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ORIGINAL PAPER

Analyses of drugs stored at home by elderly patients with chronic heart failure

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Abstract
Background Evidence-based pharmacotherapy improves morbidity and mortality in patients with chronic heart failure (CHF). Medication adherence management is important for the effectiveness and safety of treatment. This study investigated drugs stored at home by elderly CHF patients.
Methods and results One hundred and one patients with stable CHF age ≥65 years were visited at home where a standardized interview and a thorough assessment of medication were performed. Mean age of the patients was 77.7 ± 6.1 years, 53 % male, mean NYHA functional class of 2.8 ± 0.7 and a Minnesota-Living-with-Heart-Failure score of 59.4 ± 28.6 points indicating reduced quality of life. The mean number of different drug packs per patient was 13.1 ± 5.5, corresponding to a mean indexed value per patient of €403 ± 48. Cardiovascular drugs accounted for 32 % of the packs. On average, 2.4 ± 3.2 packs contained medication that was not taken by the patient (18 % of the medication, mean indexed value €61 ± 8). Fifty-six percent of the unused drugs were prescribed by general practitioners, 23 % in the hospital, and 7 % by medical specialists and 14 % were over-the-counter drugs. Sixty-three packages (5 %) of the drugs at home were expired (mean indexed value per patient €12 ± 3).
Conclusion On average, elderly patients with CHF have to manage 13 different drug packs per day at home of which a significant portion is not taken as prescribed. New strategies are needed to support medicines management at home.

Keywords Chronic heart failure · Elderly · Drugs at home · Medicines management · Healthcare costs

Introduction

Chronic heart failure (CHF) is a highly prevalent condition that significantly reduces the quality of life and causes high morbidity and mortality [1, 2]. The prevalence of CHF is 2–5 % between the age of 65 and 75 years and increases to ≥10 % at the age of 80 years and older [3]. Evidence-based pharmacotherapy has improved prognosis in patients with systolic heart failure [2]. Adherence to these medications prevents hospitalization and mortality [4].

Medication adherence is defined as the extent that patients are taking drugs according to a previous agreed medication regimen and requires both behavioral execution and persistence in medication taking [5, 6]. The estimated rates of adherence in patients with chronic heart failure—similar to other chronic conditions are 40–60 % [4, 6, 7]. A direct relationship between the number of prescribed medications and adherence rates has been observed [8]. Non-adherence is related to adverse clinical outcomes [4,

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9–12] and increase healthcare costs [13, 14]. On the other hand, good adherence to placebo is associated with lower cardiovascular mortality (healthy adherer effect) [6, 15]. Despite the socio-economic burden and the potential harmful impact of non-adherence, only very limited data are available with regard to the medications present in the homes of elderly patients with CHF. This information is needed to develop future strategies. Therefore, we visited elderly patients with CHF in their homes to assess the quantity of drugs stored, and collected medical, functional, and psychosocial characteristics.

Methods

Studied patients

We aimed to include 100 patients aged ≥65 years with CHF into the study. CHF was defined according to the European Society of Cardiology guidelines [2]. We contacted patients hospitalized for decompensated heart failure at the Saarland University Hospital and patients on a stable CHF medication at a community internal and general medicine practice (Schwemlinger Gemeinschaftspraxis, Merzig/Germany) to participate. No change in the CHF medication had to be documented in the patients' file 4 weeks prior to the visit at patients' home. In Germany, health insurance is mandatory. Care for patients with CHF is provided by hospital-based cardiologists, office-based cardiologists (specialists) and general practitioners (GP). Prescription-only drugs are dispensed in community pharmacies in pre-packed quantities corresponding to the expected treatment duration of 10 [representing norm-size (N) 1 = small-size drug packs], 30 (N2 = medium-size drug packs), or 100 (N3 = big-size drug packs) days. In addition, some drugs are available over-the-counter (OTC) without a prescription, but are usually not reimbursed by statutory health insurance funds. Community pharmacies are the primary source of OTC drugs. Most OTC drugs such as ibuprofen and paracetamol belong to the pharmacy-only category. The study was approved by the local ethic committee (identification number 212/12) in accordance with the Declaration of Helsinki. All patients gave their written consent to participate in the study.

Home visit

Fifty-eight patients hospitalized in the past were contacted and 45 patients (78 %) agreed to participate. At the medical practice, 69 patients were asked and 56 patients (81 %) agreed. Between February 1st and July 31st, 2013, 101 patients were visited at their home at a pre-agreed appointment. Demographic characteristics (gender, age), body mass index, marital status, New York Heart Association (NYHA) functional class for dyspnea, cardiovascular risk factors for the development of coronary artery disease (obesity, smoking, diabetes mellitus, hypertension, hyperlipidemia, sedentary lifestyle, and a family history of heart disease) [16], and admitting diagnosis were assessed. Heart rate and blood pressure were measured in a sitting position after resting for at least 5 min either in the hospital or in the office of the general practitioner (GP). Furthermore, the Charlson Comorbidity Index (CCI; range 0–35, with higher values indicating more comorbidities) [17, 18] was calculated, and a Mini Mental State Examination (MMSE; range 0–30, with higher values indicating lower levels of dementia, values above 25 indicates no dementia) [19] as well as the validated German version of the Minnesota-Living-with-Heart-Failure-questionnaire (MLwHF; range 0–105, with higher values indicating a lower quality of life) [20] were completed by all participants. The names of all medications stored at home (including OTC drugs), the size of the packages (N1, N2, and N3), the doses prescribed and actually taken, the expiration date, and the number of intact or open packages were recorded. If there was uncertainty about the package size (as not 100 % of the drug packs are labeled according to the N-classification), the smallest one was documented. The type of intake was defined as: "used drug packs" for drugs taken daily as prescribed, and as "unused drug packs", not taken as prescribed, if the drugs were not taken within the last 4 weeks before the visit. It was indicated whether the drugs where prescription-only or OTC. The drugs were further classified according to the Anatomical Therapeutical Chemical (ATC) classification index of the World Health Organization [21]. Medication costs were computed using the ex-pharmacy sales/list price according to the German Drug Index "Rote Liste" (www.rote-liste.de, Rote Liste® Service GmbH, Frankfurt/Main, Germany) at the day of the visit. The costs reimbursed by the health insurance fund are often lower due to rebate contracts between statutory health insurance funds and pharmaceutical companies. The details of special prize contracts between manufacturers and the health insurance funds are not available to the public.

File visit (hospital or GP's office)

A file visit of all participating patients was performed prior to the visit after the patient agreed to participate in the evaluation to list comorbidities, register NT-proBNP levels, and to record echocardiographic parameters, in particular the left ventricular ejection fraction. The NT-

Table 1 Patient characteristics

	All patients ($n = 101$)	GP ($n = 56$)	Hospital ($n = 45$)	p
Age (years)	77.7 ± 6.1	78.1 ± 6.1	77.2 ± 6.2	0.514
Male	53 (53 %)	25 (45 %)	28 (62 %)	0.08
BMI (kg/m^2)	28.6 ± 4.6	29.5 ± 4.9	27.5 ± 4.3	0.026
Married (%)	61	57.1	66.7	0.331
NYHA	2.8 ± 0.7	2.6 ± 0.6	3.0 ± 0.8	0.005
I	3	0	3	–
II	33	28	5	–
III	51	24	27	–
IV	14	4	10	–
CVRF	2.5 ± 1.0	2.6 ± 1.1	2.4 ± 1.0	0.423
Comorbidities	3.1 ± 1.2	2.9 ± 1.1	3.4 ± 1.2	0.029
Heart failure and a reduced ejection fraction (ejection fraction <50 %)	76 (75 %)	37 (66 %)	39 (87 %)	<0.001
Heart failure with preserved ejection fraction (ejection fraction ≥50 %)	25 (25 %)	19 (34 %)	6 (13 %)	<0.001
Ejection fraction (%)	45 ± 14	48 ± 12	41 ± 16	<0.001
NT-proBNP (pg/ml)	694 ± 297 ($n = 82$)	489 ± 267 ($n = 37$)	821 ± 311	<0.001
Office SBP (mmHg)	131 ± 19	134 ± 9	127 ± 26	0.045
Office DBP (mmHg)	77 ± 13	79 ± 8	74 ± 17	0.046
Office heart rate (bpm)	68 ± 13	68 ± 11	69 ± 17	0.587
CCI (0–35 points)	4.3 ± 2.8	4.0 ± 3.0	4.6 ± 2.4	0.231
MMSE (0–30 points)				
No dementia (>25)	76 (75 %)	43 (77 %)	33 (73 %)	<0.001
Mild dementia (20–25)	23 (23 %)	12 (21 %)	11 (24 %)	0.688
Moderate dementia (10–20)	2 (2 %)	1 (2 %)	1 (2 %)	–
Severe dementia (<10)	0	0	0	–
MLwHF (0–105 points)	59.4 ± 28.6	47.6 ± 27.9	73.8 ± 22.4	<0.001

proBNP levels at the hospital were measured after recovery from acute decompensation.

Statistical analyses

This evaluation is a descriptive, cross-sectional study. Data are presented as mean ± standard deviation of the mean and their distribution as percentages unless otherwise specified. Comparisons of means between groups were carried out with the Mann–Whitney U test for discrete data and Student's t test for continuous data. Relationships between sociodemographic characteristics, medical data, and number of accumulated drugs or costs were performed using Spearman correlation testing and linear regression analyses. Significance tests were two tailed with $p < 0.05$ considered significant. All statistical analyses were calculated using the SPSS statistical software (version 20.0, SPSS Inc., Chicago, Illinois).

Results

The characteristics of the 101 patients included in the study are summarized in Table 1. The participating patients were 77.7 ± 6.1-year-old, 53 % men, body mass index 28.6 ± 4.6 kg/m^2, 61 % married. They exhibited 2.5 ± 1.0 cardiovascular risk factors. Their mean heart rate was 68 ± 13 bpm. Patients recruited at the hospital had a significantly lower body mass index (−2.0 ± 4.6 kg/m^2, $p = 0.026$), higher (+0.41 ± 0.68, $p = 0.005$) NYHA functional class, a lower ejection fraction (−7 ± 13 %, $p < 0.001$), higher NT-proBNP levels (+332 ± 194 pg/ml, $p < 0.001$), more comorbidities (+0.5 ± 0.9, $p = 0.029$), and showed lower systolic (−7 ± 16 mmHg, $p = 0.045$) and diastolic (−5 ± 12 mmHg, $p = 0.046$) office blood pressures. The most common non-cardiac comorbidities were arterial hypertension (86 %), diabetes mellitus (50 %), and chronic obstructive pulmonary disease (27 %).

Mental status and quality of life

The mean CCI was 4.3 ± 2.8 points with no disparity between both groups. The MMSE showed no signs of dementia (score >25 points) in 77 % of the patients enrolled at the Schwemlinger Gemeinschaftspraxis and in 73 % of the patient recruited at the hospital ($p < 0.001$). Mild dementia (score 20–25 points; 23 % of all patients) and moderate dementia (score 10–20 points; 2 % of all patients) did not differ between groups. We detected no patient with severe dementia (score <10 points). The MLwHF score was 59.4 ± 28.6 points indicating a poor quality of life. The score was significantly higher in patients that had been hospitalized (+26.1 ± 26.7 points, $p < 0.001$).

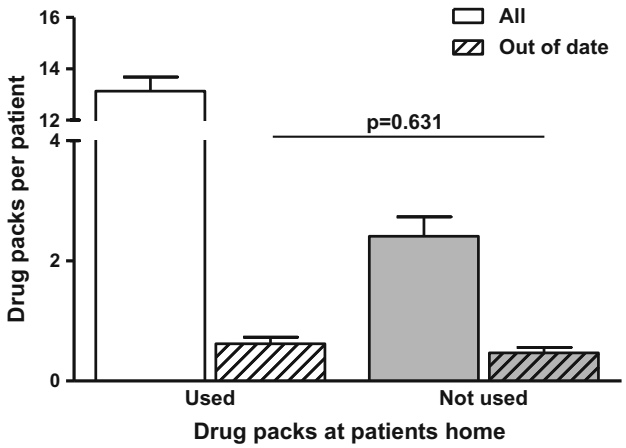

Fig. 1 Number of drug packs per patient. Data are presented in mean ± standard error

Drugs stored at home

A total of 1,326 drug packs were observed in the homes of the participants. Thus, these patients had stored at home a mean number of 13.1 ± 5.5 packs, ranging from 4 to 33, with a median of 12 (Fig. 1). Among these, 1,161 (88 %, range 3–29) drug packs were prescribed by a physician and 165 (12 %, range 0–10) packs were OTC. The mean cost per patient amounted to €403 ± 48 (range €71–1,552). Prescribed drug packs amounted to 95 % of the medication costs. Sixty-one percent (8.0 ± 4.0 packs per patient, range 3–13) of the drug packs were prescribed by a GP leading to indexed costs per patient of €244 ± 32, 19 % (2.5 ± 4.1 packs per patient, range 0–5) in the hospital leading to €86 ± 7 per patient, and 8 % (1.1 ± 1.8 packs per patient, range 0–3) by a specialist corresponding to an amount of €52 ± 6 per patient. The pack size of the medication according to treatment duration was 18 % as N1 (medication for approximately 10 days), 19 % as N2 (medication for approximately 30 days), and 63 % as N3 (medication for approximately 100 days).

Table 2 details the number of drug packs and their costs. Forty-two (3 %) packs could not be ascribed to a specific drug category (foreign drugs, drugs no longer available on the market) and were listed as "other" medication.

CHF-related medication (Table 3) accounted for 32 % of the drug packs corresponding to 30 % of the total costs. Ninety-one percent of the patients had a beta-blocker, 81 % an ACE-inhibitor or angiotensin receptor blockers, 76 % a diuretic, and 24 % a mineralocorticoid receptor antagonist at their home [2]. Digitalis (digoxin/digitoxin) was available in 13 % of the homes and ivabradine was found in 3 homes. There was no significant difference between patients enrolled in the hospital or at the GP's office.

On average, 2.4 ± 3.2 packs contained medication that was not taken by the patient (18 % of the medication, range 0–10) leading to a total amount of €6,151 (mean amount of €61 ± 7 per patient). The most common medicines not taken as prescribed were related to CHF (28 %), followed by analgesics (20 %), and drugs affecting the alimentary tract (8 %). Fifty-six percent of the unused drugs were prescribed by general practitioners, 23 % in the hospital, and 7 % by medical specialists while 14 % were OTC drugs. The pack size of the majority of the unused medication was N3 (44 %).

Sixty-three drug packs (5 %) were expired corresponding to costs of €11 ± 4 per patient. Seventy-five per cent ($n = 47$) of these packs belonged to the group not taken as prescribed. The pack size of the drug packs out of date was in 43 % N1 (small size), 32 % N2 (medium size), and 26 % N3 (big size).

In these patients, there was no significant correlation between the center of patients' enrollment, age, comorbidities, NYHA class, CCI score, drug pack size, or physician in charge for the drug prescription, and the number of drug packs or drugs not taken as prescribed. Simple and multiple regression analyses of demographic or clinical characteristics as well as comorbidities on the number of drugs or their costs identified no single statistically significant association. The same was true when these characteristics were dichotomized into normal and abnormal, and the number of drugs and their costs were log transformed to account for skewed distribution. However, patients with an MLwHF score above average ($p = 0.001$) (Fig. 2) and an MMSE score of 25 and below points ($p < 0.001$) (Fig. 3), respectively, had significant more drug packs at home not taken as prescribed. Furthermore, there was a trend for higher number of rest drug packages in patients receiving polypharmacy (intake of ≥4 different drugs per day) (2.2 ± 3.6 vs. 2.6 ± 2.8, $p = 0.108$).

Discussion

The main finding of this study is that each day an elderly patient with CHF has to manage an average of 13 different drug packs at home. 18 % of the drug packs contained medication which was not taken by the patient corresponding to an indexed value of €61 per patient. A higher number of unused drug packs were associated with a poorer quality of life (MLwHF score above average) and impaired cognitive function (MMSE score of 25 and below points).

Table 2 Analyses of all, expired, and unused drug packs stored at home according to the ATC-classification

	Count of packs		Packs per patient	Count of unused packs		Not used packs per patient
Medication						
All	1,326	(100 %)	13.1 ± 5.5	243	(100 %)	2.4 ± 3.2
All out of date	63	(5 %)	0.6 ± 1.1	47	(19 %)	0.5 ± 0.9
Chronic heart failure drugs	418	(32 %)	4.1 ± 2.1	67	(28 %)	0.7 ± 1.3
Analgetics	167	(13 %)	1.7 ± 1.7	48	(20 %)	0.5 ± 1.1
Non-prescribed drugs	144	(11 %)	1.4 ± 1.6	33	(14 %)	0.3 ± 0.7
Endocrinologic drugs other	96	(7 %)	1.0 ± 0.9	12	(5 %)	0.1 ± 0.4
Alimentary tract drugs	89	(7 %)	0.9 ± 1.1	20	(8 %)	0.2 ± 0.6
Platelet-aggregation inhibitors	63	(5 %)	0.6 ± 0.3	5	(2 %)	0.1 ± 0.1
Pneumologic drugs	61	(5 %)	0.6 ± 1.0	7	(3 %)	0.1 ± 0.3
Lipid-lowering medication	60	(5 %)	0.6 ± 0.6	5	(2 %)	0.1 ± 0.2
Anticoagulants	45	(3 %)	0.5 ± 0.6	7	(3 %)	0.1 ± 0.3
Other	42	(3 %)	0.4 ± 0.9	11	(5 %)	0.1 ± 0.4
Infectiologic drugs	36	(3 %)	0.4 ± 0.9	12	(5 %)	0.1 ± 0.4
Antidiabetics insulin	34	(3 %)	0.3 ± 0.7	1	(0.4 %)	0.01 ± 0.2
Antidiabetics oral	24	(2 %)	0.2 ± 0.6	4	(2 %)	0.04 ± 0.2
Psychotropic drugs	22	(2 %)	0.2 ± 0.5	4	(2 %)	0.04 ± 0.2
Neuroleptics	19	(1 %)	0.2 ± 0.5	7	(3 %)	0.1 ± 0.3
Noctiva	4	(0.3 %)	0.1 ± 0.2	0		
Antidiabetics others	2	(0.2 %)	0.02 ± 0.1	0		
Prescriber						
GP	803	(61 %)	8.0 ± 4.0	136	(56 %)	1.4 ± 2.1
Hospital	249	(19 %)	2.5 ± 4.1	56	(23 %)	0.6 ± 1.7
Self-medication	165	(12 %)	1.6 ± 2.0	35	(14 %)	0.4 ± 0.8
Specialist	109	(8 %)	1.1 ± 1.8	16	(7 %)	0.2 ± 0.5
Pack size						
N1 all	243	(18 %)	2.4 ± 2.3	73	(30.0 %)	0.7 ± 1.1
N1 out of date	28	(2 %)	0.3 ± 0.6	20	(8 %)	0.2 ± 0.5
N2 all	249	(19 %)	2.5 ± 2.4	64	(26 %)	0.6 ± 1.4
N2 out of date	21	(2 %)	0.2 ± 0.7	15	(6 %)	0.2 ± 0.5
N3 all	834	(63 %)	8.3 ± 3.5	106	(44 %)	1.1 ± 1.7
N3 out of date	14	(1 %)	0.2 ± 0.4	12	(5 %)	0.1 ± 0.4

GP general practitioner; Pack sizes: N1: treatment for 10 days, N2: for 30 days, N3: for 100 days

CHF is one of the most important causes of morbidity and mortality in Western countries [22]. Patients with CHF require multiple drug therapy to control symptoms, slow the progression of cardiac remodeling, as well as to decrease hospitalization and mortality [23]. According to estimates of the European Society of Cardiology, within 51 European countries representing a population of 900 million individuals, at least 15 million individuals suffer from CHF [2]. Based on our study, one could estimate for these patients' total drug costs of approximately 6.1 billion Euros and the value of unused drugs would amount to approximately 915 million Euros. Symptoms related to CHF are the leading cause of hospitalization [24], contributing to 70 % of the total treatment-related costs in patients older than 65 years [25] (in the USA approximately US$ 20.1 billion in 2009 [1]), representing approximately 2 % of the total health care expenditure in industrialized countries [25]. One half to two-thirds of all rehospitalizations have been associated with poor adherence to medication [26–28]. Strategies to improve adherence may disburden the healthcare systems. Therefore, the aim of this study was to assess the medication in the homes of elderly patients with CHF.

Besides the intake of mineralocorticoid receptor antagonists (24 % vs. 48 % in REFLECT-HF), the prescribed medication of guideline-recommended pharmaceutical treatment in this study is in line with other contemporary studies such as the REFLECT-HF registry [29]. However, a significant part of all medications which is prescribed for the treatment of chronic diseases is not taken as

Table 3 Chronic heart failure-related medication

CHF Medication	Number of patients	Prescribed by GP	Prescribed in hospital	Prescribed by a specialist
Beta-blockers	92 (91 %)	64 (70 %)	25 (27 %)	3 (3 %)
ACE-inhibitors/ ARBs	82 (81 %)	55 (67 %)	23 (28 %)	4 (5 %)
Diuretics	77 (76 %)	45 (58 %)	29 (38 %)	3 (4 %)
MRA	24 (24 %)	15 (63 %)	9 (38 %)	0
Glycosides	13 (13 %)	7 (54 %)	6 (46 %)	0

CHF chronic heart failure, *GP* general practitioner, *ACE-inhibitors* angiotensin converting enzyme-inhibitors, *ARBs* angiotensin receptor blockers, *MRA* mineralocorticoid receptor antagonists

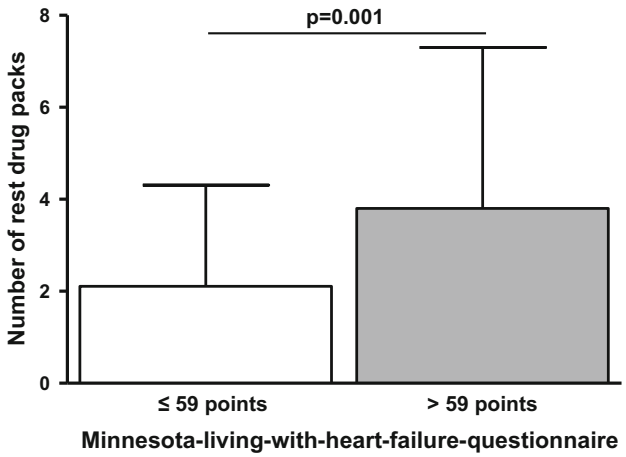

Fig. 2 Number of rest drug packs in relation to quality of life

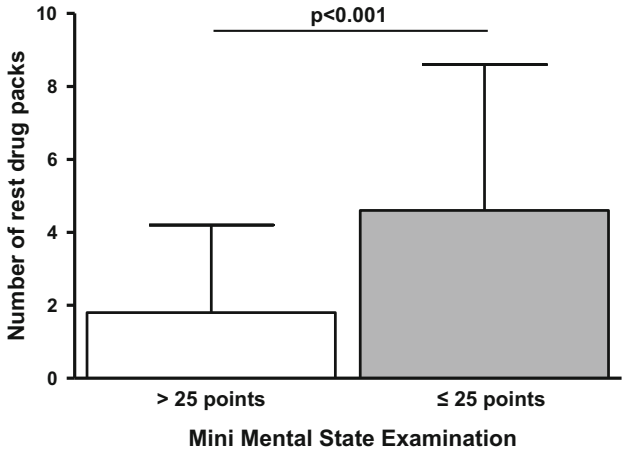

Fig. 3 Number of rest drug pack in relation to cognitive function

recommended [30, 31]. Non-adherence to medical treatments is associated with an increased risk of stroke, myocardial infarction, and cardiovascular death in patients with CHF [11, 12] as well as by other chronic diseases such as hypertension [32] or coronary artery disease [33]. Cardiovascular events are associated with lower adherence which increases event rates leading to a vicious circle of poor adherence and cardiovascular events [11]. In this study, patients with an MLwHF score above average that exhibit more CHF symptoms were characterized by a higher number of unused packs.

Patients with CHF are suffering from a high number of comorbidities that require chronic medications [34–37]. In a recent study including 1,395 participants with CHF, 58 % had 5 or more comorbid chronic conditions requiring a pharmaceutical treatment [34]. More than half of the patients had hypertension (73 %), hypercholesterolemia (54 %), or arthritis (62 %) [34]. In another cross-sectional observation of 122,630 patients with CHF the most common non-cardiac comorbidities were: hypertension (55 %), diabetes mellitus (31 %), and chronic obstructive pulmonary disease (26 %) [35]. These findings are comparable with the results observed in our study.

Polypharmacy (intake of ≥4 different drugs per day) is related to increased non-adherence rates [8]. According to a systematic review, the number of daily doses is inversely related to medication adherence [8]. In this analysis, adherence in patients taking 4 doses daily was only around 50 % [8]. Currently, 30–40 % of all German patients above the age of 65 years are prescribed four or more different drugs [38, 39]. The number of drug packs found in patients' households in this study is in line with the literature [27, 34, 40], representing a significant risk for incorrect intake [8]. However, in this study there was a non-significant trend for more rest drug packs found in patients' home and the number of prescribed agents.

In addition to comorbidities and polypharmacy, age, gender, socioeconomic status, medication characteristics (e.g., adverse effects) and psychosocial issues increase the risk of non-adherence [6, 41]. Patients with CHF often suffer from impaired cognitive function [42]. Elderly patients with CHF and impaired cognitive function are characterized by poor adherence, medication mismanagement and failure to monitor signs and symptoms of worsening heart failure or to seek for medical attention [43]. Indeed, in our analyses, an MLwHF score above average and a reduction in cognitive function were associated with more unused drug packs stored at home. The number of unused packs was similar whether they were prescribed by a hospital, specialist or general physician.

Although research in medication adherence has been only recently highlighted, a variety of interventions to improve adherence have been proposed. These range from adjustments in the medication regimen to complex multidisciplinary interventions addressing health system issues and communication between patients and healthcare

professionals [6, 41, 44]. Among these measures, an improved pharmaceutical care with thorough patient information and regular reminders by physicians, nurses, and pharmacists and the systematic use of pre-packed time-specific unit doses have shown to improve adherence in randomized studies [6]. Several types of interventions are effective in improving medication adherence, but few were able to demonstrate an impact on clinical outcomes [44]. The high number of packs found at the patients' home identifies a target for the improvement of medication management. Simplifying the drug regimen and specifically supporting elderly patients with CHF by providing the medication in weekly blister packs may be effective interventions to improve adherence.

Limitations

It is likely that some patients may have cleaned up their medication fundus prior to the scheduled home visit. Therefore, the results may be biased towards less unused and expired medications. In addition, we do not know whether medication management is worse in the patients that refused to be visited at home. Finally, all costs reported in this study are based on ex-pharmacy sales/list price according to the German Drug Index "Rote Liste" at the day of the visit. Discount agreements between suppliers and health insurance organizations as well as price changes during the study period could not be considered in the calculated indexed values of this study. Obviously, the results need to be confirmed in different populations and health care systems.

Conclusions

This study shows that elderly patients have to manage a highly complex medication regimen at their home leading to a high economic burden on the healthcare system. A significant part of the stored medication is not in use or outdated. These findings identify an important area for improvement by providing strategies and tools to improve medication adherence and safety.

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