Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-1837

Reviewer A

I congratulate the authors for this interesting retrospective observational study investigating different treatment strategies for acute type A intramural hematoma. The authors investigated the clinical outcomes of patients with acute Type A intramural hematoma or thrombosed false lumen treated with upfront surgery or watchful waiting during a time period of more than 10 years (2012-2023). Ninety three patients with Type A intramural hematoma were retrospectively reviewed. Thirty six (38.7%) patients underwent upfront surgery and 57 (61.3%) patients were offered watchful waiting with medical surveillance. Of these 57 patients, 32 were treated conservatively with medical therapy alone during the whole course including the follow up period. A satisfactory overall mortality rate (4.3%) could be achieved in the whole cohort over a median follow up of 40.5 months. Long-term survival did not differ significantly between the three groups over a time period of 5 years. On this basis, the authors concluded that watchful waiting with stringent surveillance may be justified in selected patients with Type A intramural hematoma, enabling room for individualized management of Type A intramural hematoma and potentially avoiding upfront surgery in selected cases.

These results are of great interest for the community to pave the way for an individualized approach for patients with acute type A intramural hematoma. Lately, a tailored approach as regards the timing of surgery for acute type A intramural hematoma that considers patient-, disease- and service-related factors has been gaining more interest.
After addressing the following points, I would appreciate a publication in this journal.
- The authors do describe their diagnostic and treatment approach for the patient cohort in the methods section. I would invite the authors to create a flowchart, depicting the process for treatment selection including all relevant factors which influence this decision process. This would aid understanding the clinical decision making stated by the authors for the readers.
REPLY: Thank you for your comments. We have our own set of criteria for management of Type A IMH. However, this is by no means the gold standard and patients with type A IMH in our center are still individually reviewed for the best treatment strategy. All type A IMH are reviewed by a senior aortic surgeon to decide on watchful waiting vs. upfront surgery. We follow a cut-off of 1 cm for IMH in the ascending, but this cutoff was not validated in our study and hence should not be considered as a practice recommendation. We tend to adopt watchful waiting for stable patents with uncomplicated thin IMH and non-aneurysmal ascending aortas
Changes: Figure 2 has been modified.

- Table 1: provide data for the variable "Smoker", otherwise remove it.
Reply : The variable “ Smoker” has been removed .
Changes: Changes were made to Table 1

- Figure 2: provide explanations of abbreviations
Reply: Figure 2 is completely changed.
Changes: Figure 2 has been modified.

- There is no clear referral to figure 6a in the text. Please refer to this figure, including a clear description of the findings.
Reply: Thank you for your comments. Changes have been made.
Changes: Changes have been made within the edited text and in figure legends. Line 273 page 11 and lines 409 -410 page 17

Reviewer B

The authors describe an important subject in managing patients with IMH due to acute aortic dissections Stanford A. The authors describe three patient populations presented to their medical centre in their manuscript. The first group is treated surgically within 24 hours after presentation due to clinical symptoms or hemodynamic instability. All other patients are being treated conservatively. A third group develops, however, patients initially treated conservatively and subsequently with surgery due to different causes. Although the idea of conservative treatment in patients with IMH AADA is interesting and may, in my opinion, be viable, the authors should present their data differently. Interesting would be the comparison between the patients treated surgically within 24 hours and the patients not operated at all. I agree that there is a population with IMH due to AADA that will benefit from conservative treatment, sadly this can be concluded from the data presented here.

Reply: Thank you for your comments. Patients in the watchful waiting group had uncomplicated type A IMH and had smaller mean aortic diameters. Those in the pure conservative group were the ones who did not develop any clinical or radiological indication for aortic intervention. In general, they had thinner ascending IMH and non-aneurysmal ascending aortas. This study was not designed for comparison between operative and conservative treatment; hence the data cannot be used as support for either treatment. This study was purely designed to demonstrate feasibility and safety of an individualized treatment in patients with ascending aortic IMH. To answer the question to compare between different interventions in type A IMH, a prospective comparative trial or a meta-analysis maybe required.
Changes: None

Reviewer C

Thank you very much for offering the opportunity to review your article. How to manage type A IMH or aortic dissection with thrombosed ascending false lumen has been controversial as you described in the manuscript. Your research is important as it suggested that reconsidering the guideline may be necessary. As you described in the limitation, sample size was not sufficient to reach to the definitive conclusion, however it was enough to mention that upfront surgery was not always necessary.

Several points I would like to ask.

#1 You mentioned in discussion that Patients with thicker IMH, larger aortic sizes and pericardial effusion on CT scan are more likely to have genuine intimal tear in the ascending aorta and warrant upfront surgery (line 263). Also, your supplementary table 1 showed ascending aorta calibre and PAU/ULP were associated with aortic event in group C. I was wondering why pericardial effusion and IMH thickness did not reach to the statistical significance. Please clarify this point.

Reply: Thank you for your comment. We believe that the reason pericardial effusion and IMH thickness did not reach statistical significance was due to the small sample size. This reduced the statistical significance of the impact of pericardial effusion and IMH thickness on the incidence of aortic events.
Changes: None

#2 Patients with thicker IMH, larger aortic sizes and pericardial effusion on CT scan are more likely to have genuine intimal tear in the ascending aorta and warrant upfront surgery (line 263). Could you come up with more certain number of aortic size or IMH thickness by conducting another type of statistical analysis such as linear regression if possible? Because in daily practice while we see those patients, we would like to have certain cut off value to decide whether watchful waiting or upfront surgery.

Reply: Thank you for your comment. We were not able to come up with a meaningful cut-off valve for ascending IMH thickness due to the same sample size . In our center, 1cm is our cut-off, unfortunately it was not found to be statistically significant.
Changes: None

#3 In this cohort, have you seen any patients with coronary artery malperfusion ? I assume some patients with thick IMH all around the ascending aorta could have been complicated by coronary malperfusion. If so, would you suggest another indication for upfront surgery of Type A dissection with thrombosed false lumen or IMH would be chest pain or EKG abnormality, indicating coronary malperfusion?

Reply: Thank you for your comment. We agree that an indication for upfront surgery is coronary malperfusion. In our series, none of the watchful waiting patients had

documentation of dynamic EKG changes. Amongst the 6 patients who had clinical hypotension and shock, the causes were due to pericardial effusion and rupture. Perhaps malperfusion in ascending IMH seldom happens in thin ascending IMH with no pericardial effusion, and that ascending IMH with coronary malperfusion is usually thick.
Changes: None

#4 Have you had any cases with aortic cannulation to the ascending aorta ? In all cases , you performed femoral artery cannulation in hemiarch cases ? I assume some of patients could have severe atheroscleosis, shaggy aorta, preventing from femoral artery cannulation due to the risk of retrograde embolization. Please clarify the cannulation route.

Reply: Thank you for your comment. In our center, the preferred cannulation strategy is via the femoral artery and all the patients in the series had femoral cannulation. In our series, we did not have issues with retrograde embolization from cannulating the femoral vessels.
Changes: None

Reviewer D

Please refer to numerous original articles in JTD and organize your writing according to JTD's style. I encourage you to review several original articles published in JTD. Many aspects, such as table formatting, abbreviations, capitalization, figure legends, and reference formatting, differ from JTD's style and contain typos.

Reply : Thank you for your comments. The sub-headings are kept for easy reading. References have been modified. Abbreviations are all accounted for.
Changes: Multiple changes have been made throughout the paper after referring to numerous JTD articles.

As you mentioned, the pathology of intramural hematoma and aortic dissection differs in terms of the presence of an intimal tear and other mechanisms. If you intended to study these two conditions together, I suggest indicating the ratio of IMH and aortic dissection patients in groups S, W, and C. Furthermore, a bit more elaboration is needed on why both conditions were studied together.

Reply: Thank you for your comments. The intention of the study was to demonstrate feasibility of individualized management of type A IMH and that upfront surgery is not always necessary. The contentious part of management for patients with uncomplicated type A IMH is that we cannot differentiate a true IMH from a dissection with entry tear/ thrombosed false lumen reliably from CT scan. This study does not intend to study the difference in management of dissection vs. IMH, but rather to demonstrate that a varied

approach to type A IMH on CT scan could be safely performed because of the underlying heterogeneity of the disease.
Changes: None

If possible, please recreate the flowchart, starting from the selection of 95 patients to the exclusion criteria.
Reply : Thank you for your comments.
Changes : Figure 2 has been modified

While surgical techniques may vary among surgeons, the site of aortic tear (in the case of aortic dissection) seems to have been a crucial factor determining the extent of surgery. Describing the type of surgery as solely determined by the surgeon might not be appropriate.

Reply: This was a retrospective study looking into the practice in our center throughout the study period. Unlike prospective controlled studies, we could only record decisions made in the past according to the surgeon's own judgement and discretion. Nonetheless we agree that the site of aortic tear is an important factor in deciding the extent of aortic repair.
Changes: None

Reviewer E

This is a retrospective, single-center study of 93 patients with type A Intramural Hematoma (IMH). These patients were divided into two groups: those who underwent immediate aortic surgery and those who were managed with watchful waiting. The outcomes of these two groups were then compared. While this study might not be particularly novel and primarily provides confirmatory data to existing literature on the role of watchful waiting in managing type A IMH, it remains an important contribution due to the conflicting management strategies for this condition. I would also like to commend the authors on their excellent clinical outcomes. I have the following questions and comments:

The study period should be mentioned in the 'Patients' section.
Reply: Thank you for your comments. The period has been added to the methods section.
Changes: Changes has been made on line 113, page 5.

Did all type A patients undergo CT Angiography (CTA)? Were the CTAs EKG-gated?
Reply: All patients had CTA. None of the CTAs were EKG gated as we did not have this emergency service in our unit.
Changes: None

Please clarify the meaning of “free-flowing contrast” as mentioned in line 90.
Reply: This means contrast enhancement in the false lumen in CTA.
Changes: Changes made in line 122-123 , page 5

How did you differentiate type A IMH with Ulcer-like Projection (ULP)/Penetrating Atherosclerotic Ulcer (PAU) versus type A dissection with partial false lumen thrombosis? Please provide definitions.
Reply: These entities were all CTA findings. Type A IMH with ULP / PAU consists of CT finding of ascending intramural hematoma characterized as lack of contrast in false lumen and *hyperdense crescent sign* on *plain* CT, plus presence of ulcers / PAU in the ascending or descending aorta. A classical dissection with thrombosis of false lumen in the ascending is characterized as the lack of contrast flow in the ascending aortic false lumen and contrast enhancing flow in the false lumen in the descending aorta.
Changes: None

How did the authors determine the acuteness of aortic regurgitation, as mentioned in line 100 as “acute aortic valve regurgitation”?
Reply : Acute aortic valve regurgitation was determined by the admitting office after clinical assessment and echocardiogram assessment . We consider aortic valve regurgitation to be acute
if

1. The aortic valve leaflet did not show calcification/thickening,
2. Patient displayed signs of decompensated heart failure with echo findings of a non-dilated left ventricle, or
3. There is prolapse of non-coronary cusps with eccentric regurgitant jet secondary to the dissecting flap.
4. The lack of history of aortic regurgitation also contributes to the interpretation.

Changes: None

According to line 101, patients were offered surgery within 24 hours of admission, which does not appear to be 'emergent' in nature. Could you please comment on this?
Reply: We serve a population of over 2.5 million in a specific region in Hong Kong which consists of numerous hospitals. Patients presented to different regional hospitals with variable protocols and practice. Timing of diagnosis, surgical consultation and patient transferal often takes more than 12 hours from admission. Hence, we defined emergent operation as within 24 hours of admission to include patients who did not present directly to our hospital.
Changes: None

I assume 'V scan' in line 114 refers to a bedside echocardiogram exam using a portable device. I suggest this be more clearly explained in the manuscript.
Reply: The V scan^{TM} is a pocket size portable ultrasound machine that enables point-of-care echocardiogram.
Changes: Changes have been made in line 147-148 on page 7

Line 116 states that the repeat CT was conducted within 2 weeks of admission. What is the rationale for this interval? It seems rather long for such a high-risk condition. In addition to explaining the rationale, could you provide data on the actual interval between the diagnostic and follow-up CT scans?
Reply: Our usual practice recently is to have a planned repeat CTA around 1week's time instead of 2. However, in the earlier years, due to resource limitations, early planned CT sessions for patients who did not experience any complications on watchful waiting varied.
Changes: None

The term "all-cause survival" used in line 123 sounds unusual.
Reply: Thank you for pointing this, it is changed to "overall survival" .
Changes: Changes has been made in line 170, page 7 of the latest version of the manuscript.

Please provide the number of patients who underwent emergent surgery for each indication.
REPLY: Most patients had a combination of reasons for emergent surgery, as multiple factors for emergent surgery coexisted in individual patients. 14 patients had thick pericardial effusion more than 1cm and among them , 6 had clinical manifestations of cardiac tamponade. 14 patients had ascending aorta $\geq$ 5 cm. 32 patients had ascending intramural hematoma thickness $\geq$ 1cm. 5 patients had hemodynamic instability and clinical shock. In total , 36 patients had emergent surgery performed for the above reasons, in most instances , indications for surgery overlapped in individual patients.

Lines 193-194 state: "17 out of 25 patients underwent aortic intervention during the same hospitalization (ranging from 3 to 35 days after admission). 13 patients required early surgery the next day." Assuming these patients were admitted on the day of diagnosis of type A IMH,
"next-day early surgery" would imply surgery on hospital day 2. However, the range for aortic intervention begins on day 3. Could you please clarify this discrepancy?
Reply: In the watchful waiting group, the "next day" early surgery meant surgery on the subsequent day of development of an indication for delayed surgery, e.g. if the patient had persistent pain or increasing thickness of pericardial effusion, an elective surgery was planned on the earliest next operating session on the subsequent day
Changes: None

I believe the manuscript would benefit from an English language review.
Reply: The English has been reviewed.
Changes: General improvement in word choice and sentence structures.