Effects of Left Internal Thoracic Artery Graft Use On Coronary Artery Bypass Grafting Mortality and Morbidity In Octogenerians

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ASTRACT

Introduction: Atherosclerotic heart disease is the leading cause of death in developed countries. In our country, the numbers are slightly lower, but increase each year. In 2008, the number of cases was 10,410 (12.03%) of all deaths among people aged 75 and over. The proportion of octogenarians undergoing cardiac surgery is increasing, though this high-risk population has many unknown issues to decrease mortality and morbidity. The aim of this study was to understand and compare the role of left internal thoracic artery (LITA) versus saphenous vein (SVG) to left anterior descending artery (LAD) grafting on early- and mid-term results.

Materials and Method: A retrospective analysis was conducted on 105 consecutive patients who were 80 year or older and who underwent isolated coronary artery bypass grafting (CABG) between January 2000 and January 2010. Patients with saphenous venous graft only (SVG; n: 27) were compared with those receiving arterial (LITA; n: 78) and saphenous venous grafts. Mean follow-up was 42.95±23.36 months.

Results: There was no significant difference in mortality and morbidity between the groups ($p>0.05$). Longer duration of aortic cross clamping was found to be associated with postoperative renal failure in patients with saphenous venous grafts ($p<0.05$). There was no statistically significant difference in 8-year survival rates between the groups ($p>0.05$).

Conclusion: In conclusion, octogenarians should receive complete revascularization with short aortic cross clamp time. We could not demonstrate the importance of graft choice for long-term functional outcome and survival as a prognostic factor in this age group who underwent coronary artery bypass surgery.

Keywords: Octogenarian; Coronary Artery Bypass Grafting; Left Internal Thoracic Artery; Saphenous vein graft.

Seksenli Yaş Grubunda Koroner Baypasta Sol İnternal Torasik Arter Grefti Kullanımının Mortalite ve Morbiditeye Etkisi

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ÖZET

Giriş: Aterosklerotik kalp hastalığı gelişmiş ülkelerde en önemli ölüm nedenidir. Ülkemizde de giderek artan bir yüzdeyle mortalitede üst sıralarda bulunmaktadır. 2008 yılında 75 yaş üstü nüfusun %12,03'ünde ölüm nedeninin iskemik kalp hastalığı olduğu saptanmıştır. Kalp cerrahisinde giderek artan bir yüzdeye sahip olan seksenli yaş grubunda operatif mortalite ve morbiditeyi azaltmak için araştırılması gereken pek çok başlık mevcuttur. Çalışmamızda CABG yapılan seksenli yaş grubu hastalarda sol ön inen koroner arter baypasında safen ven(SVG) veya sol internaltorasik arter grefti(LITA) seçiminin erken ve orta dönem mortalite açısından rolünü araştırdık.

Hastalar ve Metod: Ocak 2000-Ocak 2010 yılları arasında izole CABG operasyonu uygulanmış seksenli yaş grubunda 105 hasta çalışmaya dahil edilerek retrospektif olarak incelendi. LITA kullanılan [LITAgrubu (n:78)] ve kullanılmayan [SVG grubu (n:27)], hastalar kıyaslandı. Ortalama takip süresi 42.95±23.36 aydı.

Bulgular: Mortalite ve morbidite açısından her iki grup arasında istatistikî anlamlı fark izlenmedi (p> 0,05). SVG grubunda uzun aortik kros klemp süresi ile postoperatif renal yetmezlik arasında ilişki olduğu bulundu (p<0,05). 8 yıllık takipte hayatta kalım açısından her iki grup arasında istatistikî fark yoktu (p>0,05).

Sonuç: Seksenli yaş grubu hastalarda beklenen kısa yaşam sürelerine rağmen komplet revaskülarizasyon ve kısa aortik kros klemp süresi ile CABG başarıyla uygulanabilir. Bizim çalışmamızda LITA kullanımı mortaliteye etkili bulunmamıştır.

Anahtar Kelimeler: 80'li yaş grubu (oktogenaryan); Koroner arter bypass greftleme; Sol İnternal Torasic Arter; Safen Ven.

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INTRODUCTION

The percentage of the population aged over 65 years in Turkey was 3.3% during the 1950s, and increased to 5.7% in 2000s [1]. This number is estimated to reach 10 million by 2020, and 12 million by 2050 [2]. Today, life expectancy at birth for Turkey is 71 years [3]. Turkish people survived till 80 years, have expected life more 7 years for males and 9 years for women [3].

Although this patient group has more risk factors, studies have concluded both short-term and long-term survival in patients treated with surgery produce better results [4, 5]. However, for octogenarians, some points

are still unclear to decide the optimal treatment. Few studies describe or explain the risk factors for octogenarians. Because sole effect of age on mortality is more dominant in many operative risks, further studies on octogenarians are required.

The aim of this study was to understand and compare the role of left internal thoracic artery (LITA) versus saphenous vein (SVG) to left anterior descending artery (LAD) grafting on early- and mid-term results.

PATIENTS AND METHOD

Patient Population

A retrospective analysis was conducted on 105 consecutive patients 80 years of age or older, who underwent isolated coronary artery bypass grafting (CABG) between January 2000 and January 2010. During the same period 11,236 patients underwent CABG, 105 (0.93%) of who were octogenarian. Those who underwent CABG concurrently, additional procedures, and/or repeat cases were excluded from the study. We grouped patients into two groups according to their graft applied to LAD (LITA n: 78, and saphenous vein n: 27). Study was approved by ethics commitee. Complete revascularization was considered if all target vessels were revascularized. Transthoracic echocardiography was applied to all patients preoperatively. Patients were grouped according to their left ventricular ejection fraction (Group I LVEF>%55, Group II LVEF %35-55, Group III LVEF< %35)

Postoperative Morbidity and Mortality

The medical records of patients were obtained and evaluated for early postoperative MI, low cardiac output syndrome, cerebrovascular accident, renal failure, infection, and sternal dehiscence. Patients who required more than 24 hours of postoperative mechanical ventilation were included in the group of prolonged intubation.

Long term assessment was made by phone calls (LITA group: 41, (52%) saphenous vein group n: 14 (51%)).

Statistical Analysis

The findings of the study were assessed for statistical analysis with NCSS (Number Cruncher Statistical System) ® 2007 and PASS 2008 Statistical Software (Utah, USA) ® programs. The parameters for normal distribution were evaluated with the Kolmogorov-Smirnov test. The evaluation of data, descriptive statistical methods (mean, standard deviation, and frequency), as well as quantitative data were used to compare the parameters of a normal distribution. Student's t-test, a non-normal distribution of parameters between the two groups, and the Mann-Whitney U-test were used for comparisons. The chi-square test and Fisher's exact

test were used to compare the qualitative data. p values <0.05 were considered statistically significant. Survivals between the two groups were analyzed by log-rank test.

RESULTS

Patients undergoing CABG were included in the study in the octogenarian group over a ten-year period covering the years 2000-2009. The study was conducted on 39 (37.1%) females and 66 (62.9%) males for a total of 105 patients. The mean age of the patients was 81.44 ± 2.21. Among the cases, 74.3% (n = 78) received LITA and in 25.7% (n = 27) a saphenous graft was applied. The follow-up period of the patients ranged between 1.25 and 98 months, the average was 42.95 ± 23.36 months, and the median was 44 months. Pre-operative demographic data of the groups are presented in Table 1. Except for emergency operations, there was no significant difference between the groups. Emergency operations were significantly higher in the SVG group (p =0.028). There was no significant difference between the groups' intraoperative characteristics (Table 2). The groups were similar in terms of post-operative complications (Table 3). Post-operative early mortality was observed in 22 patients. In an analysis of factors affecting early mortality, incomplete revascularization was found to be the only feature that causes a difference between the two groups (Table 4). In patients who underwent urgent revascularization, mortality was seen in one patient and the patient was in the saphenous vein group. In patients with prolonged intubation, hospital mortality was observed in 10 patients (LITA group: 7, saphenous group: 3). Seven (LIMA: 5, Saphenous: 2) of the deaths were due to cardiac failure. None of the intraoperative parameters was associated with mortality (Table 4). Prolonged cross-clamp time was associated with renal failure in the patients that received the saphenous vein treatment (p = 0.028).

Survival Analysis

Forty-one patients in the LITA group were reached by telephone and 27 (65.9%) were alive. Median survival was 68.70±5.95 months. Last death was observed on the 96th month. The cumulative survival rate was 21.5±16.7%. Fourteen patients in the saphenous vein group were reached and nine (65.9%) were alive. The last death was observed on the 32nd month. The cumulative survival rate was 63.5±13.1%. Eight-year survival rates of groups were evaluated by logrank test and there was no statistical difference between the groups (p=0.72; p>0.05) (Figure 1). Thirty-six patients who survived were also questioned for NYHA classification. There was no statistical significance between the groups (Table 6, p>0.05).

DISCUSSION

The number of elderly patients is increasing and numerous advances in operative techniques and perioperative care have resulted in an increasing number of patients 80 years of age and older being referred for CABG. Although the risk factors in this patient group are higher, studies have shown both short-term and long-term survival is higher in patients treated with surgery [4, 5]. Due to long-term patency rates and positive effects on survival in CABG patients, LITA has gained wide acceptance throughout the world as the choice of graft [6, 7]. This phenomenon should be examined carefully in the elderly. In octogenarian patients, arterial grafts are approached with suspicion due to prolonged operation and CPB time, sternal fragility, poor postoperative graft flow, and shorter life expectancy. However, over the years, both the number of octogenarian patients and the number of LITA used in operations have increased [8, 9].

The saphenous vein is an outstanding graft due to ease of harvesting, accessibility, and resistance to spasm. However, thrombosis, intimal hyperplasia, and graft atherosclerosis may cause early stenosis. Ten-year patency rates ranges between 61–71% [10]. Atherosclerosis develops in the saphenous vein, which is removed without protection [11]. The incidence of patency increases in saphenous grafts, which are removed as described by Johansson et al [12], to prevent this condition. Long-term patency (8.5 years) was 91.2% in the “No-Touch” group, and 83% in the saphenous veins removed via standard method. The current developments in medical treatment and novel insights had positive effects on long-term saphenous patency and survival.

There was a male predominance in the current study (n: 66, 62.85%), but there was no statistical significance between the genders (p>0.05). According to the report released in 2008 in Turkey, the incidence of ischemic heart disease-related mortality in patients who are older than 75 years is higher in males (n:6720, 64.55%)[16]. The TEKHARF study, which was carried out in Turkey, also demonstrated that the incidence of coronary heart disease in females over 75 years was closer to males (26.2% in females, 29.5% in males) [17]. The patient population in studies that investigated CABG surgery in octogenarians had similar rates [8, 9, 18, - 19].

When hospital mortality was considered, the incidence of hospital mortality was 20.5% (n=15) in the LITA group, and 22.2% (n=6) in the SVG group [p=0.085]. According to STS, the incidence of hospital mortality for CABG was 2.5% in patients who were younger than 80 years, and was 6.8% in patients who were older than 80 years.[13] Moon et al. [11] reported 7% hospital mortality, but did not observe any correlation with LITA use (p=0.11). The study by Toker et al. in 2007 included patients older than 80 years, which included all open

heart operations, reported the incidence of operative mortality as 23.3% [14]. Kurlansky et al. investigated the effects of SVG and LITA grafts on mortality in the octogenarian patient group, and observed 11.1% mortality in the SVG group and 6.3% mortality in the LITA group (p=0.009). However, the subgroup analyses demonstrated that the correlation between graft choice and operative mortality was not significant in patients older than 84 years [9].

There was a significant reduction in mortality with an increasing number of patients in this age group in our clinic. Hospital mortality was observed in 5 out of 17 patients (29.41%) operated on in 2005 (29.41%), whereas it was observed in 1 out of 18 patients (5.55%) operated on in 2009. Similarly, Moon et al.[11] determined the operation year to be significant risk factor for hospital mortality. The second plausible reason is the improper matching between the age groups and risk factors. According to the study by Ferguson et al., which was carried out on 99,942 patients who were older than 75 years, there was a significant increase in acute phase survival in patients with LITA graft, despite including all risk factors. However, 75% of the patients were younger than 80 years in the same study, and the positive effect of LITA decreased with increasing age.[15] This outcome makes the octogenarian group unique, and causes the use of LITA in this age group to be debated. The positive effects of LITA on long-term survival were demonstrated in the same study, but non-specific patient choice brought into question “whether the results were due to the success of LITA or patients’ general characteristics”. A similar study by Kurlansky et al. demonstrated the positive effects of LITA on both early and late periods [9]. However, significant differences in pre-operative risk factors between the groups were observed in this study. There was a significant difference in mean age, presence of additional peripheral arterial disease, history of myocardial infarction and hospitalization in the pre-operative congestive heart failure clinic between in the SVG group compared to the LITA group.

When considering the parameters that have an effect on hospital mortality, there was no significant difference in the pre-operative and post-operative risk factors between the patient groups (Tables 2 and 3). Incomplete revascularization was determined as the only significant risk factor on hospital mortality (Table 4). On the other hand, Moon determined a significant correlation between complete revascularization and long-term survival, but not hospital mortality [11]. The study by Rohde et al. in 2010 investigated pre-operative and intra-operative risk factors associated with long-term survival in the octogenarian group who underwent open heart surgery, and reported the associations between mortality and renal failure, hypercholesterolemia, low LVEF, CPB duration, and nasopharyngeal temperature lower than 32.8 °C [18]. According to Rohde et al., prolonged CPB is due to the complexity of the procedure. Moon et al. reported the risk factor for hospital mortality as operation in early years, advanced age, emergency operation, and prolonged CPB duration [11].

Contrary to the aforementioned studies, Basaran et al. determined intubation as an additional risk factor for hospital mortality.[20]

In this study, there was no correlation between the graft choice and CPB duration, and the correlation between the graft choice and mortality was not significant (p=0.656 and p=0.932, respectively). According to the literature, the effects of CPB are assumed to have a differential effect between younger and elderly patients, and there are various studies on this aspect [19, 21, - 22]. These studies linked the differential effect to the low tolerance of the elderly patients to CPB's effects. As a result, they reported that CPB should be avoided in the elderly patient group that had high risk.[19, 21, 22] However, there are reports demonstrating that OPCAB CAPG has no positive effect on survival, similar to the study by Kırali et al. in 2002.[23] On the other hand, T Ivert observed a significant correlation between the CPB duration and hospital mortality. The survivors had a CPB duration of 124 ± 46 minutes, whereas patients with hospital mortality had CPB duration of 164 ± 65 minutes (p<0.05) [19]. Ngauge et al. reported that CPB was a two-fold effective risk factor in elder patients (>70 years) compared to younger patients (<70 years) [21].

Regarding hospital morbidity, prolonged intubation was observed in 13 patients (13/105 %) and 8 of these patients were in the LITA group. However, the graft choice was not a risk factor for prolonged intubation (p=0.297) (Table 3). Kurlansky et al. reported that there was no significant correlation between graft choice and prolonged intubation, a finding that supports the results of the current study [9].Basaran et al. examined CABG in octogenarian women in 2007, and detected that the presence of chronic obstructive pulmonary disease (COPD), rather than graft choice, caused prolonged intubation [20]. On the other hand, this correlation was not significant in the current study. Only 2 out of 14 patients with COPD in the LITA group had this problem. None of the six patients with COPD in the SVG groups required prolonged mechanic ventilation.

In the current study, myocardial infarction (MI) was observed in 18 patients (17.1%), and 13 of these patients were in the LITA group. There was no significant correlation between the graft choice and the post-operative MI (p=0.82) (Table 3). Similarly, Kurlansky et al. did not observe any significant correlation between the graft choice and the pre-operative MI. Interestingly, the SVG choice was determined as a risk factor for hospital mortality, but not for MI.[9] Despite a significant elevation in the incidence of emergency revascularization in the SVG group, the incidence of low cardiac output (LCO) and perioperative MI was higher in the LITA group (LITA: n=17, 21.8%; SVG: n=5, 18.5%). However, there was no significant difference in LCO between the groups (p=0.718). In the SVG group, one patient with LCO had good ventricular function, two patients had intermediate ventricular function and two patients had poor ventricular function. In the LITA group, ten

patients had intermediate ventricular function, three patients had poor ventricular function, and four patients had good ventricular function. Similarly, Kurlansky did not find a significant correlation between graft choice and LCO, but speculated that low EF might lead to only congestive heart failure [9]. On the other hand, Rohde et al. examined the patients in the octogenarian group who underwent CABG and CABG+valve, and determined that the patients with low left ventricle ejection fraction had risk for LCO [18].

In the current study, the effect of graft choice on post-operative renal failure was not significant (p=0.656) (Table 3), but aortic cross clamp duration was correlated with renal failure (p=0.046). Kurlansky et al. observed that the incidence of post-operative renal failure was significantly higher in patients who had saphenous grafts in LAD, and reported renal failure as a significant risk factor for mortality, similar to the study by Rohde et al. [9, 16].

Mediastinitis was observed in six patients (5.7%), and four of these patients were in the LITA group. While the incidence of mediastinitis was two-fold higher in the LITA group, the difference between the groups was not significant (p=0.646). According to the literature, the incidence of mediastinitis in the octogenarian group ranged between 1-9% [9, 11, 19, 20]. One of these studies by Basaran et al. reported female gender to be a risk factor for mediastinitis (p <0.01). Similar to the current study, Kurlansky et al. also reported that graft choice was not a risk factor for mediastinitis (p=0.30) [9].

The mean follow-up period was 68.00 ± 5.95 months for the LITA group, and 62.00 ± 9.97 months in the SVG group. There was no significant difference in 5-year survival between the groups (LITA: 65.9%, SVG: 63.5%, p=0.72). Similar to the results of the current study, Kurlansky et al. [9] reported 5-year survival rates of 61.5% for the SVG group, and 64.5% in the LITA group, and 10-year survival rates of 15.2% in the SVG group, and 30.2% in the LITA group. As a result of the long-term follow-up, there was no significant effect of the graft choice on survival (p=0.11). T Ivert,[19] on the other hand, reported a 3-year survival rate of 84%. Moon et al. [11] determined a higher 8-year survival rate in the LITA group. (70.30% and p=0.03). However, both Moon and Ferguson observed a reduction in the correlation between graft choice and mortality after 7 years, and determined that the significance of this correlation was diminished [11, 15].

In their study, Colin et al. stated that their patients who underwent operations were in good physical and emotional condition, were pain-free, and were satisfied with their physical functions (p<0.01). In the same study, Colins reported to have received a significantly high rate of “YES” responses when patients were asked, “Do you accept undergoing the CABP operation again, if needed?” [24]. In the current study, the patients that were accessible for questioning were asked the same question. Only two patients responded “no”. Both patients continued to live as NYHA Class 3 patients. In the current study, none of the surviving

patients in either group were NYHA Class IV patients.

The current study has all the limitations characteristic of a retrospective study. The second possible limitation is the choice bias, which may result during the decision of patient choice for grafting and the decision of complete or incomplete revascularization. The study population consisted of patients operated on at several clinics. There may be differences in patients who were considered to have high risk and who did not receive CPB support, and in patients who were chosen for LITA grafts. The degree of cooling the patients during CPB may also differ between the clinics. However, this choice bias is inevitable in observational and/or retrospective studies. In addition, choice bias may be present in intraoperative parameters. Another bias comes from the fact that some patients in the octogenarian group did not undergo an operation despite a decision for an operation. It is possible that some of these patients did not accept to undergo the operation, and some patients might be considered to have a high risk due to the presence of comorbidities and non-surgical treatment might have been continued. Another possible limitation is the small population size. Compared to the studies that included younger patients in particular, the current study had a lower number of patients. The final limitation is that the number of patients that were accessible for evaluation for the long-term survival was lower compared to the literature.

CONCLUSION

As a conclusion, octogenarians should receive complete revascularization with short aortic cross clamp time. The importance of graft choice could not be demonstrated for long-term functional outcome and survival as a prognostic factor in this age group who underwent coronary artery bypass surgery.

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TABLES AND FIGURES:

Table 1: Preoperative demographic variables

Chi-square test $p<0.05$ significant

NYHA: New York Heart Association, COPD: chronic obstructive pulmonary disease, LITA: left internal thoracic artery, SVG: saphenous vein graft

Table 2: Perioperative Variables

LITA: left internal thoracic artery, SVG: saphenous vein graft

Student t-test $p<0.05$

Table 3: Post-operative complications

Chi-square test *Fisher's exact test p<0.05

LITA: left internal thoracic artery, SVG: saphenous vein graft

Table 4: Factors affecting early mortality

LITA: left internal thoracic artery, SVG: saphenous vein graft

Student t test p<0.05 *Fisher's exact test p<0. 05

Table 5: Late-term functional capacity evaluation*

Chi-square test

* The number and rate of patients who could be followed-up on by groups of survivors.

NYHA: New York Heart Association, LITA: left internal thoracic artery, SVG: saphenous vein graft

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Figure 1: Survival Graph

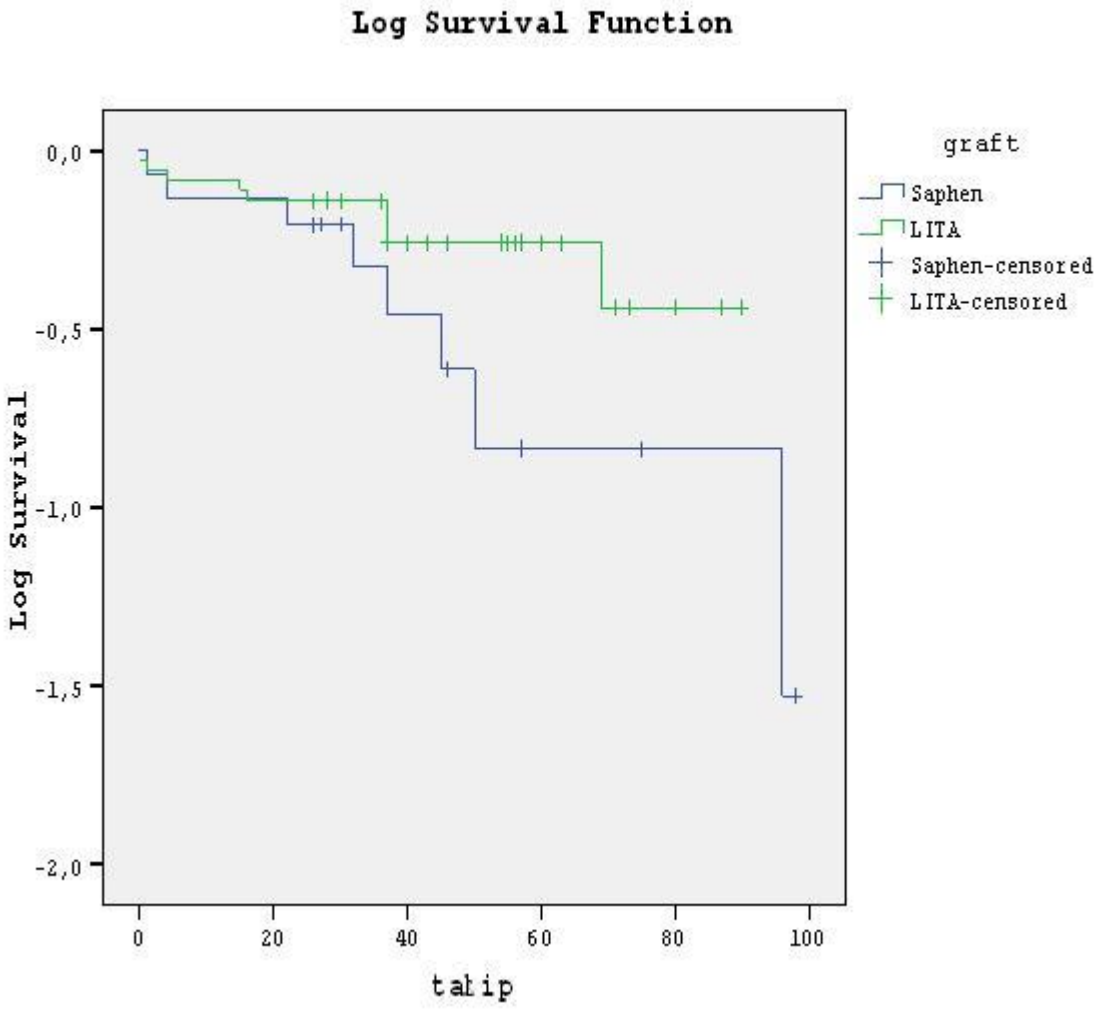

Table 1: Preoperative demographic variables

Preoperative demographic variables			
	LITA	SVG	P
Age	81.47±2.25	81.33±2.15	0.777
Female	28 (35.9%)	11 (40.7%)	0.653
Distal anastomosis X3	32 (41.0%)	12 (44.4%)	0.224
NYHA-class III	34 (43.6%)	13 (48.1%)	0.291
Emergency	1 (1.3%)	4 (14.8%)	**0.015***
Ejection Fraction 35–55%	40 (51.3%)	18 (66.7%)	0.308
Chronic Renal Insufficiency	15 (19.2%)	2 (7.4%)	0.151
COPD	14 (17.9%)	6 (22.2%)	0.626
Diabetes mellitus	16 (20.5%)	4 (14.8%)	0.516
Past Cerebrovascular Event	6 (7.7%)	3 (11.1%)	0.584
Peripheral Arterial Disease	5 (6.4%)	2 (7.4%)	0.858

Table 2: Perioperative Variables

Perioperative Variables			
	LITA	SVG	*P*
Cross-clamp time (minutes)	67.59±32.54	77.21±18.73	0.293
Cardiopulmonary bypass time (minutes)	103.14±60.66	110.53±37.75	0.656
Operation time (minutes)	192.81±70.21	161.85±81.96	0.062
Incomplete Revascularization	17 (21.8%)	6 (22.2%)	0.963
Beating Heart	23 (29.5%)	13 (48.1%)	0.078

Table 3: Post-operative complications

Post-operative complications			
	LITA	**SVG**	**p**
Prolonged ventilation	8 (10.3%)	4 (14.8%)	0.521
Peri-operative myocardial infarction	13 (16.7%)	5 (18.5%)	0.826
Low cardiac output	17 (21.8%)	5 (18.5%)	0.718
Intra-aortic balloon counter-pulsation	9 (11.5%)	4 (14.8%)	0.656
Mediastinitis*	4 (5.1%)	2 (7.4%)	0.646
Post-operative cerebrovascular event*	4 (5.1%)	2 (7.4%)	0.646
Post-operative renal insufficiency	9 (11.5%)	4 (14.8%)	0.656
Early mortality	16 (20.5%)	6 (22.2%)	0.851
Late mortality	14 (22.6%)	5 (23.8%)	0.908

Table 4**:** Factors affecting early mortality

Factors affecting early mortality			
	LITA	SAPHEN	*p*
Age	81.24±1.74	82.33±3.34	0.565
Female	6	3	0.526
Diabetes mellitus	2	6	0.931
Chronic Obstructive Pulmonary Disease	2	7	0.658
Chronic renal insufficiency	1	8	0.39
Cerebrovascular event	2	1	0.759
Peripheral arterial disease	5	2	0.858
Left Ventricular Ejection Fraction (35-55%)	9 (64.3%)	3 (60.0%)	0.323
Emergency	0	1	-
Cardiopulmonary bypass time (m)	135.33±109.41	121.00±69.91	0.932
Cross-clamp time (minutes)	76.83±34.95	80.33±40.10	0.106
Operation time (minutes)	223.18±100.78	183.33±57.76	0.882
Beating Heart	5 (21.7%)	3 (13%)	0.363
Incomplete Revascularization	5 (21.7%)	3 (13%)	**0.028**
Prolonged ventilation	7 (30.4%)	3 (13%)	0.723
Peri-operative myocardial infarction	7 (30.4%)	4 (17.3%)	0.283
Low cardiac output	15 (7.1%)	5 (21.7%)	0.759
Post-operative renal insufficiency	8 (34.7%)	3 (13%)	0.522
Post-operative cerebrovascular event	4 (17.3%)	0	-
Permanent pace implantation	1	1	0.42
Mediastinitis	2	1	0.759

Table 5: Late-term functional capacity evaluation*

Control NYHA		LITA n (%)*	SVG n (%)*	P
Class I		3 (8.3%)	1 (2.7%)	
Class II		18 (50.0%)	5 (13.8%)	*0.532*
Class III		6 (16.6%)	3 (8.3%)	
Class IV		0	0	