ORIGINAL ARTICLE

Predictors of long-term mortality in acute ST-elevation myocardial infarction patients undergoing emergent coronary artery bypass graft surgery

Akut ST elevasyonlu miyokart enfarktüsü ile acil koroner arter baypas cerrahisine giden hastalarda uzun dönem mortalite öngördürücüleri

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ABSTRACT

Objective: Coronary artery bypass graft (CABG) surgery as a primary treatment for acute ST-elevation myocardial infarction (STEMI) is still debated. This study aimed to evaluate the predictors of long-term mortality in STEMI patients undergoing emergent CABG. To the best of our knowledge, this is the first study to evaluate the long-term mortality predictors in patients with STEMI revascularized by primary CABG.
Methods: This retrospective study included 88 consecutive patients with STEMI, who did not qualify for primary percutaneous intervention and required emergent CABG between 2010 and 2017. The study population was divided into the following 2 groups: survivors and nonsurvivors. The 2 groups were compared in terms of demographics, preoperative, intraoperative, and postoperative characteristics.
Results: 23 of the 88 patients, died during the median 92.8 (69.0-105.1) months of follow-up. Data were evaluated with univariate and multivariate analyses. Killip class ($p<0.001$) was found to be an independent predictor of long-term all-cause mortality in patients with STEMI revascularized by CABG, and mortality rates increased significantly as Killip class increased (log-rank test, $p<0.001$). Moreover, age ($p=0.044$) was found to be an independent predictor of long-term mortality. Left ventricular ejection fraction, glomerular filtration rate, glucose levels, and left anterior descending artery to the left internal mammary artery graft usage ($p=0.001$, $p=0.009$, $p<0.001$, and $p=0.039$, respectively) were significantly associated with long-term all-cause mortality for our study population.
Conclusion: Killip class was found to be an independent predictor of long-term all-cause mortality in patients with STEMI who underwent emergent CABG. The patients' admission status may give valuable information about long-term mortality.

ÖZET

Amaç: Akut ST elevasyonlu miyokard enfarktüsünün (STEMI) primer tedavisinde koroner arter baypas greft (KABG) cerrahisi hala tartışılmaktadır. Çalışmamızda acil KABG geçiren STEMI hastalarında uzun dönem mortalite belirleyicilerini değerlendirmeyi amaçladık. Bildiğimiz kadarıyla çalışmamız, KABG ile revaskülarize edilen STEMI hastalarında uzun dönem mortalite belirleyicilerini araştıran ilk çalışmadır.
Yöntemler: 2010-2017 yılları arasında primer perkütan girişim için uygun olmayan ve acil KABG gerektiren 88 ardışık STEMI hastası retrospektif olarak çalışmaya dahil edildi. Çalışma popülasyonu ölenler ve sağkalanlar olarak iki gruba ayrıldı. İki grup demografik, preoperatif, intraoperatif ve postoperatif özellikler açısından karşılaştırıldı.
Bulgular: 88 hastanın 23'ü medyan 92.8 (69.0-105.1) ay takip süresi içerisinde yaşamını yitirdi. Tek ve çok değişkenli analizler ile veriler değerlendirildi. KILLIP sınıfının ($p<0.001$), KABG ile revaskülarize edilen STEMI hastalarında uzun dönem tüm nedenlere bağlı mortalitenin bağımsız öngördürücüsü olduğu ve KILLIP sınıfı arttığında mortalite insidansının da anlamlı derecede arttığı bulundu (Log-rang testi, $p<0.001$). Ayrıca yaş ($p=0.044$) uzun dönem mortalitenin bağımsız belirleyicisi olarak bulundu. Sol ventrikül ejeksiyon fraksiyonu, glomerüler filtrasyon hızı, glikoz düzeyleri ve sol ön inen arter-sol internal mamariyan arter greft kullanımı ($p=0.001$, $p=0.009$, $p<0.001$, $p=0.039$, sırasıyla) çalışma grubumuz için uzun dönem mortalite ile anlamlı olarak ilişkiliydi.
Sonuç: KILLIP sınıfının acil KABG uygulanan STEMI hastalarında uzun dönem tüm nedenlere bağlı mortalitenin bağımsız bir belirleyicisi olduğu bulunmuştur. Hastaların kabul durumları uzun dönem mortalite hakkında değerli bilgiler verebilir.

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Coronary artery disease (CAD) is the leading cause of death worldwide. It has a wide spectrum from unstable angina to ST-elevation myocardial infarction (STEMI). The primary treatment of STEMI is reperfusion by fibrinolytic therapy or primary percutaneous intervention (PCI). Emergent coronary artery bypass graft (CABG) surgery is only recommended for patients with STEMI and unsuitable anatomy of the infarct-related artery (IRA) for PCI, either a large myocardial area at jeopardy or with cardiogenic shock or mechanical complications.[1] Data for patients with STEMI undergoing emergent CABG for primary revascularization is limited. The risk stratification is an important guide for a clinician to draw a road map in that high-risk group. There are just a few studies that have investigated in-hospital mortality predictors for this patient group. However, there is no study focusing on the long-term mortality predictors. This study aimed to evaluate the predictors of long-term mortality in patients with STEMI who underwent emergent CABG.

METHODS

Patient selection

Between 2010 and 2017, a total of 97 patients with STEMI with unsuitable coronary artery anatomy for primary PCI or failed PCI accompanied by persistent angina or hemodynamic instability, who underwent emergent CABG within 6 hours after the onset of angina, were retrospectively scanned. Patients who underwent elective CABG after a balloon dilatation or stent implantation to the responsible lesion, inoperable patients owing to generalized vascular disease or anesthesia concerns, presence of left bundle branch block or pacemaker rhythm, patients accompanied with acute STEMI mechanical complications, patients who required concomitant valvular procedure, and patients with unavailable data were not included to our study. After the exclusion criteria were applied, 88 patients were included. The study protocol was approved by the Ethics Committee of University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (Approval Date: June 9, 2020; Approval Number: 2020-36), and the study was performed in accordance with the requirements of the Declaration of Helsinki.

Definitions

ECG criteria for STEMI is as follows:[2]

New ST-segment elevation at the J point in 2 contiguous leads with the cutoff point >0.1 mV in all leads other than V2 or V3.

In leads V2-V3, the cutoff point is >0.2 mV in men aged >40 years old and >0.25 in men aged <40 years old, or >0.15 mV in women.

Cardiogenic shock was defined as a Killip class of III and above which was prespecified as patients having pulmonary edema or a cardiac index of 2.0 L/(min/m^2) or less, or a systolic arterial pressure of 90 mm Hg or less, despite high-dose inotropic support.[3] Killip class was evaluated at admission. The patients provided data on their daily smoking habits. Past smokers were included in the smoker category. Hypertension (HTN) was defined as systolic arterial pressure >140 mm Hg and/or diastolic arterial pressure >90 mm Hg, or when the patient was already using antihypertensive drugs.[4] Diabetes mellitus (DM) was defined as fasting glucose levels over 126 mg/dL or the patient being prescribed glucose-lowering agents.[5] Hyperlipidemia (HL) was defined as total serum cholesterol levels >240 mg/dL, low-density lipoprotein (LDL) cholesterol >130 mg/dL, or serum triglycerides exceeding 180 mg/dL, or the patient using lipid lowering agents.[6] Chronic renal failure was defined as estimated glomerular filtration rate ≤60 mL/min. Failed PCI was defined as failure to cross the lesion, inability to advance balloons or stents and achieve flow despite multiple attempts.

Abbreviations:

AMI	*Acute myocardial infarction*
CABG	*Coronary artery bypass graft*
CAD	*Coronary artery disease*
CI	*Confidence intervals*
DM	*Diabetes mellitus*
HL	*Hyperlipidemia*
HRs	*Hazard ratios*
IRA	*Infarct-related artery*
LDL	*Low-density lipoprotein*
LIMA	*Left internal mammary artery*
LVEF	*Left ventricular ejection fraction*
PCI	*Primary percutaneous intervention*
STEMI	*ST-elevation myocardial infarction*
STS	*Society of Thoracic Surgeons*

Surgery

Mediastinum was reached via a median sternotomy under general anesthesia. Left internal mammary artery (LIMA) flap and saphenous vein grafts were prepared for hemodynamically stable patients; LIMA was not harvested for unstable patients. Arterial cannulation was made from ascending aorta, venous cannulation was performed through right atrium appendix, and cardiopulmonary bypass was initiated. Systemic hypothermia was maintained at 32ºC, and cross clamp was placed in the ascending aorta. Normothermic antegrade blood cardioplegia was administered to achieve a diastolic arrest. Distal anastomoses were made, cross clamp was removed, and systemic warming was achieved. The proximal anastomoses of the saphenous vein graft were completed with the side clamp. When the patient's temperature reached 36ºC, and the patient became hemodynamically stable with appropriate arterial blood gas analysis, the CPB was terminated, and the patient was decannulated. Following hemostasis, drainage tubes and pacemaker wires were placed, and the sternum was closed.

Patient follow-ups

The primary endpoint of the study was long-term all-cause mortality. Demographic information, cardiovascular risk factors (age, family history, smoking habits, hyperlipidemia, hypertension, and DM) together with preoperative, intraoperative, and postoperative characteristics were obtained after a systematic review of the patients' hospital records. Missing variables were obtained through telephone interviews with the patients and/or their relatives. The patients' survival data were obtained from an electronic hospital system or national population registry. The study population was divided into 2 groups on the basis of the presence of mortality. These groups were compared in terms of demographics, preoperative, intraoperative, and postoperative characteristics to evaluate the predictors of long-term mortality.

Statistical analysis

Data were analyzed using the SPSS, version 24.0 (IBM Corp.; Armonk, NY, USA). Visual (histograms, probability curves) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests) were used to evaluate whether the variables showed normal distribution. Numerical variables showing normal distribution were presented as mean±standard deviation, numerical variables not showing normal distribution were expressed as median (interquartile range) and categorical variables as percentage (%). Numerical variables were evaluated using Student t test and the Mann-Whitney U test between the 2 groups. The chi-squared or Fisher exact tests were used to compare categorical variables. Event-free survival curves were constructed using the Kaplan-Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazards model was used to calculate hazard ratios (HRs) and 95% confidence intervals (CI) for clinical endpoints. A p value of <0.05 was considered significant.

RESULTS

The mean age of the study population was 56.1±11.3 years, and 77 (87.5%) of the patients were male. During the median 92.8 (69.0-105.1) months of follow-up, 23 (mean age 60.6±12.1 years; 87.0% male of the 88 patients experienced all-cause mortality; and 65 patients were event-free (mean age 54.5±10.6 years; 87.7% male). The study population was divided into 2 groups as survivors and nonsurvivors. There was no significant difference between the groups in terms of demographic features (sex, DM, HTN, HL, and smoking habits), except age with the nonsurvivor group being significantly older (p=0.033) than the survivor group. The demographics and clinical and laboratory characteristics of 88 patients are summarized in Table 1.

Biochemical parameters showed that plasma glucose level (179 mg/dL vs 156 mg/dL, p=0.040) was significantly higher, and GFR (75.4±29.1 mL/min vs 88.4±20.1 mL/min, p=0.044) was significantly lower in the nonsurvivor group. There was no significant difference in troponin levels (p=0.801). When clinical parameters were evaluated, left ventricular ejection fraction (LVEF) was found to be significantly lower (39.8±7.5% vs 43.3±7.1%, p=0.004) in the nonsurvivor group, and nonsurvivors were more frequently admitted with cardiogenic shock (Killip class ≥III) (7 vs 2, p=0.001). The Society of Thoracic Surgeons (STS) score was significantly higher (7.2 vs 5.3, p=0.002) in the nonsurvivor group. The number of CAD involved vessels (Table 1) and the distribution of IRAs (or culprit lesion) were not significantly different between the groups (Table 2).

Intraoperative features are summarized in Table 3. Cardiopulmonary bypass time, aortic cross clamp time, and arterial revascularization with internal mammary grafts were not significantly different between the groups (p=0.943, p=0.065, p=0.063, respectively).

Postoperative ventilation time, total hospital stay, and intensive care unit stay were significantly higher in the nonsurvivor group than in the survivor group (12 hours vs 9 hours, p=0.033; 9 days vs 6 days,

Table 1. Baseline demographics, clinical, and laboratory characteristics of the study groups

	Survivors N=65	Nonsurvivors N=23	*p*
Age (years)	54.5±10.6	60.6±12.1	0.033
Sex, male, n (%)	57 (87.7)	20 (87.0)	1.0
Hypertension, n (%)	20(30.8)	10 (43.5)	0.269
Hyperlipidemia, n (%)	30 (46.2)	10 (43.5)	0.825
Smoker, n (%)	15 (23.1)	8 (34.8)	0.272
Glucose, mg/dL	156 (134-190)	179 (140-280)	0.040
LDL, mg/dL	128±33	124±29	0.635
HDL, mg/dL	38±8	38±7	0.849
Triglyceride, mg/dL	158 (118-226)	149 (103-225)	0.497
GFR, mL/min	88.4±20.1	75.4±29.1	0.044
Troponin, ng/mL	0.12 (0.05-0.35)	0.16 (0.02-0.38)	0.801
Previous PCI, n (%)	6 (9.2)	4 (17.4)	0.281
Failed PCI, n (%)	8 (12.3)	7 (30.4)	0.059
CPR before surgery, n (%)	3 (4.6)	1 (4.3)	1.0
Killip class, n (%)			
I	59 (90.8)	12 (52.2)	<0.001
II	4 (6.2)	4 (17.4)	0.198
≥III	2 (3.1)	7 (30.4)	0.001
LVEF, %	43.3±7.1	39.8±7.5	0.004
CAD			0.681
1 vessel	11 (16.9)	4 (17.4)	
2 vessels	15 (23.1)	6 (16.1)	
3 vessels	35 (53.8)	13 (56.5)	
4 vessels	4 (6.2)	0 (0.0)	
STS score	5.3 (4.3-6.5)	7.2 (5.2-11.0)	0.002

Data are expressed as percentage, mean±standard deviation, or median (interquartile range).
CAD: coronary artery disease; CPR: cardiopulmonary resuscitation; GFR: glomerular filtration rate; HDL: high density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; STS: Society of Thoracic Surgeons.

Table 2. Distribution of the infarct-related coronary artery vessels (or culprit lesion)

	Survivors N=65	Nonsurvivors N=23	*p*
LMCA	17 (26.2)	9 (39.1)	0.241
LAD	48 (73.8)	13 (56.5)	0.122
CX	1 (1.1)	0 (0)	1.0
RCA	0 (0)	0 (0)	1.0

Data are expressed as number (percentage).
CX: circumflex artery; LAD: left anterior descending artery; LMCA: left main coronary artery; RCA: right coronary artery.

Table 3. Intraoperative characteristics of study groups

	Survivors N=65	Nonsurvivors N=23	*p*
ACC time (minutes)	48.6±18.7	40.5±16.8	0.065
CPB time (minutes)	80 (55-110)	76 (55-95)	0.943
LIMA use	40 (61.5%)	9 (39.1%)	0.063

ACC: aortic cross clamp; CPB: cardiopulmonary bypass; IMA: internal mammary artery.

Table 4. Postoperative characteristics of study groups

	Survivors N=65	Nonsurvivors N=23	*p*
Ventilation time (h)	9.0 (6.5-12.0)	12.0 (8.0-29.0)	0.033
ICU stay (d)	2 (2-3)	3 (2-8)	0.010
Hospital stay (d)	6 (5-7)	9 (16-12)	0.017
Drainage (mL)	650±166	650±187	0.883

d: days; h: hours; ICU: intensive care unit.

p=0.017; 3 days vs 2 days, p=0.010, respectively) as shown in Table 4.

In the univariate regression analysis (Table 5), age, LVEF, GFR, glucose levels, Killip class, and LAD-LIMA graft usage (p=0.028, p=0.001, p=0.009, p<0.001, p<0.001, and p=0.039, respectively) were significantly associated with long-term all-cause mortality. According to the multivariate regression analysis (Table 6), Killip class (for Killip class II compared with Killip class I, HR, 5.035; 95% CI, 1.599-15.85; p=0.006; for Killip class ≥III compared with Killip class I, HR, 7.422; 95% CI, 2.768-19.90; p<0.001) and age (HR, 1.042; 95% CI, 1.001-1.085; p=0.044) were found to be independent predictors of long-term all-cause mortality in patients with STEMI who underwent emergent CABG. The Kaplan-Meier cumulative survival curve for all-cause mortality of patients grouped according to the Killip class is presented in Fig. 1. The Kaplan-Meier curve showed that as the Killip class increased, mortality rates increased significantly. Comparison of long-term mortality rates according to Killip class is shown in Fig. 2.

DISCUSSION

We investigated the predictors of long-term all-cause mortality in patients with STEMI revascularized by primary CABG. In our study, we found that Killip class

Table 5. **Univariate analysis for the predictors of long-term mortality**

	HR	95% CI	*p*
Age, years	1.041	1.004-1.079	0.028
Sex, male, n (%)	1.041	0.309-3.509	0.948
Hypertension, n (%)	1.889	0.823-4.339	0.134
Hyperlipidemia, n (%)	0.918	0.402-2.094	0.839
Smoker, n (%)	1.712	0.723-4.052	0.222
Glucose, mg/dL	1.009	1.004-1.014	<0.001
GFR, mL/min	0.974	0.955-0.993	0.009
LDL, mg/dL	0.996	0.983-1.009	0.549
HDL, mg/dL	1.000	0.950-1.052	0.993
Troponin	0.987	0.339-2.875	0.981
Killip class			<0.001
II*	4.829	1.551-15.03	0.007
≥III*	8.409	3.276-21.59	<0.001
LVEF, %	0.902	0.848-0.960	0.001
LAD-LIMA graft	0.410	0.176-0.958	0.039

*Compared with Killip class I.
CI: confidential interval; HR: hazard ratio; GFR: glomerular filtration rate; HDL: high density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; LAD: left anterior descending artery; LIMA: left internal mammary artery.

Table 6. **Multivariate analysis for the independent predictors of long-term mortality**

	HR	95% CI	*p*
Age, years	1.042	1.001-1.085	0.044
Killip class			<0.001
II*	5.035	1.599-15.85	0.006
≥III*	7.422	2.768-19.90	<0.001
LAD-LIMA graft	0.556	0.227-1.363	0.200

*Compared with Killip class I.
LAD: left anterior descending artery; LIMA: left internal mammary artery

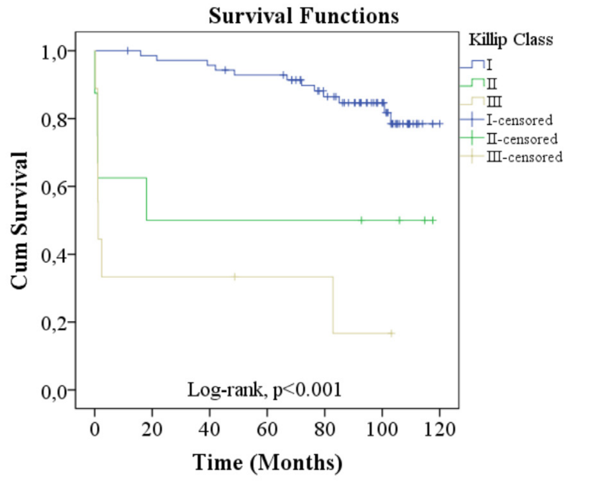

Figure 1. Kaplan-Meier curves for long-term all-cause mortality stratified by Killip class.

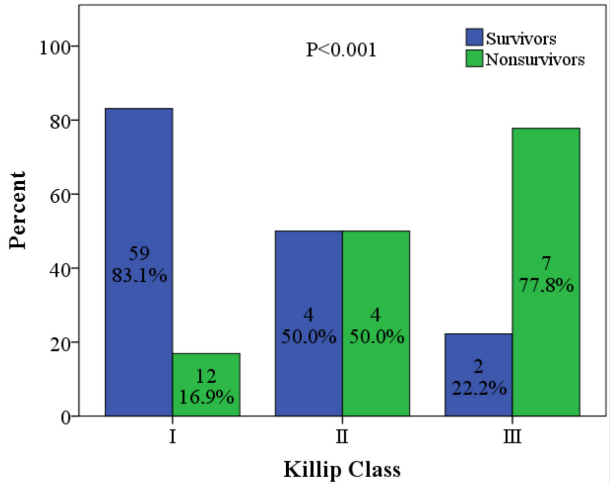

Figure 2. Comparison of long-term mortality rates according to Killip class.

and age were independent predictors of long-term all-cause mortality in patients with STEMI who underwent emergent CABG. As the Killip class increased, the mortality rates increased significantly. Moreover, LVEF, GFR, glucose levels, and LAD-LIMA graft usage were significantly associated with long-term all-cause mortality for our study population.

According to the current guidelines, CABG for the primary treatment of STEMI is still controversial. Emergent CABG is only recommended for patients with STEMI with unsuitable anatomy of IRA for PCI, either a large myocardial area at jeopardy or with cardiogenic shock or mechanical complications.[1] Mortality predictors of CABG are well established.[7] Several studies investigated the mortality predictors of CABG in acute myocardial infarction (AMI).[8, 9] In these studies, AMI definition included both STEMI and non-STEMI. In our study, we included only patients with STEMI who underwent emergent CABG and looked for predictors of long-term all-cause mortality. There are very few studies that have evaluated the in-hospital mortality predictors in patients with STEMI revascularized by primary CABG.[10-12] To the best of our knowledge, our study was the only one that evaluated the long-term mortality predictors in patients with STEMI who underwent CABG and followed up for a median of 92.8 months.

Thielmann et al.[10] and Filizcan et al.[11] have evaluated the in-hospital mortality predictors in patients with STEMI who underwent CABG. Thielmann et al.[10] found that female sex, preoperative cardiac troponin I level, preoperative cardiogenic shock, and time to surgery were major variables of mortality and morbidity. Filizcan et al.[11] reported that advanced age, elevated preoperative cardiac troponin levels, and preoperative intra-aortic balloon pump use were independent predictors of in-hospital mortality. Both studies mentioned that preoperative troponin levels were predictors of in-hospital mortality. In contrast to these studies, our study showed that preoperative troponin levels were not significantly different in the 2 groups. We only included patients who underwent CABG within 6 hours after the onset of angina; however, Filizcan et al.[11] have included patients who underwent CABG within 23 hours after the onset of angina; and Thielmann et al.[10] have included patients who underwent CABG within 15 days after the onset of angina. Therefore, their studies had a longer time period for the increase of troponin levels preoperatively. In our study, the time period between the onset of angina and surgery was shorter. This explains the different findings between the studies in terms of troponin elevation. In our study, age was found to be an independent predictor, compatible with the study by Filizcan et al.[11] Moreover, cardiogenic shock was an independent predictor similar to the study by Thielmann et al.[10]

Rohn et al.[12] have investigated the importance of timing for surgical revascularization in the early phase of STEMI for in-hospital mortality and morbidity. They found that Killip class and LVEF were associated with in-hospital mortality and morbidity; and in their study, the only independent predictor was Killip class. They concluded that cardiogenic shock, poor hemodynamic status and impaired ejection fraction were risk factors for early mortality and morbidity. Our study confirmed their results and also found that LVEF was associated with long-term mortality; the Killip class was the independent predictor for long-term mortality in patients with STEMI who underwent CABG. As Killip class increased, the incidence of mortality increased significantly.

Because the patients who underwent grafting with LIMA had relatively stable hemodynamics, they were included in the long-term survivors group, which could be seen as a bias. However, it is a well-known fact that the patency of the LIMA graft is longer than the saphenous grafts, and the long-term results with LIMA grafts are better. Therefore, our results should be interpreted with these in mind.

Limitations

Our study had some limitations. First, our study was designed retrospectively and involved a single center and a small study population. Second, the patients whose mortality information could not be accessed from the electronic hospital system or from the relatives of the patients, were checked through the national population registry. Since this system only states the existence of mortality and does not explain the cause of mortality, the primary endpoint of our study was determined as all-cause mortality, not cardiovascular mortality.

Conclusion

In our study, the Killip class was found to be an independent predictor of long-term mortality in patients with STEMI who underwent CABG. The admission status of patients may give valuable information regarding long-term mortality.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of University of Health Sciences İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (Approval Date: June 9, 2020; Approval Number: 2020-36).

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Keywords: Cardiovascular surgical procedures; coronary artery disease; prognosis; ST elevation myocardial infarction

Anahtar Kelimeler: Kardiyovasküler cerrahi prosedürler; koroner arter hastalığı; prognoz; ST yükselmeli miyokart enfarktüsü