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Euro heart failure survey

Medical treatment not in line with current guidelines

Euro Heart Survey: Unzureichende Umsetzung der aktuellen Leitlinien bei der medikamentösen Therapie der chronischen Herzinsuffizienz

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■ **Zusammenfassung** *Hintergrund* Im Euro Heart Survey – Herzinsuffizienz sollte die Umsetzung der Leitlinien der Europäischen Gesellschaft für Kardiologie untersucht werden. *Methodik* In Deutschland wurden an 7 Zentren Patienten rekrutiert, deren Entlassungsdiagnose ein akuter Myokardinfarkt, neu aufgetretenes Vorhofflimmern oder Diabetes war. Dabei musste zusätzlich mindestens eines der folgenden Kriterien erfüllt werden: (1) klinische Diagnose Herzinsuffizienz, (2) Herzinsuffizienz-bedingter Krankenhausaufenthalt innerhalb der letzten 3 Jahre, (3) Therapie mit einem Schleifendiuretikum (4) Herzinsuffizienzmedikation oder ventrikuläre Dysfunktion im Echo innerhalb der letzten 24 Stunden vor Entlassung oder Tod. *Ergebnisse* Von 2166 gesichteten Patienten wurden 747 eingeschlossen (478 Männer, 269 Frauen). Bei 93% dieser Patienten konnte die Diagnose Herzinsuffizienz gesichert werden (71% ischämischer Genese). Trotz der großen Anzahl an Patienten mit bekannter Herzinsuffizienz wurden nur 72% mit ACE-Hemmern und 62% mit β -Blockern behandelt. Die durchschnittliche Tagesdosis betrug bei den ACE-Hemmern 63% und bei den β -Blockern lediglich 54% der empfohlenen Tagesdosis. Diuretika bekamen 74% der Patienten

(Furosemid 36%, Thiazide 34%, Spironolacton 17%). *Schlussfolgerung* Die Auswahl der Medikamente und deren Dosierungen erfolgen nur bei einem unzureichenden Teil der Patienten gemäß den gültigen Leitlinien. Es sind daher weitere Anstrengungen notwendig, um alle Patienten mit einer Leitlinien-konformen und somit Evidenz-basierten medikamentösen Therapie zu behandeln.

■ **Schlüsselwörter**
Herzinsuffizienz – Leitlinien –
Medikation – Diagnostik

■ **Summary** It was the aim of the Euro Heart Survey on Heart Failure to assess whether patients are being treated according to current guidelines. *Methods* In Germany, patients were screened in 7 medical centers if their discharge diagnoses were myocardial infarction, a new episode of atrial fibrillation, or diabetes mellitus. Patients were enrolled if at least one additional criterion was fulfilled: (1) clinical diagnosis of heart failure, (2) hospital admission due to heart failure within the last 3 years, (3) therapy with loop diuretic, (4) medication for heart failure or ventricular dysfunction documented by echocardiography within the past 24 hours prior to death. *Results* 2166 patients were screened of whom 747 were in-

cluded in the study (478 men, 269 women). 93% of the patients suffered from heart failure. Despite the high number of patients with known heart failure (ischemic heart failure in 71%), only 72% received ACE inhibitors and 62% β -blockers. Average daily dose met recommendations in only 63% of

patients on ACE inhibitors and 54% on β -blockers. 74% of the patients received diuretics (furosemide 36%, thiazide 34%, spironolactone 17%). *Conclusion* An inadequately low number of patients with heart failure receives medical therapy according to guidelines, despite all the over-

whelming evidence for improved morbidity and mortality. Awareness of physicians needs to be improved.

■ **Key words** guidelines – heart failure – diagnosis – therapy – medication

Introduction

The European Society for Cardiology's guidelines recommend routine application of ACE inhibitors and β -blockers in all patients with left ventricular dysfunction since 1997 [7]. Nevertheless, it was noticed in several studies that heart failure medication at study begin was not in accordance with these guidelines in either selection or dosage (2,12). Since these studies were either monocentric or at best restricted to individual countries it is impossible to get any meaningful insight on whether or not therapy is in line with the guidelines in other European countries [2, 7, 10]. With the aim of assessing the implementation of the current guidelines, the Europe-wide EuroHeart Survey on Heart Failure was initiated [3].

Methods

In 2000 and 2001 over a period of 6 weeks 115 hospitals in 24 member countries of the ESC evaluated a total of 46788 patients [2]. In Germany the centers listed above (4 university hospitals, 3 metropolitan hospitals) participated in this study, four of these had departments of cardiac surgery. For inclusion acute myocardial infarction, first episode of atrial fibrillation or diabetes were to be diagnosed on discharge in patients who also fulfilled at least one of the following criteria: 1) clinical diagnosis of heart failure, 2) hospitalization due to heart failure within the last 3 years, 3) therapy with a loop diuretic, 4) medication for heart failure or ventricular dysfunction in echocardiography within the last 24 hours before discharge or death.

Especially the inclusion criterion „loop diuretic“ appears quite unusual at first sight. However, the Euro Heart Failure survey attempted to enroll a broad range of patients in order to explore the current practice of diagnosing and treating patients with suspected or known heart failure. It was therefore decided to include patients with loop diuretics, since this might hint at heart failure as the underly-

ing cause. Although this is a rather general inclusion criterion it was the sole criterion in only 10% of the patients. Of all the patients enrolled 93% had heart failure [3].

Results

■ Study population

Out of a total of 2166 hospitalized patients screened for enrollment 747 (37%) fulfilled the entry criteria and could be included (Table 1).

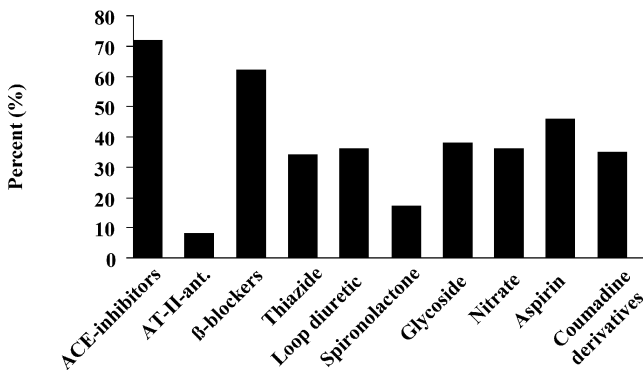
Thirty-seven percent of patients had a history of hospitalization due to heart failure, whereas the diagnosis of heart failure could be secured in 93%. Clinical signs of heart failure, angina pectoris, and arrhythmia were the primary reasons for hospital admission in 49% of the patients (Table 2). Other diagnoses resulting in hospitalization included diabetes mellitus (26%), a first episode of atrial fibrillation (13%), and myocardial infarction (8%). High blood pressure was not a common reason for admission, whereas a quarter of the patients presented with acute dyspnea, other signs of decompensation such as edema or dyspnea on exertion. Roughly a

Table 1 Patient characteristics. More females than males were among the patients older than 75 years. Most patients were classified as NYHA I and II on inclusion in this survey

Age [years]	67±11
Female [%]	35
Male >75 years [%]	12
Female >75 years [%]	36
Duration of hospital stay [d]	10±3
Treatment in cardiologic department [%]	70
Treatment in general medical department [%]	21
NYHA I [%]	24
NYHA II [%]	52
NYHA III+IV [%]	24
Heart failure: ischemic [%]	71
valvular [%]	35
dilatated [%]	8

Table 2 The primary diagnoses leading to hospitalization were heart failure and cardiac symptoms

	primary diagnosis [%]	recurrent diagnosis [%]
Heart failure	22	60
Angina pectoris	18	30
Arrhythmia	9	26
Arterial hypertension	2	28
Vertigo/syncope	1	2
Neurological deficits/insult	1	2
Cardiovascular surgery	27	42
Other cardiac surgery	7	20
Neoplasm	1	4
Gastrointestinal diseases	3	4
Respiratory illnesses	2	7
Other illnesses	6	20

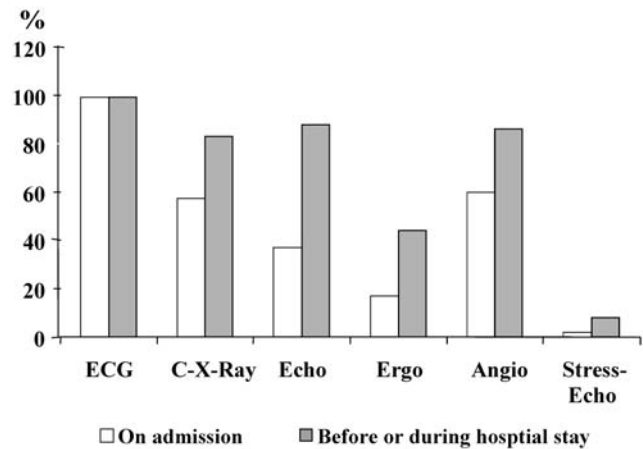
**Fig. 1** Heart failure medication. The prescription rate was insufficient for all drugs except anticoagulants. Although ACE inhibitors or (if not suitable due to side effects) AT-II-antagonists are indicated in all patients, these were not prescribed often enough. The same was found for beta-blockers

quarter of admitted patients underwent cardiovascular surgery. Average time spent in the hospital was 10 ± 3 days.

Almost two-thirds of the patients were taking diuretics upon hospitalization (Fig. 1). This high percentage can be explained by the inclusion criterion of loop diuretic therapy as an indicator of heart failure. However, this was the sole inclusion criterion in only 10% of the patients.

■ Diagnosis

Almost all patients (99%) underwent ECG, and a chest x-ray was taken in more than half (57%) of the patients (Fig. 2). Also laboratory tests were performed in nearly all patients, with quantification of hemoglobin, electrolytes and renal parameters. Evaluation of left ventricular function was done with at least one imaging technique in 87% of all patients:

**Fig. 2** Investigations performed. An ECG was recorded in almost every patient. A high but adequate proportion underwent invasive and non-invasive investigations

55% were assessed by echocardiography, 26% by angiography and 19% by scintigraphy. An ejection fraction $<40\%$ was present in 60% of the patients. Coronary angiography was performed in 60%, resulting in PTCA in 14% and bypass surgery in 9% of the patients. When considering earlier hospitalization a total of 86% underwent angiography, 32% PTCA and 29% had received bypass surgery.

■ Primary illness and other medical conditions

The main cause of heart failure was ischemic heart disease (71%). On inclusion, 70% had stable or unstable angina and 51% had suffered from myocardial infarction at some point in time (Table 3).

Heart failure associated with valvular disease (mid- to high-grade or already surgically treated valvular disease) was seen in 35%, with mitral regurgitation (25%) being the leading cause (Table 3 and 4).

■ Follow-up

During the 12 weeks of follow-up, 233 patients (43.8%) were readmitted, 22 (4.1%) due to recurrent heart failure. There were 34 deaths (6.4%) with a mean age at time of death of 74 ± 9 years.

■ Medication

The most commonly administered drugs for therapy of heart failure were diuretics (86.7%), due to diuretic therapy being an inclusion criterion as an indicator of heart failure. Furosemide was most often used (36%),

Table 3 The most frequent underlying condition was coronary heart disease and its symptoms. High blood pressure and diabetes were the most common non-cardiac diseases

	[%]
Cardiac	
CHD	82
Stable/non-stable angina pectoris	57
Myocardial infarction	51
Atrial fibrillation	41
Moderate to severe valvular disease	35
PCI	32
CABG	29
Pacemaker	8
ICD	1
Non-cardiac	
Arterial hypertension	65
Diabetes mellitus	35
Respiratory illnesses	22
Serum-creatinine >150 µmol/L	20
Cerebral insult	7
TIA	6
Dementia	6

Table 4 Echocardiographic results. Systolic dysfunction could be documented most often. Mitral regurgitation was the most frequently diagnosed valvular disease

	[%]
LV dysfunction: systolic	60
diastolic	24
LV dilation	31
LA dilation	42
Moderate – severe stenosis of aortic valve	8
aortic regurgitation	5
stenosis of mitral valve	2
mitral regurgitation	25
Right ventricular dysfunction	6
Pulmonary hypertension	23

prescribed in 60% of all recipients at a daily dose of 80 mg. 17% of patients were on spironolactone.

In patients with reduced cardiac ejection fraction, ACE inhibitors were more often used than β -blockers (84.1 vs 74.1%). A combination of ACE inhibitors and β -blockers was administered to 72% of patients, and an additional diuretic was taken by 38%.

The prescription rate of β -blockers and ACE inhibitors correlated strongly with patients' age. 73.2% of patients <70 years compared to 47.1% of patients >70 years received a β -blocker and 43.5% of patients <70 years vs 28.5% of patients >70 years were on ACE inhibitors. Also, the primary cause of heart failure resulted in a different prescription rate: Patients with ischemic heart disease took β -blockers twice as often as patients with non-ischemic causes.

Furthermore, gender made a difference to pharmacotherapy. Women received both β -blockers (58.1 vs 70%) and spironolactone less frequently than men (12.5 vs 21.1%), but were more likely to be administered calcium antagonists (22.1 vs 14.5%). Only 19.1% of patients with pulmonary diseases (COPD) were treated with β -blockers. Patients with renal failure and a serum creatinine level >176 µmol/L took ACE inhibitors in 54.6% of cases compared to 82.1% in the absence of renal failure. The dose did not vary significantly for these two groups. Diabetics received ACE inhibitors more often than non-diabetic patients (69.9% vs 56.8%).

A total of 81.3% were treated with anti-platelet agents or anti-coagulatory drugs.

Discussion

The main findings of this study are 1) ESC guidelines for the treatment of chronic heart failure are not sufficiently adhered to with regard to selection and dosage of medication. 2) Co-morbidities lead to further shortcomings in the medical treatment. 3) Patients >70 years and women are less likely to be treated according to guidelines.

Both European and German guidelines recommend for patients in NYHA class I and II a combination of ACE inhibitors and β -blockers and for patients in NYHA III and IV the addition of a diuretic [7]. Unfortunately, there were several shortcomings in the medical therapy. Although the guidelines recommend ACE inhibitors for all heart failure patients who do not have a contra-indication regardless of the presence or absence of diabetes, diabetics were treated with ACE inhibitors more frequently than normoglycemic patients. Similarly, β -blockers which should also be given to all heart failure patients was prescribed more often to patients with ischemic heart disease. Furthermore, without any obvious reason patients >70 years received β -blockers less frequently than patients <70 years. This is of importance, since many of our patients are 70 years or older. In a national survey of heart failure in French hospitals the median age was 76 years [4], which represents a clear gap between the population in clinical trials and those in routine clinical practice. Indeed, in CIBIS II the mean age was 61 years and in MERIT-HF it was 63.9 years and thus at least a decade younger than that of patients seen in clinical practice [1, 9]. This gap has now been closed with the results of the SENIORS trial, which could demonstrate nebivolol to be an effective and well-tolerated treatment for heart failure in the elderly, with significantly less all cause mortality or cardiovascular hospital admission as compared to placebo [5].

There are several factors that could possibly explain this restricted use of β -blockers and ACE inhibitors: both morbidity and mortality of heart failure but also the potential benefit of drug administration are widely underestimated by physicians. In addition, the fear of potential side-effects might lead to insufficient medication. Also, considering that β -blockers are not started within the first two weeks after cardiac decompensation, it could be speculated that β -blocker therapy had been recommended to the private physician of the patients but was not yet started in hospital prior to discharge. Indeed, a quarter of all patients were admitted with signs of congestion. However, taking unstable or decompensated heart failure into account the frequency of β -blocker prescription was still less than indicated.

The low rate of prescription of β -blockers in patients with COPD could possibly be attributed to a fear of side-effects as well. Although only bronchial asthma but not COPD is a contra-indication for β -blocker therapy, the prescription rate of 19.1% clearly shows that administration of β -blockers is not currently common practice in these patients. Etiology of heart failure had an impact on the choice of medication. As an example, although β -blockers are indicated in all heart failure patients, in the absence of coronary heart disease the prescription rate for β -blockers was less than that seen in patients with ischemic heart disease.

Indeed, β -blockers have been contraindicated for patients with obstructive lung diseases due to the potential risk for bronchospasm. However, newer evidence has shown that cardioselective β -blockers are safe in patients with obstructive lung disease, are not associated with increased respiratory symptoms or inhaler use, and do lead to an augmented FEV1 response after β -2 agonists compared with placebo. Patients with obstructive lung disease and chronic heart failure should be treated with cardioselective

β -blockers, as they are associated with significant reductions in morbidity and mortality [11].

Since 24% of the patients of this survey were in NYHA class III and IV, it is not unexpected that 38% of the patients received this triple-combination at hospital discharge. Diuretics, especially loop diuretics were administered most frequently to patients included in this study. The prescription rate of 17% for spironolactone indicates that the results of the RALES study are widely accepted considering that 24% of the patients were being classified as NYHA III and IV. It should, however, be noted that since RALES a more widespread use in patients with NYHA class I or II has been associated with an increased rate of hyperkalemia-associated morbidity and mortality [6, 8]. Therefore, spironolactone should be reserved for patients in NYHA class III or IV and should be accompanied by close monitoring of renal function and potassium levels.

A panoply of investigations were performed in order to secure the right diagnosis in these patients. It is somewhat surprising that 13% of the patients did not undergo objective assessment of left ventricular function during the index hospital admission.

Conclusions

Even at university and metropolitan hospitals there is still room for improvement in the every-day treatment of patients with chronic heart failure. These data clearly demonstrate the need for further efforts to be made in order to raise the awareness for the shortcomings of the current treatment practices, so that the number of patients receiving a medical therapy in accordance with current guidelines is as high as possible.

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