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## PERIOPERATIVE OUTCOMES OF COMBINED HEART SURGERY AND LUNG TUMOR RESECTION : A SYSTEMATIC REVIEW

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### ABSTRACT

**Background:** Cancer and cardiovascular disease are the leading causes of death in both men and women worldwide. There are concerns regarding the potentially increased mortality and complication rates of simultaneous surgery and the adequacy of lung exposure during heart surgery.

**Methods:** By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

**Result:** In the PubMed database, the results of our search brought up 14 articles, whereas the results of our search on SagePub brought up 91 articles. The results of the search conducted for the last year of 2013 yielded a total 9 articles for PubMed and 23 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

**Conclusion:** In summary, combined heart surgery and lung tumor resection had a low mortality rate and an acceptable complication rate. Subgroup analyses revealed that most patients with lung cancer underwent uncompromised anatomical resection and mediastinal lymph node sampling or dissection during combined cardiothoracic surgery, and showed off-pump CABG may reduce the complication rate compared with on-pump CABG. Further researches are still needed to verify these findings.

Keyword: Heart surgery, Lung tumor resection, Perioperative outcomes, Combined cardiothoracic surgery

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### **INTRODUCTION**

Cancer and cardiovascular disease are the leading causes of death in both men and women worldwide. The coexistence of cancer and CAD is common, and the co-incidence is expected to rise due to aging of the population and improvements of diagnostic facilities. The increasing incidence of lung cancer in China may be accelerated by the epidemic of tobacco smoking, and the major risk factors for lung cancer in nonsmoking women include passive smoking, such as tobacco smog and cooking smog. Smoking is also a major risk factor for CAD. Surgery is still the first-choice treatment for lung cancer, but treatment of resectable lung cancer and coexisting severe CAD has not been considered feasible.<sup>1</sup>

The population of patients with combined lung cancer and CHD is expected to increase, and surgical treatment for both conditions is shifting to older patients due to the increasingly aging population and the improvements in patient diagnosis. It has been reported that at least 5% of patients who require lung resection due to lung cancer also require coronary artery bypass graft surgery.<sup>2</sup>

The population of patients with combined lung cancer and CHD is expected to increase, and surgical treatment for both conditions is shifting to older patients due to the increasingly aging population and the improvements in patient diagnosis. It has been reported that at least 5% of patients who require lung resection due to lung cancer also require coronary artery bypass graft surgery. This fact creates a clinical dilemma for surgeons on how to decide on the best treatment for with combined early lung cancer and severe CHD, but because surgical techniques have continued to improve, it is now possible to conduct combined coronary artery bypass graft (CABG) surgery and lobectomy for lung cancer in a single combined surgical procedure.<sup>3</sup>

Although relatively few patients have concomitant lesions of the heart and lungs requiring surgical intervention, the prevalence of such patients is increasing. Some patients, who required cardiac surgery, found asymptomatic indeterminate lung nodules during preoperative examination. Other patients, who were scheduled to receive lung tumor resection, had heart diseases requiring surgical intervention. The management of patients who require both heart surgery and lung resection is challenging. Treatment options include either simultaneous or staged surgical procedures. Without postponing the treatment of either heart or lung diseases, simultaneous surgery can solve heart and lung lesions at the same time, thus avoiding the second operation. However, there are concerns regarding the potentially increased mortality and complication rates of simultaneous surgery and the adequacy of lung exposure during heart surgery.<sup>4</sup>

Combined heart surgery and lung resection remain a controversial issue. This method facilitates the treatment of two major problems with one intervention, reducing hospitalization cost with acceptable outcomes. On the other hand, skepticism exists related to the effects of cardiopulmonary bypass on malignancy, proper extent of lung resection from non-standard approach and to a possible greater risk of perioperative bleeding.<sup>4</sup>

To address these concerns, we conducted this systematic review to evaluate the perioperative mortality and complication rates of combined heart surgery and lung tumor resection. In the subgroup analyses, we also investigated the proportion of patients with lung cancer who underwent anatomic lung resection and mediastinal lymph node sampling or dissection, and the impact of cardiopulmonary bypass (CPB) on perioperative complications.

## METHODS

#### Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

#### **Criteria for Eligibility**

For the purpose of this literature review, we review published literature of studies to identify studies that reported the perioperative outcomess of combined heart surgery and lung tumor resection. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

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#### **Search Strategy**

We used "perioperative outcomes", "lung surgery" and "heart surgery" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: (("perioperative"[All Fields] OR "perioperatively"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields]) AND ("thoracic surgery"[MeSH Terms] OR ("thoracic"[All Fields] AND "surgery"[All Fields]) OR "thoracic surgery"[All Fields] OR ("heart"[All Fields] AND "surgery"[All Fields]) OR "heart surgery"[All Fields] OR "cardiac surgical procedures"[MeSH Terms] OR ("cardiac"[All Fields] AND "surgical"[All Fields] AND "procedures"[All Fields]) OR "cardiac surgical procedures"[All Fields]) AND (("lung neoplasms"[MeSH Terms] OR (("combinable"[All Fields]) OR "combinated"[All Fields] OR "combination"[All Fields] OR "combinational"[All Fields] OR "combinations"[All Fields] OR "combinative"[All Fields] OR "combine"[All Fields] OR "combined"[All Fields] OR "combines"[All Fields] OR "combining"[All Fields]) AND "cardiothoracic"[All Fields] AND ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "combined"[All Fields] OR "general surgery"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] Fields] OR "surgery"[All Fields] AND "operative"[All Fields]) OR "surgery"[All Fields]) OR "general surgery"[All Fields] OR "general surgery"[All Fields] OR "surgerys"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgerys"[All Fields] OR "surgerys"[All Fields] OR "surgerys"[All Fields]) OR "general surgery"[All Fields] OR "surgerys"[All Fields] OR "surgerys"[All Fields]))) AND (2013:2023[pdat]) used in searching the literature.

#### Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.





Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

#### **Quality Assessment and Data Synthesis**

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

#### RESULT

In the PubMed database, the results of our search brought up 14 articles, whereas the results of our search on SagePub brought up 91 articles. The results of the search conducted for the last year of 2013 yielded a total 9 articles for PubMed and 23 articles for SagePub. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SagePub. We included five research that met the criteria.

Li, et al<sup>1</sup> (2019) showed that the simultaneous performance of lung cancer surgery and cardiac surgery was effective and evidently safe in Group A. This treatment approach enabled earlier lung cancer resection and avoidance of the eventual complications associated with further surgical procedures. The simultaneous surgery described in this report enabled earlier tumor resection, eliminated perioperative cardiac risk and pain, and decreased medical costs by combining two operations into one session. Experienced surgeons may contribute to improved clinical outcomes in onestage surgery.

Yeginsu, et al<sup>5</sup> (2018) showed that simultaneous surgery is a safe and reliable option in the treatment of selected patients with concurrent CAD and operable lung cancer. simultaneous lung resections and OPCABG in patients with CAD accompanying LC is a safe and reliable surgical method. Several authors reported that it presented less mor-bidity and mortality compared to other options using CPB. Long-term survival is comparable in the others. On the other hand, data are not sufficient to conclude that combined OPCABG and lung resection are the best approach for the patient with concomitant LC and CAD. We need larger randomized studies for certainty.

Ma, et al<sup>6</sup> (2016) showed that combined OPCAB and pulmonary resection for early stage lung cancer patients with concurrent severe CHD is a relatively safe and effective treatment with satisfactory long-term survival rates, especially for those patients with three-vessel disease who are not usually candidates for percutaneous coronary intervention (PCI) before open surgery. Additionally, this procedure is a safe option in patients with three-vessel disease who are usually not candidates for preoperative PCI.

Author	Origin	Method	Sample	Result
Li et al, 2019 <sup>1</sup>	China	Case control study	20 patients	Twenty patients with severe CAD and coexisting lung cancer underwent simultaneous surgical interventions (Group A), and 20 patients with lung cancer underwent an isolated lung cancer operation (Group B). In Group A, the combined operations were carried out through 2 incisions in 3 patients, a single incision in 14 patients, and median sternotomy for heart surgery and thoracoscopic lobectomy for lung cancer in 3 patients. The single-incision approach was used in all patients in Group B. The operation time was longer and the blood loss volume was larger in Group A than B. No significant between-group differences were found in the 5-year

#### Table 1. The litelature include in this study

				relapse-free survival rate or 5-
Yeginsu et al, 2018 <sup>5</sup>	Turkey	Retrospective	10 patients	Mean patient age was 63.3 years (range 55-74). All patients were male. Six cases of squamous cell carcinoma, three of adenocarcinoma and one case of large cell carcinoma were diagnosed. Six patients had single-vessel CAD and 4 had two-vessel CAD. Three patients underwent OPCABG at first and then lung resection. The types of resections were one right pneumonectomy, three right upper lobectomies, one right lower lobectomies. Reoperation was performed in one patient due to hemorrhage. One patient developed intraoperative contralateral tension pneumothorax. One patient died due to acute respiratory distress syndrome at the early postoperative period.
Ma et al, 2016 <sup>6</sup>	China	study	34 patients	All patients survived the operation and no new myocardial infarctions (MIs) occurred in the perioperative period. The most frequent complications were cardiac arrhythmias (5 cases), atelectasis (4 cases), and pulmonary infections (2 cases). All patients were followed up for 5–60 months. Within this period, 6 patients (17.6%) died due to cancer recurrence. The 3- and 5-year survivals were 75% and 67% for these lung cancer patients, respectively.
Kaku et al, 2017 <sup>7</sup>	Japan	Retrospective study	18 patients	No complications associated with pulmonary resections were observed. Pathological examination revealed that 15 patients (83.3%) were diagnosed with lung cancers including 13 adenocarcinomas and two squamous cell carcinomas, with the clinical stages of 1A in 13 patients, 2A in one patient and 2B in one patient. Among them, five patients received the radical pulmonary resection subsequently, whereas 10 patients were unable to receive it due to their

				poor cardiopulmonary function. Kaplan-Meier analysis of patients with lung cancer revealed that the 5-year survival rate and progression- free survival (PFS) rate after 3 years from the surgery were 46.2% and 73.8%,
Kovacicova et al, 2014 <sup>8</sup>	Czech Republic	Retrospective study	12 patients	Group A consisted of 8 men and 4 women with the median age of $67.8 \pm 5.9$ years. In this group, 10 lobectomy procedures and 2 wedge resections for pulmonary metastasis were done. Nine patients underwent coronary artery revascularization, 2 patients underwent mitral valve replacement and one patient underwent tumor removal from the left atrium. In 5 patients, extracorporeal circulation (ECC) was needed, the remaining 7 patients underwent myocardial revascularization using an off- pump technique. Group B consisted of 7 men and 5 women with the age of $68.5 \pm$ 7.4 years. Ten lobectomy procedures and 2 wedge resections were performed.
Santavy et al, 2015 <sup>4</sup>	Czech Republic	Retrospective study	10 patients	There were nine males and one female. Their mean age was 69 (range: 59–79) years. Five patients were presented with a documented lung tumor and a concomitant heart disease. These were as follows: aortic stenosis; combined aorto-mitral disease with paroxysmal atrial fibrillation; aortic stenosis with dilatation of ascending orta; ischemic heart disease and acute non- transmural myocardial infarction. In the other group in five of the patients, pulmonary tumor was accidentally discovered on preoperative chest X-ray when cardiac procedure was planned. There was no hospital mortality. There was no reexploration because of bleeding. Cardiac part of procedures was in all cases without complications. Prolonged air-leak was found in one case. All patients with benign nathology are alive. In

the malignant group, one patient with staged approach died in terminal phase of disease and the second patient deceased because of disease- non-related reasons one year after surgery. The rest of them
after surgery. The rest of them
are followed up regularly by pneumo-oncology outpatient
department.

Kaku, et al<sup>7</sup> (2017) showed that the simultaneous resection of pulmonary tumor following cardiovascular surgery is safely performed, and is useful for the pathological diagnosis of the tumor. Further studies are warranted, however, this procedure may contribute to controlling the progression of lung cancer in patients with cardiovascular disease with comorbidities.

Kovacicova, et al<sup>8</sup> (2014) showed that the risk of simultaneously performed lung resection and cardiac surgery is not high. Despite the certain differences in clinical indicators between group A and B, the safety of simultaneous procedure, in group A, was evident. Furthermore, earlier lung resection was enabled and the eventual complications from further surgical procedure were avoided.

Santavy, et al<sup>4</sup> (2015) showed that combined heart surgery and lung resection can be performed without increased mortality and/or morbidity. The synchronous treatment avoids the necessity of a second intervention with good results and economic benefits. When indeterminate pulmonary mass at the time of cardiac operation is present, concomitant wedge excision should be performed if possible. If benign, the lesion will be appropriately managed and a second procedure will be avoided. If the lesion is malignant, the decision to proceed with a combined pulmonary resection should be individualized. In the attempt to minimize blood loss and theoretical CPB-induced tumor dissemination, off-pump revascularization techniques are preferred. In selected cases with suitable coronary anatomy, combined procedure can be performed from lateral thoracotomy using MIDCAB principles, especially in patients with left lower lobe affection.

### DISCUSSION

This systematic review involved a total of 110 patients who received combined heart surgery and lung tumor resection in 6 observational studies. Our comprehensive data analysis demonstrated that combined heart surgery and lung tumor resection had a low mortality rate and an acceptable complication rate. The incidence rate of reopening for bleeding was quite low. The incidence rates of postoperative respiratory complications and cardiac complications were similar. Overall, the present results suggest that combined heart surgery and lung tumor resection is safe with low mortality and complication rates.

Combined heart surgery and lung resection remain a controversial issue. This method facilitates the treatment of two major problems in one intervention with acceptable outcomes and overall cost reduction. With increasing age and frailty of the patient population, it is sometimes very difficult to perform two major surgeries during short time interval. Even, because of primary heart surgery complications, planned lung tumor resection can be delayed into the already inoperable condition due to malignancy spread. Psychological factor can also play an important factor, and few patients wish to have second extensive surgery.<sup>4</sup>

The combined heart revascularization with lung resection was first reported by Dalton in 1977 and Girardet in 1981. In 1985, Piehler, on his 41 patients, concluded that it is possible to perform both procedures from sternotomy safely at the same time. On the other hand, skepticism exists related to the effects of cardiopulmonary bypass on malignancy and to a possible greater risk for perioperative bleeding. There are also concerns about completeness of pulmonary resection and staging from non-standard sternotomy approach. The purpose of this report is to present our experience with the combined surgical approach and evaluate its benefits and safety.<sup>4</sup>

Patients who undergo combined heart surgery and lung tumor resection face a potential risk of postoperative bleeding. This concern raises from CPB use during heart surgery and, while performing heart and lung surgery simultaneously, the more complicated surgical procedure. Potential bleeding might be related to excessive heparin use, inadequate heparin neutralization, or platelet dysfunction during CPB. Bleeding might arise from the area of the lung resection, extensive mediastinal lymph node dissection and, not less frequently, intrapulmonary hemorrhage. Excessive bleeding increases the reexploration rate and eventually increases the mortality and complication rates. Off-pump CABG is one solution to reduce the potential risk of postoperative bleeding. During off-pump CABG, the intraoperative heparin dose was reduced and the platelet functions were less affected, leading to decreased bleeding. Alternatively, when CPB was necessary, the lung resection and lymph node dissection were best performed before heparinization or after reversal of heparin by protamine

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sulfate. Furthermore, compared with wedge excisions, anatomical lung resection was preferred to reduce the risk of intrapulmonary hemorrhage.<sup>9-11</sup>

The comparison of mortality and complication rates of combined cardiothoracic surgery and staged surgery was not performed in our study. More studies are needed to compare the mortality and morbidity of combined and staged surgery. Fifth, none of the included studies had described in detail whether complete or incomplete revascularization was achieved in coronary artery disease patients. So, the comparison between complete and incomplete revascularization for coronary artery disease patients was not performed in our study.

#### CONCLUSION

In summary, combined heart surgery and lung tumor resection had a low mortality rate and an acceptable complication rate. Subgroup analyses revealed that most patients with lung cancer underwent uncompromised anatomical resection and mediastinal lymph node sampling or dissection during combined cardiothoracic surgery, and showed off-pump CABG may reduce the complication rate compared with on-pump CABG. Further researches are still needed to verify these findings.

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