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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Total coronary revascularization via left anterior thoracotomy: Comparison of early- and mid-term results with conventional surgery

Sol anterior torakotomi ile total koroner revaskülarizasyon: Erken ve orta dönem sonuçların konvansiyonel cerrahi ile karşılaştırılması

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ABSTRACT

Background: This study aimed to evaluate the efficacy and safety of total coronary revascularization via left anterior thoracotomy (TCRAT) by comparing it to conventional coronary artery bypass grafting (CABG) with median sternotomy.

Methods: In this retrospective study, 108 patients (95 males, 13 females; mean age: 57.1±8.8; range, 41 to 75 years) who underwent TCRAT (Group 1) and 154 patients (126 males, 28 females; mean age: 61.2±9.8; range, 31 to 79) who underwent conventional CABG (Group 2) between February 1, 2021, and September 1, 2022, were evaluated. The operations were performed by the same surgical team. Preoperative, operative, and postoperative data of patients and mid-term follow-up data were analyzed.

Results: Mean cardiopulmonary bypass and cross-clamp times, respectively, were 167.70±68.93 and 77.03±38.18 min in Group 1 and 106.64±38.27 and 62.21±24.06 min in Group 2 (p<0.001). During the postoperative period, the all-cause mortality rate was 5.8% (n=9) in Group 2, while it was 0.9% (n=1) in Group 1; there was a statistically significant difference between the two groups (p=0.037). Nevertheless, the mean preoperative EuroSCORE (European System for Cardiac Operative Risk Evaluation) II was 2.59±2.3 in Group 2, which was significantly higher than the mean EuroSCORE II of Group 1 (1.37±1.5; p<0.001). The mean hospitalization duration for Group 2 was 6.99±3.37 days, and the mean hospitalization duration for Group 1 was 6.77±4.24 days. Duration of hospitalization was statistically significantly shorter in Group 1 (p=0.047). In addition, the mean perioperative number of erythrocyte suspension transfusions in Group 1 was 1.51±1.74, while it was 1.86±1.75 in Group 2. Significantly fewer erythrocyte suspension transfusions were performed in Group 1 (p=0.033).

Conclusion: The findings of our study indicate that TCRAT is a safe and viable technique when performed on a select patient group compared to the conventional method.

Keywords: Coronary artery bypass, minimally invasive surgical procedures, thoracotomy.

ÖZ

Amaç: Bu çalışmada, total koroner revaskülarizasyonun (TCRAT) etkinliği ve güvenliği, median sternotomi ile konvansiyonel koroner arter baypas greftleme (KABG) ile karşılaştırılarak değerlendirildi.

Çalışma planı: Bu retrospektif çalışmada, 1 Şubat 2021-1 Eylül 2022 tarihleri arasında TCRAT uygulanan 108 hasta (Grup 1; 95 erkek, 13 kadın; ort. yaş: 57.1±8.8; yıl; dağılım, 41-75 yıl) ve konvansiyonel KABG uygulanan 154 hasta (Grup 2; 126 erkek, 28 kadın; ort. yaş: 61.2±9.8 yıl; dağılım, 31-79 yıl) değerlendirildi. Ameliyatlar aynı cerrahi ekip tarafından gerçekleştirildi. Hastaların ameliyat öncesi, ameliyat sırası ve ameliyat sonrası verileri ile orta dönem takip verileri analiz edildi.

Bulgular: Ortalama kardiyopulmoner baypas ve kros-klemp süreleri sırasıyla Grup 1'de 167.70±68.93 ve 77.03±38.18 dk iken Grup 2'de 106.64±38.27 ve 62.21±24.06 dk idi (p<0.001). Ameliyat sonrası dönemde, tüm nedenlere bağlı ölüm oranı Grup 2'de %5.8 (n=9) iken Grup 1'de %0.9 (n=1) idi; iki grup arasında istatistiksel olarak anlamlı bir fark bulundu (p=0.037). Bununla birlikte, Grup 2'deki hastaların ameliyat öncesi ortalama EuroSCORE (European System for Cardiac Operative Risk Evaluation) II puanı 2.59±2.3 idi, ve bu değer Grup 1'deki hastaların ortalama EuroSCORE II puanına (1.37±1.5) kıyasla anlamlı derecede yüksekti (p<0.001). Grup 2 için ortalama hastanede yatış süresi 6.99±3.37 gün idi ve Grup 1 için ortalama hastanede yatış süresi 6.77±4.24 gün idi. Hastanede kalış süresi Grup 1'de istatistiksel olarak anlamlı şekilde daha kısaydı (p=0,047). Ayrıca, Grup 1'de perioperatif ortalama eritrosit süspansiyonu transfüzyon sayısı 1.51±1.74 iken, Grup 2'de 1.86±1.75 idi. Grup 1'de anlamlı derecede daha az eritrosit süspansiyonu transfüzyonu yapıldı (p=0.033).

Sonuç: Çalışmamızın sonuçları, TCRAT'nin konvansiyonel yöntemle karşılaştırıldığında seçilmiş bir hasta grubunda güvenli ve uygulanabilir bir teknik olduğunu göstermektedir.

Anahtar sözcükler: Koroner arter bypass, minimal invaziv cerrahi prosedürler, torakotomi.

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Coronary artery bypass grafting (CABG) is the most common cardiac surgical procedure worldwide. It is an important revascularization method, particularly for patients with diffuse vascular disease, diabetes mellitus, left main coronary artery disease, left ventricular dysfunction, and complex lesions.[1,2] Median sternotomy is the most commonly used incision in cardiac surgery because it provides excellent access and exposure to the heart and the surrounding anatomical and main vascular structures in the thorax. Infectious or noninfectious complications may develop after median sternotomy.

Recently, minimally invasive surgical methods have been increasingly used in cardiac surgery, particularly in treating valvular diseases. These methods aim to shorten the recovery period while still adhering to surgical principles. Some of these methods include surgery on the beating heart and the elimination of cardioplegia altogether, as well as strategies that avoid sternotomy.[3,4] The first minimally invasive direct CABG procedure was performed in the mid-1990s, followed by endoscopic total CABG in 1998.[5,6] Minimally invasive CABG, performed via a left anterior minithoracotomy, gained popularity in the late 2000s.[4] However, no technique has replaced traditional CABG surgery, which is routinely performed via sternotomy. Babliak et al.[7] reported a new method in 2019 for total coronary revascularization via left anterior thoracotomy (TCRAT), which they claimed is applicable to most patients.

Numerous studies have been conducted to determine the effectiveness and safety of TCRAT. However, due to the technical complexity of the procedure and the limited number of comparative studies, there is a lack of high-quality evidence available in the literature on this topic. The objective of this study was to assess the efficacy and safety of TCRAT, including initial experience, by comparing the early- and mid-term outcomes with those of patients who underwent CABG surgery with a standard median sternotomy.

PATIENTS AND METHODS

In this retrospective study, patients who underwent TCRAT or CABG via median sternotomy by the same surgical team at the cardiovascular surgery clinic of the Gülhane Training and Research Hospital between February 1, 2021, and September 1, 2022, were reviewed. A total of 345 patients underwent coronary artery bypass surgery between the specified dates. Eighty-three patients who underwent hybrid intervention, additional cardiovascular surgery (e.g., heart valve surgery, ascending aorta surgery, and carotid endarterectomy) in the same session, beating heart surgery, and redo CABG surgery were excluded from the study. Consequently, 262 patients were included.

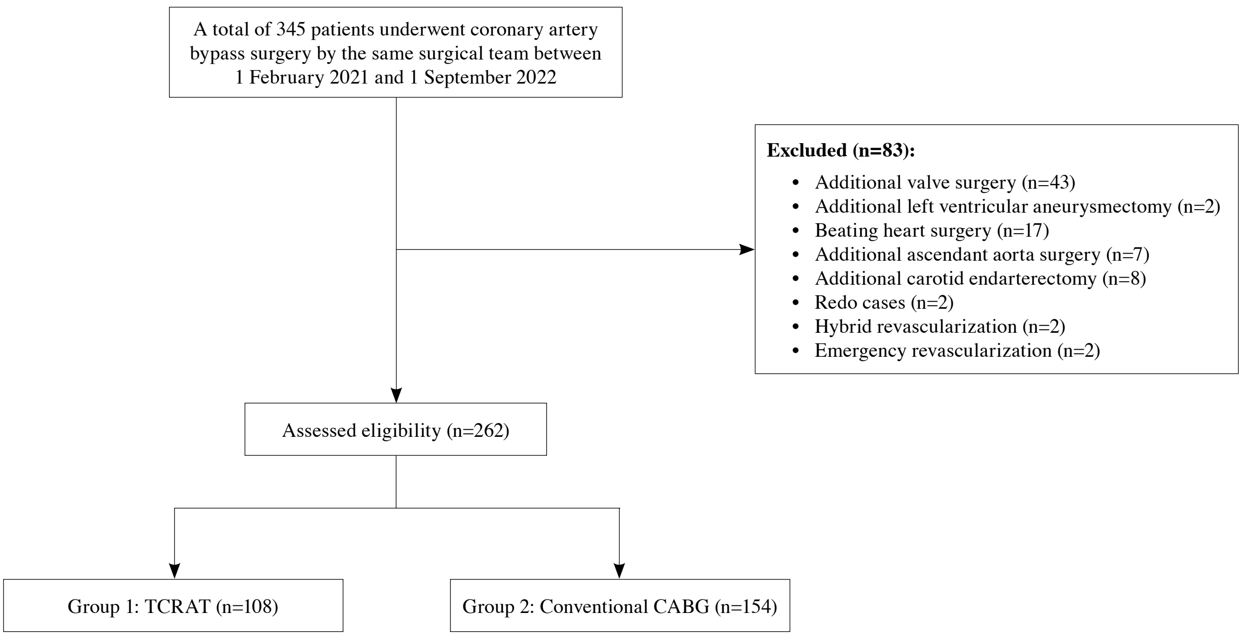

Figure 1. Flowchart of the study.

TCRAT: Total coronary revascularization via left anterior thoracotomy; CABG: Conventional coronary artery bypass surgery.

In 108 of these patients (95 males, 13 females; mean age: 57.1±8.8; range, 41 to 75 years), the operation was initiated with a thoracotomy to perform TCRAT (Group 1), while in 154 patients (126 males, 28 females; mean age: 61.2±9.8; range, 31 to 79), the operation was initiated via a routine conventional sternotomy (Group 2; Figure 1).

The pre- and postoperative data, as well as outpatient clinic attendance, were obtained from the hospital system. The data obtained from the hospitalization and outpatient clinic records of the early postoperative period (the first three months) and the mid-term postoperative period (three months to two years) were analyzed. The study protocol was approved by the Ethics Committee of the University of Health Sciences (Date: 11.04.2023, no: 46418926). Written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A perioperative myocardial infarction (MI) was defined as a 10-fold increase in cardiac troponin levels above the normal laboratory value within the first 48 h postoperatively, accompanied by compatible clinical, electrocardiographic, and imaging findings that supported graft occlusion. Furthermore, elevated troponin values to less than 10-fold and the presence of a new pathological Q wave, as well as early graft failure identified during reexploration due to hemodynamic instability within 48 h of surgery, was considered perioperative MI.

Repeat revascularization was defined as revascularization via surgical or percutaneous coronary intervention during the follow-up period in patients who had previously undergone CABG due to graft failure or native vessel lesion.

Surgical technique

In Group 1, CABG surgery was performed based on a previously published method.[7,8] Different from the technique described, left anterior minithoracotomy was performed through the third or fourth intercostal space depending on the level of the aorta, the position of the apex of the heart, and the size of the heart in preoperative studies (Figure 2). In the case of a thoracotomy performed via the third intercostal space, the distal left internal mammary artery (LIMA) graft was also harvested by reversing the retractor (MIDAccess IMA Retractor; Delacroix-Chevalier, Paris, France) after the harvest of the proximal LIMA graft. This was performed to avoid any potential shortening of the LIMA graft. The exposure of the target vessels was maintained by positioning the heart with a tape, which was used to encircle the inferior vena cava (Figure 3). In addition, unlike the technique described, the pulmonary veins were not routinely encircled with tape. The right internal mammary artery was not used as a conduit in any case in both groups. Antegrade blood cardioplegia was employed in

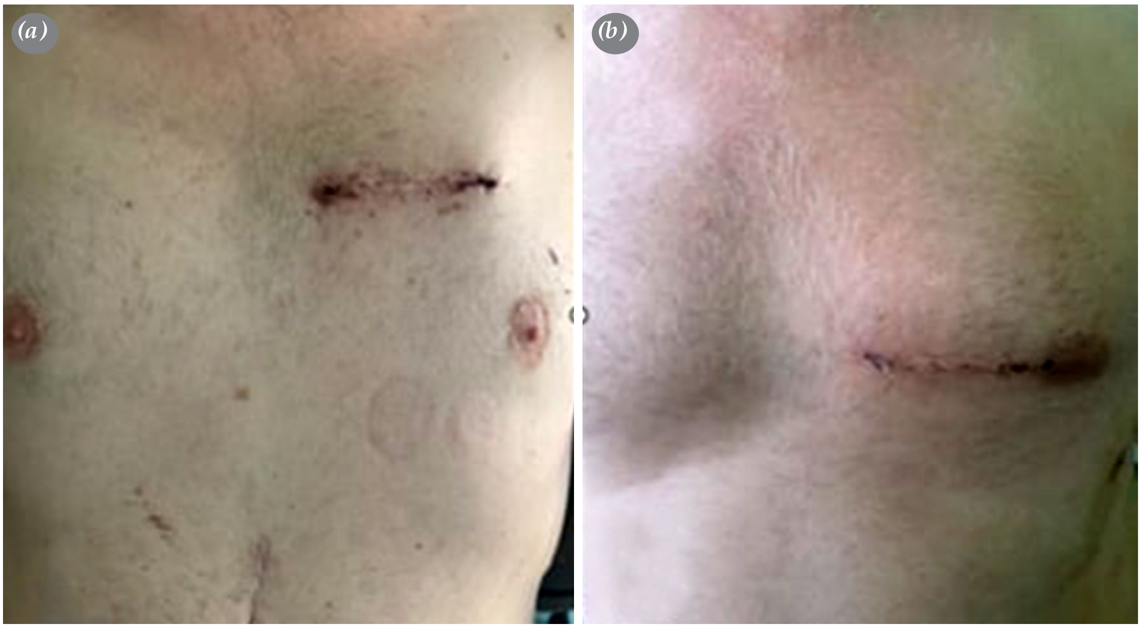

Figure 2. Left anterior mini-thoracotomy. **(a)** Third intercostal space, **(b)** fourth intercostal space.

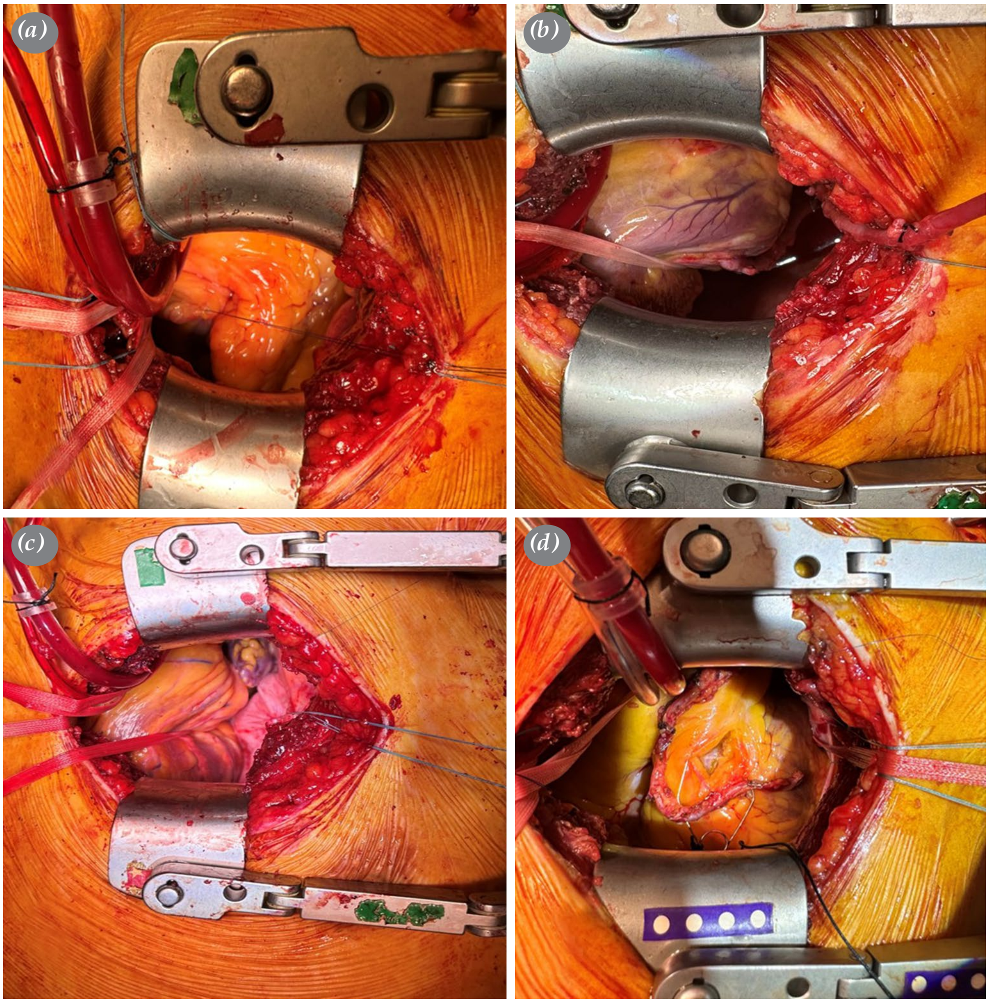

Figure 3. Intraoperative images demonstrating **(a)** right coronary artery territory, **(b)** posterior descending artery anastomosis. **(c)** Lateral wall territory of the heart, and **(d)** left anterior descending artery.

all patients across both groups. Patients who underwent CABG through median sternotomy underwent surgery using cross-clamp under cardiopulmonary bypass (CPB) with routine aortocaval cannulation.[9]

Statistical analysis

Statistical analysis was performed using SPSS version 11.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (min-max), while categorical variables were expressed as number and percentage. The Student's t-test was used to analyze significant differences between normally distributed data, while the Mann-Whitney U test was used to analyze nonnormally distributed data. The chi-square test and Fisher exact test were used to examine quantitative variables. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1 presents the patients' demographic characteristics according to groups. The median follow-up period of the patients was 15 months. The mean preoperative EuroSCORE (European System for Cardiac Operative Risk Evaluation) II was 2.59±2.3 in Group 2, which was significantly higher than the mean EuroSCORE II of Group 1 (1.37±1.5; p<0.001). There was no significant difference between the preoperative left ventricular functions in both groups (p=0.760).

Operative data and early- and mid-term results of the patients are presented in Tables 2 and 3, respectively. The mean number of distal anastomoses performed in Group 1 was 2.46±1.03, while it was 3.15±1.05 in Group 2. The mean CPB and cross-clamp times, respectively, were

Table 1. Preoperative demographic characteristics and risk factors of the patients

	Group 1			Group 2			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			57.1±8.8			61.2±9.8	<0.05
EuroSCORE II			1.37±1.50			2.59±2.3	<0.05
LVEF (%)			55.92±9.06			55.43±9.61	0.76
Sex							
Male	95	88.0		126	81.8		
Female	13	12.0		28	18.2		
Total	108	100		154	100		
Risk factors							
Smoking	76	70.4		107	69.5		0.9
Diabetes mellitus	37	34.3		82	53.2		<0.05
Hypertension	56	51.9		90	58.4		0.31
Hyperlipidemia	28	25.9		28	18.2		0.17
Prior cerebrovascular event	2	1.9		4	2.6		1.0
Prior myocardial infarction	27	25.0		68	44.2		<0.05
Peripheral artery disease	0	0		8	5.2		<0.05
Prior PCI	29	26.9		44	28.6		0.78
Chronic kidney disease (hemodialysis dependent)	0	0		2	1.3		0.51

SD: Standard deviation; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LVEF: Left ventricular ejection fraction; PCI: Percutaneous coronary intervention.

167.70±68.93 and 77.03±38.18 min in Group 1 and 106.64±38.27 and 62.21±24.06 min in Group 2 (p<0.001). In the postoperative period, the length of hospital stay was found to be significantly lower in Group 1 than in Group 2 (6.77±4.24 *vs*. 6.99±3.37 days, p=0.047; Table 3). The mean number of perioperative erythrocyte suspension transfusions was found to be significantly lower in Group 1 than in Group 2 (1.51±1.74 *vs*. 1.86±1.75, p=0.033; Table 3). The all-cause mortality rate was significantly lower in Group 1 than in Group 2 during the postoperative period (p=0.037). Four patients in Group 2 died in the postoperative period before hospital discharge. The causes of death were low cardiac output syndrome, respiratory failure after pneumonia, multiorgan failure resulting from prolonged hospitalization following a stroke, and sepsis as a result of mediastinitis. In the mid-term

Table 2. Operative data of the patients

		Group 1	Group 1	Group 2	Group 2
	Operative data	n	%	n	%
Number of vessels bypassed	1-2	58	53.7	32	20.8
	3-4	49	45.4	106	68.8
	5 or more	1	0.9	16	10.4
Vascular graft used	LIMA	104	96.3	151	98.1
	Great saphenous vein	88	81.5	148	96.1
	Radial artery	0	0	4	2.6

LİMA: Left internal mammarian artery.

Table 3. Early and mid-term postoperative outcomes

	Group 1			Group 2			
Primer endpoints	n	%	Mean±SD	n	%	Mean±SD	*p*
Hospital mortality	0	0		4	2.5		0.145
Perioperative MI	2	1.8		3	1.9		1.00
Perioperative stroke	2	1.8		3	1.9		1.00
Postoperative AF	13	12		22	14.2		0.713
Reexploration (for any reason)	7	6.4		8	5.1		0.427
Superficial wound infection	2	1.8		4	2.5		0.519
Deep wound infection	1	0.9		3	1.9		0.645
All-cause mortality	1	0.9		9	5.8		0.037*
Repeat revascularization	4	3.7		11	7.1		0,289
Duration of hospitalization			6.77±4.24			6.99±3.37	0.047*
Duration of intensive care unit stay			1.67±1.75			1.92±2.22	0.273
Perioperative red blood pack transfusions			1.51±1.74			1.86±1.75	0.033*

SD: Standard deviation; MI: Myocardial infarction; AF: Atrial fibrillation; * $p<0.05$.

follow-up, one patient in Group 2 died due to acute coronary syndrome, one died due to a stroke, and two died due to COVID-19 (coronavirus disease 2019) pneumonia. The cause of death of one patient was unknown. There was no statistically significant difference in terms of other variables (perioperative MI, perioperative stroke, postoperative atrial fibrillation, reexploration, deep and superficial wound infection, repeat revascularization, and intensive care unit length of stay; all $p>0.05$; Table 3). Among the patients who underwent CABG surgery with the conventional method, three patients underwent sternal repair in the postoperative period due to sternal dehiscence as a result of noninfectious causes.

In patients who underwent TCRAT, the rate of conversion to sternotomy in the intraoperative or early postoperative period was 7.4% (n=8; Table 4). Following the cannulation of the femoral vessels in patients who underwent TCRAT, one patient underwent a sternotomy procedure due to a retrograde aortic dissection. Two patients required graft interposition to the femoral artery, while two others required femoral artery endarterectomy. A patient presented with a superficial groin wound infection. The condition regressed with the application of wound dressing and antibiotherapy. Two patients exhibited lymphorrhoea, which regressed during follow-up with wound dressing.

Table 4. Reasons for conversion to sternotomy

	n
Intraoperative reasons	
Ascending aorta partial rupture	1
LAD intramyocardial course	1
Pericardial adhesion	1
Retrograde aortic dissection	1
Right ventricular wall perforation (Due to permanent pacemaker lead)	1
Postoperative reasons	
Perioperative MI	2
Postoperative hemorrhage/tamponade	1

LAD: Left anterior descending artery; MI: Myocardial infarction.

DISCUSSION

In 2019, Babliak et al.[7] described TCRAT as a safer anastomosis method in a bloodless field that can be routinely applied in most patients. Improved decompression of the heart allows increased target vessel access by allowing manipulation of the heart and anastomosis in a larger area (Figure 3). Furthermore, the same fundamental principles and surgical techniques are employed with CABG surgery under CPB through sternotomy, which represents the standard method.

Although CABG is an effective and safe method, perioperative MI represents a significant risk factor for mortality and morbidity. This risk is compounded by the aging population and the fact that surgery is performed in patients with more comorbidities. The present study found perioperative MI in three patients in Group 2 and two patients in Group 1, but no increase was observed in patients who underwent TCRAT. This is likely because revascularization can be easily applied to the target coronary vessels in the whole field, and the anastomosis is performed with the same technique and equipment as the conventional method. Furthermore, the incidence of acute coronary syndrome or repeat revascularization was comparable between the two groups during the early- and mid-term follow-ups.

During CABG surgery with minimally invasive techniques, conversion to sternotomy may be required. A similar retrospective study reported that the most common reason for conversion to sternotomy was an intramyocardial coronary artery.[10-12] In a study conducted by Yaşar, et al.,[10] 26 (9.5%) patients who underwent CABG with minimally invasive techniques underwent conversion to sternotomy. In the present study, five (4.6%) patients underwent a conversion to sternotomy during the intraoperative period, while three (2.7%) patients required a conversion to sternotomy in the early postoperative period. It is anticipated that these values will decrease as the indications and contraindications for TCRAT are determined and experience is gained (Table 4). No mortality was observed in any patient who underwent conversion to sternotomy. Patients with advanced age, preoperative chronic renal failure, inability to tolerate one-lung ventilation, infectious conditions or a history of previous left thoracic trauma or surgery, or a history of radiation should be considered for TCRAT with caution, as the duration of CPB is long and a return to sternotomy may be required.[10-12]

Postoperative mediastinitis is a complication that has a negative effect on mortality, with a mortality rate of 1 to 2% after CABG surgery.[13,14] In mediastinitis, the mortality rate is 12 to 50% in patients who do not undergo aggressive surgical debridement.[15-17] Furthermore, sternal dehiscence and other noninfectious complications related to bone and sternal wire may necessitate additional surgical intervention, resulting in a significant increase in mortality and morbidity, as well as cost due to prolonged hospitalization. In our study, superficial wound infection developed in five patients, and mediastinitis developed in two patients who underwent CABG with the conventional method. Patients with mediastinitis underwent surgical debridement in addition to antibiotherapy. One of the patients died. The patient who was discharged had prolonged hospitalization with vacuum-assisted closure. In addition to mediastinitis, two patients who underwent conventional CABG surgery required sternal repair due to sternal fracture and dehiscence in the postoperative period. In patients who underwent TCRAT, empyema developed in only one patient. Although the rate of deep wound infection was statistically similar in our study, studies with a larger number of patients are needed to confirm our findings. In addition, we believe that infectious complications that may develop after sternotomy have a direct effect on mortality and morbidity.

One of the primary objectives of minimally invasive surgery is to facilitate the expeditious return of patients to their normal physical activities, with a reduced incidence of trauma, blood product transfusion, and complications.[18] In the current study, patients who underwent TCRAT had a lower rate of blood product transfusion compared to the group who underwent CABG through a sternotomy. Furthermore, the early mobilization of patients and the brief recovery period resulted in a statistically significant reduction in hospital stay compared to conventional CABG surgery.

Cerebrovascular accident is one of the most significant complications following cardiac surgical procedures, with a negative impact on mortality and morbidity.[19] It may occur at a rate of approximately 1% after conventional bypass surgery.[20] However, as the rate of peripheral cannulation increased with the increase in minimally invasive methods, the incidence of ischemic cerebrovascular events was found to be higher compared to conventional methods.[21,22] However, in a meta-analysis, no significant difference was found in terms of cerebrovascular events associated with peripheral cannulation.[23] There is also increased aortic manipulation with TCRAT.

However, in our study, a similar rate of 1.9% was observed in patients undergoing minimally invasive CABG surgery, and no increased incidence of ischemic cerebrovascular events was observed in this patient group.

Femoral cannulation is the most common peripheral cannulation for CPB in minimally invasive cardiac surgery. However, it can lead to complications such as dissection and malperfusion due to retrograde arterial perfusion. In our study, one patient underwent a sternotomy procedure due to a retrograde aortic dissection that developed subsequent to femoral cannulation during a minimally invasive surgical procedure. Furthermore, coronary artery disease may be accompanied by additional vascular pathologies, with a rate of 18 to 35%.[24] In a retrospective study, the rate of traumatic injury to the femoral artery was 0.07% with femoral cannulation during minimally invasive cardiac surgery.[25] In our study, two patients in Group 1 required graft interposition, and two required femoral artery endarterectomy. To minimize the risk of complications, patients should be screened for vascular pathologies with preoperative CT angiography. Patients with renal dysfunction, contrast-induced nephropathy, or contrast allergy should undergo Doppler ultrasonography to screen for diffuse atherosclerotic plaque and occlusion. Furthermore, femoral cannulation should not be performed if intraoperative transesophageal echocardiography demonstrates diffuse plaque in the descending aorta. In such instances, axillary artery cannulation has been proposed as an alternative peripheral cannulation technique for TCRAT.

The present study revealed that TCRAT exhibited longer CPB and cross-clamp times compared to conventional CABG surgery. The mean CPB time was found to be higher in Group 1. However, this value decreased after the learning curve period and with more frequent application of the technique. Despite the longer CPB duration, there was no negative impact on the postoperative intensive care unit stay, hospitalization, postoperative atrial fibrillation, perioperative cerebrovascular events, or infection rate data in the follow-up of patients in Group 1.

Notably, the majority of patients who underwent TCRAT underwent a smaller number of vessel bypasses during the learning curve period. Consequently, despite a greater number of target vessels being bypassed in Group 2, in group 1, patients with more extensive target vessel disease underwent bypass surgery following the conclusion of the learning period. One patient in Group 1 underwent coronary artery bypass surgery on six target vessels. However, the divergence in patient selection during the learning curve period was the underlying cause of this outcome. However, it can be posited that this technique demonstrates improved efficacy and safety compared to conventional surgery in patients with left minithoracotomy.

The main limitation of the study was its nonrandomized and retrospective design. Furthermore, this study encompassed the initial 108 cases, including the learning curve period of TCRAT, within a single center. Since 2014, our clinic has accumulated experience in the field of minimally invasive valve surgery and minimally invasive direct or robot-assisted coronary revascularization surgery in single-vessel lesions. After the introduction of TCRAT in 2019, CABG for multivessel disease with minithoracotomy was started to be performed in our clinic in 2021. Consequently, the present study included patients with initial experience of TCRAT in a center with experience of minimally invasive cardiac surgical methods. Therefore, it is possible that similar results may not be obtained in centers that do not utilize minimally invasive techniques during the initial period of TCRAT. Another limitation of the study was the difference in preoperative EuroSCORE II between the patient groups. Although this was the factor that most significantly impacted the ability to make direct comparisons between the techniques under investigation in this study, we believe that it provided insight into the safety of this technique in patients undergoing TCRAT. The inclusion of the initial experience of TCRAT in the study, coupled with the favorable postoperative results, offered insights into the early safety and efficacy of the technique. Finally, to demonstrate the efficacy of TCRAT, it is essential to employ a functional measure, such as angiographic studies or a flowmeter. Further studies are required to confirm these findings. However, the study design and ethical considerations made it impossible for any patient to undergo postoperative imaging unless it was necessary. Furthermore, our clinic did not have a flowmeter, which represented a limitation of the study. Nevertheless, our study demonstrated that there was no statistically significant difference between the two groups in terms of repeat revascularization and perioperative MI. These can, therefore, be evaluated as indirect indicators. However, further prospective randomized studies with imaging and functional evaluations are required.

In conclusion, the results demonstrate that TCRAT is a safe and viable technique when performed on a select group of patients compared to the conventional method. Therefore, it is recommended that patients considered for surgery with this technique should be thoroughly evaluated in the preoperative period in terms of the feasibility of the technique and the complications that may be encountered. Although minimally invasive techniques are anticipated to become prevalent in CABG, as in many other cardiac surgical procedures, further multicenter randomized control studies with large patient populations are required to substantiate this assumption.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: T.D., M.K.; Design: T.D., M.K., K.K.; Control/supervision: T.D., M.K., E.K., K.K.; Data collection and/or processing: T.D., F.B.A., G.E., T.Ö., E.H.; Analysis and/or interpretation: T.D., F.B.A., G.E., T.Ö., E.H.; Literature review, critical review: T.D., F.B.A., T.Ö., E.H., E.K., G.E., M.K., K.K.; Writing the article: T.D., F.B.A., T.Ö., E.K., M.K.

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