

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Morbidity and Mortality Outcomes of Patients requiring Isolated Tricuspid Valve Surgery: a Retrospective Cohort Study of 537 patients in New South Wales between 2002 and 2018
<b>AUTHORS</b>	Harvey, Gregory; Chow, Vincent; Rubenis, Imants; Brieger, David; Kritharides, Leonard; Ng, Austin Chin Chwan

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Tokarek, Tomasz University Hospital in Krakow
<b>REVIEW RETURNED</b>	01-Nov-2023

<b>GENERAL COMMENTS</b>	This manuscript is well written and designed properly. However relatively low sample size and data from single centre might be serious limitation. Few questions: - how many operators performed surgery? Have authors evaluated impact of operator experience on outcome? - have authors calculated preprocedural risk? STS PROM or EuroSCORE II?
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<b>REVIEWER</b>	Sala, Alessandra IRCCS Policlinico San Donato
<b>REVIEW RETURNED</b>	15-Nov-2023

<b>GENERAL COMMENTS</b>	<p>The authors have made an extensive retrospective cohort study on patients undergoing isolated tricuspid valve surgery. A total of 537 patients have been identified, undergoing either TV repair with annuloplasty (272 patients), replacement (245 patients), valvotomy ( 5 patients) and repair other than annuloplasty (85). Results underlined a 7.4% in-hospital mortality and 40% mortality at follow-up (4 years). Predictors of mortality were history of congestive heart failure and chronic pulmonary disease. The most common complications at follow-up were congestive heart failure and new onset atrial fibrillation.</p> <p>The manuscript is overall well written and the treated topic is extremely up-to-date and considered a hot topic. Nevertheless, in my opinion, some aspects should be addressed:</p> <p>- among the baseline patient characteristics, "reintervention" was not considered. It is an extremely relevant aspect in patients undergoing isolated TV surgery, because it is well known that patients are generally medically treated for a very long time by the cardiological community before being addressed to the cardiac surgeon for treatment. this is even more true in patients that are REDOs. Therefore, this parameter should be inserted and should be evaluated. There are other published papers in the literature</p>
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	<p>that have identified reintervention as a risk factor for outcome in this population.</p> <ul style="list-style-type: none"> <li>- It would be interesting to assess outcomes according to procedure performed on the patient, therefore either repair or replacement. Matter of factly, reports in the literature have shown that patients in earlier stages more frequently undergo tricuspid valve repair and tend to have a better postoperative and long-term outcome. On the contrary, patients undergoing replacement, tend to undergo surgery in later stages of the disease, with more frequently right ventricular dilation and tend to have worse outcomes. Therefore, in this study with these numbers, it would have been interesting to assess this aspect, as it does play a major role in "Morbidity and Mortality" following isolated TV surgery.</li> <li>- the rate of patients undergoing surgery for rheumatic disease was rather high (66.5%). nevertheless, surgical repair was still feasible. It is very interesting, and this should also be underlined and explained further within the text. Also, the degree of tricuspid insufficiency (or stenosis) is not stated anywhere in the text. It is of paramount importance, especially to assess surgical indication and also outcomes.</li> <li>- Another aspect that has been strongly assessed and stressed in the literature is medical treatment in these patients. It would be interesting, since patients had CHF before surgery and a great percentage have developed CHF episodes following surgery, to know the details of their medical therapy (therefore optimal medical therapy) both prior to surgery and also following surgery, in order to correctly assess the CHF episodes, especially at follow-up.</li> <li>- Finally, the stage of disease at which patients present is extremely important in this population. Some organ involvement should be underlined: kidney (kidney function), liver (liver function tests), ascites, peripheral edema. They have not be analysed or assessed in the paper, and these are basic aspects that cannot be lacking in a paper dealing with isolated TV surgery.</li> </ul> <p>In my opinion, all these aspects should be addressed and corrected in order to increase the validity of the manuscript.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

1. This manuscript is well written and designed properly. However relatively low sample size and data from single centre might be serious limitation.

Response: We agree with the reviewer that our study does not possess a very large sample size in absolute terms, especially when compared with similar studies of isolated left-sided valvular surgery. However, given the relative rarity of isolated open TVSt, this is a relatively large study. This is the largest study to date examining medium-long term morbidity outcomes after isolated TVSt. Furthermore, there are only two larger studies which examine in-hospital mortality (1, 2). Additionally, we politely draw the reviewer's attention to the point that this is a multi-centre study, including all isolated open-TVSt in every cardiothoracic hospital in the state of New South Wales (more than 10 centres) (3).

2. How many operators performed surgery? Have authors evaluated impact of operator experience on outcome?

Response: We agree with the reviewer that operator experience has been shown in other studies to have a significant impact on outcomes after valvular surgery, and its inclusion would enhance this manuscript, and would be an important parameter to assess (4, 5). Unfortunately, our anonymised dataset does not allow for the analysis of the impact of operator experience on outcome in this study. While New South Wales had 50 active cardiothoracic surgeons in 2019 at more than 10 centres, we do not know which operations were performed by which operators, how many operators were involved with isolated TVSx, or individual operator's levels of experience (3). This limitation will be addressed in the Discussion section of the revised manuscript.

### 3. Have authors calculated preprocedural risk? STS PROM or EuroSCORE II?

Response: While important, unfortunately our administrative dataset does not contain STS PROM or EuroSCORE II pre-procedural risk scores or the granular data required to calculate these. However, our dataset does include a value for the Charlson Comorbidity Index (CCI) for each patient, a composite measure of comorbidity. Each additional point on the CCI was associated with a 25% increased relative risk of all-cause mortality at end-of-study follow up in our univariable analysis (Supplementary Table 2). Median CCI was 1 (IQR 0-2). However, the absence of STS PROM or EuroSCORE II risk scores will be addressed in the Discussion section of the revised manuscript.

#### Reviewer 2:

1. The authors have made an extensive retrospective cohort study on patients undergoing isolated tricuspid valve surgery. A total of 537 patients have been identified, undergoing either TV repair with annuloplasty (272 patients), replacement (245 patients), valvotomy ( 5 patients) and repair other than annuloplasty (85).

Results underlined a 7.4% in-hospital mortality and 40% mortality at follow-up (4 years). Predictors of mortality were history of congestive heart failure and chronic pulmonary disease. The most common complications at follow-up were congestive heart failure and new onset atrial fibrillation.

The manuscript is overall well written and the treated topic is extremely up-to-date and considered a hot topic. Nevertheless, in my opinion, some aspects should be addressed:

- among the baseline patient characteristics, "reintervention" was not considered. It is an extremely relevant aspect in patients undergoing isolated TV surgery, because it is well known that patients are generally medically treated for a very long time by the cardiological community before being addressed to the cardiac surgeon for treatment. this is even more true in patients that are REDOs. Therefore, this parameter should be inserted and should be evaluated. There are other published papers in the literature that have identified reintervention as a risk factor for outcome in this population.

Response: We agree with the reviewer that re-intervention is an important parameter to consider in patients undergoing isolated TVSx. Unfortunately, our data on re-intervention are limited in some respects. We do know that 59 (11.0%) of our patients had at least one prior prosthetic valve (Table 1), although our dataset does not specify which valve was operated on. Interestingly, prior prosthetic valve surgery was not associated with mortality in univariate analysis (Supplementary Table 2). Furthermore, we know that 19 patients had redo isolated TVSx after their index isolated TVSx within our study period. We could examine rates of prior valvular surgery, however our data only goes back to January 2001 (1 year prior to our study period beginning), and so our lookback period with regard to prior TVSx (and other valve surgery) is limited in this respect and would be affected by time-bias. The absence of comprehensive data regarding redo surgery will be highlighted as a limitation in the revised manuscript.

2. It would be interesting to assess outcomes according to procedure performed on the patient, therefore either repair or replacement. Matter of factly, reports in the literature have shown that

patients in earlier stages more frequently undergo tricuspid valve repair and tend to have a better postoperative and long-term outcome. On the contrary, patients undergoing replacement, tend to undergo surgery in later stages of the disease, with more frequently right ventricular dilation and tend to have worse outcomes. Therefore, in this study with these numbers, it would have been interesting to assess this aspect, as it does play a major role in "Morbidity and Mortality" following isolated TV surgery.

Response: We agree with the reviewer that analysis by type of isolated TV<sub>Sx</sub> surgery is an important parameter. Our analysis reflected the reviewer's observations that those with repair have better outcomes generally speaking than those who undergo TV<sub>Sx</sub> replacement, however that this may be confounded by disease severity among other factors. While our univariable analysis showed a significantly higher long-term mortality after replacement when compared with non-annuloplasty repair (Supplemental Table 2), type of TV<sub>Sx</sub> surgery was not a significant predictor of mortality in our multivariable analysis (Supplemental Table 3). These findings will be included in the Results and Discussion sections of the revised manuscript.

3. The rate of patients undergoing surgery for rheumatic disease was rather high (66.5%). nevertheless, surgical repair was still feasible. It is very interesting, and this should also be underlined and explained further within the text. Also, the degree of tricuspid insufficiency (or stenosis) is not stated anywhere in the text. It is of paramount importance, especially to assess surgical indication and also outcomes.

Response: We agree with the reviewers that the high rate of patients undergoing surgery for rheumatic disease was high. This will be discussed in the Results and Discussion sections of the revised manuscript. We will also refer to previous publications indicating the feasibility of both repair and replacement for rheumatic tricuspid valve disease (6, 7). Unfortunately, due to the administrative nature of our dataset, we do not have data regarding the severity of tricuspid insufficiency or stenosis. This will be acknowledged in in the Discussion section of our revised manuscript.

4. Another aspect that has been strongly assessed and stressed in the literature is medical treatment in these patients. It would be interesting, since patients had CHF before surgery and a great percentage have developed CHF episodes following surgery, to know the details of their medical therapy (therefore optimal medical therapy) both prior to surgery and also following surgery, in order to correctly assess the CHF episodes, especially at follow-up.

Response: We agree with the reviewer that details regarding medical therapy (and adherence) would enhance the validity of the manuscript, however unfortunately these granular data are not available owing to the administrative nature of the data set. This limitation will be addressed in the Discussion section of the revised manuscript.

5. Finally, the stage of disease at which patients present is extremely important in this population. Some organ involvement should be underlined: kidney (kidney function), liver (liver function tests), ascites, peripheral edema. They have not be analysed or assessed in the paper, and these are basic aspects that cannot be lacking in a paper dealing with isolated TV surgery. In my opinion, all these aspects should be addressed and corrected in order to increase the validity of the manuscript.

Response: We agree with the reviewers that the stage of disease, and presence/severity of organ involvement is important in this population. Unfortunately, our administrative dataset does not contain anthropometric data such as clinical findings of congestion or biochemistry (such as creatinine, or liver function tests). However, we do have data on the proportion of patients with moderate to severe kidney disease (Creatinine >270umol/L), and moderate-severe liver disease (cirrhosis with portal

hypertension). We summarised the presence of organ involvement using the Charlson Comorbidity Index (summarised in the caption to Table 1), which we will also describe in the Methods section in the revised manuscript. On the whole, our population was relatively comorbidity free with a median Charlson Comorbidity Index (CCI) of 1 (IQR 0-2). With a median age of 63.5 (IQR 43.9 – 73.8), the main contributor to CCI was age as patients gain one point on the CCI for each decade after the age of 40. The presence of congestive cardiac failure (37.2%) was the next most common contributor, giving another point. We agree that precise biochemical and anthropometric data would have added validity to this manuscript, and we this will be acknowledged in the Discussion section of the revised manuscript.

## References

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## VERSION 2 – REVIEW

<b>REVIEWER</b>	Sala, Alessandra IRCCS Policlinico San Donato
<b>REVIEW RETURNED</b>	16-Mar-2024

<b>GENERAL COMMENTS</b>	Dear authors, thank you very much for revising the manuscript and for answering all my concerns. The manuscript is well written and the topic is extremely interesting, especially for the great number of patients analysed. However, unfortunately, in my opinion, there are too many missing information in order to be able of drawing any conclusion form this study. You cannot, in my opinion, state as a conclusion that isolated tricuspid valve surgery carries a significant risk of morbidity and mortality, because you are not even capable of defining "the baseline tricuspid pathology (TR or TS), the degree of TR or TS, the stage of disease of patients, common and basic baseline information and parameters of patients". Therefore, unfortunately, your conclusions are based on limited data.
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