Eskisehir Medical Journal
Eskişehir Tıp Dergisi

Eskisehir Med J. 2023; 4(1): 11-16
doi: 10.48176/esmj.2023.97

Original Article / Araştırma Makalesi

TRENDS IN BURDEN OF HEART FAILURE MORTALITY IN TURKEY, 2009-2019

TÜRKİYE KALP YETMEZLİĞİ MORTALİTE TRENDİ, 2009-2019

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ABSTRACT

Introduction: Heart failure is the third most common cause of death after coronary artery disease and stroke. By monitoring mortality trends of heart failure, control over the disease progression can be increased. Therefore, we aimed to create a mortality trend by taking the data on deaths due to heart failure in Turkiye in the last ten years.

Methods: We obtained population estimates for Turkey from the TurkStat website. Age- and sex-specific and age-standardized rates (ASRs, using the World standard population and the method of direct standardization) were calculated. Mortality trends from heart failure were assessed using the Joinpoint regression analysis. Statistical analysis was carried out with the Joinpoint software, version 4.9.0.0. We considered p values less than 0.05 to be statistically significant.

Results: We found Turkey's 10-year standardized mortality rate is 20.63%. The highest mortality rate is in western Marmara; the lowest one is in Eastern Karadeniz. We observed a significant increase in mortality at 10 years in the total population. (p:0,008). We detected a significant growth between 2009 and 2016 (p< 0.001) and a significant decrease after 2016 (p:0.047)

Conclusion: We obtained standardized mortality rates of heart failure patients in Turkey between 2009 and 2019 according to age, sex, and years. We showed an overall mortality reduction after 2016.

Keywords: Heart Failure, Turkiye, Mortality

ÖZET

Giriş: Kalp yetmezliği, koroner arter hastalığı ve inmeden sonra en sık üçüncü ölüm nedenidir. Bu denli mortalitesi yüksek bir hastalığı kontrol altına alabilmek için öncelikle ölüm oranlarını bilmek gerekir. Biz çalışmamızda Türkiye'de son on yılda kalp yetmezliğine bağlı ölümlerin verilerini alarak bir mortalite trendi oluşturmayı hedefledik.

Yöntemler: Türkiye için nüfus tahminlerini TÜİK web sitesinden elde ettik. Yaşa ve cinsiyete özel ve yaşa göre standardize edilmiş oranlar (Dünya standart popülasyonu ve doğrudan standardizasyon yöntemi kullanılarak ASR'ler) hesaplandı. Kalp yetmezliğinden ölüm eğilimleri Joinpoint regresyon analizi kullanılarak değerlendirildi. İstatistiksel analiz, Joinpoint yazılımı 4.9.0.0 sürümü ile gerçekleştirildi. 0,05'ten küçük p değerleri istatistiksel olarak anlamlı kabul edildi

Bulgular: Türkiye'nin 10 yıllık standardize ölüm oranını %20.63 olarak bulduk. En yüksek ölüm oranı batı Marmara'da; en düşük oran Doğu Karadeniz'dedir. Toplam popülasyonda 10 yılda mortalitede önemli bir artış gözlemledik(p:0,008). 2009-2016 yılları arasında önemli bir artış (p< 0.001) ve 2016 sonrası önemli bir düşüş (p:0.047) saptandı.

Sonuç: 2009-2019 yılları arasında Türkiye'deki kalp yetmezliği hastalarının yaş, cinsiyet ve yıllara göre standartlaştırılmış ölüm hızlarını elde ettik. 2016'dan sonra kalp yetmezliğinin genel mortalite düşme eğilimindedir.

Anahtar Kelimeler: Kalp Yetmezliği, Türkiye, Mortalite

INTRODUCTION

Cardiovascular diseases are the most common cause of death in Turkiye and the rest of the World. Heart failure constitutes an important part of cardiovascular disease. Heart failure, which is more common with prolongation of life expectancy, is a global health problem with increased mortality, morbidity, and hospitalization rates. This problem is growing due to the increasing incidence every year (1).

In the Heart Failure Prevalence and Predictors in Turkey (HAPPY) study in Turkiye, Değertekin et al. estimated approximately 2.5 million heart failure patients in 2012. Considering the annual incidence of the disease is 0.001-0.005, we can evaluate over 3.5 million heart failure patients recently (2).

Since 2010, it is expected that the disease's mortality will decrease with better follow-up of the disease, increased target dose precision of angiotensin-converting enzyme (ACE) inhibitors and beta-blockers, and increased use of sodium-glucose co-transporter 2 (SGLT 2) inhibitors and valsartan/sacubitril. Nevertheless, in the 1-year mortality study conducted in Turkiye last year, the mortality of chronic heart failure was 13.7% (3).

The prevalence of heart failure increases with smoking, a sedentary lifestyle, and rising obesity. However, mortality rates are decreasing with new guideline-based treatment modalities and the development of evidence-based treatment. Our study analyzed Turkish Statistical Institute (TurkStat) data to evaluate Turkiye's heart failure mortality

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Received date: 22.08.2022 Accepted date: 06.12.2022

Cite as: Dural İE, Doğan N. Trends in Burden of Heart Failure Mortality in Turkey, 2009-2019.
Eskisehir Med J. 2023; 4(1): 11-16
doi: 10.48176/esmj.2023.97

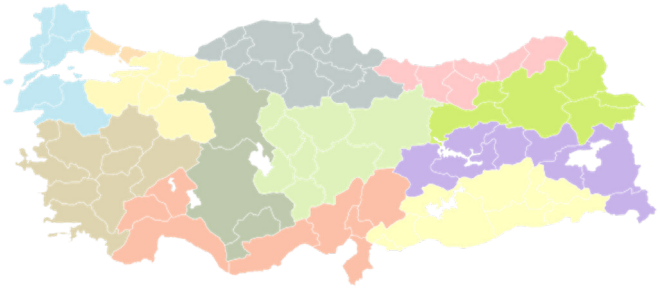

Figure 1: The twelve major regions of Turkiye.

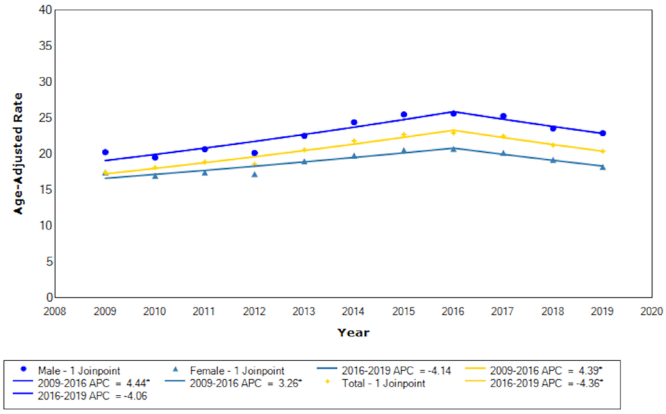

Figure 2: Trends in mortality from heart failure diseases in Turkiye, by genders, 2009–2019.

rates in the last ten years. In addition, we aimed to obtain results about the 10-year heart failure mortality by Joinpoint analysis.

METHODS

Classification of Regions

Nomenclature of Territorial Units for Statistics (NUTS) definitions are produced to collect and develop regional data, to provide analysis of the socio-economic structure of the regions, to establish regional policies, and to establish a comparable database with European Union Regional Statistical System. Figure 1 shows 12 regions of Turkiye—(TR1-İstanbul: İstanbul; TR2-Western Marmara: Balıkesir, Çanakkale, Edirne, Kırklareli, Tekirdağ; TR3-Ege: Afyon, Aydın, Denizli, İzmir, Kütahya, Manisa, Muğla, Uşak; TR4-Eastern Marmara: Bursa, Eskişehir, Bilecik, Kocaeli, Sakarya, Düzce, Bolu, Yalova; TR5-Western Anadolu: Ankara, Konya, Karaman; TR6-Akdeniz: Adana, Antalya, Burdur, Hatay, Isparta, Mersin (İçel), Kahramanmaraş, Osmaniye; TR7-Central Anadolu: Kırıkkale, Aksaray, Niğde, Nevşehir, Kırşehir, Kayseri, Sivas, Yozgat; TR8-Western Karadeniz: Zonguldak, Karabük, Bartın, Kastamonu, Çankırı, Sinop, Samsun, Tokat, Çorum, Amasya; TR9-Eastern Karadeniz: Trabzon, Ordu, Giresun, Rize, Artvin, Gümüşhane; TRA-Northeastern Anadolu: Erzurum, Erzincan, Bayburt, Ağrı, Kars, Iğdır, Ardahan; TRB-Central Eastern Anadolu: Malatya, Elazığ, Bingöl, Tunceli, Van, Muş, Bitlis, Hakkari; TRC-Southeastern Anadolu: Gaziantep, Adıyaman, Kilis, Şanlıurfa, Diyarbakır, Mardin, Batman, Şırnak, Siirt)

Data Source

We have obtained heart failure mortality data for Turkiye from the mortality database of the TurkStat (4). The underlying cause of death from heart failure was determined using the I50 codes of the International Classification of Diseases (ICD), the 10th revision. Data were available for each year in five-year age groups up to 85+ years for heart failure death data (2009-2019) , and 12 regions were grouped by year, gender, and age. However, the results are not shown for the subgroups aged <35 years due to the small number of deaths occurring in this subgroup.

Statistical Analysis

We obtained population estimates for Turkiye from the TurkStat website. Age- and sex-specific and age-standardized rates (ASRs, using the World standard population and the method of direct standardization) were calculated (5). Rates were expressed as deaths per 100,000 persons. ASRs remove the effects of historical events on age structure and control differences in age structure in populations. Age-specific mortality rates were calculated by 5-year periods (0–4, 5–9, 10–14, ..., 75–79, 80–84, and ≥85 years) for the age interval from 0 to 85 and over. This methodology was repeated within each region. For each region for, ASRs and age and sex-specific heart failure mortality rates were analyzed using Joinpoint regression to identify the years in which trends occurred. The method is widely used in epidemiological studies such as incidence and mortality. Mortality trends from heart failure were assessed using the Joinpoint regression analysis proposed by Kim et al (6). Joinpoint regression analysis identifies the best fit for inflection points (“joinpoints”) at which there is a significant change in trends and estimates the magnitude of trend changes (increases or decreases) for each period. Results include the years (period) making up each trend, as well as the annual percentage change (APC), average annual percentage change (AAPC), and 95% confidence intervals for each trend (7-8). The difference between males and females was determined with the parallelism test (9).

Statistical analysis was carried out with the Joinpoint software, version 4.9.0.0. We considered p values less than 0.05 to be statistically significant.

RESULTS

The number of deaths and mortality rates due to heart failure are given in Table 1. We found Turkiye’s 10-year standardized mortality rate to be 20.63%. The highest mortality rate is in western Marmara, and the lowest one is

Table 1. Number of deaths, distribution of standardized mortality rates by gender

Region	Deaths			ASR			Male/Female Ratio
	Male	Female	Total	Male (per 100 000 population)	Female (per 100 000 population)	Total (per 100 000 population)	
TR1	15691	20870	36561	25.86	21.02	23.23	1.23
TR2	8076	10484	18560	27.64	24.73	26.27	1.12
TR3	15397	20320	35717	20.95	18.39	19.66	1.14
TR4	10599	13175	23774	24.03	20.46	22.14	1.17
TR5	9479	11833	21312	22.54	18.70	20.84	1.21
TR6	12197	14850	27047	22.25	19.32	20.72	1.15
TR7	5621	6877	12498	22.09	18.48	20.06	1.19
TR8	9730	12052	21782	24.43	20.86	22.46	1.17
TR9	4401	5705	10106	19.21	14.17	16.33	1.36
TRA	2233	2544	4777	18.48	15.23	16.64	1.21
TRB	3776	4282	8058	22.25	17.14	19.33	1.30
TRC	6392	7229	13621	23.70	17.26	19.93	1.37
Total	103592	130221	233813	22.78	18.81	20.63	1.21

ASR: age-standardized rates

Table 2. Annual percentage change and average annual percentage change by gender (2009-2019)

	AAPC(95% CI) (2009-2019)	Trend 1		Trend 2	
		Period	APC (95% CI)	Period	APC (95% CI)
Male	1.8 (-0.4;4.1) (p=0.106)	2009-2016	4.4 (2.3;6.6) (p=0.002)	2016-2019	-4.1 (-11.2;3.6) (p=0.236)
Female	1.0 (-0.7;2.7) (p=0.251)	2009-2016	3.3 (1.6;4.9) (p=0.002)	2016-2019	-4.2 (-9.6;1.7) (p=0.128)
Total	1.7 (0.4;2.9) (0.008)	2009-2016	4.4 (3.2;5.6) (p<0.001)	2016-2019	-4.4 (-8.4;-0.1) (p=0.047)

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change.

Table 3. The annual rate of heart failure disease mortality between 2009-20019 in males.

	AAPC(95% CI) (2009-2019)	Period I		Period II		Period III	
		Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
TR1	-2.0 (-3.6;-0.4) (p=0.017)	2009-2013	-6.9 (-10.8;-2.9) (p=0.006)	2013-2019	1.4 (-0.6;3.5) (P=0.145)		
TR2	6.2 (3.5;8.9) (P<0.001)	2009-2014	14.9 (9.2;20.9) (p=0.001)	2014-2019	-1.9 (-5.4;1.8) (p=0.260)		
TR3	-0.3 (-3.4;2.9) (p=0.842)						
TR4	-2.5 (8-5.4;0.5) (p=0.101)	2009-2013	-4.9 (-9.5;-0.1) (p=0.048)	2013-2016	11.3 (-2.8;27.3) (p=0.087)	2016-2019	-11.7 (-17.1;-5.8) (p=0.009)
TR5	0.8 (-2.8;4.5) (p=0.664)	2009-2017	3.7 (1.0;6.4) (p=0.016)	2017-2019	-9.8 (-26.3;10.3) (p=0.256)		
TR6	-0.2 (-2.3;1.9) (p=0.831)	2009-2016	3.5 (1.2;5.8) (p=0.010)	2016-2019	-8.3 (-14.4;-1.7) (p=0.022)		
TR7	-0.8 (-2.2;0.7) (p=0.270)						
TR8	3.2 (1.6;5.0) (p=0.002)						
TR9	1.4 (-1.4;4.3) (p=0.280)						
TRA	8.7 (1.1;16.8) (p=0.023)	2009-2014	22.2 (5.6;41.4) (p=0.015)	2014-2019	-3.3 (-12.9;-0.8) (p=0.458)		
TRB	5.1 (0.3;10.1) (p=0.036)	2009-2015	11.2 (3.6;19.4) (p=0.010)	2015-2019	-3.4 (-12.6;6.6) (p=0.422)		
TRC	7.1 (2.5;12.0) (p=0.002)	2009-2014	16.4 (6.3;27.4) (p=0.006)	2014-2019	-1.4 (-7.4;5.0) (p=0.598)		

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change.

Table 4. The annual rate of heart failure disease mortality between 2009-20019 in females.

	AAPC(95% CI) (2009-2019)	Period I		Period II		Period III	
		Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
TR1	-3.1 (-4.6;-1.7) (P<0.001)	2009-2013	-6.5 (-10.0;-3.0)	2013-2019	-0.8 (-2.6;1.1) (p=0.360)		
TR2	3.3 (0.4;6.4) (P=0.028)	2009-2015	9.9 (5.3;14.7) (p=0.002)	2015-2019	-5.8 (-11.8;0.6) (p=0.069)		
TR3	-1.3 (-4.2;1.6) (p=0.330)						
TR4	-2.7 (-4.1;-1.3) (p<0.001)	2009-2013	-4.8 (-7.4;-2.2) (p=0.010)	2013-2017	4.9 (1.0;8.9) (p=0.028)	2017-2019	-12.6 (-18.8;-5.9) (p=0.010)
TR5	-2.2 (-4.6;0.2) (p=0.074)	2009-2011	-9.7 (-21.7;4.1) (p=0.106)	2011-2017	4.5 (1.6;7.4) (p=0.015)	2017-2019	-13.3 (-22.9;-2.5) (p=0.030)
TR6	-0.9 (-3.5;1.8) (p=0.505)	2009-2016	2.9* (0.1;5.8) (p=0.044)	2016-2019	-9.2 (-17.2;-0.6) (p=0.041)		
TR7	-1.1 (-2.5;0.3) (p=0.108)						
TR8	3.2 (1.7;4.7) (p=0.001)						
TR9	1.5 (-0.5;3.5) (p=0.122)						
TRA	3.8 (1.3;6.3) (p=0.003)	2009-2011	-0.3 (-11.7;12.7) (p=0.951)	2011-2014	24.8 (13.3;37.6) (p=0.005)	2014-2019	-5.6 (-7.3;-3.9) (p=0.002)
TRB	3.8 (-2.6;10.7) (p=0.247)	2009-2016	9.2 (1.9;17.1) (p=0.021)	2016-2019	-7.7 (-25.2;13.8) (p=0.385)		
TRC	7.3 (4.7;9.9) (p<0.001)	2009-2014	11.8 (7.6;16.1) (p<0.001)	2014-2019	0.9 (-4.1;6.1) (p=0.674)		

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change.

Table 5. Annual percentage change and average annual percentage change by gender and age groups (2009-2019)

	AAPC(95% CI) (2009-2019)	Trend 1		Trend 2	
		Period	APC (95% CI)	Period	APC (95% CI)
Male 35-64	4.0 (2.6;5.5) (p<0.001)				
65-74	1.4 (-0.1;3.0) (p=0.070)	2009-2016	3.1 (1.4;4.7) (p<0.05)	2016-2019	-2.3(-7.2;2.8) (p=0.299)
75-84	1.1 (-0.3;2.6) (p0.115)	2009-2016	3.4 (2.0;4.9) (p<0.001)	2016-2019	-4.0(-8.6;0.7) (p=0,083)
85+	-0.4 (-2.3;1.6) (p=0.698)	2009-2016	1.6 (-0.6;3.8) (p=0.136)	2016-2019	-4.8 (-10.5;1.3) (p=0.103)
Female 35-64	2.5 (0.9;4.0) (p=0.006)				
65-74	0.1 (-1.8;2.1) (p=0.905)	2009-2016	1.9 (-0.1;3.9) (p=0.059)	2016-2019	-3.9 (-10.1;2.7) (p=0.194)
75-84	-0.2 (-1.7;1.4) (p=0.815)	2009-2017	1.6 (0.6;2.7) (p=0.008)	2017-2019	-7.1 (-15.0;1.5) (p=0.087)
85+	-0.5 (-1.5;0.6) (p=0.372)	2009-2017	0.3 (-0.5;1.0) (p=0.450)	2017-2019	-3.4 (-8.8;2.4) (p=0.197)

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change

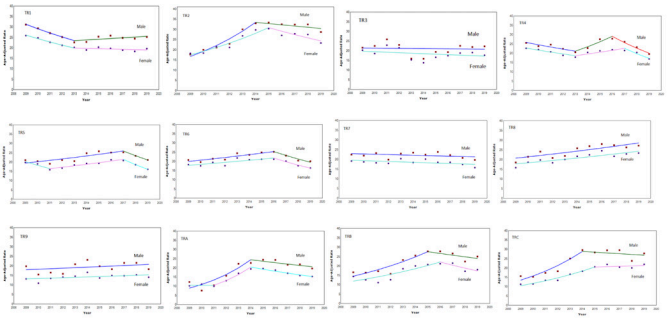

Figure 3: Trends in mortality from heart failure diseases in Turkey, by genders and region, 2009–2019.

in Eastern Karadeniz.

Annual percentage change and average annual percentage change by gender in Turkiye are given in Table 2. We observed a significant increase in mortality at 10 years in the total population (p: 0,008). We detected a significant growth between 2009 and 2016 ($p < 0.001$) and a significant decrease after 2016 (p: 0.047)

The graphs of the general annual changes in Turkiye are given in figure 2.

Average annual percentage changes by regions and annual percentage changes according to male and female gender are given in table 3 and table 4.

Trends in mortality from heart failure diseases in Turkey, by genders and region in figure 3.

Annual percentage change and average annual percentage change by gender and age are given in Table 5.

DISCUSSION

Heart failure is a common health problem with increasing mortality worldwide (10). One of the most important factors in tackling this problem is the careful examination and interpretation of data. In our study, we determined the incidence of deaths due to heart failure by examining the death reports from 12 regions of Turkiye. We tried to obtain mortality data by comparing these data to the estimated population.

Deaths due to heart failure tend to increase in Turkiye in the last ten years, as in the whole World. Especially between 2009 and 2016, the increase in mortality is higher. However, after 2016, deaths due to heart failure tend to decrease slightly in the general population. The rise in cardiology clinics and angiography units in Turkiye has greatly impacted this decreasing trend. In addition, attention to treatment standardization with the increase in guidelines and scientific congresses is a major factor in the decreasing mortality trend after 2016.

Akintoye et al., in their study published in 2017, investigated the in-hospital mortality of heart failure between 2001-2014. They showed that heart failure mortality decreased between these years (11). They found that the annual average mortality decrease was more significant after 2006. They believed that the guideline published in 2005 has a role in this decreasing trend (12). In our study, we can say that the national cardiac prevention program has a role in the mortality decline trend since 2016.

In a heart failure mortality study conducted in Japan, Shiraishi et al. investigated the 30-day and 1-year mortality of patients hospitalized with the diagnosis of acute heart failure (13). In the study, although there was a significant decrease in the length of hospitalization between 2007 and 2015, no reduction was observed in 1-year mortality rates. The fact that Japanese people have an older population may explain this situation. However, our study found a non-significant downward trend in the elderly population (+85) mortality in males and females.

In the past years, there have been studies investigating heart failure mortality in many countries in Europe. Studies to obtain mortality data from national hospital records in Denmark (1983-2012) (14), Sweden (1987-2006) (15), France (2000-2012) (16), Scotland (1986-2003) (17) and the Netherlands (1980-1999) (18) indicate that heart failure mortality decreases overall. A long-term cohort study in Denmark shows that the 5-year mortality of heart failure is decreasing. It was observed that this decrease is more prominent, especially after 2001 (14). We observed an increase in heart failure mortality between 2009 and 2019 in our study. However, we have shown that this increase has been broken in 2016 and has entered a significant downward trend. Since our study was not a follow-up study like other studies, we obtained standardized mortality data. However, we think these data will be as useful as other studies in predicting the mortality trend because Joinpoint regression analysis is the most frequently utilized analysis among the statistical methods used to determine the significant changes and breakpoints in the mortality trend over time (19).

Contrary to European data, heart failure mortality in our country has increased until 2016. The fact that the national heart health program (2007) and cardiology societies matured later than in Europe may be a reason for this situation (20). However, it has been observed that mortality has decreased after the cardiology societies and scientific congresses in our country have spread all over the country since 2016.

In the cohort study conducted in Sweden, the mortality rates of patients under 55 years were emphasized. Barasa et al. showed that mortality decreased in all age groups between 1987 and 2006. Still, they observed that this decrease was less pronounced in the under-55 age group after 2001 (15). In our study, we found a continuous increase in the age group of 35-65 years, in which died due to heart failure was reported. We can say that the most important reason for this situation is that prevalence of smoking is still high in this age group. In studies conducted in Turkiye, it is estimated that approximately 45% of men in this age group smoke cigarettes (21). We think that compliance with

treatment and regular health checks is less in Turkiye's young age group than in the elderly group. Lack of regular health checks for heart failure is an important risk factor for mortality and hospitalization (22). We think that this may be one of the reasons for the increased mortality in this age group.

Usage of SGLT-2 inhibitors and valsartan/sacubitril in Turkiye after 2016 may also affect this decrease. The inclusion of 779 patients in the angiotensin receptor neprilysin inhibitor for patients with heart failure and reduced ejection fraction: Real-world experience from Turkey (ARNI-TR) study published in 2021 shows the percentage of use of valsartan/sacubitril therapy at the national level (23).
We know that obesity has increased in young adults and children, especially in obesity studies conducted after 2009 in Turkiye (24). Obesity is one of the important risk factors for cardiovascular diseases. Therefore, one of the areas for the increase in both overall mortality and the young population's mortality may be the increase in the prevalence of obesity.

The over-65 age mortality decreases after 2016, in line with the general population. The compliance of elderly patients with treatment and their more strict cardiology outpatient follow-up seems to be compatible with these data (25).

Turkiye has seven geographical regions. However, since the population distribution of these regions is disproportionate, TurkStat divided the data into 12 regions according to the population and recorded the data. The first of these regions covers the province of Istanbul. Istanbul is the most developed province in terms of the health system (26). The highest number of hospitals and cardiology clinics are located in Istanbul. Therefore, greater access to health services may be a reason for the decrease in mortality in Istanbul between 2009 and 2019.

Another data showing the mortality effect of access to health services is the increase in deaths due to heart failure in Southeastern Anatolia, eastern Anatolia, and Eastern Karadeniz. It is more difficult for patients living in rural areas of these mountainous regions to reach hospitals. In addition, disruption of follow-up in heart failure requiring strict follow-up has been associated with mortality.

The most important limitation of our study is the lack of data on the demographic characteristics of the patients. We only have the age and gender data of the patients. Another important limitation is that our study is not a follow-up study. However, the compatibility of our data with the follow-up studies in which mortality data were obtained is one of the strengths of our study.

CONCLUSION

As a result, our country has made significant progress in managing heart failure, especially in the last five years, and has approached a national treatment standard. We observe the results of this as a decrease in mortality after 2016.

Ethics Committee Approval: The Afyonkarahisar Health Sciences University Ethics Committee approved the study protocol (approval date 16/04/2021 and number 2021/5).

Informed Consent: Retrospective study.

Authorship Contributions:
Idea/Concept: İED, ND, Design: ND, Supervision: İED, Data Collection or Processing: ND, Analysis or Interpretation: İED, ND, Literature Search: İED, Writing: İED, Critical Review: ND, References And Fundings: -, Materials: -.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

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