ORIGINAL ARTICLE

Turkish registry for diagnosis and treatment of acute heart failure: TAKTIK study

Türkiye akut kalp yetersizliği tanı ve tedavi anketi: TAKTİK çalışması

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ABSTRACT

Objective: The goal of this study was to develop a national database of patients hospitalized in Turkey with acute heart failure (AHF) using evaluations of diagnostic and therapeutic approaches.

Methods: Patient data were collected using an Internet-based survey. A total of 588 patients were enrolled from 36 participating medical centers across the country.

Results: Mean age was 62±13 years and 38% of the patients were female. Ratio of de novo AHF to study cohort was 24%. Coronary heart disease and hypertension were found in 61% and 53% of the patients, respectively. Valvular heart disease was the underlying cause in 46% of heart failure patients. The most frequent factor associated with decompensation was noncompliance with treatment, observed in 34% of patients. Systolic blood pressure was 125±28 mmHg and heart rate was 93±22 beats/minute in the cohort. The most common findings on physical examination were inspiratory fine crackles (84%), peripheral edema (64%), and cold extremities in 34%. Mean ejection fraction (EF) measured at admission was 33±13%. Preserved EF (≥%40) was present in 20% of patients. On admission, 60%, 46%, and 40% of patients were using angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, beta-blocker, or aldosterone antagonist, respectively. In-hospital events were reported as 3.4% death, 1.6% stroke and 2% myocardial infarction.

Conclusion: Compared to previous data collected around the world, AHF patients in Turkey were younger, had more frequently valvular heart disease as the underlying cause, and were more noncompliant with medical treatment, but overall mortality was lower. Drugs shown to reduce mortality, and which also form the basis of guideline-directed medical therapy, are still used inadequately.

ÖZET

Amaç: Bu çalışmanın amacı, Türkiye'deki akut kalp yetersizliği (AKY) nedeni ile yatan hastalarda tanı ve tedavi yöntemlerinin değerlendirilmesi sonucu ulusal bir veri tabanı oluşturmaktır.

Yöntemler: Hasta verileri internette yer alan anket formunun doldurulması ile toplandı. Çalışmaya Türkiye'de 36 merkez katıldı ve 558 hasta alındı.

Bulgular: Ortalama yaş 62±13 yıl olup, hastaların %38'i kadındı. Yeni ortaya çıkan AKY oranı %24 idi. Hastalarda sırasıyla, %61'inde koroner kalp hastalığı ve %53'ünde hipertansiyon eşlik etmekteydi. Altta yatan sebepler arasında kalp kapak hastalığı kalp yetersizliği hastalarının %46'sında mevcuttu. Yetersizliği tetikleyici faktörler arasında en sık tedaviye uyumsuzluk hastaların %34'ünde gözlendi. Hastaların sistolik kan basıncı 125±28 mmHg, kalp hızı 93±22 atım/dk idi. Fiziksel incelemede en yaygın bulgular akciğerde ral %84, periferik ödem %64 ve ekstremitede soğukluk %34 oranında saptandı. Başvuru sırasında ölçülen ortalama ejeksiyon fraksiyonu (EF) %33±13 idi. Korunmuş EF (≥%40) hastaların %2'sinde vardı. Hastaların kabuldeki anjiyotensin dönüştürücü enzim inhibitörü/anjiyotensin reseptör blokeri, beta-bloker ve aldosteron antagonisti kullanım oranları sırasıyla %60, 46 ve 40 idi. Hastane içi olaylar %3.4 ölüm, %1.6 inme ve %2 miyokart enfarktüsü olarak bildirildi.

Sonuç: Dünya ölçeğinde toplanmış bazı araştırma verileriyle karşılaştırıldığında, Türkiye'de AKY hastaları daha genç olup daha büyük bir sıklıkla altta yatan neden olarak kalp kapakçığı hastalığına sahipti. Tıbbi tedaviye daha fazla uyumsuz olmalarına rağmen genel mortalite oranı daha düşüktü. Mortaliteyi düşürdüğü gösterilen ve aynı zamanda kılavuzların yönlendirdiği tıbbi tedavinin temelini oluşturan ilaçlar hâlâ yetersiz kullanılmaktadır.

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Acute heart failure (AHF) is a fatal syndrome characterized by rapid onset or worsening of symptoms and/or signs of heart failure (HF).[1,2] Definition of AHF encompasses both de novo HF and recent decompensation of chronic heart failure (CHF). This syndrome has high rate of mortality and morbidity, and is a leading cause of hospitalization worldwide. Despite that, AHF syndrome has received less attention than CHF, and the majority of information regarding AHF was derived from large surveys and registries, rather than prospective clinical trials.

Large epidemiological studies, such as the Acute Decompensated Heart Failure National Registry (ADHERE) in the United States (US), the EuroHeart Failure Survey II (EHFS II) and the more recent European Society of Cardiology Heart Failure Pilot Study (ESC-HF Pilot) representing pooled data from European countries, and the worldwide Acute Heart Failure Global Survey of Standard Treatment (ALARM-HF), have provided important insights regarding background characteristics, clinical presentation, emergency diagnosis and evaluation, as well as initial and long-term treatment and short-term survival of AHF patients.[3–6] These studies also disclosed regional variations and temporal trends for evaluation and treatment of AHF and reduction in mortality with guideline-directed approach to diagnosis and treatment. Despite recent tremendous progress in the field of HF treatment, rates of both in-hospital mortality (10.7% in ALARM-HF) and 1-year mortality (17.4% for hospitalized patients in ESC-HF Pilot) remained high, and subgroup analyses revealed higher mortality in some patient subsets, such as those with reduced (<45%) ejection fraction (EF) (3.9% in ADHERE).[3,5,6]

Although large multinational surveys and registries offer important information on patient characteristics and management strategies for AHF, national surveys, such as the French Observatoire Français de l'Insuffisance Cardiaque Aiguë (OFICA) or the Italian Network on Heart Failure (IN-HF) convey essential knowledge for a particular region, since geographic variations tend to change patient characteristics.[7,8] Moreover, establishing record of regional variations in treatment strategies allows for comparison of AHF outcomes and an estimate for establishment of guidelines in a particular country. Present manuscript is the first report of a prospective nationwide AHF survey in Turkey, a country with more than 70 million inhabitants, and adds to information on clinical characteristics, patient profiles, treatment strategies, in-hospital outcomes, and prescribed medications. This study also provides a benchmark for future studies that will enable evaluation of temporal trends in AHF outcomes in Turkey.

Abbreviations:

ACE	*Angiotension-converting enzyme*
ARB	*Angiotension receptor blocker*
AHF	*Acute heart failure*
CAD	*Coronary artery disease*
CHF	*Chronic heart failure*
EF	*Ejection fraction*
GDMT	*Guideline-directed medical treatment*
HF	*Heart failure*
HFpEF	*Heart failure with preserved EF*
HFrEF	*Heart failure with reduced EF*
MRA	*Mineralocorticoid receptor antagonist*

METHODS

Turkish registry for diagnosis and treatment of acute heart failure (TAKTIK=Türkiye Akut Kalp Yetersizliği Tanı ve Tedavi Anketi) was a prospective national survey of 36 medical centers across Turkey that volunteered to collect and send data on AHF patients admitted to participating study centers between December 2007 and June 2009. At least 1 investigator was responsible for collection and electronic transmission of patient data at each study site. At centers with more than 1 investigator, a research coordinator was chosen to organize and transmit collected data. Centers included 22 university hospitals, 6 training and research hospitals, 6 state hospitals, and 2 private hospitals across the country. Figure 1 provides the distribution of study patients according to province. An electronic data collection and transmission system

Figure 1. The distribution of study patients by province.

(www.epikriz.com) was used to enter and transmit patient data to the study coordination center. Throughout the study, participating centers and investigators were free to choose diagnostic steps and management strategies according to institutional algorithms and individual decision-making.

Patient selection

All patients admitted to study institutions were included in the study if they 1) had both signs (e.g., exercise dyspnea, orthopnea, paroxysmal nocturnal dyspnea) and symptoms (e.g., hypotension, jugular venous distention, tachycardia, audible S3, pretibial edema) compatible with heart failure, and 2) there was objective evidence of pulmonary congestion (e.g., audible fine crackles over lungs or signs compatible with pulmonary congestion on chest roentgenogram). Echocardiographic or laboratory (e.g., B-type natriuretic peptide levels) findings were not required, but were recorded when available.

Data regarding demographic variables, past medical history, coexisting disease, drug use at admission, previous heart failure, or documented asymptomatic left ventricular dysfunction, clinical presentation at admission, initial examination findings, echocardiographic and laboratory findings, in-hospital treatment including pharmacological agents, percutaneous or surgical interventions, device implantation, final treatment at discharge, and in-hospital outcome, as well as complications were recorded by the investigator on an electronic questionnaire. Validity and reliability of the collected data were maintained by 6 regulators randomly assigned to 6 study centers (again selected randomly), and all data from a particular study center were rejected if any inconsistencies between actual and reported data were noted by regulators.

The study was conducted according to the principles of the Declaration of Helsinki and ethical approval was obtained from the Ege University Medical School Clinical Research Ethics Committee (decision date: December 5, 2007; decision number: 07-11/8).

Statistical analysis

All statistical analyses were performed using statistical software (SPSS version 17.0; IBM Corp., Armonk, NY, USA). Continuous data were expressed as mean+/-SD. Categorical variables were expressed as percentages.

RESULTS

Demographic, clinical findings and medications on admission (Table 1)

Mean age of patients was 62±13 years, and 38% of patients were female. Diagnosis was de novo HF in 114 of 558 patients (24%), while remaining 444 patients had known CHF (76%). 61% of patients had coronary artery disease (CAD), while 51% had hypertension, 40% had diabetes, 20% had chronic obstructive pulmonary disease, and 16% had renal failure as co-morbidities. In addition, atrial fibrillation was observed in 32% of patients, and valvular heart disease was present in 46%.

Table 1. Initial demographic and clinical findings of patients included in the TAKTIK study

	%	Mean±SD
Age (years)		62±13
Female	38	
De novo acute heart failure	24	
Coronary artery disease	61	
Hypertension	53	
Diabetes mellitus	40	
Chronic obstructive pulmonary disease	20	
Chronic renal failure	16	
Valvular disease	46	
Atrial fibrillation	32	
Acute coronary syndrome	29	
Arrhythmia	30	
Infection	22	
Noncompliance to medical regimen	34	
Systolic blood pressure (mmHg)		125±28
Systolic blood pressure <90 mmHg	3	
Systolic blood pressure 90–140 mmHg	78	
Systolic blood pressure >140 mmHg	19	
Heart rate (beats/min)		93±22
Respiratory rate (breaths/min)		23±7
Confusion	9	
Peripheral edema	65	
Cold extremities	34	
Inspiratory rales	84	
Jugular venous distention	41	
Hepatomegaly	24	

SD: Standard deviation.

The most frequent finding on physical examination was pulmonary rales, which was observed in 84% of patients. Other physical examination findings, in order of decreasing frequency, were pretibial edema (64%), jugular distention (39%), coldness in extremities (34%), hepatosplenomegaly (25%), and altered mental state (9%).

Cause of decompensation was associated with new acute coronary event in 29% of patients, ventricular or supraventricular arrhythmia in 30%, infection in 18%, and non-compliance with medical treatment in a further 34%. Some patients exhibited more than 1 cause of decompensation.

Laboratory findings on admission (Table 2)

On electrocardiography, 35% of patients had rhythm other than sinus, 23% had left bundle branch block, and 28% had ST segment abnormalities. Cardiomega-

Table 2. Initial laboratory findings of patients enrolled in the TAKTIK study

	%	Mean±SD
Electrocardiography		
Abnormal rhythm	35	
Pathological Q waves	42	
Left ventricular hypertrophy	19	
Left bundle branch block	23	
ST segment elevation	6	
ST segment depression	22	
Normal ST segment	72	
Telecardiography		
Cardiomegaly	78	
Pulmonary congestion	71	
Pleural effusion	45	
Echocardiogrphy		
Patients with available echocardiographic data	88	
Left ventricular ejection fraction		33±13
Ejection fraction >% 40	20	
Moderate-to-severe mitral regurgitation	37	
Moderate-to-severe mitral stenosis	3	
Moderate-to-severe aortic regurgitation	6	
Moderate-to-severe aortic stenosis	2	
Moderate-to-severe tricuspid regurgitation	36	
Moderate-to-severe tricuspid stenosis	1	
Complete blood count and blood chemistry		
Hemoglobine (g/dL)		12.4±2.1
Creatinine (mg/dL)		1.4±0.9
Troponin I (ng/mL)		2.2±9
Sodium (mEq/L)		136±5
Potassium (mEq/L)		4.4±0.7
Coronary Angiography		
Patients with available coronary angiographic data	52	
Three-vessel disease	41	
Significant proximal LAD or LMCA stenosis	48	
Nonsignificant/normal	30	

LAD: Left anterior descending artery, LMCA: Left main coronary artery; SD: Standard deviation.

ly (78%) and pulmonary congestion (71%) were most frequent findings on telecardiography. Mean hemoglobin level was 12.4±2.1 g/dL in study participants, while mean serum creatinine was 1.36±0.9 mg/dL. Of note, troponin I level was significantly elevated (2.2±0.9 ng/mL). Echocardiographic data was available in 88% of patients. Mean EF% was 33±13, while percentage of patients with EF% of 40% or more (preserved EF%, [pEF]) was 20%. The most frequent valvular disease was mitral regurgitation, seen in 37% of patients. Coronary angiography was performed during or before hospitalization on 52% of patients. Of patients with available coronary angiography data, 70% had significant CAD in at least one major coronary artery.

In-hospital course and outcomes (Table 3)

The most common agent used during hospitalization was diuretic, administered to 86% of patients, followed by parenteral nitrates in 55%. At least 1 inotropic agent was administered to 31% of patients during hospitalization, with dobutamine being the most common agent used (23%). Noninvasive ventilation was used on 4% of patients, and 3% needed intubation and mechanical ventilation. Left ventricular support was used on 1% of patients, and a further 1% received ultrafiltration or dialysis during hospitalization. Table 3 provides a summary of medical treatment during hospitalization.

During follow-up, 3.4% of patients died in-hospital, and stroke was seen in 1.6% of patients. Myocardial infarction was experienced by 2% of patients hospitalized with AHF, either diagnosed at admission or seen during hospitalization.

Table 3. In-hospital treatment of patients enrolled in the TAKTIK study

	%
Noninvasive ventilation	4
Invasive ventilation	3
Intravenous diuretics (bolus/continuous)	61/25
Intravenous nitrates	55
Intravenous inotropes	31
Intravenous dopamine	18
Intravenous dobutamine	23
Intravenous levosimendan	6
Intra-aortic balloon pump	1
Ultrafiltration/Dialysis	1

Medications at discharge (Table 4)

Table 4 is a summary of medications used by patients prior to hospitalization and prescribed after discharge. Before hospitalization, 60% of patients were taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), while another 46% used beta-blocker, and 40% took mineralocorticoid receptor antagonist (MRA). Slight increase was seen in percentage of patients prescribed beta-blocker (57%) and MRA (52%) after discharge, and dramatic increase in percentage of patients using cardiac glycoside was observed: Percentage rose from 4% before hospitalization to 33% after hospitalization. Finally, statins were more frequently prescribed at discharge (35%) compared to before admission (23%).

Table 4. Medications received by patients enrolled in the TAKTIK study at admission and discharge

Drugs	Admission (%)	Discharge (%)
Diuretic	62	63
Angiotensin converting enzyme inhibitor	50	54
Angiotensin receptor blocker	10	8
Beta-blocker	46	57
Mineralocorticoid receptor antagonists	40	52
Digoxin	4	33
Vitamin K antagonist	14	10
Antiaggregant	65	67
Statin	23	35
Antiarrhytmic	14	7

DISCUSSION

Present prospective survey characterized AHF patient population in Turkey on a nationwide basis, and illustrated current practice standards for AHF patients in Turkey. Findings underlined significant differences in clinical presentation of AHF patients in Turkey compared with other surveys from across the world. Furthermore, results indicated that treatment strategies were not based entirely on guideline-directed medical treatment (GDMT), emphasizing the need for further education of physicians and healthcare workers caring for AHF patients, since adherence to GDMT is associated with improved outcomes.

Registries and surveys conducted around the world have demonstrated significant differences between AHF patients admitted to emergency care, depending on particular geographic location where the study was conducted (Table 5). Patients in the US and European countries were somewhat older, with mean age ranging between 70 and 75 years.(3-5) In contrast, Damasceno et al. found mean age of patients was 52 years in Sub-Saharan Africa.[9] In the Gulf Acute Heart Failure Registry (Gulf CARE) study, which enrolled patients from Gulf countries, mean age of patients was 59 years.[10] Our figures correspond to midpoint between these extremes, with mean age of 62±13 years. Mean age was 61 years in the earlier Heart Failure Prevalence and Predictors in Turkey (HAPPY) study conducted to assess prevalence of chronic heart failure in Turkey.[11] This variance in international results reflects different etiologies of AHF in different countries. For example, frequency of valvular heart disease in the present study was higher than that seen in European and American registries, probably due to high rheumatic valve disease prevalence in Turkey.[3–6,12] Rheumatic valve disease and its sequelae affect patients at younger age than other etiologies, such as CAD. Only 22% of HF patients with reduced EF (HFrEF) in ADHERE registry had accompanying valvular disease.[3] Younger age at presentation in Turkey compared with other Western countries could have important consequences, since age group includes an important portion of active workforce, thus further adding to economic burden already increased by hospitalization.

Comorbidities in our patient cohort were somewhat similar to other reports; however, hypertension was significantly lower (51% in our cohort compared with 74% in ADHERE and 62% in EHFS II) and closer to findings of Damasceno et al. (56%).[3,4,9] Patients with HFpEF constituted roughly half of patient population in ADHERE and EHFS II registries, and had more favorable in-hospital outcome compared to HFrEF. Relatively fewer patients with hypertension, together with younger age at presentation and fewer female patients at admission (40% compared with 52% in ADHERE population), in contrast to studies conducted in the US and Europe, could explain why HFpEF was infrequent (20%) in our patient population. This trend was also seen in studies of Damascano et al. and Perna et al. conducted in Sub-Saharan Africa and Argentina, respectively.[9,13] Trend of fewer HFpEF admissions outside the Western world is intriguing and certainly deserves more study. Possible explanations include genetic influences, younger admission age, reduced incidence of hypertension in AHF population, differences in definition, or underdiagnosis in countries other than the US or Europe. In addition, to assess the actual prevalence of HFpEF, echocardiographic data must be available at both admission and discharge, as some patients with HFpEF could have temporary reduction of EF% due to precipitating factors. It is not possible to make a more definitive comment based on the present report, as echocardiography was reported voluntarily and only EF data at admission was available for our cohort.

In the present study, incidence of de novo HF was 24%; prevalence has been reported at between 12% and 70% in other registries (Table 5). Interestingly, prevalence of de novo HF shows regional distribution. Data from the US have indicated either comparable (23% in ADHERE registry) or lesser prevalence of de novo HF (12% in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure [OPTIMIZE-HF]),[3,14] while registries and surveys from eastern Asia have reported the highest figures (63% in the Korean Heart Failure [KorHF] study from South Korea and 64% in the Acute Decompensated Heart Failure Syndromes [ATTEND] study from Japan).[15,16] Frequency of de novo HF in Europe and the Middle East has been somewhere in-between, but higher than the ratio in the TAKTIK survey. However, in the majority of reports, including the present report, CHF patients with acute decompensation predominate. These findings emphasize that rehospitalizations are frequent occurrence

Table 5. Comparison of patient characteristics of TAKTIK survey and similar registries/surveys reported in the literature

	ADHERE[3] (n=105388)	OPTIMIZE-HF[14] (n=48612)	EHFS-II[4] (n=3580)	AHEAD[21] (n=4153)	TAKTİK (n=558)	IN-HF[22] (n=1855)	OFICA[7] (n=1658)	HF-Pilot[5] (n=1892)	THESUS-HF[9] (n=1006)	ATTEND[16] (n=4842)	Gulf-CARE[10] (n=5005)
	USA	USA	Europe	Czech	Turkey	Italy	France	Europe	Africa	Japan	Middle East
	2002–2004	2003–2004	2004–2005	2006–2009	2007–2009	2007–2009	2009	2009–2010	2007–2010	2007–2011	2012
Mean age (years)	72±14	73±14	70±13	72±12	62±13	72±12	76±13	70±13	52±18	73±?	59±15
Female (%)	52	52	39	42	38	40	46	37	51	42	37
New onset HF (%)	23	12	37	58	24	43	28	25	–	64	45
Coronary artery disease (%)	57	50	54	51	61	42	44	51	8	31	47
Hypertension (%)	73	71	63	73	53	58	62	62	56	69	61
Diabetes (%)	44	42	33	43	40	40	31	35	11	34	50
Atrial fibrillation (%)	31	31	39	27	32	38	38	44	18	36	12
COPD (%)	31	28	19	16	20	30	21	–	–	10	–
CRF (%)	30	20	17	–	16	33	15	26	8	–	15
Valvular disease (%)	22	–	34	10	46	–	–	–	–	20	9
SBP (mmHg)	144±33	143±33	–	135[a]	125±28	134±33	130±29	133±29	130±34	145±37	137±34
SBP <90 mmHg (%)	1	8	2	–	3	–	–	–	–	8[b]	–
SBP 90–140 mmHg (%)	70	44	48	–	78	–	–	–	–	42[b]	–
SBP >140 mmHg (%)	29	48	50	–	19	–	–	–	–	50	–
Peripheral edema (%)	66	85	23	–	65	56	–	65	–	67	54
Cold extremities (%)	–	–	–	–	34	11	–	9	–	23	–
ACS (%)	–	15	30	36	29	–	13	–	–	–	27
Arrhythmias (%)	–	14	32	8	30	–	24	–	–	–	6
Infection (%)	–	15	18	–	22	–	27	–	–	–	15
Non-compliance with treatment (%)	–	9	22	–	34	–	–	–	–	–	19
Hemoglobin (g/dL)	12.4±2.7	12.1±3.4	–	13.2[a]	12.4±2.1	12.5±2.1	–	–	12.2±2.6	12±2.6	12.6 (a)
Creatinine (mg/dL)	1.8±1.6	1.8±1.8	–	1.2[a]	1.4±0.9	1.5±1	1.5±0.9	–	1.4±1.2	1.4±1.6	1.5±1.3
Left ventricular EF (%)	34±16	39±18	38±15	37[a]	33±13	38±14	42±16	38 (a)	40±17	–	35 (a)
EF >% 40 (%)	37	51	34 (>%45)	–	20	35	45	36	–	47	31
Diuretic (%)	70	66	71	55	62	64	–	68	15	49	58
ACE-I/ARB (%)	53	52	64	60	60	59	–	60	73	45	56
Beta-blocker (%)	48	53	43	51	46	41	–	62	15	34	44
MRA (%)	9	7	28	23	40	17	–	54	65	20	17
Digoxin (%)	28	23	26	17	4	17	–	21	45	12	17
In-hospital mortality (%)	4	3.8	6.7	12.7	3.4	6.4	8.2	3.8	4.2	6.4	6.3

ACE-I: Angiotension-converting enzyme inhibitor; ARB: Angiotension receptor blocker; COPD: Chronic obstructive pulmonary disease; CRF: Chronic renal failure; EF: Ejection fraction; SBP: Systolic blood pressure. See the text for references. Data are given as mean±SD or percentage unless indicated otherwise.

[a]This value is provided as a median. [b]Hypotension was defined as SBP<100 mmHg.

for patients with CHF and that management strategies to reduce rehospitalization would be of benefit. Data obtained using US Medicare program samples indicated high rate of 30-day rehospitalization following discharge (24.8%), which could be improved with adequate treatment of congestion during hospitalization.[17] Since proportion of patients with previously known HF appears to be higher than de novo AHF in the present report, we suggest that at least a sizeable number of patients could benefit from a similar approach (e.g. obtaining dry weight before discharge) to reduce admissions of CHF patients.

As in other registries, an important proportion (approximately 50%) of patients in the present study were not receiving GDMT prior to hospitalization. Disproportionately high percentage of patients were using MRAs compared to EHFS II and ADHERE registries.[3,4] Both of those registries were created before 2010 and therefore predate universal recommendation of MRA for HFrEF; this discrepancy probably represents temporal trend rather than physician preference. Moreover, as thiazide diuretics are not available as a stand-alone product in Turkey and instead are combined with spironolactone, these findings may also represent an "unintentional" use of spironolactone in patients requiring thiazide diuretics. Importantly, GDMT reduces relative risk for rehospitalization (as illustrated in OPTIMIZE-HF registry), indicating that a large portion of these hospitalizations could have been prevented if adequate GDMT had been instituted before hospitalization.[14] Perhaps more dramatically, nearly half of the patients were not prescribed ACE inhibitor/ARB, beta-blocker, or aldosterone antagonist, despite the well-known effects of these drugs on mortality. Although present figures are very close to values provided by contemporary studies, such as Gulf CARE study conducted in 2012, analysis revealed that nearly half of patients still do not receive GDMT. Failure to comply with GDMT is a well-known risk factor for increased morbidity and mortality. In OPTIMIZE-HF study, highest mortality rates were seen in patients for whom beta-blocker treatment was either withdrawn (24%) or who did not receive treatment with beta-blocker (13%).[14] Therefore, more attention should be given to increasing GDMT awareness of primary care physicians and cardiologists to reduce mortality and rehospitalization rates. Oddly, at discharge, a large number of patients (33%) received digoxin, a drug with mild effect on rehospitalization rate and no effect on mortality at all. This drug received Class I indication from European Society of Cardiology (ESC) (when atrial fibrillation is present) and Class IIa indication (for all patients) in American College of Cardiology/American Heart Association (ACC/AHA) guidelines, but recent cohort studies and meta-analyses have cast doubt on effectiveness of digoxin even in patients with HF and atrial fibrillation.[1,2,18,19] Rather than prescribing digoxin, compliance with GDMT would probably be more effective to decrease mortality and morbidity rates. In our study, it was also observed that statins were prescribed at discharge to a significant fraction of patients who were not using statins previously. There are no proven benefits of statin use in treatment of HF.[1] Therefore, it was concluded that statins were prescribed for prevention of atherosclerotic events in patients with coexistent coronary artery disease, rather than primarily aiming at treatment of HF.

Strikingly high use of inotropic agents, particularly dopamine (18%) and dobutamine (23%), was seen in the present cohort; 31% of patients received at least 1 inotropic agent during hospitalization. In addition, 54 patients received dopamine and 55 patients received dobutamine even with pEF. In comparison, 11% and 5% of patients in EHFS II and ADHERE cohorts received dopamine, and figures are lower for other inotropic agents.[3,4] None of the inotropic agents, including levosimendan, have a positive effect on mortality, and both ESC and ACC/AHA guidelines have Class III indication of inappropriate for use due to increased mortality.[1,2]

Finally, in-hospital mortality rate (3.4%) was comparable to some other large registries. ADHERE registry cited an in-hospital mortality rate of 3.8%, but this figure is much higher in Europe (6.7% in EHFS II, 7.3% in Italian series), Canada (8.7%, Lee et al.[20]), and Japan (6.3%).[3,4,8,16,20] Whether these findings represent an adequate standard of care in Turkey remains to be investigated. Of note, Damasceno et al. cited mortality rate of 4.2%, and African-American patients in OPTIMIZE-HF registry had lower unadjusted mortality rate.[9,14] Common element in both series was that mean age of patients admitted to hospital was lower than that of other series, and age is simply the most important factor for in-hospital mortality. Since mean age in our cohort was also low (62 years), this finding may merely indicate a lower-risk cohort.

Study limitations

Although nearly all regions of Turkey were represented in the present study, number of patients included in centers from eastern Turkey was notably low, and nearly 50% of patients were recruited from 5 centers. Nonetheless, 95 patients were recruited from regions of eastern and southeastern Turkey, constituting 17% of patients. Despite presence of regional facilities, there were still many provinces in those regions where there was no study center, so sample is not entirely homogenous. Sample size (558 patients) was somewhat limited due to inadequate number of participating centers. This study was not designed as a clinical trial and daily clinical practice was registered, so effects of treatments or management strategies could not be evaluated. Longitudinal follow-up after hospitalization was not possible for the current registry. Although only registered cardiologists were invited to serve as investigators, no standardization for echocardiographic measures was possible. Analyzed data were observational.

Recommendations for AHF registries conducted in the future

Rather than depending on voluntary participation, study centers and investigators should be commissioned by a governing body for data collection and transmission. The characteristics and properties of study centers that participate in a future study should be more homogenous to assess patient characteristics and evaluate management strategies from all around Turkey. In particular, internal medicine clinics not associated with a university or training and research hospital should be invited to participate. Furthermore, sample size should be increased. Number of patients should be standardized for a better representation of all AHF patients across Turkey. To increase compliance of investigators, questions included in the survey should be reassessed and reduced, if possible. Finally, both study design and diagnostic algorithms should be updated in future studies to prevent underrepresentation of HFpEF patients.

Conclusion

TAKTIK observational registry is the first effort to define the patient characteristics and clinical management strategies for AHF patients in Turkey. Our results have shown some important differences in Turkish patients, such as younger age at admission and valvular disease as common cause of decompensation, as well as high rate of medical noncompliance (33%). GDMT use was still inadequate, and adherence to guideline recommendations did not improve at discharge. Somewhat large number of patients were prescribed digoxin at discharge. Use of inotropic agents during hospitalization was inappropriately high, but overall in-hospital mortality rate was acceptable compared with other registry data.

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Appendix

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