Author’s response to reviews

Title: Increased risk for the development of postoperative severe hypoxemia in obese women with acute type A aortic dissection

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Version: 1 Date: 19 Mar 2019

Author’s response to reviews:

Dear Vipin Zamvar:

It is my honor to submit my manuscript “Increased risk for the development of postoperative severe hypoxemia in obese women with acute type A aortic dissection” to your journal. We have revised our paper according to the reviewers’ suggestions as follows.

Reviewer #1:

1. It is well known that aortic dissection may involve bronchial artery and cause pulmonary interstitial edema. Therefore, intractable hypoxemia may occur during perioperative period. There are many related studies. There seems to be no new conclusion in your article.

Author response:

I strongly agree to your comment. The intractable hypoxemia is really a common complication during perioperative period. Although mild or moderate hypoxemia was excessively common, the incidence and risk factors of severe postoperative hypoxemia have been precisely studied in patients with acute type A aortic dissection. Moreover, we diagnosed severe postoperative hypoxemia according to new Berlin definition (PaO2/FIO2 ≤ 100 mmHg). In addition, we found that the female gender is generally considered a risk factor for aortic arch surgery. The relatively
few reports have been published regarding gender differences in patients undergoing acute type A aortic dissection. The gender-related differences in patients receiving this surgery are worth exploring. Therefore, our study’s results emphasise that more attention must be paid to the prevention of severe postoperative hypoxemia among obese women patients. Thank you.

2. Obesity and women are high risk factors for pulmonary insufficiency after thoracotomy or cardiopulmonary bypass. As can be seen from your figure 1, different patients have different degrees of hypoxemia before surgery, and there will be transient hypoxemia after surgery, and then increase, but the reduction is different. Do we need to take into account the different hypoxemia conditions before surgery?

Author response:

Among the preoperative characteristics, Table 1 showed that BMI values were higher in severe hypoxemia group when compared to the non-severe hypoxemia group (p < 0.001). Moreover, compared to the non-severe hypoxemia group, the total proportion of severe hypoxemia was greater for women than for men in severe hypoxemia group (39.0% vs. 18.3%; p = 0.02). However, there was no significant difference with respect to preoperative hypoxemia condition between 2 groups (276 ± 87 vs. 249 ± 77 mmHg; p = 0.10). In addition, chronic obstructive pulmonary disease also was no significant difference between 2 groups. Similarly, multivariate logistic regression also confirmed that preoperative hypoxemia condition was not independent risk factors for severe postoperative hypoxemia in patients with acute type A aortic dissection. Thus, we suggested that preoperative hypoxemia condition was not associated with severe postoperative hypoxemia in acute type A aortic dissection. Thank you.

Reviewer #2:

1. This is an interesting paper. Minor english corrections should be made

Author response:

We have revised as your suggestions in all manuscript. Thank you.

Reviewer #3:

1. An index between PA O2 (mmHg) divided by FiO2 (in percentages) can not be expressed in mmHg. This is simply a numerical expression used for reference. I'd like to understand why do you express this index in mmHg?

Author response:
The AECC (1994) defined ARDS as the acute onset of hypoxemia (arterial partial pressure of oxygen to fraction of inspired oxygen [PaO2/FIO2] ≤ 200 mmHg) with bilateral infiltrates on frontal chest radiograph, with no evidence of left atrial hypertension. Acute lung injury (ALI) was also described, using similar criteria but with less severe hypoxemia (PaO2/FIO2 ≤ 300 mmHg). The AECC definition was widely adopted by clinical researchers and clinicians.

Berlin definition (2011) proposed 3 mutually exclusive categories of ARDS based on degree of hypoxemia: mild (200 mmHg < PaO2/FIO2 ≤ 300 mmHg), moderate (100 mmHg < PaO2/FIO2 ≤ 200 mmHg), and severe (PaO2/FIO2 ≤ 100 mmHg) and 4 ancillary variables for severe ARDS: radiographic severity, respiratory system compliance (≤ 40 mL/cm H2O), positive endexpiratory pressure (≥ 10 cmH2O), and corrected expired volume per minute (≥ 10 L/min). Thus, we proposed severe postoperative hypoxemia based on this Berlin definition (Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012; 307: 2526-2533). Thank you.

2. A photo or drawing of the most commonly used surgical technique would be useful.

Author response:

We have revised as your suggestions. This part is highlighted in Page 6 in revised version according to your suggestion. Thank you.

3. There's some typing error in discussion (patientssuffered, differencesbetween). Must have a space between the words.

Author response:

We have revised as your suggestions in all manuscript. Thank you.

Reviewer #4:

1. This study aimed to identify the risk factors for postoperative severe hypoxemia after surgery for acute type A aortic dissection. Hypoxemia after surgery for aortic dissection remains to be very important research question. The idea is not new and innovative as the same Institution already published some research results on the very similar if not the same topic. Also, the topic has already been well researched and the data of the very similar study groups have already been published. Thus, this is not innovative study addressing some research topic that has not been already researched. I also don't see something intriguing in this, let's say so another view on known topic.

Author response:
The AECC (1994) defined ARDS as the acute onset of hypoxemia (PaO2/FIO2 ≤ 200 mmHg) with bilateral infiltrates on frontal chest radiograph, with no evidence of left atrial hypertension. The AECC definition was widely adopted by clinical researchers and clinicians. The most studies adopted this criterion for this topic. However, intractable hypoxemia was excessively common in patients with acute type A aortic dissection. Thus, the AECC definition had low sensitivity and had a difficulty to distinguishing real severe postoperative hypoxemia for patients with acute type A aortic dissection. For these reasons, we proposed severe postoperative hypoxemia based on the Berlin definition (2011). A definition proposed 3 mutually exclusive categories of ARDS based on degree of hypoxemia: mild (200 mmHg < PaO2/FIO2 ≤ 300 mmHg), moderate (100mmHg < PaO2/FIO2 ≤ 200mmHg), and severe (PaO2/FIO2 ≤ 100 mmHg).

In addition, we found that the female gender is generally considered a risk factor for aortic arch surgery. The relatively few reports have been published regarding gender differences in patients undergoing acute type A aortic dissection. The gender-related differences in patients receiving this surgery are worth exploring. Therefore, our study’s results emphasise that more attention must be paid to the prevention of severe postoperative hypoxemia among obese women patients. Thus, we thought that our study had certain new and innovative method and conclusion. Thank you.

2. This is a single centre retrospective observational study with 112 patients included into analysis. The following sentence "Patients were recruited on a consecutive basis on the condition that they agreed to provide their informed consent." remains unclear. How were patients or their relatives consented for retrospective study?? Authors need to clarify this.

Author response:

I strongly agree to your comment. I am sorry. This was our mistake in this part. Our department of cardiac surgery in Beijing Anzhen Hospital was Beijing Aortic Disease Center. The quantity of emergent aortic arch surgery referred to our team was the largest number throughout the country per year. Up to now, we underwent many prospective or retrospective observational studies for patients with acute type A aortic dissection at the same time. Thus, we have revised this question and deleted this sentence in manuscript according to your suggestion. Thank you.

3. Also, the total number of recruited patients raises my concerns on the sample size effect. Did authors do sample size calculation? Sample size effect should not be underestimated.

Author response:

I strongly agree to your suggestions. The postoperative intractable hypoxemia is a common complication during perioperative period in patients with acute type A aortic dissection. There were some similar studies. Therefore, estimation of sample size was carried out according to previous study using PASS software before study. The sample size in this study is enough to statistical analysis. Thus, our study results from these patients are believable. This is a single-
center retrospective observational study, which makes it subject to inherent selection and information biases. We have provided this study limitation in revised version according to your suggestion. This part is highlighted in Page 14. Thank you.

4. Results and conclusion: results of study are listed concisely. However, the discussion and conclusion are somewhat blurry and too general. I'm afraid that this article does not add to the current knowledge. Larger sample trials are indeed needed to elucidate some important questions in the field of acute dissection surgery. Authors selected interesting topic. Unfortunately, I think that this paper in its present form does not add to the current knowledge.

Author response:

I agreed with your point of view. Our study results demonstrated that obesity and female were two independent risk factors for severe postoperative hypoxemia in patients undergoing acute type A aortic dissection. The incidence and risk factors of postoperative hypoxemia, the mechanism of hypoxemia after surgery, and the mechanism of obesity and female for effect on severe postoperative hypoxemia were analyzed in discussion respectively. The maintaining perioperative fluid balance and inhibiting the systemic inflammatory response might reduce the incidence of severe postoperative hypoxemia in obese women with acute type A aortic dissection in conclusion. The considering the emergency nature of Stanford type A aortic dissection surgery, the identified risk factors may have been confounded by the complex interactions among different organ systems. But these factors could not be controlled in clinical study. This is indeed an important study limitation. With the experience gained in the past years and the results of this study, the present authors designed a larger sample study to determine the risk factors of postoperative hypoxemia in patients with with acute type A aortic dissection. Thank you.

Should anything further be required, please do not hesitate to contact me.

Kind regards,

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