

Peer Review File

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Reviewer A

I read with interest this narrative review by Kengo Tani et al. on the management of anterior mediastinal tumors. This manuscript represents a well conducted summary of all the peri-operative steps to manage masses of the anterior mediastinum that could present a mediastinal syndrome that is a life-threatening condition.

This review is very well conducted despite the brevity, with few weaknesses; there are just some minor issues and concerns.

Comment 1: In the introduction, authors state that giant anterior mediastinal tumors are known as mediastinal mass syndrome, but this is an error since this latter is a set of signs and symptoms related to the compression of different mediastinal structures despite the cause.

Reply 1: Thank you for pointing this out. In the abstract, we have changed the expression to avoid misunderstanding (see page 1, lines 26-27). In the introduction, we have emphasized that MMS is not giant mediastinal tumors per se, but a series of symptoms caused by compression of surrounding organs (see page 2, lines 58-62).

Changes in the text:

Page 1, lines 26-27

(Before) Giant anterior mediastinal tumors, known as mediastinal mass syndrome (MMS), may cause respiratory failure and circulatory collapse.

(After) Giant anterior mediastinal tumors sometimes may cause circulatory collapse and respiratory failure, known as mediastinal mass syndrome (MMS).

Page 2, lines 58-62

(Before) Giant anterior mediastinal tumors may cause severe respiratory and hemodynamic decompensation due to mass effects. Respiratory failure and circulatory

collapse may occur during biopsy or surgery, even in the absence of any symptoms, owing to the supine position and the use of sedatives and muscle relaxants.

(After) Since mediastinal space is narrow, giant anterior mediastinal tumors are susceptible to mechanical compression or infiltration of the surrounding organs. The circulatory collapse and respiratory failure related to the compression are known as mediastinal mass syndrome (MMS), that may occur during biopsy or surgery, even in the absence of any symptoms, owing to the supine position and the use of sedatives and muscle relaxants.

Comment 2: In MMS paragraph authors cited the role of clinical engineers in the MDT, authors should explain more in details their role.

Reply 2: We have added note about the role of clinical engineers (see page 6, lines 229-230).

Changes in the text:

Page 6, lines 229-230

Clinical engineers should be available in the operating room for the whole duration of surgery with a primed ECMO machine.

Comment 3: The pre-operative work-up discussion may benefit by reading the following article (Extended surgery of antero-superior mediastinum. CURRENT CHALLENGES IN THORACIC SURGERY, 1, 21-21).

In the same way, the discussion on the ECMO role could be improved (Extracorporeal membrane oxygenation in traumatic tracheal injuries: a bold life-saving option. Journal of Thoracic Disease, 11(7), 2660).

Reply 3: Thank you for presenting the references. We have added references (4) and (70) (see page 8, lines 317-318, page 11, lines 461-462, respectively).

Changes in the text:

Page	8,	lines	317-318
(4) Aprile V, Korasidis S, Bacchin D, et al. Extended surgery of antero-superior mediastinum. Curr Chall Thorac Surg. 2019;1:21.			

Page 11, lines 461-462

(70) Aprile V, Korasidis S, Ambrogi MC, et al. Extracorporeal membrane oxygenation in traumatic tracheal injuries: a bold life-saving option. J Thorac Dis. 2019;11:2660-3.

Reviewer B

This is a good effort manuscript offering some helpful insights into the perioperative management of giant anterior mediastinal tumors (GAMT). It is based on an extensive literature search and review of 85 cases published in the English language literature. The manuscript suggests differential approaches in management of patients with GAMT based on clinical and radiological evaluation.

Comment 1: While the manuscript analyzes a relatively large number of GAMT, it seems to fail to present its results in more scientific manner. Nowhere in the manuscript there is a documentation of actual frequencies of the discussed clinical-radiological-pathological findings and their correlations as actual number and/or percentages. Providing such analysis (perhaps with statistical evaluation of significance through p-value) would greatly benefit in improving the submission.

Reply 1: Thank you for pointing this out. We have added actual percentage or statistical figures (see page 3, lines 87-90, page 4, lines 133-138, page 5, line 178).

Changes in the text:

Page 3, lines 87-90

Some mature teratomas can grow rapidly and it has been estimated that approximately 15% of patients requires a resection extended to other structures (e.g., lobectomy, pericardiectomy) for complete tumor resection.

Page 4, lines 133-135

Orthopnea; $p=0.033$, odds ratio (OR) 5.31, 95% confidence interval (CI) 1.15-24.56, upper body edema; $p=0.035$, OR 8.00, 95% CI 1.16-55.07.

Page 4, lines 136-138

The prediction of perioperative complications were the occurrence of cardiorespiratory signs and symptoms at presentation (OR 6.2, 95% CI 1.2-31.5).

Page 5, line 178

(p=0.010, OR 12.8, 95% CI 1.5-47.1)

Comment 2: Line 183. “biopsies of pleural effusions” (?); should be “cytopathological evaluation of pleural effusions” or “biopsies of pleural lesions”.

Reply 2: We have corrected the sentence in line 189, from “biopsies of pleural effusions” to “cytopathological evaluation of pleural effusions”.

Changes in the text:

Page5, line 189

(before) biopsies of pleural effusions

(after) cytopathological evaluation of pleural effusions

Reviewer C

I would like to commend Drs Tani et al. for their well written review of the management of giant anterior mediastinal masses. These tumors represent significant diagnostic and management challenges both inside and outside of the operating room, and the presentation here reviews a number of these issues.

Comment 1: I would state that the major concern from an induction of anesthesia perspective for these patients had much more to do with the hemodynamic collapse than any physical compression of the airway. If both are to be mentioned, the hemodynamic issue should be mentioned first. The airway is fairly rigid and even with initiation of positive pressure, the airway does not usually collapse any more at the time of induction.

Reply 1: Thank you for this suggestion. We mentioned hemodynamic decompensation first, then respiratory failure (see page 1-3, lines 26-27,57, 95, 99-120).

Changes in the text:

Page 1, lines 26-27

(Before) respiratory failure and circulatory collapse

(After) circulatory collapse and respiratory failure

Page 2, line 57

(Before) respiratory and hemodynamic decompensation

(After) hemodynamic and respiratory decompensation

Page 3, line 95

(Before) acute respiratory and/or hemodynamic decompensation

(After) acute hemodynamic and/or respiratory decompensation

Page 3, lines 99-120

We have changed the order of the second and third paragraphs.

Second paragraph: Hemodynamic decompensation occurs ~

Third paragraph: Respiratory failure is caused by ~

Comment 2: The importance of the rescue position is critical, and that leaving patients in this position as long as possible during any induction for anesthesia is equally important to convey to the audience.

Reply 2: The importance of the rescue position has now been added in the revised manuscript (see page 5, lines 211-212).

Changes in the text:

Page5, lines 211-212

Leaving patients in 'rescue position' as long as possible during any induction for anesthesia is important.