

# Determinants of inpatient costs of angina pectoris, myocardial infarction, and heart failure in a university hospital setting in Turkey

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## ABSTRACT

**Objective:** This study aimed to determine the correlates of in-hospital costs for angina pectoris (AP), myocardial infarction (MI), and heart failure (HF) in a university hospital setting.

**Methods:** This is a retrospective cost-of-illness study using data from the records of patients who were admitted with AP, MI, or HF to Dokuz Eylül University Hospital during 2008. Direct medical costs were calculated from the Social Security Institute perspective using a bottom-up approach. Socio-demographic and clinical information was abstracted from patient files. Costs were presented in Turkish lira (TL). A generalized linear model was used in the multivariate analysis.

**Results:** We included 337 in-patients in total in the study. AP was present in 26.4% (n=89), MI was present in 55.8% (n=188), and HF was present in 17.8% (n=60) of patients. MI was the most costly disease (2760 TL), followed by HF (2350 TL) and AP (1881 TL). The largest proportion of the total cost was formed by medical interventions (27.5%), followed by surgery (22.2%). Presence of DM, smoking, diagnosis of MI, HF, need for intensive care, and resulting in death were strong predictors of treatment costs.

**Conclusion:** Both preadmission characteristics of patients (diabetes mellitus, smoking, use of anti-aggregant before admission) and in-patient characteristics (diagnosis, coronary artery bypass grafting, intensive care need, death) predicted the hospital cost of cardiovascular diseases (CVDs) independently. Our results may be used as input for health-economic models and economic evaluations to support the decision-making of reimbursement and the cost-effectiveness of public health interventions in healthcare. (*Anatol J Cardiol* 2015; 15: 325-33)

**Keywords:** cost of illness, economic analysis, cardiovascular disease, hospital costs, bottom-up approach, generalized linear model

## Introduction

Despite downward trends in the total number of deaths associated with cardiovascular disease (CVD) during the last decade, CVDs are the number one cause of death and a major cause of disability and loss of productivity in adults worldwide, including Turkey (1, 2). CVDs accounted for 30% of all global deaths in 2008, and 80% of these deaths occurred in low- and middle-income countries affecting men and women almost equally (3). CVDs have a significant economic impact; the total direct and indirect cost of CVD and stroke in the United States for 2009 was estimated to be \$312.6 billion, and this figure was more than the cost of all cancers and benign neoplasms, which was estimated to be \$228 billion (4). The European Union spends approximately 169 billion euros on CVDs annually, and it is estimated that of the total costs, 62% is due to health care expens-

es, 21% is due to productivity losses, and 17% is due to informal care of people with CVD. In Turkey, a recent study provided an estimate of the economic burden of acute coronary syndrome, which was around \$1.8 billion (5).

CVDs are formed by several risk factors, such as high blood cholesterol, high blood pressure, physical inactivity, obesity, smoking, and diabetes mellitus (DM). CVD and its risk factors, mainly DM and obesity, are highly prevalent in Turkey (6). In a study conducted on the 20-and-above population in Turkey in 1990, coronary heart disease prevalence was 4.1% in males and 3.5% in females (7). According to the 2010 Turkish Health Survey findings, the prevalence of self-reported angina pectoris (AP) was 4.2% in both sexes over 15 years of age. The myocardial infarction (MI) prevalence was 2.1% in men and 0.7% in women in the same study (8). Heart failure (HF) prevalence was reported as 2.9% according to a recent nationwide survey (9). Turkey is in

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the era of epidemiological transition; hence, the burden of CVDs and their economic consequences is expected to rise in the coming period in Turkey.

Since healthcare costs are rising and resources tend to be progressively limited, cost estimates for CVDs are necessary for decisions about allocating scarce resources; however, there is a paucity of studies that estimate these costs in actual clinical practice in Turkey. In other countries, earlier studies have determined the treatment costs of CVDs, but they did not compare patient subgroups and included only a limited number of determinants for costs (10, 11). Therefore, this study aimed to determine the degree of association of costs for acute myocardial infarction, heart failure, and angina pectoris in a university hospital setting.

## Methods

### Sociodemographic and clinical data

Each patient who was admitted to Dokuz Eylül University Hospital, Izmir, Turkey, for in-patient treatment of AP, MI, and HF in 2008 was included in this retrospective cost analysis. The list of patients was abstracted from the hospital admission database with the following three diagnostic groups, according to ICD-10 criteria: I 20 (Angina pectoris), I 21 [(ST elevation (STEMI) and non-ST elevation (NSTEMI)] myocardial infarction, and I 50 (Heart failure). In total, 337 individuals who were hospitalized with a diagnosis of HF, AP, or MI from January 1 to December 31, 2008 in Dokuz Eylül University Hospital formed the study group. Both the electronic discharge reports and hardcopies of patient files were examined to check the validity of the diagnosis. All medical records were screened by trained research assistants who were medical doctors. The data included detailed demographic, clinical, and process of care information. The dependent variable was hospital cost of CVDs. Independent variables were age, gender, medical history of chronic diseases (coronary heart disease, stroke, diabetes mellitus, heart failure, atrial fibrillation), smoking, hypercholesterolemia, presence of AP, MI, HF, and in-hospital treatments and procedures.

### Economic evaluation

In this cost-of-illness study, costs were estimated for the payer (Social Security Institution) perspective using a bottom-up approach. The direct medical costs considered in the study involved the following items: diagnostic procedures costs, medical supply costs, laboratory tests, interventional treatment costs (eg, angioplasty, stent), surgery [eg, coronary artery bypass grafting (CABG)], ward cost, physiotherapy, physicians' costs, and nursing costs. The total direct medical cost for each patient was calculated by multiplying the unit cost of each item with the quantity. Detailed cost data with quantities and unit costs were obtained from the database of the accounting department of Dokuz Eylül University Hospital. The total dose for the medications was assessed according to the dose prescribed in the patient charts. The unit cost per medication was

based on the pharmacy market prices, set annually by the Ministry of Health of Turkey (12). The costs of diagnostic tests (ECG, radiological procedures, and biochemical tests) and hospitalization (including beds, medication, consultation, etc.) were calculated according to the standard unit price list provided by the accounts department of the university hospital. Costs for nursing care involved costs related with monitorization, insertion of a venous cannula, intravenous drug infusion, ECG investigation, pulse oxygen screening, nasogastric tube insertion, and wound care. Costs were collected from official financial charts, listing the respective budgets and expenditures of hospital departments; the information was provided by the hospital administration. We performed all calculations, considering the prices in Turkish lira (TL) in 2008 prices. The corresponding costs, expressed in US, could be obtained by taking into account the average exchange rate in 2008 in US dollars (1 USD=1.293 TL, 2008 average) and in euros (1 euro=1.926 TL, 2008 average) (13). The researchers obtained a waiver of authorization from the local ethics committee and the institutional review board of Dokuz Eylül University Hospital with reference number 2011/39-19 to access, obtain, use, or disclose a research subject's protected health information for research purposes, without obtaining the subject's specific authorization. Data were collected retrospectively from January 2012 to June 2012.

### Statistical analysis

All data are presented as mean with standard deviation (S.D.) and median with 25th to 75th percentile range. Normality of distribution was evaluated with the Kolmogorov-Smirnov test. Non-parametric Kruskal-Wallis test was used to compare groups when the data did not follow a normal distribution. Chi-square test was used to compare the diagnostic groups' characteristics for categorized determinants. To account for the non-negativity and skewed distribution of costs and to avoid heteroscedasticity in simple least-squares models, generalized linear models (GLMs) with log link function and gamma distribution were used to study the effects of patient characteristics and medical procedures on total direct medical costs (14). The cost ratio (the exponential of the beta coefficient from the GLM estimation) was presented to show the relative increase in mean costs by increasing covariates by 1 unit. We generated two generalized linear models: the first model contained demographic and preadmission clinical data, and the second model included variables describing hospital treatment, procedures, and complications, in addition to first model. We included age as a continuous variable and other independent variables as dummy variables in the GLM. A value of  $p < 0.05$  was considered statistically significant. The data were analyzed with STATA/SE 11.0 software (Stata Corp, College Station, TX, USA).

## Results

### Patient characteristics

A total of 337 patients with a mean age of 63.6 years ( $\pm 12.1$  years) were included in the study. Of these, 89 patients (26.4%)

**Table 1. Patient characteristics of the three diagnostic subgroups**

	Diagnosis			Total	P
	Angina pectoris (n=89)	Myocardial infarction (n=188)	Heart failure (n=60)		
Distribution within diagnostic subgroups	26.4	55.8	17.8	100.0	
Men, %	64.0	74.5	56.7	68.5	0.020
Age, years±SD	61.3±9.5	63.6±12.6	66.9±13.1	63.6±12.1	0.021
History of CHD, %	42.0	26.1	61.7	38.0	0.001
History of stroke, %	1.1	2.7	11.7	3.9	0.002
Hypertension, %	67.4	61.7	73.3	34.7	0.228
Diabetes mellitus, %	30.3	26.1	46.7	30.9	0.001
Smoking, %	47.2	45.2	38.3	44.5	0.542
Hypercholesterolemia, %	48.3	29.8	38.3	36.2	0.011
Atrial fibrillation, %	0.0	1.1	20.0	4.2	0.001
Intensive care unit, %	40.4	85.1	46.7	66.5	0.001
Heart catheterization, %	88.8	89.4	21.7	77.2	0.001
PTCA, %	23.6	56.9	6.7	39.2	0.001
CABG, %	10.1	11.2	5.0	9.8	0.373
Length of stay (days)±SD	4.6±4.9	7.0±6.1	10.6±9.3	6.9±6.6	0.001
Death, %	3.4	4.8	10.0	5.3	0.185
<b>In hospital treatments</b>					
Beta-blocker, %	74.2	89.7	62.7	80.7	0.001
ACE inhibitor, %	37.1	77.0	55.9	62.5	0.001
Angiotensin receptor blocker, %	36.0	22.4	30.5	27.5	0.054
Diuretic, %	3.4	3.8	47.5	11.5	0.001
Aspirin, %	87.6	96.7	81.4	91.5	0.001
Warfarin, %	2.3	5.5	18.3	6.9	0.001
Calcium channel blocker, %	24.7	14.8	20.3	18.4	0.127
Statin, %	83.1	94.5	39.0	81.6	0.001

ACE - angiotensin-converting enzyme; CABG - coronary artery bypass graft; CHD - coronary heart disease; PTCA - percutaneous transluminal coronary angioplasty; SD - standard deviation

were diagnosed with AP, 188 patients (55.8%) were diagnosed with MI, and 60 patients (17.8%) were diagnosed with HF. The demographic and clinical characteristics of the patients are displayed in Table 1. The average ages for AP, MI, and HF patients were 61.3±9.5, 63.6±12.6, and 66.9±13.1 years, respectively. Men constituted 68.5% (n=231) of the total study population and 64.0% of the MI group, 74.5% of the AP group, and 56.7% of the HF group. A history of CHD, stroke, and atrial fibrillation was more prevalent among HF patients compared to AP and MI patients. In addition, patients in the HF group were significantly ( $p<0.05$ ) more likely to be hypertensive and diabetic and be diagnosed with AF. On the other hand, smoking rates and the presence of hypercholesterolemia were higher among patients with AP. The mean length of the in-patient stay (LOS) was 6.9±6.6 days, with a median of 5 (3-8) days. The average length of stay (LOS) was 4.6±4.9 days (median, 3 days) for AP, 7.0±6.1 days (median, 5 days) for MI, and 10.1±8.6 days (median, 7 days) for HF. The differences between groups were not significant ( $>0.05$ ).

In-hospital mortality rates were significantly higher among HF patients compared to AP and MI. The most commonly prescribed medication was aspirin (91.5%), followed by statins (81.6%) and beta-blockers (80.7%).

### Costs

The costs of diagnostic procedures, medications, physician and nursing care, surgical practices, and ward charges for the different clinical diagnoses are listed in Table 2. The total median cost per admission, independent from the diagnosis, was 1614.5 (617.7-2568.9) TL. Considering the diagnosis, specific costs per admission showed a clear and statistically significant difference in ranking. Total costs were highest for patients with MI, followed by HF patients and AP patients. When we evaluated mean cost per day for each diagnosis group, HF patients cost significantly less than AP and MI patients.

Median unit costs regarding surgery and medical interventions were the highest among the subgroups of costs, followed

**Table 2. Direct medical costs of diagnostic subgroups in Turkish lira\***

	Diagnosis			Total Mean±SD Median (IQR 25, 75)	P	Percentage of total cost
	Angina pectoris (n=89) Mean±SD Median (IQR 25, 75)	Myocardial infarctus (n=188) Mean±SD Median (IQR 25, 75)	Heart failure (n=60) Mean±SD Median (IQR 25, 75)			
Total cost per admission	1881.0±2982.6	2760.6±2832.5	2350.8±3202.9	2455.6±2956.0	0.001	-
	632 (530-1792)	1815 (1036-2976) <sup>a</sup>	1207 (412-2520)	1614 (617-2568)		
Cost per day	427.6±278.6	471.6±416.0	258.4±120.7 <sup>b</sup>	419.8±373.4	0.001	-
	358 (245-547)	410 (246-582)	121 (40-1550)	353 (175-538)		
Medications	433.7±984.6	788.4±1151.7	365.0±541.4	584±971.6	0.001	9.8
	91 (32-341)	334 (113-966) <sup>a</sup>	93 (42-436)	178 (59-750)		
Radiology	80.5±164.1	62.52±106.57	50.5±96.0	60.8±113.0	0.726	0.7
	7.4 (7-46)	15 (8-72)	14 (7-62)	14 (7-556)		
Laboratory	172.9±189.1	288.33±256.1	268.6±245.3	261.5±244	0.022	4.4
	100 (63.9-258) <sup>c</sup>	235 (152-308)	199 (120-392)	205 (99-347)		
Medical supplies	592.7±1035.7	575.4±623.3	723.5±2233.4	613.9±1260.5	0.001	15.7
	248 (43-498)	261 (248-742)	69 (6-270) <sup>b</sup>	249 (59-573)		
Ward costs	216.5±470.1	425.1±706.4	542.2±803.5	391.1±680	0.001	15.5
	50 (22-165) <sup>c</sup>	283 (178-445)	189 (91-664)	216 (84-431)		
Physician care	13.1±11.1	21.6±29.5	21.77±29.67	20.3±27.6	0.740	3.2
	11 (3-18) <sup>c</sup>	15.5 (15-21)	15 (9-21)	15 (9-21)		
Nursing care	100.9±206.6	144.6±261.8	82.00±123.1	116.8±216.4	0.014	1.7
	10 (6-61) <sup>c</sup>	53.7 (23-108)	40 (13-92)	46 (13-91)		
Medical interventions	668.2±477.4	917.9±620.9	328.5±471.1	767.8±602.8	0.001	27.5
	515 (460-613)	612 (508-1246) <sup>a</sup>	79 (41-514) <sup>b</sup>	515 (456-1246)		
Blood products	1086.3±1092.5	419.5±449.3	551.9±798	586.01±712.95	0.610	2.0
	907 (9-2200)	260 (69-695)	242 (59-1199)	349 (69-911)		
Surgery	5065.7±3399.6	4799.1±3336.4	4697.6±4738.3	4860.2±3402.3	0.890	22.2
	5216 (1507-8787)	5571 (1142-7988)	4935 (370-8787)	5571 (1142-8449)		

IQR - inter quartile range; SD - standard deviation

\*Kruskal-Wallis test compares median values of costs between diagnostic groups

<sup>a</sup>Significantly higher than groups 1 and 3. <sup>b</sup>Significantly lower than groups 1 and 2. <sup>c</sup>Significantly lower than groups 2 and 3.

by blood products, medical supplies, and ward charges. The largest proportion of the total cost was formed by medical interventions (27.5%), followed by surgery (22.2%), medical supplies (15.7%), ward cost (15.5%), medications (9.8%), and laboratory (4.4%). Costs for physician care, nursing care, blood products, and radiological procedures formed 7.6% of the total costs.

Table 3 displays the results from the generalized linear regression analysis for the total hospital costs of CVD events after controlling for demographics, co-morbidities, and hospital procedures. According to Model 1, which included pre-admission-related demographic and clinical variables, only two baseline patient characteristics were independently associated with higher costs. While the presence of DM was associated with higher costs, regular use of anti-aggregant medication reduced total costs significantly. Age and gender did not have a significant impact on total cost in the multivariate analysis. The first

model explained 11% of the variation in in-hospital costs. Model 2, including both preadmission characteristics and hospital treatments, procedures, and events, explained 60% of the variation in in-hospital costs. According to Model 2, cardiovascular disease risk factors, like smoking and diabetes mellitus, were significantly associated with higher costs (p<0.05). Coronary artery bypass grafting procedure was one of the significant predictors of total costs with the highest cost ratio (6.08, 95% CI: 4.28-8.63). Patients who received percutaneous transluminal coronary angioplasty (PTCA) treatment, calcium channel blocker, and beta-blocker treatment were associated with higher costs. Individuals diagnosed with heart failure or myocardial infarction had significantly higher mean costs compared to patients with angina pectoris (p=0.001). The need for intensive care during the stay and outcomes resulting in "death" led to significantly higher hospital expenditures.

**Table 3. Results from multivariate regression for total cost**

Variables	Model 1 Demographic and preadmission variables R <sup>2</sup> =0.11		Model 2 Demographic, preadmission and clinical characteristics R <sup>2</sup> =0.60	
	Cost ratio (95% CI)	P	Cost ratio (95% CI)	P
Age	1.01 (0.99-1.02)	0.404	1.01 (0.99-1.01)	0.265
Gender (Reference: male)	1	0.302		0.884
Female	1.15 (0.86-1.54)		0.98 (0.79-1.22)	
History of coronary heart disease (Reference: no)	1	0.140		0.926
Yes	0.82 (0.63-1.06)		0.99 (0.80-1.23)	
History of stroke (Reference: no)	1	0.415	1	0.474
Yes	1.29 (0.69-2.41)		1.19 (0.73-1.96)	
Hypertension (Reference: no)	1	0.266	1	0.179
Yes	0.85 (0.65-1.12)		0.86 (0.69-1.07)	
Diabetes mellitus (Reference: no)	1	0.005	1	0.034
Yes	1.48 (1.12-1.95)		1.27 (1.01-1.58)	
Smoking (Reference: no)	1	0.203	1	0.025
Yes	1.20 (0.91-1.56)		1.28 (1.03-1.59)	
Hypercholesterolemia (Reference: no)	1	0.505	1	0.615
Yes	0.93 (0.72-1.19)		1.05 (0.86-1.30)	
Atrial fibrillation (Reference: no)	1	0.285	1	0.356
Yes	1.40 (0.75-2.59)		0.76 (0.43-1.35)	
Regular use of anti-aggregant before admission (Reference: no)	1	0.001	1	0.049
Yes	0.49 (0.34-0.69)		0.74 (0.54-0.99)	
Coronary artery bypass graft (Reference: no)			1	0.001
Yes			6.08 (4.28-8.63)	
Percutaneous transluminal coronary angioplasty (Reference: no)			1	0.001
Yes			1.74 (1.40-2.16)	
Intensive care need (Reference: no)			1	0.001
Yes			1.36 (1.08-1.73)	
Diagnosis of myocardial infarction (Reference: angina pectoris)			1	0.021
Yes			1.35 (1.04-1.76)	
Diagnosis of heart failure (Reference: angina pectoris)			1	0.001
Yes			2.06 (1.44-2.96)	
Death in hospital (Reference: no)			1	0.001
Yes			2.05 (1.33-3.20)	
Application via emergency room (Reference: no)			1	0.465
Yes			1.01 (0.8-1.27)	
Beta-blocker (Reference: no)			1	0.821
Yes			0.97 (0.76-1.25)	
Statin (Reference: no)			1	0.003
Yes			1.57 (1.17-2.11)	
Angiotensin-converting enzyme inhibitor (Reference: no)			1	0.522
Yes			1.08 (0.85-1.38)	



Table 3. Continued

Warfarin (Reference: no)			1	0.440
Yes			1.18 (0.78-1.78)	
Aspirin (Reference: no)			1	0.164
Yes			0.76 (0.52-1.12)	
Diuretic (Reference: no)			1	0.983
Yes			0.99 (0.71-1.40)	
Angiotensin receptor blocker (Reference: no)			1	0.629
Yes			1.06 (0.83-1.35)	
Calcium channel blocker (Reference: no)			1	0.017
Yes			1.35 (1.05-2.16)	
95% CI - confidence interval				

## Discussion

The present study evaluated the direct costs of AP, MI, and HF treatments and their determinants from the Social Security Institute's perspective in a university hospital setting for the first time in Turkey. As expected, the cost of care was not uniformly distributed across patient groups. MI was the most costly disease, followed by HF and AP. Some baseline patient characteristics at admission were independently associated with increased inpatient costs. While gender and age did not have a significant impact on costs in the multivariate analysis, total cost for CVDs was predicted by both pre-admission characteristics, such as presence of DM or smoking, and inpatient care-related characteristics (diagnosis of MI, HF, need for ICU, and resulting in death). Surgery and medical interventions formed the majority of costs, where medications, nursing care, and physician costs made little contribution to the total costs from the SSI perspective.

The average LOS for patients with HF (10.6±9.3 days) was longer than the LOS of AP and MI patients in this study. A multicenter study conducted at university hospitals in Turkey reported an LOS for HF patients of 10±6 days, which is similar to our findings (15). Average LOS for HF was reported as 9.4 days in teaching hospitals according to a Turkish (16) diagnosis-related groups (DRG) development project. Based on the results of EuroHeart Survey II conducted in 133 hospitals across Europe, the average LOS for HF patients was 9 days (17). The average LOS for MI patients was 7.2 days across OECD member countries, and Turkey had the lowest average LOS for MI patients, with 4.2 days, where this finding is lower than our results (18). This could be due to the fact that our data came from only one tertiary care center that might be used as a referral hospital for rather severe patients. Therefore, our findings can not be generalized to all settings. The 2011 Turkish Statistical Yearbook also revealed that the average LOS was longer among university hospitals compared to public and private hospitals in Turkey (19), because it is likely that more severe patients are getting treatment in university hospitals compared to public hospitals, which might result in a longer LOS in our setting. The longest average LOS for AP patients was 6.4 days in Spain, and the

shortest was 2.7 days in Portugal for year, and our result was also within this range (20). A study conducted in Dokuz Eylül University Hospital during 2002 reported that among patients who were admitted with MI, 18.6% had CABG. In our case, of the patients who were admitted with MI, 11.2% received CABG, and this indicates that CABG rates decreased during the last decade in our setting, and it is likely due to increasing rates of percutaneous coronary intervention and decreasing need for emergency coronary artery bypass grafting (21, 22).

### Determinants of costs

We investigated several factors that may be predictors of total costs for CVD. In our study, neither age nor gender had a significant impact on the total costs of treatment in the multivariate analysis. While some studies reported a significant relationship between gender and older age with higher costs (23), a recent nationwide study from the Netherlands reported no association of gender and age with higher costs in a multivariate analysis (24). In our study, men had higher costs compared to women in the univariate analysis. In Poland, a recent study also reported higher costs for men and lower costs for individuals younger than 65 year old (25). In the study, death in the hospital was significantly associated with a higher cost. Studies from the USA and Thailand supported our finding that death was associated with higher inpatient costs (26, 27). This could be due to individuals who died during treatment having more severe conditions, which might have led to a higher need for care. In our study, we did not use a severity index as a proxy for severity of illness. We evaluated the nursing care procedures that are not paid by the SSI, such as eye care, foot care, positioning, feeding, fever-pulse, and blood pressure control, and according to our analysis, it was evident that individuals who died during hospitalization also used significantly more nursing care, which we think might be an indirect proxy for severity of the illness.

In our study, the regression model involving baseline characteristics, such as age, gender, co-morbidities, smoking, and use of anti-aggregant medication before admission, explained only 11% of the variation in in-hospital cost. In contrast, the model



formed by the combination of baseline characteristics, in-hospital procedures, and adverse outcomes was more strongly associated with the cost of care, accounting for 60% of the variation in cost. A cost study from the USA on acute MI reported that while demographic and clinical characteristics explained only 7% of the variation, in-hospital procedures and adverse outcomes accounted for 53% of the variation (26). A multivariate model from Switzerland used gender, age, BMI, insurance coverage, smoking, history of acute coronary syndrome (ACS), comorbidities, cardiac insufficiency, peripheral vascular disease, cerebrovascular disease, DM, renal disease, arterial hypertension, and dyslipidemia as independent variables, and this model explained 14.3% of the variation in costs for MI (23). We can conclude that there are lots of uncertainties in costs, because combining the baseline characteristics and the in-hospital procedures in the multivariate analysis still left nearly half of the variation in costs unexplained in the majority of the studies.

Some of the traditional CVD risk factors were significantly associated with higher costs, such as DM and smoking. Diabetes remained significantly associated with a higher cost in both models, but the effect size was diminished in the combined model. A study from Turkey revealed that individuals with DM had a higher risk of coronary stenosis, and they had an increased risk of coronary atherosclerotic plaques, independent of other CVD risk factors that might have a negative impact on the prognosis (28). We found that patients with diabetes experienced longer periods of in-patient cardiovascular hospitalization ( $8.6 \pm 8.2$  days) than those without diabetes ( $6.2 \pm 5.6$  days). A retrospective study from the USA and a multicenter study from Switzerland reported that diabetic patients who were hospitalized for a cardiovascular event incurred higher costs for cardiovascular care than their non-diabetic counterparts, which was as a result of longer periods of hospitalization and resource use (23, 29). Smoking, which is considered a major CVD risk factor, was not significantly associated with cost in the first model, but it was associated with a significantly higher cost in the final model, and this result is in accordance with previous research findings (26). However, some studies reported even contradicting results, like smokers having lower costs or a non-significant relation with costs by univariate analysis (23), which might be a result of the phenomenon called the "smoker's paradox," where smokers during hospitalization experience fewer adverse events (30). This is mostly explained by individuals having a younger age and more favorable clinical profile (31). It was also evident that regular use of anti-aggregants before admission significantly reduced total costs in both multivariate models, and this might be attributed to the beneficial effects of these medications in both primary and secondary prevention of CVDs (32, 33).

The cost of HF in this study ( $2455.6 \pm 2956.0$  TL) was very similar to a recent study finding based on expert panel views conducted in Turkey, where cost for HF was reported as 2435 TL (10). Based on the report of The Infrastructure Development for Strengthening and Restructuring of Health Services' Financial Management Project, aiming to generate a DRG (diagnosis-

related group)-based cost system in Turkey, the cost of HF ranged between 1721-3910 TL, and the daily cost for HF treatment was approximately 280 TL. In our study, the daily cost for HF was calculated as 260 TL. In our study, the average cost of MI was 2760 TL and the average cost of AP was 1881 TL; a multicenter hospital cost study reported hospital costs of ACS of 2706 TL for the year 2008 (16).

There is a large variation of in-hospital costs of CVDs in routine practice, and this is mostly attributable to differences in resource consumption and service costs. The most significant contributors to the total cost of ACS in Europe are in-hospital treatment costs, accounting for around two-thirds of all annual healthcare expenditures on ACS, based on estimations for the year 2004 (11). A multicountry study from Europe revealed that costs for the initial hospitalization of AMI patients vary substantially between countries as a result of heterogeneity in treatment patterns (34). Hospital costs for AMI ranged from 1182 euros in Germany to 8282 euros in England. Medication costs varied more than 50-fold, ranging from 30 euros in Spain to 1557 euros in England for AMI. In the same study, the proportion of cost of medications relative to total costs varied from 2% to 31%, and it was 15% in the Netherlands (34, 35). In our study, medications formed 9.8% of total costs. However, surgical procedures formed 22.2% of the total costs, and this figure is lower than values from France and Germany, where these costs account for around one-third of total hospital ACS expenditures, and higher than Italy and Spain, where these procedures account for between 10% and 15% of in-hospital ACS spending. In our study, CABG was a strong predictor of cost in the multivariate analysis. Even around 10% of patients received CABG therapy; its contribution to the total cost was significant, and this result is in accordance with previous research findings (26).

### Study limitations

One of the strengths of the study is that we used a bottom-up approach for calculating the costs. While cost-of-illness studies have the potential to identify the main cost drivers of a disease, the majority of studies does not provide any information on the predictors of costs (36). However, in this study, we used the number of patients and clinical characteristics, which may be able to explain the variability in treatment costs in the multivariate analysis. One of the limitations of our study to be acknowledged is its retrospective design, which may have predisposed it to a selection bias; however, we tried to deal with this problem by enrolling consecutive patients. The study's single-center nature may limit the generalizability of the findings to other hospital settings. Although confounding is a potential problem, we adjusted our analyses for potential covariates in the multivariate analysis. Some cost studies reported that overhead costs, like administration, meals, cleaning, heating, laundry, water, and electricity, which might be correlated with length of stay and costs, generally accounted for a large share of total costs. According to one study, the proportion of overhead to total cost

was on average 26% and ranged from 12% in the Netherlands to 45% in Spain (34). We did not take into account these overhead costs, which might have resulted in the underestimation of real hospital costs regarding CVDs. However, we expect that this did not have an impact on the results on the causality of cost and its determinants. Despite these limitations, to the best of our knowledge, this is the first study to quantify the hospital costs of CVDs and their determinants in Turkey using a bottom-up cost methodology. We believe that our findings could be used in economic modeling studies, formation of DRG, and calculation of cost savings by implementing preventive interventions. However, considering indirect costs will give a more definite picture of the real burden of the cost of CVDs. Another criticism can be made as to why LOS was not included as an independent variable in the multivariate analysis. As expected, LOS was highly correlated with the total cost, and in general, previous studies on hospitalization costs have argued that LOS should be treated as an endogenous variable; as a result, we did not use LOS as an independent variable (37).

## Conclusion

In summary, the current data shed light on the magnitude and determinants of in-patient costs of CVDs in a university hospital setting in Turkey. Both the preadmission characteristics of patients (diabetes mellitus, smoking, use of anti-aggregant before admission) and in-patient characteristics (diagnosis, CABG, intensive care need, death) predicted the hospital cost of CVDs independently. We believe that our results may be used as input for health-economic models and economic evaluations to support the decision-making of the registration, reimbursement, and pricing of interventions in healthcare. In order to make more accurate and comparable findings, it is recommended that multicenter cost studies be carried out in Turkey.

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