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Cardiovascular Surgery and Interventions

Letter to the Editor Open Access

Suggestion for distance and route between operator and patient during coronary angiography during pandemic

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The coronavirus is spread from person to person via aerosolized droplets and, therefore, individuals in close contact are at the highest risk. The same is also valid for healthcare workers during every procedure.[1]

Respiratory droplets can land in the upper respiratory tract. Alternatively, droplets can land on face and, the next time you touch your face or eye, you can infect yourself. Thus, even if an appropriate mask and glasses are worn, safe distance should be kept.[1]

We are all aware of that influenza virus is spread in a similar way. One study showed that, when the healthcare workers were within 1.8 m of patients with influenza, the risk of being infected increased.[2] Besides, recent studies from China revealed the importance of safe distance.[3,4]

The operator and patient distance is an important issue during this pandemic. Despite D-class protection during angiographic procedures are worn and safe distance to patient shall be kept away as much as possible.[3-5] Recent studies have suggested that secure distance without protection measures is 1.5 m, when a patient is infected or suspected with novel coronavirus 2019 (COVID-19) infection. Every safety measure must be taken. During coronary angiography, an isolated angiography room with negative pressure must be selected, and protective garments and masks must be worn. If the radial route is preferred, distance between the operator and patient poses a risk for contamination. Therefore, the femoral route, which is the one with furthest possible distance, should be preferred during angiographic procedures.

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Cardiovascular Surgery and Interventions

Interesting Image Open Access

An incidentally detected persistent left superior vena cava with an absent right superior vena cava during port catheter insertion

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A 71-year-old female patient with the diagnosis of gastric cancer was referred to our clinic for the placement of a port catheter access system. His medical history was non-specific without any cardiopulmonary symptoms. Under local anesthesia and online rhythm monitoring, a totally implantable venous access device (Venous Port, Baxter Healthcare Corp., CA, USA) was placed via the right subclavian vein uneventfully to allow the administration of chemotherapy. Subsequent control X-ray revealed that the central venous catheter (CVC) was not terminating in the right atrium as expected and the path of CVC was near the aorta (Figure 1a, b). A blood gas analysis confirmed the venous concentration. Then, computed tomography (CT) was performed to visualize the port catheter. The CT images revealed that the right subclavian vein was draining into the left persistent superior vena cava (LPSVC), while there was no evidence for a right superior vena cava (RSVC) (Figure 2). The procedure was well-tolerated by the patient and he is still on chemotherapy uneventfully.

Although LPSVC represents the most common congenital venous anomaly of the thoracic systemic venous return with a rate of 0.3 to 0.5% of individuals in the general population, coexisting absence of RSVC is extremely rare.[1] About only 10 to 20% of cases with LPSVC have this variation. As in our case, the majority of LPSVC drains into the right atrium via dilated coronary sinus without resulting in any hemodynamic consequences. Therefore, most patients remain asymptomatic.[1-3] However, some authors demonstrated the viability and safety of LPSVC for long-term CVC in the setting of both hemodialysis and chemotherapy in such patients.[1,3,4] Beyond that, this circumstance remains a challenge during pacemaker or implantable cardioverter-defibrillator

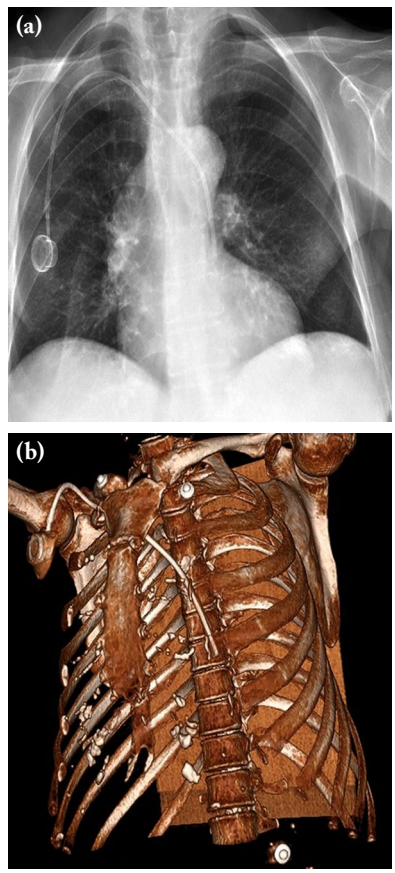

Figure 1. **(a)** Chest X-ray image. **(b)** Three-dimensional image showing unusual course of central venous catheter.

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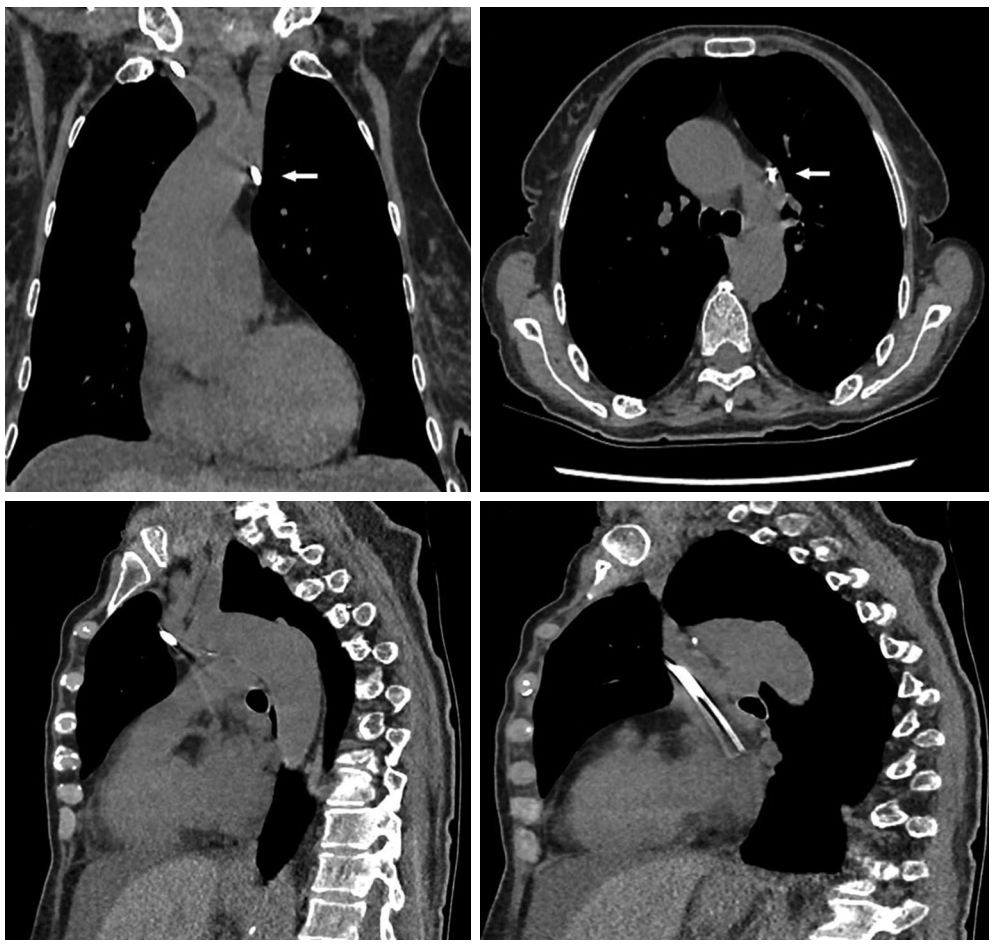

Figure 2. Computed tomography images showing venous catheter located in left persistent superior vena cava.

implantation either, as the coronary sinus ostium is not aligned with the tricuspid orifice as usual. Therefore, several techniques have been introduced to overcome this difficulty.[5]

In the presence of LPSVC, irrespective of the timing of diagnosis (i.e., before or after the intervention), a comprehensive examination of the systemic venous return should be performed to assess the suitability for continued catheterization.[6]

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Cardiovascular Surgery and Interventions

Editorial Open Access

What is wrong with extracorporeal membrane oxygenation in COVID-19: The patient or the indication?

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It is undoubtedly true that identification of novel coronavirus-2019 (COVID-19) infection, announcement of pandemic, and its social and economic effects, and reflections to the healthcare system are expected to be the subject to many researches for next years. It is a rightful interest with the actual numbers of over seven million diagnosed cases and over 400,000 deaths.[1] Debatable subjects among the healthcare professionals include diagnosis and treatment methods, epidemiological observations, and future predictions. There are many case reports and different therapy strategies of COVID-19 in recent papers about the pandemic. The relationship between COVID-19 and cardiovascular surgery is the management of surgical strategies during pandemic and extracorporeal membrane oxygenation (ECMO) use which is, itself, a subject of debate in terms of efficacy and outcomes. The special interest of healthcare professionals other than cardiovascular surgeons is, somehow, noteworthy. The number of ECMO used for COVID-19 all over the world is only 1,371 according to the Extracorporeal Life Support Organization (ELSO), which is one of the most important organizations recording ECMO data.[2] This number is quite insignificant, compared to over seven million patients. However, ECMO deserves this attention, as it can be the last option for COVID-19 patients who do not have a chance of cure with any other therapy modality.

Before discussing this subject in detail, one should know what ECMO is and is not. In particular, venoarterial ECMO (VA-ECMO) is used as the left ventricular support system for postcardiotomy cardiogenic shock, although it does not provide a left ventricular support at all. This is most probably due to easy insertion and old habits. The VA-ECMO does not help ventricular improvement, as it does not decompress left ventricle at all. On the contrary, it worsens the situation due to the increase of afterload because of the arterial cannula in such patients.[3] For sure, VA-ECMO should be used for only very serious oxygenation problems or to maintain tissue perfusion in patients with cardiogenic shock. On the other hand, there is no debate on the conditions in which venovenous ECMO (VV-ECMO) is used. It is indicated in severe hypoxic cases of severe pulmonary infections such as COVID-19.[4,5] The VA-ECMO can be used in a small number of COVID-19 patients with respiratory problems and severe circulatory disturbances.

Which COVID-19 patients should receive ECMO support? As mentioned previously, it can be used as the last option for severe hypoxia in acute respiratory distress. However, due to the limited number of data, it still remains unclear whether conventional respiratory support machines or ECMO would be more appropriate for these patients. Some reports revealed that patients who did not receive ECMO support had higher survival rates than patients receiving ECMO support.[6] As a result of this controversy, clinicians attempted to support the indication, severe respiratory distress, as mentioned above, with clinical and respiratory parameters. For instance, the ELSO has provided selection criteria needed for ECMO referral. If despite optimal ventilation strategies, neuromuscular blockade, appropriate positive end expiratory pressure, prone positioning, and the use

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of pulmonary vasodilators, patients who meet the following criteria can be referred for ECMO referral: partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) less than 60 mmHg for longer than 6 h, PaO_2/FiO_2 less than 50 mmHg for less than 3 h or pH less than 7.20 + $PaCO_2$ greater than 80 mmHg for less than 6 h, and having no contraindications.[2] In addition, some risk scoring systems can be used for the definition of indications.[7] For instance, patients having severe respiratory distress with a Murrey score of 3 to 4, it is reasonable to use ECMO.[7] Beside all these experiences, even if limited, and parameters, choosing the right patient is of utmost importance, as the results are still obscure and sources should be used very carefully. In this regard, it seems to be reasonable to use ECMO for young patients without comorbidity, and healthcare professionals who provide the greatest support in the breakthrough of pandemic.

Unfortunately, very few data are available on ECMO use for COVID-19, which are rarely used, but widely known. Recent reports demonstrated that ECMO use was not as helpful, as it was thought regardless of COVID-19 pandemic.[8-11] Based on this information, the results of COVID-19 patients with ECMO support are not very good, as well. Studies about ECMO use in small numbers of COVID-19 patients, survival was reported as ranging between 0 and 16%.[12-15] It should be kept in mind that patients who received ECMO support were in seriously poor hemodynamic conditions than the other group. Additionally, case reports of successful ECMO use led to confusion. However, it is ironic that the reason why these papers were accepted by the editors was the small number of successful ECMO use.

While debates about ECMO use for COVID-19 continue, there are also social, economic, and ethical problems particularly on this subject. The most important problem is the obligation of effective use of resources in a pandemic which puts so much burden on the healthcare system. There is an unmet need for a large organization, when it is decided to use ECMO, to protect healthcare professionals in the first place. The ECMO is more expensive than other conventional systems such as ventilators, which poses another problem. Less developed and developing countries should be more careful while using ECMO in terms of cost-saving. Another point is the necessity of a professional team to cope with the setup and complications of ECMO. This team is expected to handle these problems and get out of the system in pandemic circumstances, which is likely to reduce the number of healthcare professionals in the field. There are two other specific problems about the ECMO use. The first one is the coagulation problems commonly seen in COVID-19 patients. Many reports showed that COVID-19 patients had a tendency to thrombosis.[16-18] This makes management of anticoagulation process more difficult than it already is. The second problem is cardiomyopathy which was accounted for one-third of critical COVID-19 patients.[14,19] This is explained as myocardial damage and microvascular thrombosis caused by the cytokine storm.[5] Myocardial problems with a wide spectrum including simple electrocardiographic changes to severe cardiac insufficiency can occur in COVID-19 patients. These problems obviously make ECMO use more complicated than it is during pandemic. If such kind of myocardial damage is skipped while the VV-ECMO is inserted to a COVID-19 patient with severe respiratory distress, the results would be catastrophic. As aforementioned, choosing the VA-ECMO in such circumstances would not yield better results, particularly if there is left ventricular insufficiency due to myocardial damage.

In conclusion, the ECMO use for COVID-19 patients should be assessed in the light of these data. Regarding confusing problems and uncertain results, the most important point in this process is to choose the right patient who will benefit most. If this cannot be achieved, both waste of resources and disappointment of healthcare workers are inevitable.

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Cardiovascular Surgery and Interventions

Original Article Open Access

Off-pump versus conventional coronary artery bypass grafting for the revascularization of posterior wall arteries

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ABSTRACT

Objectives: The aim of the present study was to investigate the feasibility of revascularization of posterior wall coronary arteries with off-pump coronary artery bypass grafting (OP-CABG) versus conventional CABG (C-CABG).

Patients and methods: Between July 2001 and October 2009, a total of 104 patients (26 males, 78 females; mean age 57±10.9 years; 43 to 74) who underwent CABG were included. The patients were divided into two groups as those undergoing revascularization with OP-CABG (Group 1, n=52) and those undergoing C-CABG. Intraoperative data and postoperative coronary angiograms at six months were recorded.

Results: The OP-CABG was associated with less requirement for blood transfusion and a lower amount of postoperative drainage. Duration of intubation and the length of stay in the intensive care unit and hospital were found to be significantly shorter in the OP-CABG group. The patency of the arterial grafts was almost completely achieved in both groups, and anastomoses on the posterior vessels were patent in the OP-CABG group.

Conclusion: Based on our experience, in properly selected cases, targeted vessels on the posterior wall can be successfully revascularized with OP-CABG.

Keywords: Beating heart, coronary artery bypass grafting, graft, patency, revascularization.

Postoperative morbidity still constitutes a common problem in patients with coexisting risk factors. Arrhythmia, ventricular dysfunction, infection, gastrointestinal dysfunction, acute pulmonary injury, and renal failure are major underlying conditions problems, contributing to the non-cardiac etiology in these patients.[1]

Off-pump coronary artery bypass grafting (OP-CABG) has been shown to be superior to conventional coronary bypass grafting (C-CABG), since it is associated with less proteolytic and inflammatory response, decreased operative trauma, less postoperative complications, and shorter length of stay in the hospital and intensive care unit (ICU), leading to reduced morbidity and cost.[2] Moreover, OP-CABG offers a high rate of graft patency, less amount of blood loss, lower mortality, and reduced need for inotropic support.[2]

Owing to the fact that recent technology allows revascularization of all target vessels, OP-CABG has become a widely used surgical modality in all patient groups. This method is preferred to avoid the deleterious effects of cardiopulmonary bypass (CPB) and is more frequently performed on the descending left and right coronary arteries (RCAs).[3] Revascularization of coronary arteries in the posterior cardiac wall can be made only by the prominent displacement of the heart in the pericardial space.[2,3]

In the present study, we aimed to investigate the feasibility of OP-CABG for the revascularization of posterior coronary arteries versus C-CABG and to report short-term results of this technique.

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PATIENTS AND METHODS

In this retrospective study, a total of 442 patients who underwent OP-CABG in the cardiovascular surgery department of İzmir Atatürk Training and Research Hospital between July 2001 and October 2009 were screened. Patients with a poor vascular quality or having converted to urgent CPB during OP-CABG were excluded. Finally, a total of 104 patients (26 males, 78 females; mean age 57±10.9 years; 43 to 74) who underwent posterior wall bypass were included in the study. Among these patients, coronary revascularization for posterior wall arteries was carried out in 52 patients (OP-CABG Group), while another 52 patients who underwent C-CABG were included in the C-CABG group. Control coronary angiography was performed in the sixth months after the operation. Data including demographic and clinical characteristics of the patients and peri- and postoperative data were obtained from medical files. A written informed consent was obtained from each patient. The study protocol was approved by the İzmir Atatürk Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

All patients were operated by a single surgical team. Preparations for CABG was made routinely for all patients. General anesthesia was introduced with standardized intravenous narcotic anesthesia. Prior to CPB, heparin was applied at a dose of 300 IU/kg, maintaining an activated clotting time (ACT) at 450 sec. In C-CABG, ACT monitorization was performed every 15 min and additional doses of heparin were administered, if necessary. In OP-CABG, heparin (100 IU/kg) was introduced before proximal anastomosis, keeping the ACT at a range of 250 to 350 sec.

During C-CABG procedure, median sternotomy was followed by cannulation of the ascending aorta and, subsequent to two-stage venous cannulation from the right atrium, CPB was initiated. The pump flow and speed were set at a systemic pressure of 70 to 90 mmHg. Cardioplegia was continued every 20 min. Distal anastomoses were made using 7/0 prolene, while proximal anastomoses were performed with 5/0 prolene sutures along with lateral clamping. In distal anastomoses, the left anterior descending artery and its diagonal collaterals were initially revascularized. The RCA and its branches followed by the circumflex artery and its marginal branches on posterior wall were, then, revascularized.

In order to visualize the target vessel more clearly, wet gauzes were placed posteriorly, and the heart was elevated. Suspension sutures placed on the posterior pericardium also aided as an alternative way in the elevation of heart during anterior and lateral anastomoses. On a beating heart, anastomosis was facilitated using the Octopus® (Medtronic Inc., Minneapolis, MN, USA) to provide stabilization of the myocardium.

During the anastomosis of the RCA and its branches, the traction suture was placed in a manner that the right atrioventricular junction and RCA were involved with a thick layer of the surrounding tissues. Anastomosis could be readily accomplished after stabilization of target vessels with Octopus®.

In order to preserve the hemodynamic stability, a different technique was preferred for anastomosis of circumflex artery and its marginal branches on posterior wall. Initially, the superior vena cava was freed by dissection to allow an easier manipulation of the heart. After placement of 0-silk traction suture on posterior pericardium, the patient was rotated 20 to 30° to right in the Trendelenburg position. This maneuver caused the traction of suture at the posterior pericardium and allowed the elevation of cardiac apex. At this stage, the vacuum clamp was put on the apex keeping the heart at suspension. The circumflex artery and its marginal branches were exposed readily, and anastomoses were made after stabilization of the target vessels by Octopus®. Consecutive grafting technique was not used in any of our patients.

Control coronary angiography

In our department, control coronary artery angiography is reserved for patients who underwent CABG with revascularization of circumflex artery and its marginal branches. Therefore, it has been postoperatively performed in 52 cases operated with OP-CABG and revascularization of the posterior wall.

Statistical analysis

Statistical analysis was performed using the SPSS version 10.0 software (SPSS Inc., Chicago, IL, USA).

Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. Comparison of qualitative data was carried out using the chi-square test, while independent samples-t test was used for quantitative variables. A p value of <0.05 was considered statistically significant.

RESULTS

In both groups, there was male predominance; however, there was no statistically significant difference between the two sexes (p=0.127). The most important risk factor in both groups was smoking, lower ejection fraction (EF), and a higher incidence of chronic obstructive pulmonary disease (COPD) in the off-pump group compared to on-pump group. Demographic and clinical characteristics of the patients are shown in Table 1.

The mean duration of anastomoses performed on circumflex artery and left anterior descending artery was 8.3±1.5 min and 8.3±1.4 min, respectively (Table 2).

The number of distal anastomoses performed was more in the on-pump group than that of the off-pump group (p=0.036). A total of 124 coronary arteries in the off-pump group and 144 arteries in the on-pump group underwent anastomoses (Table 3). The consecutive grafting technique was not performed in any of our patients.

No mortality was observed in our series. However, low cardiac output syndrome necessitating intra-aortic balloon pump (IABP) occurred in two patients in the off-pump group and four patients in the on-pump group, despite inotropic support. In the on-pump group, two patients suffered from acute renal failure

Table 1
Demographic and clinical characteristics of the patients

	OP-CABG (n=52)		C-CABG (n=52)		
	n	Mean±SD	n	Mean±SD	p
Age (year)		59±11.3		54±11.7	0.13
Gender					0.26
Female	42		36		
Male	10		16		
Diabetes mellitus	12		18		0.27
Hypertension	22		28		0.29
Smoking	40		36		0.38
Peripheral arterial disease	8		10		0.50
Preoperative ejection fraction (%)		31.5±8.5		39.6±11.6	0.01
Obesity	6		8		0.50
Chronic renal failure	10		2		0.10
Cerebrovascular occlusion history	6		2		0.30
Family history	14		18		0.38
Hyperlipidemia	10		12		0.50
Preoperative history of MI	32		28		0.39
COPD	30		16		0.04
Unstable angina pectoris	6		10		0.35
Preoperative PTCA	8		10		0.50
Use of LIMA	40		38		0.50
Distal anastomoses		2.4±0.6		2.8±0.7	0.04

OP-CABG: Off-pump coronary artery bypass grafting; C-CABG: Conventional coronary artery bypass grafting; SD: Standard deviation; MI: Myocardial infarction; COPD: Chronic obstructive pulmonary disease; PTCA: Percutaneous transluminal coronary angioplasty; LIMA: Left internal mammary artery.

Table 2
Duration of anastomoses in off-pump group

	Number of anastomoses	Duration of anastomoses (min)
	n	Mean±SD
Left anterior descending	52	8.3±1.4
Circumflex	52	8.3±1.5
Right coronary artery	12	8.1±1.4
Posterior descending artery	6	9.3±0.6
Diagonal	2	8.1±1.6
Total	124	8.4±1.5

SD: Standard deviation.

Table 3
Distribution of target coronary arteries

	OP-CABG	C-CABG
Target vessels for anastomoses	n	n
Left anterior descending	52	52
Diagonal	2	8
Circumflex obtuse marginal 1	24	32
Circumflex obtuse marginal 2	28	28
Right coronary artery	12	12
Posterior descending artery	6	6
Total	124	144

OP-CABG: Off-pump coronary artery bypass grafting; C-CABG: Conventional coronary artery bypass grafting.

Table 4
Postoperative data

	OP-CABG (n=52)		C-CABG (n=52)		
	n	Mean±SD	n	Mean±SD	*p*
Intraaortic balloon pump use	2		4		0.500
Postoperative acute renal failure	0		2		
Duration of intubation (hours)		10.6±2.3		16.1±3.9	<0.001
Respiratory failure	0		2		
Drainage (mL)		519±120		655±128	0.0002
Amount of transfusion (units)		0.9±0.7		1.9±0.7	<0.001
Perioperative myocardial infarction	0		2		
Necessity for postoperative inotropic support	8		18		0.100
Intensive care unit stay (days)		2.0±0.4		2.5±0.6	0.0010
Duration of hospitalization (days)		5.3±0.6		6.7±1.0	<0.001
Postoperative atrial fibrillation	6		12		0.233
Mortality	0		0		

OP-CABG: Off-pump coronary artery bypass grafting; C-CABG: Conventional coronary artery bypass grafting; SD: Standard deviation.

Table 5
Profile of patency of grafts in target vessels in off-pump and conventional groups

	Off-pump group						Conventional group					
	LIMA		SVG		Total		LIMA		SVG		Total	
	P	O	P	O	P	O	P	O	P	O	P	O
Left anterior descending	44	0	8	0	52	0	42	0	10	0	52	0
Diagonal	0	0	2	0	2	0	0	0	8	0	8	0
Circumflex obtuse marginal 1	0	0	24	0	24	0	0	0	32	0	32	0
Circumflex obtuse marginal 2	0	0	28	0	28	0	0	0	28	0	28	0
Right coronary artery	0	0	10	2	10	2	0	0	8	3	8	4
Posterior descending artery	0	0	4	2	4	2	0	0	6	1	6	0
Total	44	0	76	4	120	4	42	0	92	4	134	4

LIMA: Left internal mammary artery; SVG: saphenous vein graft; P: Patent; O: Obstructed.

(ARF), two patients from respiratory failure, and two patients from perioperative myocardial infarction. Such complications did not occur in the off-pump group (Table 4).

The mean duration of intubation was significantly shorter in the off-pump group (8.6±2.3 h) than the on-pump group (12.1±3.9 h) ($p<0.001$). The amount of drainage was 519±120 mL in the off-pump group, while it was 655±128 mL in the on-pump group ($p<0.001$). Similarly, the amount of transfusion was significantly lower in the off-pump group (0.9±0.7 U vs. 1.9±0.7 U, respectively). The mean preoperative EF was lower in the off-pump group, although there was a need for postoperative inotropic support more often in the on-pump group (n=18/8). The frequency of postoperative atrial fibrillation did not significantly differ between the groups (n=12 in the on-pump group and n=6 in the off-pump group). The mean length of ICU stay was shorter in the off-pump group (2.0±0.4 days vs. 2.5±0.6 days, respectively) ($p=0.001$). In addition, the mean hospitalization period was also shorter in the off-pump group (5.3±0.6 days vs. 6.7±1.0 days, respectively) ($p<0.001$) (Table 4).

Control coronary angiography results revealed that the arterial graft patency rates were 100% in both groups. The venous graft patency rates in the off-pump and on-pump groups were 95% and 95.8%, respectively. In both groups, the bypass grafts performed in the circumflex arteries were patent and obstructions invariably occurred in grafts where RCA anastomoses were made. The rates of patency of the grafts in the target vessels are plotted in Table 5.

DISCUSSION

Although CPB provides some advantages in coronary surgery, it stimulates coagulation and fibrinolysis as well as elicits activation of complement system, platelets and proinflammatory cytokines.[3,4] In two distinct studies, stimulation of inflammatory pathways have been associated with increased morbidity and complications after coronary surgery and CPB.[4] Due to hazardous outcomes of adverse reactions linked with CPB, advanced age of patients planned for surgery and accompanying COPD, alternative operations that do not include CPB have been preferred.[5] Demonstration of safe anastomoses yielded an increase in OP-CABG. Publication of long-term angiographic results after OP-CABG have made this procedure popular worldwide. In our department, OP-CABG intervention has been performed since 2000 and about 20% of coronary bypass interventions have been carried out on beating heart.

We applied OP-CABG method to patients with LAD and RCA lesions and on posterior wall lesions in selected cases. The main challenge on revascularization of multiple vessels is maintenance of hemodynamic stability during access and exposure. These issues are more difficult to be accomplished on beating heart. In our series, we did not come across hemodynamic instability during revascularization of LAD. Deterioration of hemodynamics was noted on circumflex vessels located on posterior and inferior parts of heart, which constitute the most difficult regions for exposure. Experimental studies have shown that left ventricular functions were limited

and eventually hemodynamic instability was observed during anastomoses of circumflex arteries on beating heart.[6] Decrease in cardiac index and increase in pulmonary artery wedge pressure were noted during revascularization of posterior wall. We kept our patients in Trendelenburg position to maintain hemodynamic stability in ectopia cordis position and pressure on right heart was relieved with this manoeuvre.

Even though CPB is termed as a risk factor for morbidity and mortality, prospective, randomized trials have shown that there was no difference between techniques with or without CPB in terms of morbidity and mortality.[7] Revascularization on beating heart was not associated with increased mortality in early postoperative period.[4] In contrast, decreased rates of morbidity and mortality were seen in some retrospective studies investigating OP-CABG.[5,6] Incidences of perioperative mortality and perioperative myocardial infarction after OP-CABG were 1.9% and 2.9%, respectively.[8] These results imply that OP-CABG is not associated with an increased likelihood of mortality than C-CABG. Our results are in accordance of this data.

Van Dijk et al.[9] have compared OP-CABG and C-CABG in terms of surgical drainage and transfusion amounts. They reported that amounts of drainage in OP-CABG and C-CABG groups were 500 mL and 400 mL, respectively. The reason for the relatively increased amount of drainage in OP-CABG was attributed to the fact that heparin used during operation was not neutralized.

In conjunction with reports of Hoff et al.,[10] we observed that amount of drainage was more in C-CABG. Routine use of anti-platelet factors, dilutional anaemia and direct effects of CPB may be responsible for this result.

Low cardiac output syndrome diagnosed postoperatively in both groups was managed successfully with IABP. Frequencies of IABP use in OP-CABG and C-CABG in our series were slightly higher than those reported by Ascione et al.[11] Histopathological examinations demonstrated that mitochondria in the left ventricular cells were preserved better with OP-CABG.[12] Moreover, manipulations for achieving access to the target vessels resulted in serious cardiac injury.[13]

Cardiopulmonary bypass may contribute to the pathogenesis of ARF after CABG via hemodynamic, inflammatory, and nephrotoxic effects. Hemolysis, decreased perfusion, non-pulsatile flow, and hemodilution may facilitate occurrence of ARF.[14,15] Therefore, CPB has been postulated as an independent risk factor for ARF. From this point of view, OP-CABG may be an alternative for minimizing the risk of ARF. However, it should be kept in mind that low cardiac output syndrome which may occur during OP-CABG may enhance the pathogenesis of ARF. Therefore, appropriate preoperative hydration, avoidance of nephrotoxic drugs, the use of inotropic and vasodilator drugs for hemodynamic stability, and meticulous follow-up of acid-base balance are important measures for elimination of ARF.[14,15]

Adverse effects of CPB on the respiratory system may become more obvious in COPD patients. In our series, no patients with COPD who underwent OP-CABG suffered from respiratory failure postoperatively. On the contrary, respiratory failure was detected in two patients with COPD operated via C-CABG. Bull et al.[16] suggested that duration of extubation prolonged in C-CABG. Consistent with this finding, our results showed that duration of postoperative intubation were longer in the on-pump group. Shorter hospitalization accelerates the return of the patient to daily life and allows a more effective postoperative rehabilitation. In our series, the OP-CABG seems to be more favorable, since it is linked with a shorter duration of hospitalization.

Control of patency for anastomoses and grafts is an important parameter for documentation of the efficacy of OP-CABG. In the literature, the graft patency rates for C-CABG are reported between 94 to 99% in the early postoperative period and range between 51 to 98% in the long-term.[17] Mechanical stabilization yielded a better graft patency in coronary vessels including the circumflex arteries.[17,18] Compared to the OP-CABG and C-CABG, we found that the patency of the grafts was almost 100% similar to each other. At six months, the postoperative graft patency rate was 96.6% in the OP-CABG and 97% in the C-CABG. Endothelial injury due to intracoronary shunt was reported in the literature; however, we observed no stenosis or obstructions in anastomosis sites where the intracoronary shunts were used.[19,20]

Our analysis of outcomes and preoperative and operative data of OP-CABG showed that postoperative

blood transfusion and drainage was less, and the length of intubation, hospitalization and ICU stay were shorter after OP-CABG. Graft patency rates were satisfactory in both groups and, remarkably, all anastomoses performed on the posterior vessels were found to be patent in the OP-CABG group.

In conclusion, in properly selected cases, targeted vessels on the posterior wall can be revascularized effectively and safely with OP-CABG.

Declaration of conflicting interests

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What has changed in our endovascular practice at abdominal aortic aneurysms?

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ABSTRACT

Objectives: We aimed to investigate whether there was a change in the perioperative features and outcomes following endovascular repair.

Patients and methods: This retrospective study included 249 consecutive patients (223 males, 26 females; median age 70 years; interquartile range [IQR], 66 to 74 years) with abdominal aortic aneurysms (AAAs) who were treated using endovascular approach between January 2012 and February 2020. The patients were stratified into three tertiles based on the time period of the procedure (83 patients in each group) as follows: 2012-2017, 2017-2018, and 2018-2020. Trends over time were analyzed among the three patient groups.

Results: The median aneurysm diameter was 63 (IQR, 55 to 71) mm. The third tertile (2018-2020) had a significant association with lower durations of the procedure, particularly compared to the first tertile (2012-2017). The median duration of the intensive care unit stay (median 6 h, 4 h, and 4 h respectively; p<0.001) and hospital stay (median three days, two days, and two days, respectively; p<0.001) were found to be significantly shorter after the first tertile.

Conclusion: Based on these results, EVAR is a safe and feasible method of treatment in AAAs. These results support a potential link between improved outcomes, technical feasibility, and experience over time.

Keywords: Abdominal aortic aneurysm, aortic surgery, endovascular aneurysm repair, endovascular surgery, stent.

Endovascular abdominal aortic aneurysm (AAA) repair has become the standard treatment option for AAAs.[1] Trends over the years have shown the increased utilization of endovascular aneurysm repair (EVAR) over open surgery for the treatment of AAAs.[2] Short-time benefits have been well-documented in randomized-controlled trials.[3-6] However, there are some debates regarding the long-term outcomes of endovascular procedures.[7-9] Despite this controversy, EVAR is still the preferred option for treatment of AAAs. Since the registry data and observational studies also provide evidence for recent guidelines.[1,10]

There are some reports investigating the volume-outcome relationship for EVAR.[11,12] The main conclusion of these studies is that the high-volume center is associated with lower mortality and better outcomes. Therefore, it is obvious that experienced centers and surgeons are the key important issue for better outcomes. Gaining experience is related not only with high-volume, but also with technical skills changing over years.

In the present study, we aimed to investigate our clinical and technical outcomes of EVAR procedures in patients with AAAs.

PATIENTS AND METHODS

This retrospective study included 249 consecutive patients (223 males, 26 females; median age 70 years; interquartile range [IQR], 66 to 74 years) with AAAs who were treated using EVAR in the Department of Cardiovascular Surgery at Turkey Yuksek Ihtisas Hospital and Ankara City Hospital between January 2012 and February 2020. All patients were treated by experienced vascular surgeons. The patients were stratified into three tertiles based on the time period

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of procedure (83 patients in each group). The time periods were designed by an equal number of patients, rather than the standard time periods as follows: 2012-2017, 2017-2018, and 2018-2020. A written informed consent was obtained from each patient. The study protocol was approved by the Ankara City Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic variables, periprocedural parameters such as type of anesthesia, duration of operation, duration of radiation exposure, amount of contrast agent used, length of intensive care unit (ICU) and hospital stay, and outcomes of the procedures and mortality for the three groups were recorded for analysis.

Devices used in this period

The stent-grafts used in our centers have changed throughout the study period. At the earliest time of the study, the unibody stent-graft Endologix AFX®, (Endologix Inc., Irvine, CA, USA) were more common to be implanted, whereas, at the recent times, all the stent-grafts were modular types mainly Medtronic Endurant™ II (Medtronic, Minneapolis, MN, USA) and Lifetech Ankura™ AAA stent graft (Lifetech Scientific Corp., Shenzen, China).

Briefly, unibody stent-graft consists of a main bifurcated unibody and aortic extension. It mainly provides anatomic fixation at the level of aortic bifurcation. One-sided femoral exploration is sufficient for deployment. On the other hand, the deployment technique of both modular devices is remarkably similar. Bilateral femoral exploration is a standard for both stent-grafts. Contralateral limb cannulation is a limiting step for fluoroscopy durations for both stent-grafts. The main difference between the modular types is the covered graft material, which is Dacron® of the Medtronic

Table 1
Baseline characteristics by tertiles

	1st Tertile 2012-2017 (n=83)				2nd Tertile 2017-2018 (n=83)				3rd Tertile 2018-2020 (n=83)				
	n	%	Median	IQR	n	%	Median	IQR	n	%	Median	IQR	*p*
Age (year)			70	65-74			69	66-74			70	65-77	0.614
Sex Male	72	86.7			74	89.2			77	92.8			0.442
Diabetes	19	22.9			22	26.5			25	30.1			0.573
Hypertension	58	69.9			50	60.2			62	74.7			0.125
Hyperlipidemia	26	31.3			32	38.6			15	18.1			0.013
COPD	31	37.3			21	25.3			31	37.3			0.164
Renal disease	11	13.3			6	7.2			9	10.8			0.442
PAH	7	8.4			10	12.0			5	6.0			0.388
CAD	48	57.8			35	42.2			30	36.1			0.015
CABG	25	30.1			13	15.7			14	16.9			0.039
CHF	7	8.4			3	3.6			4	4.8			0.374
Smoking	27	32.5			41	49.4			35	42.2			0.086
Malignancy	9	10.8			3	3.6			2	2.4			0.039
Abdominal surgery	12	14.5			7	8.4			2	2.4			0.020
ASA score >2	51	61.4			32	38.6			39	47.0			0.012
EF			55	50-59			55	45-57			55	50-60	0.243
Diameter (mm)			60	55-67			63	55-75			61	56-71	0.201
Ruptured AAA	3	3.6			6	7.2			10	12.0			0.121

IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease; PAH: Peripheral arterial disease; CAD: Coronary artery disease; CABG: Coronary artery bypass grafting; CHF: Congestive heart failure; ASA: American Society of Anesthesiologists; EF: Ejection fraction; AAA: Abdominal aortic aneurysm.

Endurant™ II (Medtronic, Minneapolis, MN, USA) and expanded polytetrafluoroethylene (e-PTFE) of the Lifetech Ankura™ AAA stent graft (Lifetech Scientific Corp., Shenzen, China).

Statistical analysis

Statistical analysis was performed using the SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test) to determine whether they were normally distributed. Descriptive data were presented in median and IQR for the non-normally distributed and ordinal variables. The Kruskal-Wallis test was conducted to compare variables among the tertiles. A pair-wise comparison, using an adjusted alpha (α)-level of 0.017, was performed using the Mann-Whitney U test. A *p* value of 0.05 was considered statistically significant.

RESULTS

Of a total of 249 patients included in the study, there were 83 patients in each tertile. Baseline demographic and clinical characteristics are shown in Table 1. Comorbidities such as coronary artery disease, malignancy, and history of abdominal surgery were more common among the patients in the earliest tertile of the patients (p=0.015, p=0.039, and p=0.020, respectively). In addition, patients with the American Society of Anesthesiologists (ASA) Class >2 were more frequent in the earliest period (p=0.012). The other demographics, ejection fraction values, and preoperative aneurysm diameters were similar among the groups (Table 1).

Regarding the technical details, duration of operation and duration of fluoroscopy were significantly shorter at the later period of experience (p<0.001 for both). Also, the amount of contrast agents used decreased after the second tertile (60 mL, 70 mL, and 50 mL, respectively; p<0.001). Additionally, modular parts used in the procedure (particularly iliac extensions) and need for ballooning were more common at the third tertile (p=0.003 and p<0.001, respectively) (Table 2).

The median length of ICU stay was 6 h, 4 h, and 4 h, respectively (p<0.001). The median length of stay in the hospital was three days, two days, and two days, respectively (p<0.001). The decrease for ICU and hospital stays was significant by the second tertile (p<0.001 and p=0.008, respectively).

Mortality at 30 days was 1.6% (4/249) for the whole patient cohort. The rate of in-hospital mortality was similar among three groups (p=0.169), whereas both the follow-up time and late mortality decreased in the later period (p<0.001) (Table 3).

Table 2
Technical details of procedures

	1st Tertile 2012-2017 (n=83)				2nd Tertile 2017-2018 (n=83)				3rd Tertile 2018-2020 (n=83)				
	n	%	Median	IQR	n	%	Median	IQR	n	%	Median	IQR	*p*
General anesthesia	56	67.5			68	81.9			72	86.7			0.007
Type of stent-graft													<0.001
Unibody	59	71.1			9	10.8			0	0			
Modular	24	28.9			74	89.2			83	100			
Duration of operation (min)			120	120-150			150	120-180			120	90-150	<0.001
Duration of fluoroscopy (min)			18	14-20			16	10-25			12	9-18	<0.001
Amount of contrast agent (mL)			60	60-80			70	60-100			50	40-60	<0.001
Aortic extension	0	0			4	4.8			2	2.4			0.131
Iliac extension	17	20.7			13	15.7			31	37.3			0.003
Balloon usage	7	8.5			19	22.9			50	60.2			<0.001

IQR: Interquartile range.

Table 3
Outcomes and postoperative results

	1st Tertile 2012-2017 (n=83)				2nd Tertile 2017-2018 (n=83)				3rd Tertile 2018-2020 (n=83)				
	n	%	Median	IQR	n	%	Median	IQR	n	%	Median	IQR	*p*
In-hospital mortality	1	1.2			3	3.6			0	0			0.169
Endoleak	11	13.3			18	21.7			8	9.6			0.081
Type IA	0	0			2	2.4			1	1.2			
Type IB	1	1.2			3	3.6			2	2.4			0.068
Type II	4	4.8			11	13.3			3	3.6			
Type III	6	7.2			1	1.2			2	2.4			
Follow-up period (months)			44	31-56			25	18-29			13	12-14	<0.001
Late mortality	28	33.7			9	10.8			1	1.2			<0.001
Re-intervention	10	12			7	8.4			6	7.2			0.536

IQR: Interquartile range.

DISCUSSION

This study documents an evaluation of trend during the years of gaining experience on EVAR procedure. The introduction of EVAR has provided an opportunity for surgeons to treat non-operable patients and patients with comorbidities at the beginning. The satisfactory outcomes and the long-time durability of these procedures have enabled this treatment modality for almost all infra-renal AAAs. In recent years, the endovascular approach for AAAs has reached up to 75 to 80% in our clinic.[13] As shown in this study and previous studies, patients with more comorbidities (such as coronary artery disease, coronary artery bypass grafting history, malignancy, and previous abdominal operation) and increased ASA scores were treated endovascularly in earlier periods of our experience.[14] The decreased rates of these comorbidities in later periods may have contributed to the increased utilization of endovascular procedures in almost all patients, even those with no comorbidities.[13]

The shorter periods of procedure and fluoroscopy and decreased amounts of contrast agents used coincided with the last period. We observed a trend with a stabilized decrease in these parameters in each time period; however, the significant decrease was seen only in the latest period. This can be attributed to the type of the stent-graft used. In the earlier periods, we used more commonly the unibody stent-graft (71%) which provided only one-sided femoral exploration and shorter fluoroscopy and procedure time. At the second tertile, modular stent-grafts gained popularity in our clinic (89%) and, currently, we implant only modular stent-grafts. Modular stent-grafts requires more technical procedures during deployment (such as two-sided femoral exploration, contralateral limb cannulation) which prolongs the procedure and fluoroscopy time and increases the amount of contrast agent used. An increase of these parameters (i.e., procedure duration, fluoroscopy duration, and amount of contrast agents) at the second tertile may be understandable. However, with gaining experience with a large volume of patients, we provided a plateau phase during the first and second tertiles and a decrease in the third tertile with increased experience. This decrease significantly manifested even with more use of iliac extensions and balloons which are technically time-consuming. The increased use of iliac extensions and balloons can be attributed to the increased complexity of aneurysms (angulated and elongated) over time, as the instruction-for-use criteria of the endograft types and technical experience have extended day by day. Recently, the median fluoroscopy duration of our procedures is only 12 min (IQR, 9 to 18 min), which appears to be very convenient. There are some reports documenting techniques for contralateral limb cannulation and these reports particularly aim to decrease fluoroscopy times.[15-17] In these reports, about 12 to 15 min of contralateral limb cannulation has been documented, indicating longer fluoroscopy times for whole procedure. Therefore, a 12-min

total fluoroscopy time is quite considerable for our experienced team.

The ICU and hospital stays following the endovascular procedure was significantly shorter as of the beginning of second tertile, corresponding to 2017. The patients with less comorbidities may have contributed to this finding, as the EVAR procedure gained popularity for a greater population of AAAs.

The decrease at the mid-term mortality at the latest period is quite understandable, since the follow-up period was longer for the earlier periods (44 months, 25 months, and 13 months, respectively). Overall long-term mortality rate was 15.3% (2-38/249) over a median period of 26 months. However, supporting evidence of decreasing mid-term mortality over time was published by Varkevisser et al.[18] who documented that four-year survival tended to improve in recent years, due to technical improvements and increased experience.

Nonetheless, there are some limitations. Firstly, the groups were non-heterogenous regarding stent-grafts used and comorbidities. Secondly, mid-term mortality should be assessed with comparable follow-up periods for each group.

In conclusion, technical success of the procedure and perioperative outcomes have improved in more recent years. We believe that the relative perioperative outcome benefits of EVAR such as shorter ICU and hospital stay have increased over time.

Declaration of conflicting interests

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A comparison of renal failure development between endovascular and open aortic aneurysm repair in patients older than 80 years

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ABSTRACT

Objectives: In this study, we aimed to compare open surgery and endovascular aneurysm repair in terms of renal failure development in patients over 80 years of age.

Materials and methods: The literature search was carried out in PubMed, Ovid, Web of Science, and Scopus electronic databases without publication date and language restriction. Clinical studies involving the group of patients over 80 years old, comparing open surgery and endovascular aneurysm repair, including post-procedural renal failure rates, were included in the analysis. The results of the studies were evaluated according to the presence of heterogeneity (I^2>25%) by the random or fixed effect model.

Results: A total of 7,845 articles were reached. After reviewing the article titles and abstracts, 10 articles including 9,027 patients were included in the analysis. As a result of the analysis, there was a significant difference between open surgery and endovascular aneurysm repair in terms of renal failure development (odds ratio [OR]: 0.378, 95% confidence interval [CI]: 0.187-0.765 and p=0.007). Studies were observed to be heterogeneous (I^2=83.8%). Possible publication bias results were not significant using the Begg test (tau^2=0.70).

Conclusion: Our study results suggest that aortic aneurysm repair with both techniques carries serious risks for renal failure, and the risk is higher with open surgical technique in patients over the age of 80.

Keywords: Aortic aneurysm, elderly, endovascular repair, open repair.

The most frequent diseases of aorta are atherosclerosis and aneurysms.[1] True aneurysms defined as a permanent localized dilatation of an artery, having at least a 50% increase in diameter compared to the normal diameter".[2] Aortic aneurysms may be located in the abdomen (62.7%), thorax (25.9%), thoracoabdominal region (8.3%), and unspecified (3.0%) sites.[2]

The risk factors for aortic aneurysms include age, male sex, smoking, family history of abdominal aortic aneurysms (AAAs), coronary artery disease, hypertension, peripheral artery disease, and previous myocardial infarction.[3] In particular, age older than 65 years is the main risk factor for aortic aneurysms.

In the interventional treatment of aneurysms, two options can be selected: conventional open surgical repair (OSR) or endovascular aneurysm repair (EVAR). In a recent meta-analysis performed by Powell et al.,[4] early mortality was found to be lower in EVAR compared to OSR. However, five-year survival rates were comparable between the groups.[4] In a more recent analysis for long-term outcomes, there was no significant difference between the EVAR and OSR.[5]

Factors causing renal failure in aortic aneurysm repair are thought to be problems such as atheroembolism, intraoperative hypotension, and renal ischemia.[6] Saratzis et al.[7] reported that 18.8% of acute renal injuries occurred in a cohort study including 149 patients. In another study, Toya et al.[8] observed that a similar rate (19%) of renal failure in their cohort. Previous studies demonstrated that post-procedural

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acute renal injury increased the aneurysm-related mortality and cardiovascular morbidity rates and prolonged the length of hospital stay.[7,8]

To the best of our knowledge, there is no meta-analysis available in the literature comparing EVAR and OSR for renal failure in patients older than 80 years. We, therefore, aimed to compare OSR and EVAR in terms of renal failure development in this patient population.

MATERIALS AND METHODS

Literature search

We performed database search according to the systematic review and meta-analysis guidelines published in 2015.[9] In the initial stage, we conducted our electronic database search to determine whether postoperative renal failure could differ between EVAR and OSR. Researchers screened the PubMed, Scopus, Web of Science and Ovid electronic databases up until 01.02.2020 without no publication or language restriction. In the search, the following keywords were used: "aortic aneurysm", "thoracic aortic aneurysm", "abdominal aortic aneurysm", "endovascular repair", "open surgical repair", "renal failure", "renal insufficiency", "renal injury", "kidney failure", "kidney insufficiency", and "kidney injury".

Selection criteria

All studies (i.e., retrospective/prospective; randomized/observational) were included without sample size restriction. Inclusion criteria were as follows: *(i)* clinical human study, *(ii)* adult patients, *(iii)* articles in English language. Exclusion criteria were as follows: *(i)* experimental studies and *(ii)* case studies or case series. Studies which were relevant to our subject of study, but were unable to investigate development of postoperative renal failure were not included in the analysis. A meta-analysis was carried out for studies in which comparative data were reported. In addition, articles in which relevant data were presented as figures or graphs were excluded from the analysis.

Data collection

Researchers recorded the related data (including name of the first author, date of publication, sample size, research design, and prevalence of renal failure) independently from each other. Disagreements were resolved by consensus.

Statistical analysis

Data were analyzed using the Jamovi® version 1.2 (The jamovi project; 2020) and Open MetaAnalyst® for Windows 8 version (Brown University, Rhode Island, USA) software. The results were presented in odds ratio (OR) and 95% confidence interval (CI). Heterogeneity was evaluated using the I^2 statistics. No heterogeneity: $I^2<25\%$, low heterogeneity: $50\%<I^2>25\%$, moderate heterogeneity: $75\%<I^2>50\%$, and high heterogeneity: $I^2>75\%$. When there was a significant heterogeneity, analysis of moderators was evaluated for the cause of heterogeneity. The meta-analysis was carried out using fixed or random models and results were presented with forest plot. In the presence of heterogeneity ($I^2>25\%$), the random effects model was used; otherwise for ($I^2<25\%$), the fixed effect model was used. Publication bias was evaluated using the Begg's test.

RESULTS

After the screening of databases, we obtained a total of 7,845 articles. After removing the duplications and unrelated articles, a total of 10 articles were included in the analysis.[10-19] The database search flow diagram is shown in Figure 1.

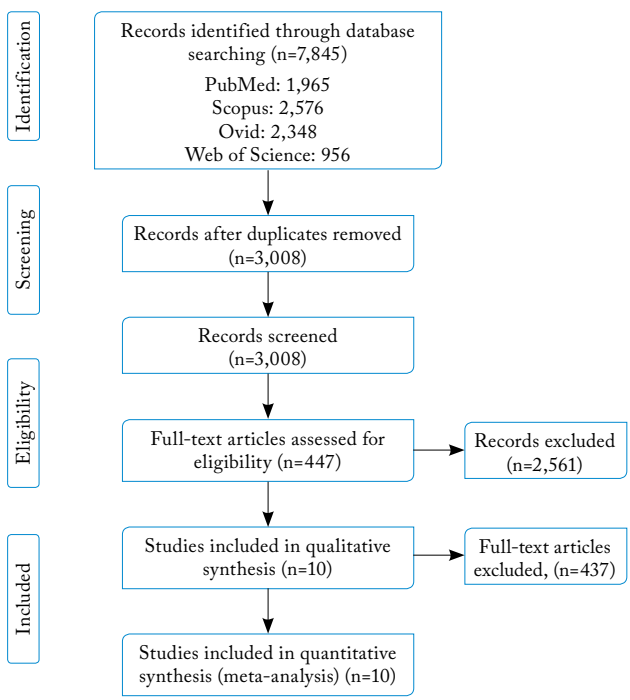

Figure 1. Database search flow diagram.

Table 1
Relevant features of studies included in the analysis

Study	Year	Country	Period	EVAR (n)	OSR (n)	Trial design	Weight on results
Morisaki et al.[10]	2016	Japan	2007-2011	117	90	R	5.83
Sicard et al.[17]	2001	USA	1997-2000	52	38	P	3.79
De Donato et al.[16]	2007	Italy	2004-2007	32	12	P	3.71
Raval et al.[15]	2012	USA	2005-2008	1634	391	R	14.76
Tan et al.[19]	2017	USA	2005-2014	450	598	R	17.62
Martelli et al.[11]	2017	Italy	2006-2010	42	55	R	8.96
Law et al.[13]	2018	China	1999-2013	11	23	P	9.49
Locham et al.[12]	2018	USA	2006-2015	242	306	R	13.80
Karimi et al.[14]	2016	USA	2006-2013	41	54	R	3.79
Hicks et al.[18]	2016	USA	2003-2014	4074	765	R	18.21

R: Retrospective; P: Prospective.

Relevant features of the studies included in the analysis are summarized in Table 1. As a result of the analysis, heterogeneity was observed (Q: 55.56, df,[9] p<0.001, I^2: 84%). The random effect model was used for the final analysis due to the heterogeneity, indicating that the difference between two techniques for the development of renal failure was statistically significant (OR: 0.378, 95% CI: 0.187-0.765; p=0.007). According to this result, possibility of renal failure development was higher in ORS than EVAR (Table 2).

When we analyzed heterogeneity among the studies, the main reason of heterogeneity was the retrospective design of the studies (I^2: 88.79%). The results on the heterogeneity analysis are summarized in Table 2.

Model fitting weights were between 3.71% (De Donato et al.[16]) and 18.21% (Hicks et al.[18]). Four of the studies[12,15,18,19] included in the analysis had 64.3% effect on the results.

Possible publication bias results were not significant according to the Begg's test (tau 2=0.7). Fail-safe number (possible articles overlooked or inaccessible during the literature search) according to file drawer analysis was calculated as 10 using the Orwin approach.

DISCUSSION

In this analysis, we included 10 articles to determine the possibility of renal failure risk between EVAR and OSR in elderly patients older than 80 years. The results demonstrated that there was a significant difference for the development of renal failure. The heterogeneity among the studies was very high, but the possibility of publication bias was not statistically significant. The main reason for the presence of heterogeneity was the retrospective design of the studies.

In their study, Bagia et al.[20] showed that elective AAA repair caused higher treatment costs in patients over 80 years of age. However, the opposite result

Table 2
Results of analysis

	OD	95% CI	*p*	Q	df	*p*	I^2 (%)	Publication bias
Retrospective studies	0.370	0.16-0.82	0.014	53.52	6	<0.001	88.79	0.75
Prospective studies	0.50	0.13-1.87	0.669	1.39	2	0.499	0	0.0
Overall	0.378	0.187-0.765	0.007	55.56	9	<0.001	83.8	0.7

OD: Odds ratio; CI: Confidence interval.

was obtained in the emergency surgery setting. Nevertheless, as a result of analyzing the ratio of treatment cost to survival, emergency AAA repair caused an eight-fold increase over 80 years.

In a recent meta-analysis of 15,580 patients and 13 studies, patients who underwent thoracic aortic aneurysm repair were examined.[21] In this study, OSR was applied to younger patients and EVAR was chosen for mostly elderly. According to this meta-analysis, the rate of renal failure development was higher in the OSR (p=0.01). On the other hand, the age difference between the groups appeared to be an important issue in this analysis. However, Scheer et al.[22] concluded that the development of renal insufficiency did not show a significant difference between the octogenarian and younger patients.

In another study, Grant et al.[23] examined the risk factors of renal failure in patients undergoing elective OSR with a logistic regression model. As a result, age >75 years, symptomatic AAAs, respiratory disease, hypertension, juxta-/supra-renal AAAs, and a serum creatinine level of >150 μmol/L were found to be risk factors. According to the data obtained from this study, for the renal insufficiency in the scoring system, the age of >75 years was 1.5 and serum creatinine >150 μmol/L was 2.5, while the other factors were evaluated with 2 points.

Geriatric patients and renal failure are two important issues for aortic aneurysm repair. Egorova et al.[24] evaluated 66,943 patients who underwent EVAR and recommended a scoring system for 30-day mortality risk. In this scoring system, age and renal failure were the factors which increased the risk. For age between 75 and 79 years one point, 80 and 84 years two points, and ≥85 years four points were determined. On the other hand, the highest risk factor was renal failure (7 points) requiring dialysis. A recent study by Saratzis et al.[7] investigated the development of renal insufficiency due to EVAR in 146 patients, and demonstrated that the rate of renal insufficiency was significant (18.8%) and was associated with mortality. Wald et al.[25] also compared EVAR and OSR in terms of renal failure in their retrospective study including 6,516 patients. Renal failure developed in 6.7% of the patients. However, the authors observed that EVAR had a lower probability (OR: 0.42, 95% CI: 0.33-0.53). In addition, EVAR was more advantageous, as it reduced renal failure requiring dialysis (OR: 0.30, 95% CI: 0.15-0.63). Our analysis and results were an update of a previous meta-analysis performed with only three studies.[26] This current meta-analysis applied with 10 versus three studies in 9,027 versus 2,159 patients. According to these results, retrospective studies have more weight. The total weight of prospective studies was 16.99%.[13,16,17] The weight of four studies with a high sample size was 64.39%.[12,15,18,19] Also, these were retrospective studies. Among the studies we included in the quantitative analysis, there was no study with a randomized-controlled design.

In their research, Hagiwara et al.[27] retrospectively examined 350 patients and 25.7% had chronic renal failure. After 30 months of follow-up, the rate of chronic renal failure increased to 33.4%. On the other hand, 27.5% of them had acute renal failure postoperatively. In this study, the authors concluded that being over 65 years of age was a risk factor for chronic renal failure development, but not for acute renal failure. In another study, Patel et al.[28] examined the effect of renal failure on clinical outcomes in 8,701 patients with chronic renal failure. They analyzed the patients by classifying them as mild, moderate, and severe renal insufficiency and EVAR or OSR. When the groups with mild and severe renal insufficiency were compared, a significant relationship was observed between renal failure severity and 30-day mortality, prolongation of ventilation, and acute renal failure in both EVAR and OSR groups. However, an increased amount of blood transfusion and cardiac arrest differed only in the EVAR group. The development of renal insufficiency in the aneurysm repair may increase the risk for morbidity, leading to an increase in the cost of treatment and mortality due to secondary causes.

There are some limitations to the present research. The lack of randomized-controlled trials which fulfilled the inclusion criteria are the main limitation. On the other hand, although many studies included patients over 80 years of age, the fact that the age variable for renal failure development was not examined by age subgroups reduced the number of studies we analyzed.

In conclusion, our study results suggest that repair of aortic aneurysms with both techniques carries a risk for renal failure development, and the risk is higher with open surgical technique in patients over the age of 80 years. However, further large-scale, randomized-controlled studies are needed to confirm these results.

Declaration of conflicting interests

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Does pleurotomy have any effect on postoperative respiratory system functions after cardiac surgery?

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ABSTRACT

Objectives: The aim of this study was to evaluate the effects of pleural integrity on respiratory system functions after cardiac surgery.

Patients and methods: In this prospective, cohort study, a total of 114 patients (84 males, 30 females; mean age 56.3±13.1 years; range, 21 to 76 years) who underwent on-pump cardiac surgery between February 2016 and June 2016 were included. The patients were divided into two groups: open (Group 1, n=56) and intact pleura (Group 2, n=58). Arterial blood gas values (pH, partial pressure of oxygen [PaO_2], partial pressure of carbon dioxide [$PaCO_2$], and oxygen saturation [SaO_2]), and respiratory and heart rates were evaluated per-operatively. Preoperative and the fifth postoperative day values of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC% were compared between the groups.

Results: Extubation time and duration of mechanical ventilation were similar in both groups ($p>0.05$). There was a significant decrease of FEV1 and FVC of open versus intact pleura group in terms of preoperative and the fifth postoperative day values ($p<0.001$ and $p<0.001$, respectively). There was no significant difference in the $PaCO_2$ in arterial blood gas between the groups (open; 38.6±3.5 vs. 39.0±4.2 mmHg, Intact; 37.8±2.3 vs. 38.1±2.1 mmHg, respectively $p=0.49$) at room air before surgery and on the first postoperative day ($p>0.05$). However, a significant decrease was observed in the PaO_2 ($p=0.006$ vs. $p<0.001$, respectively) and SpO_2 ($p<0.001$ vs. $p<0.001$, respectively) values of the groups between the preoperative and the fifth postoperative day values. The only significant difference regarding postoperative complications, which was higher in Group 1 ($p=0.003$), was observed in bleeding on the first postoperative day.

Conclusion: Based on our study findings, opened pleura seems not to be associated with a higher incidence of pulmonary complications, compared to the intact pleura.

Keywords: Blood gas analysis, cardiac surgical procedures, pleural effusion, respiratory insufficiency.

The causes of postoperative respiratory complications depend on several factors during cardiac surgery, and the underlying pathophysiological mechanisms include adverse effects of general anesthesia, mechanical ventilation, atelectasis, systemic inflammatory response related to cardiopulmonary bypass (CPB) procedure and various surgical techniques which may lead to deterioration in the respiratory functions.[1-5]

Previous studies have shown that possible opening of the pleura during internal mammary artery (IMA) harvesting may cause respiratory dysfunction after coronary artery bypass grafting (CABG).[1,2] On the contrary, few researches have demonstrated that preservation of the pleural integrity during IMA harvesting significantly reduces postoperative bleeding without affecting pulmonary functions.[6-8] Although limited, there are studies investigating the effect of pleural integrity in patients undergoing isolated valve operations or both valve and CABG operations.[9-11] In the present study, we aimed to evaluate the effects of pleural integrity on respiratory system functions and complications after cardiac surgery.

PATIENTS AND METHODS

In this prospective, cohort study, a total of 114 patients (84 males, 30 females; mean age 56.3±13.1

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years; range, 21 to 76 years) who underwent on-pump cardiac surgery between February 2016 and June 2016 were included. The patients were divided into two groups depending on whether the pleura was opened or intact during the surgical procedure as Group 1 (n=56, 49.1%) with an opened pleura and Group 2 (n=58, 50.9%) with an intact pleura. The preoperative and the first postoperative week data were recorded. The parameters of the study included chest X-rays, and spirometric respiratory functional tests, and arterial blood gas analysis. A written informed consent was obtained from each patient. This study was approved by the Institute Research Medical Ethics Committee at Kosuyolu Heart Training and Research Hospital. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Arterial blood gas analysis (pH, partial arterial oxygen pressure [PaO_2], partial arterial carbon dioxide pressure [$PaCO_2$], and arterial oxygen saturation [SpO_2]), heart rate and respiratory rate were evaluated preoperatively and within 8 h after extubation on the first postoperative day. Spirometric studies (forced expiratory volume in one second [FEV1]%, forced vital capacity [FVC]%, and FEV1/FVC%) were conducted preoperatively and on the fifth postoperative day.

Patients with prior cardiac surgery, emergency surgery, reduced lung function test, abnormal clotting parameters or coagulation disorders, pleural adhesions, reduced left ventricular ejection fraction (<30%), degenerative alterations of the vertebral column, or psychiatric disturbances were excluded. In our institute, preserving pleural integrity is primarily aimed in patients undergoing median sternotomy. According to the American Thoracic Society/ European Respiratory Society (ATS/ERS) Position Statement on the diagnosis and treatment of chronic obstructive pulmonary disease (COPD), patients with mild-to-moderate COPD with FEV1 ≥50% and FEV1/FVC ≤0.7 were not included in the study.[12]

Pleural effusion was considered relevant, when it was moderate (pleural effusions represented a significant accumulation of pleural fluid, but did not produce respiratory symptoms and did not require thoracentesis) or large (pleural fluid which resulted in dyspnea and required thoracentesis), while atelectasis was considered significant when a clear radiological shadow with a width more than 15 mm was observed on chest X-ray. The anteroposterior chest X-rays were taken 24 h after extubation and, if possible, on the sixth postoperative day or before discharge.[13] Chest X-rays were interpreted by a single radiologist and the spirometric studies and arterial blood gases were interpreted by a single anesthesiologist who were both blinded to the study groups. Median sternotomy was performed in all patients. Intermittent inflation of the lungs was the ventilator management strategy during CPB. The remaining steps were carried out in a standard fashion.

Chest tube drainage was documented for 24 h postoperatively. Chest tubes were removed, when drainage was less than 100 mL/day. Acetylsalicylic acid (150 mg/day) was given on the first postoperative day, and sodium warfarin was additionally used for patients who underwent valvular operations. Reoperation for bleeding was defined as bleeding which required early surgical re-exploration after the end of the operation. The criteria were as follows: the drainage of more than 500 mL of blood during the first 1 h, more than 400 mL during each of the first 2 h, more than 300 mL during each of the first 3 h or more than 1,000 mL in total in the first 4 h; sudden massive bleeding; obvious signs of cardiac tamponade; and excessive bleeding despite correction of coagulopathies.[14] All patients were transferred to the intensive care unit (ICU) after the operation. The lungs were initially ventilated in synchronized intermittent mandatory ventilation at 12 to 14 breaths/min, an inspiratory/ expiratory ratio of 1:2, positive end-expiratory pressure (PEEP) of 3 cmH_2O, and tidal volume of 8 mL/kg of body weight for keeping arterial oxygen saturation above 90%. All patients received similar analgesic protocol administered during the initial five postoperative days and were given daily chest physiotherapy until discharge. If an acute respiratory insufficiency episode was diagnosed with regard to criteria for acute respiratory distress (dyspnea, respiratory rate more than 24 breaths/min, use of accessory muscles of respiration, arterial blood gas analysis with pH<7.35 and partial pressure of oxygen in arterial blood PaO_2/fraction of inspired oxygen (FiO_2) ratio less than 200 mmHg or PaO_2 less than 60 mmHg, while the patient was breathing oxygen through an air-entrainment mask), patients received bilevel positive airway pressure (BiPAP) in addition to standard therapy.[13] Standard treatment included diuretics, inhaled beta-agonist, and inhaled

ipratropium bromide, and intravenous theophylline, if clinically indicated.

On the second postoperative day, all catheters, urinary catheters, and central venous and arterial lines were removed and the patients were mobilized as soon as possible. The hospital mortality was defined as death for any reason occurring within 30 days after the operation.[15] Respiratory failure was defined as pulmonary insufficiency requiring intubation and ventilation for a period of 72 h or longer at any time during the postoperative stay. Low cardiac output syndrome was defined as a cardiac index of 2.0 L/min/m^2, requiring pharmacological support of more than one inotropic agent and/or use of intra-aortic balloon pump.[16] Postoperative renal dysfunction was defined as an increment in the creatinine level of ≥1 mg/dL compared to the preoperative value. Neurological complications as any focal brain lesion were confirmed based on clinical findings or cranial computed tomography imaging.[17] The critical hematocrit value is patient- and organ-specific and varies intraoperatively according to the duration and temperature of bypass, as well as for a variable postoperative period.[18]

Statistical analysis

Statistical analysis was performed using the Number Cruncher Statistical System (NCSS) version 23 (NCSS LLC, Kaysville, Utah, USA) & and Power Analysis and Sample Size (PASS) version 23 (NCSS LLC, Kaysville, Utah, USA) statistical software. Normal distribution was evaluated using the Kolmogorov-Smirnov test. Descriptive data were presented in mean ± standard deviation (SD), median (min-max) or number and frequency. Categorical variables between the groups were compared using the Student t-test, while the paired sample t-test and Wilcoxon signed-rank test were used to evaluate normally and non-normally distributed variables, respectively. Roentgenographic data were analyzed using the Fisher's exact test. Qualitative data was compared using the chi-square and Fisher's exact test, when appropriate. A p value of <0.05 was considered statistically significant.

RESULTS

There was no significant difference in the demographic characteristics, pre- and intraoperative

Table 1
Demographic characteristics and perioperative data

	Total (n=114)			Opened pleurae (Group 1; n=56)			Intact pleurae (Group 2; n=58)			
Variables	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	p
Age (year)			56.3±13.1			58.1±11.7			54.6±14.3	0.15
Body surface area (m^2)			1.8±0.2			1.8±0.2			1.7±0.2	0.14
Men (%)		73.7			75			72.4		0.75
Smoking history (%)		42.1			39.3			44.8		0.55
Ejection fraction (%)			57.6±8.2			56.2±9.3			59±6.7	0.07
EuroSCORE			2.7±2.1			2.7±2.4			2.6±1.7	0.58
Hematocrit (preoperative) (%)			43.3±3.5			44.3±3.6			42.6±3.5	0.69
CC time (min)			59.7±32.8			57.8±27.4			61.5±37.4	0.55
CPB time (min)			92.8±34.5			93.7±30.4			91.8±38.2	0.77
Isolated CABG	83			44			39			0.33
Combined CABG and valve surgery	6			2			4			0.21
Valve surgery	25			10			15			0.19
Distal anastomoses, (number of vessels)			2.6±0.7			2.7±0.7			2.5±0.8	0.27
LIMA		95.4			95.8			95		0.98

SD: Standard deviation; CC: Cross-clamp; CPB: Cardiopulmonary bypass; CABG: Coronary artery bypass grafting; LIMA: Left internal mammary artery.

Table 2
Pre- and postoperative spirometric respiratory function test results after extubation

	Opened pleurae (n=56)	Intact pleurae (n=58)	
	Mean±SD	Mean±SD	*p**†
FEV1 (%)			
Preoperative	92.3±25.0	88.9±16.4	0.55
Postoperative	59.3±18.6	63.7±14.7	0.09
p‡	0.001*	0.001*	
FVC			
Preoperative	90.3±18.7	89.1±16.3	0.7
Postoperative	57.9±19.1	64.2±13.9	0.07
p‡	0.001*	0.001*	
FEV1/FVC (%)			
Preoperative	104.4±14.2	103.4±12.5	0.69
Postoperative	104.1±12.3	101.7±9.2	0.23
p‡	0.88	0.38	

SD: Standard deviation; FEV1: Forced expiratory volume in one second; FVC%: Forced vital capacity (FVC%); * p<0.05; † Student t-test; ‡ Paired sample t-test.

data of the patients including type of operations, EuroSCORE, and ejection fraction between the groups. A total of 72.8% of the patients underwent CABG, while 22% had valve surgery. Medications of pulmonary and cardiac systems prior to operation were similar (p>0.05) (Table 1).

Comparison of pre- and postoperative (Day 5) spirometric values showed no significant difference between the groups in terms of FEV1, FEV1(%), FVC, and FEV1/FVC (p>0.05). However, there was a significant decrease in the FEV1(%) and FVC of both groups on the fifth postoperative day compared to the preoperative values (p<0.001 and p<0.001, respectively). Pre- and postoperative FEV1/FVC ratios of the groups were similar (p>0.05) (Table 2).

A comparison of clinical data and arterial blood gas parameters are presented in Table 3. There were no significant differences between the two groups with respect to the respiratory rate, heart rate, arterial blood gas values at room air such as pH, PaO_2, $PaCO_2$, and SpO_2, comparing the preoperative period through the first postoperative day (p>0.05). However, there were significant differences in the PaO_2 and SpO_2 levels comparing the preoperative and post-extubation period between Group 1 and Group 2 (p<0.05).

In addition, there was no significant difference in the perioperative incidence of atelectasis or pleural effusions. However, atelectasis in each group increased significantly 24 h after extubation (p<0.05). Also, atelectasis at 72 h after extubation showed a significant difference compared to preoperative values (p<0.05); however, no significant change was observed on chest X-ray between the two groups (p>0.05). Pleural effusion significantly increased on the third postoperative day compared to preoperative in both groups (p=0.01 and p=0.001, respectively), although

Table 3
Respiratory rate, heart rate, and arterial blood gases preoperatively and on the first postoperative day

	Opened pleurae (n=56)			Intact pleurae (n=58)		
	Before operation	After operation on day 1		Before operation	After operation on day 1	
Parameters	Mean±SD	Mean±SD	*p*	Mean±SD	Mean±SD	*p*
RR (rate/min)	23.0±1.3	24.5±3.2	0.09	24.9±2.3	26.8±2.6	0.21
HR (rate/min)	106.8±14.6	108.3±11.6	0.43	104.4±13.3	105.6±10.6	0.48
Ph	7.36±0.0	7.36±0.0	0.33	7.4±0.0	7.4±0.0	0.5
PaO_2 (mmHg)	86.2±7.5	82.6±10.2	**0.006***	85.6±7.04	80.2±11	**<0.001***
$PaCO_2$ (mmHg)	38.6±3.5	39.0±4.2	0.49	37.8±2.3	38.1±2.1	0.49
SpO_2 (%)	95.9±1.8	93.9±2.4	**<0.001***	96±1.4	93.9±2.5	**<0.001***

SD: Standard deviation; RR: Respiratory rate (breaths/min); HR: Heart rate (bpm); PaO_2: Partial pressure of arterial oxygen; $PaCO_2$: Partial pressure of arterial carbon dioxide; SpO_2: Oxygen saturation; * p<0.05.

Table 4
Postoperative respiratory system-related complications

	Opened pleurae (n=56)		Intact pleurae (n=58)		
	n	%	n	%	*p*
Reentubation†	2	3.6	2	3.4	0.97
Atelectasis‡					
Preoperation	0	0	0	0	1
Postextubation (24 h)	12	21.4	10	17.2	0.57
Postextubation (72 h)	16	28.6	17	29.3	0.93
p§	**0.01***		**0.007***		
Pleural effusion‡					
Preoperation	2	3.6	2	3.4	0.57
Postextubation (24 h)	4	7.1	3	5.1	0.73
Postextubation (72 h)	15	26.7	9	15.5	0.2
p§	**0.001***		**0.01***		
Bilevel positive airway pressure‡	16	28.6	10	17.2	0.15

SD: Standard deviation; † Fisher's exact test; ‡ Chi-square test; § Wilcoxon signed-rank test; * p<0.05.

there was no significant change between the two groups (p>0.05) (Table 4). Comparison of respiratory complications in the ICU revealed that there were no significant differences between the groups in terms of the reintubation, atelectasis, or pleural effusion and patients requiring BiPAP treatment (p>0.05) (Table 4). The extubation time and duration of mechanical ventilation were similar in both groups (p>0.05) (Table 5). There were no signs of perioperative myocardial infarction in either group.

There was significant difference only in the postoperative bleeding of the first postoperative day between the two groups. The mean amount of bleeding was higher in Group 1 (612.5±274.2 mL) compared to Group 2 (481.0±182.2 mL) (p=0.003) (Table 5). No significant difference was observed in the rate of arrythmias, low cardiac output syndrome, and renal dysfunction (p>0.05). None of the patients had sternal infection, mediastinitis, sternal dehiscence, or neurological or gastrointestinal complications. In addition, there were no cases of 30-day mortality in two groups. The length of ICU and hospital stay was similar between the two groups (p>0.05).

Table 5
Postoperative data of the patients

	Total (n=114)			Opened pleurae (n=56)			Intact pleurae (n=58)			
Parameter	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Bleeding (mL/24 h)†			545.6±240.2			612.5±274.2			481.0±182.2	**0.003***
Ventilation time (h)‡			11.4±4.4			11.1±4.7			11.7±4.2	0.39
ICU stay time (days)‡			2.9±2.7			3.0±1.8			2.6±1.2	0.26
Hospital stay time (days)‡			9.3±3.0			9.7±3.4			8.9±2.5	0.20
LCOS§	4	3.4		2	3.6		2	3.4		0.57
Renal dysfunction¶	4	3.5		2	3.6		2	3.4		1.00
Mortality	0	0		0	0		0	0		1.00

SD: Standard deviation; ICU: Intensive care unit; LCOS: Low cardiac output syndrome; * p<0.05; † Student t-test; ‡ Mann-Whitney U test; § Chi-square test; ¶ Fisher's Exact test.

DISCUSSION

Although we aim to preserve pleural integrity during cardiac surgery in our institution, some surgeons perform routine pleurotomy prior to IMA harvesting to expose and prevent tension. This approach led us to constitute this study. Altered respiratory system functions are frequently observed after cardiac surgery. Reduced FVC and arterial oxygen tension are found to be responsible for the changes in the lung functions and are related to increased morbidity and mortality in the early postoperative period.[1,18] The effect of pleurotomy on pulmonary function can be explained by a higher incidence of pleural effusion and atelectasis, increased intrapulmonary shunting, and postoperative pleuritic chest pain.[6] However, some studies showed that restrictive defect in pulmonary function observed during the first 72 h after cardiac operations with CPB was unaffected by the interference with the pleural integrity.[11,19,20] Another important finding in our study is that FEVI/FVC values on the fifth postoperative day did not significantly differ from preoperative values, indicating a lack of significant pulmonary obstruction (Table 2). All patients received chest physiotherapy, as well as early mobilization, to prevent retention of secretions to be a source of decrease in the functional residual capacity (FRC) or atelectasis.[21] In the evaluation of arterial blood gas values, some authors reported a negative influence of pleurotomy in the PaO_2 and PaO_2/FiO_2 during on-pump CABG with the use of the left internal mammary artery (LIMA).[16,17] Unlike many other studies, decrease in the PaO_2 occurred in both groups on the first postoperative day and the decrease within the groups did not significantly differ ($p>0.05$) (Table 3).

In a meta-analysis of 19 randomized-controlled studies comparing IMA harvesting with intact versus open pleura, all patients demonstrated significant deterioration in the pulmonary function tests and radiographic appearance postoperatively.[20] Although pleurotomy seemed to have increased rates of atelectasis and effusions, the study showed no impact on clinical outcomes and length of hospital stay. As in our study, we found no impact on the postoperative outcomes. In contrast to these findings, decrease in the lung volume, as well as FRC, atelectasis and postoperative reduction of the PaO_2 were similar. We observed no complications directly related to pleurotomy. Many studies showed that the incidence of atelectasis was limited in preserved pleural integrity,[20,21] although there was no significant difference in the atelectasis rate of our patient groups. We believe that it could be due to pain-related breath restriction and mucus retention, leading to atelectasis. Unlike most published researches, we believe that pleurotomy reduces some adverse effects, such as tamponade or pneumothorax, in the early postoperative period. Another issue related to oxygenation is the placement of pleural drainage tube or thoracostomy tube and it has been shown that such a procedure is associated with decreased oxygenation secondary to chest wall pain, splinting, and reluctance of the patient to cough, sigh, and taking deep breaths.[21] Some authors reported that pleural effusion was more common following the LIMA harvesting.[4] Other studies, unlikely, found that pleural effusion occurred with the same frequency after CABG, even in the absence of the LIMA harvesting.[22] However, Labidi et al.[23] reported 11.9% incidence of symptomatic pleural effusion in their prospective study. We showed that the pleural integrity has no effect on pleural effusions (Table 4). Both groups of this study consisted of patients undergoing IMA harvesting, as well as valve surgery. This result has been also supported by findings of Iskesen et al.[8] showing that preservation of the pleural integrity during LIMA harvesting did not have any effect on atelectasis or pleural effusions. Lim et al.[9] divided 206 patients into three groups: isolated CABG patients (n=138), valve surgery patients (n=39), and combined procedure patients (n=29). Although patients with a left pleurotomy (n=164) had a higher incidence of left lung atelectasis (67.7% vs. 45.2%, respectively; $p=0.007$), there was no significant difference in pleural effusion (42.5% vs. 46.3%, respectively; $p=0.66$) and these results were not associated with an adverse clinical outcome.

It is crucial that postoperative bleeding, which was fewer with the preserved pleural integrity ($p=0.003$) in our study, has been shown in many studies.[7,8] Excessive bleeding in our opened pleurotomy group did not cause any pulmonary complications. Besides, postoperative anticoagulation in valve operations may increase the risk for cardiac tamponade, and pleurotomy may act as a safeguard against such a complication. This study found no significant association between bleeding and cardiac tamponade. We excluded patients with previous lung disease, such as chronic obstructive pulmonary disease, to prevent possible source for a higher incidence of respiratory related complications.

Nonetheless, there are some limitations to our study that we were unable to measure postoperative long-term respiratory tests to detect changes over time. On a chest X-ray, it can be difficult to identify atelectasis visually. However, uniform analysis was used to avoid bias of data evaluation.

In conclusion, our study results suggest that opened pleura seems not to be associated with a higher incidence of pulmonary complications, compared to the intact pleura. However, further large-scale, prospective studies are needed to establish a definitive conclusion.

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Cardiovascular Surgery and Interventions

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Effect of entering cardiopulmonary bypass prior to sternotomy on outcomes in redo open heart surgery

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ABSTRACT

Objectives: In this study, we aimed to investigate the effect of the initiation of cardiopulmonary bypass (CPB) before sternotomy on the postoperative outcomes in patients undergoing redo open heart surgery.

Patients and methods: A total of 104 patients (58 males, 46 females; mean age 48.2 years; range, 13 to 77 years) who underwent CPB via femoral cannulation before and after sternotomy between January 1990 and December 2016 were retrospectively analyzed. The patients were divided into two groups as those with femoral cannulation before sternotomy (Group 1, n=34) and those with sternotomy without femoral cannulation (Group 2, n=70). Both groups were compared in terms of pre-, intra-, and postoperative data.

Results: There was no significant difference in the pre- and intraoperative results between the groups. The rates of 24-h drainage, extubation time, length of intensive care unit and hospital stay, surgical revision for bleeding, the amount of blood transfusion, prolonged use of inotropic agents, and postoperative acute renal failure were significantly higher in Group 1.

Conclusion: Due to the lack of a significant difference in the pre- and intraoperative data of the patients and the absence of a positive contribution to the outcome of CPB before sternotomy, it is more reasonable to use this method in only high-risk patients for cardiac injury.

Keywords: Cardiopulmonary bypass, redo open heart surgery, resternotomy.

Due to the rising number of cardiac interventions and increased life expectancy, the number of recurrent cardiac procedures has dramatically increased.[1] Patients undergoing cardiac reoperations are older and have also more comorbid factors. In addition, operation procedures are more complicated compared to the initial surgery. When it is decided that it is difficult and risky to reach the heart in terms of surgery after preoperative evaluation in patients scheduled for cardiac reoperation, cannulation of the femoral artery and vein is one of the methods which can be preferred. Patients with mediastinal adhesion (i.e., recent operations, mediastinitis, or mediastinal radiation), patent graft available, an enlargement in the ascending aorta, and severe right ventricular dilatation should be evaluated as the risky group. This procedure allows the surgical team to make a safe dissection and it is also thought that the patient has secured with the chance of starting cardiopulmonary bypass (CPB) at the onset of a sudden injury which may occur.

In the present study, we aimed to investigate whether the initiation of CPB via femoral arterial and venous cannulation prior to sternotomy affected the operative results of the patients scheduled redo open heart surgery.

PATIENTS AND METHODS

In this retrospective study, a total of 104 patients (58 males, 46 females; mean age 48.2 years; range, 13 to 77 years) who underwent CPB via femoral cannulation before and after sternotomy between January 1990 and December 2016 were retrospectively analyzed. The patients with a previous cardiac surgery who underwent standard unicaval, bicaval, or femoral artery cannulation were included in the study. Those with axillary artery, subclavian artery and jugular

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venous cannulation, and undergoing off-pump surgery were excluded from the study. The patients were divided into two groups as those with femoral cannulation before sternotomy (Group 1, n=34) and those with sternotomy without femoral cannulation (Group 2, n=70). Patient data were obtained from the hospital registry system. Data including baseline demographic and clinical characteristics of the patients and intra- and postoperative data were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Izmir Katip Çelebi University Atatürk Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation, median (min-max) or number and frequency. The distribution of the variables was analyzed using the Kolmogorov-Smirnov test. Independent samples t-test and Mann-Whitney U test were used to examine quantitative independent variables. The chi-square test was used to analyze qualitative independent variables, while the Fisher's exact test was performed to analyze data not suitable for chi-square test conditions. A p value of <0.05 was considered statistically significant.

RESULTS

There was no statistically significant difference in the preoperative characteristics such as age, EuroSCORE, ejection fraction, pulmonary artery pressure, smoking habit, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, or chronic renal failure between the groups (p>0.05). However, the number of male patients was significantly higher in Group 1 (p<0.05) (Table 1). There was no statistically significant difference in the operative data of the patients (p>0.05) (Table 2).

In addition, the patients were compared in terms of the data obtained from postoperative intensive care unit and ward follow-up. There was no significant difference between the groups in terms

Table 1
Baseline demographic and clinical characteristics of patients

	Group 1 (n=34)				Group 2 (n=70)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	p
Age (year)			49.1±12.1	50.5			47.9±15.4	47.5	0.680*
Sex									0.034†
Male	24	70.6			34	48.6			
Female	10	29.4			36	51.4			
EuroSCORE			5.6±2.1	5.0			6.1±2.2	6.0	0.277‡
Ejection fraction			55.1±6.9	57.5			55.3±7.8	60.0	0.841‡
Pulmonary artery pressure			32.8±13.3	30.0			40.9±21.0	35.0	0.072‡
Smoking habit	18	52.9			27	38.6			0.165†
Hypertension	16	47.1			23	32.9			0.161†
Diabetes mellitus	7	20.6			10	14.3			0.377†
COPD	3	8.8			6	8.6			0.966†
Chronic renal failure	0	0.0			1	1.4			1.000†
LIMA use in first operation	6	17.6			9	12.9			0.514†
Total surgery									0.595†
2	32	94.1			68	97.1			
3	2	5.9			2	2.9			

SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; LIMA: Left internal mammary artery; * t-test; † Chi-square test; ‡ Mann-Whitney U test.

Table 2
Intraoperative data

	Group 1 (n=34)				Group 2 (n=70)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
Duration of operation (min)			301.6±71.8	293			276.1±62.2	270	0.097†
Duration of CPB (min)			139.3±48.3	132.5			132.2±54.0	117.0	0.262†
Duration of aortic cross-clamping (min)			92.3±40.1	94.5			87.1±39.2	76.5	0.425†
Cardiac injuring during sternotomy	2	5.9			1	1.4			0.249‡

SD: Standard deviation; CPB: Cardiopulmonary bypass; † Mann-Whitney U test; ‡ Chi-square test.

of the need for intra-aortic balloon pump support, premature mortality, and development of neurological complications (p>0.05). In Group 1, 24-h drainage, extubation time, the length of intensive care unit stay and discharge time, the need for postoperative revision surgery for bleeding, the amount of blood product use, prolonged use of inotropic agents, and postoperative acute renal failure development were significantly higher (p<0.05) (Table 3).

The rate of mitral valve replacement was found to be higher in Group 2 (p<0.05). However, there was no statistically significant difference between the two groups, when the first operations were compared (p>0.05). In addition, there was no significant difference in the time interval between the first operation and the second operation between the groups (Table 4).

DISCUSSION

At the present time, open heart surgery has dramatically evolved owing to the increased experience and technological developments. With the increase in life expectancy, the number of patients with cardiac reoperations has been increasing day by day.[1] Patients who need cardiac reoperation are older and have also more comorbid factors. In addition, mediastinal exploration is thought to be more difficult in these patients. One of the preferred methods is the initiation of CPB through femoral cannulation before sternotomy to prevent the complications which may occur due to these factors. Therefore, the operation was started by the initiation of CPB via femoral cannulation before sternotomy for patients who were at risk for cardiac injury in our center.

Table 3
Postoperative data

	Group 1 (n=34)				Group 2 (n=70)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
24-h drainage			982.9±617.8	1000			735.3±680.1	535	0.022†
Blood product use (IU)		3.6	5.5	5		1.3	2.3	2	0.000†
IABP use	6	17.6			6	8.6			0.174‡
Extubation time (h)			23.2±19.7	17.5			18.6±20.7	14.0	0.009†
ICU staying (day)			8.2±7.8	4.0			6.9±13.3	3.0	0.011†
Discharging time (day)			19.5±12.5	16.0			12.3±9.6	8.0	0.000†
Bleeding revision operation	19	55.9			8	11.4			0.000‡
Prolonged use of inotropic agents (24 h)	27	79.4			31	44.3			0.001‡
Premature mortality (in 30 day)	4	11.8			8	11.4			0.960‡
Neurological complications	6	17.6			8	11.4			0.358‡
Postoperative ARF development	12	35.3			9	12.9			0.008‡

SD: Standard deviation; IABP: Intra-aortic balloon pump; ICU: Intensive care unit; ARF: Acute renal failure; † Mann-Whitney U test; ‡ Chi-square test.

Table 4
Comparison of operations

	Group 1 (n=34)				Group 2 (n=70)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
Previous operation									
Mitral valve replacement	9	26.5			30	42.9			0.107‡
Other operations	6	17.6			12	17.1			0.949‡
Aortic and mitral valve replacement	2	5.9			8	11.4			0.329‡
Aortic valve replacement	6	17.6			4	5.7			0.054‡
Open mitral commissurotomy	3	8.8			5	7.1			0.764‡
Coronary artery bypass grafting	8	23.5			11	15.7			0.336‡
Duration between operations (month)			103.2±109.7	60.5			91.4±78.3	79.5	0.760†
New operation									
Mitral valve replacement	9	26.5			37	52.9			0.014‡
Other operations	11	32.4			8	11.4			0.009‡
Aortic and mitral valve replacement	1	2.9			4	5.7			0.537‡
Aortic valve replacement	6	17.6			8	11.4			0.385‡
Open mitral commissurotomy	0	0.0			3	4.3			0.222‡
Coronary artery bypass grafting	7	20.6			10	14.3			0.417‡

SD: Standard deviation; † Mann-Whitney U test; ‡ Chi-square test; Other operations include aortic valve repair, atrial septal defect Repair, Bentall procedure, supracoronary aortic replacement, pericardiotomy, Tetralogy of Fallot, tricuspid valve replacement, ventricular septal defect patchplasty.

In the light of this information, the idea of making a serious preoperative evaluation before the onset of cardiac reoperation is in the foreground. Apart from the standard approach, we are confronted with the literature on the advantages and disadvantages of various techniques such as computed tomography (CT), magnetic resonance imaging (MRI), transesophageal electrocardiography (TEE), and nuclear MRI.[2-6] Among them, we believe that CT plays an important role in the preoperative evaluation of patients scheduled for cardiac reoperation. However, we do not recommend CT to be used routinely for the reasons of financial burden and time lost. In our clinical practice, we prefer using it in patients in whom the internal mammary artery was used as a graft in the previous operation, patients who have risk factors on their chest X-ray, and those exposed to sternotomy at least two times previously.

It is thought that the initiation of CPB via femoral cannulation prior to the sternotomy leads to a complete evacuation of the heart without compromising the hemodynamic parameters during the sternotomy, allows an easier dissection, and causes less injury to the mediastinal structures and less bleeding. Review of the literature reveals that the initiation of CPB before resternotomy may avoid heart injuries, leading to hemodynamic disturbance along with heart decompression and allows a safer and easier dissection.[7,8] However, some authors have reported that re-entry injuries which can be occurred during redo open heart surgery do not produce any significant differences, when compared to the initial sternotomy.[7-11] In our study, three patients in the total of two groups had cardiac injury which did not impair hemodynamics during resternotomy. There was no statistically significant difference between the two techniques, consistent with the literature data.

There are many studies in the literature regarding the parameters related to postoperative mortality and morbidity. In a study, Merin et al.[12] reported a mortality rate of 9%, while O'Brien et al.[10] reported a mortality rate of 2.9% and Salehi et al.[2] reported a mortality rate of 3%. In our study, the mortality rate was found to be 11.8%, indicating no statistically significant difference between the two groups. These findings are consistent with the current literature. In addition, based on these findings, we conclude that the comparison of the duration of operation and the duration of CPB is of utmost importance for redo open heart surgery patients. In the literature, the only study comparing two techniques reported that the duration of operation was statistically significantly shorter in the group in which CPB was initiated before resternotomy, while the duration of CPB

was found to be longer in the group without CPB before resternotomy.[13] In our study, we observed no statistically significant difference in this respect. Therefore, we believe that the duration of femoral cannulation preparation is short and that our clinic has sufficient surgical experience in peripheral cannulation.

On the other hand, Luciani et al.[13] found that the patients who underwent CPB prior to resternotomy were less likely to have postoperative bleeding and prolonged use of inotropic agents. Again, in the same study, the patients were found to have shorter periods of the intensive care unit stay. In our study, Group 1 was found to have higher values of postoperative 24-h drainage, prolonged inotropic support need, and surgical revision for bleeding. This can be attributed to the fact that coagulopathy can be more frequent due to prolonged systemic heparinization. However, in our study, unlike Luciani et al.,[13] the duration of extubation, length of intensive care unit stay, and discharge time were significantly higher in the patients who underwent CPB before resternotomy. We believe that this is due to the higher amount postoperative bleeding and the increased need for blood product use in our study.

In the present study, the primary objective was to investigate the effect of CPB before resternotomy on postoperative mortality and morbidity. In addition, there are many studies in the literature reporting the mortality and morbidity rates in patients requiring resternotomy.[10-12,14] Yet, in our study, the mortality rate was found to be 11.6%, indicating no statistically significant difference between the two groups. These findings are consistent with the current literature. Furthermore, postoperative mortality and morbidity were examined in the study of Luciani et al.,[13] which is the only study comparing the patients who did and did not receive CPB before resternotomy, as in our study. According to this study, the mortality, stroke, myocardial infarction, sepsis, and lung failure rates were similar in both groups. Unlike our study, in this study, acute renal failure was found to be more frequent in patients who did not receive CPB prior to resternotomy. In our study, the development of acute renal failure was found to be statistically significantly higher in the group of patients who underwent CPB before resternotomy. We believe that this difference in our study is the result of a higher amount of blood products used due to the greater amount of bleeding in the patient group who underwent CPB prior to sternotomy. Based on many studies, it was shown that increasing need for blood use increased the rate of deterioration of renal function.[15,16]

The complications which may develop after femoral cannulation have been discussed in many studies. These include vascular injury, hematoma, pseudoaneurysm, lower extremity ischemia, and wound infections.[13] In our study, no complication was encountered in the patient group in which the femoral artery cannulation was performed.

The main limitation of our study is its retrospective design with a relatively small sample size. However, we believe that our study is valuable, as it shows the differences in initiation of CPB before resternotomy compared to the conventional method.

In conclusion, patients who are scheduled for resternotomy are at a particular risk than those who are scheduled for surgery for the first time. Therefore, preoperative management of these patients is crucial. Starting of CPB prior to resternotomy may reduce the risk of cardiac injury and help surgeons feel more secure. However, it should be taken into account that there may be adverse effects on postoperative results, particularly due to the increased amount of bleeding and the use of blood. Nevertheless, the initiation of CPB should be considered as an alternative for patients who are at risk for preoperative cardiac injury.

Declaration of conflicting interests

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Association between non-dipping status and carotid intima-media thickness in patients with elevated blood pressure category

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ABSTRACT

Objectives: This study aims to evaluate the relationship between non-dipping pattern and carotid intima-media thickness (CIMT) in patients with elevated blood pressure (BP).

Patients and methods: Between November 2019 and April 2019, a total of 150 consecutive patients (84 males, 66 females; mean age 52.3±10.1 years; range, 40 to 65 years) with elevated BP (systolic BP between 120 and 129 mmHg and diastolic BP less than 80 mmHg) were included. The patients were divided into two groups as the dipper (n=92) and non-dipper (n=58) groups according to the ambulatory BP measurements. The CIMT was measured using ultrasonography and compared between the groups.

Results: The CIMT was significantly higher in the non-dipper group (0.7±0.2 mm vs. 1.0±0.2 mm, respectively; p<0.001). The CIMT was an independent predictor of non-dipping pattern in the multivariate logistic regression analysis (odds ratio: 1.098, 95% confidence interval: 1.062-1.135; p<0.001).

Conclusion: Our study results show that the non-dipping status is closely associated with the known indicator for atherosclerosis such as CIMT in elevated blood pressure category.

Keywords: Carotid intima-media thickness, levated blood pressure, non-dipping status.

A meta-analysis of observational studies has shown that elevated blood pressure (BP) is closely related to cardiovascular diseases, subclinical atherosclerosis, and all-cause death.[1] Recent studies have shown that 24-h ambulatory BP monitoring (ABPM) is more accurate compared to office BP measurements in predicting adverse cardiovascular events, particularly due to the opportunity of nocturnal BP measurements.[2-6] During the sleep period, the BP should decrease by more than 10% compared to daytime (dipping status). If the mean systolic BP (SBP) and diastolic BP (DBP) levels decrease by less than 10% or do not fall, it is considered a non-dipping status.[7] There is an insufficient cardiac index, pulse index, and sympathetic activity reduction at night compared to daytime in non-dipping status.[8] The association of the non-dipping pattern with target organ damage and worsening cardiovascular outcomes is due to the relatively high BP exposure of the cardiovascular system during the night, and the compensatory structural and functional changes in the vascular structures lead to irreversible damage in the entire vascular system.[9]

Elevated BP term, newly included in the classification of 2017 American College of Cardiology (ACC)/American Heart Association (AHA) High Blood Pressure in Adults Clinical Practice Guideline, refers to an SBP of 120 to 129 mmHg and a DBP of <80 mmHg.[10] This definition covers lower levels of BP and should not to be confused with the prehypertension term which was previously defined in the JNC 7 report, as SBP 120 and 139 mmHg and DBP of 80 to 89 mmHg in more than two or more separate readings in two or more separate occasions.[11]

Increased carotid intima-media thickness (CIMT) is a thickening of intima, media, or both layers. While intimal thickening is more likely a result of

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similar pathogenetic mechanisms of atherosclerotic plaques, thickening of media is primarily related to hypertension. That is why CIMT is one of the most reliable markers of preclinical atherosclerosis. Also, CIMT is an important surrogate marker of target organ damage in the hypertensive patient.[12] High BP, as one of the most important cardiovascular risk factors, has been shown to be associated with the progression of CIMT.[13]

The association between non-dipper pattern and increased CIMT is shown in essential hypertension and some normotensive cohorts such as overweight men or polycystic ovary syndrome patients in different studies.[14] However, as a result of the literature search, we found no study investigating the relationship between CIMT and elevated BP patients' non-dipping status, as a novel issue.

In the present study, we aimed to evaluate the relationship between the CIMT and non-dipping pattern in patients with elevated BP.

PATIENTS AND METHODS

In this cross-sectional study, a total of 150 consecutive patients (84 males, 66 females; mean age 52.3±10.1 years; range, 40 to 65 years) who were admitted to our clinic with elevated BP (systolic BP between 120 and 129 mmHg and diastolic BP less than 80 mmHg) between November 2019 and April 2019 were included. Patients with hypertensive history were not included in this study. In the initial phase, 172 patients were enrolled in our study. However, five with coronary artery disease, three with severe heart valve diseases (one severe aortic stenosis and two moderate mitral insufficiencies), three with diabetes, and two with chronic renal insufficiency with an abnormal approximate glomerular filtration rate were excluded from the study. A 24-h ABPM was done. Six with normal BP and two with masked hypertension (based on ABMP) and one extreme dipper subject were excluded. Finally, 150 patients were eligible to include in our study. The patients were divided into two groups as the dipper (nocturnal decline in mean BP ≥10%; n=92) and non-dipper (nocturnal decline in mean BP <10%; n=58) groups according to the ambulatory BP measurements. The body weight and height measurements were recorded according to standard protocols with ultimate calibrated instruments. Echocardiographic examination and CIMT measurements were performed once at the time of admission. A written informed consent was obtained from each patient. The study protocol was approved by the Ethics Committee of Sanko University (Date: 27.05.2018, No: 2018/6). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Definitions

All patients were comprehensively assessed for clinical risk factors such as age, sex, and smoking status, and office DBP and SBP, and heart rate (HR) measurements were recorded. The patients were considered to have elevated BP if they had a SBP between 120 and 129 mmHg and DBP less than 80 mmHg on average of at least two measurements obtained on two occasions, according to 2017 High Blood Pressure Clinical Practice Guideline.[15] Smoking was defined as at least one pack/year of smoking history.

Office and ambulatory BP measurements

The HR and BP were measured using a non-invasive automated system (Mobil-O-Graph NG, I.E.M., Stolberg, Germany) at 30-min intervals for 24 h. The British Hypertension Association and the European Hypertension Association have approved the use of this device following BP measurement.[16] All patients underwent ABPM for 24 h with the same usual working day.[17] The patients were kept on a regular schedule throughout the study, at 08:00 A.M. (wake up), and the room lights were closed at 10:00 P.M. The records were not accepted without at least 50 measurements in 24 h and at least one measurement was performed every 2 h. The mean day and night SBP and DBP of each patient were calculated.

Carotid artery ultrasonographic measurements

The common carotid artery (CCA) was visualized using a Vivid E9 (Bioject Medical Technologies Inc., OR, USA) with an MLA-15 transducer. The CIMT measurement was performed on the supine position at an angle of 45°. One-cm segment was identified within the first 2 cm distal region from the main carotid artery bulb and the images were recorded on the computer. From these images, the mean CIMT (CIMTmean) values of the segment studied were determined based on the remote edge measurement method with a special intima-media thickness measurement program (M'Ath ver 2.0; Metris, Argenteuil, France). The measurement was performed for both main carotid

arteries. Later, these values were evaluated separately and averaged. All measurements were performed by an experienced radiologist who was blinded to the study data.[18]

Echocardiographic measurements

Echocardiographic recordings were obtained by two qualified cardiologists who were blinded to the study data. Standard two-dimensional and M-mode echocardiographic parameters were obtained using the Vivid 7 GE echocardiography device (GE Healthcare, Little Chalfont, UK). Parasternal long and short axis, apical four-space, and apical two-chamber images were used for the evaluation of the left ventricular (LV) and valve functions. Pulsed Doppler ultrasonic examination was performed with a 2.5 MHz transducer. Parasternal and apical images were acquired, while the patient lied in the left lateral decubitus position. M-Mode measurements were applied according to the guidelines from the American Society of Echocardiography.[19] Posterior wall thickness (PWT), interventricular septum (IVS) thickness, end-diastolic, and end-systolic diameters, and LV ejection fraction were measured with M-mode echocardiography in the parasternal long-axis position (at the level of the mitral valve, perpendicular to the ventricular long axis). All measurements were calculated over three successive heartbeats.

Using pulsed-wave Doppler sample-volumes (before and during Valsalva maneuver), LV inflow velocities were recorded 0.5 cm above the mitral valve annulus in the apical four-chamber view. From the obtained data, mitral E and A velocities, isovolumetric relaxation, and contraction times (IVRT and IVCT), deceleration time (DT) were measured. The three left atrial dimensions (LAD) were obtained: D1 was measured from the middle of the mitral annular plane to the

Table 1
Baseline characteristics of the study population

	Dipper group (n=92)			Non-dipper group (n=58)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			51.8±9.9			52.8±10.6	0.560*
Sex Male	49	53.3		35	60.3		0.395**
Smoking	24	26		33	56		0.498**
Body mass index (kg/m^2)			28.2±2.7			28.7±2.5	0.222*
Glucose (mg/dL)			92.6±8.5			95.9±3.3	0.134*
Creatinine (mg/dL)			0.83±0.12			0.86±0.12	0.155*
Creatinine clearance (mL/min)			67.0±19.8			75.4±31.8	0.076*
Total cholesterol (mg/dL)			185.5±47.9			191.5±36.7	0.415*
Triglyceride (mg/dL)			175.8±30.1			201.0±34.2	0.266*
High density lipoprotein (mg/dL)			36.3±8.1			36.4±8.7	0.954*
Low density lipoprotein (mg/dL)			116.9±26.9			121.1±27.2	0.361*
Heart rate (beats/pm)			79.8±10.9			78.9±10.0	0.674*
Office SBP (mmHg)			122.2±8.6			123.2±7.8	0.672*
Office DBP (mmHg)			72.6±6.4			72.9±6.2	0.822*
Ambulatory 24-h SBP (mmHg)			115.7±10.8			116.2±9.3	0.492*
Ambulatory 24-h DBP (mmHg)			70.1±5.6			70.9±6.3	0.724*
Ambulatory day-time SBP (mmHg)			120.8±9.6			117.9±10.1	0.117*
Ambulatory day-time DBP (mmHg			72.8±7.1			72.3±7.4	0.251*
Ambulatory night-time SBP (mmHg)			106.1±5.8			117.6±6.9	**0.024***
Ambulatory night-time DBP (mmHg)			64.8±6.2			70.1±6.9	**0.046***

SD: Standard deviation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; * Student t test and Mann-Whitney U test; ** Chi-square test.

superior aspect of the left atrium (LA); D2 was the orthogonal short-dimension to D1 in a four-chamber view; and D3 was the anterior-posterior diameter measured in a parasternal long-axis. The LA volume calculated with an ellipsoid formula: LA volume (mL)= π/6 (D1)(D2)(D3).[20] The left atrial volume index (LAVI) formula is LA volume/body surface area (BSA).[21] The LV mass index (LVMI) was calculated using the Devereux formula.[22] with diastolic measurements of LV internal diameter (LVID), interventricular septal thickness (IVST), and PWT.

Laboratory parameters

All biomarkers were examined in the serum samples obtained from the patients' blood. Blood samples were drawn after 20 min of rest, following 12-h starvation and centrifuged at 2,000 rpm for 10 min within 20 min. The samples were flash-frozen in the liquid nitrogen and immediately stored at -80°C until analysis. Standard biochemical parameters including blood glucose, creatine, and lipid panels were measured.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 24.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine the normality of data distribution. Categorical variables were expressed in number and frequency, while continuous variables were expressed in mean ± standard deviation (SD) or median (min-max). Continuous parametric variables were compared using the Student t-test. The chi-square (χ^2) test was used to compare groups with categorical variables. The Mann-Whitney U test was used to compare groups with continuous non-parametric variables. In the univariate logistic regression, variables with a significance level of $p<0.25$ were identified as the potential risk-takers and were included in the multivariate model as covariates. The last model was formed by determining the discriminant factors between the groups based on logistic regression analysis. A p value of <0.05 was considered statistically significant.

RESULTS

Table 1 summarizes the baseline characteristics of the study population. The baseline characteristics were similar between the groups ($p>0.05$ for all) (Table 1). The LAD, LA volume, and LAVI were significantly higher in the non-dipping group than the dipping

Table 2
Carotid intima-media thickness and echocardiographic parameters

	Dipper group (n=92)	Non-dipper group (n=58)	
	Mean±SD	Mean±SD	p
Left ventricular ejection fraction (%)	58.3±6.2	59.2±2.8	0.334
Intraventricular septum (cm)	13.8±1.5	14.3±2.2	0.254
Posterior wall thickness (cm)	11.8±1.7	12.5±1.9	0.352
End diastolic diameter (cm)	35.6±4.5	36.3±4.7	0.428
End systolic diameter (cm)	27.4±4.0	27.4±3.4	0.949
Left ventricle mass index (g)	101.1±22.4	112.5±22.7	0.022
Left atrial diameter (mm)	31.8±3.6	34.3±2.6	<0.001
Left atrium volume (mm^3)	28.2±2.2	38.6±2.8	<0.001
Left atrial volume index (mL/m^2)	21.3±5.5	28.5±6.7	<0.001
E/A	0.83±0.14	0.76±0.13	0.009
Deceleration time (msec)	243.1±35.2	246.4±36.6	0.703
Isovolumetric relaxation time (msec)	74.1±5.3	74.9±5.5	0.380
Isovolumetric contraction time (msec)	75.3±2.6	75.2±2.4	0.758
Carotid intima-media thickness (mm)	0.74±0.17	0.97±0.15	<0.001

SD: Standard deviation; E: Mitral early diastolic velocity; A: Mitral late diastolic velocity; All tests were made by Student t test and Mann-Whitney U test.

Table 3
Independent determinants of non-dipping status

	Linear regression analysis			Logistic regression analysis		
	Coefficients	95% CI	*p*	OR	95% CI	*p*
Body mass index	0.016	-0.007-0.039	0.162			
Smoking	0.072	-0.058-0.202	0.273			
Age	0.004	-0.002-0.011	0.155			
Heart rate	-0.001	-0.007- 0.004	0.660			
Low density lipoprotein	0.002	-0.004-0.004	0.096			
Left ventricular ejection fraction	0.003	-0.009-0.015	0.653			
Left ventricle mass index	0.001	-0.001-0.004	0.212			
Left atrial volume index	0.008	0.002-0.014	<0.001	1.055	1.007-1.106	0.025
E/A	0.475	0.031-0.920	0.036			
Carotid intima-media thickness	1.211	0.911-1.511	<0.001	1.098	1.062-1.135	<0.001

E: Mitral early diastolic velocity; A: Mitral late diastolic velocity; Variables with p<0.25 in univariate regression were included into multivariate regression.

group (p<0.001 for all). The E/A ratio was lower and LVMI was moderately higher in the non-dipping group than the dipping group (p=0.009 and p=0.022, respectively). The CIMT was significantly higher in the non-dipping group than the dipping group (p<0.001) (Table 2).

The LAVI and CIMT were found to be associated with the non-dipping status. Both were independent predictors of non-dipping status in the multivariate analysis (odds ratio [OR]: 1.055, 95% confidence interval [CI]: 1.007-1.106; p=0.025 and OR: 1.098, 95% CI: 1.062–1.135; p<0.001, respectively) (Table 3).

DISCUSSION

To the best of our knowledge, this is the first study to investigate the possible relationship between elevated BP category and CIMT. In this study, we found the following findings: *(i)* CIMT was significantly higher in the non-dipping group than the dipping group; *(ii)* CIMT was strongly correlated with the non-dipping status; and *(iii)* CIMT was independent predictors of the non-dipping status.

The European Society of Hypertension (ESH)/ European Society of Cardiology (ESC) guidelines for the management of hypertension suggest a cut-off value for CIMT greater than 0.9 mm as being a conservative estimate of asymptomatic organ damage.[23] The main results of the study showed that patients with elevated BP had increased CIMT values and those with non-dipping status had statistically significant higher CIMT values, independent from other risk factors.

The relationship between the time of the BP variation and the increased CIMT has been proven by a previous study.[17] The relationship between high BP and carotid artery hypertrophy was also reported.[24] The presence of intima-media thickening and carotid plaques of CCA may be a sign of subclinical atherosclerosis and a predictor of future adverse cardiovascular events.[25] Pierdomanico et al.[26] showed a significant increase in the prevalence of CIMT in non-dippers. Pellegrino[27] also reported that CIMT was higher in individuals with high BP than in normal subjects and higher in non-dippers versus dippers. Similarly, in our study, the mean CIMT was higher in the non-dippers compared to the dippers.

The pathophysiological mechanisms of the link between non-dipping pattern and carotid intima-media thickening have not been fully elucidated, yet. However, higher BP effects on endothelial cells during day and night, high molecular levels associated with endothelial dysfunction and atherosclerosis, procoagulant processes and increased platelet activation have been thought to be possible mechanisms of this relationship.[28] In a study, Ren et al.[29] showed a relationship between BP and CIMT in the Chinese population living in the rural Tianjin region, where the incidence of stroke and prevalence of hypertension were high. A study showed SBP elevation and hypertension history as the main risk

factors for CIMT development.[30] Slightly elevated SBP in middle-aged men had a great influence on the progression of CIMT, and there was a strong and direct effect of SBP on CIMT.[13] It has was also shown that SBP had a linear and continuous correlation with high CIMT across the BP levels.[31]

To date, several studies have reported that DBP does not affect the CIMT increase.[13,31] Only one study reported a weak, direct association between the DBP and maximal CIMT increase after adjusting for other risk factors, but not after further adjusting for SBP.[13] Su et al.[33] found that the mean time-weighted 24-h ambulatory DBP was a negative predictor of CIMT. It was also shown that high pulse pressure levels caused the progression of CIMT, and increased CIMT was associated with pulse pressure widening.[32]

Many studies have claimed that males have increased CIMT values than females and age and sex strongly affect the CIMT measurement, while older age is a significant predictor of increased CIMT.[33] Vicenzini et al.[34] reported that the mean CIMT had a linear relationship with age. In our study, dipper and non-dipper groups were similar in terms of age. The increased CIMT in smokers was previously reported,[35] but in our study, there was no significant difference in terms of smoking between the non-dipper group and the dipper group which can be attributable to a small sample size. Richey et al.[36] also observed that individuals with ambulatory hypertension had increased LVMI after controlling for BMI and race. Previous studies demonstrated an increase in the LV mass index in non-dipper patients.[37,38] Similarly, our study suggested that non-dippers had significantly increased LVMI, compared to dippers. Seo et al.[39] showed that non-dippers had impaired LV systolic and diastolic dysfunction without significantly altered levels of LVMI and LAVI parameter. Nevertheless, in our study, the LAVI was higher and E/A ratio was lower in the non-dippers, as expected.

Elevated BP is the category following normal BP, in which no pharmacological treatment is recommended, whereas it is associated with an increased risk of cardiovascular diseases, end-stage renal disease, subclinical atherosclerosis, and all-cause death compared to normotensives.[40] Measurement of CIMT can be considered a determinant of early target organ damage and is valuable in the identification of elevated BP subjects with higher cardiovascular risk. Moreover, considering worse cardiovascular prognosis in patients with an increased CIMT and increased CIMT values in non-dipper group, the ABPM should be recommended in elevated BP group not only for screening for masked hypertension but to distinguish dipper and non-dipper status.

The main limitation of this study is its relatively small sample size in both groups. The lack of observation of coronary anatomy by angiography is another limitation, although we attempted to overcome this problem by excluding the suspicion of coronary artery disease according to its clinical features, medical history, and electrocardiographic findings. Positive lifestyle habits such as weight loss, regular exercise, and salt restriction were unable to be evaluated, as this study is not a follow-up study in nature. Therefore, further larger scale, prospective, randomized studies are needed to confirm these results.

In conclusion, our study results indicate that higher levels of CIMT are seen in elevated BP patients with non-dipping status. In our study, we found a correlation between the non-dipping status and the known indicator for atherosclerosis such as CIMT. Besides, the increased CIMT level was an independent predictor of non-dipping pattern. This result suggests that it is important to control nocturnal BP to prevent cardiovascular disease and target organ damage in elevated BP individuals. Of note, it has been suggested that non-dipping BP pattern in our study may be a useful risk indicator for cardiovascular events and may need close follow-up for this pattern.

Declaration of conflicting interests

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Do thromboembolic events increase in the emergency department during COVID-19 era?

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ABSTRACT

Objectives: In this study, we aimed to investigate whether thromboembolic events increased in the emergency department (ED) setting due to asymptomatic carriers.

Patients and methods: This single-center, retrospective study included a total of 40,633 patients who were admitted to ED after the first case of COVID-19 in Turkey, between 11 March 2020 and 26 May 2020 and the corresponding dates in 2019. The number of patients and demographic and clinical characteristics were compared between the two years for cardiovascular surgery (CVS)-related venous and arterial thromboembolism events.

Results: Emergency department admissions requiring CVS consultations decreased by 41.6% from 77 patients in 2019 to 45 patients in 2020. Total CVS consultations over the 11-week period per 1,000 ED admissions increased from 2.9 to 3.2. The number of deep vein thrombosis decreased from 14 to 9 during pandemic, while there was no significant difference in weekly cases of venous thrombosis. The number of arterial thromboembolism cases was 11 in 2019 and six in 2020. Weekly arterial thromboembolism admissions were not significantly different between the two years.

Conclusion: Our study results showed that the rate of thromboembolic events did not increase in the general population admitted to the ED during the first 11 weeks of the COVID-19 pandemic in Rize province of Turkey.

Keywords: Arterial thromboembolism, COVID-19, deep vein thrombosis, SARS-CoV2, thrombosis, venous thromboembolism.

Since its emergence in December 2019 in Wuhan, China, the novel coronavirus 2019 (severe acute respiratory syndrome coronavirus-2 [SARS-Cov-2]) has spread worldwide causing a pandemic. As of June 1st, more than six million cases were diagnosed across the world.[1] Mainly presenting with pneumonia of varying severity, clinicians were challenged with the wide range of clinical spectrum with which the COVID-19 is associated, pursuing to battle the public health emergency and understand it at the same time. Typical symptomatology of COVID-19 includes fever, cough, and shortness of breath.[2,3] Limiting diagnosis and screening to these symptoms overlooks many cases with COVID-19 as an estimated 30 to 50% of all infected individuals transmitted the disease with no or atypical symptoms, including but not limited to gastrointestinal, neurological, and cardiovascular complaints.[4]

Recent observations have revealed that, in hospitalized patients with COVID-19 infection, venous and arterial thrombotic events are frequent, even in low-risk and anticoagulated patients.[5-7] Deep vein thrombosis and pulmonary embolism, coronary and limb ischemia complicate the course of the disease. Both COVID-19 infection itself, the inflammatory response in severe cases, and the drug-drug interactions in the admitted patients with underlying risk factors can predispose to thrombosis.[8] Due to this predisposition and the risk of drug-drug interactions, low-molecular-weight heparin or unfractionated heparin is recommended for prophylaxis in all patients without a contraindication for COVID-19.[9] However, it is still unclear whether COVID-19 itself directly plays a role in thromboembolism or the immune system response to the infection with varying

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scale has thrombotic effects, and patients with no evident respiratory symptoms may be affected by the prothrombotic changes.

In the present study, we aimed to investigate whether thromboembolic events increased in the emergency department (ED) setting due to asymptomatic carriers in the COVID-19 era.

PATIENTS AND METHODS

This single-center, retrospective study included a total of 40,633 patients who were admitted to ED after the first case of COVID-19 in Turkey, between 11 March 2020 and 26 May 2020 and the corresponding dates in 2019 in Rize province. All patients with ED admissions throughout the study were included. Pediatric patients with <18 years of age were excluded. Patients consulted to the cardiovascular surgery (CVS) department for any cause were classified as CVS-related admissions. Data including demographic and clinical characteristics of the patients, diagnoses and comorbidities were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdoğan University Training and Research Hospital Ethics Committee and the Republic of Turkey, Ministry of Health. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All lower and upper extremity deep vein thrombosis, and central venous thrombosis were classified as venous thrombosis. Upper and lower limb arterial thromboembolisms (ATEs) were classified as arterial thrombosis. Cerebral venous thrombosis, stroke, or acute coronary syndrome cases were excluded, as they were not consulted to the CVS department. Aortic dissections included all types of acute aortic dissections, and aortic aneurysms included all aortic aneurysms of any location with or without rupture. Vascular traumas included isolated vascular injuries or multi-trauma with vascular injuries.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and percentage. The chi-square test was used to analyze categorical variables, while the Student's t-test was used to analyze normally distributed continuous

Table 1
Emergency Department Admissions between March 11-May 26 of 2019 and 2020

	2019				2020				
	n	Median	Mean±SD	IQR	n	Median	Mean±SD	IQR	*p*
Emergency department admissions									<0.001
All admissions	26,698				13,935				
Admissions per week	2,270			2167-2327.5	1,027			918.5-1332	
Cardiovascular surgery consultations									
CVS consultations	77				45				
CVS consultations/1,000 ED admissions		2.9				3.2			
Weekly CVS consultations			7.1±3.2				4.0±1.9		0.013
Weekly CVS consultations/1,000 ED admissions			3.1±1.3				3.5±1.4		0.496
CVS related hospitalizations									
Emergent CVS hospitalizations	24				19				
Emergent CVS hospitalizations/1,000 ED admissions	2	0.90			1	1.36			
Weekly emergent CVS hospitalizations				2-3				1-2.5	0.171
Weekly emergent CVS hospitalizations/1,000 ED admissions			1.0±0.5				1.5±1.2		0.248

SD: Standard deviation; IQR: Interquartile range; CVS: Cardiovascular surgery; ED: Emergency department.

Table 2
Presenting Diagnoses of Cardiovascular Surgery-related Emergency Department Admissions

	2019			2020			
	n	Median	IQR	n	Median	IQR	*p*
Emergency CVS diagnoses							
Venous thrombosis	14			9			
Venous thrombosis per week		1	0-2		1	0-1.5	0.519
Arterial thromboembolism	11			6			
Arterial thromboembolism per week		1	0.5-1.5		0	0-1	0.193
Acute aortic dissections	3			2			
Aortic aneurysm	5			8			
Vascular trauma	25			13			

IQR: Interquartile range; CVS: Cardiovascular surgery.

variables. Non-normally distributed variables were compared using the Mann-Whitney U test. A *p* value of <0.05 was considered statistically significant.

RESULTS

Throughout the study period, there were 26,698 ED admissions in 2019 and 13,935 ED admissions in 2020. Details on ED admissions are presented in Table 1. Considering all ED admissions per week, there was a decrease in weekly ED admissions in 2020 (1,027 vs. 2,270, p<0.001). The ED admissions requiring CVS consultations decreased by 41.6% from 77 patients in 2019 to 45 patients in 2020. Total CVS consultations per 1,000 ED admissions increased from 2.9 to 3.2. Similarly, the mean total CVS consultations per week decreased (7.09 vs. 4.00, p=0.013), although this decrease was likely caused by the drop in total admissions as the mean total CVS-related admissions per 1,000 ED admissions increased (3.08 vs. 3.47, p=0.496), indicating no statistical significance.

In addition, CVS-related hospitalizations decreased from 24 patients in 2019 to 19 patients in 2020. In contrast, the ratio of CVS-related hospitalizations per 1,000 ED admissions increased from 0.90 in 2019 to 1.36 in 2020. Weekly CVS-related hospitalizations per 1,000 ED admissions increased from 1.00 to 1.46, indicating no statistical significance.

All CVS admissions were classified according to the presenting pathology (Table 2). Total cases of deep vein thrombosis decreased from 14 to 9 during the study, and there was no significant difference in weekly cases of venous thrombosis. Concerning ATE, the number of cases was 11 in 2019, whereas six patients had ATE during the same period in 2020. Weekly arterial thrombosis admissions were not significantly different between 2019 and 2020.

All ED admissions in 2019 and 2020 were compared for comorbidities (Table 3). Among all patients consulted to CVS, there were fewer cases with chronic renal failure in 2020 (2.2% vs. 15.6%, p=0.030), while there were no significant differences in other comorbidities. Venous thrombosis patients and ATE patients in 2019 and 2020 showed no significant difference for documented comorbidities. In total, there were three cases of aortic dissection in 2019 and two cases in 2020. The number of patients consulted for aortic aneurysm with or without rupture was five in 2019 and eight in 2020. A major cause of CVS consultations was vascular trauma in 25 cases in 2019 and in 13 cases in 2020.

DISCUSSION

In this single-center study, the rate of thrombotic diseases did not increase in the general population as evidenced by ED admissions during the COVID-19 era, compared to the same period in the previous year. In addition, there was no significant difference in the number of venous and arterial thrombotic cases between the two years.

Our hospital serves a city of approximately 350,000 population. Within one week of the first COVID-19 case in Turkey, patients suspected of COVID-19 infections were diagnosed in the study hospital. The ED was arranged in accordance with the Republic of

Table 3
Patient demographics in emergency department admissions during COVID-19 era

	2019 (n=77)			2020 (n=45)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
CVS related admissions (n=122)							
Age (year)			59.2±18.1			64.6±19.8	0.127
Diabetes mellitus	2	2.6		1	2.2		1.000
Hypertension	35	45.5		23	51.1		0.546
Coronary artery disease	9	11.7		6	13.3		0.789
Congestive heart failure	3	3.9		6	13.3		0.054
Chronic renal failure	12	15.6		1	2.2		0.030
Malignancy	5	6.5		2	4.4		1.000
Atrial fibrillation	2	2.6		2	4.4		0.625
Venous thrombosis (n=23)	2019 (n=14)			2020 (n=9)			
Age (year)			62.9±20.7			72.0±18.1	0.243
Diabetes mellitus	0	0		0	0		
Hypertension	6	42.9		5	55.6		0.552
Coronary artery disease	2	14.3		0	0		0.502
Congestive heart failure	1	7.1		2	22.2		0.538
Chronic renal failure	2	14.3		0	0		0.502
Malignancy	4	28.6		1	11.1		0.611
Atrial fibrillation	0	0		0	0		
Arterial thromboembolism (n=17)	2019 (n=11)			2020 (n=6)			
Age (year)			73.7±19.6			76.3±8.1	0.756
Diabetes mellitus	1	9.1		0	0		1.000
Hypertension	6	54.5		4	66.7		0.627
Coronary artery disease	1	9.1		3	50.0		0.099
Congestive heart failure	1	9.1		1	16.7		1.000
Chronic renal failure	1	9.1		0	0		1.000
Malignancy	0	0		0	0		
Atrial fibrillation	0	0		0	0		

SD: Standard deviation; CVS: Cardiovascular surgery.

Turkey, Ministry of Health guidelines, with suspected COVID-19 patients examined in an area separate from the other ED admissions. If a patient carried the COVID-19, but did not show any infectious or respiratory symptoms, they would be unaware of their infection and might have presented with other atypical symptoms, and such cases would not be initially suspected of COVID-19. There are reported cases of COVID-19 presenting with venous thrombotic events or stroke and subsequently being diagnosed with COVID-19.[10,11] We believe that such cases would result in more ED admissions for thrombotic events during the pandemic, but failed to show an increase in thrombotic events in the ED of the study center.

Most reports of venous or arterial thrombosis in COVID-19 patients are based on patients with a severe course of infection and in the intensive care unit (ICU) setting.[12-15] However, not all thrombotic events related to COVID-19 were associated with ICU requirement, and severe arterial or venous thromboembolism (VTE) were detected in patients with milder symptoms [5,6,16-18] or even as presenting

symptoms.[10,19] It is likely that the risk of thrombosis is high in severe cases and low in mild or asymptomatic cases. As the patients with CVS-related admissions did not present with typical symptoms of COVID-19 and they were not tested for the novel coronavirus, the number of COVID-19 infections among this patient group may be undetermined.

There was a drop in the absolute number of total ER admissions during the COVID-19 era. Self-isolation, stay-at-home orders by the government, or fear of contracting the virus at the hospital may have prevented patients from seeking emergency care. Despite the drop in total ED admissions, there was an insignificant increase in the number of CVS-related admissions. The demographic factors were overall not different between the two years, except for chronic renal failure which was less frequent in 2020; therefore, the lack of increase in thrombotic events cannot be attributed to the differences in comorbidities. It is possible that patients with more severe symptomatology opted to seek emergency care during the pandemic and patients with mild symptoms of any cause did not admit to the ED. Due to similar reasons, some minor VTE or ATE may not have reached the hospital due to fears of leaving the house or waiting in the hospital. Italy is one of the European countries with the largest impact of COVID-19 and the association with thrombosis notwithstanding, admissions for acute coronary syndrome reduced in all parts of the country.[20] Likewise, recorded cases of strokes diminished in a neurological center in Italy during the March.[21] The prominent explanation in both cases in Italy and our case is the fear of contact with the virus, while seeking medical attention for other causes. It is a point of concern that some patients with minor thrombotic disease, such as a distal deep vein thrombosis or a mild new-onset claudication may wait, until the pandemic recedes to seek medical attention and their disease may complicate the course of treatment.

The main limitation of this study is its retrospective design and insufficient data collection. Another limitation is that our study was conducted in a single state hospital serving a city of a relatively small population. Although the study hospital is the largest in the city, there could be patients admitted to smaller distant hospitals and, therefore, not included in the study. Thus, further studies from larger cities or multi-center studies are needed to confirm our results.

In conclusion, the rate of thromboembolic events did not increase in the general population admitted to the ED during the first 11 weeks of the COVID-19 pandemic in Rize province of Turkey. However, further studies from other centers are needed to determine whether thromboembolic events tend to increase due to mild or asymptomatic cases of COVID-19.

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Outcomes of antecubital perforating vein-radial artery arteriovenous fistula for hemodialysis: Gracz fistulas

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ABSTRACT

Objectives: In this study, we present our midterm results of arteriovenous fistulas constructed with the antecubital perforating vein and radial artery.

Patients and methods: In this single-center, retrospective study, a total of 62 patients (27 males, 35 females, mean age 59±13.5 years; range, 34 to 77 years) who underwent antecubital perforating vein-radial artery arteriovenous fistula at Istanbul Medeniyet University, Göztepe Training and Research Hospital between January 2017 and January 2019 were analyzed. Complications, primary failure, primary patency, and secondary patency rates were evaluated at 6, 12, 18, and 24 months.

Results: The mean follow-up was 25 (range, 19 to 28) months. Primary arteriovenous fistula failure was seen in seven patients (11.2%). The primary patency rates during follow-up were 79.3% at six months, 67.7% at 12 months, 53.2% at 18 months, and 35.4% at 24 months. The secondary patency rates were 82.2% at six months, 75.8% at 12 months, 69.3% at 18 months, and 54.8% at 24 months.

Conclusion: Construction of an arteriovenous fistula with the antecubital perforating vein and radial artery is a feasible method with acceptable patency rates. This type of arteriovenous fistulas has also a lower complication rate, particularly for steal syndrome.

Keywords: Neosinus; pericardial patching; right ventricular outflow tract stenosis.

The radiocephalic arteriovenous fistula (AVF) is widely recommended as the first choice for hemodialysis vascular access in patients with end-stage renal disease.[1-4] A native AVF should be created before a prosthetic graft is attempted. For the first time, Gracz et al.[5] described to creating a native AVF by anastomosing the antecubital perforating vein to the brachial artery. Bender et al.[6] and Konner et al.[7] reported modifications of the Gracz fistula. In all reports concerning this type of access, brachial artery was usually preferred, whereas the radial artery was used less frequently.[5] The Gracz fistula with the radial artery should be a favorable option for patients with complete destruction or abnormalities of the superficial forearm veins with heavily calcified distal radial artery and with occluded distal radiocephalic AVFs.[8]

In this study, we present our experience in creating Gracz fistula formed by anastomosis of the antecubital perforating vein to the radial artery in an end-to side fashion.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at a referral vascular access center of Istanbul Medeniyet University, Göztepe Training and Research Hospital between January 2017 and January 2019. A total of 73 patients in whom a Gracz AVF was created by antecubital perforating vein and radial artery were screened. Inclusion criteria were as follows: age between 18 and 80 years, the presence of a complete destruction or abnormalities of the superficial forearm veins, heavily calcified distal radial artery, and occluded distal radiocephalic AVF. Pediatric cases

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and those with a previous antecubital vascular access operation were excluded. Finally, a total of 62 patients (27 males, 35 females, mean age 59±13.5 years; range, 34 to 77 years) who met the inclusion criteria were included in the study. In all patients, vessels were evaluated preoperatively with ultrasonography (USG) by the surgeon, and a proximal radial artery diameter of ≥2 mm and an antecubital perforating vein diameter of ≥2 mm under tourniquet were deemed appropriate for Gracz fistula. Arteries were also assessed using the modified Allen's test to prevent postoperative hand ischemia. A written informed consent was obtained from each patient. The study protocol was approved by the Istanbul Medeniyet University, Göztepe Training and Research Hospital Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All operations were performed under local anesthesia using 1% lidocaine. A 5 to 6-cm transverse incision was made in the median forearm, 1 to 3-cm distal to the antecubital crease. The antecubital perforating vein, which was usually a deep branch of median cubital or cephalic vein, was exposed, ligated at its deep portion, and mobilized. The vein was flushed with heparinized saline only, and systemic heparin was not used. Then, the proximal radial artery was prepared, and the vessel loop was placed around the artery. All anastomoses were performed with the end of the antecubital perforating vein to the side of the radial artery (Figure 1). The distal part of the median cubital or cephalic vein was ligated to prevent possible hand edema. All patients were discharged either on the same day or first postoperative day with prescribed acetylsalicylic acid (100 mg) only. If needed, a second additional superficialization procedure was performed three to four weeks later for arterialized basilic vein in patients in whom no eligible upper arm cephalic vein or enough long cubital veins were present for needling. All patients were followed in the outpatient setting and AVFs were evaluated with USG at 6, 12, 18, and 24 months. Patients who were lost to follow-up, had kidney transplantation, or died during the follow-up period were excluded from the analysis. The primary outcome of the study were primary failure, primary patency, and secondary patency rates. Primary failure was defined as immediate AVF failure as indicated by the loss of bruit or thrill within 15 days. Patency was determined clinically by the presence of a thrill or bruit and also by the flow in the vein part of the fistula visualized on USG. Primary patency was defined as the interval from the time of AVF creation, until any intervention or surgery to maintain or re-establish the patency. Secondary patency was defined as the interval from the time of access placement until access abandonment, including all performed surgical and endovascular interventions.

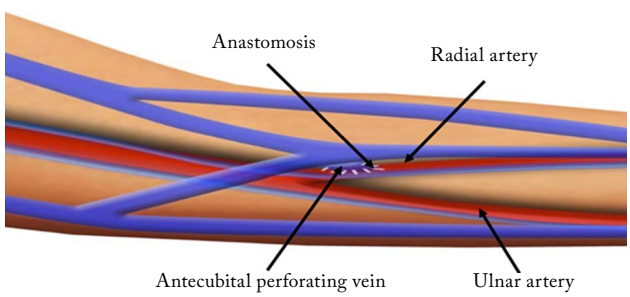

Figure 1. Illustration of end-to-side anastomosis between antecubital perforating vein and radial artery.

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean and standard deviation (SD) and median (min-max) values, while categorical data were expressed in number and frequency. The Kaplan-Meier analysis was used to calculate the patency rate of AVFs. A p value of <0.05 was considered statistically significant.

RESULTS

Of the patients, diabetes mellitus was seen in 42 (67%), hypertension in 45 (72%), congestive heart

Table 1
Baseline demographic and clinical characteristics of patients

Demographic parameters	n	%
Female	35	56
Diabetes mellitus	42	67
Hypertension	45	72
Congestive heart failure (EF <40%)	4	6.4
Peripheral vascular disease	17	27
Previous failed arteriovenous fistula	29	46
Ipsilateral catheter	3	4
Contralateral catheter	34	55

failure with an ejection fraction of <40% in four (4.8%), peripheral vascular disease in 17 (27%), previous failed AVF in 29 (46%), ipsilateral catheter in three (4%), and contralateral catheter in 34 (55%) patients (Table 1).

Primary AVF failure was seen in seven patients (11.2%), and all of them were caused by thrombosis. Three patients (4.8%) who were lost to follow-up, two patients (3.2%) who underwent successful kidney transplantation, and six patients (9.6%) who died during follow-up were excluded from the study.

In nine patients (14.5%) with a functioning fistula, the antecubital venous part was too short for needling and, therefore, a basilic vein superficialization procedure was performed as a second-stage intervention. Early hematoma and bleeding were seen in five patients (8.6%) and only two of them required re-intervention. Seroma developed in two patients (3.2%) and healed during follow-up. Mild wound infection was detected in one patient (1.6%) which healed with oral antibiotics. None of the patients developed steal syndrome or ischemic monomelic neuropathy. Aneurysms and pseudoaneurysms were seen in eight patients (12.9%) which were repaired by aneurysmorrhaphy repair techniques. Stenosis and occlusion at the fistula tract were detected in three patients (4.8%). Two of them developed juxta-anastomotic stenosis which was treated with percutaneous transluminal angioplasty, and one patient had central vein occlusion with hand edema. In this patient, the lesion was unable to corrected using endovascular salvage techniques and, therefore, the AVF was ligated due to increasing severe edema at the extremity. The primary failure rate and complications during follow-up were summarized in Table 2.

Table 2
Primary failure and complications during follow-up

Follow-up period	n	%
Primary failure	7	11.2
Vein superficialization procedure	9	14.5
Hematoma and bleeding	5	8.6
Seroma	2	3.2
Wound infection	1	1.6
Steal syndrome	0	0
Ischemic monomelic neuropathy	0	0
Aneurysm and pseudoaneurysm	8	12.9
Stenosis and occlusion at fistula tract	3	4.8

Table 3
Patency outcomes of the AVFs

	Primary patency	Secondary patency
	%	%
6 months	79.3	82.2
12 months	67.7	75.8
18 months	53.2	69.3
24 months	35.4	54.8

AVF: Arteriovenous fistula.

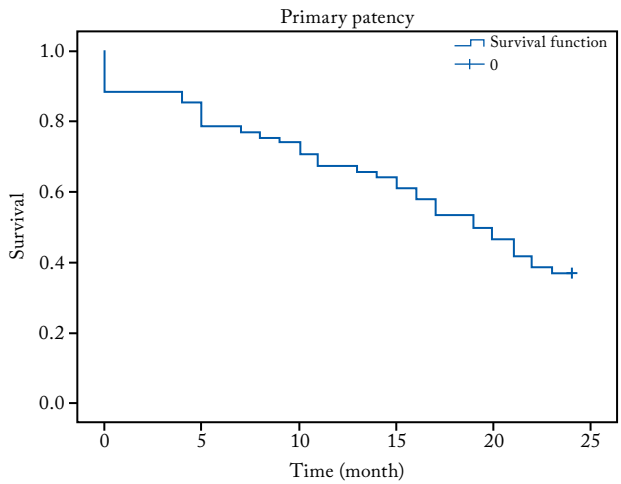

Figure 2. Kaplan-Meier survival analysis of primary patency rates for arteriovenous fistulas.

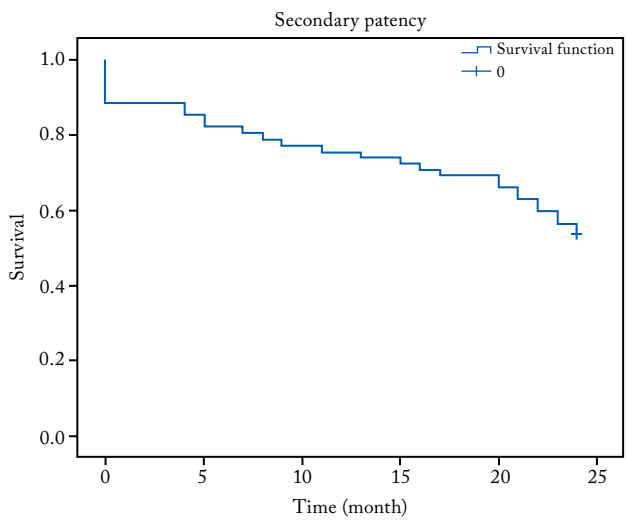

Figure 3. Kaplan-Meier survival analysis of secondary patency rates for arteriovenous fistulas.

The primary patency rates during the follow-up period were 79.3% at six months, 67.7% at 12 months, 53.2% at 18 months, and 35.4% at 24 months. The secondary patency rates were 82.2% at six months, 75.8% at 12 months, 69.3% at 18 months, and 54.8% at 24 months. The follow-up patency rates are given in Table 3. The Kaplan-Meier analysis of the primary patency and secondary patency is shown in Figure 2 and Figure 3, respectively.

DISCUSSION

Arteriovenous fistula at the wrist region is the most recommended type of vascular access, and antecubital area fistulas created with anastomosis of veins to particularly radial artery are good access options.[9] Our study showed the feasibility of AVF construction between the antecubital perforating vein and proximal radial artery with acceptable primary and secondary patency rates up to 24 months. Our patency results are consistent with other published reports using the cubital perforating vein and radial artery for AVF creation.[6,8] In the study by Weyde et al.,[8] the AVF between the antecubital perforating vein and radial artery had primary patency rates of 47% at one year and 43% at two years with cumulative patency rates of 67% at one year and 56% at two years.

In another study, Elcheroth et al.[10] reported the cumulative patency rates of antecubital perforating vein-brachial artery fistulas as 80.3% at one year and 68.0% at four years. In this study, the patency results are higher than our patency rates. The use of brachial artery instead of radial artery is the probable explanation of this fact and the radial artery has a smaller diameter and slower blood flow, compared to the brachial artery. In contrast, using brachial artery also provoked steal syndrome and hand ischemia as reported in the study, which did not develop in any of our patients. In the literature, acute or chronic ischemia symptoms have been reported in up to 20% with brachial artery-based access procedures and 2% with radial artery procedures, and also nearly half of the patients with the brachial artery required interventions due to severe hand ischemia.[11,12]

The blood flow through the AVF is limited by anastomosis width and diameter of the fistula vein, making anastomosis with brachial artery may produce steal syndrome or cause hyperkinetic blood flow with a possibility of circulatory insufficiency. That is the exact reason of why Konner[13] advised AVF creation with proximal radial artery at the antecubital region, particularly for diabetic patients with probability of peripheral circulatory insufficiency. In our study, we observed no symptoms of steal syndrome even in diabetic and older patients.

Our method for harvesting and preparing the antecubital perforating vein was relied on ligating the vein at the connection point with deep veins without any damage to the deep vein circulatory system. Using this method may prevent severe hand edema during hemodialysis and during future vascular access attempts.

The modest-flow AVFs constructed with the radial artery offer a lower risk for patients with congestive heart failure and should be preferred for particularly in older patients.[14] These modest-flow AVFs are also more likely to remain asymptomatic without severe edema in patients with central venous occlusion or stenosis, as the existing collateral venous return is usually enough for the flow.[15] It is speculated that the vein wall shear stress is directly related to the high flow and turbulence and, thus, lower flows may decrease neointimal hyperplasia in the veins with less turbulence and pressure.[16] In our study, stenosis and occlusion at the AVF tract were rare and two juxta-anastomotic stenoses and one central vein occlusion were noted.

The origin and the proximal part of the radial artery is usually free from occlusive vascular disease.[14] This advantage gives a few more vascular access options via the proximal radial artery as anastomosed with the proximal cephalic vein or antecubital perforating vein. This type of AVFs provide a more accessible cannulation length compared to typical brachiocephalic fistulas. In brachiocephalic AVFs, the possible cannulation length may be shortened by rotating the vein to the brachial artery.

Nonetheless, the single-center, retrospective design with a small sample size are the main limitations to the present study. In addition, we were unable to evaluate the results of Gracz AVFs created with the perforating antecubital vein and brachial artery in this study.

In conclusion, arteriovenous fistulas constructed with the antecubital perforating vein and radial artery is a feasible method with acceptable patency and low complication rates, particularly for steal syndrome. The arteriovenous fistula creation failure at the wrist

region in the distal part of the forearm may cause a dilemma regarding the second site selection for another access. The arteriovenous fistula creation through the antecubital vein may be the second choice, when the forearm vasculature is exhausted. In such cases, antecubital perforating vein-radial artery arteriovenous fistulas should be kept in mind with low complications before creating an arteriovenous fistula through the brachial artery.

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Cardiovascular Surgery and Interventions

Case Report Open Access

Replacement of ascending aorta and aortic arch and its main branches with reimplantation of coronary arteries in aneurysmatic aorta

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ABSTRACT

Aortic aneurysm is one of the vascular pathologies which may results in fatal complications such as rupture and dissection. Dilatation of the aortic vessels increases the pressure on the entire aortic wall, leading to more dilatation and risk of dissection or rupture. Surgical intervention should take place, when the aortic diameter reaches the level that may associate with such complications. Herein, we report a case with previous aortic valve replacement due to an ascending aorta, aortic arch, and proximal descending aortic aneurysm, extending to the aortic arch branches and right subclavian artery.

Keywords: Artery reimplantation, cardiopulmonary bypass, Dacron® graft, intensive care unit.

Aortic aneurysm is one of the vascular pathologies which may results in fatal complications such as rupture and dissection.[1] Dilatation of the aortic vessels increases the pressure on the entire aortic wall, leading to more dilatation and risk of dissection or rupture according to the Laplace's law.[2] According to the guidelines, surgical intervention should take place, when the aortic diameter reaches the level that may associate with such complications.[3]

In this report, we present a case with previous aortic valve replacement due to an ascending aorta, aortic arch, and proximal descending aortic aneurysm, extending to the aortic arch branches and right subclavian artery and discuss its surgical treatment in the light of literature.

CASE REPORT

A 57-year-old male patient was presented to our clinic with the chief complaint of recurrent episodes of chest pain, palpitation, and numbness in both lower limbs. He underwent aortic valve replacement surgery 32 years ago due to rheumatic heart disease. Five years ago, coronary angiography revealed no abnormal findings. Echocardiography showed a functional artificial aortic valve with an ejection fraction of about 60%. Contrast-enhanced computed tomography (CT) demonstrated an aortic root of 56 mm, an ascending aorta of 54 mm, an aortic arch of 46 mm, and a proximal descending aorta of 40 mm with a brachiocephalic artery of 28 mm and a right subclavian artery of 19 mm (Figure 1). The diameter of infrarenal abdominal aorta was 60 mm. Surgery was decided and a written informed consent was obtained from the patient. After all preoperative preparations were done, the patient was taken to the operating room.

Operative technique

After full intravenous heparinization, the artery was clamped by vascular clamps to allow anastomosis to an 8-mm polytetrafluoroethylene (PTFE) graft. This graft was, then, connected to the arterial line of cardiopulmonary bypass (CPB) machine. Median sternotomy was done in a regular fashion, as it is a case of resternotomy using the micro-oscillating saw. Substernal adhesions were resolved gently with caution. Two-stage venous cannulation was done via the auricula of the right atrium. The ascending aorta, aortic arch, and its branches were all dissected gently from the surrounding tissues (Figure 2). A vascular

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cross-clamp was applied at the distal ascending aorta and, then, antegrade isothermic blood-enriched cardioplegic cardiac arrest was achieved. On the other hand, a continuous retrograde cardioplegic solution was given via a retrograde cannula replaced into the coronary sinus through the right atrium. Excision of the aneurysmatic segment was done with caution to the aortic root in order to excise the coronary ostia as buttons. The previous artificial aortic valve was checked and found to be clean from any pannus formation and to be functional; therefore, it was kept in place. A 30-mm Dacron® graft was sewn to the mechanical valve using 3.0 polyester sutures in a continuous fashion and the left coronary ostium was, then, re-implanted into the graft using 6.0 polypropylene sutures (Figure 3a). At the beginning of the operation, a 28-mm Dacron® graft was prepared by implanting four pieces of 8-mm Dacron® grafts in an end-to-side fashion to a 28-mm polyester graft by the second assistant to obtain a special arch branch graft. The brachiocephalic artery was clamped and antegrade selective cerebral perfusion was done under 28°C. The left carotid artery was cannulated by a line taken from the arterial line and perfused during the antegrade cerebral perfusion. The left subclavian artery was snared. Meanwhile, all the branches of the arch were divided proximally from the aneurysmatic arch. The proximal descending aorta with a dilatation was resected as possible as we could. The 28-mm Dacron® graft was anastomosed to the descending aorta leaving about 3-cm free edge into the descending aorta as an elephant trunk. After the distal aortic anastomosis, the proximal 8-mm graft branch was cannulated by Y-line from the arterial line which was previously prepared (Figure 3b). Distal body perfusion was instituted and CPB was increased up to the normal level. The left subclavian artery and left carotid artery branches were anastomosed to the distal 8-mm graft branches. The 30-mm and 28-mm grafts were anastomosed to each other in an end-to-end fashion.

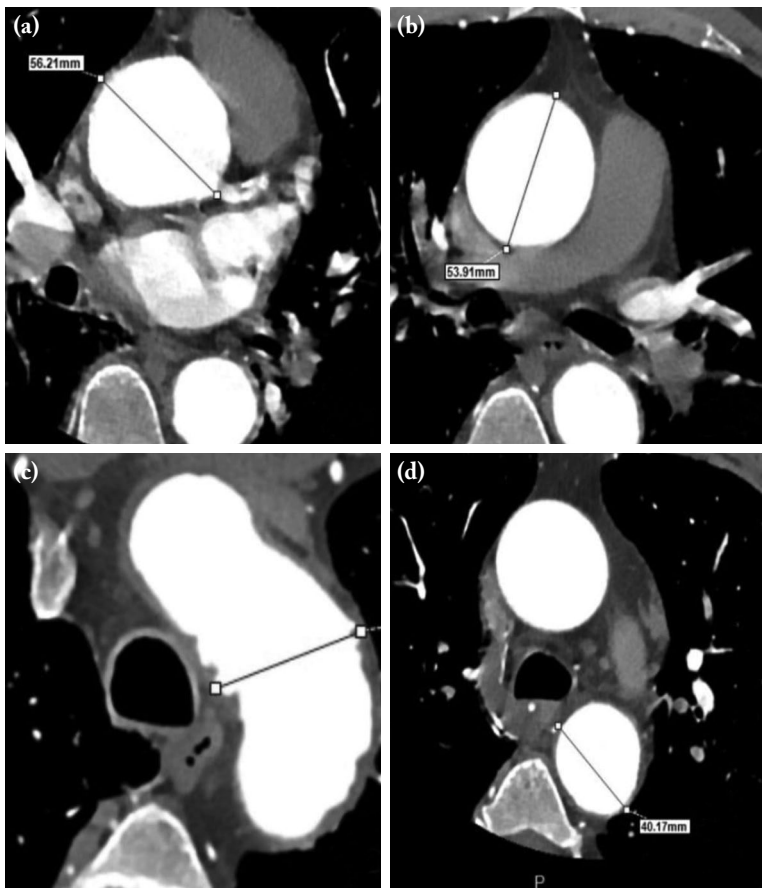

Figure 1. Contrast-enhanced computed tomography scans. **(a)** Aortic root. **(b)** Ascending aorta. **(c)** Aortic arch. **(d)** Descending aorta.

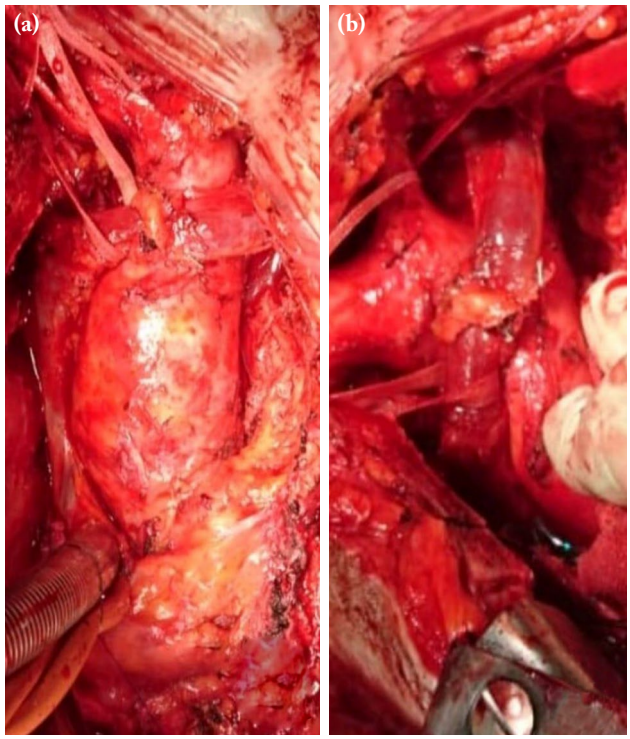

Figure 2. An intraoperative view. **(a)** Aneurysmatic ascending aorta. **(b)** Aneurysmatic brachiocephalic and right subclavian artery.

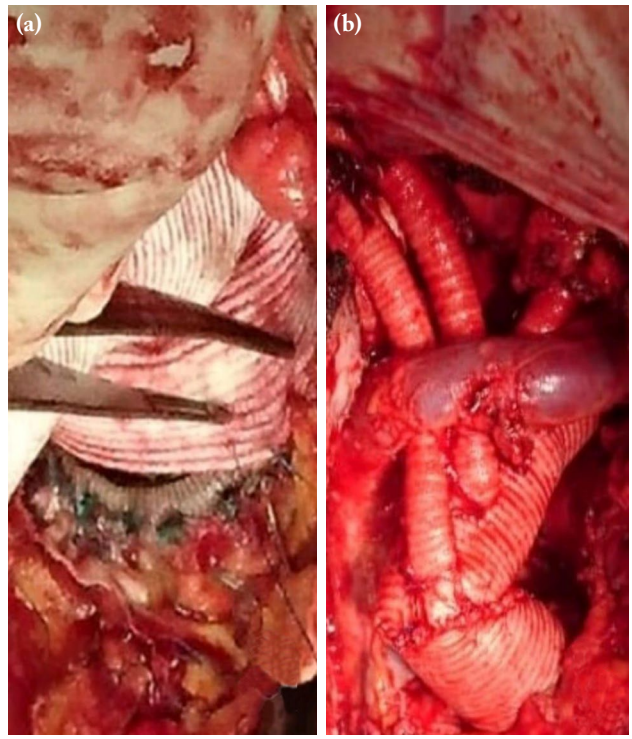

Figure 3. An intraoperative view. **(a)** Sewing 30-mm Dacron® graft to old artificial aortic valve. **(b)** Dacron® grafts after vascular clamps were released.

The right coronary artery button was anastomosed and cross-clamp was removed. The right carotid artery was anastomosed to the second 8-mm branch graft. After protamine administration the connection of the CPB was withdrawn. The proximal side branch was used for axillary artery bypass. The graft was passed through an anatomic tunnel to the right subclavian artery. The proximal and distal ends of the subclavian artery, the internal thoracic artery branch and its costocervical main thyrocervical branches were all ligated. The last anastomosis was done to the right subclavian artery using a right-sided 8-mm Dacron® graft. Embolectomy was done to the graft and distal axillary artery for a blood clot before tying the anastomosis suture due to protamine neutralization previously. Hemostasis was secured (Figure 3). At the end of the operation, two drains were placed into the mediastinum where one drain into the right and another one into the left thorax were placed. Sternum was closed in a standard manner and the patient was taken to the cardiovascular intensive care unit (ICU). The total CPB perfusion time was 204 min, while the total cross-clamp time was 119 min. Three units of erythrocyte suspension and two units of fresh frozen plasma were transfused.

For the first three days postoperatively, the patient was monitored in the ICU. The total drainage was about 450 mL. On Day 4, he was transferred to the ward. During ward stay, daily routine blood and imaging studies with daily dressing were done. On Day 10, the patient started doing well and was discharged on medication with scheduled follow-up visit one week later.

DISCUSSION

Aortic aneurysm is a vascular pathology with possible serious complications which can be prevented considerably by regular controls, proper medications, and appropriate and timely surgical interventions. The type of the operation and surgical technique used have also a key role for lifelong. In general, for all aortic aneurysms, surgical interventions have a high complication risk. On the other hand, the location of the aneurysm is critical in planning and achieving the operation. An isolated ascending aortic aneurysm operation surely has a lower risk than that one extending to the arch. Our case is a complicated case presenting with the ascending and

aortic arch aneurysm associated with an aneurysm of the brachiocephalic and right subclavian arteries which were all successfully treated. The cornerstone of a successful operation of all types of operations is the timing and planning of the operation steps.

Review of the literature reveals similar cases treated by similar surgical techniques. Many cases were managed by synthetically prepared branched grafts. In our case, we prepared the branched graft in the operating room by ourselves. Our patient had a diffuse aneurysm which involved all the aorta and brachiocephalic artery, extending to the right subclavian artery, as well. Most of the cases in the literature underwent dissection with a high mortality rate. In a study including 220 patients who underwent total arch replacement from 1990 to 1999, the mortality rate was about 12.7% and 3.3% of the patients had permanent neurological dysfunction postoperatively. However, no neurological problem was observed in our patient, which can be attributed to the fact that we perfused both of the carotid arteries during the operation. The only non-perfused period was during the left and right carotid artery anastomosis which were five and four min, respectively.

There are also several studies regarding the combined open surgical techniques and endovascular interventions. To the best of our knowledge, endovascular interventions have been increasingly used over the last two decades and widely adopted in the management of aortic aneurysms, mainly in thoracic and abdominal aneurysms. Unfortunately, ascending aorta and aortic arch aneurysms still have not the similar ability to be treated using such endovascular stents, due to their valuable branches and angularity.

For the aneurysmatic arch of the aorta, several endovascular techniques can be used including endoanchors, in situ laser fenestration, chimney grafts, and elephant trunk.[4] For all techniques, the main goal is to preserve the patency of the great vessels during treatment of the main pathology of the aorta. In a case report by Sonesson et al.,[5] a ruptured aortic arch was treated by in situ fenestrated endovascular stenting technique using a centrifugal pump to perfuse both carotid arteries from the right femoral artery. In another study, 41 patients underwent total thoracic aorta repair with the frozen elephant trunk stent graft due to acute type A aortic dissection.[6] The authors emphasized that, in such cases, treatment with the single-session frozen elephant trunk technique was safe with a high successful rate.

In some cases, patients can be operated before for other types of aortic pathologies such as dissection, followed by another dissection in the other site of the aorta. In a case report, a patient had secondary repair of the descending thoracic aorta with previous arcus aortic replacement and elephant trunk extension, and the authors concluded that endovascular elephant trunk could improve morbidity and mortality in high-risk patients.[7] In our center, we are unable to utilize such fenestrated stents and the health insurance of the does not cover that types of the stents. We did our operation as a case of resternotomy and left a graft extension of about 3 cm into the descending aorta to perform thoracic endovascular aortic repair (TEVAR) later. In addition, we attempted to decrease the total circulatory arrest time by perfusing the whole body immediately after we anastomosed the distal aortic anastomosis. The left subclavian, left carotid artery, and right carotid artery were anastomosed respectively under normal CPB circumstances during perfusion of the distal aorta and right axillary antegrade cerebral perfusion.

In the literature, Kreibich et al.[8] performed the first endovascular conduit stent graft for a case of dissected ascending aorta. However, those types of stent grafts have constricted indication and many limitations. In our case, we observed both ascending aorta and aortic arch aneurysms along with brachiocephalic and right subclavian artery aneurysms which was impossible to treat all of them by an endovascular intervention. Therefore, we left a 5-cm neck arch graft distal to the left subclavian artery branch and a 3-mm elephant trunk graft inside the descending aorta for a possible aneurysm formation in the descending aorta. In the future, we are expected to put an endovascular graft in such cases. Our patient was operated previously with aortic valve replacement. That was another cause to have more difficulties than a virgin case. We performed this operation very well and planned the steps before starting to shorten the time of CPB and cross-clamp and to reserve the full perfusion and normothermia, as soon as we could.

In conclusion, careful preoperative planning, perfusing as many aortic branches as possible, and a prompt surgery are the mainstays for surgical success in such extensive aneurysmal diseases.

Declaration of conflicting interests

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Cardiovascular Surgery and Interventions

Case Report Open Access

Quick decision and right management in coronary artery vasospasm following on-pump coronary artery bypass grafting

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ABSTRACT

The importance of early diagnosing of coronary artery vasospasm (CAV) which can cause serious, life-threatening hypotension immediately after coronary artery bypass grafting (CABG) is well-known. High endogenous catecholamine levels, vasopressor treatments, vascular endothelial damage due to physical manipulation of the perioperative coronary artery, hypothermia and increased inflammatory response during cardiopulmonary bypass can be counted among the various factors thought to induce CAV in the postoperative period. However, quick decision and right management can be life-saving in CAV. Herein, we present successful treatment of CAV after CABG operation in a 48-year-old active smoker, female patient with cardiological follow-up due to stable angina preoperatively.

Keywords: Angina pectoris; coronary artery bypass grafting, coronary artery vasospasm, myocardial infarction, variant angina.

It was the first time in 1959 that Prinzmetal et al.[1] identified a syndrome with ischemic chest pain which was not stimulated by emotional stress and physical exercise accompanied by myocardial ischemia findings and ST segment elevation. This syndrome, also called variant angina pectoris, was associated with acute myocardial infarction, ventricular tachycardia, ventricular fibrillation, and sudden death.

Variant angina pectoris may exist after coronary artery bypass grafting (CABG) and is usually accompanied by generalized vasospastic diseases such as Raynaud's phenomenon and migraine.[1] While the most common involvement is the right coronary artery (RCA), the left anterior descending artery (LAD) or co-involvement are less frequently observed.[2] Coronary artery vasospasm (CAV) developing after CABG may be manifested by refractory angina, malignant arrhythmias, ST segment elevation on electrocardiography (ECG), myocardial infarction, sudden hypotension, bradycardia and myocardial wall motion abnormalities, and sudden cardiac arrest.

The relationship between coronary artery disease (CAD) and CAV is frequently investigated in the literature. However, there are limited case reports related to CAV after CABG. Herein, we present that successful treatment of CAV after CABG operation in a 48-year-old, active smoker, female patient with cardiological follow-up due to stable angina preoperatively.

CASE REPORT

A 48-year-old female patient was admitted to our clinic with stable angina. The patient, who was not found to be suitable for percutaneous coronary intervention by the cardiologist due to long-segment LAD lesion previously, was operated for single-vessel CABG without any problems. Her medical history revealed active smoking (20 pack year), exercise intolerance and effort angina. There was no abnormality in the blood gas and other respiratory criteria to explain tachypnea (24 breaths/min) after extubation. However, while under nitroglycerin infusion therapy (0.25 µg/kg/min; Perlinganit®, ADEKA Pharmaceuticals, Istanbul, Turkey),

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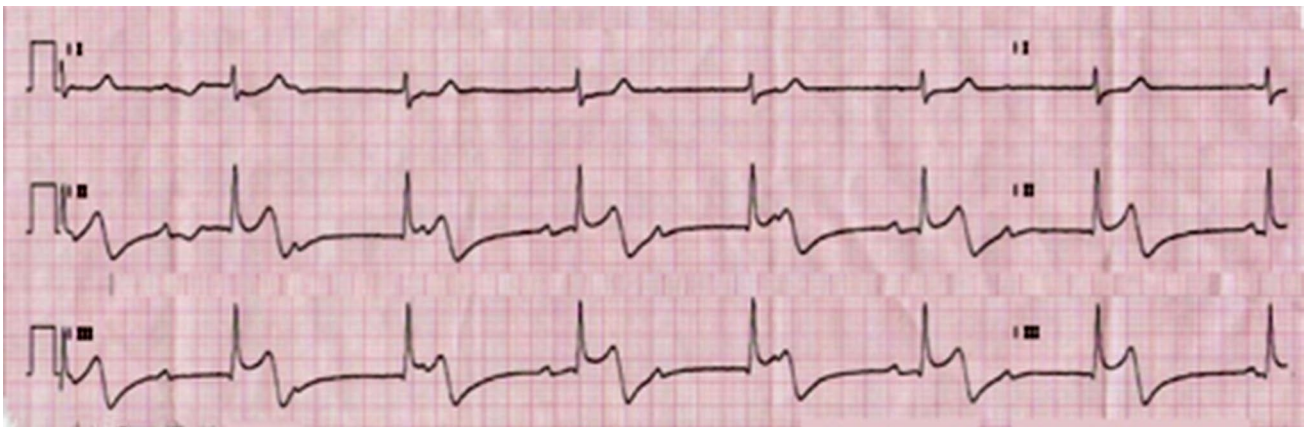

Figure 1. ST segment elevation and third-degree atrioventricular block on electrocardiography.

severe chest pain followed by sudden hypotension (55/35 mmHg), sudden bradycardia (45 bpm), signs of right heart failure symptoms developed at 6 h after the operation. The patient was quickly evaluated by ECG, followed by echocardiography. There were ST segment elevation in the D2-D3 and AvF leads of ECG, and also third-degree atrioventricular block (Figure 1). A pacemaker was inserted through the right internal jugular vein and right ventricular myocardial wall motion abnormality was detected on the echocardiogram. The patient was rapidly taken to coronary angiography after hemodynamic stability was achieved. A written informed consent was obtained from the patient.

Firstly, RCA imaging was performed on coronary angiography. The RCA, which was completely normal preoperatively (Figure 2a), suffered from a totally spasm from the proximal segment to distal segment (Figure 2b). The vessel was reached using a guidewire, and intracoronary nitroglycerin was applied (Figure 2c). However, percutaneous coronary angioplasty (PTCA) was applied to the RCA, as the vasospasm did not regress and hemodynamic instability persisted (Figure 3a). The patient was taken to the intra-aortic balloon pump (IABP) (Datascope CS300®, Getinge, Sweden) support instead of increasing the positive inotropic support due to possible vasospasm effects. The RCA was clear on control angiography, and the patient provided hemodynamic stability rapidly after IABP support. Subsequently, other coronary imaging studies were performed, and the graft anastomosis was well-perfused and clear (Figure 3b). The IABP

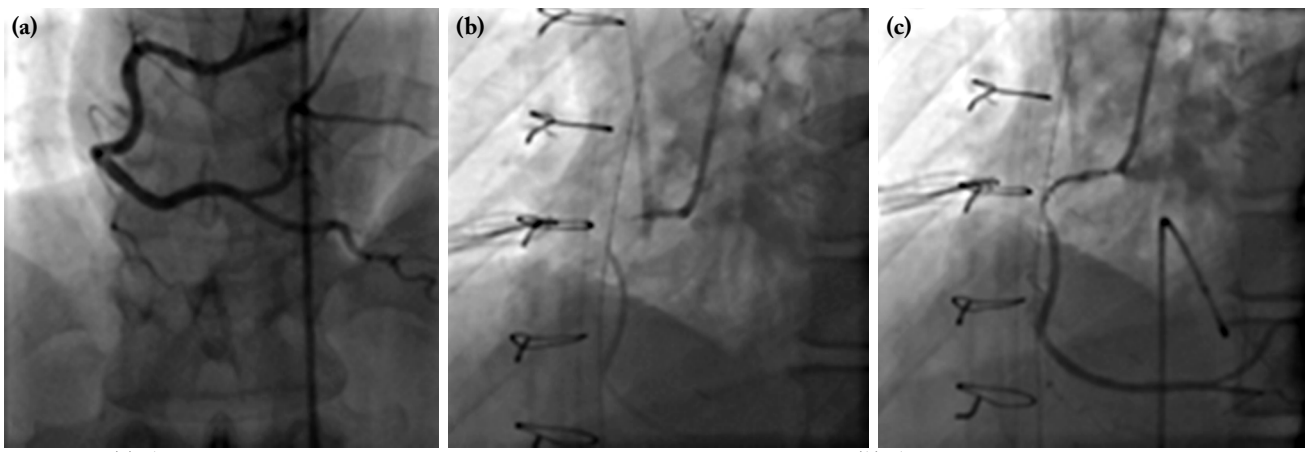

Figure 2. **(a)** Angiographic imaging of right coronary artery before the operation. **(b)** Angiographic imaging of right coronary artery suffering from vasospasm after operation. **(c)** Angiographic imaging of ostial vasospasm continuing after nitroglycerin treatment.

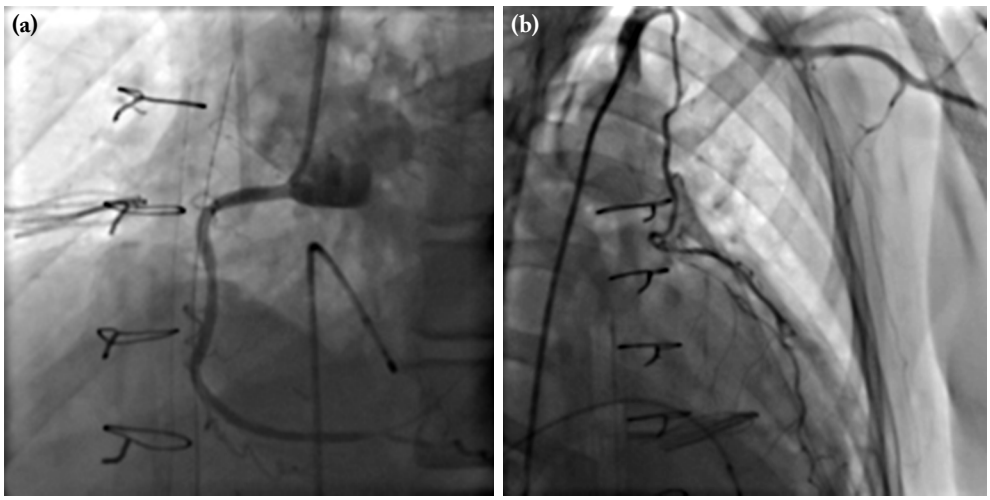

Figure 3. **(a)** Angiographic imaging of right coronary artery after percutaneous coronary intervention. **(b)** Angiographic imaging of left internal mammary artery-left anterior descending artery perfusion after surgery.

support was continued, until the third postoperative day. Meanwhile, intravenous nitroglycerin treatment (0.25-1 μg/kg/min; Perlinganit®, ADEKA Pharmaceuticals, Istanbul, Turkey) with a calcium channel blocker (5-15 mg/h; Diltizem®, Gensenta Pharmaceuticals, Istanbul, Turkey) was applied. On daily echocardiographic evaluation, right ventricular myocardial wall motion abnormality was unable to be seen. The patient was taken to the ward. Nitroglycerin (50 mg/day; Monoket Long®, ADEKA Pharmaceuticals, Istanbul, Turkey) and diltiazem (90 mg/day; Diltizem SR®, Gensenta Pharmaceuticals, Istanbul, Turkey) treatment continued orally. On Day 6 after the operation, the patient was discharged with recommendations.

DISCUSSION

There may be many potential causes of malignant arrhythmia and cardiogenic shock which develop shortly after CABG. Myocardial infarction may also cause this situation after CABG. Despite the technical advances and development of myocardial protection strategies in recent years, perioperative myocardial ischemia associated with increased morbidity and mortality rates is seen in 3.5 to 10% of cases.[3] Myocardial infarction which occurs shortly after CABG may be caused by graft failure or stenosis or incomplete revascularization. However, it should be kept in mind that CAV may cause myocardial infarction and cardiogenic shock, and CAD is a well-known cause of CAV.[4] The latter can be seen at rates ranging from 0.8 to 1.3% after CABG.[4] High endogenous catecholamine levels, the use of vasopressor treatments, vascular endothelial damage due to physical manipulation of the perioperative coronary artery, hypothermia and increased inflammatory response during cardiopulmonary bypass can be counted among the various factors thought to induce CAV in the postoperative period. However, the effects and potency of these factors on patients have not been fully elucidated, yet. In most cases, as in our case, CAV has usually been noted to develop within the first 8 h (mean: 5.6 h) after surgery.[5]

The importance of diagnosing early CAV, which can cause serious, life-threatening hypotension immediately after CABG, has been well-documented in the literature.[4] In our case, emergency coronary angiography was performed to the patient to confirm our suspicion of CAV, to rule out graft failure or possible new-onset stenosis, and to allow intracoronary administration of vasodilators agents, after the patient became hemodynamically suitable for transportation. Calcium channel blockers or nitroglycerin administered intracoronary have been shown to be effective in most cases.[6] However, as in this case report, while nitroglycerin infusion treatment continued, PTCA was applied as the next treatment step to ensure hemodynamic stability in the patient who developed

CAV and the patient was, then, successfully followed with long-term nitrate and calcium channel blocker therapy.

In conclusion, in this case report, we emphasize that the hemodynamic instability developed after a routine and successful operation in the early period following CABG should be managed correctly and that CAV should not be overlooked. In the course of CAV extending to variant angina, myocardial infarction, malignant arrhythmia and even sudden cardiac arrest, we believe that early diagnosis and proper treatment are life-saving for these patients.

Declaration of conflicting interests

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Cardiovascular Surgery and Interventions

Case Report Open Access

A glomus tumor of left lower extremity arising from left superficial femoral artery: A case report

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ABSTRACT

Glomus tumors, usually used as a synonym of carotid body tumors, are of neuroectodermal origin and a part of the extra-adrenal neuroendocrine system pathologies. These lesions are the most frequent paragangliomas located in the neck. Herein, we present a rare case of mass lesion on the left leg arising from the left superficial femoral artery. After successful excision and removal, the pathological examination result was reported as a glomus tumor.

Keywords: Glomus tumor, lower extremity, surgical excision.

Typically, glomus tumors, also known as carotid body tumors, chemodectomas or carotid body paragangliomas, are vascular component dominant tumors which often arise from paraganglioma cells of the carotid body area. In most cases, these tumors are located at the carotid bifurcation. A small number of patients are familial forms with an autosomal dominant inheritance associated with conditions such as tuberous sclerosis, neurofibromatosis type 1, von Hippel-Lindau disease, and Carney triad. Malignant transformation is rare and may occur via bone, lung, liver, and lymph node metastases. The lower extremity is an extremely rare location of the involvement.[1]

In this report, we present a case of surgical excision of a glomus tumor arising from the left superficial femoral artery.

CASE REPORT

A 53-year-old male patient was admitted to the emergency department with an history of a slowly growing and painful bulky lesion on his left leg above the knee for three years. His medical history included the use of antihypertensives for 10 years, right knee surgery with implantations, and tobacco abuse for over 20 years. His medical prescription before the admission included acetylsalicylic acid 300 mg/day, omeprazol 30 mg/day, and metoprolol 100 mg/day. Physical examination findings were normal, except for a non-pulsatile bulky mass lesion located medially of his left leg above knee. There was no active bleeding. The lesion was non-sensitive and non-flexible. Ultrasonography and Doppler ultrasound in the emergency setting revealed two mass lesions together around 5×4 cm in diameter, each (Figure 1). There was no evidence of intravascular thrombosis. Magnetic resonance imaging was unable to be performed due to the knee implant. The electrocardiogram showed a normal sinus rhythm for 90 bpm. On auscultation, the lungs and heart were clear. There were no significant pathological findings on the abdominal evaluation. Laboratory blood tests showed no abnormalities including the cardiac panel. The arterial vessel pulses were detectable on both side of upper and lower extremities. Chest radiographs and M-mode echocardiograms were also normal. Surgery was decided and a written informed consent was obtained from the patient.

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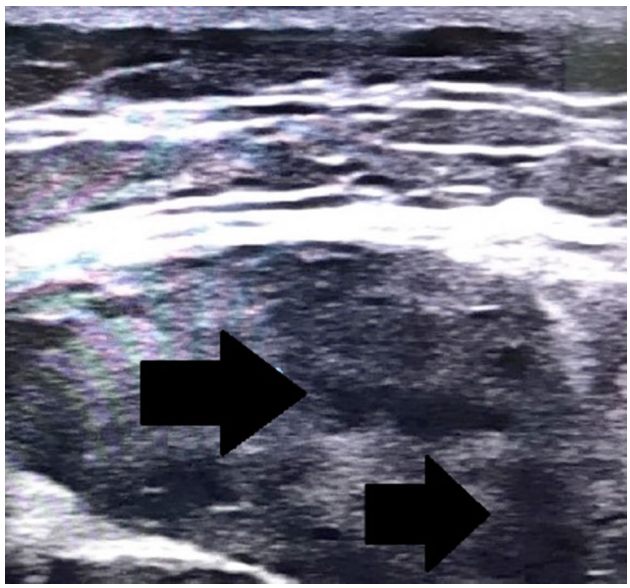

Figure 1. A preoperative ultrasonographic image of mass lesion.

Following preoperative preparation, the patient was operated under general anesthesia and endotracheal intubation. A surgical skin incision was made over and along the mass lesion. There were two distinct lesions approximately 3×4×5 cm, which were immobile and tightened to surrounding tissue (Figure 2). Total mass excisions were achieved with multiple ligations of the collateral vascularity and careful dissection. Despite the fact that the mass was located at the close neighborhood of the vessels such as artery and veins of the area, we observed no direct vascular invasion other than dense attachments. A fine dissection was made, but a further vascular surgery including graft interpositioning was not necessary. Operation was carried out free of any complications with total excision (Figure 3). The patient was transferred to the cardiovascular surgery intensive care unit. Early postoperative clinical follow-up was uneventful. The patient discharged at the postoperative fifth day.

The pathological examination of the specimens obtained from the excision material showed a glomus tumor (Figure 4).

DISCUSSION

The first reports of glomus tumors date back to the 16th century. Von Haller,[2] in 1762, described a mass at the carotid bifurcation area in a glomus body-like structure. In 1812, Wood[3] described a glomus tumor as painful subcutaneous tubercles. In 1840, Valentin[4] defined it as ganglia tympanica. A glomus jugulare tumor case was first reported by Rosenwasser[5] in 1945. A long time after von Haller,[2] Mulligan,[6] in 1950, introduced the term chemodectoma to describe glomus tumors for their chemoreceptor tissue origin. In 1974, Glenner and Grimley[7] renamed the tumor as paraganglioma and introduced a classification according to the localization, innervation, and histopathological features of the tumor. Four types of glomus tumors are defined according to its origin of carotid body or nodosum of vagus: Type 1 is defined as within 2 cm of carotid bifurcation and no cranial

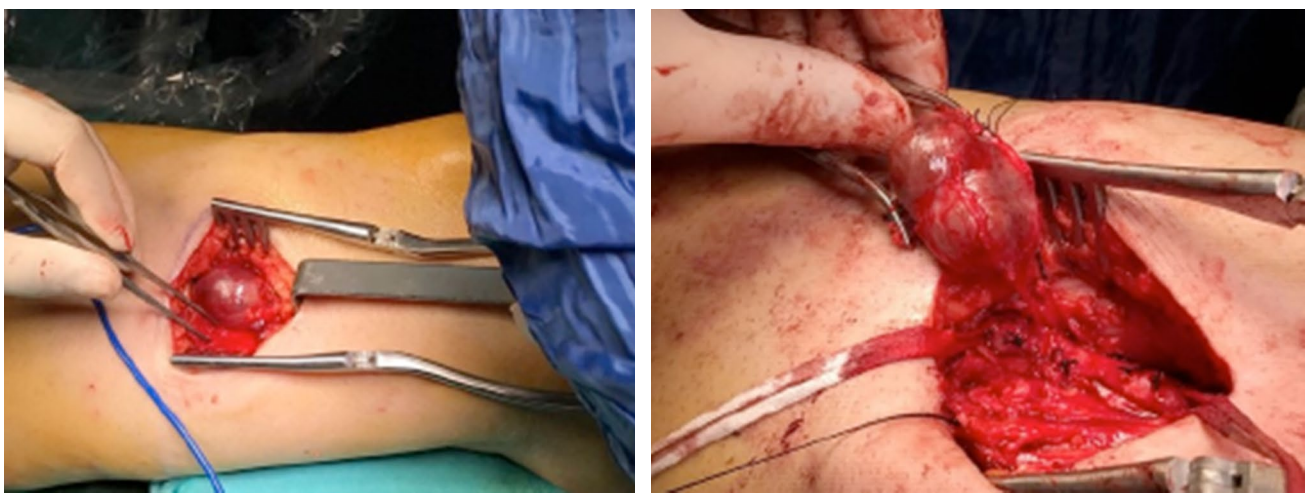

Figure 2. Intraoperative excision of mass lesion.

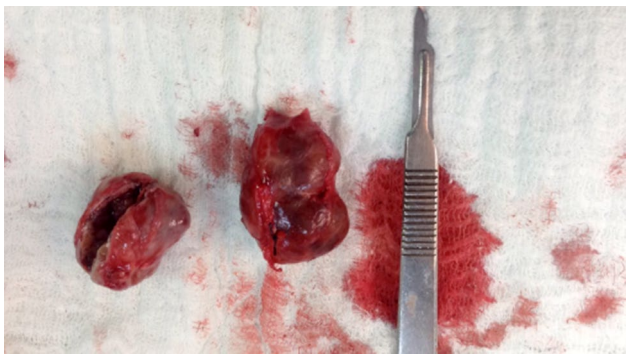

Figure 3. The excised mass lesion.

nerve deficits; Type 2 extending 2 cm beyond carotid bifurcation or encases internal carotid artery; Type 3 extending within 2 cm of or through skull base; and Type 4 bilateral/multiple and/or atypically located tumors. In our case, the tumor was Type 4.

Rarely, as in our case, paraganglionic cells of the extra-adrenal neuroendocrine system may occur in various localizations of the body including orbit oculi, pterygopalatine fossa, larynx, pharynx and dermis, and upper and lower extremity.[8] These cells in these localizations seem to involve atypical accumulation of glomus caroticum cells. Malignancy is related to size, deeper location, infiltrative growth, mitotic activity, and nuclear pleomorphism with necrosis.

The reported surgical mortality for carotid body tumors of the neck is around 8 to 10%, which is mainly due to a major neurological complication and/or deficit at the postoperative period.[9] Glomus tumors of the extremities are rarely reported in the literature. Nonetheless, we believe that the mortality may be significantly lower in these extremity regions than the rate of neck tumors.

Alternative treatment techniques such as coil embolization and gamma knife surgery have been advocated in the literature.[10] Due to the dense vascularity of these tumors, despite a preoperative definitive diagnosis of these inner and surrounding tumor vessels, a complete treatment by a coil embolization and/or gamma knife surgery is difficult to achieve. Furthermore, a massive bleeding during these alternative approaches may complicate excision, the second step of surgery, with higher morbidity and mortality rates. In our opinion, a direct surgical removal is the treatment of first choice, particularly in cases larger than 2 cm.

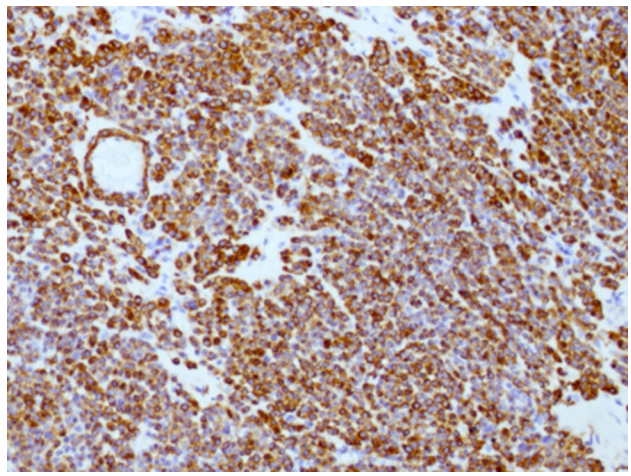

Figure 4. Histopathological appearance of excision material (H-E ×100).

In conclusion, glomus tumors of the lower extremity are extremely rare. A total excision and removal of the mass lesion can be achieved with appropriate measures.

Declaration of conflicting interests

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