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

# Summer 2023

# The Academy Newsletter

# Message from the AACP President - Summer 2023

Summer is here! By the time you read this message, we would have celebrated the July 4th Independence Holiday. Nothing represents the summer months better than fireworks, BBQs, the lingering scent of chlorine and sand, and family festivities. More importantly, the 4th serves as a day of national pride and patriotism, as we recognized ourselves as an independent nation. As a fan of summer weather, it's been my favorite time of year since childhood.

While not reaching the level of national independence, one of the monumental dates that also recently passed is the anniversary of Dr. John Gibbon's 1st successful use of CPB. This past May we celebrated 70 years of cardiopulmonary bypass. It's amazing to realize how far our profession has come in such a short period of time. To think that during this time we have taken a very dangerous surgery and made it so safe and conventional that most patients we serve will have a 98% percent chance or greater of survival. Records indicate that there were at least 18 other reported operations by several groups using CPB in the years 1951–1954 with no known survivors1. In fact, by July 1953, Dr. Gibbon had declared a moratorium on the use of CPB and would abandon cardiac surgery altogether.



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#### Editor

David Palanzo Fogelsville, PA

**Contributing Editors** 

Tom Frazier Nashville, TN

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*Student Section* Deborah L. Adams *Houston, TX*  Had it not been for the contributions of Drs. C. Walton Lillehei and John Kirklin, we may all be celebrating this summer much differently without the field of perfusion. To quote the late Jerry Garcia after 70 years, "What a long, strange trip it's been".

What will the next 70 years have in store for our profession? Will artificial intelligence and machine learning change the way we interact with patients? AI is ubiquitous in society, ranging from smart devices, apps, and credit cards, to entertainment, purchasing, and travel. Significant advancements in healthcare are already being reported in the fields of personalized medicine, drug discovery, early disease detection, and predictive analytics. Machine learning and AI in perfusion may incorporate real-time data analysis for clinical guidance and minimize human error which leads to safer surgeries and improved patient outcomes. AI-powered robotic systems could enhance surgical precision and efficiency. Surgeons may leverage robotic platforms equipped with AI algorithms to perform complex procedures with greater accuracy and dexterity. The rise of machines is here.

The integration of AI technologies into cardiac surgery will require careful planning, training, and collaboration between healthcare professionals and technology experts. Will the science of perfusion evolve into a profession of data scientists and engineers? Despite the perceived benefits of machine learning, AI lacks creativity and compassion for direct patient care. As such, caring and compassionate perfusionists are paramount in tailoring the clinical experience to meet the needs of our patients.

The 2024 Program Committee is excited to share the theme of the 2024 AACP Meeting- The past, present, and future of perfusion. The program will not only honor and recognize the seminal contributions of our pioneers but discuss the present and future opportunities in perfusion technology. The scientific panel will feature experts throughout our industry's extraordinary history and help us celebrate significant achievements along the way. This year's conference is hosted in Nashville (February 7-10, 2024). Please be sure to make your arrangements now. You don't want to miss this event!

Have a happy and safe summer.

Yours in service,

Dave Fitzgerald President, AACP



Reference: Kurusz M. May 6, 1953: the untold story. ASAIO J. 2012;58(1):2-5

### **Brendan Boyson**

CV Perfusion Program Rush University Chicago, Illinois



Brendan Boyson is currently a firstyear perfusion student at Rush University Medical Center in Chicago. He is a lowa native who received his Bachelors of Science at Weber State University. Prior to going to Rush University, Brendan was a respiratory therapist for four years and an ECMO specialist for one year. Outside of school he enjoys working out and spending time outside. He is interested in pediatric perfusion after graduation.

### HIT The Ground Running: A 5K into Heparin-Induced Thrombocytopenia and Heparin Alternative Strategies

Early recognition of clinical changes, quick thinking and willingness to communicate alternatives for patients can be the difference between a short ICU or long ICU stay for many Cardiovascular patients. One of the recognition signs for Heparin-Induced Thrombocytopenia (HIT) is a decreased platelet count. Although this early clinical representation is a good starting point to recognition, treating preoperatively, perioperatively and postoperatively is an area in which more research is needed. Luckily, a team at Lausanne University Hospital in Lausanne Switzerland looked to find and compile a large-scale systematic review of what HIT is and different strategies for pre, post and perioperative alternatives to mitigate HIT's potentially lifethreatening outcomes.

Heparin-induced thrombocytopenia can be categorized into two types: Type 1 HIT, characterized as a mild drop of platelet count generally around the one to four day mark of heparin use, that recovers without the discontinuation of heparin and Type 2 HIT: The more rare, but severe adverse drug reaction leading to potential life threatening thrombotic events. HIT begins with platelet activation through two separate pathways: The FcyRIIa receptor pathway and the IP receptor pathway. Most notably platelets secrete a large amount of platelet factor 4 (PF4) that negatively bonds to heparin creating complexes. This in turn creates an antigen from which immunoglobulin G class antibodies link to, creating larger scale complexes. These complexes bind to FcyRIIa receptors sites, leading to intracellular signaling and eventual platelet aggregation (Revelly et al, 2023). Within this context, HIT essentially leads to increasing thrombin generation, decreasing platelets counts from both aggregation and from macrophages working to remove these platelets.

The use of a low platelet count can be one of the indicators for HIT but the timing, the amount of decrease and any formation of thrombus can lead to a greater identifier of whether a patient is truly HIT positive, among other tests. All these factors are actually used in the 4T scoring system which grades the patient based on specific criteria and gives the medical provider a good insight into the possibility of the patient having HIT. The gold standard remains the Serotonin Release Assay (SRA) and any 4T score should be followed up with an SRA or a PF4 ELISA test. The ELISA test looks for specific antibodies while the SRA looks at the actual activation of the platelets through the release of serotonin (Nicolas et al, 2022). Still, at this time, the only course of action recommended after recognition of HIT is the discontinuation of Heparin and the initiation of alternative anticoagulants.

The current practice at most institutes is a bolus of heparin administration prior to the initiation of Cardiopulmonary bypass (CPB) to minimize complement activation and clot formation while on CPB during surgery. The team at Lausanne investigated two main types of alternative management: Non-Heparin anticoagulants and the use of antiplatelets in conjunction with the standard heparin protocol. The two non-heparin anticoagulants discussed were Bivalirudin and Argatroban. Bivalirudin is both recommended by AmSECT as a heparin alternative and by the American Society of Hematology (Nicolas et al, 2022). Bivalirudin is a direct thrombin inhibitor which is used and found to be useful in off pump coronary bypass surgery, ventricular assist device implantation and with ECMO use. Its half-life is around 25 minutes if the patient has normal renal function and it is actually cleared by thrombin catalyzing the reaction to create a proteolytic cleavage of Bivalirudin (Revelly et al, 2023). Normally monitoring is performed through activated partial thromboplastin time (aPPT) but the use of ACT over >400 can be used for CPB in cardiac surgery. Multiple trials investigated the use of Bivalirudin, one of them most notably being the EVOLUTION-On trial, looking at 150 patients undergoing cardiac surgery with CPB for CABG and valve replacement and comparing it to that of typical heparin strategies. The EVOLUTION-ON team found similar "comparable success rates between strategies" but did find that there was more postoperative bleeding within the first 2 hours. Due to Bivalirudin having no reversing agent and for a drug to be removed it needs to have an average of about 5 half life cycles, it would make sense for this to be true for patients within the first 2 to 3 hours. Another concern with Bivalirudin is that it rapidly undergoes cleavage in stagnant blood, requiring more constant monitoring and a new protocol for overall management on bypass. Argatroban on the other hand is a small molecule that reversibly binds to the thombin and is also a direct inhibitor. Its half-life is around 60 minutes and is eliminated via liver metabolism. Argatroban has far less literature relating to its use in CPB. Among the literature that is out, Argatroban led to major bleeding episodes requiring reexploration and, in some cases, requiring larger amounts of blood product during surgical cases. Due to these findings, it was found not to be recommended for use.

The secondary approach the team discussed was that of antiplatelet agents in conjunction with the typical heparin protocol. The prevailing thought behind this is the ability to have a reversible anticoagulant that is well known by the cardiovascular team and adding an additional agent to assist with HIT management. Three main classes were addressed: Prostacyclin receptor agonists, GP IIb/ IIa antagonist and P2Y12 receptor antagonists. The Prostacyclin drug discussed was Epoprostenol which is a pulmonary and systemic vasodilator and works to create cyclic adenosine monophosphate (cAMP), which in turn can inhibit many processes such as platelet activation. The biggest concern with using this drug is the hypotension created and the need to counteract it with high vasopressors that make it a less suitable drug for HIT patients. The GPIIb/IIa antagonist was Tirofiban which inhibits the fibrinogen receptor. Much like Argatorban, there is limited literature regarding its effectiveness in the cardiac OR setting. One case used Tirofiban prior to the initial heparin bolus with 47 patients during CPB cases. There was not extra postoperative blood loss or transfusion requirements compared to normal. Cangrelor is a reversible P2Y receptor inhibitor that works to block ADP-induced platelet activation and aggregation by 99% when used as a bolus dose followed by a continuous infusion (Revelly et al, 2023). Many cases were discussed regarding the use of Cangrelor, but each one was addressing subacute or remote HIT who had minimal antibodies within their system, leaving its effectiveness on more active HIT patients lacking.

The final alternative addressed was the use of Immunoglobulins. The IgG within Intravenous Immunoglobulin (IVIG) works to bind to all Fcy receptors to block them, but it is unknown fully how it assists in HIT. Intravenous Immunoglobulin has been used as treatment for acute HIT since 1989 and is recommended as an adjunct therapy for patients with known HIT who are going to be re-exposed to heparin. Based on the recommendation by case reports and the Lausanne team, the use of IVIG either intraoperatively or preoperatively can greatly benefit these patients. Through thorough investigations into case reports and literature, small steps are being made to recognize HIT and find means to minimize it detrimental outcomes to the patients. There are alternative strategies that are being researched in order to continue furthering our understanding of managing HIT, although nothing is foolproof at this time. Further research is needed but we hopefully have a foundation to move forward and see positive outcomes for our patients.

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### Timing of Initiation of COVID VV ECMO: Did it matter? Did it not matter? Why are we asking?

The timing of initiation for venous venous extracorporeal membrane oxygenation (VV-ECMO) in COVID-19 patients is a heavily debated topic in the perfusion world today. Many factors are involved in those decisions, but I wanted to discuss how perfusionists were most affected by the COVID-19 pandemic. There was a constant lack of supplies, ECMO machines, and even beds for our patients. Another problem that we are still facing today is staffing shortages. Many perfusionists worked more hours in the last few years than they ever have before. Lastly, perfusionists were often put into situations they had not been trained for. Speaking with loved ones and giving medical advice were two I noticed in my own experiences. This brings me to my question, "Does the amount of time on mechanical ventilation prior to VV-ECMO initiation for COVID-19 patients really matter"? Before I dive into answering that question, there are a few definitions and criteria I'd like to go over since the following studies all used them.

The Berlin Definition for ARDS is centered around PaO2/FiO2 ratios. If your ratio is between 200-300, you have a mild case of ARDS, if it is

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between 100-200 you are moderate, and below 100 is considered a mild case of ARDS. The EO-LIA Criteria of ARDS for VV-ECMO initiation is a PaO2/FiO2 ratio < 50 for more than 3 hours, < 80 for more than 6 hours, or an arterial pH of 7.25 and pCO2 > 60 for more than 6 hours. Now that I've got those definitions out of the way, I will be comparing two articles that support early initiation, and two that say it does not matter.

The first study was in support of early initiation and was a retrospective study out of Geneva University Hospitals in Switzerland (Giraud et al., 2021). They had 10 patients on VV ECMO with an average age around 57 years and an average BMI around 31.5. The mean mechanical vent time prior to ECMO and time on ECMO was 7 days  $\pm$  3 and 19 days  $\pm$  11. These patients were cannulated through femoral and internal jugular veins. The results showed that any patients that had less than 7 days of mechanical ventilation had a 100% survival rate to discharge. The group that had more than 150 hours of mechanical ventilation prior to ECMO had a 0% survival rate. This study's results were so strong towards the early initiation opinion that the researchers stated that initiation after the 7th day of ventilation is futile.

The next study was also in support of early initiation and was a retrospective study out of China (Li et al., 2021). There were 31 patients split into two groups. There were 17 in the delayed ECMO group, which was placed on ECMO within 2-5 days of meeting the ECMO criteria. The other group had 14 patients, and that was the early initiation group, which was within 24 hours of meeting the criteria. The median age was 58 and there were 19 men and 12 women. The average length of symptom onset to hospital admission was 11 days, and median duration ECMO was 14 days. The study had > 75 years of age, mechanical ventilation longer than 7 days, and multi organ failure all listed as their exclusion criteria. The results stated that the 60 day mortality for the early initiation group was 50%, while the late initiation group was 88%. The early initiation group maintained their mean arterial pressure around 75mmHg, the PaO2 and CO2 clearance were both improved, and had significantly increased ECMO weaning success. They stated early application successfully improves weaning and increases survival compared with the delayed initiation of ECMO.

The next two studies cover why they believe initiation and ventilation times do not matter. This was a retrospective study run out of the Medical University of Vienna Austria, that had 101 patients with a mean age of 56(Hermann et al., 2022). The median time from intubation to ECMO was 7.7 days and the median ECMO duration was 16.4 days. Fifty-two percent of the patients had pre ECMO invasive mechanical ventilation over seven days. This study found that 60 of the 101 patients survived to discharge. Specifically, of the 53 patients with pre ECMO IMV duration > 7 days, 33 patients (62%) survived to the ICU. For the 35 patients that had pre ECMO IMV > 10 days, 21 patients (60%) survived to the ICU. The researchers stated that there was no difference in survival for patients with pre ECMO IMV less than seven days, compared to greater than seven days.

The last study was a retrospective study done in Angers University Hospital in France (Oliver et al., 2021). There were 56 patients, 49 men and 7 women, and the age ranged from 24-71 years old. The pre ECMO mechanical ventilation time ranged from 0-36 days. The results stated that 48% of patients were discharged from the hospital after an average VV-ECMO run of 17.5 days. The researchers mentioned that there was no significant association between duration of mechanical ventilation prior to VV-ECMO. The results were consistent with data showing a strong association between age and mortality for COVID-19 patients on VV-ECMO.

After a deep dive of all of these studies, I felt that I left with more questions than answers. I had the opinion that less mechanical ventilation time prior to ECMO was better but am now believing there is another factor at play here than just ventilation times. The seven-day rule of mechanical ventilation prior to ECMO was developed after the H1N1 pandemic about a decade ago. That was proven to be accurate for H1N1 patients but did not seem to be as big as a factor for COVID-19 patients on VV-ECMO. The studies had multiple limitations that hindered my ability to come to a conclusion. The studies rarely mentioned their treatment regimens, specifically physical therapy or medications that the patients were on throughout their ECMO run. There were also too few patients included, and the retrospective nature caused some data to be left out of the study. Due to this, there are many more steps to take to figure out the best course of treatment for our COVID-19 patients that need VV-ECMO. We need to develop better treatments and therapy regimens for the patients. What perfusionists can do to help is continue to do more research on what the best time is for COVID-19 patients to be put on VV-ECMO. Mechanical ventilation times may not be the main source of mortality for our COVID-19 patients, but there is still something that is holding us back from achieving higher success rates, and I believe we can find that in the near future.

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# Expanding The Donor Pool: Uncontrolled Cardiac Death Lung Allografts in The United States

Lung disease is one of the top causes of death in the United States and the third leading cause of death worldwide (1,2). Although the case volume of lung transplants has increased, demands are still exceeding the supply. Based on the Organ Procurement and Transplant Network (OPTN) data, there were 2,524 lung transplants in 2022. However, there were 1,065 unmatched candidates who remained on the waitlist, 150 were removed because they became too sick for transplantation and 128 died awaiting a donor match. The inclusion of uncontrolled donation after circulatory determination of death (uDCD) has the potential to ameliorate the shortage of suitable lungs for transplant.

The first lung transplantation was performed in 1963 from a donor who suffered a myocardial infarction in the University of Mississippi emergency room (2). By 1970, twenty-three lung transplants had been reported world-wide, and all came from Non-Heart-Beating Donors (NHBD) (2). Out of the forty lung transplantations attempted by 1983, none reported immediate deaths from graft failure, despite all being recovered from NHBDs (2). After the FDA approval of the immunosuppressant cyclosporine in 1983, patients continued to have increased rates of survivability and there was a massive growth in lung transplant programs across the United States. By 1996, the United Network for Organ Sharing (UNOS) received reports from 75 centers having fully functional lung transplant programs.

As transplantations became more standardized, there grew an ethical desire for an exact definition of death, which led to the Uniform Determination of Death Act (UDDA) in 1981 (2). In 1995, the Maastricht classification for NHBD was released which categorized organ ischemic times based on the conditions in which cardiac arrest took place. Controlled donation after circulatory determination of death (cDCD), classified at Type III and IV, are donors who experienced a devastating, irreversible injury deemed non-recoverable at which time the decision to voluntarily withdraw life support leads to imminent death via hypoxia and hypercarbia. If death occurs swiftly, the organs can be recovered for transplant. In the case of Type I or Type II, death happens unexpectedly either inside or outside the hospital, making them uncontrolled DCDs.

The lung's unique physiology makes it exponentially more tolerant of longer ischemia periods due to the utilization of diffusion over perfu-

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Christine is a recent graduate from Rush University in Chicago, Illinois. She attended the University of Wyoming where she received her Bachelor's Degree in Biology with a minor in human physiology. Christine is excited to be going the team of cutting edge perfusionists at UW Health in Madison, WI. sion for its primary method of cellular respiration. Studies have shown that lungs could be recovered one hour following circulatory arrest and transplanted with excellent gas exchange (2,3). However, if the deceased donor were ventilated following cardiac arrest, lungs could be recovered four hours postmortem with good gas exchange (3).

The first successful cDCD was performed in 1993 and many programs continue to utilize these sudden death donors with acceptable outcomes and data suggests cDCDs and DBDs appear to experience similar outcomes (2,5). In addition to increased incidence of aspiration pneumonia and neurogenic pulmonary edema in DBD lung allografts, there is growing awareness of the importance of the innate immune system activation as a mediator of ischemia-reperfusion injury and its correlation with early primary graft dysfunction (PGD) (4). It is possible that ex-vivo perfusion may allow for down-regulation of innate immune signaling pathways, and lead to better outcomes with ex-vivo perfused organs than organs from conventional donors. This superiority has been demonstrated in kidney transplantations (5). Thus, it is possible that lungs retrieved from victims of sudden death may function better than lungs retrieved from conventional brain-dead organ donors.

Expanding the lung transplantation donor pool to include uDCD allografts is not a novel idea. Documentation from other countries show the feasibility of implementing successful uDCD protocols; there has yet to be a uDCD lung transplant in the United States (2,3). In 2001, the first uncontrolled lung transplantation was performed in Sweden. Today approximately 10 programs have successfully extended their donor criteria to include uDCDs, most notably in Spain. However, the application of these published parameters may be challenging for aspiring teams in the United States. The adequacy of uDCD lung allografts measured against traditional donors has already been proven, yet the United States fails to apply these accounts of success towards building their own programs. The long-term respiratory effects of COVID-19 are still being realized which have been a contributing factor to increase demand for available lung allografts.

Theorized obstacles include ethical considerations, commitment of time from stakeholders and early associated costs. However, as increased demands for organ donation, a future which includes uncontrolled sudden death donors might not be far off.

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# **Contact Information for Our Sponsoring Partners**

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# Important Academy Dates

The ACADEMY ANNUAL MEETING DEADLINES

ABSTRACT DEADLINE	October 15, 2023
MEMBERSHIP DEADLINE	December 1, 2023
PRE-REGISTRATION	January 18, 2024
HOTEL REGISTRATION	January 18, 2024
2024 ANNUAL MEETING	February 7-10, 2024

### 45th Annual Seminar of The American Academy of Cardiovascular Perfusion Loews Vanderbilt Hotel 2100 West End Avenue, Nashville, TN 37203 February 7-10, 2024

### (Tentative Program)

### Wednesday, February 7, 2024

- 11:00 AM 4:00 PM REGISTRATION
- 3:30 PM 4:00 PMOpening Business Meeting<br/>Fellow, Member, Senior and Honorary Members4:00 PM 7:00 PMManufacturers' Breakout Rooms

### Thursday, February 8, 2024

- 7:00 AM REGISTRATION
- 7:00 AM 8:00 AM Video Presentations
- 8:00 AM 09:30 AM Scientific Paper Session
- 9:30- AM 11:30 AM Fireside Chats
- 11:30AM 12:30PM Lunch (Speaker)
- 12:30 PM 2:30 PM Special Scientific Panel Session Our Early Years of Cardiopulmonary Bypass: A Blast from the Past Moderator: Thomas Frazier

Pumps and Hardware - Steven Sutton Circuit Components - David Palanzo Myocardial Protection - James MacDonald Perfusion Safety - Mark Kurusz ECMO- John Toomasian Panel Discussion

- 2:30 PM 2:50 PM Break
- 2:50 PM 4:20 PM **Special Scientific Panel Session Future Innovation: Al and HLMs** *Moderators: Vincent Olshove, John St. Onge*

Big Data / Predictive Analytics Future of Hardware / Safety Future of Simulation Future of Education Panel Discussion

05:00PM Sponsor's Hands-On Workshop & Reception

### Friday, February 8, 2024

7:00 AM	REGISTRATION
7:00 AM – 8:00 AM	Video Presentations
8:00 AM – 9:30 AM	Scientific Paper Session
9:30- AM – 11:30 AM	Fireside Chats
11:30AM - 12:30PM	Lunch (Historical Videos)
12:30 PM – 2:30 PM	<b>Special Scientific Panel Session – ECMO Update</b> Moderators: Allison Weinberg, Dana Mullin
	Adult ECMO Pediatric ECMO Hybrid Cannulations / MCS ECPR ECMO Patient Interview Panel Discussion
2:30 PM – 3:00PM	Break
3:00 PM – 5:00 PM	Memorial Session Moderator: Justin Resley
	Introduction – <i>Justin Resley</i> Charles C. Reed Memorial Lecture Thomas G. Wharton Memorial Lecture ( <i>David Fitzgerald</i> )
6:30 PM	Induction Dinner All Attendees and Guests

### Saturday, February 10, 2024

7:00 AM	REGISTRATION
7:00 AM – 8:00 AM	Video Presentations
8:00 AM – 9:30 AM	Scientific Paper Session
9:30 AM – 10:00 AM	Break
10:00 AM – 11:30 AM	Special Scientific Panel Session - Pediatrics Moderator: Joseph Deptula
	Adult Congenital Fetal Interventions Pediatric Registry Complicated Cases Panel Discussion

11:30 AM – 12:30 PM	Lunch (Historical Videos)
12:30 PM – 1:30 PM	Special Scientific Panel Session – Pro / Con Debate
	ECMO and MCS Coverage (CCP vs. Specialist) Flow vs. Neo-Synephrine Recredentialing for all CCPS Del Nido Cardioplegia vs. the field
1:30 PM – 3:00 PM	Special Scientific Panel Session – Heart Transplantation
	Donation After Circulatory Death (DCD) Organ Procurement Normothermic Regional Perfusion (NRP) Reallocation of Organs Partial Domino Heart Transplant Panel Discussion
3:00 PM – 5:00 PM	Fireside Chats
5:00 PM	Closing Business Meeting Fellow, Senior and Honorary Members Only

# THE ACADEMY TO OFFER <u>LIVE</u> <u>WEBCAST</u> AGAIN THIS YEAR

The American Academy of Cardiovascular Perfusion will again be offering a live webcast of our 2024 Annual Meeting in Nashville, Tennessee. The General Sessions of the meeting and two virtual Fireside Chats each day will be broadcast in high quality streaming video. There will also be an opportunity for attendees to ask questions, thus qualifying for Category I CEUs from the American Board of Cardiovascular Perfusion.

# 2024 Annual Meeting



# Nashville, Tennessee



# Our Host Hotel Loews Vanderbilt Hotel

2100 West End Avenue, Nashville, TN 37203

### Reservations: 888-879-0462 or 615-340-5778

### Single/Double Occupancy: \$249.00

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

### AACP 2023 Officers and Council

**President** David Fitzgerald *Mt. Pleasant, SC* 

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