

Peer Review File

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Reviewer A

Congratulations to the authors for the work done. I think it has the potential to be published but I would like to draw their attention to several aspects that I think could improve the document.

Comment 1: Line 184 - One of the factors associated with the appearance of POAF is the extent of lung resection. The authors describe a higher percentage of POAF in patients who underwent multiple wedges than in cases of lobectomies or pneumonectomies. Perhaps it would be appropriate to comment on this.

Reply: We have added a comment in the discussion part.

Changes in the text: see page 9, line 219-220

Comment 2: Line 192 - 18% of the patients who received MgSO₄ suffered intraoperative hypotension. The authors do not describe whether they required treatment to compensate for this side effect.

Reply: We added an explanation in the methods section

Changes in the text: see page 6, line 139-141

Comment 3: Line 207- The initials THKT are not defined.

Reply: We deleted this abbreviation and replaced it with non-cardiac thoracic surgery

Changes in the text: see page 10, line 234-235

Comment 4: Table 1- It would be interesting to know the pulmonary function tests of the patients and the presence or absence of heart disease.

Reply: Data were not collected

Changes in the text: NA

Comment 5: Within the possible future lines of research discussed by the authors, it would be interesting to consider the application of minimal invasive surgery and enhanced recovery protocols.

Reply: We take the advice and modified our text

Changes in the text: see page 14, line 316-318

Reviewer B

This manuscript is interesting research regarding the effect of perioperative magnesium sulphate (MgSO₄) application on the incidence of postoperative atrial fibrillation (POAF). They concluded that prophylactic MgSO₄ application is a safe and easy way to reduce the incidence of POAF

thoracotomy and lung resection. However, there are several crucial issues in this manuscript to be accepted for JTD.

Comment 1: Authors described that one of the main findings that prophylactic MgSO₄ application is a safe and easy way to reduces the incidence of POAF thoracotomy and lung resection. This finding could interest thoracic surgeon, but almost half patients were conducted the wedge resection. This analysis should be conducted for patients performed in lobectomy.

Reply: We commented to this issue in the discussion section

Changes in the text: see page 9-10, line 219-223

Comment 2: Diagnostic criteria of POAF were unclear in method section.

Reply: We clarified the POAF criteria in the methods section

Changes in the text: see page 7, Assessment of postoperative atrial fibrillation line 156-162

Comment 3: Although this study was prospective study, the study was approved by Ethics Committee of the local medical board at 2013. Is this study prospective study?

Reply: Yes, it is a prospective observational study. Patients were included after approval of the Ethics committee. The inclusion years of the study are put down wrong.

Changes in the text: we corrected this mistake, see page 5 line 118-119

Comment 4: Why this study was conducted more than ten years ago?

Reply: Due to heavy workload, organizational changes in the hospital and the covid pandemic writing the publication was delayed

Changes in the text: NA

Reviewer C

Authors reported the relationship between prophylactic MgSO₄ application and postoperative atrial fibrillation after lung surgery. POAF is an important complication experienced in clinical practice. However, it needs to be revised for publication in this journal.

Comment 1: Was all postoperative atrial fibrillation symptomatic? Survey of ECG would not detect asymptomatic POAF, which would affect the results.

Reply: Most of POAF is asymptomatic. We addressed this issue in the modified text.

Changes in the text: see page 9 line 217-219

Comment 2: How was POAF detected? Routine detection of ECG only? Have you detected it in unscheduled ECG attempts, or is there no difference between the two groups?

Reply: POAF was detected via routine ECG, only if there was a symptomatic POAF an unscheduled ECG would have been performed. There was no difference between the two groups.

Changes in the text: We made modifications in the Methods section. See page 7 line 156-162

Comment 3: Short-acting β -blockers have been used in recent years, and previous report demonstrated no side effects. In this study, the incidence was significantly lower when β -blocker was used, suggesting that preoperative use of β -blocker may be better than Mg use. Also, perhaps the combination of Mg and β -blocker may have superior prophylactic effects. Please discuss and comment this problem.

Reply: Prophylactic use of β -blockers reduces the incidence of POAF in cardiac surgery patients. There has been research about the prophylactic capacity of β -blocker. It decreases the risk of cardiovascular complications but increases the risk of stroke and death. Therefore, a new onset of β -blocker is not recommended.

Changes in the text: We modified the text in the discussion section, see page 11 line 258-267

Comment 4: Is there any difference in the degree of lymph node dissection, intraoperative blood.

Reply: All operations were conducted by the same team of surgeons with the same operational approach. There was no difference between the two groups.

Changes in the text: NA

Reviewer D

Overall, the study hypothesis is interesting, and the results add to existing knowledge. However, the manuscript is hard to read and follow and the results are not properly displayed and presented.

I advise the authors to find a native English speaking to revise the manuscript and moreover to keep the same structure when presenting the aim, the methods, the results and the discussion.

Furthermore, the subgroups (ASA, betablocker) needs to defined in the purpose section as well as in the methods section. The selection of these subgroups needs to be presented in the introduction.

Below comments and suggestions for revision.

Abstract:

Introduction:

Comment 1: In general, the introduction needs a thorough revision by a native English speaking.

Reply: The whole text was revised by a native English-speaking person

Changes in the text: Text was changed as advised.

Comment 2: Furthermore, it is mentioned that the study is observational, however an effect of change in standard care is investigated. This design is not randomized, however not observational. This needs to be addressed.

Reply: We created a new anesthesiologic standard operating procedure and assessed its efficacy in preventing POAF. We observed the incidence of POAF before we changed our anesthesia standard operating procedure and after the implementation of the new standard operating procedure. This meets the criteria of an observational prospective study.

Changes in the text: NA

Methods:

Study group:

Comment 3: The selection of the study group needs to be defined in this paragraph.

Reply: We have modified our text as advised.

Changes in the text: See page 5 line 119-121

Comment 4: How and by whom was the need for catecholamine decided? At the discretion of the clinician?

Reply: We have modified our text as advised

Changes in the text: See page 6 line 139-141

Comment 5: What is the rationale between presenting data from day one, three and seven?

Reply: ECG monitoring on postoperative day 3 and 7 was hospital standard procedure. We have modified our text as advised

Changes in the text: See page 7 line 157-160

Statistics:

Comment 6: When was χ^2 or Fisher exact test used and why?

Reply: We have modified our text as advised

Changes in the text: See page 7-8 line 169-175

Results:

Comment 7: What does the sentence: 'All data could be recorded before 174 and within the immediate postoperative period of 8 days', mean?

Reply: We had no drop outs. We clarified it in the text.

Changes in the text: See page 8 line 178-179

Comment 8: I think it need to be clearly stated: 1. There was no POAF during the first 24 hours. Furthermore, what was the incidence on day 2, day 3 and day seven and how where the numbers in the control arm and the intervention arm, including p-values, as is done for patients with and without betablocker.

Reply: We have modified our text as advised

Changes in the text: See page 8 line 181-183

Comment 9: Furthermore, the difference between ASA groups is not mentioned in the methods section or introduced in the introduction.

Reply: We have modified our text as advised

Changes in the text: See page 4 line 91-95

Comment 10: Similarly, the occurrence of atrial fibrillation in different surgery categories are described. This is to my understanding common knowledge. It is not clearly stated the divided into intervention groups.

Reply: We have modified our text as advised

Changes in the text: See page 4 line 89-91

Discussion:

Comment 11: I advise the conclusion to be toned down, as the reduction is not proven causal.

Reply: we changed the text as advised

Changes in the text: see page 13 line 311-318

Comment 12: In this discussion of previous studies, the characteristics of the trials would be helpful, for instance when and how was the incidence of POAF recorded in these trials. This would help the reader in the comparison to this trial and the numbers for patients with and without betablocker needs to be put in context.

Reply: We have modified the text as advised

Changes in the text: see page 9 line 212-217

Figures:

Comment 13: Figure 1 and 2 would preferably be changed into a table, it is hard to compare groups in this format and the numbers for day 1,2,3 and 7 should be added to the table.

Reply: We changed Figure 1 and 2 into a table as advised and added the data for day 3. There are no data for day 2.

Changes in the text: See Table 2 and 3 (new)

Tables:

Comment 14: Table 2 and 3:

Should be changed, so that only the incidence of POAF is shown, by standard care and magnesium sulfate-groups.

Reply: We have modified the tables as advised

Changes in the text: See table 2,3,4,5

Specific comments:

Comment 15: 81-82: I believe this conclusion is a bit far-fetched and should be toned down.

Reply: We have modified our text as advised

Changes in the text: See page 3 line 70-72

Comment 16: 93: please rewrite

Reply: We have modified our text as advised

Changes in the text: See page 4 line 81-83

Comment 17: 95-96: There is now reference on the increased risk of thromboembolism, stroke, myocardial infarction and heart failure. To my knowledge, atrial fibrillation is not associated with increased risk of myocardial infarction.

Reply: We have modified our text as advised

Changes in the text: See page 4 line 83-86

Comment 18: 99-100: what is meant by ‘The incidence of atrial flutter or fibrillation ranges from 10 to 42% (7) and is based....’, maybe associated is the correct word?

Reply: We have modified our text as advised

Changes in the text: See page 4 line 88-89

Comment 19: 101: patient risk factors for what?

Reply: We have modified our text as advised

Changes in the text: See page 4 line 91-93

Comment 20: 144: Need to be revised by a native English speaking: ‘As already has been shown is an epidural 145 analgesia not superior to a standardized opioid regime’.

Reply: We have modified our text as advised

Changes in the text: See page 7 line 149-151

Comment 21: 150: I believe this sentence needs to be rewritten as previously suggested.

Reply: We have modified our text as advised

Changes in the text: See page 7 line 153-155

Comment 22: 153-157: ‘Perioperatively?’ Again, this paragraph needs to be rewritten.

Reply: We have modified our text as advised

Changes in the text: See page 7 line 157-162

Comment 23: 161: ‘in the medicinal history’ may be deleted

Reply: We have modified our text as advised

Changes in the text: See page 7 line 165-167

Comment 24: 174-175: I believe the term ‘patient characteristics’ is enough to describe the contents of table 1.

Reply: We have modified our text as advised

Changes in the text: See page 8 line 179-180

Comment 25: 176: ‘illustrated variables’ may be deleted.

Reply: We have modified our text as advised

Changes in the text: See page 8 line 179-180

Comment 26: 186: Needs to be changed to: Fifteen patients in the MgSO₄ 187 group and eleven (22%) in the standard group (p=0.362).

Reply: We have modified our text as advised

Changes in the text: See page 8 line 193-194

Comment 27: 212-215: Divide the following sentence in two: ‘If there are contraindications for β -blocker therapy a prophylactic 213 therapy with amiodarone is recommended and patients who have contraindications to β 214 blocker therapy and to amiodarone therapy intravenous magnesium should be considered 215 to prevent postoperative AF’.

Reply: We have modified our text as advised

Changes in the text: See page 10 line 240-241

Comment 28: 215: 'But better strategy than treating POAF seems to prevent it', this sentence needs revision.

Reply: We have modified our text as advised

Changes in the text: See page 10-11 line 242-245

Comment 29: 229: The preventive effect of betablocker is mentioned above.

Reply: We have modified our text as advised

Changes in the text: See page 11 line 256-260

Comment 30: 258: I do not believe that the word confirm is appropriate, supports, may be better.

Reply: We have modified our text as advised

Changes in the text: See page 12 line 288-291