THE AMERICAN ACADEMY
OF
CARDIOVASCULAR PERFUSION
515A EAST MAIN STREET
ANNVILLE, PA 17003
(717) 867-1485
OFFICEAACP@AOL.COM
HTTP://WWW.THEAACP.COM

Spring 2020

The Academy Newsletter

The Roaring 20's Invade the 2020 AACP!

Inside this issue








GRAND
3rd 12
0 to 0
18 to 36
2 to 1
2 to 1
2 to 1


StO2




Nathan Minie

Cardiovascular Perfusion Program

Quinnipiac University

Hamden, CT

Neurocognitive Function Days, Weeks and Months Post Cardiopulmonary Bypass

Neurocognitive function is a major consideration in adult patients undergoing cardiac surgery. Numerous patient risk factors, as well as pre-operative neurocognitive function, can be used as indicators for risk of post-operative neurocognitive impairments.[1,2,4,5,6,7,8] Post-op delirium (POD) can also indicate poor post-operative neurocognitive function outcomes.[1] The method of assessing neurocognitive function pre-operatively, and post-operatively needs to be considered, as well as what specifically, in cardiac surgery, influences these outcomes.

Stroke, encephalopathy, and neurocognitive disorders are the causes of decline. These can lead to different classifications of outcome.[1,3] A Type I outcome is most likely associated with cardiopulmonary by-pass.[1,3] Type I consists of cerebral death, nonfatal stroke, or a new transient ischemic attack (TIA).[1,3] A Type II outcome would be intellectual decline at discharge, or new onset of seizures.[1,3]

When we asses neurocognitive function we look at visuoconstriction, language, verbal memory, attention, executive function, visual memory, motor speed, and response to stimuli. These parameters can be measured by comparing pre-operative and post-operative test results.[1,2,4,5] The Confusion Assessment Method, the Mini Mental State Exam, and the Trail Making Test, can be used in these instances. MRI and CT scan can also be used to directly examine the brain for injury. It is important to note that some test results prior to discharge from CT ICU may have fault due to pain, medications, and sleep deprivation.[1,2,4,5]

Any patient undergoing cardiopulmonary bypass (CPB), is at increased risk. Stroke risk increases 1-9% on CPB, while there is a 10-80% higher incidence of neurocognitive deficit.[1] Approximately 5-20% of patients retain these deficits 3 to 6 months post-op.[1] Long term decline occurs in 10-30% of patients.[2] Patients of advanced age show the most dramatic changes.[1,2] Prior history of neurological events, aortic and/or carotid disease, low cardiac output, atrial arrhythmias, hypertension, and diabetes also increase the risk of poor outcomes.[1]

Age alone is very important due to the increased risk of stroke. Approximately 50% of cardiac surgery-related strokes occur post-op.[1] Over the last 2 decades, patients greater than 60 years old undergoing cardiac surgical repairs requiring CPB have doubled.[1] Patients under age 60 have less than 1% stroke risk post-op.[1] The population of patients greater than 70 years old, have increased 7-fold resulting in an additional 4-9% risk of stroke or coma post op.[1.]

One study examining adult patients post-operatively, who had a history of stroke pre-operatively, showed that 44% of patients developed a neurological deficit post-op.[8] In the same study 8.5% of patients developed a new deficit, 27% had a re-appearance of an old deficit, and 8.5% showed worsening of an old deficit.[8] Of note, about 5% of patients will have an abnormal MRI pre-op with an absence of known clinical stroke.[4] This 5% is also more likely to have a new post-op deficit.[4]

Continued on Page 4

Continued from Page 3

Early post-op incidence of decline in neurocognitive function occurs in 35-85% of adult patients.[2] Patients who experience strokes in the first 30 days after cardiac surgery have a mortality rate upwards of 20%, compared with 2-4% for patients without stroke.[4] Transfusion of autologous blood in cardiac surgery does not completely eliminate lipid micro-emboli in blood that is eventually returned to the patient. Lipid micro-emboli can lead to an increased risk of post-op delirium, as well as TIA.[4]

POD commonly occurs in 26-52% of adult patients.[1] It is also a major indicator in neurocognitive decline during the post-op recovery period.[1] Age, depression, stroke/TIA, decreased baseline MMSE score, increased baseline serum creatinine, abnormal serum albumin, and neuro imaging findings can correlate to post-op delirium.[1,6] Despite the identification of these risk factors, the pathophysiology of POD remains unclear.[1] It is important to note that patients with Alzheimer's have an increased risk for post-op delirium, but Alzheimer's pathology begins decades prior to observable cognitive defects.[7]

In 2012, Saczynski et al[6] compared adult patients with POD versus adult patients without POD, patients with POD were typically older, female, and had lower baseline education and pre-op scores.[6] The study also measured significant Mini Mental State Exam decline on post-op day 2, but increases on days 3 -5.[6] A slow improvement was documented through the first 6 post-op months, but stabilized by 1 year without return to baseline.[6] Patients without POD had a general lower functional impairment, and returned to cognitive baseline by 1 month post-op. [6]

Arensen et al[6] assessed 1000 post-op adult ICU patients, at two different hospitals. Approximately 15% of patients tested positive for signs of delirium.[6] All patients were more than 65 years old, had post-operative stroke, mechanical ventilation greater than 24hrs, post-operative renal insufficiency, post-operative blood product administration, concomitant CABG-valve surgery, and/or pre-operative benzodiazepine use. [6]

The exposure to the CPB circuit is what is attributed as the reason for neurocognitive outcomes compared to other surgeries performed without use of the heart-lung machine (HLM).[1] One study of adult patients requiring coronary artery bypass grafting compared the outcomes of those exposed to CPB and compared their outcomes to those undergoing cardiac surgical procedures that did not utilize CPB. Patients were only included if they completed both the pre-op and post-op tests. Both groups were similar with respect to age, pre-operative neurologic and intellectual status, anesthetic methods, duration of operation, peri-operative complications, and time spent in the CT ICU. Certain potential risk factors for cerebrovascular disease were more common in the control (non-CPB) than the CPB patients.[1] The authors concluded that cardiac surgery, especially on CPB has a much higher risk of effecting neurocognitive function.[1] 55% of CABG patients had mild deterioration, compared to 31% of the surgical control.[1] 19% of CABG patients showed moderate deterioration, and 4.7% severe deterioration, when compared to the surgical control having 0% deterioration in both the moderate, and severe categories.[1]

Comparing on pump vs. off pump CABG neurocognitive outcome testing compared the effect of CPB as well. It was postulated that off pump surgery would reduce blood loss and blood transfusion, as well as reduce risk of renal dysfunction, atrial fibrillation, stroke, and neurocognitive decline.[2] The trial randomized 142 off pump versus 139 on pump CABG cases in adults.[2] Patients were assessed pre-op, 3 months post-op, and 12 months post-op in the areas of verbal and visual memory, language, visuoconstruction, psychomotor skills, and motor speed.[2] In the first 3 months post-op, 21% of patients in the off-pump category showed a cognitive decrease compared to 29% in the on-pump cohort.[2] At the 1-year mark, 31% of off pump patients had a neurocognitive decline vs. 34% of on pump patients.[2]

Neurocognitive injury in children post-op will manifest itself differently than adults, which suggests a different etiology.[1] Signs of decline or defect in pediatric patients are observed as seizures, movement disorders, or developmental delays.[1]

Neurocognitive decline after cardiac surgery is still a significant factor in a large population of patients. Screening patients properly, and using appropriate testing tools is vital, as some tests like the MMSE have a floor and ceiling effect.[7] Timing of testing can also be a factor in patient response and outcome.[7] Consideration of the patient's cognitive changes from baseline should be conducted approximately 30 days post-op due to pain, medications, anesthesia, and mechanical ventilation.[7] Development of an

intraoperative management bundle assessing all variables of the operation, with all members of the operative team, including neurology, will hopefully improve neurocognitive outcomes in the future.[7]

References

1. Gravlee, G. P. (n.d.). Cardiopulmonary Bypass and Mechanical Support Principles And Practices (4th ed.). Philadelphia, PA: Wolters Kluwer.
2. Ghosh, S. (n.d.). Cardiopulmonary Bypass (2nd ed.). Cambridge Medicine.
3. Smith, Michael. Neuromonitoring PowerPoint Presentation. Physiological Monitoring. Quinnipiac University. 2019.
4. Gottesman, R. F., McKhann, G. M., & Hogue, C. W. (2008). Neurological Complications of Cardiac Surgery. Seminars in neurology, 28(5), 703–715. doi:10.1055/s-0028-1105973
5. Cognitive Outcome After Coronary Artery Bypass: A One-Year Prospective Study. McKhann,MD, Guy M et al. The Annals of Thoracic Surgery, Volume 63, Issue 2, 510 – 515
6. McDonagh, D. L., Berger, M., Mathew, J. P., Graffagnino, C., Milano, C. A., & Newman, M. F.(2014). Neurological complications of cardiac surgery. The Lancet. Neurology, 13(5), 490–502. doi:10.1016/S1474-4422(14)70004-3
7. Miles Berger, Niccolò Terrando, S. Kendall Smith, Jeffrey N. Browndyke, Mark F. Newman, Joseph P. Mathew; Neurocognitive Function after Cardiac Surgery: From Phenotypes to Mechanisms. Anesthesiology 2018;129(4):829851.doi: https://doi.org/10.1097/ALN.0000000000002194.
8. Bojar, R. (2014). Manual Perioperative Care in Adult Cardiac Surgery (5th ed.). Worcester, MA: Wiley-Blackwell

Contact Information for Our Sponsoring Partners

EDWARDS LIFESCIENCES
Phone:800-424-3278
website: www.Edwards.com/HemoSphere

INVOSURG
Fax: 617-507-6462
Website: www.invosurg.com

LIVANOVA
SORIN GROUP USA, INC.
Phone: 800-221-7943 or 303-467-6517
Fax: 303-467-6375
Website: www.soringroup.com

MEDTRONIC PERFUSION SYSTEMS
Phone: 763-391-9000
Websites: www.medtronic.com
www.perfusionsystems.com

QUEST MEDICAL, INC.
Phone: 800-627-0226 or 972-390-9800
Fax: 972-390-2881
Website: www.questmedical.com

SPECTRUM MEDICAL, INC.
Phone: 800-265-2331
Fax: 803-802-1455
Website: www.spectrummedical.com

TERUMO CARDIOVASCULAR SYSTEMS
Phone: 734-663-4145 or 800-521-2818
Fax: 734-663-7981
Website: terumo-cvs.com

A SINGLE CENTER INITIATIVE TO CUT BLOOD USE IN CARDIAC SURGERY PASSION, PERSEVERANCE AND PATIENCE

For many years we were hesitant to change at our hospital. We used the same tubing pack, and same oxygenator. We were transfusing 77% of female patients and 41% of male patients. We knew we could do better. Unable to get a monthly blood use report, we created our own database and developed our own data set

By creating a blood conservation committee we increased awareness and began using smaller packs and smaller oxygenators, reducing pre-bypass fluid, keeping blood in the pump on bypass, and not in the cell saver. In three years we cut our RBC usage by 83%. This saved over $750,000 in just three years for RBCs only. Since 2012 our stroke has dropped from 2.0% to 0.7% and AKI has dropped 53% from 5.8% to 2.7% in 2019. Transfusion dropped to 14% intra-operatively and 18% post-operatively for isolated CABG patients. Deep sternal wound infections dropped to 0.0% in 2018.

Charles F. Krumholz, CCP, MSA

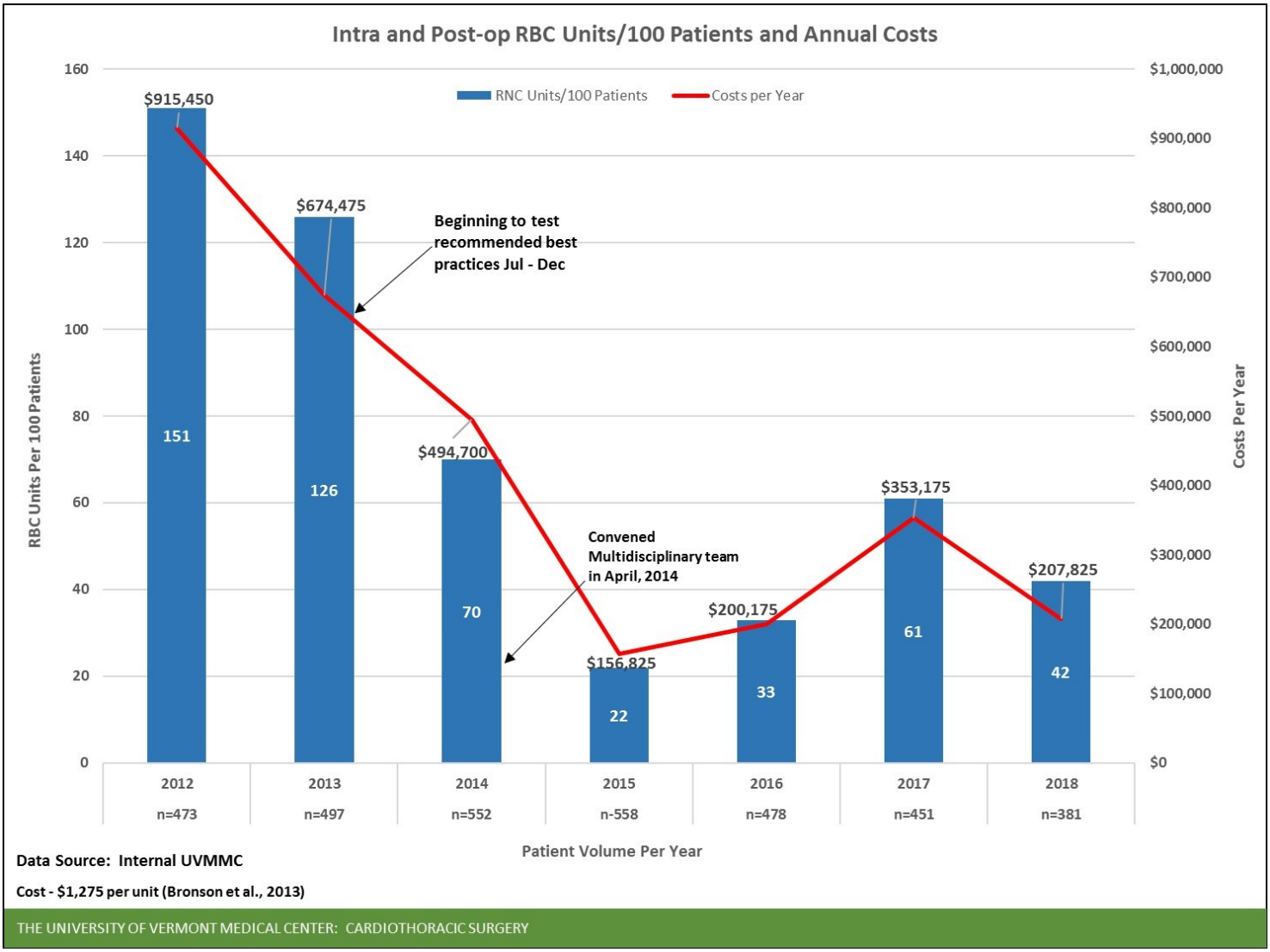
University of Vermont Medical Center

Burlington, VT

The full manuscript of this article has been submitted to the journal Perfusion for possible publication.

How did this all happen? Many small steps, each team member working together to effect change. It cost very little to achieve. Reducing protamine was an important change…35% decrease from 2012 to 2020. Our database with 32 variables for over 3,500 patients at one institution directed change with facts. A second database with 1,150 patients tracked heparin, protamine and chest tube output. Reducing protamine from 2017 to 2020 reduced chest tube output each year, as well as transfusion.

We can all do more to improve our outcomes. Each of us has to work at this every day. Make it better, make it more efficient, and make it cost effective. Don't let hematocrits drop, don't transfuse unless clinically necessary. Remember stroke, AKI and infection are associated with transfusion and lower hematocrits on CPB. Recent data shows AKI costs one billion dollars per year in the US. A 10% drop in AKI would save $100,000,000 in one year. Follow the STS guidelines. Protamine/heparin ratios of 0.5% are a starting point. Track your patient's chest tube output. Old habits are hard to change, but without change we are falling behind. It takes passion, perseverance and patience.



This graph shows Intra-operative and post-operative blood use per one hundred patients. It also shows cost of RBCs transfused by year from 2012 to 2018. The number of cases per year is below each column. The cost per unit is from a 2013 paper by Shanna Bronson et al. Saving blood reduces cost. It does not cost a lot to make this happen, but it requires a willingness to change.

Comparison of Biocompatible Circuit Coatings Used in Cardiopulmonary Bypass Surgery

Breanna Hackworth B.S., M.S.
Robin Schwartz, B.S.
Nathanial Darban, Ph.D, CP

Cardiovascular Science Program

Midwestern University

Glendale, AZ

The use of biocompatible coatings on extracorporeal circuits (ECC) during open heart bypass surgery has increased over the past decade. Numerous surface coatings have been developed and extensively studied to show improved blood compatibility of biomaterials[1,2]. This biocompatible surface is made to help minimize the patient's inevitable immune response to the ECC while on bypass[3,4]. The effectiveness of four ECC coatings were compared directly by measuring protein adhesion to each circuit surface with the use of scanning electron microscope (SEM). In this study, the platelet preservation was also considered as blood samples were taken at the same time as each tubing sample.

The biocompatible circuit coatings where evaluated using bovine blood; an affordable and feasible alternative to human blood. The circuits tested were Trillium by Medtronic, Balance Biosurface by Medtronic, Cortiva BioActive Surface by Medtronic, and X-Coating by Terumo[5-8]. The bovine blood was circulated through each circuit for a total of 50 min; reflective of a bypass procedure. Blood samples and tubing samples were collected at three different time and temperature intervals (37^{0}C at 10 min, 30^{0}C at 30 min, and 37^{0}C at 50 min). The blood samples were drawn into Monoject blood collection tubes containing EDTA, and small pieces of circuit tubing were cut and processed according to SEM protocol. The Monoject blood samples were analyzed and evaluated by a medical laboratory professional at ANTECH Diagnostics. The parameters measured included; hematocrit, hemoglobin, platelets, neutrophils, lymphocytes, monocytes, eosinophils, and basophils. Circuit tubing samples were treated for molecule fixation using varying strengths of alcohol and 4% glutaraldehyde. Tubing samples were stored within a vacuum chamber and later evaluated using the SEM. The SEM provided a visual image of the number of molecules adhered to the circuit tubing. These images were analyzed and quantified using an image software called imageJ. Percentage of molecular coverage was calculated for each image. In total 60 pictures were taken and processed.

The SEM images revealed a layer of protein coverage on all tubing samples. Cortiva BioActive Surface had the highest percentage of protein adhesion with an average of 46.8% coverage across all temperature and time intervals. The remaining samples were observed to have coverage across all temperature and time intervals as follows; Trillium 25.8% coverage, Balance Biosurface 16.6% coverage, and X-coating 10.7% coverage. The blood samples showed that Balance Biosurface and Trillium had the highest platelet preservation across all temperature and time intervals, where Cortiva and X-coating platelet counts varied throughout the trial. The average adhesion across all the time and temperature intervals is consistent with the results achieved at the individual time and temperature intervals.

The results demonstrated all biocompatible tubing has the potential to be coated by protein, activate an immune response, and increase the patients' platelet count. Further research investigating the activation of platelets

and specific antigen/antibody complexes would help provide a more detailed representation of the immune response to the ECC. This information could be used alongside previously stated results to aid in the advancement of bioactive coating strategies, helping minimize the patient's response to the ECC.

1. Shapira OM, Korach A, Pinaud F, et al. Safety and efficacy of biocompatible perfusion strategy in a contemporary series of patients undergoing coronary artery bypass grafting – a two-center study. *J Cardiothorac Surg.* 2014;9.
2. Lindholm L, Westerberg M, Bengtsson A, Ekroth R, Jensen E, Jeppsson A. A closed perfusion system with heparin coating and centrifugal pump improves cardiopulmonary bypass biocompatibility in elderly patients. *Ann Thorac Surg.* 2004;78(6):2131-2138; discussion 2138.
3. Mariani E, Lisignoli G, Borzì RM, Pulsatelli L. Biomaterials: Foreign Bodies or Tuners for the Immune Response? *Int J Mol Sci.* 2019;20(3).
4. Xu LC, Bauer J, Siedlecki CA. Proteins, Platelets, and Blood Coagulation at Biomaterial Interfaces. *Colloids Surf B Biointerfaces.* 2014;124:49-68.
5. Medtronic. Balance Biosurface. https://www.medtronic.com/us-en/healthcare-professionals/products/cardiovascular/cardiopulmonary/balance-biosurface.html. Published 2019. Accessed.
6. Medtronic. Cortiva BioActive Surface for CPB Circuit Devices. https://www.medtronic.com/us-en/healthcare-professionals/products/cardiovascular/cardiopulmonary/cortiva-bioactive-surface.html. Published 2019. Accessed.
7. Medtronic. Trillium Biosurface for CPB Procedures. https://www.medtronic.com/us-en/healthcare-professionals/products/cardiovascular/cardiopulmonary/trillium-biosurface.html. Published 2019. Accessed.
8. Corporation TM. Terumo. http://www.terumomedical.com/about/the-terumo-family.html. Published 2019. Accessed.

Important Academy Dates

The ACADEMY ANNUAL MEETING DEADLINES

ABSTRACT DEADLINE	**October 15, 2020**
MEMBERSHIP DEADLINE	**December 10, 2020**
PRE-REGISTRATION	**January 15, 2021**
HOTEL REGISTRATION	**January 15, 2021**
2020 ANNUAL MEETING	**February 10-13, 2021**

Sal and his wife, Ann, at the recent AACP Meeting in Reno

In Memoriam: Sal Guercio 1954-2020

Salvador "Sal" V. Guercio, age 65 of Houston, passed away unexpectedly on Sunday, the 1st of March 2020.

He was a clinical instructor for twenty-seven years at the Texas Heart Institute School of Perfusion Technology. Sal gave generously of his skill and knowledge to countless students. His consistent character, affable demeanor and quick wit will be missed.

He was recently voted into Honorary Membership in The Academy at the Annual Seminar in Reno.

Awards Committee Selects Winning Paper Presentations

Three students received **Lawrence Awards** for their paper presentations at the Annual Seminar in Reno.

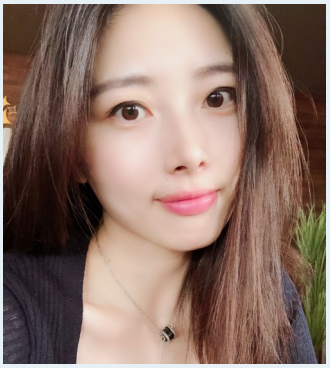
Hongting Diao - "Does Cardioplegia Provide Cardiac Protection By Inducing Nuclear Factor Erythroid 2 - Related Factor 2 (Nrf2)? "

Adam Murphy - "A Survey Of Perfusionists' Communications During Critical Events"

Caitlin Murdock - "The Effects Of Cardioplegia On Non-Diabetic Patient Glucose Levels"

The Lawrence Award is a $500 cash award for the best student paper presentations.

In addition, Christine Chan was awarded the **Best Paper of the Conference** - a $750 cash award funded by the journal *Perfusion* for her presentation entitled, "Peripheral Veno-Arterial Extracorporeal Membrane Oxygenation: Distal Perfusion Cannulation Complication."



Welcome to New Members

The American Academy of Cardiovascular Perfusion would like to welcome the following individuals whom were voted into membership at the Closing Business Meeting of our annual meeting in Reno, Nevada.

Fellow Members

Desiree Bonadonna
Colette Calami
Alex Gum
Emily Kahring
Charles Krumholz
Ray Wong

Members

Beshah, Amsalu
Calaritis, Christos
Catricala, Joseph
Dell'Aiera, Laura
Evans, Matthew
Hunter, Paul
Lee, Min Ho
London, Morgan
Magnusson, Cheryl
McIlwain, Rodney
Mora, Frank
Pitts, Stuart
R, Manu
Savoy, Eileen
Smith, Trevor
Wittenauer, Matt
Zalfa, Jeffrey

Students

Adler, Amanda
Alexander, Jeffrey
Anderson, Nicholas
Anderson, Warren
Azmat, Ramsha
Baig, Sumbell
Baldwin, Laurie
Barba, Audrey
Beck, Matthew
Bertrand, Morgan
Boley, Jeremy
Bopardikar, Priyanka
Boyne, Grace
Camberato, Gabrielle
Candela, Chandler
Carlos, Cara
Carneglia, Joshua
Cirillo, Kathryn
Davidson, Kraig
Derk, Alexis
DeSimone, Stevie
Diao, Hongting
Donelan, Lucas
Edwards, Adrian
Enriquez, Samuel
Farrow, Kourtney
Gitchell, Dustin
Gonzalez, Leslie
Grimm, Linda
Hackworth, Breanna
Hernandez, Herson
Honey, Kate
Hoskins, Erica
Ishee, Taylor
Jack, Andrew
Jaskula-Dybka, Michelle
Johnson, Stephanie
Keck, Heather
Kelly, Madeleine
Konermann, Rebecca
Kutateladze, Nikoloz
Lambert, Zachary
Lester, Brian
Ly, Kaitlynn
McDaniel, Allison
Middleton, Demetria
Minie, Nathan
Moore, Ashley
Morency, Nicole
Morrow, Emily
Murphy, Adam
Nguyen, Randy
Oettinger, Phill
O'Shaughnessy, Sydney
Otis, Jonathan
Pankrez, Tiffany
Patel, Mohini
Pearson, Charles
Peaytt, Morgan
Peng, Gavin
Pierce, Jennifer
Plomondon, Maria
Pollock, Sean
Powell, Benjamin
Quiambao, Laurice
Reeder, Amanda
Reid, Edward
Reyes, Christopher
Santana, Yamil
Scherpich, Dylan
Schmidt, Mihailo
Scullion, Mark
Senajor, Brian
Slack, James
Stickler, Lindsey
Strickland, Victoria
Swanson, Alysha
Thompson, Sara
VanderPloeg, Brett
Walker, Kaiti
Ward, Gabrielle
Weiss, Ryan
Williams, Talia
Williams, Shivani
Wood, Alexa
Woomer, Madeleine

Ischemic Preconditioning for Neuroprotection of Infants Undergoing Cardiopulmonary Bypass for Correction of Congenital Heart Disease

Jennifer Pierce

Cardiovascular Perfusion Program

Quinnipiac University

Hamden, CT

Neonates with congenital heart defects (CHD) are at increased risk of neurological injury due to various etiologies. Delayed or abnormal brain development increases that risk, as well as periventricular leukomalacia, which is the most common neuropathologic lesion found in preterm infants. It is associated with 20% of full-term infants with CHD and increases to greater than 50% post-surgery. This suggests an increased risk of white brain matter injury and possible delayed brain development. An immature brain increases the risk of micro emboli, oxidative stress, inflammation, and hemodynamic disturbances when theses infants are placed on cardiopulmonary bypass (CPB). One study showed a 10% risk of stroke in neonates with CHD and most occurring preoperatively.[1] Neonates with CHD also have unique hemorrhagic events due to hemosiderin deposits and an increased risk of air emboli or thromboembolism from either the cardiac lesion itself, the palliative surgical procedure, or the repair surgery. Postoperative conditions may lead to neurologic complications such as hyper coagulopathies, residual right-to-left shunts, low cardiac output syndrome, chronic cyanosis, and arrhythmias.[1]

As many as 50% of children with congenital heart defects will have neuropsychological defects by school age that affect the children, as well as their families. These neurological deficits may manifest as attention disorders or academic issues that lead to social and economic difficulties. These insults to the brain may not occur in surgery alone, but may occur in utero, the immediate post-natal period, or postoperatively. If a patient requires multiple operations, this may increase their risk of brain injury.[1]

Multiple neuroprotective interventions are in place to protect neonates undergoing CPB for CHD. Perioperative interventions that target prevention of neuronal cell damage, minimize cerebral oxygen demand, and optimize blood flow are taken prior to infants arriving in the operating room. Techniques in the operating room include deep hypothermic circulatory arrest (DHCA), continuous low flow CPB (as an alternative to DHCA), temperature-corrected (Ph-stat) blood gas management strategies during patient cooling, protocols for hemodilution, hypothermia, and rewarming during CPB. Pharmacologic therapies used to provide neuroprotection include anesthetic gases, methylprednisolone, and allopurinol but are not clinically proven to improve outcomes. These intraoperative strategies have been modified for over twenty years despite long term neuroprotective improvements.[1] Since the current strategies are not showing consistent, long term improvements, more must be done. Ischemic preconditioning is one method of interest.

"Preconditioning is a phenomenon in which prior exposure to sublethal insults results in up-regulation of endogenous defense mechanisms which then protect the organ system from subsequent lethal insults".[2, p.14]

Numerous animal studies have been conducted to measure the effects of ischemic preconditioning. One study using twelve newborn piglets that were subjected to ischemic preconditioning demonstrated a decrease in cardiac apoptosis and overall preservation of cardiac performance. Cardiac performance was measured by ejection fraction, cardiac index, and

stroke volume.[3] Since ischemic preconditioning was beneficial in a cardiac model, the technique was applied to protection in organs such as the brain.

Neurologic ischemic preconditioning was first introduced in a canine model in 1986.[4] A study using newborn pigs subjected them to 8% oxygen and 92% nitrogen for 3 hours. 24 hours later the piglets were exposed to hypoxic-ischemic events be breathing 5% 02, and at the same time manipulating the mean arterial pressure (MAP) to less than or equal to their baseline for 10 minutes. The results showed an increase in mRNA expression of the hypoxia-induced factor 1 alpha (HIF-1a) and its target gene, vascular endothelial growth factor (VEGF), which started at 0 hours and continued to rise for seven days.[5] This signified that hypoxia-conditioning provided protection against hypoxic ischemic injury in the newborn piglet and correlated with the pathophysiology of an asphyxiated human neonate. This HIF factor is a transcription factor that promotes hundreds of genes when hypoxia occurs. Some increase production of nitric oxide (NO), erythropoietin (EPO), glucose transporters, and angiogenesis. Anaerobic glycolysis and mitochondrial function preservation are all enhanced by the HIF 1a as well.[1]

The results of these studies were encouraging, and the discovery of remote ischemic preconditioning allowed the protective actions of ischemic preconditioning to be utilized in humans.[1]

Remote ischemic preconditioning was first demonstrated in 1993[4] and is achieved by applying a blood pressure cuff to the leg or arm to induce ischemic preconditioning to a distant target such as the brain or heart. Four cycles of ischemia lasting 5 minutes are then followed by 5 minutes of reperfusion. The exact mechanism of action is unknown. Neuroprotective benefits are thought to be derived from activation of mechanisms for cell survival, increased cerebral blood flow, and attenuation of neuroinflammation. Many hurdles regarding remote ischemic preconditioning continue to exist, such as the safety of producing limb ischemia with and without cooling therapy while on bypass. There is debate on the number and duration of ischemic cycles required to provide protection. Also unknown are what are the detrimental effects and the exact protective mechanisms.[6] However, clinical trials showed cerebral infarct was reduced by 70% in hypoxia-ischemic conditioned neonatal rats[7] and currently there is a clinical trial in progress for "Neuroprotective Effects of Remote Ischemic Preconditioning (RIPC) During Infant Cardiac Surgery".[8]

Neonates with CHD undergoing cardiopulmonary bypass continue to have increased risk of neurological vulnerabilities without significant improvements in neuroprotective techniques over the years. Neurologic ischemic preconditioning techniques are showing promising results in multiple animal studies with remote ischemic preconditioning providing benefits for many organs. Currently, there is a clinical trial in progress to determine the effects of ischemic preconditioning on neuroprotection in infants undergoing cardiac surgery, and there is hope that improvements in neuroprotection will be clinically demonstrated, furthering much needed advances in neuroprotection for neonates with CHD undergoing CPB.

References

Albers, E.L., Bichell, D.P., & McLaughlin, B. (2010). New approaches to neuroprotection in infant heart surery. Pediatric Research, 68(1), 1-9. https://doi.org/10.1203/PDR.0b013e3181df5402

Mahan, V.L. (2017). Current neuroprotective strategies for cardiopulmonary bypass and deep hypothermic circulatory arrest in newborns. Advances in Cardiothoracic Surgery, 2, 1-93. Retrieved from http://www.avidscience.com/wp-content/uploads/2017/09/current-neuroprotective-strategies-for-cardiopulmonary-bypass-and-deep-hypothermic-circulatory-arrest-in-newborns.pdf.

Continued on Page 14

Continued from Page 13

Rachmat, J., Sastroasmoro, S., Suyatna, F.D., & Soejono, G. (2014). Ischemic preconditioning reduces apoptosis in open heart surgery. Asian Cardiovascular and Thoracic Annals, 22(3), 276-283. https://doi.org/10.1177/0218492313481223

Healy, D.A., Moloney, M.C., McHugh, S.M., Grace, P.A., & Walsh, S.R. (2014). Remote ischaemic preconditioning as a method for perioperative cardioprotection: Concepts, applications and future direction. International Journal of Surgery, 12(10), 1093-1099. https://doi.org/10.1016/j.ijsu.2014.08.352

Ara, J., Fekete, S., Frank, M., Golden, J.A., Pleasure, D., & Valencia, I. (2011). Hypoxic-preconditioning induces neuroprotection against hypoxia-ischemia in newborn piglet brain. Neurobiology of Disease, 43(2), 473-485. doi: 10.1016/j.nbd.2011.04.021

Hassell, K.J., Ezzati, M., Alonso-Alconada, D., Hausenloy, D.J., & Robertson, N.J. (2015). New horizons for newborn brain protection: enhancing endogenous protection. Arch Dis Child Fetal Neonatal Ed, 100, 541-552. doi: 10.1136/archdischild-2014-306284

Tropak, M.B., Shi, H., Li, J., Dai, X., Redington, A.N., & Askalan, R. (2011). Potent neuroprotection induced by remote preconditioning in a rat model of neonatal cerebral hypoxic-ischemic injury. J Thorac Cardiovasc Surgery, 142, 233-235. doi: 10.1016/j.jtcvs.2011.04.003

CenterWatch. (2018). Neuroprotective effects of remote ischemic preconditioning (RIPC) during infant cardiac surgery. Retrieved from https://www.centerwatch.com/clinical-trials/listings/165984/heart-defects-congenital-neuroprotective-effects-remote-ischemic/?&radius=50

YOU

Affinity Fusion™
Oxygenation System

autoLog IQ™
Autotransfusion System

HMS Plus
Hemostasis Management System

GOT US.

Committed to cardiopulmonary.
Committed to life.

CAUTION: Federal Law (USA) restricts these devices to sale by or on the order of a physician. For a listing of indications, contraindications, precautions, and warnings, please refer to the Instructions for Use, which accompanies each product.

UC201908989a EN 02/2020

medtronic.com

Medtronic

Vasoplegic Shock: A Summary of Current Standings

Cara Carlos

Cardiovascular Perfusion Program

Quinnipiac University

Hamden, CT

What is Vasoplegia?

Vasoplegic syndrome (VS), also known as vasodilatory shock (VDS), is a well-documented adverse effect of cardiopulmonary bypass (CPB) surgery, often occurring in parallel to systemic inflammatory response syndrome (SIRS). In the early postoperative period following CPB circuit exposure, patients will commonly present with a lack of vascular tone leading to inadequate tissue perfusion and the potential for organ failure. The hypotensive event is coupled with a cardiac output that is within normal limits or even elevated.[1] In its refractory form, this type of maldistributive shock can manifest as a resistance to vasopressors, rendering treatment less straightforward. While multiple therapeutic avenues are currently in practice, more focused research will aid in proper identification, treatment and (most importantly) prevention of vasoplegia.

Vasoplegia has been appreciated in 5-44% of postoperative CPB patients.[3,4,7] Retrospective hospital studies have found a correlation between VS and increased hospital stay, extended ventilator dependence, blood product usage and mortality in CPB patients.[1,4,7] While certain traits within this patient population have been pinpointed as indicative of increasing the likelihood of vasoplegia development, such as the accumulation of comorbidities as well as mean arterial pressure (MAP) upon induction. The occurrence of vasoplegia does not always behave in a predictable fashion.
The presenting parameters of vasoplegic shock are reported to correlate with a MAP of less than 50-70 mmHg and a CVP of less than 5 mmHg, a normal or elevated cardiac index (greater than or equal to 2.5 L/min/m^2), a low peripheral resistance (800-1400mmHg) and persistent vasopressor requirements.[5,6] One of the most challenging aspects of this disorder is identification. Since vasoplegic shock presents in a frustratingly nonspecific manner that can be attributed to a myriad of etiologies, ruling out alternative sources of hypotension is often the suggested route (via double checking a radial artery reading or the correction of a hypovolemia, for example).

The Link Between SIRS and VDS

Several factors are theorized to contribute to the cardiac patient's risk of developing vasoplegia. Immediately upon initiation of CPB, cardiac surgery activates many inflammatory pathways with detrimental effects that propagate long into the postoperative period. Complement, leukocyte, and contact activation result in the release of cytokines, kallikrein, inducible NO and other inflammatory mediators in a snowballing effect that depletes vital molecules such as clotting proteins and ATP. ATP depletion in conjunction with acidosis will disrupt the membrane gradient and render calcium channel-regulated vasoactivity ineffective, even in the presence of catecholamines. Duration of circuit exposure and reperfusion injury are factors that can increase levels of circulating inflammatory mediators and can therefore be categorized as contributors to vasoplegia risk.[1,3]

When blood passes through the synthetic CPB circuit, plasma proteins adhere to the lumen of the circuitry, causing the aggregation of proteins and subsequent molecular changes to occur. The activation of inflammatory and vasoactive molecules such as reactive oxygen species (ROS), endothelins, platelet activators, inducible NO, cytokines and prostaglandins leads to a massive systemic insult that the body struggles to recover from because vital components such as vasopressin, platelets and ATP have been depleted.

Where Has All the Vasopressin Gone?

The depletion of vasopressin can be exacerbated by historical angiotensin-converting enzyme inhibitor (AChI) drugs used preoperatively to control essential hypertension (HTN). Blocking the renin-angiotensin-aldosterone (RAA) pathway, coupled with a procedure that literally bypasses the site of bradykinin metabolism (lungs) can result in loss of vasomotor tone.[5,7] While not a concrete prognostic indicator, the reaction of MAP to bypass initiation, including the degree and duration of a hypotensive change and its responsiveness to vasoactive drugs, can be utilized as a clue to the extent of inflammatory response and whether endogenous vasopressor levels persist at levels adequate enough to compensate.[7] Other factors such as induction duration, history of congestive heart failure (CHF), previous surgeries, increased BMI and the use of bridge devices exacerbate the risk.[1,7] Interestingly, the case demographic with the lowest incidence of vasodilatory shock are aortic cases, perhaps due to the use of DHCA to maintain the patient during repair.[4]

Treatment

Once a hypovolemia has been ruled out or corrected, practitioners turn to pharmaceutical intervention for vasoplegic shock. Instinctually, the first line treatment for this presentation would be a vasoconstrictive agent. But what can be done when vasoplegia proves refractory to vasopressors? Vasopressin supplementation, to replenish depleted hypophyseal stores, given prophylactically preoperatively, or in adjunct to a catecholamine has been shown to decrease the required dosage.[3,4,6] Methylene blue, a direct NO binding competitor, has come into light as a valid option for treating vasoplegia. Success has been reported in preoperative, intraoperative and single post CPB doses; however it has not proved to be of use post onset of organ failure There is also the known drawback of pulse oximetry interference to consider.[1,3,11] Corticosteroids such as methylprednisolone and dexamethasone have also been administered to mitigate inflammatory mediators, reverse the vasodilatory shock state and as an adjunct to reduce the vasopressor dosage via adrenergic receptor upregulation. However the detrimental impact on wound healing is a consideration. Several studies returned data that failed to support an improvement in mortality with intraoperative administration of these steroids, however they were not specifically focused on VDS and it appears more focused research is warranted.[3] Two other studies supported corticosteroid prophylactic use with an observed decrease in hospital stay and decrease in time of mechanical ventilatory dependence.[1] Exploratory therapies currently include vitamin C for anti-inflammatory and microcirculatory reasoning, hydroxocobalamin (for a hypertensive effect), telipressin (the longer-acting vasopressin analog) and angiotensin II (as encouragement for the natural release of vasopressin).[3]

Prophylaxis

In addition to pharmaceutical interventions (preoperative vasopressin treatment and ACE inhibitor discontinuation, for example), other steps can be taken to reduce patient risk. For the perfusionist, the measures taken to mitigate vasoplegia are the same steps taken to minimize the inflammatory response: short pump runs, judicious use of blood products, minimized circuits and careful hemodynamic monitoring of the patient. It is theorized that an additional thirty minutes

Continued on Page 18

Continued from Page 17

of pump exposure time can increase a patient's risk of developing VDS by 38%.[4] With the increased popularity of MICS and off-pump CABG, hopefully fewer patients will be exposed to the risk. Knowing the patient history and predicting how it will impact the pump run will help the operating team to provide the best patient care. In our time, we are sure to see more research on vasoplegic shock that will hopefully uncover more insight into how we can protect and treat patients. Because vasoplegic shock and septic shock share a similar presentation, most of this knowledge is based upon publications for the latter. With the increase in prevalence of bypass surgeries around the globe, we will hopefully see an increase in investigations dedicated specifically to this life-threatening event. In the meantime, let's keep it short, keep it cold and maintain the MAP!

References

1. Omar, S., Zedan A., and Nugent K (2015). Cardiac Vasoplegia Syndrome: Pathophysiology, Risk Factors and Treatment. Am J Med Sci., Jan;349(1):80-8. doi: 10.1097/MAJ.0000000000000341.
2. Hosseinian, L., Weiner, M., Levin, M., and Fischer, G. (2016). Methylene Blue: Magic Bullet for Vasoplegia? Anesthesia & Analgesia, 122(1):194–201. doi: 10.1213/ANE.0000000000001045
3. Shaefi, S., Mittel, A., Klick, J., Evans, A., Ivascu, N., Gutsche, J., and Augoustides, J. (2018). Vasoplegia After Cardiovascular Procedures—Pathophysiology and Targeted Therapy. Journal of Cardiothoracic and Vascular Anesthesia, 32(2):1013-1022. doi: 10.1053/j.jvca.2017.10.032.
4. Fischer, G. and Levin, M. (2010). Vasoplegia During Cardiac Surgery: Current Concepts and Management. Seminars in Thoracic and Cardiovascular Surgery, 22(2):140-144. doi: 10.1053/j.semtcvs.2010.09.007
5. Mekontso-Dessap, A., Houël, R., Soustelle, C., Kirsch, M., Thébert, D., Loisance, DY (2001). Risk factors for post-cardiopulmonary bypass vasoplegia in patients with preserved left ventricular function. The Annals of Thoracic Surgery, 71(5): 1428 – 1432. doi: 10.1016/s0003-4975(01)02486-9
6. Masetti, P., Murphy, S. F. and Kouchoukos, N. T. (2002). Vasopressin Therapy for Vasoplegic Syndrome Following Cardiopulmonary Bypass. Journal of Cardiac Surgery, 17: 485-489. doi:10.1046/j.1540-8191.2002.01002.x
7. Levin M., Lin, H., Castillo, J., Adams, D., Reich, D., and Fischer, G. (2009). Early On–Cardiopulmonary Bypass Hypotension and Other Factors Associated with Vasoplegic Syndrome. Circulation, 120:1664–1671. doi: 10.1161/CIRCULATIONAHA.108.814533
8. Lambden, S., Creagh-Brown, B., Hunt, J., Summers, C., Forni, L. (2018). Definitions and pathophysiology of vasoplegic shock. Critical Care, 22:174. doi: 10.1186/s13054-018-2102-1
9. Truby, L., Takeda, K., Farr, M., Beck, J., Yuzefpolskaya, M., Colombo, P., Topkara, V., Naka, Y., and Takayama, H. (2018). Incidence and Impact of On-Cardiopulmonary Bypass Vasoplegia During Heart Transplantation. ASAIO J.,64(1):43-51. doi: 10.1097/MAT.0000000000000623.
10. Badke, C. M., Marsillio, L. E., Weese-Mayer, D. E., & Sanchez-Pinto, L. N. (2018). Autonomic Nervous System Dysfunction in Pediatric Sepsis. Frontiers in Pediatrics, 6, 280. doi:10.3389/fped.2018.00280
11. Hosseinian L., Weiner M., Levin M.A., Fischer G.W. (2016). Methylene Blue: Magic Bullet for Vasoplegia? Anesthesia and Analgesia, 122(1):194-201. doi: 10.1213/ANE.0000000000001045

Spectrum Medical

CE Approved

Spectrum Medical is proud to present its newest addition to the Quantum family of Perfusion technologies.

A powerful and revolutionary Heater Cooler technology

Eliminates the growth environment for Mycobacterium Chimaera bacteria

Eliminates the disruption of O.R. based laminar flow systems

Eliminates hazardous cleaning procedures

Quantum PureFlow

Specifically developed to operate exclusively with the Quantum Heater-Cooler technology and its Glycol heat transfer fluid.

USA Business Inquiries:
Call 800 265 2331
ussales@spectrummedical.com

UK, EU and ROW Business Inquiries:
Call +44 (0) 1242 650120
eusales@spectrummedical.com

www.spectrummedical.com

Disclaimer: Quantum Heater-Cooler is not FDA cleared.

"Inside Perfusion"

Webinar Series

Wednesday April 8 & 15, 2020

12PM to 1:15PM EST

"2019 European Adult Cardiopulmonary Bypass Guidelines"

Luc Puis, ECCP

Brussels, Belgium

Please Register Here:

https://zoom.us/webinar/register/WN_0ZJgund4TOChBbwKfUWfCA

ABCP has Awarded 1.5 CEUs for April 8th and 1.5 CEUs for April 15th (Total of 3 CEUs)


ONI SAC

2021 Annual Meeting

Lost Pines, Texas
February 10-13, 2021

Our Host Hotel
Hyatt Regency Lost Pines Resort & Spa
(23 miles outside Austin)

www.hyatt.com › hyatt-regency-lost-pines-resort-and-spa › auslp

Reservations: 512-308-1234 or 877-803-7534

Single/Double Occupancy:
$239.00 (includes daily resort fee)

Remember to mention that you will be attending the Annual Conference of The American Academy of Cardiovascular Perfusion (AACP).

AACP 2020 Officers and Council

President
William Riley
N. Weymouth, MA

Vice-President
Justin Resley
Evans, GA

Secretary
Tami Rosenthal
Aston, PA

Treasurer
Kenmund Fung
New York, NY

Council Members
Carmen Giacomuzzi
Portland, OR
Past President

Molly Bryant
Oronoco, MN

David Fitzgerald
Mt. Pleasant, SC

Richard Melchior
Woodbury, NJ

Mat Tyndal
Birmingham, AL