Cost of heart failure management in Turkey: results of a Delphi Panel

Dursun Aras, Sinan Aydoğdu, Engin Bozkurt[1], Yüksel Cavuşoğlu[2], Mehmet Eren[3], Çetin Erol[4], Sadi Güleç[4], Pınar Kızılırmak[5], Zeki Öngen[6], Oktay Özdemir[7], Mete Saylan[5], Lale Tokgözoğlu[8], Ekrem Yeter[1], Mehmet Birhan Yılmaz[9]

Department of Cardiology, Faculty of Medicine, Karabük University; Zonguldak-*Turkey*, [1]Department of Cardiology, Faculty of Medicine, Yıldırım Beyazıt University; Ankara-*Turkey*, [2]Department of Cardiology, Faculty of Medicine, Eskişehir Osmangazi University; Eskişehir-*Turkey*, [3]Department of Cardiology, Siyami Ersek Cardiovascular Surgery Training and Research Hospital; İstanbul-*Turkey*, [4]Department of Cardiology, Faculty of Medicine, Ankara University; Ankara-*Turkey*, [5]Medical Department, Novartis; İstanbul-*Turkey*, [6]Department of Cardiology, Cerrahpaşa Faculty of Medicine, İstanbul University; İstanbul-*Turkey*, [7]Department of Statistics, Yorum Consulting Ltd.; İstanbul-*Turkey*, [8]Department of Cardiology, Faculty of Medicine, Hacettepe University; Ankara-*Turkey*, [9]Department of Cardiology, Faculty of Medicine, Cumhuriyet University; Sivas-*Turkey*

Abstract

Objective: To analyze health-related cost of heart failure (HF) and to evaluate health-related source utilization aiming to provide data on the economic burden of HF in actual clinical practice in Turkey.

Methods: The study used the Delphi process of seeking expert consensus of opinion including 11 cardiologists who are experienced in HF. The standardized questionnaire comprised items to reflect the opinion of the expert panelists on the distribution of the HF patients in terms of demographic and clinical characteristics and background disease states. Costs related to out-patient follow-up, in-patient follow-up, medications, and other therapies were also evaluated.

Results: 34.1% of the HF patients were in the age range of 60–69 years, and 62.3% were males. Coronary heart disease was the leading cause of HF (59.6%); 63.6% of the HF patients had reduced ejection fraction (rEF) and 42.3% were in New York Heart Association (NYHA)-II class. Approximately 75 % of the patients were followed up by a cardiology unit. The total annual visit number was estimated as 3.41. Approximately 32% of HF patients were hospitalized 1.64 times a year, for an average of 6.77 days each time. The total annual costs of all HF patients and HF-rEF patients were estimated as 1.537 TL and as 2.141 TL, respectively.

Conclusion: The analysis demonstrating the magnitude of the economic impact of HF management on Turkey's healthcare system may help facilitate health and social policy interventions to improve the prevention and treatment of HF. *(Anatol J Cardiol 2016; 16: 554-62)*

Keywords: heart failure, cost, economic burden, Turkey, Delphi

Introduction

Heart failure (HF) is a global epidemic in health care and a leading cause of mortality and morbidity worldwide (1). Approximately 5.7 million individuals suffer from HF and over 550,000 are newly diagnosed as having HF every year in the United States (2). The Heart Failure Prevalence and Predictors in Turkey (HAPPY) Study conducted in Turkey reported the prevalence of HF as 2.9% in the adult population, and estimated that 1 million adults suffer from HF symptoms (3). Approximately 5% of all acute medical admissions are HF-related in Europe (4). It has been stated that in 2006, 1 in 8.6 death reports in the United States mentioned HF (5).

Besides its high prevalence and mortality rate, the disease places a huge economic burden on the health-care system. Heart failure hospitalization represents 1%–2% of all hospital admissions, which makes it the leading cause of hospitalization for patients older than 65 years (6). The estimated direct and indirect costs of HF in the United States in 2010 were $39.2 billion in total (5). The cost of HF care was reported to be two times higher than the cost of breast cancer and three times higher than the costs of colorectal cancer and lymphoma care in the USA (7). The burden of HF has increased due to increasing elderly population as well as improved survival of patients with risks of HF such as acute myocardial infarction, hypertension, and diabetes mellitus.

In a study analyzing the annual global economic burden of HF in 197 countries, the overall economic cost of HF in 2012 was estimated as $108 billion per annum with direct costs accounting for ~60% ($65 billion) and indirect costs account-

Address for correspondence: Dr. Mehmet Birhan Yılmaz, Cumhuriyet Üniversitesi Fakültesi, Kardiyoloji Anabilim Dalı, Sivas-*Türkiye*
Phone: +90 346 219 10 10 E-mail: mehmet.birhan.yilmaz@tkd.org.tr

Accepted Date: 14.06.2016

DOI:10.14744/AnatolJCardiol.2016.6999

ing for ~40% ($43 billion) of the overall spend (8). A study by Heidenreich et al. (9) stated that by 2030, one of every 33 Americans, more than eight million individuals, will have HF and that total costs for HF in the 18–44 age group will increase from $1.51 billion to $2.48 billion, while the costs for the 65–79 age group will increase from $11.50 billion to $29.9 billion in 2030. In high-income countries, the economic burden of HF is high because it is associated with frequent hospital admissions (10,11). Heart failure currently accounts for approximately 5% of all emergency medical admissions to hospital (12). In the USA, in 2008 the total inflation-adjusted cost of HF admissions was US$ 10.7 billion, compared with US$ 6.9 billion in 1997 (13).

As HF admissions are expensive, reducing admissions, thereby reducing costs while improving the quality of life for patients with HF, is highly desirable. A retrospective cost-of-illness study conducted in a university hospital setting in Turkey in 2008 used in-hospital cost data from the records of patients who admitted to the hospital with angina pectoris, myocardial infarction, or HF and stated that HF was the second most costly disease (14). It was reported that patients diagnosed with HF or myocardial infarction had significantly higher mean costs compared to patients with angina pectoris (14). They calculated the daily cost of HF patients as 258 TL and the total cost per admission as 2351 TL (14). These findings were very similar to a recent data based on expert panel views conducted in Turkey by Fak et al. (15), where cost for HF was reported as 2435 TL per patient. When all these observations are taken into account, an up-to-date documentation of the cost of HF management considering both in-patient and out-patient source utilization in Turkey may help to demonstrate the economic burden of HF in actual clinical practice in Turkey. Thus, the present study was designed to analyze health-related cost of HF and to evaluate health-related source utilization for patients diagnosed with HF in Turkey.

Methods

The study used the Delphi process of seeking expert consensus of opinion and was conducted in 2015. A Delphi study is a structured process that invites experts to complete a series of 'rounds' to gather and refine information on the study question, until expert consensus is reached (16). In the present study, the panel included 11 cardiologists experienced in HF, who are currently working at university hospitals (ten experts from seven institutions) or one from a training and research hospital in Turkey. The cities where these institutions are located are Ankara, İstanbul Eskişehir, Sivas, and Zonguldak.

Questionnaire forms

The standardized questionnaire form was prepared by an independent consultant under the supervision of an expert panelist representing the group. The questions were determined considering the cost items in the management of HF. For this purpose, the literature data related to the subject and HF guidelines (i.e., Turkish Society of Cardiology HF Guideline, European Society of Cardiology HF Guideline, American Heart Association HF Guideline) were examined thoroughly. The questionnaire was prepared comprising the subjects included in these guidelines.

The questionnaire included items to reflect the opinion of the expert panelists on the distribution of the HF patients in terms of demographic and clinical characteristics (age, gender, level of ejection fraction, and New York Heart Association classification) and background disease states (hypertension, diabetes mellitus, coronary heart disease, valvular diseases, cardiomyopathies, and myocarditis). Costs related to out-patient follow-up (frequency of visits, consultations, medical tests), in-patient follow-up (emergency unit, intensive care unit, and other services), medications (in-patient and out-patient), and other therapies (invasive and non-invasive interventions) were also evaluated. The finalized questionnaire form was reviewed by one of the experts (ZO) and sent to the expert panelists via e-mail. The panelists were asked to send back the filled forms within 7 days. Then, an expert meeting was organized to review and finalize the answers given by the panelists.

As a principle set by the expert panel, the costs related with diagnosis, treatment, and follow-up of complications (rhythm abnormalities, cerebrovascular complications, renal complications, etc) or underlying pathologies (valvular disease, diabetes mellitus, etc) were not taken into account in the analysis, in order to avoid such cost items to be double-counted amongst possible several cost studies. This approach ensures that published costs of various disease states can be summed up to calculate the disease burden nationwide. Otherwise, simply adding the costs provided from various publications would lead to an over-estimation in the burden calculation.

For the estimation of utilization rate of medical devices per patient, including implantable cardioverter defibrillator (ICD), cardiac resynchronization therapy-defibrillator (CRT-D), and cardiac resynchronization therapy-pacemaker (CRT-P), the annual numbers of devices sold throughout the country were divided by the estimated number of HF patients (data from HAPPY Study). These figures were then multiplied with the unit costs of ICD, CRT-D, or CRT-P. The expert panelists did not include CPAP (continuous positive airway pressure) and BiPAP (bi-level positive airway pressure) into the calculations, since the patients are supplied with these devices by SSI when needed, and the devices are given back when treatment is terminated. Thus, the net financial burden of these items to SGK can be neglected. Since the perspective of our analysis is SGK (i.e., we calculated the costs from the viewpoint of SGK), the costs of these devices are not included.

Statistical analysis

The analysis was performed from the perspective of reimbursement agency of Turkey (SGK). All data were analyzed

using descriptive statistics. The costs were provided in Turkish Lira (TL), and the cost model was based on the following equation: Cost=Σ (Frequency; %) X (Unit price; TL). Cost per day was calculated from the price lists stated in the Declaration of Health Care Implementation (SUT) published by Social Security Institute of Turkey (SSI).

Data were expressed with mean and minimum and maximum values.

Results

Basic characteristics

According to experts' view, the majority of the HF patients (34.1%) were in the age range of 60–69 years. Approximately 27.3% of the patients were ≥70 years old. Two-thirds of the patients were males (62.3%); 63.6% of the HF patients had reduced ejection fraction (HF-rEF), and 42.3% were in NYHA-II class (Table 1). Coronary heart disease was the leading cause of HF (59.6%), and it was followed by cardiomyopathies (13.7%) (Table 1).

Table 1. The demographic and clinical characteristics of HF patients

	% of patients		
	Mean	**Min**	**Max**
Age, years			
<40	5.6	2	10
40–49	12.3	5	25
50–59	20.7	10	30
60–69	34.1	20	50
≥70	27.3	10	50
Gender			
Male	62.3	60	70
Female	37.7	30	40
Ejection fraction			
Reduced	63.6	40	90
Preserved	36.4	10	60
NYHA classification			
NYHA-I	18.4	10	30
NYHA-II	42.3	20	70
NYHA-III	29.1	10	50
NYHA-IV	10.3	5	20
Primary underlying disease			
Coronary heart disease	59.6	50	72
Cardiomyopathy	13.7	5.5	25
Hypertension	13.3	3.8	20
Valvular diseases	8.0	3	15
Diabetes mellitus	2.9	0	6
Others	2.5	0	5

NYHA - New York Heart Association

Follow-up data

According to experts' view, 75.9 % of the patients were followed up by a cardiology unit. The average annual number of out-patient visits was 3.64 for cardiology, 3.00 for the internal medicine, and 1.91 for the cardiovascular surgery clinics. Total annual number of visits weighted by branch was estimated as 3.41 (Table 2). Out-patient management is assumed to be same in all HF patients, not differing with regard to preservation of left ventricular EF.

According to experts' view, 29.5% of HF patients admitted to the Emergency Unit with an average annual number of visits of 2.0. When all HF patients were considered, the annual number of visits was estimated to be 0.67. On the other hand, 40% of HF-rEF patients admitted to Emergency Unit with an annual number of visits of 2.0, and when all HF-rEF patients were considered, this figure was estimated to be 0.93 visits per year (Table 2).

Hospitalization

Overall, 32.3% of HF patients were hospitalized. The lengths of stay of HF-rEF and HF-pEF were assumed to be equal. The average annual number of hospitalizations was 1.64 stays per year with an average 6.77 days of length of stay per each stay. This figure was averaged to 3.52 days when all patients (including the ones who have not been hospitalized within a year) were taken into account, as well. On the other hand,

Table 2. Utilization of healthcare resources: Out-patient data of HF patients

	% of patients			Annual number of visits/ consultations		
	Mean	**Min**	**Max**	**Mean**	**Min**	**Max**
Out-patient visits*						
Cardiology	75.9	60	90	3.64	2	5
Internal medicine	15.0	5	30	3.00	2	5
Cardiovascular surgery	5.2	0	10	1.91	0	5
Other out-patient admission	3.9	0	10	1.55	0	5
Consultations*						
Cardiology	0.0	0	0	0.00	0.0	0.0
Internal medicine	18.6	5	40	0.34	0.05	0.8
Cardiovascular surgery	5.7	0	20	0.07	0.0	0.2
Chest diseases	20.9	10	30	0.38	0.1	0.1
Others	2.7	0	10	0.06	0.0	0.3
Emergency unit admission						
All patients	29.5	5	60	2.00	1	4
HF-rEF patients	40.0	5	100	2.00	1	4

*Out-patient management, including consultations, is assumed to be same in all HF patients, not different between reduced or preserved EF. HF-rEF - HF patients had reduced ejection fraction

Table 3. Utilization of healthcare resources: Hospitalization data of all HF patients and HF-rEF patients

	All HF patients			HF-rEF patients		
	Mean	Min	Max	Mean	Min	Max
Hospitalization						
% of patients	32.3	20	40	43.2	26.7	71.1
Number of hospital stays per year						
All patients	0.52	0.25	0.80	0.70	0.40	1.42
Hospitalized patients*	1.64	1	2	1.64	1	2
Length of each stay (days)*	6.77	4	9	6.77	4	9
Total length of stay (days per year)	3.52	1.38	6.40	4.58	2.20	8.53
Initial admission to cardiac intensive care unit (CICU)						
% of patients	9.7	2.5	20	16.9	5	50
Length of each stay in CICU (days)*	2.41	2	3.5	2.41	2	3.5
Length of each stay in medical ward followed by CICU (days)*	4.36	2	7	4.36	2	7
Total length of stay in CICU (days per year)	0.35	0.06	0.80	0.62	0.13	1.50
Total length of stay in medical ward followed by CICU (days per year)	0.63	0.08	1.20	0.16	0.15	3.00
Initial admission to medical ward						
% of patients	22.6	10	35	26.3	6.2	55.1
Length of each stay in medical ward (days)*	6.77	4	9	6.77	4	9
Total length of stay in medical ward (days per year)	2.53	0.80	4.80	2.91	0.49	6.61

*Length of stay is assumed to be same in all types of wards in all HF patients, not different between reduced or preserved EF. HF-rEF - HF patients had reduced ejection fraction

hospitalization rate was 43.2% among HF-rEF patients. When the length of stay in HF-rEF patients was assumed to be not different from patients without reduced EF, average length of stay was calculated as 4.58 days per stay in HF-rEF patients. It is assumed that, when patients with preserved EF need to be hospitalized, they are admitted directly in medical ward. On the other hand, some HF-rEF patients may need to stay in cardiac intensive care unit (CICU) for a while before being transferred to a medical ward. Therefore, one-tenth (9.7%) of all HF patients and 16.9% of HF-rEF patients were hospitalized in CICU. Following an average 2.41 days of stay in CICU, the patients were transferred to medical ward and stayed there for 4.36 more days. The percentage of patients who were admitted directly to medical ward was 22.6% and 26.3% for all HF patients, and for HF-rEF patients, respectively (Table 3).

Treatment

Beta blockers were the most commonly used drugs by the HF patients. The rate of beta blocker use was almost equal or even higher than renin-angiotensin system blocker use. The major medications used by HF patients were as follows: 75% beta blockers, 70% diuretics, 57% angiotensin-converting enzyme (ACE) inhibitors, 32% spironolactone, 20% angiotensin receptor blockers, and 20.5% digitalis (Table 4). Chronic use of medications on out-patient basis is assumed to be same in all HF patients, not different between reduced or preserved EF. However, interventional treatments with devices were assumed to be used only in patients with HF-rEF. When all patients were considered, regardless of the degree of EF, the proportions of HF patients who need to be treated with interventional modalities are 8.4% for ICD, 5.5% for CRT-D, and 1.9% for CRT-P. These figures increased to 13.9% for ICD, 9.8% for CRT-D, and 4.0% for CRT-P in HF-rEF patients. Annual rates of interventional treatments were estimated to be one-fifth of these figures, since average life-time of these devices is about five years, and reimbursed once in every five years by national reimbursement agency (Table 4 for annual rates).

Unit costs

The unit cost of out-patient follow-up items and the cost of hospitalization including consultations, medical tests, medications and interventional treatments are given in Table 5, 6 and 7.

Annual cost of HF management

As demonstrated in Table 8, the annual cost of out-patient follow-up was 216.54 TL (176.31 TL for visits, 5.09 TL for consultations and 35.14 TL for medical tests). The annual cost of Emergency Unit admission was 92.65 TL and of CICU was 111.19 TL. On the other hand, the annual cost of hospitalization at medical ward was 206.52 TL. The average cost of a hospital stay was calculated as 599.57 TL, with daily cost of stay of 143.21 TL/day in all HF patients. These figures were higher in HF-rEF patients; corresponding figures were 989.46 TL for the average cost of a hospital stay, and 353.63 TL/day for the daily cost of stay.

Table 4. Utilization of medications and interventional treatments in all HF patients and HF-rEF patients

	All HF patients			HF-rEF patients		
	% of patients					
Medications	**Mean**	**Min**	**Max**	**Mean**	**Min**	**Max**
Chronic use on out-patient basis*						
Furosemide PO	70.0	45	100	70.0	45	100
Beta blocker	75.0	50	100	75.0	50	100
ACEI	57.3	40	80	57.3	40	80
ARB	20.0	5	40	20.0	5	40
Spironolactone	32.3	20	50	32.3	20	50
Digoxin PO	20.5	10	40	20.5	10	40
Ivabradine	5.5	0	10	5.5	0	10
Oral nitrate	8.7	2	20	8.7	2	20
ASA	57.3	20	80	57.3	20	80
Warfarin	15.5	5	30	15.5	5	30
Acute use on in-patient basis						
Furosemide IV	76.0	50	90	96.9	76.9	100
Nitroglycerin	24.1	5	55	36.8	8.3	100
Digoxin IV	4.6	0	20	7.8	0	30.8
Dobutamine	8.7	3	25	15.0	5.0	55.6
Dopamine	8.1	3	20	13.8	5.0	44.4
Levosimendan	4.7	1	10	7.7	1.7	15.4
Heparin	11.8	0	50	17.3	0	66.7
Interventional treatments	**annual rate per 100 patients**					
ICD	1.68	0.2	5	2.77	0.44	8.33
CRT-D	1.11	0.2	3	1.95	0.22	5.00
CRT-P	0.38	0	3	0.81	0	5.00
LVAD	0.019	–	–	0.030	–	–
Heart transplantation	0.006	–	–	0.009	–	–

ACEI - angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; ASA - acetylsalycilic acid; CRT-D - cardiac resynchronization therapy-defibrillator; CRT-P - cardiac resynchronization therapy-pacemaker; HF-rEF - HF patients had reduced ejection fraction; ICD - implantable cardioverter defibrillator; LVAD - left ventricular-assist device
*Chronic use of medications on out-patient basis is assumed to be same in all HF patients, not different between reduced or preserved EF

The cost of medical tests (109.53 TL) seemed to be the major component of the total cost of stay at medical ward. When the costs of medications (403.76 TL) and interventional treatments (505.96 TL) were included, the total annual cost of HF patients was estimated as 1,537 TL.

According to the experts' view, the total annual cost of HF-rEF patients was 2,141 TL. This included the out-patient follow-up (216.54 TL), admission to Emergency Unit (126.93 TL), hospitalization at CICU (192.22 TL), hospitalization at medical ward (263.73 TL), medications (435.37 TL), and interventional treatments (906.07 TL) (Table 8).

Table 5. Unit costs of utilization of healthcare resources in HF patients

	Cost per patient
Out-patient visits	**15.50 TL/visit**
Cardiology	54.00 TL/visit
Internal medicine	42.80 TL/visit
Cardiovascular surgery	46.00 TL/visit
Other	33.80 TL/visit
Emergency unit admission	**15.50 TL/visit**
Stay at CICU	**278.75 TL/day**
Primary step CICU	200.00 TL/day
Secondary step CICU	425.00 TL/day
Tertiary step CICU	800.55 TL/day
Stay at medical ward	**300.00 TL/day**

CICU - cardiac intensive care unit

Discussion

In the present analysis using the Delphi process, the estimations of an expert group on demographic and clinical characteristics of HF patients and cost of HF management were evaluated. The findings demonstrated the magnitude of the economic impact of HF management on Turkey's healthcare system.

Heart failure imposes both direct costs to healthcare systems and indirect costs to society through morbidity, unpaid care costs, premature mortality, and lost productivity. The cost resulting only from HF represents 2% of the total healthcare expenditure (17). In a recent study analyzing the data of 197 countries (covering 98.7% of the world's population), the overall economic cost of HF in 2012 was estimated as $108 billion per annum (18). Direct costs accounted for 60%, and indirect costs accounted for 40% of the overall spend (18). The economic burden of HF results from its high prevalence, the demanding medical, device, and surgical therapies, the frequent comorbid conditions, and primarily from the frequent hospital admissions. The HAPPY Study conducted in Turkey reported the prevalence of HF as 2.9% in the adult population (3). The rapid aging of the population in developed countries, lack of a fall in incidence, and improving prognosis of HF are all acting to increase the number of people with chronic HF.

A recent meta-analysis using the published and unpublished data of nearly 240,000 hospitalizations for acute and chronic HF provided important data on the presentation, causes, management, and outcomes of HF in 31 low- and middle-income countries including Turkey (19). According to their data, the mean age of the HF patients was 63 years (range: 42–77 years) being males 58% (95% CI: 54%–62%) of the patients. Across all low-and middle-income countries, the ischemic heart disease and hypertension were found to be the leading causes of HF. In line with these observations, our analysis demonstrated that 34% of HF patients were within the age range of 60–69 years, and 27% were ≥70 years old. According

Table 6. Unit costs and payment status* of consultations and medical tests utilized in HF patients

	Unit cost	Paid at			
		Out-patient basis	Emergency unit	CICU	Medical ward
Consultation					
Cardiology	6.00 TL	Yes	Yes	Yes	Yes
Internal medicine	6.00 TL	Yes	Yes	Yes	Yes
Cardiovascular surgery	6.00 TL	Yes	Yes	Yes	Yes
Chest diseases	6.00 TL	Yes	Yes	Yes	Yes
Others	6.00 TL	Yes	Yes	Yes	Yes
Medical tests					
Chest X-ray	11.37 TL	No	Yes	No	Yes
Electrocardiogram	3.00 TL	No	Yes	No	Yes
Echocardiogram	32.20 TL	No	Yes	No	Yes
Treadmill	42.00 TL	No	Yes	No	Yes
Holter monitoring	60.00 TL	Yes	Yes	No	Yes
Myocardial perfusion scintigraphy	320.26TL	Yes	Yes	Yes	Yes
BUN, creatinine, and glucose	3.20 TL	No	Yes	No	Yes
Electrolytes	5.30 TL	No	Yes	No	Yes
Liver function tests	6.39 TL	No	Yes	No	Yes
Lipid profile	6.40 TL	No	Yes	No	Yes
eGFR	3.40 TL	No	Yes	No	Yes
NT-proBNP and BNP	30.00 TL	Yes	Yes	No	Yes
CK and troponin	10.90 TL	No	Yes	No	Yes
Microalbuminuria	6.00 TL	No	Yes	No	Yes
Thyroid tests	22.00 TL	No	Yes	No	Yes
Hemogram	3.00 TL	No	Yes	No	Yes
PT, aPTT, INR	11.40 TL	No	Yes	No	Yes
Blood gases	5.10 TL	No	Yes	No	Yes

aPTT - activated partial thromboplastin time; BUN - blood urea nitrogen; CICU - cardiac intensive care unit; CK - creatine kinase; eGFR - estimated glomerular filtration rate; INR - international normalization ratio; NT-proBNP - N terminal pro brain natriuretic peptide; PT - prothrombin time
*Most of the tests are included in out-patient visit package and CICU stay package. Therefore, the setting where the patient is followed at, is considered, whether to include or not the costs derived from these tests

to our experts' view, 62% were males, and the ischemic heart disease was the leading cause of HF (60%).

Heart failure is the most common reason for hospitalization in the elderly and exceeding a million admissions per year both in US and in Europe (20–22). Despite therapeutic advances, the overall 5-year mortality rate remains approximately 50%. The prognosis of the syndrome is mainly driven by the poor outcome of patients hospitalized for HF. Readmission rates are quite high, reaching 30% during the first 3 months and exceeding 50% at 6 months post-discharge (22). Overall, within a year after discharge, one third of patients are expected to die and two-thirds to be re-admitted because of HF (23). In the United States, the annual HF-related expenses were calculated as $31 billion in 2012, and this cost is expected to rise to $97 billion in 2030 (24). A study by Stewart et al. (10) estimated that 69% of the total expenditure related to HF results from hospitalizations, while drug therapy contributed to 18% of the cost. The direct mean cost of a single episode of hospital admission for HF in Europe lasting a median of 7 days has been calculated to €3200, an expenditure that represents only ward costs, laboratory tests, and drug therapies, excluding diagnostic or therapeutic interventions or hospitalization in Intensive Care Unit (25).

Our analysis revealed that 32% of all HF patients and 43% of HF-rEF patients were estimated to be hospitalized with a hospital stay period of 6.77 days. A meta-analysis of HF care in low- and middle-income countries reported the average of stay in hospital as 10 days (18). In a recent study by Ergene et al. (26) on chronic HF patients in a state hospital in Turkey, the average duration of hospitalization was found to be 7.0 days. Turkish Atherosclerosis Cost Study (2009), which provided data from five centers related with the hospitalizations due to HF in 2007,

Table 7. Unit costs of medications and interventions used in HF patients

Treatment	Unit cost
Medications	**Cost per day**
Chronic use on out-patient basis	
Furosemide PO	0.09 TL
Beta-blocker	0.49 TL
ACEI	0.23 TL
ARB	0.38 TL
Spironolactone	0.26 TL
Digoxin PO	0.02 TL
Ivabradine	1.86 TL
Oral nitrate	0.29 TL
ASA	0.07 TL
Warfarine	0.20 TL
Acute use on in-patient basis	
Furosemide IV	0.53 TL
Nitroglycerine	14.46 TL
Digoxin IV	0.88 TL
Dobutamine	15.24 TL
Dopamine	12.47 TL
Levosimendan	599.51 TL
Heparin	8.68 TL
Interventions	**Cost per procedure**
ICD	12.674.73 TL
CRT-D	16.053.94 TL
CRT-P	13.834.60 TL
LVAD	202.715.96 TL
Heart transplantation	78.323.04 TL

ACEI - angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; ASA - acetyl-salicylic acid; CRT-D - cardiac resynchronization therapy-defibrillator; CRT-P - cardiac resynchronization therapy-pacemaker; ICD - implantable cardioverter defibrillator; LVAD - left ventricular-assist device

reported the mean duration of hospitalization as 6.6 days, the total cost of stay as 1617 €, and daily cost of stay as 245 €/day (Unpublished data). On the other hand, the length of stay for HF patients reported by Sözmen et al. (14) and Ergin et al. (27) was 10.6 and 10 days, respectively. Average length of stay for HF was reported as 9.4 days in academic hospitals in Turkey (28). In a previous study by Malki et al. (29), the clinical presentation, hospital length of stay, and readmission in HF-pEF and HF-rEF patients were evaluated, and it was reported that among consecutively hospitalized patients with HF, hospital length of stay and readmission rates within 6 months of discharge were not statistically different between patients with HF-pEF and HF-rEF. This finding was in accordance with the data of a national survey of HF in French hospitals demonstrating the length of hospital stay to be 11 days in both HF-pEF and HF-rEF patient groups (30). These observations imply that HF-rEF patients do not have a markedly longer hospital stay in comparison to HF-pEF patients as the latter group are older and have more comorbidities in comparison to the former group. Thus, in our study, all cost analyses were performed considering the hospital stay to be same in both patient groups.

The one-year cost per congestive HF patient was established to be $3,802, based on an analysis of a state Medicaid dataset (31) with 52.1% of costs being related to prescriptions. Compared with other cardiovascular conditions among this Medicaid population, the annual cost per HF patient was found to be higher than the costs associated with diabetes or hypertension (31).

A cost analysis study by Fak et al. (15) was based on identification of total costs related to management of acute coronary syndrome, HF, stroke, and the drug related adverse events in patients with atrial fibrillation, the average total cost of HF was reported as 4,524 TL (2,436 TL within the first month and 2,088 TL within a year excluding the first month) according to experts' view. In our analysis, the total annual cost of HF management was found to be 1,537 TL. In HF-rEF patient population, the calculated total annual cost was 2,141 TL. We demonstrated that the majority of the costs attributed to HF in this population was related to medication (435.37 TL/year) and out-patient follow-up (216.54 TL/year) when the diagnostic/therapeutic interventions were excluded. The costs of diagnostic/therapeutic interventions and medications represented 42% and 20% of the total cost respectively. Medications used during the out-patient follow-up (336.94 TL/year) constituted the major component of all medication costs; the cost of in-patient medication was only 98.43 TL/year. The calculated costs of management (including hospitalization, consultations, and medical tests) in Emergency Unit, CICU, and medical ward were 126.93 TL/year, 192.22 TL/year, and 263.73 TL/year, respectively.

According to the results of the study by Sözmen et al. (14), the total in-hospital cost of a HF patient per admission is 2.351 TL, and cost per day is 258 TL. They reported that unit cost regarding surgical interventions was the highest, followed by medical supplies, laboratory tests, and ward costs. They also found that patients diagnosed with HF or myocardial infarction had significantly higher mean costs compared to those with angina pectoris.

In the cost analysis by Ergene et al. (26), the total cost of stay was 1,537 €, and average daily cost of stay was 221 €/day for HF patients in 2011. The retrospective cost-of-illness study conducted in a university hospital setting in Turkey in 2008 by Sözmen et al. (14) calculated the total cost of HF patients per admission as 2351 TL. The recent data based on expert panel views by Fak et al. (15), reported the cost for HF as 2435 TL per patient.

The reason why our cost figures are lower than those reported in these earlier studies might be that the duration of hospital stay and costs are lower public hospitals compared

Table 8. Components of total cost in all HF patients and HF-rEF patients

	All HF patients				HF-rEF patients			
Cost components	**Cost (TL/year)**			**Cost (%)**	**Cost (TL/year)**			**Cost (%)**
	Mean	**Min**	**Max**		**Mean**	**Min**	**Max**	
Out-patient follow-up	**216.54**	**111.22**	**324.66**	**14.1**	**216.54**	**111.22**	**324.66**	**10.1**
Visit (incl. basic laboratory tests)	176.31	99.52	257.35	11.5	176.31	99.52	257.35	8.2
Consultations	5.09	1.20	12.00	0.3	5.09	1.20	12.00	0.2
Tests not included in the basic package	35.14	9.00	56.51	2.3	35.14	9.00	56.51	1.6
Emergency unit admission	**92.65**	**6.47**	**336.96**	**6.0**	**126.93**	**6.47**	**561.59**	**5.9**
Admission (incl. basic laboratory tests)	10.32	0.78	37.20	0.7	14.44	0.78	62.00	0.7
Consultations	6.98	0.40	21.75	0.5	9.47	0.40	36.25	0.4
Tests not included in the basic package	75.35	5.30	278.01	4.9	103.02	5.30	463.34	4.8
Stay in cardiac intensive care unit (CICU)	**111.19**	**19.10**	**288.73**	**7.2**	**192.22**	**38.20**	**469.31**	**9.0**
Stay (incl. basic laboratory tests and treatments)	98.74	17.42	223.00	6.4	172.07	34.84	418.12	8.0
Consultation	0.65	0.08	1.68	0.0	1.11	0.15	3.15	0.1
Tests not included in the basic package	11.80	0.00	64.05	0.8	19.03	0.00	98.54	0.9
Stay in medical ward	**206.52**	**90.38**	**317.95**	**13.4**	**263.73**	**143.86**	**443.33**	**12.3**
Stay (incl. basic laboratory tests)	94.95	39.37	180.00	6.2	118.84	51.69	222.40	5.6
Consultation	2.05	0.75	6.29	0.1	2.91	1.20	11.18	0.1
Tests not included in the basic package	109.52	50.25	203.00	7.1	141.97	80.41	249.85	6.6
Medications	**403.76**	**269.69**	**716.55**	**26.3**	**435.37**	**307.31**	**746.49**	**20.3**
Out-patient basis	336.94	211.38	447.07	21.9	336.94	211.38	447.07	15.7
In-patient basis	66.81	17.94	269.48	4.3	98.43	29.28	299.42	4.6
Interventional treatment	**505.96**	**153.84**	**1,186.39**	**32.9**	**906.07**	**190.90**	**2,198.20**	**42.3**
Total	**1,536.60**	**1,014.89**	**2,034.48**	**100**	**2,140.85**	**1,198.72**	**3,552.00**	**100**

HF-rEF - HF patients had reduced ejection fraction, ICD

to university hospitals. In addition to this, these variations may be due to the differences in the estimation of existing co-morbidities, and the cost of treating the co-morbidities. Although the majory of the HF patients (42%) were in NYHA-II class, 29% were in NYHA-III, and 10% were in NYHA-IV class. In general, mild HF patients visit their family physicians regularly more than a few times to get their prescriptions. On the other hand, the management of the severe cases should be considered as an additional factor to increase the cost.

In addition to the direct costs, indirect, and societal costs of HF, which are not estimated in our study, may also influence the total cost of the patient. The number of patients with HF in 32,7 million Turkish population (of >35 years of age in 2014) could be calculated as 930 thousand, considering the prevalence of HF as 2.9% as reported in HAPPY study (3). Thus, total annual national economic burden of HF has been calculated as 1,4 billion TL.

Study limitations

The study has some limitations. The major limitation is that the respondents may not be representative for "all" experts on HF, and the hospitals may not be representative of all regions in Turkey. These might limit the generalizability of the findings. Secondly, the results of this study only reflect current practice patterns. As healthcare technology and treatment guidelines change, the results are likely to become outdated.

Conclusion

To summarize, our findings reveal the extent of the economic burden of HF management on healthcare systems in our country. With the aging of the population, the impact of HF may increase. Thus, enhancing cardiovascular health strategies, new therapies, and improving implementation of existing preventative measures and therapies may be considered to improve the prevention and treatment of HF.

Acknowledgements: The authors are sorted alphabetically according to their family names. All authors have equivalent contributions regarding the processes related with planning, conduct, analysis and manuscript writing.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – All authors; Design- All authors; Supervision- All authors; Analysis and/or interpretation– All authors; Writing – All authors; Critical review- All authors.

References

1. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. Heart 2007; 93: 1137-46.
2. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2012 update: A report from the American Heart Association. Circulation 2012; 125: e2-e220.
3. Değertekin M, Erol Ç, Ergene O, Tokgözoğlu L, Aksoy M, Erol MK, et al. Heart failure prevalence and predictors in Turkey: HAPPY study. Arch Turk Soc Cardiol 2012; 40: 298-308.
4. Cowie MR, Fox KF, Wood DA, Metcalfe C, Thompson SG, Coats AJ, et al. Hospitalization of patients with heart failure. A population-based study. Eur Heart J 2002; 11: 877-85.
5. American Heart Association. Heart Disease and Stroke Statistics: 2010 Update. A Report from the American Heart Association Statistics Committee and Stroke Statistics. Circulation 2010; 121: e46-e215.
6. Alla F, Zannad F, Filippatos G. Epidemiology of acute heart failure syndromes. Heart Fail Rev 2007; 12: 91-5.
7. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brow M. Projections of the cost of cancer care in the United States 2010–2020. J Natl Cancer Inst 2011; 103: 117-28.
8. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. Int J Cardiol 2014; 171; 368-76.
9. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, et al; American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013; 6: 606-19.
10. Stewart S, Jenkins A, Buchan S, McGuire A, Capewell S, McMurray JJ. The current cost of heart failure to the National Health Service in the UK. Eur J Heart Fail 2002; 4: 361-71.
11. Ryden-Bergsten T, Andersson F. The health care costs of heart failure in Sweden. J Intern Med 1999; 246: 275-84.
12. National Institute for Health and Clinical Excellence. New NICE guidance will improve diagnosis and treatment of chronic heart failure. London: NICE, 2010. Available from: URL: https://www.nice.org.uk/guidance/cg108/documents/new-nice-guidance-will-improve-diagnosis-and-treatment-of-chronic-heart-failure.
13. Healthcare Cost and Utilization Project (HCUP). HCUP facts and figures. Statistics on hospital-based care in the United States, 2008. Available from: URL: https://www.hcup-us.ahrq.gov/reports/factsandfigures/2008/TOC_2008.jsp
14. Sözmen K, Pekel Ö, Yılmaz TS, Şahan C, Ceylan A, Güler E, et al. Determinants of inpatient costs of angina pectoris, myocardial infarction, and heart failure in a university hospital setting in Turkey. Anatol J Cardiol 2015; 15: 325-33.
15. Fak AS, Küçükoğlu MS, Fak NA, Demir M, Ağır AA, Demirtaş M, et al. Expert panel on cost analysis of atrial fibrillation. Anadolu Kardiyol Derg 2013; 13: 26-38.
16. Okoli C, Pawlowski SD. The delphi method as a research tool: An example, design considerations and applications. Inf Manag 2004; 42: 15-29.
17. Farmakis D, Stafylas P, Giamouzis G, Maniadakis N, Parissis J. The medical and socioeconomic burden of heart failure: A comparative delineation with cancer. Int J Cardiol 2015; 203: 279-81.
18. Cook C, Cole G, Asaris P, Jabbour R, Francis D. The annual global economic burden of heart Failure. Heart 2014; 100: A28-A29.
19. Callender T, Woodward M, Roth G, Farzadfar F, Lemarie J-C, Gicquel S, et al. Heart failure care in low- and middle-income countries: A systematic review and meta-analysis. PLoS Med 2014; 11: e1001699.
20. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation 2015; 131: 29-322.
21. Farmakis D, Parissis J, Filippatos G. Acute heart failure: epidemiology, classification, and pathophysiology. In: Tubaro M, Vranckx P, Price S, Vrints C, editors. ESC Textbook of Intensive and Acute Cardiac Care. Oxford; Oxford University Press; 2015.
22. Farmakis D, Parissis J, Lekakis J, Filippatos G. Acute heart failure: epidemiology, risk factors, and prevention. Rev Esp Cardiol 2015; 68: 245-8.
23. Kociol RD, Hammill BG, Fonarow GC, Klaskala W, Mills RM, Hernandez AF, et al. Generalizability and longitudinal outcomes of a national heart failure clinical registry: comparison of Acute Decompensated Heart Failure National Registry (ADHERE) and non-ADHERE Medicare beneficiaries. Am Heart J 2010; 160: 885-92.
24. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. Circulation 2011; 123: e18-e209.
25. Parissis J, Athanasakis K, Farmakis D, Boubouchairopoulou N, Mareti C, Bistola V, et al. Determinants of the direct cost of heart failure hospitalization in a public tertiary hospital. Int J Cardiol 2015; 180: 46-9.
26. Ergene O, Kocabaş U, Akyıldız I, Eren NK, Tan M, Özdemir O. Macrocosting analysis of hospital stay in heart failure patients in Turkish setting. Value In Health 2012; 15: A521.
27. Ergin A, Eryol NK, Ünal S, Delicea A, Topsakal R, Seyfeli E. Epidemiological and pharmacological profile of congestive heart failure at Turkish academic hospitals. Anatol J Cardiol 2004; 3: 32-8.
28. The Infrastructure Development for Strenghtening snd Restructuring of Health Services' Financial Management Project. Ankara: Hacettepe University 2007.
29. Malki Q, Sharma ND, Afzal A, Ananthsubramaniam K, Abbas A, Jacobson G, et al. Clinical presentation, hospital length of stay, and readmission rate in patients with heart failure with preserved and decreased left ventricular systolic function. Clin Cardiol 2002; 25: 149-52.
30. Cohen-Solal A, Desnos M, Delahaye F, Emeriau JP, Hanania G. A national survey of heart failure in French hospitals. The Myocardiopathy and Heart Failure Working Group of the French Society of Cardiology, the National College of General Hospital Cardiologists and the French Geriatrics Society. Eur Heart J 2000; 21: 763-9.
31. Garis RI, Farmer KC. Examining costs of chronic conditions in a Medicaid population. Manag Care 2002; 11: 43-50.