



# Exploring Regional Disparities in Heart Failure Epidemiology and Outcomes: A Comprehensive Study Across Geographical Regions in Türkiye

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**Background:** Heart failure (HF) is a common condition that affects 1-3% of the general population. Its prevalence exhibits notable international and intranational disparities, partly explained by socioeconomic status, religion, ethnic diversity, and geographic factors. A comprehensive understanding of the epidemiological symptoms of HF in different regions of Türkiye has yet to be revealed.

**Aims:** To examine epidemiological data from 2016 to 2022, focusing on crucial patient characteristics and geographical regions, to determine the incidence and prevalence of HF in Türkiye across seven diverse geographical regions.

**Study Design:** A nationwide population-based retrospective cohort study.

**Methods:** The comprehensive National Electronic Database of the Turkish Ministry of Health was used in this study to obtain data that covers the whole Turkish population from January 1, 2016, to December 31, 2022. The International Classification of Diseases-10 (ICD-10) codes were used to identify adults with HF (n = 2,701,099) and associated comorbidities. Türkiye is divided into seven geographically distinct regions. Epidemiological characteristics and survival data of these regions were analyzed separately. All-cause mortality was set as the primary outcome.

**Results:** In , the total estimated prevalence of adult patients with HF is 2.939%, ranging from 2.442% in Southeastern Anatolia to 4.382% in the Black Sea Region. Except for the Eastern Anatolia Region, the three most often reported comorbidities were hypertension, dyslipidemia, and anxiety disorders. The rates of prescribing guideline-directed medical therapy (GDMT) for HF and other medications varied significantly. GDMT prescription rates were lowest in the Eastern Anatolia Region (82.6% for beta-blockers, 48.7% for RASi, 31.8% for mineralocorticoid receptor antagonists, and 9.4% for SGLT2i). The Mediterranean and Aegean regions had the highest median N-terminal brain natriuretic peptide (NT-proBNP) levels of 1,990,0 pg/ml (518.0-6,636,0) and 1,441,0 pg/ml (363.0-5,000,0), respectively. From 2016 to 2022, 915,897 (33.9%) of 2,701,099 patients died. The Eastern Anatolia Region had the lowest all-cause mortality rate of 26.5%, whereas the Black Sea Region had the highest all-cause mortality rate of 35.3%.

**Conclusion:** Our real-world analysis revealed geographic disparities in HF characteristics, such as decreased mortality in socioeconomically challenged regions. Higher stress susceptibility in developed regions may increase the likelihood of adverse outcomes.



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Received: October 04, 2023 Accepted: November 09, 2023 Available Online Date: January 03, 2024 • DOI: 10.4274/balkanmedj.galenos.2023.2023-10-5

Available at [www.balkanmedicaljournal.org](http://www.balkanmedicaljournal.org)

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Cite this article as:

Şahin A, Çöllüoğlu T, Çelik A, et al. Exploring Regional Disparities in Heart Failure Epidemiology and Outcomes: A Comprehensive Study Across Geographical Regions in Türkiye. *Balkan Med J.*; 2024; 41(1):47-53.

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## INTRODUCTION

Heart failure (HF) has been characterized as a widespread global phenomenon, affecting an estimated 64.3 million people worldwide in 2017.<sup>1</sup> In addition to the medical challenges it presents, HF imposes a significant financial burden on healthcare systems.<sup>2</sup> The HF prevalence rate ranges from 1% to 3%, with disparities between countries.<sup>3</sup> Additionally, within the same country, different HF prevalence rates have appeared in various regions, with various regional determinants, including socioeconomic status (SES) and multiethnic composition.<sup>4</sup> Our nation comprises seven distinct geographic regions, each with different characteristics based on SES and ethnic factors. People from various ethnic backgrounds live in different geographical regions of Türkiye. Furthermore, the Southeastern Anatolia Region has a higher prevalence of refugees than other regions.<sup>5</sup> The eastern regions of have a higher birth rate, a lower maternal age at the time of childbirth, and a lower average income per household.<sup>6</sup> With our hypothesis centered on the idea that regions with varying ethnic and socioeconomic characteristics may yield different results, we designed this study accordingly.

Socioeconomic deprivation and ethnic differences have an inverse correlation with overall health status and are significant determinants of increased mortality and morbidity associated with HF.<sup>7,8</sup> In patients with HF who live in lower SES regions, an increased prevalence of cardiovascular risk factors has been observed, as well as an increased susceptibility to mortality risk.<sup>9,10</sup> Data on racial and regional differences can be quite perplexing. According to studies, Black individuals have a higher rate of HF mortality and hospitalization than individuals of Spanish origin and those with lower socioeconomic status.<sup>11</sup> In contrast, findings from the “Get With The Guidelines” initiative show a significant disparity in mortality among individuals of different racial backgrounds. In particular, the results indicated that Black patients have lower mortality rates than their White counterparts.<sup>12</sup>

However, the comprehensive epidemiological insights into the manifestation of HF within distinct regions are veiled by uncertainty. Considering the regional differences in ethnicity, culture, and SES, incorporating this registry would be an important contribution to the epidemiological data pool and prognostic insights specific to different geographical locations from the perspective of HF.<sup>8</sup> While data from other countries show regional variations in heart failure, no such data are available for our country. The primary objective of this study, which mainly focused on essential patient characteristics and geographical regions, was to thoroughly investigate the epidemiological data and outcomes of HF in Türkiye between 2016 and 2022 based on the seven geographical regions.

## MATERIALS AND METHODS

### Study population and study design

This retrospective cohort study includes a cohort of adult patients with HF (Figure 1). The study protocol was approved by the Turkish Ministry of Health and was documented under the reference number 95741342-020. The study’s design and procedures were

utterly consistent with the principles of the Helsinki Declaration. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies were rigorously followed with a complete checklist in preparation for this manuscript.

### Data collection

This registry is a detailed analysis focusing on adult patients with HF, using deidentified patient data acquired from the National Electronic Database of the Turkish Ministry of Health. This electronic dataset contains health-related records for a substantial population of around 85 million individuals. The Turkish Ministry of Health has successfully integrated all databases, making it easier to correlate diagnoses with prescriptions and record follow-up data for medical treatments. The diagnosis of HF and comorbid conditions was determined using the International Classification of Diseases, tenth revision (ICD-10) codes.

The inclusion criteria for the study were as follows:

- Over 18 yr;
- Any of the following ICD-10 codes [I50.0 (congestive HF), I50.1 (left ventricular dysfunction), I50.9 (HF with unspecified), I11.0 (hypertensive heart disease with congestive HF), I13.0 (hypertensive heart and chronic kidney disease with congestive HF), I13.2 (hypertensive heart and chronic kidney disease with congestive HF and renal failure), and I42.0 (dilated cardiomyopathy)]; and - receiving at least one HF drug for at least 1 month.

The database included age and sex, as well as comorbidities, such as hypertension, dyslipidemia, anxiety disorders, diabetes mellitus, chronic obstructive pulmonary disease, anemia, atrial fibrillation, acute myocardial infarction, hypothyroidism, chronic kidney disease, pulmonary embolism, ischemic stroke, and hemorrhagic stroke (Supporting Information Table S1). The study included data from all drug prescriptions categorized using the Anatomical Therapeutic Chemical classification system. The specific procedures and tests were screened using the Health Implementation Declaration codes specified by the Republic of Türkiye Health Implementation Declaration. Data on deceased individuals were obtained from the Turkish Death Notification System to obtain information on mortality.

Laboratory parameters, such as hemoglobin, B-type natriuretic peptide (BNP), N-terminal BNP (NT-proBNP), and estimated glomerular filtration rate (eGFR), were obtained from the National Electronic Database.

### Prevalence and incidence estimation

The HF prevalence was calculated by dividing the number of surviving adult patients with HF at the end of 2022 by the Turkish population for that year. From 2017 to 2022, annual HF incidence rates were calculated. The HF incidence was calculated by dividing the number of adult patients diagnosed with HF for the first time in a given year by the population of Türkiye in the same year. In the study, we calculated the incidence of 2019, 2021, and 2022 because

the number of accessible adults in our country was available for those years.

### Statistical analysis

The data on adult patients with HF was divided into seven distinct geographical regions. For categorical variables, cross-tables were created, with data presented as case numbers and percentages. For adult patients with HF, continuous variables were presented as mean and standard deviation, median, and interquartile range (IQR: 25-75%). We used the Cox regression model to obtain the hazard ratio for all-cause deaths in seven regions. Confounders in the Cox-regression model included age, sex, eGFR, previous myocardial infarction, diabetes mellitus, chronic obstructive pulmonary disease, and atrial fibrillation. The life-table method was used to calculate the probability of survival at specific points in time, such as 1, 5, and 7 yr. The statistical analyses were conducted using SPSS version 25.0 software (IBM Corp., Armonk, New York) and E-PICOS AI (MedicReS, New York).

## RESULTS

### The prevalence and incidence of heart failure in Türkiye

Between 2016 and 2022, there were 2,701,099 adult patients with HF, with females accounting for 51.8% of this population. At the end of 2022, there were 1,785,202 living adult patients with HF; the adult population was 60,721,745. In Türkiye, the total prevalence of HF is 2.939% (Figure 2). The annual incidence rates of HF per 1,000 person-years were 6,130 in 2019, 4,234 in 2021, and 5,030 in 2022 (Figure 3).

When the prevalence and incidence rates of HF were compared across seven distinct regions, it was shown that the Black Sea Region had the highest population-based prevalence of HF per 1,000 individuals, whereas the Southeastern Anatolia Region had the lowest prevalence, 2,442% (Figure 2). The annual HF incidence rates for each geographical region in 2019, 2021, and 2022 are shown in Figure 3. The Southeastern Anatolia Region had the lowest incidence in recent years, with 4,693%, 3,304%, and 4,370%, respectively.

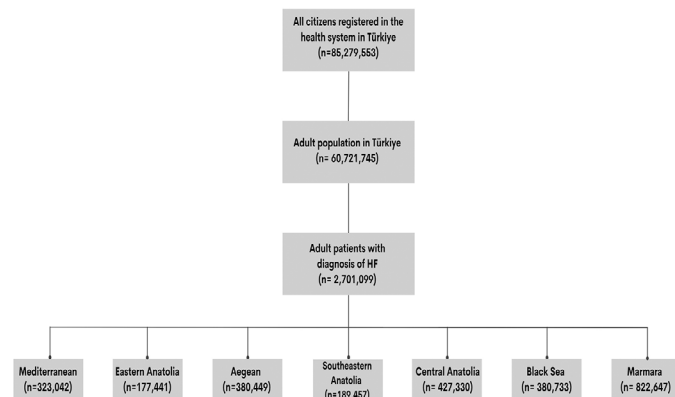


Fig 1. Study flowchart.

### The baseline characteristics of patients with heart failure in

The mean age at the index diagnosis was  $68.8 \pm 12.9$  yr. The Southeastern Anatolia Region had the lowest mean age among adult patients with HF, at  $66.5 \pm 13.7$  yr, whereas the Black Sea Region had the highest mean age, at  $70.5 \pm 12.2$  yr (Table 1).

Hypertension was found to be the most prevalent comorbidity, followed by dyslipidemia, anxiety disorders, diabetes mellitus, and chronic obstructive pulmonary disease (Table 1). When the data were analyzed regionally, the three most common comorbidities had similarities across geographical regions, except the Eastern Anatolia Region (Table 1).

The Eastern Anatolia Region had relatively low prevalences of anemia, atrial fibrillation, and chronic kidney disease compared with the other regions. The prevalence of acute myocardial infarction was notably lower in the Marmara Region than in the different regions (Table 1).

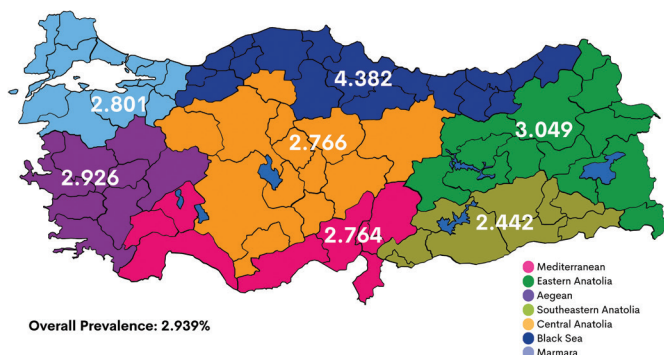


Fig 2. Distribution of heart failure prevalence by regions in Türkiye (per 1,000 person-years).

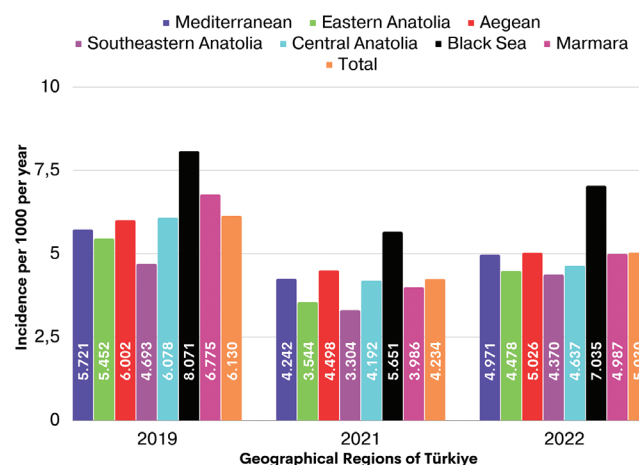


Fig 3. Incidence of patients with heart failure by geographic regions.

### Heart failure treatment in Türkiye

The majority (83.9%) of adult patients with HF received beta blockers as part of their treatment regimen. This was followed by the use of renin-angiotensin-aldosterone system inhibitors (RASi, 52.9%), mineralocorticoid receptor antagonists (MRA, 38.9%), and sodium-glucose cotransporter-2 inhibitors (SGLT2i, 11.1%). When examining the highest utilization rates in HF treatment, beta-blockers were most widely used in the Southeastern Anatolia Region at 87.1%, RASi in the Marmara Region at 56.5%, MRA in the Aegean Region at 41.4%, and SGLT2i in the Mediterranean and Aegean regions at 11.8%. Other medical treatments are shown in Table 2. The Eastern Anatolia Region had the lowest prescription rates of guideline-directed medical therapy for HF and other medications, whereas the highest prescription rates for each drug varied across distinct geographical regions (Table 3).

In adult patients with HF, the implantation rates for cardiac resynchronization therapy (CRT) and implantable cardioverter defibrillators (ICDs) were 0.9% and 0.3%, respectively. The

Central Anatolia Region had the highest implantation rate of ICD. The implantation rates for the Central Anatolia Region were nearly similar across the seven distinct geographical regions (Table 3).

### Laboratory parameters in patients with heart failure

The median values for hemoglobin, BNP, NT-proBNP, and eGFR were 11.5 (9.0-13.4) g/dl, 864.0 (210.1-3,327.9) pg/ml, 1,316.0 (327.0-4,665.0) pg/ml, and 73.7 (52.0-90.5) ml/min/1.73 m<sup>2</sup>, respectively. The Mediterranean Region had the highest median natriuretic peptide levels [1,506.0 (227.6-4,256.0) pg/ml for BNP and 1,990.0 (518.0-6,636.0) pg/ml for NT-proBNP]. The Aegean Region had the lowest median eGFR [64.2 (41.2-85.5) ml/min/1.73 m<sup>2</sup>] compared with the other regions. The Marmara Region had the lowest median hemoglobin levels [10.7 (7.3-12.8) g/dl] compared with the other regions (Table 2).

### Survival rates in patients with heart failure

Between 2016 and 2022, the all-cause mortality rate for adult patients with HF was 33.9% (915,897 out of 2,701,099). The

TABLE 1. Demographic Characteristics of Patients with Heart Failure in Türkiye According to Regions.

	Total (n=2,701,099)	Mediterranean (n=323,042)	Eastern Anatolia (n=177,441)	Aegean (n=380,449)	Southeastern Anatolia (n=189,457)	Central Anatolia (n=427,330)	Black Sea (n=380,733)	Marmara (n=822,647)
<b>Female, n (%)</b>	1,398,055 (51.8)	161,782 (50.1)	91,206 (51.4)	196,973 (51.8)	101,280 (53.5)	218,832 (51.2)	202,386 (53.2)	425,596 (51.7)
<b>Age, years</b>	68.8 ± 12.9	68.5 ± 13.1	66.5 ± 13.5	69.7 ± 12.8	66.5 ± 13.7	68.9 ± 12.8	70.5 ± 12.2	68.8 ± 12.9
<b>Hypertension, n (%)</b>	2,647,861 (98.0)	316,359 (97.9)	172,174 (97.0)	369,741 (97.2)	183,685 (97.0)	419,677 (98.2)	376,348 (98.8)	809,877 (98.4)
<b>Dyslipidemia, n (%)</b>	1,618,621 (59.9)	195,019 (60.4)	97,430 (54.9)	204,969 (53.9)	112,707 (59.5)	271,135 (63.4)	226,692 (59.5)	510,669 (62.1)
<b>Anxiety disorder, n (%)</b>	1,306,712 (48.4)	168,385 (52.1)	69,007 (38.9)	187,538 (49.3)	84,900 (44.8)	191,419 (44.8)	205,114 (53.9)	400,349 (48.7)
<b>Diabetes mellitus, n (%)</b>	1,229,833 (45.5)	147,705 (45.7)	76,426 (43.1)	150,908 (39.7)	89,542 (47.3)	200,878 (47.0)	168,269 (44.2)	396,105 (48.2)
<b>COPD, n (%)</b>	1,185,498 (43.9)	125,843 (39.0)	76,980 (43.4)	173,929 (45.7)	74,896 (39.5)	198,910 (46.5)	180,558 (47.4)	354,382 (43.1)
<b>Anemia, n (%)</b>	1,097,968 (40.6)	137,801 (42.7)	42,968 (24.2)	176,886 (46.5)	72,114 (38.1)	152,568 (35.7)	161,448 (42.4)	354,183 (43.1)
<b>Atrial fibrillation, n (%)</b>	1,009,653 (37.4)	111,413 (34.5)	52,878 (29.8)	142,007 (37.3)	53,127 (28.0)	160,187 (37.5)	166,716 (43.8)	323,325 (39.3)
<b>Prior myocardial infarction, n (%)</b>	591,906 (21.9)	81,119 (25.1)	35,489 (20.0)	89,890 (23.6)	61,909 (32.7)	90,620 (21.2)	91,617 (24.1)	141,262 (17.2)
<b>Hypothyroidis, n (%)</b>	524,192 (19.4)	56,119 (17.4)	29,306 (16.5)	77,946 (20.5)	28,504 (15)	84,790 (19.8)	84,914 (22.3)	162,613 (19.8)
<b>Chronic kidney disease, n (%)</b>	480,922 (17.8)	56,525 (17.5)	22,312 (12.6)	68,539 (18)	26,856 (14.2)	74,025 (17.3)	67,650 (17.8)	165,015 (20.1)
<b>Pulmonary embolism, n (%)</b>	211,419 (7.8)	18,335 (5.7)	14,394 (8.1)	25,729 (6.8)	17,288 (9.1)	42,585 (10.0)	35,495 (9.3)	57,593 (7.0)
<b>Ischemic stroke, n (%)</b>	178,098 (6.6)	21,194 (6.6)	7980 (4.5)	19,865 (5.2)	13,389 (7.1)	25,610 (6.0)	29,756 (7.8)	60,304 (7.3)
<b>Hemorrhagic stroke, n (%)</b>	22,695 (0.8)	2143 (0.7)	476 (0.3)	3947 (1.0)	587 (0.3)	2214 (0.5)	1559 (0.4)	11,669 (1.4)

Comorbidities are ranked by frequency of occurrence, Categorical variables are presented as n (%). COPD, Chronic obstructive pulmonary disease.

Eastern Anatolia Region (26.5%) had the lowest HF mortality rate, whereas the Aegean Region had the highest all-cause mortality of HF (36.4%, Table 4). The projected survival probability for HF in the adult population at 1, 5, and 7 yr were 79%, 54%, and 49%, respectively. At the end of the 7-yr follow-up period, the Eastern Anatolia Region (59%) had the highest survival rate, whereas the Mediterranean and Aegean regions (47%) had the lowest survival rate (Table 4).

## DISCUSSION

In our previous TREnds HF study, which included all age groups, we found a prevalence of 2,114%.<sup>13</sup> This study found a slightly higher prevalence as we focused on the adult population. This

study analyzed the data by geographical regions, highlighting the regional differences.

This registry provides an in-depth and current evaluation of the epidemiological landscape of HF in the adult Turkish population across seven distinct geographical regions. The estimated overall prevalence rate is 2,939%, which is consistent with previous Western and European observations.<sup>14</sup> Notably, the rate exceeds the prevalence rates reported in South America, China, Japan, South Korea, and Thailand.<sup>1</sup> However, there are significant differences in prevalence between these regions, ranging from 2,764% to 4,382%. Furthermore, as previously reported, our comprehensive registry found a positive correlation between increasing age and HF prevalence.<sup>15,16</sup> Notably, the Black Sea Region exhibited a

**TABLE 2.** Selected Laboratory Parameters of Heart Failure Patients in Türkiye According to Regions.

	Total (n=2,701,099)	Mediterranean (n=323,042)	Eastern Anatolia (n=177,441)	Aegean (n=380,449)	Southeastern Anatolia (n=189,457)	Central Anatolia (n=427,330)	Black Sea (n=380,733)	Marmara (n=822,647)
<b>BNP (pg/ml)</b>	864.0 (210.1-3327.9)	1516.8 (373.0-5000.0)	1056.0 (227.6-4256.0)	956.9 (248.6-3453.9)	690.0 (177.0-2992.0)	595.0 (140.7-2716.0)	1071.0 (277.0-3780.0)	720.6 (186.2-2664.0)
<b>NT-proBNP (pg/ml)</b>	1316.0 (327.0-4665.0)	1990.0 (518.0-6636.0)	1069.0 (252.9-4054.0)	1441.0 (363.0-5000.0)	1270.0 (337.3-4708.0)	1289.0 (330.0-4545.5)	1348.6 (343.7-4560.0)	1227.0 (296.6-4425.0)
<b>eGFR (ml/ dk/1.73m<sup>2</sup>)</b>	73.7 (52.0-90.5)	68.4 (44.4-88.9)	74.3 (50.9-91.9)	64.2 (41.2-85.5)	72.7 (48.7-91.2)	68.3 (44.9-88.1)	66.5 (42.5-87.2)	67.0 (43.2-87.9)
<b>Hemoglobin (g/dl)</b>	11.5 (9.0-13.4)	11.5 (9.1-13.5)	12.4 (9.8-14.2)	11.6 (9.2-13.3)	11.9 (9.3-13.7)	12.2 (10.1-13.9)	11.7 (9.9-13.3)	10.7 (7.3-12.8)

Continuous variables are presented as mean (SD) and median (IQR 25-75th). BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-brain natriuretic peptide.

**TABLE 3.** Treatment of Heart Failure Patients in Türkiye According to Regions.

	Total (n=2,701,099)	Mediterranean (n=323,042)	Eastern Anatolia (n=177,441)	Aegean (n=380,449)	Southeastern Anatolia (n=189,457)	Central Anatolia (n=427,330)	Black Sea (n=380,733)	Marmara (n=822,647)
<b>Beta blocker, n (%)</b>	2,265,067 (83.9)	279,291 (86.5)	146,542 (82.6)	317,008 (83.3)	164,963 (87.1)	358,707 (83.9)	314,982 (82.7)	683,574 (83.1)
<b>RASi, n (%)</b>	1,427,651 (52.9)	168,068 (52.0)	86,343 (48.7)	191,965 (50.5)	100,223 (52.9)	224,583 (52.6)	191,509 (50.3)	464,960 (56.5)
<b>MRA, n (%)</b>	1,051,704 (38.9)	132,049 (40.9)	56,500 (31.8)	157,690 (41.4)	73,561 (38.8)	174,502 (40.8)	140,859 (37.0)	316,543 (38.5)
<b>SGLT-2i, n (%)</b>	298,581 (11.1)	38,043 (11.8)	16,647 (9.4)	45,014 (11.8)	21,818 (11.5)	45,173 (10.6)	40,662 (10.7)	91,224 (11.1)
<b>Ivabradin, n (%)</b>	168,826 (6.3)	23,231 (7.2)	8,170 (4.6)	29,696 (7.8)	11,702 (6.2)	21,821 (5.1)	25,766 (6.8)	48,440 (5.9)
<b>Digoxin, n (%)</b>	405,368 (15.0)	53,635 (16.6)	18,959 (10.7)	63,629 (16.7)	25,324 (13.4)	66,120 (15.5)	61,634 (16.2)	116,067 (14.1)
<b>Acetylsalicylic acid, n (%)</b>	2,162,793 (80.1)	267,541 (82.8)	142,826 (80.5)	299,277 (78.8)	163,478 (86.3)	342,192 (80.1)	298,721 (78.5)	648,258 (78.8)
<b>ICD, n (%)</b>	23,024 (0.9)	2683 (0.8)	1603 (0.9)	3755 (1.0)	1502 (0.8)	5173 (1.2)	2601 (0.7)	5707 (0.7)
<b>CRT, n (%)</b>	8890 (0.3)	1310 (0.4)	718 (0.4)	1131 (0.3)	708 (0.4)	1648 (0.4)	1022 (0.3)	2353 (0.3)

Categorical variables are presented as n (%). CRT cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; MRA, mineralocorticoid receptor antagonist; RASi, renin angiotensin system inhibitor; SGLT-2i, sodium/glucose cotransporter 2 inhibitor.

**TABLE 4.** Outcomes of Heart Failure Patients in Türkiye According to Regions.

	Total (n=2,701,099)	Mediterranean (n=323,042)	Eastern Anatolia (n=177,441)	Aegean (n=380,449)	Southeastern Anatolia (n=189,457)	Central Anatolia (n=427,330)	Black Sea (n=380,733)	Marmara (n=822,647)
<b>All cause mortality, n (%)</b>	915,897 (33.9)	112,045 (34.7)	47,086 (26.5)	138,356 (36.4)	58,441 (30.8)	143,167 (33.5)	134,573 (35.3)	282,229 (34.3)
<b>Survival rates (%)</b>								
<b>1 year</b>	79	78	85	77	81	79	79	78
<b>5 year</b>	54	53	64	52	58	55	53	54
<b>7 year</b>	49	47	59	47	53	49	47	49

positive relationship between advancing age and the highest prevalence rate of HF. The Southeastern Anatolia Region had the lowest prevalence rate despite comparable comorbidities and mean age rates compared with other regions. This might imply that HF is caused by diverse pathophysiological mechanisms other than the conventional and well-known cardiovascular risk factors. Moreover, chronic obstructive pulmonary disease and atrial fibrillation were shown to be more prevalent in regions with a higher prevalence of HF.

The temporal trends of HF incidence have been explained in our nation, with rates of 6.13, 4.23, and 5.03 per 1,000-person years recorded in 2019, 2021, and 2022, respectively. During the same period, regional HF incidence rates ranged from 3.30 to 6.77 per 1,000 person-years. These observations provide important insights into the dynamics of HF incidence at the national and regional levels. A similar trend in HF incidence rates was observed in other countries, ranging from one to 20 cases per 1,000 person-years.<sup>14</sup> In 2021, national and regional HF incidence rates showed a downward trend, possibly due to lower hospital admissions throughout the country during the coronavirus disease-19 pandemic. In 2022, there was a return to actual incidence levels.

All-cause mortality rates varied across the seven distinct geographic regions. The Eastern Anatolia Region has the lowest all-cause mortality rates, followed by the Southeastern Anatolia Region. Despite the predominant lower SES stratum that characterizes these specific regions, there is a clear emphasis on adopting a natural lifestyle. This inclination is exacerbated by geographical separation from the negative health consequences of industrialization. Aside from that, it is noteworthy that the government has uniformly established healthcare institutions equipped with modern diagnostic and treatment methods in every country province, regardless of SES. Furthermore, the lower population density in these geographic areas allows for increased accessibility to healthcare facilities, thereby expediting patients' proximity to hospitals and receiving essential medical services. Finally, the limited number of immigrant settlements within these geographical regions, relatively significant of whom have Turkish citizenship, poses an important consideration. The enrollment of these patients from diverse ethnic and genetic backgrounds in the registry's statistical analysis might explain the observed variance in mortality rates. This demographic diversity highlights the importance of carefully interpreting the registry's findings regarding mortality differentials in patients with HF.

In our country, beta-blockers were the most commonly prescribed medications among the GDMTs for HF, regardless of geographical region. The use of angiotensin receptor neprilysin inhibitors (ARNIs) exhibited a notably low rate in each region of our country. Although ARNI is available on the market, it has yet to be reimbursed by the nationwide healthcare system in Türkiye. As a result, its use is less common in each geographical region, although it is recommended. The current HF guidelines recommend using SGLT2i, regardless of the left ventricular fraction (LVEF).<sup>18,19</sup> Nevertheless, the use of SGLT2i showed low rates among distinct geographical regions, ranging from 9.4% to 11.8%. The main factor behind the limited use of SGLT2i among adult patients with HF appears to be its exclusive prescription for patients with concomitant type 2 diabetes mellitus. In Türkiye, SGLT2i is not covered under reimbursement for patients with no diabetes. Although we were unable to differentiate patients according to EF in our study, ICD and CRT implantation rates were relatively low in all regions in our country. These rates are quite low compared with European registries.<sup>20</sup> This is because ICD and CRT insurance payments are only available in state hospitals, and ICD implantation shows an LVEF of < 35%. No distinction has been made in our population based on LVEF, and patients from all LVEF groups are present.

All-cause mortality rates are increasing in more developed areas, such as Aegean. These regions exhibit widespread industrialization linked to various health problems. In the realm of industrialized regions, prevalent concerns include anxiety disorders, depression, and related issues.<sup>21</sup> According to a meta-analysis, anxiety disorders are associated with an increased risk of cardiovascular mortality.<sup>22</sup> The coexistence of patients diagnosed with HF within an environment characterized by increased stress levels has been proposed to potentially contribute to the exacerbation of anxiety disorders among this patient cohort. Such physiological distress, which results from the interaction of the physiological complexities of HF and the physical implications of stress, is thought to have a multifaceted impact. Notably, it is hypothesized that this increased anxiety burden might have a negative effect on the overall prognosis of these patients, potentially manifesting as an increased susceptibility to mortality risk. Given these complex associations, a comprehensive understanding of the interaction of physiological and psychological factors is imperative, as it may yield insights that might drive holistic patient care and management strategies.

This study has some limitations. Our data were obtained by retrospective analysis of an electronic dataset. Because of the retrospective nature of the study, sources of bias from the selection process and variables confounding the outcomes may be introduced. Because the study design inherently promotes associations over causation, the retrospective nature of the data may limit our ability to establish causal relationships or draw definitive conclusions. The lack of explicit categorizations for HF phenotypes in the used database and ICD-10 codes does not precisely define HF phenotypes. Due to the inability to integrate the discrete echocardiography reports into the main database, we were unable to obtain data on the EF of the patients. Because the database lacked explicit HF phenotypic classifications, we were unable to analyze the distribution of HF<sub>rEF</sub>, HF<sub>mrEF</sub>, and HF<sub>pEF</sub> cases. We have no information on the patient's functional abilities. Individual income level would have helped elucidate the relationship between regional income level and patient characteristics; however, this was not available in our study.

Our study analyzed real-world data to reveal significant geographical region-related differences in HF demographics, comorbidities, biomarkers, medications, and outcomes. Patients with HF who live in lower SES regions had lower mortality rates. This interesting phenomenon may be attributed partly to inherent lifestyle factors prevalent in such areas and easier access to healthcare resources. In contrast, patients with HF in more developed regions appeared to be more susceptible to higher stress levels, potentially leading to an increased propensity for acute coronary syndrome and associated adverse outcomes. Moreover, the status of migrants in these regions may emerge as an essential factor determining HF-related results.

**Ethics Committee Approval:** Ministry of Health of Türkiye, approval number: 95741342-020.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Authorship Contributions:** Concept- A.Ş., T.Ç., A.Ç., A.K., D.U., N.A., M.O.A., M.M.Ü., Ş.B., M.B.Y.; Design- A.Ş., T.Ç., A.Ç., A.K., D.U., M.O.A., M.B.Y.; Data Collection or Processing- A.Ş., T.Ç., M.O.A.; Analysis or Interpretation- A.Ş., T.Ç., A.K., M.O.A.; Literature Search- A.Ş., T.Ç., A.Ç., D.U., M.B.Y.; Writing- A.Ş., T.Ç., A.Ç., D.U., M.B.Y.

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

**Funding:** The authors declared that this study received no financial support.

**Supplementary:** <http://balkanmedicaljournal.org/uploads/pdf/2023.2023-10-5-53-supplemantry.pdf>

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