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The Impact of Atrial Fibrillation on the Cost of Stroke: The Berlin Acute Stroke Study

Bernd Brüggenjürgen, MD, MPH,[1] Karin Rossnagel, MD,[1] Stephanie Roll, MSC,[1] Fredrik L. Andersson, PhD,[2] Dagmar Selim, MSC,[1] Jacqueline Müller-Nordhorn, MD,[1] Christian H. Nolte, MD,[3] Gerhard J. Jungehülsing, MD,[3] Arno Villringer, MD,[3] Stefan N. Willich, MD, MPH[1]

[1]Institute for Social Medicine, Epidemiology and Health Economics, Charité—Universitätsmedizin Berlin, Germany; [2]AstraZeneca R&D, Lund, Sweden; [3]Department of Neurology, Charité—Universitätsmedizin Berlin, Germany and Competence Network Stroke

ABSTRACT

Objectives: Atrial fibrillation (AF) is an important risk factor for stroke. The primary purpose of this study was to determine the resource use for patients admitted to hospital with acute stroke and to calculate stroke-related direct costs, stratifying the results according to the presence of AF as a risk factor.

Methods: Data from 558 consecutive patients hospitalized with confirmed acute stroke between August 2000 and July 2001 were analyzed as part of the Berlin Acute Stroke Study. Sociodemographic variables were assessed by direct interview, while hospital data were derived from patient medical records. Patients or their carers completed a follow-up questionnaire about resource utilization and absenteeism from work during the 12-month period after hospital admission.

Results: Out of the 367 patients with follow-up data and ECG findings, 71 (19%) had AF. Patients with AF were generally older, more likely to be female, and had more severe strokes compared with those without AF. Mean direct costs per patient were significantly higher in those with AF-related strokes (€11,799 vs €8817 for non-AF-related strokes; $P < 0.001$). After adjustment for confounding factors, direct costs were comparable in the two groups, except for acute hospitalization costs, which remained significantly higher in the group with AF ($P < 0.05$).

Conclusion: Medical care for stroke patients with AF is associated with higher costs compared with those without AF; this is explained mainly by confounding factors and driven essentially by a significant difference in acute hospitalization costs.

Keywords: atrial fibrillation, burden of disease, cost analysis, stroke.

Introduction

Stroke is a debilitating and potentially fatal disease with a significant long-term economic and social burden. In the United States alone, for example, the annual cost of stroke has been estimated at $53.6 billion [1]. A major share of strokes are cardioembolic, and the presence of atrial fibrillation (AF) is a strong risk factor in this regard [2]. Indeed, this common cardiac arrhythmia, which has an estimated age-dependent prevalence of 1% to 9%, is responsible for approximately 15% of all strokes [3]. Such events also tend to be of greater severity and associated with increased risk of poorer neurological outcomes, medical complications, and death than in patients with non-AF-related strokes [4,5]. To the best of our knowledge, however, there are no studies that have examined whether the presence of AF impacts on costs among patients with stroke [6]. If an impact on costs is present and it is neglected, economic evaluations will underestimate the cost-effectiveness of future anticoagulation treatment resulting in a reduced risk of stroke.

Therefore, the primary aim of the present study was to determine the short- and long-term medical resource use for patients admitted to hospital with acute stroke and to calculate stroke-related direct costs, stratifying the results according to the presence of AF as a risk factor. In addition, labor-force-related indirect costs were assessed.

Methods

This study used data from the Berlin Acute Stroke Study, an ongoing study of consecutive patients admitted to four German hospitals for treatment of acute stroke over a 1-year period (August 1, 2000 to July 31, 2001). Details of the study have been reported elsewhere [7]. Briefly, the study was conducted at four hospitals in the city of Berlin (population approximately

Address correspondence to: Bernd Brüggenjürgen, Institute for Social Medicine, Epidemiology and Health Economics, Charité—Universitätsmedizin Berlin, 10098, Berlin, Germany. E-mail: bernd.brueggenjuergen@charite.de

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420,000), including two university hospitals and two general community hospitals, all with primary responsibility for the treatment of patients with acute stroke in their geographic areas. A total of 1094 patients with stroke symptoms were admitted to the respective emergency departments. Patients were eligible for inclusion if they were judged by a neurologist to display signs or symptoms of an acute stroke upon emergency department (ED) admission, during which the National Institutes of Health Stroke Scale (NIHSS) score was recorded (using the validated German version of this questionnaire [8]). The exclusion criteria were presentation after 7 days of symptom onset, discharge or transfer to a nonparticipating hospital within 24 hours, death within 24 hours of ED admission, or in-hospital stroke. Thirteen non-German speaking patients were also excluded from enrollment. A total of 471 (mean age 72.6 ± 14.3 years) could not be interviewed because of immediate transfer to another hospital, lack of informed consent, or inability to participate in the interview without any proxies around. The study was approved by the local ethics committee.

A total of 623 patients with suspected stroke were able to participate in the study and consented to face-to-face interviews that were conducted between 24 and 72 hours after hospital admission. The 50-item interview (available at http://www.mosby.com/AnnEmergMed) captured information on type and course of symptoms, patient's interpretation of symptoms, lifestyle and medical history, help-seeking behavior, awareness about stroke and medication, and socio-demographic factors. In-hospital management data, including final diagnosis, were collected by chart reviews after the patient had been discharged. The final diagnosis was based on neurological assessment and imaging. The diagnosis of stroke was determined as "a clinical syndrome characterized by rapidly developing clinical signs of focal or global loss of cerebral function, lasting more than 24 hours or leading to death, with no other apparent causes other than of vascular origin" [9], while a diagnosis of transient ischemic attack (TIA) followed the definition of "a neurological symptom of vascular etiology that resolved within 24 hours" [10,11]. The neurologist's initial diagnosis of stroke on ED admission was changed after thorough investigation in 65 patients (10%), who were subsequently excluded from the analysis. The final diagnoses in these patients were mainly other neurological diseases, such as epileptic seizures with history of stroke, multiple sclerosis, neuritis vestibularis, myasthenia gravis, and Miller–Fisher syndrome. The study population therefore comprised 558 patients with confirmed stroke and baseline interview. This group received a follow-up postal questionnaire 12 months after hospital admission regarding resource utilization and absenteeism from work, which was to be completed by the patient or carer. A reminder was sent after 4 weeks if there was no reply; thereafter, the patient was contacted by telephone. One hundred seventy-five patients did not respond to the follow-up form, of which 96 could not be contacted by the local residents' registration office, 28 were not willing to participate, and 51 died. Direct costs were subsequently calculated by multiplying medical resource units used with cost per unit, while indirect costs (productivity loss of the labor-force participants) were calculated by multiplying days off work or days of early retirement with the average cost factor per day (Table 1). A subanalysis was completed by stratifying the data according to the presence of confirmed AF. The time horizon of the study was 1 year.

Baseline variables were compared between groups using appropriate statistical tests. Socioeconomic sta-

Table 1 Unit costs

	Cost (€)
Hospitalization (cost/day)*	
Acute treatment	
Stroke unit/intensive care	853
General ward	250
Readmission	309
Rehabilitation	
Inpatient (cost/day)†	118
Day rehabilitation (cost/day)†	60
Outpatient (cost/session)‡	
Physiotherapy	13.94
Massage	9.37
Heat pack	7.85
Exercise therapy	11.30
Occupational therapy	25.28
Speech therapy	21.22
Nursing care (cost/month)§	
Nursing home	1023–1432
Nursing care at home	250–857
Visits to a health-care professional (cost/visit)‖	
General practitioner	12.3
Neurologist	30.6
Internal medicine specialist	30.6
Psychologist/psychotherapist	40.2
Other specialist	30.6
Lost productivity (cost/day)¶	
Absenteeism from work	78.13
Early retirement	78.13
Other	
Medication	Per item#
Aids/modifications of home	Per item#
Transport (cost/trip)	
Ambulance	52
Emergency medical services	212
Emergency physician	317
Taxi	14

*Statistisches Taschenbuch Gesundheit 2002, Tab 7.7, Krankenhauskosten je Pflegetag nach Ländern für Deutschland (per diem hospital costs according to Länder). 2000.
†Verband deutscher Rentenversicherungsträger. From Landesversicherungsanstalt Niederbayern-Oberpfalz [12].
‡Vergütungsliste für krankengymnastische Leistungen, Massagen und med. Bäder (reimbursement scheme for physiotherapies, massages, and medical spa) (§ 125 Sozialgesetzbuch V). 2002.
§Pflegeversicherungsgesetz (nursing insurance law) § 15, 36, 37, 43 SGB XI.
‖Zentralinstitut für die kassenärztliche Versorgung in der BRD. Die 50 häufigsten Diagnosen von Patienten, Kontakthäufigkeit und angeforderter Leistungsbedarf in Punkten. 2002.
¶VdR, Durchschnittliche Bruttojahresarbeitsentgelte (average yearly gross income). From Weimar et al. [12].
#Gelbe Liste Pharmindex (German Yellow pharmacopoiea). Neu-Isenburg. 2002.
Exchange rate: €1 = $1.32 (January 2005).

Table 2 Baseline sociodemographic and clinical characteristics

	AF (n = 71)	Non-AF (n = 296)	*P*-value*	Responders with ECG findings (n = 367)†	Nonresponders/ no ECG (n = 191)	*P*-value‡
Mean age (± SD)	73.7 ± 9.4	63.9 ± 13.5	<0.001	65.8 ± 13.4	68.4 ± 14.0	0.04
Female (%)	52	39	0.06	42	52	0.03
Education ≥12 years (%)	18	28	0.13	26	18	0.04
Living alone (%)	44	28	0.01	31	43	<0.001
Gainfully employed (%)	3	30	<0.001	24	19	0.13
NIHSS score (%)						
0–2	31	43	0.03	41	24	<0.001
3–6	38	39		39	41	
≥7	31	18		20	35	
Mean NIHSS score (± SD)	5.5 ± 4.6	4.1 ± 4.1	0.008	4.3 ± 4.2	6.4 ± 5.4	<0.001
Diagnosis (%)						
TIA	17	33	0.03	30	18	0.02
Stroke	77	62		65	72	
Hemorrhage	6	5		5	10	
Comorbidity (%)§						
Diabetes mellitus	49	27	0.08	23	27	0.34
Hypertension	65	51	0.05	54	51	0.59
Cardiac insufficiency	23	6	<0.01	20	9	<0.01
Myocardial infarction	16	7	0.03	20	9	<0.01
Hyperlipidemia	25	35	0.16	30	33	0.56
Prior stroke (%)§	30	17	0.02	20	22	0.43

*Comparison of AF and non-AF patients.
†Patients with questionnaire follow-up data (at 12 months) and ECG findings.
‡Comparison of responder and nonresponder patients.
§From patient recall.
AF, atrial fibrillation; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

tus was measured via length of education and gainful employment. Resources used were compared with the chi-square test, while costs were compared with the Mann–Whitney *U*-test because of non-normal distribution of data. Cost data were analyzed in three ways: unadjusted, adjusted for confounding factors, and adjusted for confounding factors on a logarithmic scale (to test the impact of skewed data). These adjustments were completed given the importance of confounding factors in this patient population and were carried out using general linear model (GLM) analysis. All baseline sociodemographic and clinical characteristics reported in Table 2 were initially included, tested for interaction, and consecutively excluded based on statistical significance. As the severity of stroke could also be considered a result of the presence of AF, we performed the adjustment both including and excluding the severity variable from the NIHSS score. No adjustment for multiple testing was performed. All statistical analyses were performed with SAS version 8.1 (SAS Institute, Inc., Cary, NC). Costs are presented in euros (€)—exchange rate: €1 = $1.32 (January 2005).

Results

Patient Characteristics

A total of 558 patients with confirmed stroke were interviewed (mean age 66.8 years; mean NIHSS score 5.0). ECG findings were available for 531 (95%) patients. AF was diagnosed in 116 patients (22%).

A total of 383 patients (69% of total population) filled out the follow-up questionnaire at 12 months after hospital admission, of whom 16 had missing baseline ECG information. Of the remaining 367 patients, 71 (19%) had AF. Overall, patients with AF were generally older, more likely to be female and living alone, had more frequent comorbidity and prior stroke, and experienced more severe strokes than those without AF (Table 2). Patients with AF were also less likely to be gainfully employed than non-AF patients (2 (31%) of 71 patients and 87 (30%) of 294 patients, respectively).

Resource Use and Costs

Resource use, stratified according to AF status and for all patients combined, is shown in Table 3. Overall, stroke patients with AF tended to consume more resources than non-AF patients, including longer lengths of hospital stay and increased use of nursing care. Of those 65 patients with medication a total of nine (13%) patients with AF had received anticoagulation therapy before the stroke event, of which six (8%) patients were receiving such treatment for secondary prevention.

Direct and indirect costs, stratified according to AF status and for all patients combined, are shown in Table 4. Overall, total direct costs were approximately €3000 higher in patients with AF-related strokes ($P < 0.001$), and this was primarily driven by significantly increased costs for acute hospital treatment and nursing care at home. The percentage of direct-cost components for AF and non-AF patients is shown in Figure 1. Total indirect costs were significantly higher for non-AF patients than for those with AF

Table 3 Mean (± SD) resource use of patients, stratified according atrial fibrillation (AF) status and for all patients combined, unadjusted

	AF (n = 71)		Non-AF (n = 296)			All patients (n = 367)	
	n (%)	LOS or frequency (median)	n (%)	LOS or frequency (median)	*P*-value	n (%)	LOS or frequency (median)
Hospitalization							
Acute treatment	71 (100)	16 ± 10 days (15)	296 (100)	14 ± 8 days (11)	1.0	367 (100)	14 ± 8 days (12)
Stroke unit/intensive care	37 (52)	5 ± 4 days (3)	143 (48)	4 ± 3 days (3)	0.60	180 (49)	4 ± 3 days (3)
General ward	67 (94)	15 ± 10 days (13)	282 (95)	12 ± 8 days (11)	0.76	349 (95)	13 ± 8 days (11)
Readmission	13 (18)	26 ± 25 days (18)	51 (17)	16 ± 21 days (10)	0.86	64 (17)	18 ± 22 days (11)
Rehabilitation							
Inpatient	25 (35)	33 ± 28 days (22)	106 (36)	27 ± 17 days (20)	1.0	131 (36)	28 ± 20 days (20)
Day rehabilitation	2 (3)	40 ± 28 days (40)	9 (3)	28 ± 20 days (20)	1.0	11 (3)	30 ± 21 days (20)
Outpatient	20 (28)	NA	72 (24)	NA	0.54	92 (25)	NA
Nursing care							
Nursing home	3 (4)	281 ± 34 days (273)	4 (1)	209 ± 83 days (209)	0.14	7 (2)	240 ± 73 days (252)
Nursing care at home	16 (23)	247 ± 100 days (224)	40 (14)	198 ± 95 days (224)	0.07	56 (15)	211 ± 98 days (224)
Visits to a health-care professional							
General practitioner	54 (76)	17 ± 14 visits (12)	216 (73)	13 ± 14 visits (10)	0.66	270 (74)	14 ± 14 visits (10)
Neurologist	21 (30)	4 ± 5 visits (3)	110 (37)	5 ± 5 visits (3)	0.27	131 (36)	5 ± 5 visits (3)
Internal medicine specialist	20 (28)	8 ± 11 visits (4)	68 (23)	6 ± 7 visits (4)	0.36	88 (24)	6 ± 8 visits (4)
Psychologist/psychotherapist	1 (1)	4 visits (4)	43 (15)	13 ± 13 visits (10)	<0.001	44 (12)	12 ± 12 visits (10)
Other specialist	7 (10)	7 ± 9 visits (1)	28 (9)	6 ± 6 visits (4)	1.0	35 (10)	6 ± 7 visits (4)
Other							
Medication	65 (92)	NA	274 (93)	NA	0.80	339 (92)	NA
Aids/modifications of home	30 (42)	NA	70 (24)	NA	0.003	100 (27)	NA
Transport	20 (28)	NA	58 (20)	NA	0.007	78 (21)	NA
Lost productivity (age < 65)	(n = 11)		(n = 150)			(n = 161)	
Absenteeism from work	2 (18)	150 ± 127 days (150)	59 (39)	96 ± 88 days (60)	0.209	61 (38)	97 ± 89 days (60)
Early retirement	1 (9)	140 days (140)	19 (13)	159 ± 111 days (148)	1.0	20 (12)	158 ± 108 days (144)

LOS, length of stay; NA, not applicable.

($P < 0.001$), and work absenteeism was the major cost driver in this regard (Table 4).

Further statistical analysis of the cost data was completed, adjusting for confounding factors such as age, sex, TIA, number of comorbidities, and with and without NIHSS score (the logarithmic GLM adjustment analysis provided no different results and is not further reported). The GLM procedure indicated that, in addi-

Table 4 Mean (± SD) costs per patient (€), stratified according to atrial fibrillation (AF) status and for all patients combined, unadjusted

	AF (n = 71)	Non-AF (n = 296)	*P*-value	All patients (n = 367)
Hospitalization				
Acute treatment	5447 ± 3363	4423 ± 2774	0.004	4620 ± 2920
Readmission	1467 ± 4476	847 ± 3224	0.66	966 ± 3503
Rehabilitation				
Inpatient/day rehabilitation*	1559 ± 2755	1313 ± 2128	0.81	1360 ± 2261
Outpatient	140 ± 419	129 ± 477	0.52	131 ± 466
Nursing care				
Nursing home	438 ± 2118	114 ± 1048	0.11	177 ± 1327
Nursing care at home	683 ± 1524	357 ± 1108	0.05	419 ± 1204
Visits to a health-care professional				
General practitioner	396 ± 446	291 ± 409	0.05	311 ± 418
Neurologist	37 ± 100	53 ± 121	0.18	50 ± 117
Internal medicine specialist	67 ± 207	39 ± 124	0.24	44 ± 143
Psychologist/psychotherapist	2 ± 19	74 ± 261	0.002	60 ± 236
Other specialist	21 ± 105	16 ± 75	0.94	17 ± 81
Other				
Medication	829 ± 655	808 ± 879	0.29	812 ± 840
Aids/modifications of home	532 ± 2037	284 ± 1501	0.003	332 ± 1618
Transport	182 ± 366	71 ± 194	0.002	92 ± 241
Total				
Total direct costs	11,799 ± 8292	8817 ± 7251	<0.001	9394 ± 7544
Lost productivity for age < 65 years	(n = 11)	(n = 150)		(n = 161)
Absenteeism from work	2131 ± 5698	2940 ± 5650	0.25	2885 ± 5638
Early retirement	994 ± 3298	1572 ± 5123	0.73	1533 ± 5014
Total indirect costs for age < 65 years	3125 ± 6211	4513 ± 7348	0.27	4418 ± 7268

*Rehabilitation in Germany within a clinic could be both on an inpatient and on a per day basis.
Exchange rate: €1 = $1.32 (January 2005).

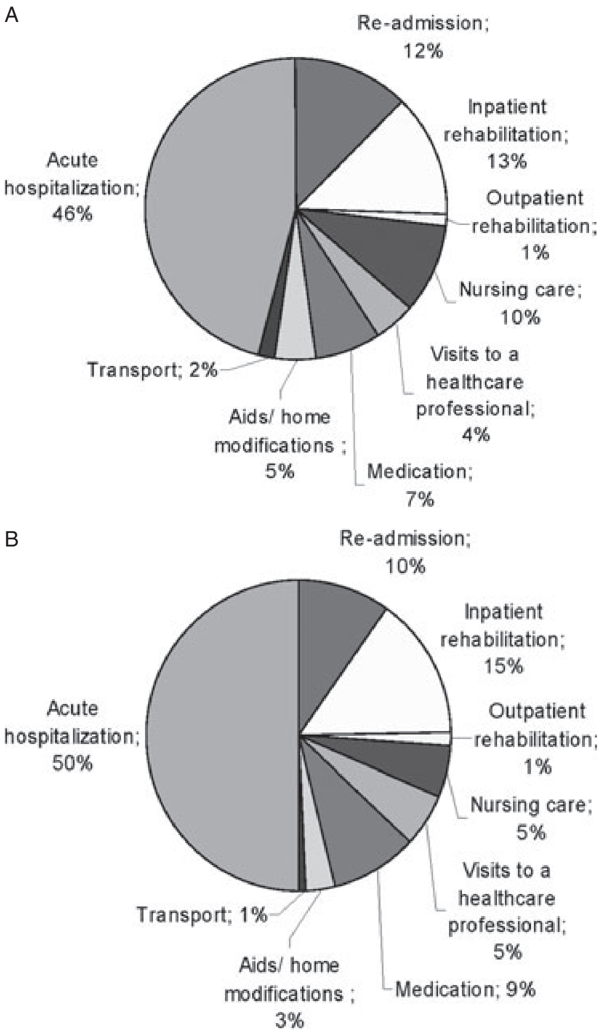

Figure 1 Percentage of direct-cost components for patients with (A) and without (B) atrial fibrillation (acute hospital data based on hospital chart reviews; follow-up data based on patient questionnaire).

tion to the latter variables, the interaction between AF and both sex and comorbidity had an impact for some cost variables (Table 5). Despite adjustments for various potentially confounding factors, acute hospitalization costs were still significantly higher in patients with AF than in the non-AF group ($P < 0.05$) (Table 5).

Discussion

The results of the present study, conducted at four German hospitals in a large metropolitan area and with patient- and/or carer-reported feedback, show that the direct and indirect costs of stroke during a 12-month period are considerable. The largest contributors to the total direct costs were initial hospital stay (49%) and rehabilitation (16%), while indirect costs due to loss of productivity accounted for 18% of the total costs. Furthermore, the present article shows that the burden of stroke, with regard to resource utilization and the resulting costs, differs according to AF status. Indeed, patients with AF tended to experience more severe strokes (in terms of higher NIHSS score), giving rise to significantly increased costs for acute hospitalization. This significant difference was somewhat unexpected and may reflect perhaps a more intense and prolonged level of care. This difference remained after adjustments for age, gender, stroke type, prior stroke, number of comorbidities, and stroke severity. Total indirect costs due to productivity loss per patient for AF-related strokes were lower than for non-AF related strokes. This difference, however, may be somewhat of an artifact as the non-AF patients, on average, were about 10 years younger and with 87 of a total of 294 non-AF patients more likely to be in gainful employment compared with 2 of 71 total AF patients. Consequently, the information value with regard to indirect costs is limited.

Comparison with Other Studies

According to Weimar et al. [13], the mean hospitalization cost of patients with ischemic stroke in Germany is €4749, which is in line with the mean cost of acute hospitalization in the present study (€4620). Similar findings are apparent for comparative costs of outpatient care (€2444) and inpatient rehabilitation (€1633).

There is a limited amount of data on resource use and costs in patients with AF-related strokes [6]. One Danish study, by Jørgensen et al. [14], compared outcomes data in stroke patients with and without AF and showed that patients with AF-related stroke had a 20% increase in hospital stay and a lower discharge

Table 5 Direct costs (€), adjusted for confounding factors

Target Variable	Interaction included	AF	Non-AF	*P*-value	Observations used (n)
NIHSS + AF, sex, age, TIA, comorbidity					
Acute hospitalization		4,539	3,675	0.03	359
Total direct costs		13,095	12,552	0.56	359
Without NIHSS, only AF, gender, age, TIA, comorbidity					
Acute hospitalization	AF * comorbidity	4,687	3,445	0.02	360
Total direct costs	AF * gender; AF * comorbidity	12,727	13,344	0.59	360

Exchange rate: €1 = $1.32 (January 2005).
NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

rate to their own homes (both $P < 0.001$). Nevertheless, the influence of AF became insignificant when the severity of stroke (as determined by the Scandinavian Stroke Scale) was included in the analysis.

Sex was an important confounding factor in the present analysis. This is in accordance with the findings of Ghatnekar et al. [15], who reported that stroke costs in Sweden were generally higher in women than in men.

Underuse of Prevention Therapy

Many of the patients with AF in the present study would be candidates for oral anticoagulation therapy, either because of prior stroke or in view of their risk profile and the need for primary stroke prevention. Only 13% of patients with AF, however, had received anticoagulation therapy before the stroke event. This is consistent with reported underuse of oral anticoagulation for stroke prophylaxis both in Germany [16] and elsewhere [17], and reflects the fact that numerous barriers exist to the effective and safe use of such therapy, including the risk of bleeding and inconvenience [18]. Although we do not have information on possible reasons for failure to use oral anticoagulation in the present study population of patients with AF-related strokes, it is reasonable to assume that some of the events (and therefore resources and costs) in this real-life population could therefore have been avoided with effective anticoagulation.

Limitations of the Study

The exclusion criteria restricted the studied population to the German-speaking population staying in the admission hospital and surviving the initial 24 hours after admission, as the study setting did not allow for follow-up in other hospitals. This might have introduced a bias toward higher costs as the deceased patients consumed less resources. The present study was based on a detailed interview with the patient (and/or a carer) that was carried out within 72 hours of ED admission for acute stroke. Consequently, some selection bias was inevitable, not only because some patients were unwilling to participate but also because it was difficult to obtain interview information in some patients (e.g., because of severe stroke and/or aphasia). Indeed, the inability of certain patients to participate probably explains why nonresponders were characterized by more severe strokes than the interviewed population (see Table 2). Given that more severe strokes tend to be more costly [19], this bias might have resulted in an underestimation of the cost of stroke in the present study. However, those having died during the last 12 months might have consumed fewer resources. Similarly, we relied on patient and/or carer recall of resource utilization at 12 months after hospitalization, which may have also introduced a bias toward under-reporting. However, the key cost drivers were acute hospitalization and hospital readmissions (together accounting for about 60% of total costs), the data for which were provided empirically via patient records. Future studies should perhaps try to map resource use on a more frequent basis.

Discharge from hospital to a residential or nursing facility (in view of functional impairment and dependency), rather than the patient's home, can significantly increase the cost of postacute stroke care. Although such costs accounted for less than 10% of total costs in the present analysis, this can be explained by the fact that resource use was only captured for the first 12 months after hospitalization for stroke. The full picture therefore will only arise after several years of follow-up. It is also important to consider that even if the patient returns home, this can be associated with a great deal of unpaid informal care and financial burden on family members [20], an aspect that was not captured in the present study. This issue may be especially relevant to health-care systems where poststroke rehabilitation services and institutional care are not formally provided.

Another important consideration is that we only studied patients who were alive after 12 months. We have no information as to resource use for those who died within 12 months of the stroke event (31 (7.5%) of 415 patients and 19 (16.4%) of 116 patients) of non-AF and AF patients, respectively, as the burden to patients and carers because of follow-up contacts should be reduced to a minimum. Selective survival of non-AF patients, however, may have occurred and biased the results.

Conclusion

Patients admitted to hospital in Germany with acute stroke use significant health-care resources that, in turn, account for a considerable economic burden. Medical care for stroke patients with AF is associated with higher costs compared with those without AF; this is explained mainly by confounding factors and driven essentially by a significant difference in acute hospitalization costs.

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