Peer Review File

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Reviewer A

In this report authors describe the outcome of Hybrid ablation approach in the treatment of atrial fibrillation in patients with prior coronary artery bypass grafting surgery. This is a retrospective review of patients undergoing a planned Hybrid ablation approach with prior coronary bypass grafting surgery. Safety of Hybrid ablation was described in terms of 30-day STS complications. This is a technically very demanding patient subset and as such descriptive report may provide newsworthy results.

I have following remarks.

1) this is purely a descriptive feasibility type of report with no comparator group. Efficacy can not be analyzed using this setting. Safety signal can be assessed. This should stated in more detail. Thank you. We have adjusted the manuscript accordingly to reflect only the Rhythm success and safety of the procedure.

2) N is relatively low and this limits the generalizability of the results. This needs to discussed in the limitations section. Thank you. We have adjusted the limitations to include, "due to the small sample size of twenty-three patients in this report, these findings have limited generalizability. We are an experienced Hybrid ablation center and these findings may not be similar with less experienced surgeons or arrythmia centers."

3) There is no description of how patients were screened for the procedure, how they were followed up. Please add details. This is not a routine operation.
Thank you. We have included the following information.

"All adult patients (> 18 years of age) in our Atrial Fibrillation database between 2013 to 2018 who underwent the 1st Stage Epicardial VATS surgical ablation for isolated atrial fibrillation were reviewed for eligibility (n=455). Patients who then had a prior isolated coronary artery bypass grafting (CABG) were then specifically reviewed to be included in this study (n=23). Patients who completed both stages of the Hybrid approach (epicardial VATS and endocardial ablation) and at least 24 hours of continuous ambulatory rhythm monitoring were then reviewed for Rhythm success [Heart Rhythm Society (HRS) <30 seconds of Atrial fibrillation, Atrial Tachycardia, Atrial Flutter and off anti-arrhythmic medications (AAD) with 24-hours of continuous ambulatory monitoring] (n=17). Patients who failed to undergo the second stage of the intended combined hybrid approach were excluded from the Rhythm success category."

"Rhythm monitoring was performed by the Saint Helena Hospital Arrythmia Center team at regular intervals of 3-months and 12-months post-operatively and

annually thereafter and monitored by the atrial fibrillation nurse navigator (Co-Author: CP). Rhythm data were obtained from standard permanent pacemaker interrogations and transdermal Ziopatch monitors, which provide continuous 24-hr rhythm data for up to 14-days. Rhythm data were then reviewed by our research team and adjudicated as a "Rhythm success" if it met HRS criteria of less than 30 seconds of atrial fibrillation, atrial tachycardia or atrial flutter without the use of Class I or III antiarrhythmic medications."

Reviewer B

The authors provide a thoughtful evaluation of an emerging technique with a focus on preliminary safety and efficacy of the hybrid ablation approach.

1. Although the results demonstrate an impressive 76% success rate for the persistent AF population, the small sample size significantly limits extrapolation of this data. Furthermore, the cohort is not compared to a control with endocardial only ablation or even medical management. As such, I would recommend refraining from use of success rate as an endpoint and take it out of the conclusion from the abstract. I would also remove the word "efffective" from the conclusion and emphasize that this study is underpowered to determine efficacy in the discussion of the results. Thank you. A similar critique was raised by another reviewer and we have made corrections to the manuscript to refrain from applying efficacy or effectiveness of this procedure.

2. It is unclear why freedom from anticoagulation appears to be contingent on rhythm control at follow up in this cohort. Per HRS guidelines, anticoagulation is not based on perceived success of rhythm control, including after ablation, and without LAA management it is recommended that anticoagulation is continued indefinitely. In the presence of LAA management (Watchman device or Atriclip), anticoagulation can be discontinued even in the presence of ongoing atrial fibrillation. The authors should likely remove this endpoint entirely unless a very substantial explanation can be made for why there was a rhythm contingency in this particular population. Thank you. We wanted to be completely forthcoming regarding the use of OAC in this patient cohort. That being said we do defer to our referring electrophysiologist, cardiologist and primary care physicians to manage the use of OAC post-procedure.

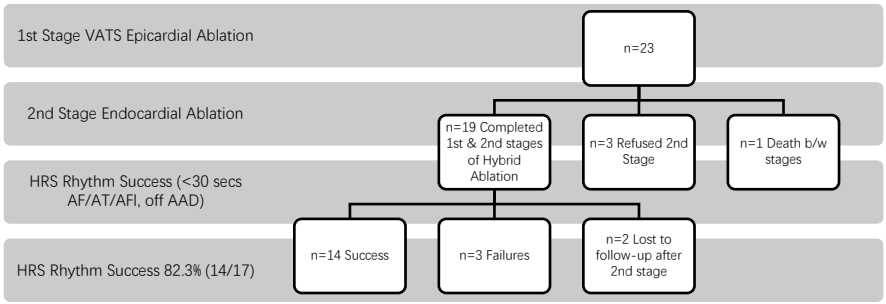
3. The authors review the single mortality in the study in detail, which is appreciated. Given the small sample size, however, a single death is still a very substantial outcome, and it cannot be determined if this was an outlier. The authors focus on the pulmonary toxicity and rightfully suggest that this population may be at substantial risk for a hybrid approach. Nonetheless, other factors may have contributed and are not reviewed. For example, it is possible that the longer surgical time and extensive manipulation needed for lysis of adhesions pre-disposed to respiratory failure and this result may have occurred despite the

pulmonary disease. There was also a significant bleed due to adhesions. Overall, the complication rate appears significantly higher from this small cohort compared to an endocardial only approach (10% of patient's had a major complication resulting in further surgical intervention or death) and there is no control group for comparison. While this is a very much needed study to explore the potential complications of such an approach in order to guide proper patient selection, I do not think that we can conclude from these results that this is a safe approach. I recommend concluding that we have identified specific features that increase the risk of this approach and potential techniques to mitigate those risks.
Thank you and we agree. We have made corrections to the manuscript to reflect these recommendations.

Reviewer C

I would like to congratulate the authors for the great job they demonstrate in this manuscript. No doubt, post-operative atrial fibrillation remains a major health issue with significant early- and long-term impact on our cardiac surgical patients. I have a few comments/suggestions for the authors and I would appreciate if they can provide some clarifications.

1- Please clarify the following:
Authors mentioned that out of 23 patients, only 19 patients made it to the 2nd stage of the hybrid procedures. However, in the follow-up section, authors report the results of 21 patients who were followed up (2 patients were missed to follow-up). I don't agree with adding the 2 patients who only underwent the 1st stage of the Hybrid procedure (and refused the 2nd stage) to the final list of patients included in the study. By definition, these 2 patients did not receive the 2 stages of the Hybrid procedure and therefore do not belong to the "post-Hybrid procedure" cohort. Follow-up data should be limited to the 19 patients who underwent both stages minus the 1 patient who was missed for follow-up (ie 18 patients only)
Thank you, an additional reviewer had similar concerns have we provided the following corrections to the manuscript.
We errantly reported a patient as "lost to follow-up after 2nd stage" after they have refused a 2nd stage. Therefore, on correction, there were 2 patients lost to follow-up after 2nd stage.
HRS Hybrid success as defined by completing both stages of the hybrid procedure (epicardial and endocardial) and < 30 secs of AF/AT/AFl without Class I and III AAD was 14/17 (82.3%) (corrected Figure 2).



2- What was the timeframe of the study? How long did it take to recruit 23 patients?
All adult patients (> 18 years of age) in our Atrial Fibrillation database between 2013 to 2018 who underwent the 1st Stage Epicardial VATS surgical ablation for isolated atrial fibrillation were reviewed for eligibility (n=455). Patients who then had a prior isolated coronary artery bypass grafting (CABG) were then specifically reviewed to be included in this study (n=23). Patients who completed both stages of the Hybrid approach (epicardial VATS and endocardial ablation) and at least 24 hours of continuous ambulatory rhythm monitoring were then reviewed for Rhythm success [Heart Rhythm Society (HRS) <30 seconds of Atrial fibrillation, Atrial Tachycardia, Atrial Flutter and off anti-arrhythmic medications (AAD) with 24-hours of continuous ambulatory monitoring] (n=17). Patients who failed to undergo the second stage of the intended combined hybrid approach were excluded from the Rhythm success category.

3- Please clarify the following:
In Figure 2, you mentioned 3 patients refused 2nd stage, however, in line no. 43 you mentioned 2 patients refused 2nd stage, which statement is correct?
Thank you, we have corrected the manuscript and figure as above.

4- Again, in Figure 2, you mention that out of 3 patients who refused the 2nd stage, 2 had successful rhythm control, I'm not sure these 2 patients should be considered as part of the "Hybrid" procedure as these patients did not undergo the 2 stages of the procedure.
Thank you, we have corrected the manuscript and figure as above.

5- In Table 1, you mention 4 patients had pre-op PPM, however, in line no. 167 you mention only 3 had pre-op PPM, please clarify.

6- Please advise on when was the oral anti-coagulation therapy stopped after the procedure.
OAC discontinuation was deferred to the referring physicians and we can not provide an exact time of discontinuation. However, that being said, typically OAC was discontinued after the 3-month rhythm assessment, if patients demonstrated HRS Rhythm success (<30 sec AF/AT/AFl off AAD).

7- in line no. 70, I suggest you replace "will" with "may" as it is not certain that these patients will require any further management of their AFib. Similarly, in line no. 182 I suggest you replace "will" with "may" for the same reason.
Thank you, we have made these corrections.

8- Did you check the complete exclusion of LAA on intra-operative trans-oesophageal echo? This would be interesting to add given the technical challenges that are encountered in positioning these devices in this group of patients.
Yes, great question. We did check intra-operative TEE's in each of these patients

and are happy to report that we had complete exclusion in these cases as defined by (<1 cm pouch, no device leak, no device related thrombus). We have included this in the manuscript.

9- The first paragraph of the discussion is a mere repetition of results section (lines no. 184-188), please address.
Thank you. We have made adjustments to this section of the manuscript.

10- Line no. 271, you mention “effective early rhythm control strategy” in your conclusion, I’m not sure this was proven by your study, moreover, how “early” is early? Days, weeks, months? Please advise or remove from the sentence.
Thank you, other reviewers noted the same concern and we have adjusted the manuscript accordingly.

11- Please check the citations of references no. 4 and 5