Multicenter Perioperative Outcomes Group (MPOG)
PCRC Meeting Notes – Friday, October 11, 2013

Attendees: P=Present; A=Absent; X=Expected Absence

Active PIs		**In Progress PIs Continued**	
P	Kenneth Abbey, MD - OHSU	**X**	Scott Springman, MD – Wisconsin
P	Michael Aziz, MD - OHSU	**P**	Wilton van Klei, MD – Utrecht
P	Mitchell Berman, MD - Columbia	**Chairs**	
P	Daniel Biggs, MD – Oklahoma	**X**	Wolfgang Buhre, MD - Utrecht
P	Robert Craft, MD –Tennessee	**X**	David Brown, MD – Cleveland Clinic
P	Douglas Colquhoun, MD –Virginia	**X**	Michael Cahalan, MD - Utah
X	Jerry Epps, MD - Tennessee	**X**	Timothy Morey, MD - Florida
P	Jesse Ehrenfeld, MD - Vanderbilt	**X**	Jerry Epps, MD – Tennessee
X	Ana Fernande-Bustamente, MD - Colorado	**X**	Alex Evers, MD – Wash U
X	Alexander Friend, MD –Vermont	**X**	Jane Fitch, MD – Oklahoma
X	Sandra Holtzclaw, MD - Vanderbilt	**X**	Thomas Henthorn, MD –Colorado
P	Leslie Jameson, MD - Colorado	**P**	Jeffrey Kirsch, MD - OHSU
P	Sachin Kheterpal, MD - Michigan	**X**	Mervyn Maze, MD - UCSF
X	Fabian Kooij, MD – AMC Amsterdam	**P**	Marco Navetta, MD – Santa Barbara Cottage
P	Philip Lirk, MD – AMC Amsterdam	**P**	Robert Pearce, MD, PhD - Wisconsin
P	Bhiken Naik, MD - Virginia	**P**	Wolfgang Schlack, MD - AMC
P	Nathan Pace, MD – Utah	**P**	Kevin Tremper, PhD, MD - Michigan
P	William Paganelli, MD – Vermont	**P**	Warren Sandberg, MD, PhD – Vanderbilt
X	Stephen Robinson, MD - OHSU	**X**	Howard Schapiro, MD - Vermont
X	Kelley Smith, MD – Utah	**X**	George Rich, MD – Virginia
P	Jonathan Wanderer, MD - Vanderbilt	**P**	Wilton van Klei, MD – UMC Utrecht
X	Kevin Wethington, MD - Utah	**X**	Jeanine Wiener-Kronish, MD - MGH
In-Progress PIs		**X**	Margaret Wood, MD - Columbia
X	Maged Argalious, MD – Cleveland Clinic		
X	Michael Avidan, MD - Wash U	**MPOG**	
P	Brian Bateman, MD - MGH	**P**	Mark Dehring
P	Jorge Caballero, MD – Stanford	**P**	Robert Freundlich, MD
X	Matthias Eikermann, MD - MGH	**P**	Tory Lacca, MBA
P	Dan Helsten, MD – Wash U	**P**	Jenny Mace
P	Bassam Kadry, MD – Stanford	**P**	Michael Mathis, MD
P	Marco Navetta, MD – Santa Barbara Cottage	**X**	Amy Shanks, MS, PhDc
X	W. Pasma - Utrecht	**P**	Tyler Tremper
X	David Robinowitz, MD - UCSF	**X**	John Vandervest
P	Leif Saager, MD – Cleveland Clinic		

Ground Rules for PCRC:

1. Each protocol must have specific testable hypothesis with data available in MPOG data structure
2. People requesting specific data elements must also supply that data type to MPOG. If you don't submit that data type currently, then you can't get that type of data type out. However, if you have a co-investigator from another site that does supply that data, then you can ask for that

type of data. The reason is so someone on the research team understands the limitations of each data element being requested and used

3. To ensure that there is not a lack of clarity about what the status of the proposal is, each proposal will get the following overall decision at the end of each presentation and discussion
    a. Accept with minimal or no changes required
    b. Accept with major changes required
    c. Revise and reconsider at future meeting
    d. Reject
4. Meeting will be recorded to be shared later with members of MPOG via the MPOG website. There were no objections to this via the members that were on the call.

Presentation

Title: Role of Beta Blockers in Perioperative Stroke

Proposed Authors: George A. Mashour, MD, PhD, Brian Bateman, MD, Laurel Moore, MD, Robert Freundlich, MD, Milad Sharifpour, MD, Sachin Kheterpal, MD, MBA

Primary Institution: Michigan

Presented by: George Mashour, MD, PhD

Discussion Points:

- General questions posed to the audience by Dr. Mashour
    - What timeframe do we use to identify post-operative stroke? 7 days (POISE) or 30 days (NSQIP)
    - What cases should we include?
        - All cases except hearts, carotids, and brains?
        - Or a set number of high-risk non-cardiac surgeries?
        - Should we only include patients on beta-blockers?
    - For beta-blocker compliance, how robust are these data collected across the MPOG institutions?

- Dr. Ehrenfeld: Suggestion for outcome: It would be easier as the consortium is constructed to get the outcome of stroke during the initial hospitalization. Because although we have indicator flags, the ICD-9 codes just tell you that there was a stroke during hospitalization. We would have to do a manual chart review to figure out when during the hospitalization occurred. That is feasible if it there are only 100 cases to review. But it might guide your ultimate determination.
    - Dr. Kheterpal: We have the level of granularity to look at stroke during hospital stay or during readmission within X-days.
    - Mashour: This is reasonable based on the two NSQIP studies. You see the peak on postop day one. We should be able to capture the bulk of the patients.
    - Dr. Kheterpal: If you do a second IRB, each site can look at the 80 patients you find and get their record number and look at the management. Is this something we should we complicate this proposal with? As a reviewer if I saw not just discharge ICD-9 of stroke, but discharge ICD-9 of stroke confirmed by manual record review it is more believable.

        - The small number is worth the extra detail, because it adds a level of rigor.
        - Mashour: We screened for neuroimaging, Ashes and colleagues used ICD-10 and confirmed with neuroimaging.
            - Dr. Laurel Moore and I did a study on the inpatient strokes and how the patients who went home and came back to the ED had better neuroimaging. The patients who were in house had a longer period of time before they were neuro-imaged and treated. The ED has a protocol to recognize the signs of a stroke. Exploring this across a number of institutions could have some interesting clinical implications in terms of policy and setting up stroke networks to recognize inpatient strokes.
        - Since this is regarding six types of veno-blockade plus your outcomes the number of events are going to be much less. Is there a point in which you can look at those levels and if the numbers of events are much less, stop and maybe after a year or so, start doing the whole thing again?
            - Mashour: That seems reasonable. I was thinking we would primarily be focusing on metoprolol, atenolol and bisoprolol. We have the data and they are more commonly prescribed. We are going to first see what that instances see if it's worth analyzing.
- Analysis issues: Without knowing the prevalence and the use of the different beta blockers, that creates some difficulty in creating the propensity score. Matching might tremendously reduce your data sets. You can try some other types such as inverse probability weighing. If there is a huge imbalance in the amount of different drugs being used both preop and intraop, once again, you might have great difficulty in estimating the parameters to find any effect size?
    - Dr. Mashour: Excellent point, we actually didn't have any problem with metoprolol and atenolol. In the Ash's studies they were able to do the three, but it's an important point.
    - Dr. Kheterpal: Based on the Scott and Michigan papers (which were both single centers) there were 2,500 patients per group after propensity score matching, which was an interesting coincidence. Based on the data from MPOG we should expect a 5 to 7 time increase. Our sample size should be around 12,000 – 15,000, given on what we've seen from the data diagnostics.
        - Suggestion: Put into the proposal, what is enough to take the next step in the analytic process? We will reach out to Dr. Pace on what type of analysis we should be using for this to determine how many events we need and how many beta blockers we want to assess and whether or not we can assess all betablockers. Need to determine whether we can assess bisoprolol at all in the US, because it is an underutilized drug.
            - Commentary: maybe that there may be large limitations on which agents. How to keep the power up while keeping our selection bias managed and find the balance.
            - Question: Can you do beyond 1 to 1 matching? Potentially do many to one matching or propensity score adjustment?
                - Stratification as opposed to matching analysis?
- Dr. Kheterpal: Is the concept of going into each EHR a reasonable expectation? Are people willing to go into their records? If we submit another IRB, people will go into their source system and verify the records.
    - Dr. Mashour: Would be nice in setting up the validity for future studies and when there are more centers we may not have to do this.

    - Will you have a check list?
        - The MPOG system will have a pick list of the secondary outcomes and each investigator will see the same check list.
- Dr. Kheterpal: Do you want to look at the other paper that you mentioned with Dr. Moore?
    - Dr. Mashour: I have spoken with Dr. Moore and we want to look at a multicenter approach. We are thinking about a prospective approach and may have translational potential.
    - Dr. Kheterpal: Maybe will make some progress on this and once we make progress on the sample size we will back a separate proposal regarding whether we want to collect the management data for a separate proposal using the same dataset.
    - Dr. Moore: Not familiar with the methodology. But, this is dirty data on when the stroke occurring and the management of the stroke.
- Dr. Kheterpal: What journal should we target?
    - Dr. Eisenach, this is general interest and you should try a more generalized journal.
    - Dr. Kheterpal: JAMA, BMJ, Lancet
    - Dr. Mashour: It may be good to speak with a cardiologist to see what drives the decision as to what beta blocker is chosen and how to control for the bias.
- Dr. Kheterpal: Do we do our risk adjustment and selection bias adjustment based on discharge ICD-9 data or preoperative H&P data or both? Historically I have done one or the other and it may be a bit too specific. Centers that have discharge ICD-9 data what are your thoughts? Is it okay to be that dirty?
    - Dr. Jameson, we have a problem because 80% of our population is a referral base. The only real data we have would be the ICD-9 or the discharge data because the hospital can bill. There is a small portion of our patients who come in with an extensive list. Epic does not filter the intake data very well so you will have a long list that is not helpful. I would advocate for discharge because it will be more accurate broadly across institutions.
    - Dr. Kheterpal: We were thinking of the discharge ICD-9 data plus the EHR H&P clinical data.
    - Dr. Pace: There are some data independence issues. You have multiple hospitalizations on one patient being allowed. In your propensity scoring you may have to include a random effect for the center.
- Dr. Kheterpal: We were going to include every hospitalization over a three year period. Should we include each procedure as an index procedure? That was the initial plan and clinically we thought that made sense. Multiple procedures within a given hospitalization were going to affect the index procedure within that hospitalization.
    - Dr. Paganelli: The fact that they needed more surgery they were sicker, but they were exposed more. They got away the first two times without a stroke.
    - Dr. Kheterpal: Do we have to address the first two cases that didn't involve a stroke, but the third one that did?
        - Those are interesting patients and involves a sub group analysis and is a separate paper.
    - Co-investigators feel that only one hospitalization should be taken per patient.
        - Dr. Jameson, we will not know if they have been hospitalized three other times. We could not give that data.
        - Conclusion: One case per patient through the study period.
- Other feedback?
    - Separate proposal for the management with Dr. Moore
    - Yes to go into EHR to validate

- Mixture of EHR plus ICD-9 data for risk adjustment is okay
- ICD-9 discharge data okay
- Beta blocker – using Anesthesia H&P to define that with good data across the thirteen centers. The compliance piece Dr. Mashour raises a question because I have seen variant levels of documentation on did they meet their 'skip card' ten measure or not and whether they got it in 24-hours. Therefore not going to include compliance information.
    - Overall medication data is good
    - Overall compliance data is variable
        - Dr. Jameson, Epic compliance data is good and will be pretty accurate.
        - OHSU: Medication data is not good and hard to tell and relying on medication from Epic may not be good.
        - Vanderbilt: We have good medication documentation. We capture beta blockers well.
        - Virginia: Medication data is in Epic. There is system wide problems with drugs
        - Vermont: We have Picis and Epic and preop manager the nurses are good about checking beta blocker use. The Epic at our place is very accurate. You are not getting our Epic data yet.

- Any comments?
    - How are you going to decide whether to only choose patients on beta blockers or have you decided?
        - Should we do an overall analysis on all patients or just betablocker patients?
            - First paper is overall patients with a sub group analysis of patients on beta blockers.
                - Dr. Pace: If you only analyzed the people on beta blockers how do you know the stroke rate on those who are not on beta blockers?
                - Dr. Kheterpal: Do we comment on the stroke incidence overall? Is it of value to this paper?
                - Dr. Bateman: I worry about not having enough comparators in the setting where are not measuring confounding beta blocks. Clearly patients who are not on any beta blockers are very different than those who are on beta blockers and a study design where you have a way to compare would create less issues.
                - Dr. Kheterpal: This is how it is designed now. The current plan is to include that control group of no beta blocker at all and then compare to other patients. Are we consistent with this plan?
            - Conclusion: Yes include all patients

Institution	Vote
Academic Medical Center (AMC), Amsterdam	**Accept with moderate revision**
Columbia	**Accept with moderate revision**
Oklahoma University Medical Center	**Accept with moderate revision**
Oregon Health Science University	**Accept with moderate revision**
University of Colorado	**Accept with moderate revision**
University of Florida	**Not available**
University of Michigan	**n/a**
University of Tennessee	**Accept with moderate revision**
University of Vermont	**Accept with moderate revision**
University of Utah	**Accept with moderate revision**
University of Virginia	**Accept with moderate revision**
Vanderbilt	**Accept with moderate revision**
Washington University, St. Louis	**Accept with moderate revision**

Final Decision: Accept with moderate revisions. Dr. Mashour makes a revision and then it will be sent out via e-mail.

Dr. Pace: I accept with moderate revisions, but it depends on what if found with the project and if it is something different it will need to be represented.

Dr. Kheterpal: We have several manuscripts that are being re-presented to the group.