Trends in heart failure between 2016 and 2022 in Türkiye (TRends-HF): a nationwide retrospective cohort study of 85 million individuals across entire population of all ages

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Summary

Background Data on the burden of heart failure (HF) outside western countries are limited, but available data suggest it may present differently in other countries. The aim of this study was to examine the incidence, prevalence, and survival rates of HF in Türkiye, with a specific focus on how these rates vary according to age, sex, comorbidities, and socioeconomic status (SES).

Methods We harnessed the extensive National Electronic Database of the Turkish Ministry of Health, covering Turkey's entire population from January 1, 2016, to December 31, 2022, to identify 2,722,151 cases of HF and their associated comorbidities using ICD-10 codes. Analyzing the primary endpoint of all-cause mortality, our study utilized anonymized data to examine patient demographics, comorbidities, socioeconomic status, and survival patterns, employing statistical techniques to delve into relationships and trends. The data were segmented by gender, socioeconomic status, and age, involving cross-tabulations and statistical metrics to explore connections, odds ratios, and survival rates.

Findings The estimated prevalence of HF was 2.114% in Türkiye at the end of 2022, with an annual incidence ranging between 3.00 and 6.06 per 1000 person years. Females were older than males (69.8 ± 13.9 years vs. 66.8 ± 13.9 years, respectively). The most common comorbidities were congenital heart diseases and anemia under the age of 20, and hypertension and atherosclerotic cardiovascular disease in the adult population. Only 23.6% (643,159/2,722,151) of patients were treated with any triple guideline-directed medical therapy (GDMT) and 3.6% (96,751/2,722,151) of patients were on quadruple GDMT. The survival rates for patients with HF at 1, 5, and 7 years were 83.3% (95% CI: 83.2–83.3), 61.5% (95% CI: 61.4–61.6), and 57.7% (95% CI: 57.6–57.8) among females, and 82.1% (95% CI: 82.0–82.2), 58.2% (95% CI: 58.1–58.3), and 54.2% (95% CI: 54.0–54.3) among males. Despite a tendency for an increase from the highest to the lowest SES, the prevalence of HF and mortality were paradoxically lowest in the lowest SES region.

Interpretation The prevalence, incidence, and survival rates of HF in Türkiye were comparable to western countries, despite the notable difference of HF onset occurring 8–10 years earlier in the Turkish population. Drug usage statistics indicate there is a need for effective strategies to improve treatment with GDMT.

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Research in context

Evidence before this study

We conducted comprehensive searches in PubMed and Google Scholar for articles published until May 10, 2023, using the search terms "heart failure", "prevalence", "incidence", "co-morbidities", "trend", "epidemiology", "nationwide", "morbidity", "mortality", "pediatric", "children". We also reviewed the related articles of identified publications to determine other relevant articles. To ensure a comprehensive approach, we also accessed and reviewed articles from journal families of Lancet, Circulation, American College of Cardiology and European Society of Cardiology. For reliable and up-to-date epidemiological data for our country, we referred to the annual reports of the Turkiye Statistical Institute. We found only one study evaluating epidemiology and mortality rates in adult Turkish heart failure patients and a limited number of studies reporting prevalence of heart failure including pediatric range, though they were not integrated with socioeconomic status.

Added value of this study

This is the first study to model the nation-wide epidemiologic data of heart failure in Turkiye. It involves one of the largest comprehensive set of data with 2,722,151 heart failure patients, obtained from the Electronic Database of the Turkish Ministry of Health covering over 85 million Turkish citizens. Our registry fills an important gap in terms of frequent co-morbidities accompanying different age groups in the heart failure population. Moreover, it provides contemporary epidemiological data on pediatric heart failure with a prevalence of 0.069%. An eye-catching finding of TRENDs-HF study is related to the critical role of fully covered health insurance system that enables a rather homogeneous survival among heart failure patients living in different socioeconomic regions, and even a better survival trend for patients living in the lowest socioeconomic region on the contrary of the existing literature.

Implications of all the available evidence

Our findings have significant implications for practice in the following ways: Our findings can guide practitioners in choosing the most appropriate and effective course of action. Informing policy development: The results of our research can inform policy development by providing evidence to support specific policy changes on health coverage or program implementation. Policymakers can use our research to design or modify health policies in line with identified effective approaches, leading to more efficient and effective interventions. Addressing challenges: Our research can shed light on key challenges or barriers in a particular area (cardiac device implantation, heart transplantation), providing insights into potential solutions or mitigation strategies for the heart failure syndrome according to specific age categories as one size does not fit all. By understanding the underlying issues, cardiologists can proactively develop strategies to overcome barriers and improve practice for precision medicine.

Introduction

Heart failure (HF) is a severe and life-threatening condition that affects a significant number of individuals worldwide, with a prevalence exceeding 37.7 million people. The global burden of HF is expected to rise in the coming decades due to the aging population and improved survival rates among individuals with heart disease.[1,2] While the epidemiology and prognostic impact of HF in the adult population have been extensively studied in Europe and the USA, there is limited data available from other regions. Existing data point to potential differences in the presentation and outcomes of HF between various nations.[3,4] Population characteristics, socioeconomic factors and health infrastructure affect epidemiological characteristics, implementation of contemporary clinical practice guidelines and mortality in different countries.

Age and sex have a significant impact on the epidemiology of HF. Although HF is more prevalent in elderly, there has been a notable increase in its prevalence and incidence among younger patients. The data in this population subset are scarce probably due to challenges in diagnosis and the limited number of affected patients.[5,6] Sex-specific differences in HF epidemiology and prognosis have been well-documented, potentially influenced by type of HF, usage of guideline-directed medical therapies (GDMT) and variations in comorbidities such as diabetes mellitus, hypothyroidism, anemia, and depression between males and females. Therefore, it is crucial to identify these differences and develop targeted health policies and strategies to address the specific needs of each population and improve outcomes in HF.

Türkiye has a relatively younger population, with a median age of 33.5 years. The mortality rate from cardiovascular diseases is relatively high compared to European countries, and females are more likely than males to die from cardiovascular diseases. Türkiye's health status has significantly improved over the past three decades, especially after the Health Transformation Program was put into place. In 2022, the average life expectancy at birth reached 75.6 years for males and 81.1 years for females.[7] Some risk factors like smoking and hypertension showed a decline with nationwide legislation, whereas other risk factors like obesity and diabetes either increased or remained stable.[8,9]

This study aims to identify epidemiological trends in the incidence and prevalence of HF in Türkiye between 2016 and 2022, considering population characteristics such as age, sex, and comorbidities. Additionally, the study will explore hospitalization and survival rates among patients with HF in Türkiye to provide insights into the management and prognosis of this condition in the country.

Methods

Study population and study design

Our study was a nationwide population-based retrospective cohort study. The study protocol was approved and conducted in accordance with the Ministry of Health of Türkiye's approval number 95741342-020. The design and procedure of the study were in accordance with the Declaration of Helsinki. STROBE guidelines for cohort studies and a checklist were used in the preparation of this report (Supplementary Material).[10] The primary endpoint was all-cause mortality according to population characteristics.

Data collection

This study used anonymized data from the Turkish Ministry of Health's National Electronic Database. The database consisted of over 85 million citizen records between January 1, 2016, and December 31, 2022. The Turkish Ministry of Health has been governing the national electronic database, which merges all other databases, including procedures, laboratory results, medications, and deaths, since 2016. It is officially required to report all data since 2016 for all hospitals. Since the Turkish Ministry of Health has governed and merged all databases, it is possible to cross-check the diagnoses, for example, with compatible medications after index diagnoses or planned follow-up data for procedures. Of note, all medications and medical equipment are digitally followed up and recorded into this database; otherwise, no reimbursement occurs. Following International Statistical Classification of Diseases and Related Health Problems (ICD)-10 codes were used to identify patients with HF: I50.0 (congestive HF), I50.1 (left ventricular dysfunction), I50.9 (HF, 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) (Supplementary Figure S1). The database contained on age and sex, while comorbidities including hypertension, atherosclerotic cardiovascular disease (ASCVD), dyslipidemia, anxiety disorders, diabetes mellitus, chronic obstructive pulmonary disease, anemia, atrial fibrillation, acute myocardial infarction, hypothyroidism, chronic kidney disease, pulmonary embolism, iron deficiency, depression, ischemic stroke, hyperthyroidism, morbid obesity, hemorrhagic stroke, congenital heart disease, primary muscle disorders, and primary cardiac tumors were recorded using the ICD-10 codes (Supplementary Table S3). To analyze the frequency of comorbidities among different age groups, we stratified our study population into four subpopulations based on the age strata: (I) 0–19 years, (II) 20–49 years, (III) 50–79 years, and (IV) ≥80 years. All prescribed drugs were recorded according to the Anatomical Therapeutic Chemical Classification (ATC) system. Specific procedures and tests were recorded based on the Health Implementation Declaration codes. Data on deaths was obtained from the Turkish Death Notification System. Variables including age, date of birth, sex, socioeconomic status (SES), comorbidities, all prescribed drugs, investigations, and procedures, date of hospitalization, length of stay (LOS) in hospital, date of death, and time from diagnosis to death were reported. Laboratory variables, including natriuretic peptides (BNP or NT-proBNP), estimated glomerular filtration rate (eGFR, based on chronic kidney disease [CKD]-epi), and hemoglobin, were obtained from the National Electronic Database.

Prevalence and incidence estimation

The prevalence of HF was calculated by dividing the number of patients with HF who were alive at the end of 2022 by Türkiye's population in 2022. The annual incidence of HF was estimated for each of the years from 2017 to 2022. The incidence of HF was calculated by dividing the number of patients first diagnosed with HF in a given year by Türkiye's population in that year.

Socioeconomic status definition

In this study, province and region rankings were obtained from a 52-variable model in the socioeconomic status (SES)-2017 research report of the Turkish Ministry of Industry and Technology. In this report, provinces were classified according to their level of socioeconomic development (Supplementary Table S1). Of note, SES is rather reported per region, aiming to improve regional status for specific healthcare policies. Hence, outputs might be different from per-patient

analyses. The SES of patients with HF was assessed using the SES-2017 Research Report, which was ranked into sixtiles (from the most affluent group [SES-1] to the most deprived group [SES-6]).[11]

Statistical analysis

The big data were stratified by sex, socioeconomic sixtiles, and age groups. Cross-tables were created for categorical variables, and values were expressed as the numbers of cases and percentages (%). Age and laboratory parameters at index HF diagnosis time described by mean and standard deviation, median and interquartile range [25th–75th]. The number of HF cases by age and sex groups was shown by the population pyramid. The association between comorbid conditions and sex was expressed as an odds ratio and confidence interval without any adjustment using the case–control study design model. Because of the big data, all comparisons might be statistically significant, but we have preferred to calculate the effect size and confidence interval (CI) to decide whether they are clinically significant or not.[12] Comorbidities based on sex were shown by a forest plot with odds ratios and CIs. In survival analyses, the Kaplan–Meier method was used for estimating the median overall survival time (days), the Life Tables method was used to obtain survival rates (%) at certain time points as 1-5-7 years, and the Cox regression method was used to obtain hazard ratios along with an adjustment for age when necessary. Age was adjusted as a continuous variable in all of the analyses. We assessed the proportional hazards assumption for the mortality outcome using the graphical (Log minus Log) method. We plotted the Log minus Log of the survival function against time for age, sex, and SES groups. SPSS 25.0 software (IBM Corp., Armonk, NY, USA) and E-PICOS AI (MedicReS, NY) were used for statistical analyses.

Results

The prevalence and incidence of HF in Türkiye

Between January 1, 2016, and December 31, 2022, there were 2,722,151 patients (51.7% female, 48.3% male) of all ages who received a diagnosis of HF. Of them, 23,443 patients were under the age of 19, 201,773 were between the ages of 20 and 49, 1,906,039 were between the ages of 50 and 79, and 560,896 were over the age of 80. The flow chart of the TRends-HF study was shown in Supplementary Figure S1. At the end of 2022, the number of alive patients with HF was 1,803,637 and the population was 85,279,553. The overall prevalence of HF in Türkiye is 2.114% (21.14 per 1000 people) (Table 1). The prevalence of HF per 1000 people was 22.30 (2.230%) in females and 19.99 (1.999%) in males. The distribution of HF prevalence by province in Türkiye was illustrated with a map in Supplementary Figure S2.

The annual HF incidence rates per 1000 person-years were 6.06 in 2017, 4.92 in 2018, 4.28 in 2019, 3.09 in 2020, 3.00 in 2021, and 3.61 in 2022. The mean age at the time of HF diagnosis was 68.3 ± 13.8 years. The age at initial diagnosis in females was 3 years older than in males (69.8 ± 13.9 years vs. 66.8 ± 13.9 years, respectively). Age-adjusted prevalence of HF increased from 0.98 per 1000 people in the age group 0–9 years to 153.3 per 1000 people in the age group 80–89 years. However, after the age of 90, the age-adjusted prevalence rates started to decline, with the age-adjusted prevalence of HF of 97.28 per 1000 people.

The numbers of patients by age group and sex were shown in Fig. 1A and the sex-specific HF prevalence by different age groups was shown in Fig. 1B. When analyzed by age groups, males had a predominance until ages of 60–69, while females surpassed males after age 70. The overall sex-specific incidence of HF was consistently higher in females than in males for each year between 2017 and 2022 (Fig. 1C).

When analyzed according to SES groups, the SES-5 group had the highest population-based prevalence of HF per 1000 people, while the SES-6 group had the lowest. Patients in the SES-6 group were 2.43 years younger at HF diagnosis than patients in the SES-1 group (Table 1).

Comorbidities in patients with HF

Hypertension was the most common comorbidity, followed by ASCVD, dyslipidemia, anxiety disorders, diabetes mellitus, chronic obstructive pulmonary disease, anemia, and atrial fibrillation (Table 1). Females had a higher rate for atrial fibrillation, anemia, extreme obesity, diabetes mellitus, hypertension, hypothyroidism, pulmonary embolism, and anxiety disorders than males. On the other hand, males had a higher rate of ASCVD, acute myocardial infarction, chronic obstructive pulmonary disease, dyslipidemia, and chronic kidney disease than females (Fig. 2). Congenital heart disease was the most prevalent comorbidity in patients under the age of 20, whereas ASCVD, hypertension, hyperlipidemia, and diabetes mellitus were the most prevalent comorbidities in the adult population (Supplementary Table S4) Comorbidities were similar across the SES groups (Table 1 and Supplementary Table S2).

Laboratory parameters in patients with HF

The median hemoglobin, BNP, NT-proBNP, and eGFR at index diagnosis were 11.5 g/dL, 972.1 pg/mL, 1374.0 pg/mL, and 68.1 mL/min/1.73 m^2, respectively. The median BNP level was higher in females (1000.0 pg/mL) compared to males (947.8 pg/mL). In contrast, the median NT-proBNP was higher in males (1417.0 pg/mL) than in females (1332.0 pg/mL) (Table 1).

	All patients	Sex		Socio economic status					
	(n = 2,722,151)	Female (n = 1,407,927)	Male (n = 1,314,224)	SES—1[a] (n = 1,120,680)	SES—2[a] (n = 472,755)	SES—3[a] (n = 426,184)	SES—4[a] (n = 265,063)	SES—5[a] (n = 237,634)	SES—6[a] (n = 199,835)
Age, years	68.3 ± 13.8	69.8 ± 13.9	66.8 ± 13.9	68.2 ± 14.3	69.4 ± 13.3	68.3 ± 13.9	69.0 ± 13.2	68.4 ± 13.7	65.8 ± 15.4
Female				575,040 (51.3%)	243,101 (51.4%)	222,567 (52.2%)	137,241 (51.8%)	124,579 (52.4%)	105,399 (52.7%)
Prevalence	2.114%	2.230%	1.999%	1.997%	2.378%	2.408%	2.410%	2.712%	1.344%
Comorbidities									
Hypertension	2,655,730 (97.6%)	1,378,865 (97.9%)	1,276,865 (97.2%)	1,094,849 (97.7%)	461,419 (97.6%)	416,127 (97.6%)	258,772 (97.6%)	232,526 (97.9%)	192,037 (96.1%)
Atherosclerotic CVD	2,312,456 (84.9%)	1,151,782 (81.8%)	1,160,674 (88.3%)	950,563 (84.8%)	397,332 (84.0%)	365,667 (85.8%)	226,379 (85.4%)	202,909 (85.4%)	169,606 (84.9%)
Dyslipidemia	1,619,065 (59.5%)	782,408 (55.6%)	836,657 (63.7%)	698,574 (62.3%)	261,614 (55.3%)	258,890 (60.7%)	149,928 (56.6%)	137,116 (57.7%)	112,943 (56.5%)
Anxiety disorder	1,308,584 (48.1%)	772,792 (54.9%)	535,792 (40.8%)	524,224 (46.8%)	246,575 (52.2%)	230,775 (54.1%)	117,154 (44.2%)	114,159 (48.0%)	75,697 (37.9%)
Diabetes	1,230,323 (45.2%)	671,540 (47.7%)	558,783 (42.5%)	533,723 (47.6%)	190,001 (40.2%)	196,230 (46.0%)	121,705 (45.9%)	102,248 (43.0%)	86,416 (43.2%)
COPD	1,185,821 (43.6%)	552,810 (39.3%)	633,011 (48.2%)	475,563 (42.4%)	220,649 (46.7%)	177,932 (41.8%)	119,892 (45.2%)	104,258 (43.9%)	87,527 (43.8%)
Anemia	1,105,450 (40.6%)	670,604 (47.6%)	434,846 (33.1%)	472,909 (42.2%)	208,860 (44.2%)	179,367 (42.1%)	95,878 (36.2%)	87,831 (37.0%)	60,605 (30.3%)
Atrial fibrillation	1,010,148 (37.1%)	552,168 (39.2%)	457,980 (34.8%)	429,361 (38.3%)	182,542 (38.6%)	154,769 (36.3%)	95,769 (36.1%)	88,030 (37.0%)	59,677 (29.9%)
Acute miyocardial infarction	592,154 (21.8%)	250,238 (17.8%)	341,916 (26.0%)	205,047 (18.3%)	113,272 (24%)	114,589 (26.9%)	53,426 (20.2%)	58,698 (24.7%)	47,122 (23.6%)
Hypothyroidism	526,761 (19.4%)	357,444 (25.4%)	169,317 (12.9%)	238,905 (21.3%)	85,682 (18.1%)	80,416 (18.9%)	45,753 (17.3%)	47,585 (20.0%)	28,420 (14.2%)
Chronic kidney disease	481,776 (17.7%)	234,610 (16.7%)	247,166 (18.8%)	218,273 (19.5%)	85,573 (18.1%)	74,063 (17.4%)	40,710 (15.4%)	35,538 (15.0%)	27,619 (13.8%)
Pulmonary embolism	211,552 (7.8%)	120,534 (8.6%)	91,018 (6.9%)	90,181 (8.0%)	34,897 (7.4%)	36,584 (8.6%)	18,463 (7.0%)	19,197 (8.1%)	12,230 (6.1%)
Selected lab parameters									
BNP, pg/ml	972.1 (247.5–3454.2)	1000.0 (259.0–3722.3)	947.8 (237.5–3273.0)	837.8 (206.0–3058.0)	592.0 (182.7–1790.8)	1842.0 (544.0–5008.0)	1586.0 (503.9–4408)	1183.0 (283.1–4950.5)	980.5 (133.8–3477.5)
NT-proBNP, pg/ml	1374.0 (350.2–4366.0)	1332.0 (335.4–4379.0)	1417.0 (368.9–4358.5)	1442.0 (375.0–4502.1)	1222.5 (351.3–3802.0)	947.9 (233.8–3376.0)	1721.0 (391.0–5442.0)	1906.0 (603.7–5348.0)	1430.0 (351.4–4480.0)
eGFR, (CKD-EPI)	68.1 (44.2–88.6)	64.9 (41.7–86.7)	71.4 (47.4–90.2)	67.1 (43.4–87.9)	66.4 (43.3–87.3)	68.4 (44.3–88.8)	67.7 (43.0–88.5)	70.8 (46.5–90.1)	74.5 (50.9–92.3)
Hemoglobin, g/dL	11.5 (9.0–13.4)	11.1 (8.8–12.7)	12.1 (9.3–14.1)	11.4 (8.9–13.3)	10.7 (6.4–13.0)	12.0 (10.0–13.6)	12.1 (9.8–13.8)	11.7 (9.4–13.5)	11.9 (8.4–13.8)
Medications									
Beta blocker	2,272,491 (83.5%)	1,150,579 (81.7%)	1,121,912 (85.4%)	931,685 (83.1%)	392,932 (83.1%)	361,266 (84.8%)	220,956 (83.4%)	195,152 (82.1%)	170,500 (85.3%)
ACE-i	1,207,761 (44.4%)	559,196 (39.7%)	648,565 (49.3%)	527,337 (47.1%)	203,979 (43.1%)	181,533 (42.6%)	107,148 (40.4%)	94,906 (39.9%)	92,858 (46.5%)
ARB	434,661 (16.0%)	239,803 (17.0%)	194,858 (14.8%)	199,051 (17.8%)	71,108 (15.0%)	68,318 (16.0%)	39,610 (14.9%)	31,595 (13.3%)	24,979 (12.5%)
ARNI	16,822 (0.6%)	5206 (0.4%)	11,616 (0.9%)	8679 (0.8%)	2697 (0.6%)	2519 (0.6%)	1054 (0.4%)	701 (0.3%)	1172 (0.6%)
MRA	1,058,504 (38.9%)	532,481 (37.7%)	529,300 (40.2%)	440,607 (39.3%)	196,064 (41.5%)	165,935 (38.9%)	100,308 (37.8%)	82,726 (34.8%)	72,865 (36.5%)
SGLT-2i	298,607 (11.0%)	150,448 (10.7%)	148,159 (11.3%)	125,438 (11.2%)	49,275 (10.4%)	50,664 (11.9%)	28,125 (10.6%)	25,395 (10.2%)	19,710 (9.9%)
Loop diuretic	1,677,344 (61.6%)	892,168 (63.4%)	785,176 (59.7%)	680,374 (60.7%)	298,463 (63.1%)	270,725 (63.5%)	166,362 (62.8%)	145,633 (61.3%)	115,787 (57.9%)
Device therapy									
ICD	23,133 (0.8%)	4990 (0.4%)	18,143 (1.4%)	11,123 (1.0%)	3073 (0.7%)	3240 (0.8%)	2396 (0.9%)	1624 (0.7%)	1677 (0.8%)
CRT	8894 (0.3%)	3042 (0.2%)	5852 (0.4%)	3860 (0.3%)	1047 (0.2%)	1512 (0.4%)	985 (0.4%)	650 (0.3%)	840 (0.4%)
LVAD	401 (0.0%)	57 (0.0%)	344 (0.0%)	218 (0.0%)	62 (0.0%)	57 (0.0%)	18 (0.0%)	21 (0.0%)	25 (0.0%)
Heart transplant	148 (0.0%)	38 (0.0%)	110 (0.0%)	87 (0.0%)	6 (0.0%)	24 (0.0%)	11 (0.0%)	7 (0.0%)	13 (0.0%)
RRT	141,102 (5.2%)	63,764 (4.5%)	77,338 (5.9%)	58,086 (5.2%)	26,931 (5.7%)	22,144 (5.2%)	14,232 (5.4%)	10,766 (4.5%)	8943 (4.5%)

(Table 1 continues on next page)

	All patients	Sex		Socio economic status					
	(n = 2,722,151)	Female (n = 1,407,927)	Male (n = 1,314,224)	SES–1[a] (n = 1,120,680)	SES–2[a] (n = 472,755)	SES–3[a] (n = 426,184)	SES–4[a] (n = 265,063)	SES–5[a] (n = 237,634)	SES–6[a] (n = 199,835)
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Outcomes									
Annual ED visits	5 (2–10)	5 (2–10)	5 (2–11)	4 (2–9)	5 (2–11)	5 (2–11)	5 (2–11)	5 (3–12)	7 (3–14)
Annual cardiology outpatient visits	3 (1–6)	3 (1–5)	3 (1–6)	3 (1–6)	3 (1–6)	3 (1–6)	3 (1–5)	3 (1–5)	3 (1–6)
Patients without any hospitalization	1,112,349 (40.9%)	641,885 (45.6%)	470,464 (35.8%)	467,718 (41.7)	188,006 (39.8)	165,632 (38.9%)	111,025 (41.9%)	107,288 (45.1%)	73,380 (36.7%)
LOS in hospital	6 (2–13)	6 (2–14)	6 (2–13)	6 (2–13)	6 (2–14)	6 (2–14)	6 (2–15)	6 (2–14)	5 (2–12)
All cause mortality	918,514 (33.7%)	458,108 (32.5%)	460,406 (35.0%)	377,220 (33.7%)	172,316 (36.4%)	145,993 (34.3%)	88,890 (33.5%)	75,936 (32.0%)	58,159 (29.1%)
Survival rates (%, 95% CI)									
1 year	82.7 (82.7–82.8)	83.3 (83.2–83.3)	82.1 (82.0–82.2)	82.3 (82.3–82.4)	80.9 (80.8–81.0)	82.5 (82.4–82.6)	83.5 (83.4–83.7)	85.2 (85.0–85.3)	85.6 (85.5–85.8)
5 year	59.9 (59.8–60.0)	61.5 (61.4–61.6)	58.2 (58.1–58.3)	60.0 (59.9–60.1)	57.0 (56.8–57.1)	59.0 (58.8–59.1)	60.0 (59.8–60.2)	63.2 (63.0–63.4)	64.4 (64.2–64.7)
7 year	56.0 (55.9–56.1)	57.7 (57.6–57.8)	54.2 (54.0–54.3)	56.1 (56.0–56.2)	52.9 (52.8–53.1)	54.9 (54.7–55.1)	56.1 (55.8–56.3)	59.4 (59.2–59.7)	61.0 (60.7–61.2)

Comorbidities are ranked by frequency of occurrence, Categorical variables are presented as n (%). Continuous variables are presented as mean (SD) and median (IQR). ACE-i = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, ARNI = angiotensin receptor-neprilysin inhibitors, BNP = brain natriuretic peptide, CVD = cardiovascular disease, COPD = Chronic obstructive pulmonary disease, CRT = cardiac resynchronization therapy, eGFR = estimated glomerular filtration, ED = emergency department, ICD = implantable cardioverter defibrillator, LOS = length of stay, LVAD = left ventricular assist device, MRA = mineralocorticoid receptor antagonist, NOAC = non-vitamin K antagonist oral anticoagulant, NT-proBNP = N-terminal pro-brain natriuretic peptide, RRT = renal replacement therapy, SES = socioeconomic status, SGLT-2i = sodium/glucose cotransporter 2 inhibitor. [a]SES-1 represents the least deprived region; SES-6 represents the most deprived region.

Table 1: **Characteristics of patients with heart failure in Türkiye according to sex and socioeconomic status.**

The use of drug therapies in patients with HF

Among patients with HF, 83.5% were treated with beta blockers, followed by angiotensin converting enzyme inhibitors (ACEI) (44%), mineralocorticoid receptor antagonists (MRA) (38.9%), angiotensin receptor blockers (ARB) (16%), and The angiotensin receptor–neprilysin inhibitor (ARNI) (0.6%). The proportion of patients with HF on any oral antidiabetic drug was 45.2%. Sodium glucose co-transporter-2 (SGLT2) inhibitors were used 11% of patients with HF, mostly in the presence of diabetes mellitus. Additionally, the use of conventional HF medical therapies, including beta blockers, ACEI/ARB/ARNI, MRA, and SGLT2 inhibitors, was higher in males compared to females (Table 1). The total number of patients using quadruple GDMT was 96,751 (3.6%), and for females and males 42,081 (3.0%) vs. 54,670 (4.2%) respectively. Any triple GDMT was noted in 643,159 (23.6%) of all patients, 299,521 (21.3%) vs. 343,638 (26.1%) of females and males, respectively. Other medical therapies were shown in Supplementary Table S2. The use of beta blockers, RAS inhibitors, MRA, and SGLT2 inhibitors was found to be lowest in the SES-5 group and highest in the SES-1 group (Table 1).

Advanced therapies in patients with HF

Of the 2,722,151 patients, 148 patients underwent heart transplantation, and 401 patients received a ventricular assist device between 2016 and 2022. The implantation rates for cardiac resynchronization therapy (CRT) and implantable cardioverter defibrillator (ICD) were, 3 per 1000 person-years and 8 per 1000 person-years, respectively (Table 1). The rate of heart transplantation was the highest in the SES-1 group.

Outpatient visits, emergency visits and hospitalizations in patients with HF

The median number of annual emergency department (ED) visits was 5 (2–10). Patients in the SES-6 group had the highest median ED visit of 7 (3–14) per year, while the least frequent ED visit was observed in the SES-1 group (4 [2–9] per year) (Table 1). Median annual cardiology outpatient visits were 3 (1–6) per year and were also similar among SES groups (Table 1). Of the study population, 41% were not hospitalized for any reason during the follow-up period, while the 1-year hospitalization rate is 36.7%. The median length of stay (LOS) in the hospital was 6 days per year for hospitalized patients with HF and was similar in both sex. The median LOS was longer in the first decade and in patients over 80 years of age (7 days/year). The median LOS was the shortest in patients with HF in the SES-6 group (5 days/year) (Table 1).

Survival rates of patients with HF

The mortality rate of patients with HF between January 1, 2016 and December 31, 2022 was 33.7% (918,514 out

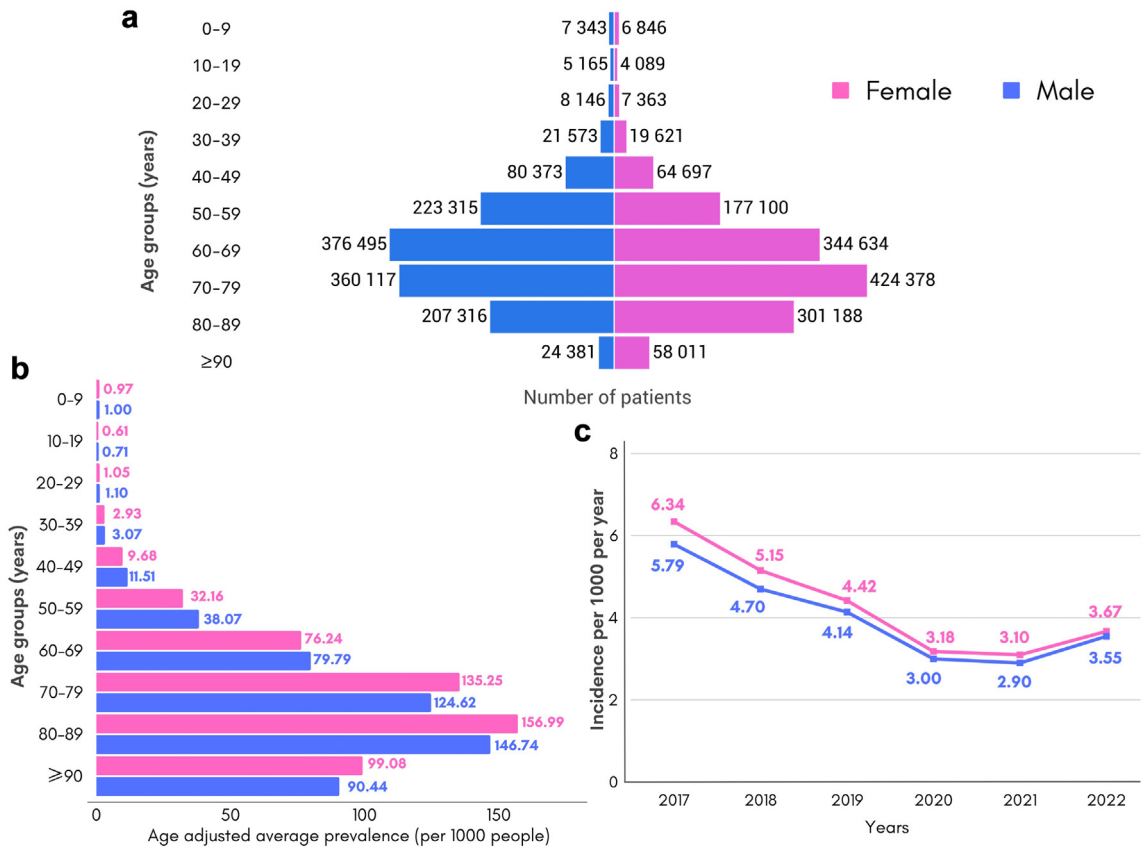


Fig. 1: Incidence and prevalence of patients with heart failure by age and sex. a) Turkish heart failure population pyramide. b) Age adjusted prevalence of heart failure in Türkiye. c) The incidence of heart failure in Türkiye between 2017 and 2022.

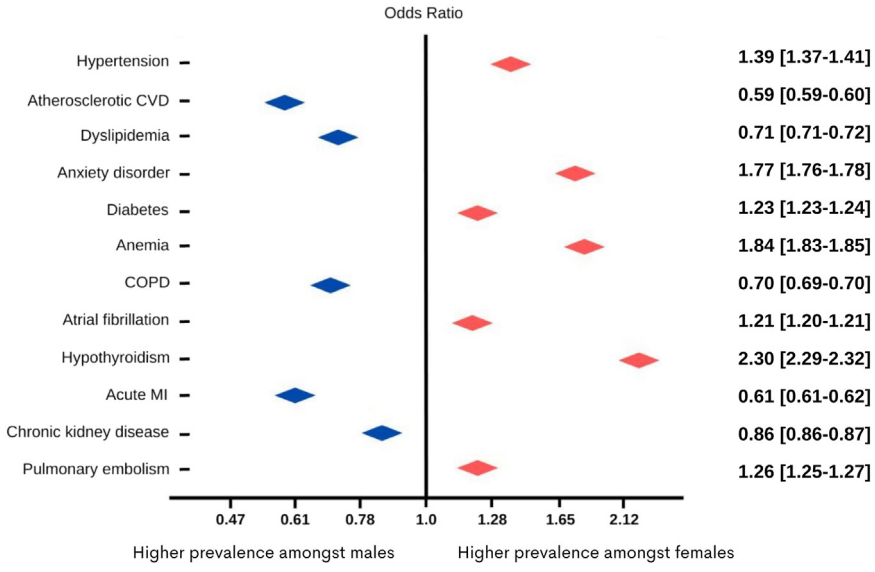


Fig. 2: Unadjusted comparison of males and females according to the frequency of comorbidities in heart failure (odds ratios >1 indicate a greater prevalence of the condition amongst females, whereas odds ratios <1 indicate a greater prevalence of the condition amongst males).

of 2,722,151). During this period, 32.5% of females (458,108 of 1,407,927) and 35% of males (460,406 of 1,314,224) died. The mortality rates were lowest in the SES-6 group (29.2%) and highest in the SES-2 group (36.4%) (Table 1). For the entire population, the survival rates at 1 year, 5 years, and 7 years stood at 82.7% (95% CI: 82.7–82.8), 59.9% (95% CI: 59.8–60.0), and 56.0% (95% CI: 55.9–56.1), respectively. Among patients diagnosed with HF, the survival rates at 1, 5, and 7 years were as follows: for females, 83.3% (95% CI: 83.2–83.3), 61.5% (95% CI: 61.4–61.6), and 57.7% (95% CI: 57.6–57.8), while for males, the rates were 82.1% (95% CI: 82.0–82.2), 58.2% (95% CI: 58.1–58.3), and 54.2% (95% CI: 54.0–54.3). The disparity in survival rates between male and female became more pronounced in age-adjusted survival analyses (Fig. 3).

Fig. 4 displays the survival analysis of patients with HF according to age and sex groups. Patients younger than 20 years old yielded no discernible sex difference. In patients with HF older than 20 years, females had a higher survival rate.

Discussion

Our study provides comprehensive and contemporary data on HF epidemiology in Türkiye. The prevalence of 2.114% across all age groups is close to previous reports from Western Europe and the USA, but higher than South America, China, Japan, South Korea, and Thailand, and lower than Germany and Canada.[12] Between 2017 and 2022, the incidence rates of HF in our nation ranged from 3.00 (in 2021) to 6.06 (in 2017) per 1000 person-years. These numbers were in line with the incidence rates (3.2 per 1000 person-years) reported in the 2019 HFA Atlas as well as studies conducted in various nations (1–20 cases per 1000 person-years).[3,13] A decline in HF incidence was observed in the years 2020 and 2021, but this decline was possibly linked to lower hospital admissions during the COVID-19 pandemic rather than a true decrease in HF incidence. The overall prevalence of HF was higher in females (2.23%) than in males (1.99%). When analyzed by age groups, males had a predominance until ages 60–69, while females overtook males after age 70. This finding is different

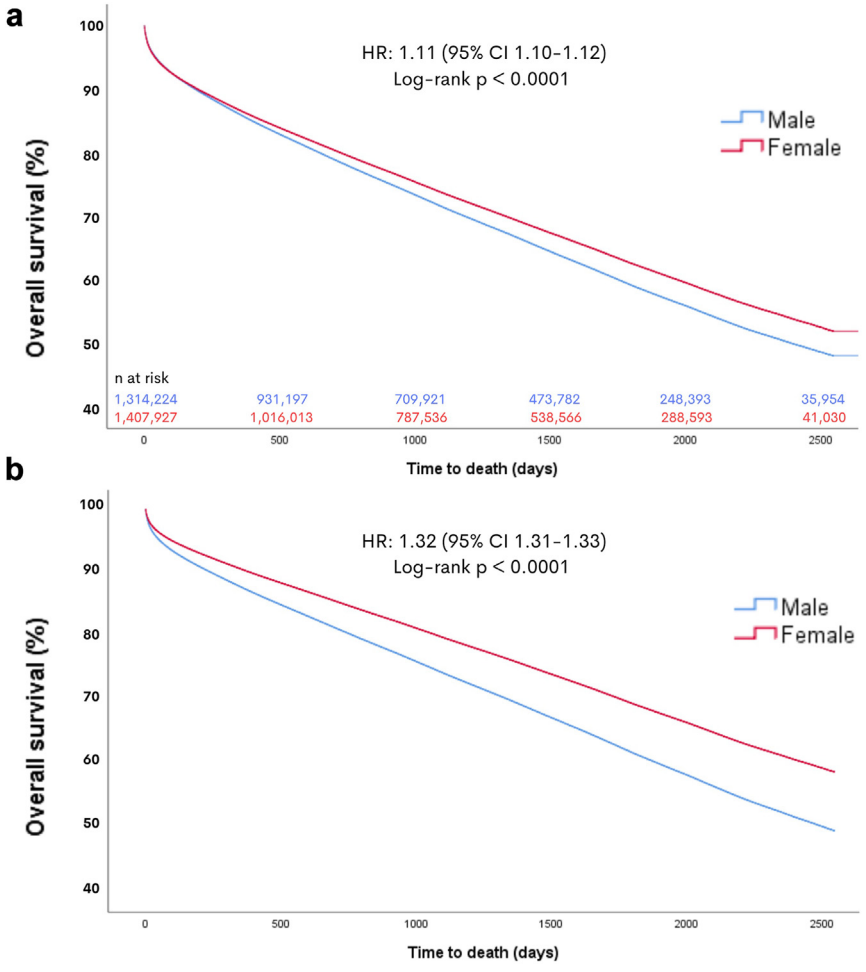


Fig. 3: a) Unadjusted survival curves of patients with heart failure by sex. b) Age adjusted survival curves of patients with heart failure by sex. The hazard ratios were calculated for males versus females.

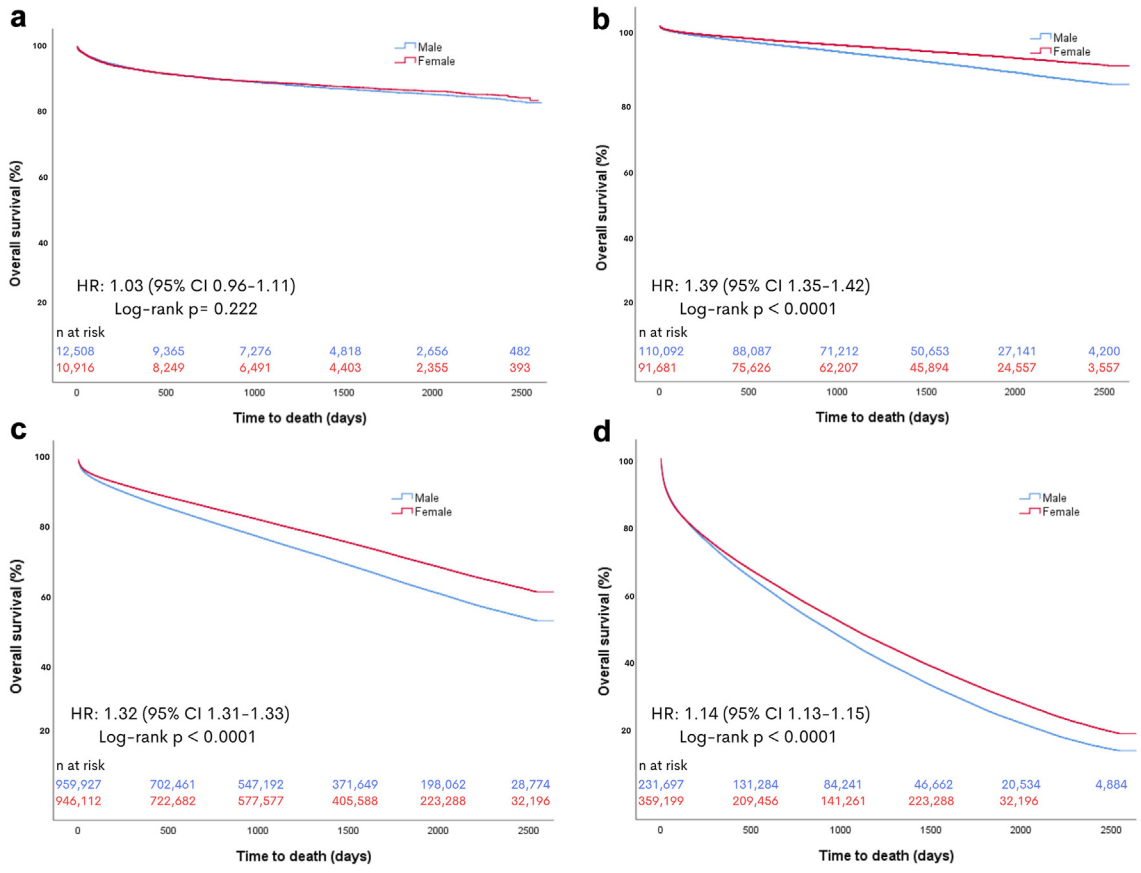
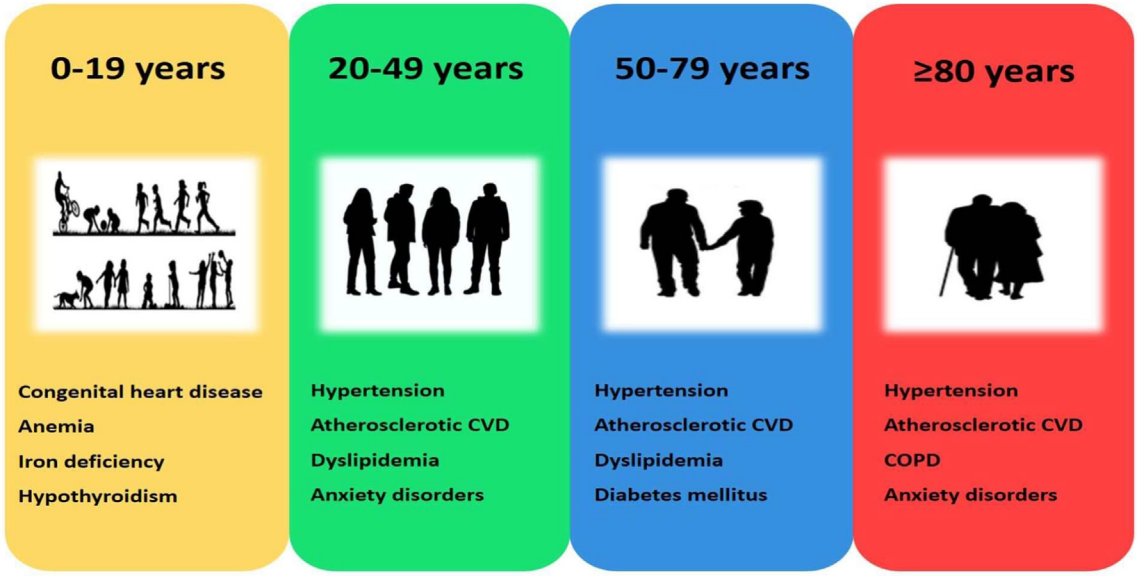


Fig. 4: Survival analysis of patients with heart failure according to age and sex groups (a: 0–19 years, b: 20–49 years, c: 50–79 years, d: ≥80 years). The hazard ratios were calculated for males vs. females.

from that in many countries, where the prevalence of HF was slightly higher in males.[14] The higher prevalence of HF in Turkish females is likely caused by their higher rates of obesity and diabetes than Turkish males as reported in previous meta-analyses[8,9] which may raise their risk for HF with preserved EF (HFpEF).[15] Of note, this finding was comparable to a previous national study, which reported a higher prevalence of asymptomatic diastolic dysfunction in females.[16]

The mean age at the onset of HF was ~8–10 years younger compared to European nations.[15] Earlier studies have shown that myocardial infarctions, the primary cause of HF in Türkiye, happen roughly 10 years earlier than in western nations and that the rate of acute coronary syndromes in people under the age of 50 is high.[17] HF in the young, i.e., those aged <50–55 years, is a growing issue in the western world, comprising around 3–12% of all adult patients with HF and affecting males more than females.[18,19] In our study, the prevalence of young patients with HF (i.e., 18–50 years) was 12% and the incidence was 0.3%, placing Türkiye among the countries with the highest burden of young patients with HF. These alarming statistics highlight the significance of risk factor management through lifestyle changes and promoting sports and physical activity among young Turks.

We believe that our study is the first to demonstrate the most common comorbidities among patients with HF across different age groups (Fig. 5). Data on patients with HF under 20 years of age are quite scarce in the existing literature, but recent studies show a trend towards increasing HF hospitalizations in this population.[6] In a systematic literature review, the incidence of HF in children showed a wide variation between 0.87 and 7.40 per 100,000 person-years depending on the different definitions of HF, statistical methods, and studied populations.[20] In a recent study using a health insurance database of >10 million people, the crude prevalence of HF in children was reported as 5.46 per 1000 people in Japan.[21] In our study, we identified 23,000 patients with HF at this age range, indicating a prevalence of 0.5 per 1000 people for ages 0–9 and 0.3 per 1000 people for ages 10–19. Congenital heart disease was the top issue, affecting 69.5% of those in the



CVD, cardiovascular disease; COPD: chronic obstructive pulmonary disease.

Fig. 5: The most common comorbidities according to age groups in patients with heart failure.

HF population aged 0–9 years. In the contemporary era, accurate and early diagnosis of congenital heart disease starting in the antenatal period might reduce the rate of HF in children.

Analysis according to SES showed that the rate of HF increased from the group of highly developed provinces (SES-1) to the group of less developed provinces (SES-5), but decreased in the SES-6 group. When the population-adjusted prevalence of HF is examined, provinces belonging to the SES-5 group had the highest prevalence, while those belonging to the SES-6 group had the lowest incidence. A population-based study conducted in the UK with about 4 million participants revealed that people with low SES had a 1.6-fold higher likelihood of developing HF and that their risk of doing so was 3.51 years earlier.[22] It is interesting to note that, despite a trend towards an increase in prevalence concomitant with the decline in SES in our study, the prevalence of HF was lowest in the SES-6 category, which is the least developed province group. Patients with HF in the SES-6 group were about 3 years younger than those from the other provinces, which may explain the lower prevalence of HF, though they had a higher rate of ED admissions. Noteworthy, the National Social Security Institution provides full coverage of health expenses for all insured and uninsured individuals living in Türkiye with comprehensive and non-discriminatory access to healthcare services, regardless of their economic status. Hence, it remains to be established whether this system may have eliminated major changes in the incidence and prevalence of HF at various socioeconomic levels.

Anxiety and depression were reported in 40.8% and 48.1% of the patients, respectively. Females had a 1.7-fold higher risk of developing mood disorders than males. As this rate is not derived from systematic screenings but from ICD-10 codes reported by the physicians during their daily practice, we may assume that the true frequency of anxiety and depression is even higher. A systematic review analyzing data from 23 countries reported the pooled prevalence of any severity of depression as 41.9%, and a higher prevalence was noted in the EMRO region (70.1%) and lower economic status countries (56.7%).[23] Of note, anxiety disorders are reported in up to 30% of patients with HF.[24] However, this rate might be higher if systematic prospective evaluation is provided in an outpatient HF clinic. The link between anxiety disorders and outcomes in patients with HF is less well established compared to depression.

Diabetes was diagnosed in nearly half (45.7%) of the Turkish patients with HF. On a global scale, the prevalence of diabetes among individuals with HF ranges from 10% to 47%, positioning Türkiye among the countries with one of the highest rates.[25,26] Consistent with previous epidemiological data, the prevalence of diabetes among female patients with HF significantly surpasses that among their male counterparts (47.7% vs. 42.5%, Table 1).[9] Considering the recent guidelines, it is advisable to conduct comprehensive screening for HF in patients with diabetes, aiming to identify the condition even before the manifestation of symptoms and signs.[27]

In our study, medications used for the treatment of HF were assessed regardless of ejection fraction (EF). Similar to global data, beta blockers were the most widely prescribed agents among the GDMT for HF in our country. RAS inhibitors were given at relatively low rates, however, since EF data was not available, we could not identify what percentage of heart failure with reduced EF (HFrEF) patients received RAS blockers. ARNI use was remarkably low in our nation. Despite being on the market, ARNI has not received reimbursement from the universal health coverage system in Türkiye and this yields much less frequent use, though it is recommended. In the latest guidelines, SGLT2 inhibitors are recommended for all patients with HF regardless of the EF, however, only 11% of patients with HF receive SGLT2 inhibitors in Türkiye.[28] These agents are currently not reimbursed for patients without diabetes, though, they could be out-of-pocket prescribed by cardiologists in Türkiye.

The use of device therapies including ICD and CRT was again strikingly low in Türkiye. ICD implantation was reported to be 20%, and CRT was about 15% in the European registry data.[29] Although all patients with HF, regardless of their EF, were included in our study, the rate of ICD and CRT in our nation was still very low (0.8% and 0.3%, respectively) expecting nearly half of the patients to have HFrEF, and considering the eligibility criteria for device therapies. We think that the reasons for the underutilization of device therapies may be related to problems in reimbursement of ICD/CRT devices.

A small percentage of patients have advanced HF and may need specialized care, including heart transplantation or ventricular assist devices. This study found that, when compared to global statistics, the number of heart transplants performed in our nation (148 patients) was noticeably lower. Additionally, only 401 patients received left ventricular assist devices, which are primarily used as a bridge to transplantation. It is known that the poor heart transplantation rates worldwide, including in our country, are mostly associated with the shortage of donor organs due to the public's refusal to accept donor hearts because of cultural, religious, and psychosocial factors. Other challenges in Türkiye are the relatively low number of centers and experienced staff capable of performing cardiac transplantation and ventricular support device implantations despite fully reimbursements of those procedures. Moreover, increasing awareness of cardiology specialists for referring patients may be a solution for the underutilization of ventricular assist device therapies.

Mortality and hospitalization rates are the main outcomes in HF studies. In a systematic review of 1.5 million patients with HF from Europe or North America, survival estimates at 1, 5 and 10 years were 86.5%, 56.7%, and 34.9%, respectively.[30]

When the mortality rates of patients with HF were subcategorized based on sex, it was observed that males had a 1.114-fold higher death risk than females. This finding might be related to the better prognosis of HFpEF, which is the more prevalent phenotype of HF in females in international registries. The impact of sex on mortality was not evident in patients with HF under 20 years of age. This can be explained by the fact that congenital heart diseases are the primary cause of HF in this age group. Hence, the absence of a significant sex effect on mortality in this context is an anticipated finding.

Limitations

There are some limitations worth mentioning. The main limitation of the study was missing data on EFs and some laboratory tests at index diagnoses due to system-based shortcomings in the coincident reporting. Country-wide integration of the laboratory data into the merged database has not been completed until 2018, since then, all accompanying laboratory data have been available for each patient. Transthoracic echocardiography was performed in all patients, however, as the integration of the discrete echocardiography reports with the main database could not be established, we were unable to analyze the patients according to their EFs. Of note, a separate analysis is being thoroughly discussed in a representative, randomly selected sample. Secondly, since measurement of natriuretic peptides was not part of the usual practice for diagnosis, particularly for HFrEF, we were limited by the acquired number of tests, which needs to be improved. Thirdly, since the whole coverage of the Ministry of Health dates back to 2016, we did not acquire data before that time due to a lack of representativeness of the whole country. Fourthly, since we are not commissioned to have access to the data of 85 million citizens, we were unable to compare patients with HF with the non-HF population, limiting some of the conclusions. Last but not least, a word of caution is required for the reality that these electronic healthcare records are based on administrative claims that are, as a rule, contemplated for reimbursement by the paying bodies, and there are challenges when they are aimed at research. However, it is a matter of all the similar studies in the literature. Of note, Türkiye, is somewhat uniform in this regard, as there is universal health insurance for all citizens, covered and hence regulated by a single major payer, the Social Security Institution. Besides, since the Ministry of Health has currently merged and governed all healthcare data, i.e., not only ICD-10 codes but also medication, admission, cost data, etc., there is always a chance to scan for any ambiguities. Fiftly, the survival analyses displayed were exclusively adjusted for age, raising the possibility of residual confounding. And finally, failure of some patients to apply to any heathcare

institution during the study period might have resulted in underestimating the true prevalence of HF.

In conclusion, HF is a significant healthcare issue that is linked to high resource consumption and the expense of care. In Türkiye, HF develops at a younger age compared to western populations, but the survival rates of the patients are quite similar to the rates reported in those countries. Despite the significant advantages of a full health coverage system, usage of device therapies and the number of cardiac transplantations are low, and this requires increased awareness among physicians and the population along with specific regulations to enhance patient referral.

Contributors

AC-study design, writing, DU-data interpretation, writing, AS-data collection, writing, ITC, data collection, writing, EAK-study design, resources, NA-study design, resources, EA-data collection, MOA-data analysis, MMU-study design, AT-data collection, YC-data collection, RDA-data collection, SN-data collection, LDA-data collection, SM-data collection, SB-resources, MBY-study design, writing.

Data sharing statement

The data supporting the findings of this study are available at a secure server at Turkish Ministry of Health. Access to data requires permission from Turkish Ministry of Health.

Editor note

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Declaration of interests

The authors declare no conflicting interests.

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None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2023.100723.

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