Experiences of a University Hospital on Adhering to ESC Guidelines in Patients with Chronic Ischaemic Heart Failure

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ABSTRACT

Introduction: Ischaemic heart failure (HF) is a common public health problem that is associated with increased mortality, morbidity and medical costs. This study aimed to investigate the percentage of patients with HF who are taking target doses of the drugs to improve the mortality rate and assess the reasons for the patients' non-adherence to treatment guidelines during the follow-up period.

Patients and Methods: Between January 2017 and December 2018, 480 patients who had been diagnosed with ST elevation myocardial infarction (STEMI) and had undergone primary percutaneous coronary intervention with a left ventricular ejection fraction (LVEF) of < 40% were enrolled in this study at our centre. The percentage of patients taking target doses of drugs that improved the mortality rate according to the 2016 European Society of Cardiology Guidelines for the treatment of HF, such as beta blockers (BB), angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB) and mineralocorticoid receptor antagonists (MRA) at the time of discharge and at the 6-month follow-up period was investigated.

Results: Of the 480 patients, the follow-up data of 430 patients were available and the percentages of patients prescribed with ACEI/ARB, BB and MRA at discharge were 86%, 89% and 28%, respectively. At the 6-month follow-up, the percentages of patients using ACEI/ARB, BB and MRA were 72%, 78% and 42%. About 7% of patients using BB switched to a different BB and 5% of the patients using ACEI were found to switch to an ARB. The percentages of patients taking target doses of ACEI/ARB, BB and MRA were 28%, 22% and 24%, respectively. Metoprolol succinate, ramipril and spironolactone were the most prescribed agents. Worsening of renal function, hyperkalaemia and bradycardia were the main reasons for non-achievement of target doses during the follow-up period.

Conclusion: In clinical practice, the percentage of patients with ischaemic HF who were receiving optimal target doses of BB, ACEI and MRA was far below the desired levels as compared to the European Society of Cardiology (ESC) guidelines.

Key Words: Guidelines; heart failure; medication adherence

İskemik Kalp Yetersizliği Hastalarında Klinik Kılavuz Önerilerine Uyumun Değerlendirilmesi

ÖZET

Giriş: Kalp yetersizliği (KY) önemli bir sağlık sorunu olup artmış mortalite, morbidite ve sağlık harcamasıyla ilişkilidir. Bu çalışmada, KY hastalarında mortaliteyi azalttığı gösterilen ilaçların klinik pratikte hedef doza ulaşılma oranları ve bunu etkileyen faktörlerin araştırılması amaçlandı.

Hastalar ve Yöntem: Ocak 2017-Aralık 2018 tarihleri arasında ST segment yükselmeli miyokart enfarktüsü (STYME) tanısıyla pimer perkütan koroner girişim (PPKG) yapılan ve sol ventrikül ejeksiyon fraksiyonu (SVEF) < %40 olan 480 hasta çalışmaya dahil edildi. Hastaların taburculuk ve altıncı ay vizitlerinde 2016 Avrupa Kardiyoloji Derneği Kalp Yetersizliği Tedavi Kılavuzu önerileri doğrultusunda mortaliteyi azalttığı gösterilmiş olan anjiyotensin dönüştürücü enzim inhibitörü (ACEI), anjiyotensin reseptör blokeri (ARB), beta-bloker (BB) ve mineralokortikoid reseptör blokeri (MRA) kullanım ve hedef doza ulaşma oranları araştırıldı.

Bulgular: Taburculuk esnasında ACEI/ARB, BB ve MRA reçete edilme oranları sırasıyla %86, %89 ve %28 idi. Altıncı ay takip vizitinde hastaların ACEI-ARB, BB ve MRA kullanım oranları sırasıyla %72, %78 ve %42 olarak saptandı. Altıncı ayda ACEI/ARB, BB ve MRA için hedef doza ulaşılma oranları sırasıyla %28, %22 ve %24'tü. Renal fonksiyonlarda bozulma, hiperkalemi ve bradikardi hedef doza ulaşmada en çok karşılaşılan önleyici nedenler oldukları tespit edildi.

Sonuç: KY hastalarında mortaliteyi azalttığı gösterilen ilaçların kullanımı ve hedef doza ulaşılma oranları istenilen düzeyin oldukça altındadır.

Anahtar Kelimeler: Kalp yetersizliği; kılavuzlar; ilaç uyumu

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INTRODUCTION

Heart failure (HF) is a clinical condition that is associated with increased mortality and morbidity. It's frequency is anticipated to increase in the future, especially in ageing populations[1]. Patients with HF are commonly prescribed multiple medications for which they have low treatment adherence, resulting in poor health outcomes[2]. Pharmacological agents such as beta blockers (BB), angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB) and mineralocorticoid receptor antagonists (MRA) have proven to play an effective role in reducing the mortality related with HF. The guideline-directed medical therapies have decreased the disease progression and improved outcomes in HF[3]. Currently, several studies have reported that there is a significant discrepancy between the accepted treatments published in clinical guidelines and the approaches seen in daily practice[4]. Even when the prescription rates of guideline-based treatments are optimal, patients who do not meet their target doses may have adverse outcomes[5,6].

Although there is evidence that good adherence to medical treatment guidelines by HF patients is associated with better clinical results, the data specific to this issue in Turkey is scarce. The aim of this study was to estimate the percentage of HF patients who received the target doses of drugs as recommended in the 2016 HF treatment guidelines of the European Society of Cardiology (ESC) and to assess the reasons for non-adherence to the guideline-recommended treatment during the follow-up period[7].

PATIENTS and METHODS

Between January 2017 and December 2018, 480 patients who were diagnosed with ST elevation myocardial infarction (STEMI) and underwent primary percutaneous coronary intervention (PCI) with a left ventricular ejection fraction (LVEF) of < 40% were enrolled in this study in our centre. An analysis was performed to determine whether these patients received the treatments recommended in the 2016 ESC-HF guidelines, specifically with respect to ACEI/ARB, BB and MRA. Additionally, the dose of each drug was determined and it was also assessed whether the dose used was the target dose established in clinical trials. The reasons for patients' non-adherence to guidelines were identified by searching 6 months of digital medical records of outpatient follow-up clinic visits. The prescription data was also confirmed by analysing the medical drug outputs of the social security systems of the patients. The impact of patient and physician behaviours on non-adherence to the guidelines were surveyed by a questionnaire form. The results for continuous variables were expressed as a median (interquartile range) and the results for categorical variables were expressed as percentages. The study was approved by the local ethics committee of our centre and all patients gave their informed consent for inclusion in the study.

RESULTS

Of the 480 patients, 455 patients were accepted to participate in this study and the follow-up data of 430 patients were finally available. The patients' characteristics are given in Table 1. The general pharmacological treatment properties of patients at discharge and during the follow-up period are given in Table 2. The percentages of prescription for ACEI/ARB, BB and MRA at discharge were 86%, 89% and 28%, respectively. The main reason not to initiate the treatment with ACEI/ARB was the appearance of symptomatic hypotension at discharge. The main reason not to initiate the treatment with BB was the presence of asthma/chronic obstructive pulmonary disease at discharge. The main reason not to initiate the treatment with MRA was the functional status of patients (NYHA), which did not require MRA at discharge. At the 6-month follow-up, the percentages of patients using ACEI/ARB, BB and MRA were 72%, 78% and, 42%. During the follow-up period, 7% of patients using BB were found to switch to a different BB and 5% of patients using ACEI were found to switch to an ARB. Additionally, 6% of the patients on ACEI therapy switched to being treated with an angiotensin receptor-neprilysin inhibitor. The percentages of patients who were meeting the target dose of ACEI/ARB, BB and MRA were 28%, 22% and 24%,

Table 1. Patients characteristics at discharge

Patients (n)	430
Age, years	62 (48-84)
Male, n (%)	318 (74)
BMI	28 (25-34)
SBP, mmHg	120 (95-160)
HR, bpm	70 (60-90)
EF, %	30 (20-40)
NYHA functional class I-II, n (%)	361 (84)
Type 2 DM, n (%)	154 (36)
Atrial fibrillation, n (%)	65 (15)
Hypertension, n (%)	236 (55)
COPD, n (%)	52 (12)
Chronic renal failure (GFR < 30 mL/minute), n (%)	94 (22)

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; EF: Ejection fraction; GFR: Glomerular filtration rate; HR: Heart rate; NYHA: New York Heart Association; SBP: Systolic blood pressure.

Table 2. Pharmacological treatment in patients with heart failure at discharge and at the 6-month follow-up

Treatments	At discharge time	At the 6-month follow-up visit
ACEI/ARB, n (%)	370 (86)	310 (72)
Ramipril, n (%)	209 (48.5)	151 (35)
Captopril, n (%)	22 (0.5)	0 (0)
Enalapril, n (%)	13 (3)	9 (2)
Lisinopril, n (%)	0 (0)	0 (0)
Trandolapril, n (%)	0 (0)	0 (0)
Others (Perindopril, etc.), n (%)	65 (15)	47 (11)
Valsartan, n (%)	30 (7)	43 (10)
Candesartan, n (%)	43 (10)	52 (12)
Losartan, n (%)	9 (2)	9 (2)
Beta-blockers, n (%)	383 (89)	335 (78)
Carvedilol, n (%)	95 (22)	103 (24)
Metoprololsuccinate, n (%)	206 (48)	151 (35)
Bisoprolol, n (%)	47 (11)	26 (6)
Nebivolol, n (%)	34 (8)	56 (13)
MRA, n(%)	120 (28)	181 (42)
Spironolactone, n (%)	120 (28)	172 (40)
Eplerenone, n (%)	0 (0)	9 (2)

ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blockers; MRA: Mineralocorticoid receptor antagonists.

respectively. Metoprolol succinate, ramipril and spirinolactone were the most frequently prescribed agents. The reasons for guideline non-adherence during the follow-up period are summarised in Table 3. The main reason for non-achievement of the target dose for ACEI/ARB usage was the worsening of renal function, while a development of cough was the main reason for switching from ACEI to ARB. The main reason for not achieving the target dose for BB usage was bradyarrhythmia. The main reason for not achieving the target dose for MRA usage was hyperkalaemia. According to the questionnaire form, 1 of 4 physicians were concerned about the side effect profile when the drug dose was increased. Only 18% of the physicians declared that the relatively good functional capacity of the patients (NYHA I-II) made them reluctant to reach the target dose. Due to the fact that the medications prescribed in the previous visits were still unfinished, 28% of the patients were unable to take the increased dose according to the changed prescription. During the follow-up period, 22% percentage of patients (n= 102) were re-hospitalised due to decompensation. Although 36% of the patients were euvolemic, it was observed that they used loop diuretics (e.g. furosemide) regularly.

DISCUSSION

This study showed that the use of both drugs reduced the mortality rate and that the percentage of patients with ischaemic HF who were receiving optimal target doses of BB, ACEI and MRA was far below the desired levels as compared to the recommendations in the ESC guidelines. Another result highlighted by this study was that the physicians' and patients' behaviours during the follow-up period significantly

Table 3. Attainment of the target dose in recommended treatments for patients with heart failure

Total patient number (n= 430)	Not achieved target dose n (%)	Reason for not achieving target dose	Patient number n (%)
ACEI/ARB	310 (72)	Worsening of renal function	93 (30)
		Symptomatic hypotension	66 (21)
		Cough	44 (14)
		Others/Unknown	107 (35)
Beta-blockers	335 (78)	Bradyarrhythmia	117 (35)
		Worsening of HF	65 (19)
		Sexual dysfunction	34 (10)
		Others/Unknown	119 (35)
MRA	327 (76)	Hyperkalaemia	137 (42)
		Gynaecomastia	13 (4)
		Others/Unknown	177 (56)

ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blockers; HF: Heart failure; MRA: Mineralocorticoid receptor antagonist.

prevented optimal treatment. Furthermore, this study allowed comprehensive information on the treatments and doses administered in HF patients to be gathered, along with the reasons why the indicated drugs were not prescribed or why their administered doses did not reach the targets defined by ESC guidelines in Turkey.

In clinical practice, even in the high-quality centres, defining the reasons for non-adherence to guideline-directed treatments might not possible because of the nature of the HF management process. In general, HF treatment is performed by different professionals who work over time in several settings. The dose adjustment requires numerous outpatient visits and laboratory tests to carefully tailor the treatment to each patients' properties. A previous report from the European Heart Failure Pilot Survey (ESC-HF Pilot) estimated that the number of patients treated with ACEI/ARB, BB and MRA were 88.5%, 86.7% and 43.7% of patients, respectively[6]. Another registry Spain showed that ambulatory patients with HF who were prescribed ACEI/ARB, BB and MRA were distributed as 92.6%, 93.3% and 74.5%, respectively. According to the same study, target doses were reached in 16.2% of the patients receiving ACEI, 13.2% of patients with BB and 23.5% of those with MRA. Interestingly, after the reasons for not prescribing a certain treatment were considered, the true problem of undertreatment percentages were 3.4% and 1.8%, with regard to ACEI/ARB and BB, whereas a wider value was obtained with respect to MRA, i.e., 19%[8].

In the QUALIFY (Quality of Adherence to guideline recommendations for Life-saving treatment in HF survey) study, the rate of prescription was 66.5% for ACEIs, 21.3% for ARBs, 86.9% for BBs and 70.3% for MRAs. The recommended medications were often underdosed, as per the following distribution: 27.3% of patients treated with ACEIs, 49.9% of those on ARBs and 48.5% of those on BBs. This study showed that the physicians' adherence (with > %50 of recommended dosages at baseline) to guideline recommendations was associated with better outcomes (reduction in cardiovascular and HF-related death, rehospitalisation, etc.) at the 18-month follow-up[9].

Giezeman et al. from Sweden reported that in patients with chronic HF in primary healthcare, the percentages of prescribing an inhibitor of the renin-angiotensin system and BBs were 78% and 76%, respectively. In this study, the target prescription rates of these drugs were 29% and 18%[10]. In general, our findings were compatible with those of the previous literature, such as underdosing, which remains widespread, with less than one-third of patients taking guideline-recommended doses for most of the key drugs.

Patient-related factors may also affect guideline adherence over the time[11]. Co-morbidities, frailty, age, emerging contraindications of drugs (commonly hypotension, worsening of renal function, hyperkalaemia, bradycardia) and adverse events play an important role in guideline adherence as patient-related factors. Other factors such as physicians' post-discharge inertia, public health insurance problems, variations between the physicians responsible for drug prescription and dose optimisation, and limited access to clinical follow-up facilities may have contributed to guideline non-adherence[12].

Patient education and self-care behaviour play an essential role in guideline adherence in HF patients. Currently, in many European countries, to optimise and increase the achievement of pharmacological treatment and patient education, HF clinics are considered as promising centres[13,14]. For our country, centres having specific HF management programmes with multidisciplinary approaches may improve guideline adherence in HF patients.

LIMITATIONS

There are several limitations to this study. Firstly, this is an observational, single-centre study that only provides descriptive results. Secondly, patients with the diagnosis of non-ischaemic HF were not included. Thirdly, newer drugs such as sacubitril/valsartan and ivabradine that have been shown to improve HF outcomes were not included in adherence analysis. Finally, the follow-up period after discharge was slightly shorter than 6 months and did not include the mortality data.

CONCLUSION

Adherence to guidelines for pharmacological treatment practice in HF patients is still suboptimal for our country. Lack of patient education and questionable physician behaviours seem to be important factors that negatively impact treatment and prevent the completion of targets. These issues need to be addressed and improved. Further research on how treatment guidelines can be adapted to clinical practice may optimise the treatment results.

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CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: VO
Analysis/Interpretation: VO
Data Acquisition: VO
Writting: VO
Critical Revision: VO
Final Approval: VO

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