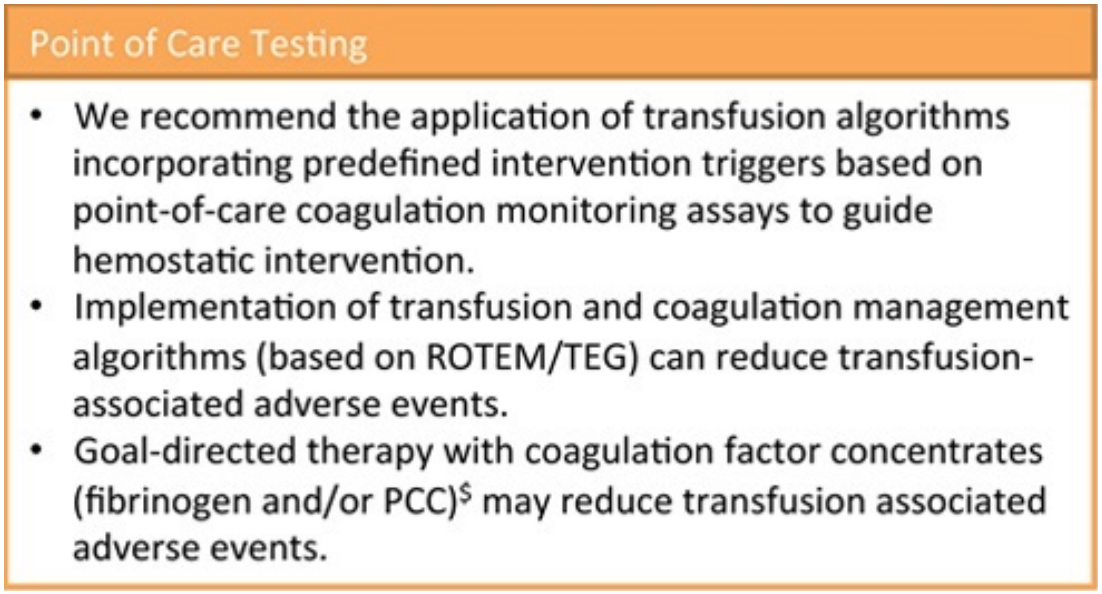


Figure 6. Part of the 2019 SCA Summary Statement on Blood Conservation and Transfusion in Cardiac Surgery[49]

Conclusion and the Authors Opinion

While no study has shown a reduction in mortality, numerous randomized control studies have demonstrated a reduction in morbidity through a reduction in transfusions across all components of blood. A significant reduction in blood product usage can have profound impacts across a healthcare system. Blood is an expensive and scarce resource. Not only do fewer transfusions reduce the risk of transfusion reactions in patients but it allows more blood to be available to patients in need. Routine use of this next generation may even save money overall when considering the saved cost of blood products. They say, "all bleeding stops eventually" with these advances in point of care testing we should be able to shorten the time to "eventually". As the technology advances and investment of many vendors in viscoelastic POC devices, it is a matter of time before this type of coagulation monitoring be an integral part of management of the cardiac surgery patients inside the operating room and outside.

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Viscoelastic Tests Are Not Necessary Post Cardiopulmonary Bypass to Guide Hemostasis Management

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Introduction

Despite advances in surgical techniques, anesthetic management, and perioperative care, major bleeding is a well-recognized, complex clinical problem in cardiac surgery.[1,2] Allogenic blood product administration and emergency reoperation for bleeding are associated with increased morbidity, mortality, and healthcare cost.[1, 3-6] Prompt diagnosis and treatment of major bleeding, either surgical or coagulopathic, must be rapidly instituted to avoid the "bloody vicious cycle" of bleeding and coagulopathy.[7]

Multiple randomized clinical trials (RCTs), and subsequently systematic reviews and meta-analyses, have been published on the role of point-of-care viscoelastic hemostatic assays (VHAs), including TEG (Thromboelastography) and ROTEM (Rotational Thromboelastometry), in cardiac surgery.[8-16] The majority of the primary literatures are deemed to be "unclear" or at "high risk" of bias, with the possible exception of the clustered RCT by Karkouti and colleagues, which enrolled 7402 adult patients undergoing cardiac surgery in 12 Canadian Hospitals.[17] It has been shown that VHA-guided algorithms reduce the number of patients requiring transfusions; however, its role in improving clinical outcome metrics, including postoperative acute kidney injury (AKI), stroke, emergency reoperation for bleeding, prolonged intubation, ICU/hospital length of stay, and mortality, is either absent or at best insubstantial. The weak quality of existing evidence to support routine use of VHAs in cardiac surgery, in addition to lack of important clinical end point benefits, have led some authors to conclude that VHAs lacks clinical effectiveness, and benefits conferred by VHAs are not sufficiently robust to recommend the universal implementation of this technology in adult patients undergoing cardiac surgical procedures.[10, 11]

The authors reviewed the findings of seven meta-analyses published since 2016, with a focus on some of the methodology and statistical nuances, contents, limitations, and strengths (Table 1), in order to interpret their findings into actionable conclusions.

Summary of Findings

I. Blood Product Transfusion

Six out of seven meta-analyses reported statistically significant reduction in RBC transfusion in favor of VHA-guided algorithms.[8-13] However, the reported relative risk (RR) of 0.86 to 0.91 in different studies leaves doubt about the clinical relevance of this finding. Six out of seven meta-analyses reported a significant reduction in FFP transfusion in favor of VHA-guided treatments, with FFP showing the greatest effect reported among different blood products (RR 0.57-0.68).[8, 9, 11-14] All seven meta-analyses found a statistically significant reduction in platelet transfusion in VHA group compared to the controls, with RR ranging from 0.54 to 0.81.[8-14] Six meta-analyses reported no difference in the use of other hemostatic agents, including cryoprecipitates, PCC, fibrinogen, or factor VIIa[9-14]; however, the paucity of data from the primary literature and the small sample sizes, hinders any conclusion to be made in this regard.

II. Major Morbidity and Mortality Outcomes

Deppe et al. showed a statistically significant decrease in the incidence of postoperative

AKI when pooling data from RCTs and observational studies. This finding did not reach statistical significance in the subgroup analysis of patients included in RCTs.[8] In contrast, three meta-analyses reported decreased risk of AKI and dialysis-dependent renal failure in the TEG/ROTEM group, however, acknowledging the high risk of bias and the weakness of existing evidence.[9, 10, 14] Thromboembolic events and stroke are other major, but rare, complications that have been sparsely reported,[8, 10, 14] making any conclusion drawn not clinically meaningful given the small, heterogenous sample sizwes.

The existing data on postoperative bleeding is scarce and confounded by lack of uniformity among various studies with regards to reporting measurements and varied definitions of major/massive/clinically significant bleeding postoperatively. Deppe et al. reported no difference in chest tube volume drainage in the first 24 hours.[8] Wikkelsø ewt al. reported no difference in excessive bleeding or massive transfusion between the two groups.[9] Li et al. reported a statistically significant decrease in postoperative bleeding (though with a negligible clinical significance of -103 ml mean difference), along with no difference in massive bleeding/transfusion events between the VHA group and the controls.[12] In the meta-analysis by Meco et al., postoperative bleeding at 12 hours and 24 hours were both reported to be decreased in favor of VHA guided algorithms with relatively long 95% CI associated with small sample size and number of events.[13] Surgical re-exploration was reported in all 7 meta-analyses,[8-14] although only two reported statistically significant difference in favor of POC VHA.[8, 13] The small sample size and paucity of data from the primary literature limits any conclusion to be drawn.

With regards to mortality outcome, only one study reported a significant difference in all-cause mortality in the ROTEM/TEG compared with the control groups in a mix of surgical procedures.[14] In the cardiac surgery subgroup analysis, the mortality benefit was no longer statistically significant at 5% in a random-effects model.[14]

III. Healthcare Costs

Hospital and ICU length of stay, as an indirect measure of healthcare cost, was significantly decreased in the TEG/ROTEM group in the meta-analysis by Meco et al.[13] The other 6 meta-analyses did not show a difference in time to extubation, hospital or ICU length of stay.[8-12, 14]

A meta-analysis by Whiting et al. published in 2015 demonstrated a reduction in RBC transfusion rate attributable to the use of VHAs, and using assumptions based on historical data showing strong associations between RBC transfusion and adverse clinical outcomes, the authors concluded that VHAs were likely cost-effective.[19] Their analysis directly informed current National Health Service (NICE) Guidelines, which recommend routine use of VHAs in cardiac surgery in England. Of note, while blood conservation can reduce cost, VHAs is also an added expense. No study has examined whether the reduction in blood product use with the addition of VHAs is cost effective, an outcome worthy of future consideration.

Conclusion

Our review of seven recently published meta-analyses showed statistically significant benefits of VHAs on rate of blood product transfusions (with FFP showing the greatest effect among different blood products); although data from the primary literature on use of cryoprecipitates, PCC, fibrinogen, or factor VIIa is insufficient. When interpreting the above findings, one should note that a host of other factors could potentially affect the efficacy of VHAs in reducing patients' exposure to allogenic blood products, such as preoperative anemia, preoperative thrombocytopenia and acquired platelet dysfunction (liver and kidney disease and preoperative use of antiaggregant therapy), intraoperative routine use of antifibrinolytics, percentage of high-risk surgical procedures, and standardized transfusion protocols in the control group. Not all of the above items are comparable in the primary literature. In addition, most RCTs conducted on the use of

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TEG/ROTEM in cardiac surgery have little or no allocation concealment or blinding of clinical personnel, and since there is a hypothesis that suggests the transfusion of blood products maybe associated with adverse clinical outcomes, these RCTs are considered to be at high risk of procedural bias. While the transfusion algorithms in the intervention groups are based on TEG or ROTEM, the control groups rarely have a standard transfusion protocol, and treatments are guided mainly based on standard laboratory tests, the clinician's discretion, or both. In the absence of clearly defined transfusion protocols in the control group (which by itself can lead to decreased rate of transfusion), the decision to transfuse can be significantly influenced by product availability, center-specific transfusion cultures, clinician's preference, and secular trends over time. Furthermore, other than the statistical significance, it is also important to assess the clinical relevance and impact of the above findings.

The effect of VHA testing on the incidences of major morbidities, massive blood loss/transfusion and re-exploration have been demonstrated in a few meta-analyses, although not as consistent as its beneficial effect on reducing the rate of blood product transfusion in cardiac surgery patients. The majority of evidence did not support the beneficial effect of VHA testing on more complex, multifactorial clinical outcomes, such as length of hospital/ICU stay and mortality. In patients undergoing cardiac surgery, transfusion is only one of many potential variables affecting morbidity and mortality, including surgical length and complexity, duration on extracorporeal circulation, duration of cross-clamping, hematocrit level, thrombocyte count, temperature on arrival to the ICU and pre-existing comorbidities. Therefore, it might be exceedingly difficult to establish a robust cause-effect association.

In conclusion, in the authors' opinions, in the absence of adequately powered, strictly designed RCTs and until further strong evidence is uncovered either way, the jury is still out

Table 1: Summary of seven meta-analyses published since 2016 on point of care VHAs in cardiac surgery patients

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
Deppe et al., 2016 [8]	17 trials (n=8332): 9 RCTs (n=848) 8 observational studies (n=7484)	Cardiac surgery; adults only	**All products combined (P<0.0001)** **RBC (P<0.0001)** **FFP (P<0.0001)** **Platelets (P=0.0292)**	**AKI (P= 0.0278)** **Thromboembolic events (P= 0.0005)** CVA (P=0.1345) Drainage volume (P=0.0873) **Re-exploration (P<0.0001)** Mortality (P=0.4520)	Ventilation time (P=0.4546) ICU LoS (P=0.3995) Hospital LoS (P=0.5899)	Quality assessment of included studies were performed by using the Downs and Black score for all studies (11 studies rated poor, 6 studies rated good), and the Jaded score for RCTs (mean value 2.0±0.9 points; poor quality <3). Publication bias was assessed visually by funnel plots and excluded using the Eggers' statistics. Patients receiving transfusion analyses of all included studies revealed a significant publication bias (P=0.0075). This was not observed in subgroup analyses with only RCT (P=0.5232). Fixed effects model was used in the absence of heterogeneity between included studies (I^2<50%). Random effects model was used in the presence of heterogeneity (I^2>50%).
Wikkelsø et al., 2016 [9]	17 RCTs (n=1493), 15 RCTs (n=1185) were used in	Cardiac (13, 96% of pts), liver (1), burn (1) surgeries; adults	**RBC (RR 0.86, 95% CI 0.79-0.94)** **FFP (RR 0.57, 95% CI 0.33-0.96)**	**Dialysis-dependent renal failure (RR 0.46, 95% CI 0.28-0.76)** Surgical reintervention (RR	Time to extubation, ICU and hospital LoS with skewed data, no meta-analysis was performed	The quality of evidence was graded as low based on the high proportion of trials at high risk of bias, large clinical and statistical heterogeneity, small and inadequate information size (as indicated by TSA analyses), low number of events, imprecision,

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
	meta-analyses	(13) and peds (2)	**Platelets (RR 0.73, 95% CI 0.60-0.88)** **Combined FFP or platelets (RR 0.44, 95% CI 0.28-0.81)** Fibrinogen, PCC, or recombinant factor VIIa (2 trials, no significant difference)	0.75, 95% CI 0.50-1.10) Excessive bleeding or massive transfusion (RR 0.82, 95% CI 0.38-1.77) Mortality (RR 0.52, 95% CI 0.28 to 0.95 with fixed effects model vs RR 0.57, 95% CI 0.30 to 1.07 with random effects model)		and wide CI for many of the meta-analyses in this review. All included trials except two were marred by high risk of bias. If I^2=0, the results from the fixed effects model were reported. If I^2>0, the results from the random-effects model were reported; unless one or two trials contributed more than 60% of the total evidence provided, in which case, the random-effects model may be biased.
Serraino et al., 2017 [10]	15 RCTs (n=8737)	Cardiac surgery; adults (13) and peds (2)	**RBC (RR 0.88, 95% CI 0.79–0.97)** FFP (RR 0.68, 95% CI 0.46-1; significant heterogeneity I^2=79%) **Platelets (RR 0.78, 95% CI 0.66–0.93)** Fibrinogen and PCC (4 trials, no difference)	**AKI (RR 0.42, 95% CI 0.20-0.86; I^2=26%, 4 trials with moderate heterogeneity and high risk of bias)** Stroke (RR 1.73, 95% CI 0.41-7.23) Reoperation for bleeding (RR 0.82, 95% CI 0.55-1.23) Mortality (RR 0.55, 95% CI 0.28-1.1)	Ventilation time (MD 0.28, 95% CI -0.66 to 1.23) ICU LoS (MD -31.76 h, 95% CI -94.68 to 31.17) Hospital LoS (MD -3.11 days, 95% CI -9.57 to 3.34)	GRADE assessment demonstrated that the quality of the evidence was low or very low for all estimated outcomes. No trial was judged to be at low risk of bias. Heterogeneity was defined as follows: I^2=0–40%, no or mild heterogeneity; I^2=40–80%, moderate heterogeneity; and I^2>80%, severe heterogeneity. In the presence of severe heterogeneity, meta-analysis was not performed. As a result of the inclusion of multiple small studies with significant heterogeneity, the primary analyses were performed using random-effects

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
						models. Results of random-effects model were compared with a fixed-effects model to assess the effects of small studies.
Lodewyks qt al., 2018 [11]	11 RCTs (n=8294)	Cardiac surgery; adults only	Any products (RR 0.9, 95% CI 0.79-1.02) **RBC (RR 0.91, 95% CI 0.85-0.96)** **FFP (RR 0.58, 95% CI 0.34-0.99; I^2=87% with significant heterogeneity)** **Platelets (RR 0.66, 95% CI 0.49-0.9)** Cryoprecipitate and fibrinogen concentrate (1 trial, RR, 1.77; 95% CI 1.01 to 1.86)	Reoperation rate (RR 0.74, 95% CI 0.42 to 1.31) All-cause mortality (RR 0.73, 95% CI 0.47-1.13)	ICU LoS (MD -1.85, 95% CI -5.16 to 1.47) Hospital LoS (MD -0.14, 95% CI -1.81 to 1.54)	Quality of included RCTs/Quality of evidence were not reported. Three trials were adjudicated to be at high risk of bias because of lack of participant and personnel blinding; the remaining 8 trials were classified as unclear primarily because of poor reporting. If significant heterogeneity was encountered with an I^2 value greater than 50%, further subgroup analyses were conducted.
Li et al., 2019 [12]*	19 trials (n=15320): 13 RCTs (n=14766) 6 observati	Cardiac surgery; adults only	**RBC (RR 0.89, 95% CI 0.80-0.98; I^2 =0%)** **FFP (RR 0.59, 95% CI 0.42-0.82, I^2 =55%; P<0.01)**	**Blood loss (103 ml, MD -103.50, 95% CI -156.52 to -50.48; I^2=0%)** Massive bleeding or massive transfusion (RR	ICU LoS (MD -2.06, 95% CI -4.34 to 0.22; I^2=0%) Hospital LoS (MD -0.05, 95% CI -	Quality of included RCTs/Quality of evidence were not reported. Only one RCT included was classified as having an overall low risk of bias.

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
	onal studies (n=554)		**Platelets (RR 0.81, 95% CI 0.74-0.90; I^2 =0%)** Fibrinogen or cryoprecipitate (RR 0.98, 95% CI 0.80-1.19; I^2 =22%) PCC (RR 0.62, 95% CI 0.18-2.07; I^2=86%)	0.86, 95% CI 0.60-1.24; I^2=0%) Surgical re-exploration (RR 0.74, 95% CI 0.50-1.10; I^2=0%) Mortality (RR 0.50, 95% CI 0.26-0.96; I^2 =1%, P=0.04)	0.38 to 0.27; I^2=0%)	I^2 ³50% indicates a substantial level of heterogeneity. Random effects model was used for overall studies. In RCTs only analyses, results from fixed effect models were reported when I^2 ≤25%. When I^2 >25%, relevant subgroup analyses were performed, and when it failed, the results from random effect models were reported.
Meco et al, 2020 [13]	8 RCTs (n=1035)	Cardiac surgery; adults only	**All products combined (OR 0.85, 95% CI 0.74-0.97, P=0.002; I^2=58%)** **RBC (OR 0.55, 95% CI 0.34-0.88, P=0.01; I^2=64%)** **FFP (risk difference 0.24, 95% CI 0.12-0.36, P<0.0001; I^2=81%)** **Platelets (OR 0.54, 95% CI 0.30-1, P=0.05; I^2=73%)**	**Postoperative bleeding at 12 hours (3 RCTs, MD -178.7, 95% CI -308.9 to -48.4, P=0.007; I^2=84%) and 24 hours (4 RCTs, MD -175.4, 95% CI -305.78 to -40.9, P=0.01; I^2=6%)** **Redo surgeries (OR 0.51, 95% CI 0.28-0.94, P=0.03; I^2=3%)** Mortality (OR 0.57; 95% CI 0.18-1.74, p=0.38; I^2: 42%)	**ICU LoS (OR -4.03, 95% CI -6.28 to -1.78, P=0.005; I^2=91%)**	Quality of included RCTs/Quality of evidence were not reported. No trial was judged to be at low risk of bias. I^2 values from 50% to 75% were considered to represent substantial heterogeneity and from 75% to 100% considerable heterogeneity. A random-effects model was used for primary analysis and a fixed-effects model for sensitivity analysis. The results from the 2 models were compared. If the results between the 2 models were similar, the results from the random-effects analysis were reported, and if the results differed substantially, the authors evaluated for small-study effects.

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
			Cryoprecipitates (3 trials, OR 0.31, p5% CI 0.04-2.32, P=0.26; I^2=78%)			
Santos et. Al, 2020 [14]	21 RCTs (n=8932)	Cardiac (16), liver (2), orthopedic (1), burn (1), trauma (1) surgeries; adults (19) and peds (2)	RBC (RR 0.93, 95% CI 0.87-1,01, P=0.07; I^2=37%) **FFP (RR 0.57, 95% CI 0.41-0.81, P=0.001; I^2=85%, P<0.001)** **Platelets (RR 0.74, 95% CI 0.59-0.92, P= 0.006; I^2 =47%, P= 0.03)** Fibrinogen (RR 0.94, 95% CI 0.76-1.17, P=0.54; I^2=22%) Prothrombin complex (RR 0.39, 95% CI 0.07-2.16, P=0.28; I^2=91%) Factor VIIa (RR 0.19, 95% CI	**AKI (10.5% vs. 17.6%; RR 0.53, 95% CI 0.34-0.83, P=0.005)** Thrombotic events (RR 1.17, 95% CI 0.36-3.81, P=0.80; I^2=0%) Re-exploration for bleeding (RR 0.82, 95% CI 0.55-1.23, P=0.34; I^2=0%) **Mortality (7.3% vs. 12.1%, RR 0.64, 95% CI 0.43-0.96, P=0.03; I^2=0%)**	Hospital LoS (RR -0.39, 95% CI -3.30 to 2.52, P=0.79; I^2=67%) ICU LoS (RR -31.76 h, 95% CI -94.68 to 31.17, P=0.32; I^2=59%)	The quality of evidence was considered between low and very low. Many outcomes showed inconsistency and imprecision. All outcomes were considered to be at high risk of bias and the level of evidence was lowered at one point since the intervention influences the use of allogeneic blood products and there was no masking in the studies. Analyzes with I^2 > 30% were considered to have moderate heterogeneity, I^2 > 50% to have substantial heterogeneity, and I^2 > 75% to have high heterogeneity. Heterogeneity data with a p-value of the $\chi 2$ test < 0.10 were considered statistically significant.

Author, Year	#RCTs (#Pts)	Patient Population	Exposure to Allogenic Blood Products	Major Morbidity and Mortality Outcomes	Healthcare Cost Outcomes	Quality of RCTs Included/Quality of Evidence Risk of Bias Data Heterogeneity
			0.03-1.24, P=0.08; I^2=33%) **Volume of RBC (MD -1.63 U, 95% CI -3 to -0.26, P=0.02; I^2=73%, P=0.005)** **Volume of FFP (MD -0.90, 95% CI -1.4 to -0.41, P=0.0003; I^2=53%, P<0.09)** Volume of platelets (MD -0.60, 95% CI -1.66 to 0.45, P=0.26; I^2=91%, P<0.001)			

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