NEWS FROM THE NEUROPROTECTION SUB-COMMITTEE

Summary of Group Project or Activities – Posted June 2024

Name of Project or Activity	Description	Project Status (New, Ongoing, Complete, Near Completion, Long Term, Abandoned)
STS database study nadir temp during CPB and outcomes	An ambitious STS database study including data from almost 2million CABG, Valve and CABG and Valve procedures spanning over the most recent decade. This study is being done given the lack of high-level evidence guidance and highly variable practice globally pertaining to temperature management during CPB. The outcomes of interest are primarily neuro outcomes such as stroke and encephalopathy, but also secondary outcomes such as kidney injury, pneumonia and bleeding related complications.	Ongoing: We heavily rely on Vanderbilt Department of Anesthesiology Statisticians to process the data and perform the analyses. We had 2 statisticians dedicated to this work, and initially met weekly and still on an ongoing basis. We have the results on the whole dataset now and almost completed the first draft of the manuscript. Given the complexity and very large data set we needed a supercomputer, which Vanderbilt made available for us to use. All of this took time, but we are very excited to share results soon.
Proposal for SCA 2025 submitted	We submitted a proposal for a session based on the results from the above study.	Submitted
Neuro-outcomes after CABG on-pump vs off pump: data from the STS database	While analyzing the data for our temperature study, we realized the STS included data on off pump CABG patients. Since we have the data, for a small additional we can request STS approval for a sub-study.	We first want to complete the original study and submit the manuscript, but this is a proposal we want to discuss with our sub-committee at the SCA meeting.

Summary of Group Meetings – Posted June 2024

Type of Group Meeting	Date	Action Items from Meeting
Zoom call	Multiple meetings and constant communication between the core research group to bring this huge study to completion.	

POSTED NOVEMBER 2023

Summary of Group Meeting 1 - Date: May 6, 2023
The well attended meeting focused the STS database study on the effects of lowest temperature during CPB for CABG and valve surgeries. Dr Kertai presented preliminary results and statistical approach. We discussed the findings (which remain preliminary). The group had an opportunity to provide feedback. We discussed whether to plan for 1 higher impact vs 2 lower impact manuscripts.

Completed work: The goal with this STS database study is to examine the association between lowest temperature during CPB and perioperative brain injury outcomes, and secondary outcomes related to infection, bleeding and kidney injury. After carefully considering suitability and quality of individual variables of interest, the a priori decision was made to use stroke as primary outcome, and include encephalopathy, coma, pneumonia, reoperation for bleeding and acute kidney injury as secondary outcomes. Guided by our group of statisticians (Vanderbilt Department of Anesthesiology) we decided to do 3 analyses for each outcome:
      1)association between outcome and temperature

2)association between outcome or death and temperature
3)association of outcome and interactions with surgery type (CABG only/ valve only/ CABG and valve).

The Inverse Probability Weighting (IPW) approach is used to balance for possible confounding associations with exposure to different temperatures. The IPW approach is very general, and some details (e.g., choosing an appropriate weight calculation model for the primary and secondary analyses, identifying the correct algorithm for constructing weights for the subgroup analysis, estimating the quality of weighting) need to be tailored to specific outcomes and exposures. Because our analytic cohort is about 1.9 millions, figuring out details of the statistical analysis is extremely time consuming, therefore, we had to work with a subsample first to finalize the analytic details. The steps that we completed include finalizing:

- Construction and selection of variables
- Model selection for weights
- Method for weight computation for the secondary analysis
- Method for evaluating the quality of weighting
- Multiple imputation for missing data
- Analytic cohorts (inclusion/exclusion criteria)
- Primary and secondary outcomes
- Fitting preliminary models (16 models total with 6 different sets of weights) on the subgroup of 10,000 subjects
- Statistical analysis draft

Ongoing work: In the ongoing work, we fucus on ensuring that our models work well and our analysis can be scaled up to the entire cohort:
- Refining the approach for computing weights based on the quality-of-weighting – This is an iterative process, if the weights do not sufficiently balance the exposure groups, the model for weights has to be revised.
- Fine-tuning the model for the weights to make sure it converges.
- Upscaling the analyses from the testing sample of 10,000 to the entire sample of over 1,900,000
- Developing visual and numeric summaries of the results

Estimated timeline for finishing data analysis, manuscript writing and submission for publication: Currently, we estimate that the analyses can be completed by the end of November. I would say that this is an optimistic estimate given that the large sample size inflates the computational time.

Manuscript draft: In the mean time we have started to write a first draft of the manuscript. At this stage we have an introduction and the statistical analysis sections completed.

COLLABORATION
We are working in close collaboration with Dr Miklos Kertai (SCA STS Database Sub-Committee) and rely extensively on his and 3 statisticians in the Department of Anesthesiology, Vanderbilt University Medical Center. They are pouring in hours and hours of work into the data processing and analysis.

FUTURE PROJECTS
The goal is to propose to present the finding of this study at a future SCA meeting.

POSTED JUNE 2023

Meeting Summary: 11/14/2022
Karten Bartels, Miklos Kertai, Willem Lombard, Svetlana Eden (statistician) and Sarah Feng (statistician).
We reviewed and discussed the summary statistics report for our STS PUF study:
o   Reviewed the exclusion criteria and data description.
o   Reviewed code for data imputation.
o   We identified missing variables previously requested not included in the dataset, and a few additional variables we previously omitted to request.
•   Significant action items: Requested additional variable from STS, subsequently approved and data received.

COLLABORATION
This is primarily a Neuroprotection Sub-committee project. To date we could not have done this ourselves, and the nature of the work so far has not been conducive to involving a large group: Karsten Bartels and I wrote the study protocol which we presented to the Neuroprotection group for review and discussion. The rest largely involved

administrative effort on my behalf, with significant guidance from Miklos Kertai to get the STS, VUMC IRB and VUMC Office of Contracts to approve protocols and the DUA agreement. The next stage that kept us busy over the past 6 months was data processing, which Miklos and VUMC statisticians helped with. Given their unique expertise and familiarity with the dataset they essentially managed this part of the project, again, not something the Neuroprotection group could have contributed to in an efficient way.

I should also mention that Bruce Bollen has been closely involved all along and provided much appreciated guidance and perspective.

The next year is going to be critically busy for the Neuroprotection Sub-Committee: pertinent literature reviews, manuscript writing and submission and then hopefully prepare to present our findings at next year's meeting.

In summary therefore, we are working in close collaboration with Dr Miklos Kertai (SCA STS Database Sub-Committee) and rely extensively on his and 3 statisticians in the Department of Anesthesiology, Vanderbilt University Medical Center. They are pouring in hours and hours of work into the data processing and analysis.

Moving into the manuscript writing section, we will make use of VUMC Librarian, Rachael Walden to assist in literature searches.

POSTED NOVEMBER 2022

Summary of Group Meeting 1: 05/14/2022
This meeting focused on our current PUF project on the association between intraoperative temperature management and neuro outcomes. We discussed the merits of various primary and secondary outcomes and reviewed the variables to be included.

We also reviewed progress on the administrative aspects of the project.

- The proposal was submitted to the STS, reviewed and approved.
- The research protocol was submitted to VUMC IRB and under review
- STS Data Use Agreement (DUA) was submitted to VUMC Office of Contracts Management and under review.

Summary of Group Meeting 2:
Several informal phone discussions took place between Dr Lombard, Bartels and Kertai to move the PUF project through various administrative hurdles.

DESCRIPTION & GOALS
We now have all the regulatory approvals for the project and have our first meeting with our group of VUMC statistician scheduled for 10/06/2022. This meeting will be an opportunity to discuss and work toward a final statistical approach. Once this is agreed upon, we will submit our final research protocol (and statistical methods) for publication to Open Science Framework (OSF). We just received the dataset from the STS and expect that it may include close to 1 million patients. Analyzing this dataset will likely take several months. In the meantime we will also begin to work on the manuscript draft.

COLLABORATION
We are collaborating with VUMC Department of Anesthesiology Statisticians on this project. The VUMC office of Contracts Management facilitated DUA negotiations with STS.

FUTURE PROJECTS
We are planning to do a systematic review on intraoperative temperature management and neuro outcomes. This review, in combination with our PUF project will provide the basis for our CPI advisory.

POSTED JUNE 2022

We had several small group discussions to strategize and plan. We wrote a study proposal, received SCA funding and STS approval for a database study to examine the impact of lowest intraoperative temperature on outcomes, in particular neurological outcomes, during various surgical procedures. When we receive the data, this will be a very large dataset on patients in the STS database from 2011 onwards. This proposal was well received by the STS review panel. Given the small group size and frequent informal calls (to promote efficiency) we did not keep meeting minutes.

DESCRIPTION & GOALS
With this project we will have a very large dataset with a wide range of variable pertaining to neurologic outcomes. Contemporary data reflecting on current use of intraoperative hypothermia for neuroprotection is lacking. The goal with this project is to examine the association between lowest intraoperative temperature with neurologic outcomes and mortality, while carefully controlling for confounding variables.

COLLABORATION
We are working with the Vanderbilt Medical Center Office for Grants and Contracts to process complex legal contracts with STS. Vanderbilt University Medical Center IRB is processing our research proposal. Vanderbilt Department of Anesthesiology statisticians, well versed in the STS database (with several peer reviewed publications), will help with the statistical analysis of the data. Given legal complexities and restrictions (Vanderbilt requires that all personnel in the study proposal are Vanderbilt employees), and an STS requirement to involve a cardiac surgeon, Vanderbilt Chair of Cardiac Surgery, Dr, Ash Shah is also collaborating on the project. In no way do any of the restrictions apply to authorship on papers that will stem from the project, and several other SCA projects have benefitted from the mechanisms put in place at Vanderbilt to process STS database study proposals.

FUTURE PROJECTS
Our next meeting will be at the SCA meeting. Emerging from pandemic restrictions and challenging work schedules, we are looking forward to having the group meet in person. At this meeting we will begin to work towards putting a writing group together for the above project. A second potential project we will discuss at the meeting to gauge interest involves the use of NIRS during cardiac surgery. A recent thorough systematic review on NIRS, spearheaded by Dr Bob Thiele, provides excellent groundwork for a spinoff study on the dataset we have. We believe such a study, combined with the completed systematic review will enable our group to develop a practice advisory on the use of NIRS during cardiac surgery.

POSTED OCTOBER 2021

DESCRIPTION & GOALS
1. Goal: Practice advisory on temperature management for optimal neurologic outcomes
   a. Systematic review: I am working with Dr Sun to get the protocol finalized. This protocol will be discussed between Drs Sun, Bartels, Grocott and Mackensen. With the help of Vanderbilt library, we

do the literature searches. Once that is completed the group will convene and put to work to review and grade the abstracts.

b. STS PUF study to examine the relationship between intraoperative temperature and neuro outcomes. I am working with Drs Bartels and Kertai, and Vanderbilt statistician Matt Shottwell. We are running some test analyses to help with our ultimate sample size. The protocol will be completed in the next couple of weeks and submitted to the SCA and then the STS.

c. Two manuscripts will be produced resulting from a and b. They will be submitted simultaneously along with the practice advisory, which will likely be incorporated in the systematic review.

COLLABORATION

We are working with Vanderbilt library, Vanderbilt Center for Knowledge, Vanderbilt Library and Vanderbilt Department of Anesthesiology Statisticians. Also working in close collaboration with Dr Miklos Kertai (STS database) to make sure we align the 2 projects as much as possible to optimize the impact of these two projects.

FUTURE PROJECTS

Dr Kertai and I just completed an STS PUF analysis on the impact of processed EEG on neuro outcomes after cardiac surgery, that we submitted for publication. Based on the findings (under review) and a subsequent systematic review, we plan to produce a practice advisory on pEEG during cardiac surgery.

POSTED JUNE 2021

The group worked on establishing methodology for practice advisories for 4 topics previously identified:
1. Temperature management during Cardiopulmonary Bypass
2. Neuromonitoring during Cardiac Surgery
3. Blood Pressure management during Cardiac Surgery
4. Atherosclerosis Assessment during Cardiac Surgery
5. (Depending on progress on the above, me may also include Spinal Cord Ischemia during Aortic Surgery)

Our goal is to conduct high quality unbiased systematic reviews, adherent to PRISMA guidelines, and produce advisories that are as closely as possible in line with the National Academies of Sciences published Standards for developing trustworthy clinical practice guidelines. We hope this will streamline the peer review process for publication and promote wider acceptance. We consulted and met with various methodologists, including the Joanna Briggs Institute, the ASA, GRADE and The Vanderbilt Center for Knowledge Management. Our goal is to first focus on Temperature Management and then rapidly progress to the other items.