

**Peer review file**

**Article information:** <http://dx.doi.org/10.21037/jtd-20-3032>

**Reviewer A**

**Comment:** One comment regards the missing descriptive statistical explanation in the methods. In general, well written and clear results.

**Reply:** You are correct. I added the statistical explanation. See page 9, lines 217-220

**Reviewer B**

Background

**Comment 1:** In my experience and centers' experience, mini-thoracotomy is often more painful than sternotomy for some patients. Line 77 suggests "better pain control".

**Reply 1:**

In our center experience, mini- thoracotomy is often less painful than sternotomy. Therefore, we prefer this approach not only in younger patients but also in in patients with osteoporosis or diabetes, in which the thinned out sternum may take a long time to heal and be associated with a significant amount of pain. Our data agree with the experience of other authors and centers. I added reference n. 2 in the text

1. Goyal A, Chhabra L, Parekh A, Bhyan P, Khalid N. Minimally Invasive Aortic Valve Surgery. 2020 Oct 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. PMID: 29261951.
2. Kara KA, Caner T. Comparison of pain in the early post-operative period using VAS score in patients after cardiac surgery who had minimally invasive incisions vs. full median sternotomy. *Ann Ital Chir.* 2019;90:3-9. PMID: 30394365
3. Diegeler A, Walther T, Metz S, Falk V, Krakor R, Autschbach R, Mohr FW. Comparison of MIDCAP versus conventional CABG surgery regarding pain and quality of life. *Heart Surg Forum.* 1999;2(4):290-5; discussion 295-6. PMID: 11276489.
4. Hu CX, Tan J, Chen S, Ding H, Xu ZW. Comparison of clinical outcomes and postoperative recovery between two open heart surgeries: minimally invasive right subaxillary vertical thoracomy and traditional median sternotomy. *Asian Pac J Trop Med.* 2014 Aug;7(8):625-629. doi: 10.1016/S1995-7645(14)60105-X. PMID:25149376

Methods

**Comment 2:** How were 48 patients selected for analysis? Are they consecutive?

**Reply 2:** In our center, we usually performed mitral valve surgery through a right antero- lateral minithoracotomy except in presence of contraindications (exclusion criteria). We consecutively enrolled 48 patients underwent mitral valve repair through mini-thoracotomy in our Cardiac Surgery Unit, between January 2015 and July 2018. As per your advice, I specified in the text (see pag. 3 lines 55-56 and pag.5 line 112-113)

**Comment 3:** How were the patients selected for the actual surgery for minithoracotomy versus sternotomy? This is a major limit of retrospective design that is not acknowledged as a limitation and means there may be biases in the results.

**Reply 3:** As I mentioned before, in our center we usually performed mitral valve repair through a right antero- lateral minithoracotomy except in presence of contraindications (exclusion criteria). We consecutively enrolled 48 patients underwent mitral valve repair through mini-thoracotomy in our Cardiac Surgery Unit, between January 2015 and July 2018. I specified the exclusion criteria in the text (see page 5-6 lines 126-132).

**Comment 4:** I presume, as indicated above, that patients with strokes or neurologic damage, aortic atherosclerosis, re-do surgeries, and certain indications (endocarditis) may have been excluded. Clearly state the exclusions in terms of aortic size (all that is stated is sinus > 35 mm but presumably the ascending aortic dimension was evaluated). What constitutes "severe vessels pathology" and "right chest disease"? Presumably patients were excluded for an aorta that was not "regular and circular" line 184.

**Reply 4:** We considered as exclusion criteria: sino-tubular junction > 35 mm; aortic regurgitation > 2+; aorta tortuosity; strokes or neurologic damage; aortic atherosclerosis; severe vessels pathology; right chest diseases; endocarditis. (see page 5-6 lines 126-132).

Re-do cardiac surgery was not considered as exclusion criteria. (see page 5 lines 114)

We defined "right chest diseases" previous thoracic surgery or other potential causes of significant pleural adhesions in the right hemithorax. In this situation, the increased risks of significant intra-operative hemorrhage and/or bronchopleural fistulas may outweigh the benefits of minimally invasive surgery, and the patient and surgical team should discuss (and be prepared for) the possibility of a conversion into an open sternotomy (see page 6 lines 130-132)

We defined "severe vessels pathology" severe calcification and stenosis of femoral artery and severe aortic atherosclerosis (grade 2 to 5 of Katz and colleagues classification). (see pag.5 lines 128-130)

Katz ES, Tunick PA, Rusinek H, Ribakove G, Spencer FC, Kronzon I. Protruding aortic atheromas predict stroke in elderly patients undergoing cardiopulmonary bypass: experience with intraoperative transesophageal echocardiography. *J Am Coll Cardiol.* 1992 Jul;20(1):70-7. doi: 10.1016/0735-1097(92)90139-e. PMID:1607541. (see reference 13)

**Comment 5:** How methodologically does a retrospective study use a standard protocol? Line 104.

**Reply 5:** You are right. Our retrospective analysis allowed us to explain an effective, safe and reproducible method using an intra-aortic occlusion device. In order to propose a standard protocol it needs to be performed a multicenter randomized study. I corrected the text (see page 3 lines 52-54; pag.3 lines 69-72; pag.5 lines 102-106; pag.13 lines 321-324)

**Comment 6:** How can a retrospective study guarantee the same anesthesiologist performed every procedure line 145 or same surgeon line 172?

**Reply 6:** In our cardiac surgery unit, there is a "Dedicated Team" to minimally invasive valve surgery. This team consists of: one Consultant Cardiac Surgeon who has performed all mitral and tricuspid valve surgery through a right mini-thoracotomy using the intra-aortic occlusion device; two Cardiac Surgery Registrars who have collaborated in the surgical procedure; anesthesiologists dedicated to monitoring the patients; one Consultant Cardio Anesthetist dedicated to perform TEE during minimally invasive surgery; perfusionists and nurses.

**Comment 7:** Please take time to explain why right coronary flow is in jeopardy. Explain why patency of the right coronary sinus is key line 177. Acknowledge that visualization of the RCA is difficult on TEE and needs a superior or upper window.

**Reply 7:** In a certain number of patients the right coronary artery shows an upper origin. Moreover, as you mentioned in your comment, the visualization of the right coronary artery on TEE could be challenging. For those reasons, we consider mandatory to search for and identify the origin of both coronary arteries in order to prevent insufficient delivery of cardioplegia and consequent myocardial ischemia. Upper oesophagus, Midesophageal windows and x-plane technique should be considered in this case. I added the explanation in the discussion (see pag. 12, lines 299-308).

**Comment 8:** Type 1 neurological damage is never defined nor referenced and I have never heard this term.

**Reply 8:** We identified neurological damage in Type I (focal injury, or stupor or coma at discharge) and Type II (deterioration in intellectual function, memory deficit, or seizures) according to Roach GW et al.'s definitions. I added the definition in the text (see pag. 9, lines 212-215) and the relative reference (see reference 14).

Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R, Aggarwal A, Marschall K, Graham SH, Ley C. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. *N Engl J Med.* 1996 Dec 19;335(25):1857-63. doi: 10.1056/NEJM199612193352501.

**Comment 9:** How does TEE help guide femoral vein cannulation line 155?

**Reply 9:** TEE guidance of the procedure allows us to confirm the presence of the guide wire (Seldinger technique) in the right atrium and afterwards to assess the correct position of the two stage venous cannula passing through the right atrium and its insertion in the superior vena cava. Midesophageal bicaval view, transgastric long axis view and X-plane techniques are strongly recommended for this purpose (see Figure1 and Video 1 and 2).

**Comment 10:** Line 162 "over the nipple" is unclear - is it superior to or directly through the nipple?

**Reply 10:** It is directly through the nipple. I changed the text as per your advice (see page 7 line 170)

**Comment 11:** Monitoring: justify why you measured cardiac enzymes (presumably RCA related). What enzymes did you measure? Why did you not also monitor ECG? When did TTE occur postoperatively?

**Reply 11:** In our clinical practice, we always measure cardiac enzyme after the operation to assess the ischemic myocardial damage potentially related to the cardiopulmonary bypass and to an ineffective myocardial protection. In particular, during the minimally invasive surgery performed with an intraortic occlusion device the risk of coronary artery ostia occlusion is increased (presumably RCA related).

Routinely we measure myoglobin, creatine kinase MB, hs Troponine at the laboratory tests. Finally, in all cases we performed a 12 leads ECG and a TTE 24 hours after surgery. The ECG and the TTE is repeated in every patient when he is discharged from the ICU and in 4<sup>o</sup> and 6<sup>o</sup> POD. (see pag. 9, lines 205-215).

**Comment 12:** There is no monitoring for postoperative neurologic complications or dissection; there is not one word on this in the methods. I have no idea how the paper can state that there were no complications when there was no monitoring.

**Reply 12:** all patients were evaluated for clinical follow up one month after surgery in our out-patient clinic. At this time, the neurological clinical evaluation and a transthoracic echocardiography showed no signs of neurologic dysfunction or aortic dissection in all cases.

**Comment 13:** Additionally, again this was a retrospective paper so unless there was a protocol I don't think the paper can comment on these complications.

**Reply 13:** You are right. Our retrospective analysis allowed us to explain an effective, safe and reproducible method using an intra-aortic occlusion device. In order to propose a standard protocol it needs to performed a multicenter randomize study. We do not want comment the complications but only report our experience.

**Comment 14:** Overall the paper is very lengthy. There is way too much detail in the pages 5-7 about TEE, monitoring, and surgical technique. Much of this is standard, and the verbiage detracts from focus on the balloon. -Yet there is no discussion of key parameters like aortic or neurologic monitoring.

**Reply 14:** As per your advice we added more details about the aortic monitoring.

During the perioperative TEE in all patients we collected the following aortic key parameter: annulus, aortic root, sinutubular junction and ascending aorta were measured inner edge to leading edge in midesophageal long axis view. The diameter and quality of the thoracic aorta was studied through a midesophageal long axis and short axis vie (see pag. 6, lines 156-159)

In order to avoid aortic deadly complications (embolism, dissection or rupture) we excluded patients with grade 2 to 5 according to the Katz and colleagues classification of aortic atherosclerosis. (see pag. 6, lines 128-130)

Katz ES, Tunick PA, Rusinek H, Ribakove G, Spencer FC, Kronzon I. Protruding aortic atheromas predict stroke in elderly patients undergoing cardiopulmonary bypass: experience with intraoperative transesophageal echocardiography. *J Am Coll Cardiol.* 1992 Jul;20(1):70-7. doi: 10.1016/0735-1097(92)90139-e. PMID:1607541. (reference 13)

The intraoperative neurological monitoring was performed using the near infrared spectroscopy (INVOS™ Cerebral/Somatic Oximeter, Somanetics Corp., Troy, MI 48083, USA) and Bispectral Index (BIS VISTA™ monitoring System, Aspect Medical Systems, Inc., Newton, MA 02464, USA). In the post operative period and at follow-up it was performed by clinical examination. (see pag. 6, lines146-148; pag. 9, lines 212-215)

**Comment 15:** Not until Table 1 do we learn there were concurrent TV repairs. Despite all the detail in the protocol there is no mention of concurrent valve surgery, or eg the surgical approach to these (eg exquisite detail about the approach to the LA, nothing of the RA/TV, nor why these patients were included).

**Reply 15:** In cases of concurrent surgery, the tricuspid valve was exposed through a conventional oblique right atriotomy. As per your advice I added this surgical details (see pag.7, lines 176-177). In 7 patients (14%) concurrent tricuspid valve repair has been performed. In particular, three of them had severe secondary tricuspid regurgitation and four of them had moderate secondary tricuspid regurgitation with dilated annulus ( $\geq 40$  mm or  $> 21$  mm/m<sup>2</sup> by 2D echocardiography). As per you advice I added this surgical indications in the text (see page 9-10, lines 228-231)

## Results/Discussion

**Comment 16:** What are risk factors for migration in the cases discussed?

**Reply 16:** During the procedure, the distal migration of intra-aortic occlusion device could be related to a systemic hypotension, increase antegrade cardioplegia flow, catheter retraction (see Figure 6-7 and Video 5). The proximal migration could do to increase perfusion pressure and

increase root vent suction (see Figure 8 and Video 6).

**Comment 17:** How can migration be mitigated?

**Reply 17:** The distal migration can be mitigated giving vasopressor drugs such as norepinephrine or increasing the systemic perfusion pressure rising up the pump flow.

**Comment 18:** line 211: you did not do "cross clamp"

**Reply 18:** You are right. As per your advice I corrected the text (page 10 line 220) and the Table 1

**Comment 19:** There are no control values to contextualize the operation, CPB, and aortic occlusion times.

**Reply 19:** You are right. There are no control values to contextualize the operation, CPB, and aortic occlusion times because this is not a case-control study but is a retrospective study through which we analyse our center experience in minimally invasive mitral valve surgery using intra-aortic occlusion device and we showed our monitoring and imaging method.

**Comment 20:** Line 214 does not refer to Figure 1

**Reply 20:** You are right. This was a mistake.

**Comment 21:** Hospital postoperative stay of 7 days for mini-thoracotomy seems quite long. Explain.

**Reply 21:** You are right. In most cases, the hospital postoperative stay was 4-5 days. Unfortunately, one patient developed a dehiscence of the inguinal wound site (femoral cannulation) and this caused an increasing of the median hospital postoperative stay.

**Comment 22:** As above, line 216 and 248, this analysis has no basis to state the incidence of aortic dissection and neurologic damage was zero.

**Reply 22:** You are right. I delete the word incidence in the text (see pag. 3 line 64 and pag. 10 line 237).

**Comment 23:** Were any vasodilators used in this series? This is not mentioned. eg line 257. Did any patients have femoral pressure exceed 200 mmHg? also not mentioned.

**Reply 23:** No, we did not use any vasodilators in this series because any patients have femoral pressure exceed 200 mmHg. As per your advice I modified the discussion

**Comment 24:** How can a study with n=48 patients have a 99% freedom from reoperation rate at 2 years? If one patient required reoperation the rate would be 98%.

**Reply 24:** You are right. It was a mistake. The freedom from reoperation rate was 98% because only one patient required reoperation.

**Comment 25:** The discussion starts with talking about comparison of aortic balloon and clamp, yet this paper did NOT do any comparison.

**Reply 25:** You are right. I modified the text as per your advice. (see page 10-13, lines 242-318)

This is a major flaw.

**Comment 26:** The conclusion is wholly inaccurate - nothing about this paper allows one to conclude that adverse events and complications were reduced in the absence of a control data set.

**Reply 26:** Our study is not a case-control analysis but its aim was to report our center experience through a case series. As per your advice I changed the conclusion. (see page 13, lines 321-324).

**Comment 27:** Limitations: this section by authors is incomplete. Please refer to this review to augment the limitations section.

**Reply 27:** You are right. I have augmented the limitations of the study (see page 13, lines 315-318)

**Comment 28:** I would reframe this paper as a single center experience with imaging for the aortic occlusion device, and as a hypothesis generating paper.

**Reply 28:** You are right. As per your advice and I changed the title (see pag. 1, lines 3-4)

## Figures

**Comment 29:** Figure 1 is irrelevant and not necessary to this paper.

**Reply 29:** We think you are right and I attached one image and two videos that describe the TEE guided procedure of venous cannulation with a two stage cannula. (Figure 1 and Video 1 and 2)

**Comment 30:** Figure 2: annotate the RCA origin on both panels; Figure 2B is likely an upper esophageal view to find the RCA origin and state this.

**Reply 30:** I modified the Figure as per your request. Figures 2a and 2b now have the RCA origin annotation.

**Comment 31:** Figure 3: the balloon is not well visualized in long axis, which I infer was part of the point of the figure, however why not image the ascending aorta more superiorly? (see the Hahn guidelines which authors cited). What about 3D imaging? Annotate 3B - novice readers will have no idea where the balloon is.

**Reply 31:** We choose an x-plane view of the ascending aorta to underline the importance of this technique and how it helpful is in this case: the wire is not always clearly visualizable in a long axis view but we can confirm the presence of the wire clearly detected in a short axis xplane view. The video attached images the ascending aorta more superiorly (video 3).

**Comment 32:** -Figure 4: There is no legend for panels C and D. Please annotate A and B with balloon and lumen. Panel A does not appear to be complete occlusion; please clearly differentiate from B - noting these appear to be orthogonal planes.

**Reply 32:** In figure 3 we annotate L for lumen and B for balloon. We also added the video 3 to clarify the concept of incomplete occlusion.

**Comment 33:** Figure 5: does this really add anything to show bilateral arterial lines? Picture quality is limited, or crop the left side.

**Reply 33:** We have improved the image by cropping its left side.

**Comment 34:** Figure 6: annotate A to show a reader how displacement is measured. B does not explain to me the increased cardioplegia flow. C can you show the transition in the RRA tracing rather than the flat line?

**Reply 34:** We substitute figure 6 with video 5 that illustrates the distal displacement of the balloon.

**Comment 35:** -Figure 7: A label and annotate the balloon versus landmarks.

**Reply 35:** We substitute figure 7 with video 6.

**Comment 36:** -Table: also refers to cross-clamp erroneously.

**Reply 36:** You are right I modified the table as per your request.

English language and grammar needs attention in a resubmission:

**Comment 37:** line 60 monitoring has been "detected"

**Reply 37:** As per your advice, I corrected the text (see pag. 3, line 62).

**Comment 38:** line 63 "us"

**Reply 38:** As per your advice, I changed the text.

**Comment 39:** line 81 "open discussions"

**Reply 39:** As per your advice, I corrected the text (see pag. 4, line 82).

**Comment 40:** line 90 "under the innominate" - proximal is likely more accurate and descriptive

**Reply 40:** As per your advice, I corrected the text (see pag. 4, line 91).

**Comment 41:** line 133 "in" should be "Inc."

**Reply 41:** As per your advice, I corrected the text (see pag. 6, line 138).

**Comment 42:** line 150 "in order to grading"

**Reply 42:** As per your advice, I corrected the text (see pag. 7, line 155).

**Comment 43:** line 169 what is "custodiol"

**Reply 43:** "Custodiol" is the name of the cardioplegia that we used. It is an intracellular crystalloid cardioplegia solution used in minimally invasive surgery or complex surgery.

**Comment 44:** line 189 "right drop of cerebral oxymetry". Oxymetry is misspelled

**Reply 44:** As per your advice, I corrected the text but in the new version of the paper the description of balloon migration is in the discussion (see pag. 10-13, lines 242-318).