The catastrophe of hypoxia in complex aortic surgery

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Running head: Brain damage in aortic surgery

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Acute type A Aortic Dissection (AAAD) is a catastrophic disorder and a surgical emergency associated with a high mortality rate when no intervention is performed in the acute setting (1). Several schools exist for managing this lethal pathology, depending on the extent of the disease; this could range from an interposition graft to replacing the ascending aorta to aortic root replacement and total arch replacement with the frozen elephant trunk (FET) in a more extensive approach. However, the novel Triple Branched Stent Graft (TBSG) implantation approach has been proven to shorten intraoperative parameters such as cardiopulmonary bypass time, aortic cross-clamp time, circulation arrest time and the duration of ventilator-assisted breathing (2). TBSG implantation was first described by Chen et al (3) in 2010 and is effective in the treatment of type A aortic dissections, however, the procedure, as with most cardiac surgeries is not without risk. Risks associated with this technique include occlusion and disruption of the aorta, paraplegia, and hypoxaemia (4,5).

Wang and colleagues (6) attempted to develop a predictive nomographic model to identify postoperative hypoxic risk factors in patients following TBSG implant surgery. A population of 97 patients were included in this study, all of whom underwent TBSG implantation at Fujian Union Hospital in the Fujian Province of China within a 3-month window. The predictive nomogram was based on the result of their study, being that postoperative lactic acid, creatinine, intraoperative and aortic occlusion time were all independent risk factors for hypoxemia, and that age, sex and body mass index (BMI) were clinically relevant for predicting postoperative hypoxemia. (6) The methodology Wang et al. (6) utilise, although practical in approach, is not without its limitations.

When involving patients in the sample population, Wang et al (6) failed to report their individual demographics. In patients with aortic dissections, certain demographic features could be considered independent risk factors for morbidity and mortality. For example, in the United States of America, acute type B aortic dissections occur more frequently in the black population (7). As a result of this, applying the results of the predictive nomogram developed by Wang et al (6) to an international population will not be possible. To be reliable, the application of such models should be demonstrated on varied validation datasets in the same setting. Furthermore, the imbalance of the male to female ratio (75% to 25%) of the sample population affects the generalisation and applicability of the results, as the female sex is a known risk factor in cardiac surgery, mainly coronary and valve surgery (8). Although these criticisms are true, the population used was homogenous, supporting the validation of the dataset.

As postoperative hypoxemia is the focus of this study (6), it is expected that the variables collected should pertain to the precise definition of hypoxia. However, Wang et al (6) refer to hypoxemia in the context of ARDS with a PaO2/FiO2 ratio of less than or equal to 200 mmHg, not coinciding with the Berlin Definition of a PaO2/FiO2 ratio of equal to or less than 300 mmHg (6,9). Additionally, there was no mention of the different severities of hypoxia, as hypoxemia is classified into mild hypoxemia for PaO2/FiO2 ratios between 300 and 201 mmHg, moderate hypoxemia for PaO2/FiO2 ratios between 200 and 101 mmHg, and severe hypoxemia for PaO2/FiO2 ratios below or equal to 100 mmHg (10). Additionally, regarding the exclusion and inclusion criteria, the decision to exclude patients from the study who had severe preoperative pulmonary insufficiency was adequate in this context, however, such exclusion should have been extended to include preoperative inflammatory conditions. This is true as it could severely affect intraoperative systemic inflammatory degree during aortic dissection surgery (11). The preoperative inflammatory state relates directly to postoperative hypoxaemia due to the physiology of postoperative hypoxaemia: alveolar accumulation and activation of macrophages and neutrophils occur due to the release of pro-inflammatory cytokines, leading to the release of toxic mediators and proteolytic enzymes which allow the permeability of epithelial and endothelial cells, pulmonary vascular pressures, affect the alveolar surfactant function, impair the oxygenation function, and cause postoperative hypoxaemia (12). This serves to be another significant limitation recognized from this study, causing a diagnosis purity bias to be present in the data collection.

The absence of imperative operative variables is apparent when considering risk factors for postoperative hypoxia. Such variables include the circulatory arrest time, known to affect neurological outcomes of the FET for acute type A aortic dissection, and may therefore also influence the outcomes of the TBSG implantation. Furthermore, there was no consideration of prolonged bypass time, disease severity, and neurological status. Both the performance and length of time that the patient is under cardiopulmonary bypass are important factors which influence the occurrence of postoperative hypoxemia in aortic dissection patients undergoing surgery. This is evidenced in a retrospective single-centre study by Wang et al (13) which highlighted the fact that 12.2-27% of patients undergoing cardiopulmonary bypass experienced postoperative hypoxemia. Failure to consider the neurological status of patients further limits the study, as an observational study by Lin et al (5) concluded that hypoxaemia following the insertion of a TBSG increases the risk of postoperative delirium, calling to attention its significance. Still, as mentioned by Wang et al (6), there exists a scarcity of studies assessing the risk factors of postoperative hypoxemia after TBSG implantation.

Further limitations of the study exist in the exclusion of postoperative interventions. Wang and colleagues neglected to mention any oxygen supplementation provided to the patients within the 6-hour interval of blood collection. Such an intervention could either prove beneficial or detrimental to the patient, significantly affecting the results of this study. Moreover, the 6-hour postoperative duration of blood collection was not justified. Providing a lack of insight into this time interval allows for speculation into the varying laboratory values such as lactic acid which is Wang et al's (6) primary predictive factor of hypoxemia (14). Despite the limitations described above, the study does provide valuable insight into the independent risk factors which may affect the occurrence of hypoxemia postoperatively.

Statistically, Wang et al. provided reliable analysis and interpretation of the data collected in their study. Internal validation was performed via bootstrapping and a concordance index was utilised to measure the predictive ability of the nomogram graph. This resulted in a value of 0.76 which suggests that the validation was between a good (C-index: 0.7) and a strong level (C-index: 0.8), corroborating the efficacy of the study (15). Using univariate and multivariate logistic regression to screen independent risk factors also provided localised rather than generalised results. Finally, the utilisation of decision curve analysis (DCA) in the study was appropriate due to the relatively high incidence and significant volume of information available on aortic dissections (16,17).

Overall, it can be concluded that Wang et al. have provided valuable insights into the relatively new procedure of triple branched stent graft implantation for type A aortic dissections. Developing a predictive model for the risk factors of postoperative hypoxemia will carve a path for other studies to follow. This work was strengthened by a strong internal validity and the reproducibility of its results due to the clear description of his methods. However, the lack of a more extensive list of operative variables, omission of data regarding levels of hypoxemia, and insufficient justification of follow-up time limits the applicability of the study. The authors need a more extensive approach to the perioperative state of the patient, along with a long-term follow-up to heighten its suitability for more widespread use. The study serves as a stepping stone for further investigation into the risk factors and confounding variables for postoperative hypoxaemia, providing the scope for larger multi-centred studies and developing an international risk model.

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