Effects of preoperative mildly elevated pulmonary artery systolic pressure on the incidence of perioperative adverse events undergoing thoracoscopic lobectomy: an observational cohort study protocol

Yu Fu,1 Jiameng Gao,1 Zhiyuan Zhang,1 Nan Zhang,1 Jing Yu,1 Chang Chen,2 Zongmei Wen1

ABSTRACT

Introduction Echocardiography provides a non-invasive estimation of pulmonary artery systolic pressure (PASP) and is the first diagnostic test for pulmonary hypertension. Recent studies have demonstrated that PASP of more than 30 mm Hg related to increased mortality and morbidity. However, perioperative risks and management for patients with mildly elevated PASP are not well established. This study aims to explore the association between mildly elevated PASP and perioperative adverse outcomes.

Methods and analysis This will be a retrospective cohort study conducted at Shanghai Pulmonary Hospital in Shanghai, China. Eligible patients are adults (≥18 years) who performed preoperative echocardiography and followed thoracoscopic lobectomy. Our primary objective is to determine the effect of preoperative mildly elevated PASP on the incidence of hypotension during surgery. Whether mildly elevated PASP is related to other perioperative adverse events (including hypoxaemia, myocardial injury, new-onset atrial fibrillation, postoperative pulmonary complications, 30-day readmission and 30-day mortality) will be also analysed. An estimated 2300 patients will be included.

Ethics and dissemination The study has been approved by the institutional review board of Shanghai Pulmonary Hospital (approval No: 2022LY1143). The research findings intend to be published in peer-reviewed scientific publications.

Trial registration number Chinese Clinical Trial Registry (ChiCTR2200066679).

INTRODUCTION

Lung cancer was the second most common cancer and the leading cause of cancer death, with approximately 2.2 million new cases and over 1.8 million deaths from lung cancer worldwide in 2020.1 Furthermore, the incidence of lung cancer and disease burden still increased in the last decades in China, seriously threatening public health. More recent studies revealed that lung cancer was the most commonly diagnosed cancer as well as the first leading cause of cancer death in China.2 Surgical resection is seen as the primary and preferred treatment modality for stage I–II non-small cell lung cancer,3 4 and lobectomy remains the preferred approach to stage IB and large tumours.5 Although lung resection contributes to improved survival, thoracic surgery also brings about a high risk of perioperative cardiorespiratory complications and a high burden of long-term morbidity,6 7

The presence of impaired right ventricle (RV) function after lung resection has been well demonstrated.7 To be more specific, short-term intraoperative pathophysiology during one-lung ventilation and lung resection significantly affect heart rate, right ventricular ejection fraction, pulmonary vascular resistance and even long-term RV function.8 9 Unfortunately, RV dysfunction may be implicated in perioperative myocardial injury, atrial fibrillation, hypotension and even more severe cardiorespiratory complications.10–12 Therefore, further work is required to identify specific and sensitive risk factors to predict perioperative adverse events.
Pulmonary artery systolic pressure (PASP) measurement by Doppler transthoracic echocardiography is non-invasive, inexpensive, widely available and adequately reliable. In healthy individuals who undergo echocardiography, the average PASP is in the range of 18–24 mm Hg, and PASP over 30 mm Hg is uncommon. Recent studies have demonstrated that elevated PASP of more than 30 mm Hg is associated with increased mortality and morbidity. Furthermore, when the PASP is higher than 40 mm Hg, prompting further evaluation for pulmonary hypertension is recommended by expert consensus opinions. It is likely that anaesthesiologists will have increased exposure to patients with mildly elevated PASP (30–40 mm Hg). However, there are missing recommendations for the perioperative management of patients with mildly elevated PASP who do not have underlying severe pulmonary vascular disease. To our knowledge, the association of preoperative mildly elevated PASP and perioperative adverse events have not been previously reported, especially in patients undergoing lung resection with the unique perioperative physiology. Understanding the effect of mildly elevated PASP on perioperative adverse events is important to anaesthesiologists, since such information may influence management and aggressive risk-reduction strategies.

Objectives
We will perform an observational cohort study on patients undergoing thoracoscopic lobectomy. Our objectives are to explore the association between mildly elevated PASP and perioperative adverse outcomes (including hypotension, hypoxaemia, myocardial injury, new-onset atrial fibrillation (NOAF), postoperative pulmonary complications (PPCs), 30-day readmission and 30-day mortality).

METHODS AND ANALYSIS

Ethics statements
The protocol of this study has been approved by the institutional review board of Shanghai Pulmonary Hospital (approval No: 2022LY1143). This study has been registered on chictr.org.cn.

Study design
This study protocol has been designed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology. This study will be a single-centre, observational cohort study.

Patient selection
We will collect data from records of adult patients aged above 18 years who followed thoracoscopic lobectomy from 1 September 2021 to 1 March 2022 in our institution, which is a tertiary thoracic surgery centre in China.

Inclusion criteria
- Age ≥18 years old, regardless of gender.
- American Society of Anesthesiologists (ASA) grade I–III.
- Already performed preoperative echocardiography and recorded the value of PASP.
- Underwent elective thoracoscopic lobectomy.
- Complete case data.

Exclusion criteria
- History of lung resection surgery.
- History of respiratory failure within 1 year.
- History of radiotherapy, chemotherapy or immunotherapy before surgery.
- Known pulmonary hypertension (including but not limited to using prostacyclin or similar conditions).
- Pre-existing heart failure (ejection fraction <40%), severe respiratory disease, renal or metabolic diseases.
- Pre-existing arrhythmia, atrial fibrillation, sick sinus syndrome or atrioventricular block.
- Underwent simultaneous bilateral lung resection surgery.
- Loss of the data.

Main exposure
We will create a normal-PASP cohort: PASP<30 mm Hg (the control cohort) and a mildly elevated-PASP cohort: 30 mm Hg ≤ PASP <40 mm Hg (the exposure cohort). Doppler transthoracic echocardiography is used to estimate PASP by measuring the tricuspid regurgitation jet velocity doppler signal. Specifically, the value of PASP is determined by calculating the estimated maximum tricuspid regurgitation jet velocity (using the modified Bernoulli equation) and adding the estimated right atrial pressure.21

Data collection
Clinical variables will be retrospectively collected by two trained physicians and closely supervised by two independent physicians. Clinical data will be collected from the electronic anaesthesia record system (Medicalsystem, Nanjing, China) and thoracic surgery registry system (Winning Health Technology Group, Shanghai, China). The data will be entered into the clinical trial management public platform ResMan (www.medresman.org.cn) using anonymised case report forms.

Observation index
We will retrospectively collect relevant information, including demographic characteristics (age, gender, body mass index, ASA physical status, smoking, pulmonary function tests and echocardiographic reports); past systematic comorbidities (hypertension, diabetes and cardiac diseases); intraoperative data (dosages of anaesthetic medications, blood loss, fluid infusion, transfusion, hypoxaemia, hypotension, NOAF, location of resection, tumour staging and the duration of surgery); and postoperative data (PPCs, perioperative myocardial injury (PMI), the length of stay (LOS), 30-day readmission and 30-day mortality).

The primary outcome is intraoperative hypotension, which is defined as the duration of a systolic arterial pressure of <100 mm Hg, because there is best available
Evidence suggested that duration and magnitude of systolic arterial pressure below 100 mm Hg during non-cardiac surgery in adults are associated with myocardial injury and death. In the case of patients with preoperative hypertension, we will use the relative threshold (30% below baseline systolic arterial pressure) as a supplement to prevent the scenario wherein the intraoperative blood pressure may have decreased by more than 30%, but not below 100 mm Hg. Furthermore, we categorised this outcome variable into groups of no intraoperative hypotension as well as a short (<15 min) and a prolonged (≥15 min) duration of intraoperative hypotension.

The secondary outcomes are intraoperative hypoxaemia, intraoperative NOAF, PPCs, PMI, LOS, 30-day readmission and 30-day mortality. In the retrospective study, hypoxaemia was defined as any SpO2 value ≤90%, for at least 1 min and not being the result of an artefact. NOAF was defined when the electrocardiograph recordings with features of atrial fibrillation, for at least 30 s. According to the European Perioperative Clinical Outcome consensus statement, PPCs was defined as a circumstance involving newly developed pulmonological symptoms, including atelectasis, pulmonary infection and respiratory failure. PMI was identified by a high-sensitivity troponin-T>20 ng/L within 3 days postoperatively.

**Statistical analysis**

Descriptive statistics (frequencies, means and medians) will be initially undertaken. Significant differences between the two cohorts will be tested by two independent sample t-test or Mann-Whitney U test for continuous variables. Categorical variables will be compared by $\chi^2$ test or Fisher’s exact test depending on the sample size.

A 1:1 propensity score matching (PSM) will be used to reduce discrepancies in the characteristics of the study cohort. Cases will be matched with a calliper size of 0.01. All demographic and intraoperative characteristics will be included in the PSM. Then, HRs will be calculated for dichotomous variables such as hypotension, hypoxaemia, NOAF, PPCs and PMI. All data processing and statistical analysis will be performed by statistical software SPSS V.26.0 (SPSS, Chicago, Illinois, USA). Two-tailed $p$ values of less than 0.05 will be considered statistically significant.

**DISCUSSION**

Pulmonary hypertension (PH) is a complex and serious pulmonary vascular disease that is associated with adverse clinical outcomes. The perioperative morbidity and mortality are substantially increased in patients with PH undergoing general anaesthesia for surgical procedures. Currently, echocardiography provides a non-invasive estimation of PASP based on the tricuspid regurgitation velocity doppler signal and is the first diagnostic test for PH. Based on available data, a PASP of less than 30 mm Hg seems to be appropriate pressure, and elevated PASP is a common (over 40% of individuals) and high-risk finding on echocardiography. While there are several guidelines to help direct patients with PH, perioperative risks and management for the high numbers of patients with elevated PASP who do not have confirmed PH are not well established. This will be the first study to provide clinical evidence about the association of mildly elevated PASP on perioperative adverse events.

Video-assisted thoracoscopic surgery lobectomy, the technique of choice for the resection of early-stage lung cancer in many institutions, has become mainstream in modern thoracic oncology practice. However, lung resection surgery is understood to confer a high risk of perioperative cardiovascular complications and postoperative respiratory complications. Due to undesirable effects on right ventricular performance, patients with mildly elevated PASP undergoing thoracoscopic lobectomy may further exacerbate these complications. Additionally, right ventricular volume overload associated with fluid shifts during operation may diminish left ventricular filling due to ventricular interdependence, resulting in reduced cardiac output and hypotension.

It is well-known that intraoperative hypotension has been proven related to increased risk of myocardial injury, acute kidney injury, cardiac or cerebrovascular adverse events, and even mortality. Thus, we will perform an observational cohort study in patients undergoing thoracoscopic lobectomy. Our...
primary objective is to determine the effect of preoperative mildly elevated PASP on the incidence of hypotension during surgery. Whether mildly elevated PASP is associated with other perioperative adverse events (including hypoxemia, myocardial injury, NOAF, PPCs, 30-day readmission and 30-day mortality) will be also analysed. With the resulting evidence, we will design an intervention study about the perioperative management of patients with mildly elevated PASP undergoing lung resection, with the ultimate goal of preventing or decreasing the incidence of perioperative adverse events. However, this study focused on thoracoscopic lobectomy and the generalisation of the results may require further validation in other thoracic surgery.

ETHICS AND DISSEMINATION

The study has been approved by the institutional review board of Shanghai Pulmonary Hospital (approval No: 2022LY1143). The research findings intend to be published in peer-reviewed scientific publications.

Author affiliations

1Department of Anesthesiology, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, People’s Republic of China
2Department of Thoracic Surgery, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, People’s Republic of China

Contributors

The following authors make contributions to this manuscript: Conceptualisation: YF, JG and ZZ. Data collection: JG, NZ and JY. Data monitoring and analysis: YF and ZZ. Drafting the manuscript: YF and JG. Funding acquisition: ZZ and CC. Supervision: ZZ and CC. Revision of the article: All participating authors. YF and JG contributed equally to this work.

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Competing interests

None declared.

Patient and public involvement

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Not applicable.

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ORCID iDs

Yu Fu http://orcid.org/0000-0003-0881-7165
Zhiyuan Zhang http://orcid.org/0000-0001-7362-3362

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