



# Should Cardiac Surgery and Lung Cancer Be Operated Simultaneously?

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## ABSTRACT

**Introduction:** There are limited studies regarding the concomitant surgical outcomes of resectable lung cancer (LC) and cardiac surgery (CS). This study aims to present the outcomes of cases with major pulmonary resection due to LC and CS that were operated upon simultaneously, and also present the literature associated with this procedure.

**Patients and Methods:** From October 2011 to May 2019, 10 LC patients (8 men, 2 women) who had undergone concomitant CSs were included in the study. The median age of the patients was 67 years (43-78). All patients underwent sternotomy, with left thoracotomy added after sternotomy for 1 left lower lobe tumour. Cardiac operations were performed for coronary artery problems in 7 cases, for aorta stenosis of 1 case, for mitral stenosis for 1 case and for an intra-atrial mass in 1 case.

**Results:** No mortality was observed in the early period. Re-operation linked to postoperative haemorrhage was not encountered. The most common complication was atrial fibrillation, which was seen in 3 cases. Nine cases underwent lobectomy, with 1 case undergoing bilobectomy. Four cases had adenocarcinoma, 2 cases had squamous cell carcinoma, 1 case had small cell carcinoma, 1 case had large cell carcinoma, 1 case had undifferentiated round cell carcinoma, and 1 case had atypical carcinoid tumour. The median duration of hospital stay was 5.5 days (4-10). Median follow-up was 74 months (1-91), with mortality observed in a total of 3 cases (30%); 2 due to recurrence and 1 due to cardiac arrest. Seven cases were tumour-free.

**Conclusion:** When limited cases studies and previous literature were investigated, the concomitant LC and CS method was observed to result in the highest number of appropriate, reliable and satisfactory outcomes.

**Key Words:** Lung cancer; cardiac surgery; cardiopulmonary surgery; concomitant heart lung operation

## Kalp Cerrahisi ve Akciğer Kanseri Eş Zamanlı Opere Edilmeli mi?

### ÖZET

**Giriş:** Rezektabl akciğer kanseri (LC) ve kardiyak cerrahi (CS) birlikte uygulanmasının cerrahi sonuçları açısından sınırlı sayıda çalışma mevcuttur. Bu çalışmada eş zamanlı LC nedeniyle majör akciğer rezeksiyonu ve CS uygulanan olgularımızın sonuçlarını literatür eşliğinde sunmayı amaçladık.

**Hastalar ve Yöntem:** Ekim 2011-Mayıs 2019 tarihleri arasında eş zamanlı CS ile opere edilen 10 (sekiz erkek, iki kadın) akciğer kanseri olgusu çalışmaya alındı. Olguların median yaşı 67 (43-78) yıl idi. Tüm olgularda sternotomi uygulandı, bir sol alt lob tümörüne sternotomi sonrası sol torakotomi eklendi. Yedi olgu koroner arter cerrahisi, bir olgu aort darlığı, bir olgu mitral darlığı ve bir olgu intraatriyal kitle nedeniyle kalp operasyonuna alındı.

**Bulgular:** Erken dönem mortalite izlenmedi. Postoperatif kanamaya bağlı reoperasyona rastlanmadı. En sık komplikasyon atriyal fibrilasyon ile üç olguda izlendi. Dokuz olguya lobektomi, bir olguya bilobektomi uygulandı. Dört olguda adenokarsinom, iki olguda skuamöz hücreli karsinom, bir olguda küçük hücreli karsinom, bir olguda büyük hücreli karsinom, bir olguda indifferansiye yuvarlak hücreli karsinom ve bir olguda atipik karsinoid saptandı. Median yatış süresi 5.5 gün (4-10) idi. Median 74 ay (1-91) takip süresinde iki olgu nüks, bir olgu kardiyak arrest nedeniyle toplam 3 (%30) olgu da mortalite görüldü. Yedi olgu tümör saptanmamış olarak takip edilmektedir.

**Sonuç:** Sınırlı vaka sayısı ve literatürler eşliğinde incelendiğinde LC ve CS eş zamanlı cerrahi uygun, güvenilir ve tatmin edici sonuçları ile tercih edilebilir.

**Anahtar Kelimeler:** Akciğer kanseri; kalp cerrahisi; kardiyopulmoner cerrahi; eş zamanlı kalp-akciğer operasyonu

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**INTRODUCTION**

Cardiac surgery (CS) and lung cancer (LC) are rarely encountered simultaneously. In 10% of LC cases, coronary artery disease is observed<sup>(1)</sup>. LC is frequently encountered with CS in preoperative tests and should not be primarily operated upon due to high cardiac risks, which are particularly dangerous risks while performing two-stage surgery. The reason for this is that after the coronary stent is inserted or if CS has been performed earlier, it leads to a delay in LC surgery by 6 weeks. This delay may cause dissemination or inoperability after some time is allowed to elapse. Performing LC surgery is generally not possible due to high cardiac risks. CS with concomitant thoracic surgery was reported for the first time by Dalton and Girardet<sup>(2,3)</sup>.

Simultaneous operations with coronary artery bypass surgery (CAB) with LC are reported at a rate of 0.4%<sup>(4)</sup>. Concomitant surgery may be chosen if the patient does not require a second operation, if tumoural spread needs to be prevented in the event of delayed LC treatment, to provide a good clinical outcome and for economic reasons. However, this combined surgery can increase morbidity and mortality. In this study, we aimed to present the cases and outcomes of CS with concomitant major lung resection operations, accompanied by the relevant scientific literature.

**PATIENTS and METHODS**

A total of 10 cases who underwent cardiac and LC operations from October 2011 to May 2019 were evaluated in this study. Lung resections for all cases were performed by a single surgeon (MA). All cases showed a negative N<sub>2</sub> on preoperative PET/CT. Seven cases were operated upon for coronary heart disease (CHD), 1 case for mitral stenosis (MS), 1 case for aor-

tal stenosis (AS) and 1 case for an intracardiac floating mass (Table 1). All cases underwent detailed physical examinations and blood biochemistry evaluations with routine LC evaluation methods, such as thoracic CT, brain MR, PET/CT, respiratory function tests, bronchoscopy, and, if necessary, transthoracic-transbronchial needle biopsy procedures. In addition to the cardiac tests, EKG, echocardiography and coronary angiography tests were also performed. CS was performed before major lung resection. Secondary pathologies were identified during the CS preoperative tests in 9 cases and during the LC preoperative test in 1 case. Three cases showed preoperative LC histologic diagnoses. In 6 cases, the questionable mass was excised with wedge resection without achieving a diagnosis, and a lobectomy was performed after CS. One case was diagnosed using a preoperative biopsy, with the resection being performed after the off-pump CAB. In 7 cases with coronary surgery, 3 underwent off-pump CAB and 4 underwent on-pump CAB. Surgeries were completed with sternotomy in 9 cases and with sternotomy and thoracotomy in 1 case. Major lung resection was performed with lobectomy with CS for 9 cases, while 1 case underwent bilobectomy. The demographic data, tumour measurements, operation outcomes, durations of hospital stay, and follow-ups of the cases were retrospectively evaluated. Permission to conduct the study was granted by the ethics committee (2019/27).

**Statistical Analysis**

The normally distributed data were evaluated using the Shapiro-Wilk test. Descriptive values without normal distribution were recorded as median values (minimum-maximum). Categorical data were stated as case numbers and percentages.

**Table 1. Preoperative patient characteristics**

No	Age	Sex	Tumour size (cm)	Smoking status (p/y)	Preoperative diagnosis
1	73	M	3.5	40	NSCLC
2	49	M	3	25	CHD
3	52	M	8	30	CHD
4	66	M	2	20	AS
5	68	F	2.5	0	CHD
6	59	F	4	0	CHD + NSCLC
7	78	M	4	45	CHD
8	43	M	5.5	28	MS
9	68	M	12	45	Atrial mass
10	71	M	4.5	30	CHD

cm: Centimetre, p/y: packets/year, NSCLC: Non-small cell lung cancer, CHD: Coronary heart disease, AS: Aorta stenosis, MS: Mitral stenosis.

### Surgical Technique

The concomitant heart and LC surgeries were mainly performed with median sternotomy. Thoracotomy incisions were also performed, but at lower rates. Median sternotomy ensured sufficient exposure for all major resections, apart from tumours in the left lower lung lobe.

Median sternotomy in the supine position was more easily applied than double lumen intubation surgery. Lung resection can be performed either on- or off- pump, however, off-pump resection was chosen, with the aim of not lengthening the pump duration and reducing complications. Cases without a diagnosis underwent wedge resection or biopsy, which was evaluated as a frozen section. All major lung resections were performed after the completion of CS. Heparin neutralisation was done with protamine. The side with LC was elevated and the operation table was turned 30 degrees. The distance between the heart and sternum was expanded with a left internal mammary artery retractor. The pleura was opened and after the adhesions were separated and the inferior ligament was freed, gas compressors were placed behind the lung and the hilus was pushed upwards. Grafts for CAB were brought near the pericardium to ensure that they remained within the pericardium. On the tumour side, the hilus was pulled upward by passing 3-4 silk sutures through the pericardium, a manoeuvre that made accessing and dissecting the hilus easier.

Major resections commonly began by binding the main lobal vein. The intrapericardial vein and main pulmonary artery were checked in case of tumours with central and hilar involvement. Lymph node dissection of the mediastinum was done through stations 2, 3, 4, 10 and 11 in the surgical field. Tumours on the left were easily reached via the 5<sup>th</sup> and 6<sup>th</sup> surgical stations and were completely removed. A single drain was placed in the resected hemithorax. For left lower lobectomy cases after closing the sternotomy, a left thoracotomy and standard oncologic left lower lobectomy was performed. All cases were taken to the intensive care unit under intubation. When the haemodynamic and ventilator parameters were stable, the patients were extubated.

### RESULTS

Of all the cases, 8 were male (80%) and 2 were female (20%), with a median age of 67 years (43-78). Eight cases (80%) were smokers who consumed a median of 30 packets/year (20-45). The median tumour size was 5.5 cm (2-12). Pre-operatively, 1 CAB case developed hypotension and bradycardia so off-pump CAB was changed to on-pump CAB. Four cases underwent left upper lobectomy, 3 cases underwent right upper lobectomy, 1 case underwent right upper bilobectomy, 1 case underwent right lower lobectomy and 1 case underwent a left lower lobectomy. Pathologic evaluation reported 4 cases of adenocarcinoma (1 case of bronchoalveolar carcinoma), 2 cas-

es of squamous cell carcinoma, 1 case each of small cell, large cell, atypical carcinoid and undifferentiated round cell carcinoma. Two cases were staged as T4 due to atrium invasion, with 1 case of severe mitral stenosis and another case of intra-atrial tumour-related floating thrombus. The median duration of ICU stay was 1.5 days (1-3), with the median hospital stay being 5.5 days (4-10). Complications were observed in 6 cases (60%). In 3 cases with developing atrial fibrillation, the sinus rhythm was managed with amiodarone. One case with developing atelectasis underwent a bronchoscopy procedure, while the other underwent clinical amelioration with physiotherapy. Developing pneumonia in one case was made to regress with antibiotic therapy. After sternotomy, the left lower lobectomy and thoracotomy case showed a prolonged air leak, which was controlled with conservative treatment (Table 2). All the patients were administered aspirin on the 1<sup>st</sup> postoperative day, while those with valve operations were also administered warfarin on the 2<sup>nd</sup> postoperative day. The follow-up duration was a median of 74 months (1-91), with recurrence observed in 2 cases (20%). Mortality was not observed in the early period, but in the long-term, 3 cases (30%) showed postoperative mortality. One patient died due to sudden cardiac arrest in the 6<sup>th</sup> month, while 2 patient died due to recurrence of cancer in the 24<sup>th</sup> and 36<sup>th</sup> month. Seven cases (70%) (stage I-II) were tumour-free.

### DISCUSSION

Initially, surgeons avoided performing CS simultaneously with LC surgery due to a high risk of haemorrhage that was linked to heparinisation<sup>(5)</sup>. However, after a few case studies were published, the concomitant LC and CS morbidity and mortality rates appeared to be within acceptable limits and the combined surgery began to be performed more frequently.

Median sternotomy is generally chosen for concomitant heart and lung operations. LC surgical treatment requires anatomic resection. Performing a median sternotomy may make it more difficult to perform oncologic surgery, however, it does not prevent anatomic resection. Even for cases with early-stage tumours (T1N0M0), non-anatomic or limited surgical resection lowers the expectations of survival<sup>(6)</sup>. As a result, all our patients underwent anatomic lobectomy operations.

Median sternotomy is reported to be less painful, have lower analgesic requirements, cause rapid amelioration of pulmonary functions and cause lower pulmonary complications<sup>(7,8)</sup>. It also appears to be better tolerated in patients with lower pulmonary reserves and insufficient pulmonary functions<sup>(9)</sup>. However, it is very technically difficult to perform a left lower lobectomy with median sternotomy. As a result, in our case series, the one case with left lower lobectomy had to have the sternotomy closed, following which the left thoracotomy was performed.

**Table 2. Preoperative and postoperative outcomes**

No	Incision	Cardiac procedure	Lung resection	Histology	Stage	ICU S/d	Postop complications	LOS	Follow-up/m
1	S	OPCABX1	RUL	Squamous Cell Ca	IB	1	AF	5	91
2	S	OPCABX1	Wedge + RUL	Small Cell Ca	IB	3	AF + Atelectasis	6	89
3	S	OPCABX1	Biopsy + LUL	Squamous Cell Ca	IIIA	1		4	88
4	S	AVR	Wedge + RUL	Adenocarcinoma	IA	2		9	86
5	S + T	ONCABX2	Wedge + LLL	Adenocarcinoma (BAC)	IB	3	Prolonged Air leak	7	82
6	S	ONCABX5	Wedge + RLL	Atypical Carcinoid	IIA	2		7	66
7	S	ONCABX3	Wedge + RUBL	Adenocarcinoma	IIA	1		5	37
8	S	MVR	LUL	Large Cell Ca	IIIB	1	AF	5	36
9	S	Atrial mass	LUL	Undifferentiated round Cell Ca	IIIB	2	Atelectasis + Pneumonia	10	24
10	S	ONCABX2	Wedge + LUL	Adenocarcinoma	IIB	1	Atelectasis	5	1

S: Sternotomy, T: Thoracotomy, OPCAB: Off-pump coronary artery bypass, ONCAB: On-pump coronary artery bypass, BAC: Bronchoalveolar carcinoma RUL: Right upper lobectomy, LUL: Left upper lobectomy, LLL: Left lower lobectomy, RLL: Right lower lobectomy, RUBL: Right upper bilobectomy, Ca: Carcinoma, ICU S/d: Intensive care unit stay/day, AF: Atrial fibrillation, Postop Cx: Postoperative complications, LOS: Length of stay, m: Month.

CAB cases with heart surgery carry a high risk of haemorrhage<sup>(10)</sup>. The causes of haemorrhage may range from the use of heparin, insufficient neutralisation of heparin with protamine and temporary functional insufficiency of platelets during cardiopulmonary bypass (CPB). Haemorrhage may develop in both fields during concomitant surgery. In the lung field, haemorrhagic foci are commonly observed in the resection field and in the lymph node dissection locations. The re-operation rates linked to haemorrhage are 5-15%<sup>(1,5,10,11)</sup>. In our study, none of our cases had haemorrhage that may have required a postoperative re-operation.

CPB may activate the inflammatory response syndrome, lower the immune response, disrupt the complementary system factors, cause lymphopaenia, neutropaenia, polymorphonuclear cell pulmonary accumulation or natural killer cell suppression<sup>(11,12)</sup>. Suppression of the immune system with CPB also causes malignant tumour growth and dissemination<sup>(3,4)</sup>. Additionally, no randomised studies were encountered that showed the specific effect of CPB on LC growth and dissemination<sup>(13,14)</sup>. In a study comparing on-pump and off-pump CAB LC resection cases, Suzuki et al.<sup>(15)</sup> observed no significant differences in dissemination-linked cancers and 2-5 year mortality rates. Additionally, if possible, it has been recommended that LC surgery be performed first for off-pump CPB<sup>(16)</sup>. In our series, all 7 CAB cases had the mass excised by wedge resection, with 3 having off-pump CPB performed in an attempt to minimise the dissemination risk. The remaining

4 CAB cases and 1 case each of MS-AS and intra-atrial mass were not appropriate for off-pump CPB, so lung resection was applied after performing on-pump CPB. One of the two T4 cases with atrium invasion had locally advancing tumours causing an intra-atrial floating thrombus, while the other had mitral valv replacement performed due to severe mitral stenosis. In both cases, advanced-stage (IIIB) tumour recurrence was observed.

Comparative studies identified fewer complications for off-pump CPB as compared to on-pump CPB<sup>(16-18)</sup>. Complication rates are reported as 59-80%. The most common complications in order of frequency of occurrence were atrial fibrillation, prolonged air leak, atelectasis, pneumonia, ventricular arrhythmia and pleural effusion<sup>(4,19)</sup>. In our study, the rate of appearance of complications was similar to the literature (60%) (Table 2).

Mortality rates in the early periods have varied from 0-6% in previous publications<sup>(5,7,11,20,22)</sup>. In our study, mortality was not observed in the early period. In spite of the median hospital stay being 12-15 days in the previous literature, in our study it was shorter than many series (5.5 days)<sup>(7,11,13,20)</sup>.

In the long-term follow-up (median 74 months) of concomitant operations, survival is frequently linked to the stage of LC. With median sternotomy, hilar and mediastinal lymph node dissection is accepted as being more difficult<sup>(21)</sup>. For concomitant surgeries, Miller et al.<sup>(22)</sup> reported that a poor long-term survival rate was related to inappropriate or insufficient lymph node dissection. For our limited case numbers, during a median follow-up of 74 months, 7 cases were identified as

tumour-free (70%). These 7 cases were early-stage (stage I-II) cases. In the literature, it appears that early-stage LC cases show better survival rates after concomitant surgery<sup>(1,19,23)</sup>. Publications report the 5-year survival to be 34-85%<sup>(5,7,18,22,24)</sup>.

In our study, concomitant surgery for LC and CS was the chosen method and had a number of advantages, such as non-requirement of a second operation, prevention of danger due to delayed treatment of LC, less pain and requirement of less analgesia, allowance of surgery in accordance with oncologic principles, better surgical outcomes, satisfactory survival expectations and economic costs. The morbidity rate of the same was acceptable. As per our recommendation, if an undiagnosed, resectable pulmonary mass is identified during cardiac operation testing, wedge resection may be performed first, followed by anatomic resection after CS. In appropriate cases, performing off-pump CPB may minimise dissemination of the cancer.

### LIMITATIONS

The study is limited by the small number of cases and its retrospective evaluation method. There is a need for broad-erisive comparative-controlled randomised trial studies.

### CONCLUSION

When limited cases studies and previous literature were investigated, the concomitant LC and CS method was observed to result in the highest number of appropriate, reliable and satisfactory outcomes.

### CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

### AUTHORSHIP CONTRIBUTIONS

*Concept/Design:* MA

*Analysis/Interpretation:* MA

*Data Acquisition:* MA

*Writing:* MA

*Critical Revision:* MA

*Final Approval:* MA

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