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ORIGINAL ARTICLE

Lung Cancer Surgery in Patients With a History of Coronary Artery Bypass Graft: A Multicentre Study

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Background Lung cancer surgery may be required for patients with a history of coronary artery bypass graft (CABG). In this study, we evaluated the general characteristics of patients, the difficulties experienced during and after lung cancer surgery and complications and mortality rates.

Method Patients who were operated on for primary lung cancer between January 2012 and July 2017 in the participating centres were analysed retrospectively (n=7,530). Patients with a history of CABG (n=220) were examined in detail. This special group was analysed and compared with other patients operated on for lung cancer who did not have CABG (n=7,310) in terms of 30-day mortality and revision for haemorrhage.

Results Of the 7,530 patients operated on for primary lung cancer, 2.9% were found to have undergone CABG. Surgical revision was required in the early postoperative period for 6.8% of those who had CABG and 3.5% in those who did not have CABG (p=0.009). Thirty-day (30-day) mortality was 4.5% in those who had CABG and 2.9% in those who did not have CABG (p=0.143). Further analysis of patients who had undergone CABG demonstrated that video-assisted thoracoscopic surgery (VATS) resulted in fewer complications (p=0.015). Patients with a left-sided left internal mammary artery (LIMA) graft had a higher number of postoperative complications (p=0.30).

Conclusions Patients who had CABG suffered postoperative haemorrhage requiring a revision twice as often, and a tendency towards higher mortality (non-statistically significant). In patients with a history of CABG, VATS was demonstrated to have fewer complications. Patients with a LIMA graft who had a left-sided resection had more postoperative complications.

Keywords Coronary artery bypass surgery • Lung cancer surgery

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Introduction

Cardiovascular disorders are the most common cause of death around the world [1], and coronary artery bypass grafting (CABG) surgery is a life-saving procedure in patients suffering from such disorders. Lung cancer is the leading cause of cancer-related death [2], although lung cancer and coronary artery disease, which have similar aetiologies, may co-exist in the same patient. Various difficulties can be encountered given the need to operate in anatomically confined areas for patients with a history of CABG and who will be operated on for lung cancer. Only limited studies of patients with lung cancer with a history of CABG surgery have been published [3–6].

Adhesions that occur after CABG surgery, resection site of a bypass graft, and vascular graft injuries are the leading problems faced by patients following lung cancer surgery. Although mechanical causes are thought to be risky for patients, the history of cardiac disease in the CABG patient group and the applied medical treatments increase the risk of operations to a significant degree. In particular, left upper-side operations have been evaluated in the literature, while full evaluations of patients are lacking [3,6,7].

In this study, patients with a previous history of CABG surgery were considered to have undergone more complicated lung cancer surgery, and that recovery may be different in these patients when compared to other patient groups. Accordingly, we evaluated the perioperative status of all patients who underwent CABG in the past and who were operated on for lung cancer and compared them to other patients operated on for lung cancer who did not have CABG in terms of only 30-day mortality and revision for haemorrhage. To begin with, the prevalence of this condition was investigated, after which we aimed to gather a wide range of information on the potential difficulties associated with the need for lung cancer surgery in patients with a previous history of CABG, while also investigating the feasibility of lung cancer surgery in such patients.

Materials and Methods

This study was conducted with the participation of seven academic centres that actively provide training in thoracic surgery, that carry out important studies related to thoracic surgery, that perform a large number of lung cancer operations, and that employ at least three thoracic surgeons. The study period was kept up to date and narrow in order to avoid differences between centres in their approach to the patients. Particular attention was paid to the patient evaluation methods applied by each centre to ensure alignment with literature, particularly in recent years. The study was designed to facilitate the enrolment of similar number of patients from seven different centres, and a retrospective analysis was conducted of the patients operated on for primary lung malignancy in these centres between January 2012 and July 2017. Patients who were operated on for diagnostic or exploratory purposes, and those who underwent both CABG and lung resections in the same session were excluded from the study. Patients with a previous history of CABG surgery were examined in detail. In order to reveal the difference between this patient group and the other patient group with no history of CABG surgery, who underwent surgery for lung cancer, a comparison was made between two groups in terms of revision for haemorrhage and 30-day mortality. The data collected from CABG patients included age, sex, comorbidities, information about previous CABG surgery, operations performed for lung cancer, and the time between operations, lung cancer histology, and stage (according to the 8th Edition Cancer Staging System [8]), anticoagulant/antiplatelet drug use, difficulties encountered during the operations, postoperative period and complication status (prolonged air leak, blood product replacement, pneumonia, atelectasis requiring bronchoscopy, pulmonary embolism, postoperative haemorrhage, arrhythmia and other cardiac pathology, wound infection, and postoperative liver and kidney pathologies). duration of hospitalisation, blood transfusion status, revision surgery requirements, and 30-day mortality status. CABG and non-CABG patients were compared in terms of revision for haemorrhage and 30-day mortality.

Patients who underwent repeat surgery as a result of haemorrhage prior to being discharged after the initial lung surgery were considered to have undergone revision surgery. The revision criterion for all centres participating in the study was determined to be continuous postoperative bleeding. The collected data were merged in line with the data determined by the investigators prior to launching the study. Any conflicting data submitted by the centres were excluded. Cases with conflicting information about surgical procedure were excluded. The pooled data were shared with a statistician.

Preoperative evaluations were made of all patients in line with the standard oncological procedures related to primary lung malignancy. Patients with a history of CABG were evaluated preoperatively in terms of cardiac status, and such tests as transthoracic echocardiographs and treadmill stress tests were performed when necessary. Patients who were found to be at high risk during the cardiological examination were considered as medically inoperable cases, and surgery was postponed in patients who were found to have a new focus of ischaemia, decompensated heart failure, severe arrhythmia and symptomatic valvular heart disease, and those who required a new line of cardiological therapy and alternative treatment methods were investigated. Accordingly, these patients were excluded from the study, while patients who remained stable after CABG surgery were retained. Unless otherwise stated by cardiology physicians, anticoagulant/antiplatelet therapy was discontinued 2 or 7 days prior to surgery.

The outcome was major complications, reoperations for bleeding, and first 30-day mortality between patients undergoing lung cancer operations with and without a CABG operation in their history.

Table 1 Demographic data of patients with a history of coronary artery bypass grafting surgery.

	N=220
Sex	
Male	209 (95.0)
Female	11 (5.0)
Operation Type	
Thoracotomy	191 (86.8)
VATS	29 (13.2)
Resection Type	
Left upper lobectomy	44 (20.0)
Left lower lobectomy	19 (8.6)
Left pneumonectomy	19 (8.6)
Right upper lobectomy	45 (20.5)
Right superior bi-lobectomy	10 (4.5)
Right inferior bi-lobectomy	5 (2.3)
Right lower lobectomy	30 (13.6)
Right middle lobectomy	14 (6.4)
Right pneumonectomy	14 (6.4)
Segmentectomy	12 (5.5)
Wedge	8 (3.6)
Histology	
Adenocarcinoma	86 (38.4)
SCC	117 (52.2)
Others	21 (9.4)
Stage	
IA1	16 (7.3)
IA2	13 (5.9)
IA3	14 (6.4)
IB	51 (23.2)
IIA	25 (11.4)
IIB	49 (22.3)
IIIA	37 (16.8)
IIIB	7 (3.2)
IVA	3 (1.4)
T0N0	5 (2.3)
Concomitant diseases	
Hypertension	106
COPD	32
Diabetes mellitus	60
Other cardiac diseases	14
Secondary malignancy	13
Other	15
Complication	
Prolonged air leak	32
Atelectasis	11
Pneumonia	19
Arrhythmia	39
Other	20
Use of Bypass graft	
Left internal mammary artery	174 (79.1)
Right internal mammary artery	11 (5.0)
Bilateral internal mammary artery	14 (6.4)
Other	21 (9.5)

Data are n or n (%).

Abbreviations: VATS, video-assisted thoracoscopic surgery; SCC, squamous cell carcinoma; COPD, chronic obstructive pulmonary disease.

The study protocol was approved by the Institutional Review Board of the Ege University Medical School (decision no: 17-11.1/38), and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Statistical Analysis

The statistical analysis was carried out using SPSS version 22.0 software (IBM Statistics for Windows version 22; IBM, Armonk, NY, USA). For the comparison of categorical data, Pearson's chi square test was used. Multiple regression analysis was performed for multivariate analysis on CABG patients. Continuous data were expressed as mean ±standard deviation (minimum–maximum), while categorical data were expressed as n (%) in Table 1. A confidence level of 95% was selected, and a p-value of <0.05 was considered to be statistically significant.

Results

Of the 7,530 patients who were operated on for primary lung cancer in the participating centres in the study between January 2012 and July 2017, 220 (2.9%) were found to have undergone a CABG operation, while 7,310 had no history of CABG. The mean duration between the lung operation and CABG surgery was 71.41±60.87 months (range, 1–300 months). In the CABG group, 209 (95.0%) patients were male, 11 (5.0%) were female, and mean age was 65.92±7.17 years (range, 48–84 years).

Of the CABG patients, 127 (57.7%) were found to have been operated on from the right side, while 93 (42.3%) patients were operated on from the left. Eight (8) (3.6%) underwent a wedge resection, while all other patients underwent an anatomical resection (Table 1). In addition to these operations, 14 patients underwent sleeve resections, while six had wedge resections, three had vertebra resections, three had segmentectomies, and two had rib/chest wall resections in addition to a complete resection. Four (4) cases had synchronous lung cancer and in two of these cases, the tumours were excised through the wedge, while a segmentectomy was used for the excision of the other two. Five (5) cases had T0N0 disease due to neoadjuvant treatments. The mean operation duration was 216±78.79 minutes (range,

50–540 minutes), and the mean duration of hospitalisation was 8.8±14.61 days (range, 1–210 days).

A thoracotomy was performed on 191 patients, while video-assisted thoracoscopic surgery (VATS) was planned for 33. A thoracotomy was preferred in the presence of severe pleural adhesions, accounting for four patients in whom a thoracoport insertion was not possible, and an operation was completed with VATS in 29 patients. Severe pleural adhesions were observed in 94 patients (42.7%), whereas parenchymal adhesions to the left internal mammary artery (LIMA) graft were seen in 47 patients (21.4%). No adhesion was reported in 79 patients (35.9%). Some parenchymal tissue was left so as not to damage the graft in 15 (6.8%) patients with adhesion to the graft, while there was no need to leave any parenchymal tissue in 32 patients with adhesion to the graft, and no patients were observed to have myocardial infarction or graft injuries during their operations. Severe bleeding from foci other than the graft was observed in 20 (9.1%) cases during operation, although all of the bleeding foci were controlled during the operation and no mortalities were recorded.

Patients with a history of LIMA grafts who underwent a left-side operation were compared with those who underwent a right-side operation. The number of complications, mortalities, revisions, and blood product replacements were found to be similar in both groups, with no significant difference observed (Table 2). Patients who underwent a LIMA graft were compared with those who underwent surgery on the same side without using the LIMA. As a result, 81 patients who underwent surgery on the left side using LIMA were compared with 12 patients who underwent surgery on the same side without using LIMA graft. Comparison of the two groups showed no statistically significant difference in terms of mortality or revision surgery (in patients with LIMA graft, the number of patients requiring revision was four [4.9%], without a LIMA graft, one patient required revision [8.3%; p=0.627]; in those with a LIMA graft, six patients died [7.4%] and in those without a LIMA graft, one patient died [8.3% p=0.910]), although complications were noted in 59 patients (72.8%; in the respiratory tract in 25 patients and in the heart in 16 patients, with other complications occurring in 18 patients). Of the 44 patients who underwent left upper lobectomy (LUL), mortality occurred in four (9.1%), and while complications were noted in 29 (65.9%) of these patients, none underwent a revision. Compared with other resection types, the revision rates of the patients who received LUL were found to be lower, with no difference was seen in the other factors (Table 3). A total of three patients underwent a right upper lobectomy and a graft on the same side, and all of these patients had no revision.

Comorbidities were observed in 155 patients (70.5%) who were known to have undergone CABG surgery, aside from their coronary pathologies (Table 1). There were 173 stage I and II patients, while there were 47 stage III and IV patients. Only two advanced-stage patients required revision, and one patient died. Forty-one (41) patients underwent neoadjuvant therapy. Preoperative anticoagulant/antiplatelet use was present in 203 patients (92.3%). Of the patients using anticoagulant/antiplatelets, 188 (acetylsalicylic acid, n=162; clopidogrel, n=25; dipyridamole, n=1) were using antiplatelet medication and 15 were using an anticoagulant. The mean preoperative international normalised ratio (INR) value of the patients was found to be 1.05±0.29 (range, 0.79–4.49), while the mean activated partial thromboplastin time (aPTT) value was 26.63±7.24 (range, 10.1–55). Unless otherwise stated by cardiologists, anticoagulant/antiplatelet therapy was discontinued 2–7 days prior to surgery and low-molecular-weight heparin was started for 208 (94.5%) patients. The remaining 12 (5.5%) patients received no treatment.

The CABG operation notes of the cardiovascular surgeons were obtained for the patients, from which a LIMA graft was found to have been used in the majority of patients (n=174).

In the CABG group, complications occurred in 143 (65.0%) patients; blood product replacement was needed in 106 (48.2%) patients, with erythrocytes replaced in 99 of these patients. Fifty-six (56) underwent plasma replacement. In patients requiring erythrocyte replacement, approximately 2.89 units of replacement were needed in each. For those requiring plasma replacement, around 2.23 units of replacement were used in each.

In a multivariate analysis of the data on the interval between two operations in patients undergoing CABG, as well as their age, operation side, type of lung surgery, use of internal mammary artery (IMA), INR–aPTT, anticoagulant/antiplatelet use, and VATS, it was found that no single factor affected revision and mortality. In terms of revision for haemorrhage and 30-day mortality, 15 (6.8%) of the patients in CABG group were found to require surgical revisions in the early postoperative period, whereas this rate was 255

Table 2 Left-side operated patients (using left internal mammary artery) versus patients operated on with the right side.

	Patients (n)	Revision Requirement	Mortality in the First 30 d	Complication
Left-sided operated patients (using LIMA)	81	4 (4.9)	6 (7.4)	59 (72.8)
Right-sided operated patients	99	6 (6.1)	3 (3.0)	61 (61.6)
P		0.744	0.180	0.112

Data are n (%) unless otherwise indicated.

Abbreviation: LIMA, left internal mammary artery.

Table 3 **Left upper lobectomy (LUL) patients versus other patients.**

	Patients (n)	Revision Requirement	Mortality in the First mo	Complication
LUL	44	0	4 (9)	29 (66)
Other resection type	176	15 (8.5)	6 (3.4)	114 (64.8)
P		0.045	0.106	0.888

Data are n (%) unless otherwise indicated.

(3.5%) for the non-CABG group. The patients in the CABG group were observed to need more revision (p=0.009). Ten (10) (4.5%; five due to cardiac causes and five due to respiratory tract complications) patients were determined as having experienced 30-day mortality versus 209 (2.9%) patients in non-CABG group. No statistically significant difference was observed between the groups in this regard, although the mortality rate was higher in CABG group (p=0.143) (Table 4).

No early mortality or revision was observed in the patients operated on with VATS, and no statistical difference was identified when a comparison was made with other patients. However, it is noteworthy that complications were observed in 13 (44.8%) patients who underwent VATS, whereas this rate was 130 (68.1%) in the thoracotomy group. In short, significantly fewer complications were observed in the VATS group (p=0.015). Among patients operated on with VATS, 15 (51.7%) underwent ipsilateral surgery with an IMA graft and 13 (44.8%) underwent contralateral surgery with an IMA graft. Five (5) patients (17.2%) operated on with VATS underwent a wedge (two patients) or segmentectomy, whereas 15 of the 191 thoracotomy patients (7.8%) underwent a wedge (six patients) or segmentectomy. There was no statistical difference in terms of distribution.

Discussion

LIMA grafts are the preferred option in most CABG surgeries [9]. During the preparation of the LIMA graft, the pleura may be opened, and inflammation may increase in the area being operated on, resulting in the possibility of severe adhesions developing in the apex, chest wall, and mediastinal region [6]. In some cases, lung tissue may adhere to the graft [6,10,11], and fatal complications may occur during the separation of the LIMA graft from the lung, or the dissection of the lung from the chest wall and mediastinum [10,11]. Hypotension, myocardial ischaemia, infarction, and death may develop as a result of LIMA injury [3], although Halkos et al. [4] developed a technique aimed at preventing such a situation that allows some of the parenchymal tissue adjacent to the LIMA graft to be left on the graft. Santini et al. [12] reported that the amount of lung tissue left could be minimised through the use of certain instruments, and Shah et al. [6], accordingly, performed a LUL with VATS in 14 patients with previous LIMA grafts, completing the operation while leaving some lung tissue on the LIMA graft. Wei et al. [3] suggested that this was not necessary, claiming that, if necessary, an open surgical intervention would be more appropriate according to oncological principles, and reported severe adhesions in 26/28 patients. Funaki et al. [7] performed upper lobectomies with VATS on two patients who had undergone a previous CABG, and observed similarly severe adhesions. In another study, LUL was able to be resected since the LIMA graft was sacrificed due to invasion [10], although dissections to be performed in these areas are reported as requiring particular attention [6]. In our study, LIMA was used in the majority of patients (79.1%), and a parenchymal adhesion was observed on the LIMA grafts in 47 patients (21.4%). Some of the parenchymal tissue was left behind so as not to damage the graft in 15 (6.8%) patients with adhesion to the graft. However, some of us, including the senior author, prefer to dissect the LIMA from lung parenchyma (Figure 1). It was recommended that a small amount of lung tissue should be left on the graft in cases where there is no distinction despite dissection. Oncological principles were followed as much as possible. We consider that there is no obstacle to the performance of full oncological procedures, provided that there are no dense adhesions to the IMA graft. No LIMA injury was reported in our case series, and no development of myocardial infarction was observed during surgery, although we believe that a more controlled dissection should be carried out in CABG than in other cases. Graft injuries can be fatal, but a cardiac pump may alleviate the problem if activated on time. Thus, it would be more appropriate to perform these surgeries in centres where cardiac interventions can be made. Furthermore, electrocardiogram monitoring and catheterisation procedures should be followed during the operation to

Table 4 **Revision and mortality status of patients in the coronary artery bypass grafting (CABG) and non-CABG groups.**

	Patients	Revision Requirement	Mortality in the First 30 d
CABG group	220	15 (6.8)	10 (4.5)
Non-CABG group	7,310	255 (3.5)	209 (2.9)
p		0.009	0.143

Data are n (%) unless otherwise indicated.

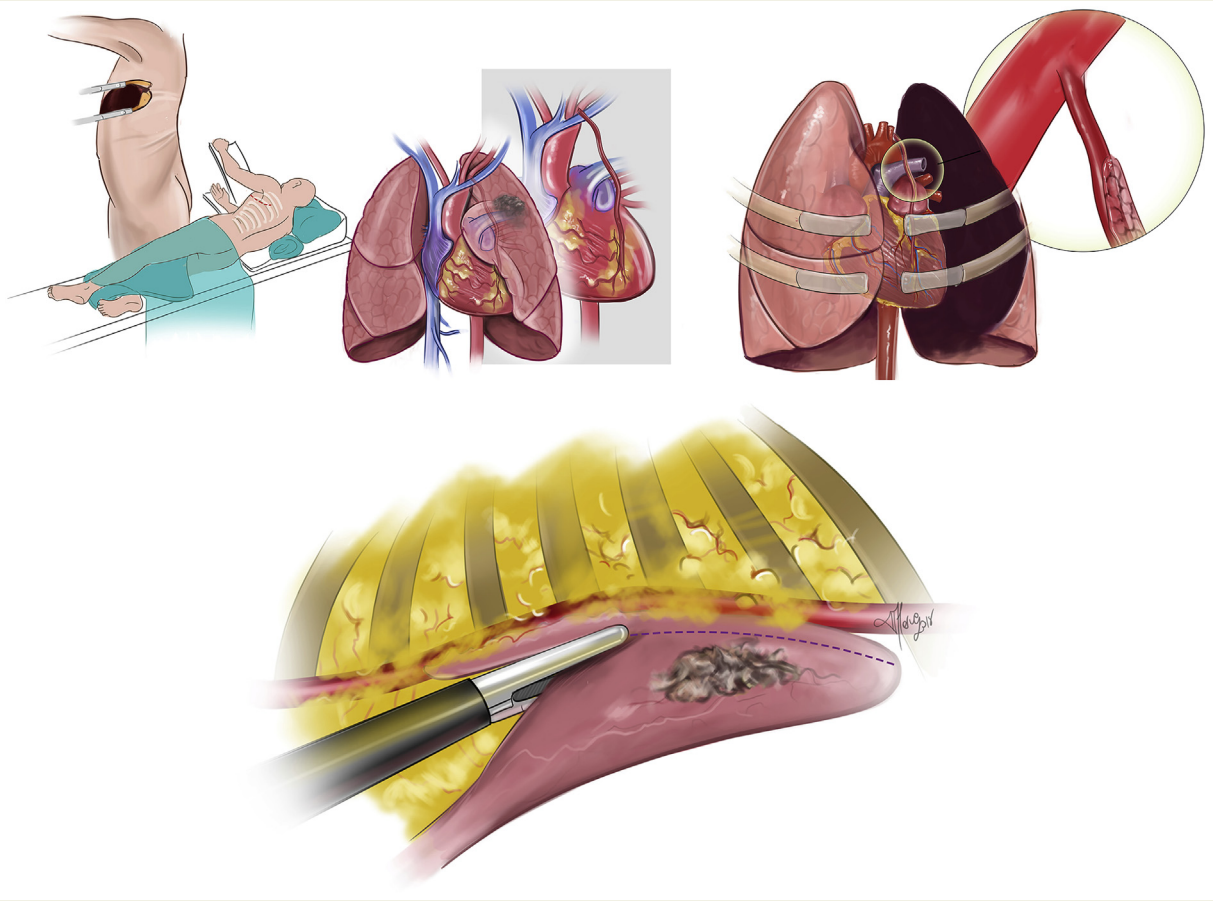


Figure 1 Left upper lobe parenchymal fragment left on a left internal mammary artery graft.

monitor for possible infarctions, allowing for necessary interventions to be made.

In a study by Wei et al. [3], it was found that 28 of 458 patients who underwent LUL had CABG, and only one of these patients was able to be operated upon with robotic surgery. Shah et al. [6] reported that 14 of 290 LUL cases had undergone CABG in the past, 13 of whom were operated on with VATS LUL. In a study by Papiashvili et al. [5], successful operations were reported in three of the eight CABG-treated patients with VATS. Singhatanadgige et al. [11] reported a successful upper lobectomy on a patient with history of CABG but noted that possible adhesions around the LIMA could lead to numerous problems in the future. In another study, more frequent mortality and complications were observed in VATS procedures performed on patients who had previously undergone a sternotomy [13]. In our study, VATS was planned for 33 of the cases, and a thoracotomy had to be carried out as a result of severe adhesions in four cases. Operations were able to be completed with VATS in 29 cases, of which 18 were left-side procedures. In our study sample, when cases treated with VATS were compared with those treated with a thoracotomy, fewer complications were found to have occurred in the VATS cases, although there was no difference between these groups in terms of revision and early mortality. Based on these findings, it can be concluded that the authors should consider abandoning the notion that a history of CABG surgery precludes VATS, and that VATS may also be attempted in patients with a history of CABG surgery.

There is a paucity of data on patients who underwent left-sided operations, although in the present study 93 (42.3%) patients in the study sample underwent such a procedure. A comparison of LIMA patients who underwent a left-sided operation and those who underwent a right-sided operation revealed no difference in terms of mortality, revision, or complication rates. When only LUL-treated patients were compared with all other treatments, no difference was observed in complication or mortality rates, and no revision was needed in the LUL patients. This was attributed to the fact that dissection is performed more carefully in LUL patients. Based on these results, it can be concluded that all cases with CABG should be evaluated as a whole, rather than evaluating them only in terms of the risk associated with LIMA grafts.

In conclusion, lung cancer surgical techniques are being kept up to date, although the treatable patient population is increasing daily as incidences of lung cancer continue to increase. The population of patients who received CABG

represent an important group among these patients. No clear data relating to the co-existence of these two conditions is present, although in the present study the ratio of patients who underwent CABG surgery prior to lung cancer operations was determined to be 2.9% (n=220/7,530), and lung cancer surgeons are more likely to encounter such a condition, given its prevalence. The efficacy of the antiplatelet/anticoagulation therapy undertaken by these patients, the existing cardiac pathology, and the presence of more dense adhesions associated with the previous surgery attach particular importance to this patient population. These factors can be considered to cause an increase in mortality rates during and after surgery, and especially in the rate of revision for haemorrhage in patients undergoing CABG. Persistent dissections of the LIMA may lead to fatal consequences, and it must be kept in mind that reoperations will be inevitable if more meticulous bleeding and leakage control is not carried out than in the normal patient population. Despite all these measures, it is necessary to be both aware of and prepared for such a situation, both during and after the operation.

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