

Resource use and costs in systolic heart failure according to disease severity: a pooled analysis from the German Competence Network Heart Failure

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Received: 9 December 2010 / Accepted: 26 September 2011 / Published online: 26 October 2011
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Abstract

Aim Systolic chronic heart failure (CHF) is currently one of the most prevalent cardiac diseases. The present analysis sought to estimate the 1-year disease-related resource use and associated management costs of patients with CHF.

Subject and methods A total of 2,710 individuals with systolic CHF [mean age 62.9 years±13.6, 25.2% female, New York Heart Association (NYHA) I–IV] were included from the German Competence Network Heart Failure. Disease-related resource use was assessed with regard to outpatient contacts with physicians,

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hospitalizations including rehabilitation stays and drug utilization.

Results During 1 year, patients had on average 6.1 contacts with their general practitioner, 1.7 contacts with cardiologists and 0.8 hospital stays per year. Overall disease-related health care costs per patient were calculated at 3,150 € per year. The largest component related to hospitalizations (2,328 €, 74%), while costs of rehabilitation (294 €, 9%), medication (290 €, 9%) and outpatient contacts (238 €, 8%) were considerably lower. Compared with 2,474 € in NYHA class I, there was a cost increase in NYHA II, III and IV of 14, 48 and 71%, respectively. About 76% of this cost increase resulted from augmented hospital (inpatient) resource use.

Conclusion The present analysis demonstrates a high disease-related resource consumption of heart failure care. In particular, patients in higher NYHA classes require increased inpatient resources. Hence, improved treatment strategies need to be developed to optimize care thus reducing hospitalization rates.

Keywords Economic evaluation · Heart failure · Resource use · Costs

Introduction

Heart failure is one of the most common and severe diseases in developed countries (Cleland et al. 2003; Komajda et al. 2003). It is assumed that more than 23 million people suffer from heart failure worldwide (Bui et al. 2010; Cleland et al. 2001; McMurray et al. 1998). Each year, 5–600,000 new cases are diagnosed in Western countries (Cleland et al. 2001; Lloyd-Jones et al. 2010). Hence, appropriate management of patients with heart failure is an ongoing medical challenge and the aging of most Western societies in the next decades will lead to a growing impact of this relevant cardiovascular disease.

Heart failure is also characterized by its natural history and severity of this disease. Even if managed according to current guidelines, a 50% mortality rate has to be expected in the 4 years after first hospital admission. Furthermore, patients suffering from heart failure have a high morbidity, expressed by a 24% rehospitalization rate within 3 months after hospital admission (Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology et al. 2008). Therefore, it is obvious that heart failure constitutes a major and still growing economic burden for the social systems of most countries (Cowie and Zaphiriou 2002; Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology et al. 2008). In particular, the severe stages of the disease have

been assumed to be associated with elevated resource consumption and associated costs. However, there is a paucity of specific data on this topic.

Against this background, the current analysis investigated disease-related resource utilization and costs in systolic heart failure for Germany in a large sample of well-characterized patients from various cohort studies and randomized controlled trials (RCTs) within the framework of the German Competence Network Heart Failure (CNHF), taking into account the dependency of costs on clinical severity.

Methods

Sample

The target population included patients from ten sub-projects of the CNHF, one of Europe's largest heart failure research programmes. Patients were eligible for the present analysis if they suffered from symptomatic systolic chronic heart failure [CHF; New York Heart Association (NYHA) functional class I–IV], had proven reduced left ventricular ejection fraction (LVEF < 50%), were aged 18 years or above and were mentally and linguistically able to participate in the study. Patients of the different projects who met these inclusion criteria were included in the analysis. All patients provided written informed consent prior to participation in any of the CNHF studies.

In conjunction with the scientific projects within the CNHF, a comprehensive obligatory clinical data set was developed and implemented into all scientific projects, including relevant parameters about disease-related resource consumption. Data were successively collected from all patients within the CNHF and recorded using standardized case report forms (CRFs) and finally fed into a standardized database, which allows for pooled data analyses of study results (Mehrfhof et al. 2010). Patients were questioned at baseline in a standardized way about the disease-related resource use in the last 12 months. Hence pooled analyses of the requested data were feasible. Patient selection criteria of the different studies were present and might influence the results, but due to the high numbers of patients these differences can be considered as secondary. The aim of the study is ultimately a representation of the resource utilization for the patients of the CNHF with systolic CHF. Therefore, detailed information of the studies included is provided in Table 1.

Economic analysis

Resource use Information on disease-related resource use comprised outpatient physician contacts with general practitioners (GP) and cardiologists. With regard to the

Table 1 Description of the studies which provided data

Study	Description of study and patients included	Total no. (included in analysis)	Number of patients in NYHA class	Mean age (\pm SD)	Sex (% female)
HH-BNP	Handheld BNP study: objectification of cardiac dysfunction based on a handheld echocardiography device and/or a BNP test in an outpatient general practitioner setting	918 (51)	I: 1 II: 25 III: 21 IV: 4	70.7 (11.7)	56.9
extended INH	extended INH study: prospective randomized comparison of a comprehensive disease management (consisting of medical care, cardiac patient education and telephone) with the usual care in patients with CHF	1,032 (844)	I: 15 II: 463 III: 333 IV: 33	67.7 (12.5)	29.3
Diast-CHF	Diastolic CHF study: prevalence and history of diastolic dysfunction and diastolic heart failure ^a	1,937 (54)	I: 19 II: 25 III: 9 IV: 1	69.1 (8.2)	20.4
HIV&Heart	HIV and heart study: study investigated the frequency of cardiac disease in patients with HIV infection	806 (21)	I: 2 II: 13 III: 5 IV: 1	51.8 (8.2)	0.0
Gene	Gene study: genetic study of mutations in patients suffering from dilated or hypertrophic cardiomyopathies	758 (515)	I: 51 II: 270 III: 174 IV: 20	54.9 (13.0)	19.2
CIBIS-ELD	CIBIS-ELD: comparison of bisoprolol and carvedilol in elderly patients with CHF	445 (211)	I: 19 II: 119 III: 73 IV: 0	72.8 (6.1)	28.9
IKARIUS	IKARIUS study: manifestation of inflammatory DCM as a process of autoimmune diathesis. Estimate of the prevalence of familial DCM in DCM patients	441 (332)	I: 36 II: 136 III: 153 IV: 7	51.4 (12.9)	25.3
HELPS	HELPS study: Heidelberg study of longitudinal evaluation of quality of life and psychosocial variables in depressed heart failure patients	351 (267)	I: 10 II: 141 III: 115 IV: 1	62.0 (12.0)	21.3
TTT	Train-the-trainer study: evaluation of a training approach for family doctors to improve the life and quality of care of CHF patients	208 (145)	I: 1 II: 80 III: 61 IV: 3	68.0 (10.2)	31.7
ACVB-Out	ACVB outcome study: influence of heart failure, hormone status and psychosocial factors on the outcome after bypass surgery depends on gender	1,605 (270)	I: 43 II: 129 III: 89 IV: 9	65.7 (9.6)	18.5

NYHA New York Heart Association functional classification, BNP B-type natriuretic peptide, INH Interdisciplinary Network for Heart Failure, HIV human immunodeficiency virus, CIBIS-ELD Cardiac Insufficiency Bisoprolol Study in Elderly, DCM dilated cardiomyopathy, ACVB aortocoronary venous bypass

^aRegarding this study only patients with systolic dysfunction were included in the analysis

outpatient and inpatient care resource use data were available in more than 97%. In the case of missing data it was assumed that no resources had been utilized. Medication data were determined for five groups of heart failure

medication: beta blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II type 1 (AT1) receptor antagonists, aldosterone antagonists and cardiac glycosides. Inpatient resources comprised inpatient hospital as well as

rehabilitation stays. These data were recorded for a period of 12 months before baseline. Data were patient reported while trained nurses were asking the patients at baseline about the disease-related resource use in the last 12 months.

Costs The economic evaluation was performed from the societal perspective and focused on resource use regarding CHF. The costing of resource use concerning outpatient contacts was done by a proposal of the Working Group of Methods in Health Economic Evaluation (Krauth et al. 2005). Market values of cardiac drugs were determined by published prices (Schwabe and Paffrath 2010). The relevant agents of beta blockers in heart failure therapy were defined as metoprolol, bisoprolol, nebivolol and carvedilol. The agents considered as aldosterone antagonists were spironolactone and eplerenone. The price for a defined daily dose (DDD) was calculated by a weighted mean of the respective agents. The calculation of treatment costs was determined for a time period of 1 year.

In the case of inpatient costs, unit costs for hospitalization concerning heart failure were identified based on the relevant diagnosis-related groups (DRG; F62A, F62B and F62C) by calculating a weighted mean price using data of the Institute for the Hospital Remuneration System (InEK), since the acquired hospital stays were not directly assigned to a DRG. Because hospital care in Germany is dually funded, this must be taken into account in determining the hospital costs. Hence the capital costs have to be included in a survey from a societal perspective. The capital costs per patient day were determined according to Krauth et al. 2005. Costing of resource use regarding rehabilitation was done in accordance with the proposal of the Working Group of Methods in Health Economic Evaluation (Krauth et al. 2005). All costs were adjusted for the year 2009.

Indirect costs (e.g. absence from work or early retirement) were not included in the CRFs and therefore not considered in the present analysis. Study-related costs (e.g. in RCTs) were excluded.

Statistical analysis

Data management for the study was coordinated by the Clinical Trial Centre Leipzig (Leipzig, Germany), which independently managed the database and performed statistical analyses. Statistical analysis was performed with the statistical package SPSS version 18.0 (SPSS Inc., Cary, NC, USA). Descriptive statistics are presented as means \pm standard deviation. Analyses by disease severity, i.e. trends across NYHA classes, were examined by Kendall's Tau b statistical test. A p value of <0.05 was considered as significant. Estimates adjusted for centre effects were calculated by mixed models including centre as a random factor.

Results

Population

The following results are based on 2,710 patients (female 25.2%; 62.9 ± 13.6 years) of the CNHF with systolic CHF (Table 2). The mean LVEF in the patient population was $31.3 \pm 9.0\%$. Of all patients, 61.3% had an LVEF between 30 and 50%, whereas 38.7% had an LVEF $<30\%$. The most common cause of heart failure was dilated cardiomyopathy (47.4%), followed by coronary artery disease (33.5%).

The majority of patients were in NYHA functional classes II (51.7%) and III (38.1%). Patients with a higher NYHA class were older (NYHA I: 57.3 ± 14.8 years; II: 61.9 ± 13.0 ; III: 65.0 ± 13.6 ; IV: 66.4 ± 15.4). Furthermore, the proportion of females increased with heart failure severity (NYHA I: 10.2%; NYHA II: 23.0%; NYHA III: 30.6%; NYHA IV: 32.9%).

Of all patients with CHF, 11.4% had a coronary aortic bypass graft, 18.1% a percutaneous coronary intervention (PCI), 3.3% valve operation, about 19.7% a one- or two-chamber implantable cardioverter-defibrillator and 7.3% a system with biventricular stimulation. The rates of patients taking beta blockers, ACE inhibitors, AT1 receptor antagonists and aldosterone antagonists were 84.4, 74.9, 17.0 and 46.5%, respectively. Aldosterone antagonists and cardiac glycosides were more frequently used in the NYHA classes III/IV vs I/II.

Out- and inpatient disease-related resource use

On average, CHF patients had 6.1 ± 9.0 GP and 1.7 ± 2.5 cardiologist contacts. The average number of inpatient hospital stays was 0.8 ± 1.2 and of rehabilitation stays 0.1 ± 0.5 . Patients in lower NYHA classes consulted the GPs significantly less often compared with patients in higher NYHA classes ($p < 0.001$). A similar trend was also seen in cardiologist contacts: the mean number of contacts was 1.6 ± 2.1 in NYHA class I and increased to 1.9 ± 4.1 in NYHA class IV. However, this increase was not statistically significant ($p > 0.2$). Nevertheless, patients with higher NYHA class did less often visit the cardiologist at all ($p = 0.004$), but those who have contact with a cardiologist have more frequent visits with increasing NYHA class ($p = 0.001$).

With regard to the inpatient hospital stays, frequency of hospitalizations increased with NYHA class ($p < 0.001$). In addition, the mean number of hospitalizations increased from 0.7 ± 0.9 in NYHA class I to 1.2 ± 1.6 in NYHA class IV. A detailed presentation of out- and inpatient resource use including rehabilitation is given in Table 3.

Table 2 Patient characteristics

	NYHA I	NYHA II	NYHA III	NYHA IV	Total
<i>n</i> (%)	197 (7.3)	1,401 (51.7)	1,033 (38.1)	79 (2.9)	2,710 (100)
Demographics					
Age	57.3±14.8	61.9±13.0	65.0±13.6	66.4±15.4	62.9±13.6
Sex (% female)	10.2	23.0	30.6	32.9	25.2
BMI (kg/m ²)	27.6±4.6	27.7±4.8	27.6±5.2	27.2±6.2	27.6±5.0
Haemodynamics					
Systolic BP	129.0±20.0	123.7±19.4	120.4±19.4	118.2±23.2	122.7±19.7
Diastolic BP	76.3±11.9	73.7±11.2	72.6±11.8	70.4±13.5	73.4±11.6
Heart rate (min ⁻¹)	70.7±14.0	74.8±16.0	78.9±17.9	84.1±18.2	76.3±16.9
Aetiology, <i>n</i> (%)					
Dilated CM	105 (53.3)	666 (47.5)	477 (46.2)	37 (46.8)	1285 (47.4)
CAD	52 (26.4)	473 (33.8)	357 (34.6)	25 (31.6)	907 (33.5)
Other	40 (20.3)	262 (18.7)	198 (19.2)	17 (21.6)	517 (19.1)
Echocardiography					
LVEF (%)	34.6±8.8	32.2±8.7	29.7±9.0	27.0±9.5	31.3±9.0
LVDD (mm)	61.5±9.7	62.3±10.2	62.7±10.1	63.6±10.2	62.4±10.1

All values expressed as mean ± SD if not otherwise specified

NYHA New York Heart Association functional classification, BMI body mass index, BP blood pressure, CM cardiomyopathy, CAD coronary artery disease, LVEF left ventricular ejection fraction, LVDD left ventricular end-diastolic diameter

Estimation of disease-related costs

The estimated costs per physician contact were 19 € for GP and 69 € for the cardiologist. Medication costs per year were 30 € for ACE inhibitors, 88 € for cardiac glycosides, 106 € for beta blockers, 215 € for AT1 receptor antagonists

and 234 € for aldosterone antagonists. Estimated costs per inpatient hospital stay were 2,874 € and 2,943 € per inpatient rehabilitation stay. A complete list of the costs is presented in Table 4.

Overall disease-related health care costs per patient were 3,150 € per year (Table 5). With 74%, the costs of inpatient

Table 3 Disease-related resource use by NYHA class

	NYHA I	NYHA II	NYHA III	NYHA IV	Total
Contacts with GP					
0–1	48.8%	41.0%	35.6%	34.2%	39.3%
2–4	29.4%	27.2%	23.9%	17.7%	25.8%
5–12	17.3%	21.8%	25.1%	24.1%	22.8%
>12	4.6%	10.1%	15.4%	24.1%	12.1%
Mean±SD	3.5±4.9	5.6±8.6	7.1±9.6	9.8±12.5	6.1±9.0
Contacts with cardiologist					
0–1	64.0%	58.0%	57.2%	72.2%	58.5%
2–4	32.0%	35.3%	35.1%	19.0%	34.5%
5–12	3.6%	6.2%	6.8%	6.3%	6.2%
>12	0.5%	0.5%	0.9%	2.5%	0.7%
Mean±SD	1.6±2.1	1.7±2.5	1.8±2.5	1.9±4.1	1.7±2.5
Inpatient hospital stays					
0	49.7%	55.5%	46.6%	48.1%	51.4%
1	37.6%	30.6%	29.6%	24.1%	30.6%
2+	12.7%	13.9%	23.8%	27.8%	18.0%
Mean±SD	0.7±0.9	0.7±1.1	1.0±1.3	1.2±1.6	0.8±1.2
Inpatient rehabilitation stays					
0	98.5%	90.9%	90.6%	91.1%	91.4%
1+	1.5%	9.1%	9.4%	8.9%	8.6%
Mean±SD	0.02±0.1	0.1±0.7	0.1±0.4	0.1±0.4	0.1±0.5

All values expressed as mean ± SD if not otherwise specified

NYHA New York Heart Association functional classification

Table 4 Values for costing

	Costs in 2009 (€)
Physician contacts (costs per contact)	
GP	19
Cardiologist	69
Medication (costs per year)	
Beta blockers	106
ACE inhibitors	30
AT1 receptor antagonists	215
Aldosterone antagonists	234
Cardiac glycosides	88
Hospital (costs per inpatient stay)	2,874
Rehabilitation (costs per inpatient stay)	2,943

hospital care were the largest component of direct costs (2,327 €), while costs of rehabilitation (294 €), medication (290 €) and outpatient physician contacts (238 €) were significantly lower (9, 9 and 8%, respectively). Costs of heart failure care strongly increased with NYHA class. Compared with 2,474 € in NYHA class I, there was an increase of cost in NYHA II, III and IV by 14, 48 and 71%, respectively. About 76% of these incremental costs resulted from increased hospital (inpatient) resource use.

When adjusting for the centre effect, using a mixed model with centre as a random factor, the overall cost per patient was estimated at 2,927 €/year (95% confidence interval 2,394–3,461). In NYHA classes I–IV, the average costs were 2,169 (1,221–3,117), 2,617 (2,046–3,188), 3,656 (3,048–4,265) and 4,466 (3,279–5,654) €/year. NYHA classes I and II differed significantly from III and IV (overall $p=0.003$, pairwise p values from 0.003 to 0.015), but the differences between I and II ($p=0.42$) and III and IV ($p=0.23$) did not reach statistical significance. This could be explained by the fact that groups I and IV

were quite small and the cluster effect was significant (intraclass correlation coefficient 0.1).

Discussion

The present analysis of a current large-scale cohort of systolic CHF patients showed that (1) CHF has a high level of disease-related resource consumption, (2) is cost intensive and (3) costs exhibit a remarkable increase regarding severity of disease.

The present analysis showed that the number of GP contacts increased substantially with the severity of the disease (i.e. by 181% from NYHA class I to IV). However, the number of contacts with the cardiologist increased only slightly by 19%. The present analysis also showed a high rate of hospitalization, which increases with the severity of the disease. Inpatient hospital resources rose by 67% between NYHA class I and IV.

New treatment and care programmes are increasingly designed to improve disease management and to optimize both the sectoral supply and to promote the self-management as well as the empowerment of the patients. Not only the clinical but also the economic benefit of such management strategies to reduce hospitalizations and mortality was previously shown in several studies (Biermann et al. 2010). However, it has been observed that patients in higher NYHA classes show increased inpatient resource use while in the less severe disease categories outpatient contacts dominate. This corresponds to recent results of studies that have dealt with the treatment of CHF patients (Miller et al. 2009).

With regard to the costs of the management of heart failure patients, the analysis showed that costs increase with disease severity as well. This is accordant with previous analyses (Berry et al. 2001; Liao et al. 2007). The total

Table 5 Annual disease-related costs per patient by NYHA class (€)

	NYHA I	NYHA II	NYHA III	NYHA IV	Total	
Subtotal physician	174	224	263	315	238	
GP	67	107	138	188	118	
Cardiologist	107	117	125	127	120	
Subtotal medication	258	290	298	280	290	
Beta blockers	91	91	88	77	90	
ACE inhibitors	23	23	22	23	23	
AT1 receptor antagonists	34	39	36	16	37	
Aldosterone antagonists	87	105	117	125	109	
Cardiac glycosides	23	31	35	40	32	
Hospital (inpatient stays)	1,983	1,954	2,816	3,305	2,328	
Rehabilitation (inpatient)	59	353	294	324	294	
All costs were adjusted for the year 2009	∑	2,474	2,821	3,671	4,224	3,150

costs increased by 71% between NYHA class I and IV. Overall, the highest proportion of costs related to inpatient hospital stays (74%), while the percentage of costs for medication and physician contacts was nearly the same for both components (9 or 8%, respectively). Concerning the external validity, the proportion of costs in our study is comparable to the results of a nationwide data analysis referring to the cost-of-illness accounts of the Federal Statistical Office of Germany (Neumann et al. 2009). In that analysis, 60% of the costs of illness were attributable to hospital stays. Physician contacts resulted in 6% and drugs in 10% of the total expenditures (Neumann et al. 2009). In contrast to the present analysis, Neumann et al. (2009) referred to a top-down approach to determine costs of illness and based on data of the Federal Statistical Office of Germany from 2006 and the authors did not differentiate between systolic and diastolic CHF. Regarding epidemiological data patients with systolic heart failure seem to be a major part of all patients with CHF (Owan et al. 2006). International studies showed that in Western industrialized countries, inpatient hospitalization costs for patients with heart failure accounted for 50–70%, which is comparable to our results (Lloyd-Jones et al. 2010; Stewart et al. 2002; Szucs 2003). Furthermore, the international study results show that physician contacts accounted for 6–8% of the total expenditures and medication costs for 11–18% (Lloyd-Jones et al. 2010; Stewart et al. 2002; Szucs 2003). Nevertheless, cost-of-illness studies for the diagnosis of heart failure are limited in the German health care system. Therefore, the present analysis exhibits a novel and notable estimation of costs for heart failure patients since it is based on nationwide data from more than 2,500 patients.

In addition, the present analysis is predicated on a bottom-up approach to determine the resource consumption. Details of the single patient information about resource use were available and used for the present analysis. The estimation of costs was carried out by a macro-costing approach, where aggregated values were applied. Macro-costing approaches may result in deviations from the true social opportunity costs if the assessment is based on regulated prices and tariffs (Brouwer et al. 2001). Data from macro-costing approaches, however, are generally robust to regional and institutional variations (Luce et al. 1996). This is very important in the present context because the patients were recruited from different institutions and clinics in Germany.

To further improve the quality of the analyses, the present study includes an adjustment of centre effects. Due to comprehensive calculations, this adjustment is the most restrictive statistical analysis and also includes almost the complete cluster effect being performed by different studies. The heterogeneity between different centres highlights the importance of multicentre analyses for the

generation of reliable resource consumptions and associated costs.

Limitations of the present analysis could be further ascertained with regard to the costing of the medication. The application of mono-preparations may overestimate medication costs, because the use of combination preparations would result in lower costs. Nevertheless, such a trend would be similar across the groups. Our analysis evaluated costs associated with disease-related inpatient and outpatient utilization, but we did not examine indirect costs such as loss of productivity. This will lead to an underestimation of the true societal costs. Due to the different NYHA classes there were expectable differences in age and gender. Patients were recruited from different studies across the CNHF, e.g. having different section criteria. Proportions in the study population could therefore not reflect the general population. This may not absolutely represent the German heart failure population, so that real costs will differ from the present analysis. Nevertheless, the aim of our study was to evaluate the disease-related resource utilization and costs for the broad population of the CNHF.

The present work shows that the care of patients with heart failure is associated with high disease-related resource consumption and illustrates for a well-defined cohort of more than 2,500 patients the current health care situation in Germany. However, other treatment strategies have to be developed to optimize care while considering the resource consumption. In light of an aging society and therefore of an expected increase in heart failure patients (Neumann et al. 2009), these aspects represent challenges in health care for the coming years.

Acknowledgement This work was supported by the Competence Network of Heart Failure funded by the Federal Ministry of Education and Research (BMBF), FKZ 01GI0205.

Conflict of interest The authors declare that they have no conflict of interest.

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