

Original Article

Impact of different stages of chronic kidney disease on in-hospital costs in patients with coronary heart disease

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Abstract

Background. Chronic kidney disease (CKD) is associated with markedly increased in-hospital morbidity and mortality. Its effect on in-hospital costs for the treatment of coronary heart disease (CHD) has not been assessed, although it is of interest due to the exponential increase in its prevalence.

Methods. Clinical and costing data were retrospectively assessed from 765 consecutive patients who suffered from CHD requiring percutaneous coronary interventions. Based on their estimated glomerular filtration rate (eGFR), patients were classified in accordance with the *National Kidney Foundation*. Patient-level in-hospital costs for this single hospitalization were thoroughly calculated from precise in-house assessments for the national DRG database.

Results. In univariate analysis, the average total in-hospital costs increased with each stage of CKD [€2926; €3466; €4208; €9687 (stages 4 and 5 combined), $P < 0.0001$]. Treating patients with CKD stages 4 and 5 utilized markedly more resources than patients with ST-elevation myocardial infarction (€4916), coronary three-vessel disease (€4659), severely impaired left ventricular function (€6072) or diabetes (€4495). Multivariate analyses identified, even after adjustment for confounding comorbidities, that CKD was a significant and independent predictor of in-hospital costs; with each loss of 1 ml/min in the eGFR, the expenses for this hospitalization increased by €18 (95% CI, €13–23).

Conclusions. Although the absolute amount of costs may vary between different countries, this work showed, for the first time, that in all stages of CKD, there is a significant increase of in-hospital costs when treating patients with both CHD and CKD.

Keywords: chronic kidney disease; coronary heart disease; costs; mortality

Introduction

During recent years, the prevalence of chronic kidney disease (CKD) has markedly increased and is expected to double continuously every 8 to 10 years [1,2,3,4,5]. The massive increases in the prevalence of obesity, diabetes and hypertension will further augment this dramatic development [2,5,6]. This increase in affected patients is associated with markedly higher utilization of resources and costs which must be borne by the health care systems [3,5,6]. Apart from the direct costs of treating patients in all stages of CKD (specific drugs, renal replacement therapy), the high risk for the development of coronary heart disease (CHD) represents the major cause for morbidity and mortality in this population [7,8,9], thus, being responsible for additional markedly higher expenses. However, although the high economic burden has been outlined by many authors [2,7,8,9], there are no concrete calculations available about the impact of CKD on direct in-hospital costs when treating patients with CHD. This is even more of interest since the presence of CKD is currently not taken into account by any of the national reimbursement systems.

As a fundamental change in the hospital reimbursement system in Germany during the last few years, the Australian system of diagnosis-related groups (DRGs) has been introduced [10]. This now allows us to obtain detailed costing data. Some selected German hospitals calculate their costs for each individual patient very thoroughly including all expenses for personnel, drugs, procedures, implants and others, e.g. hospital overhead. These patient-level costing data together with all diagnoses and procedures are given to the national DRG institute, which thereby calculates the treatment costs for more than 1000 DRGs. These are then used as prices for the revenues in the 2000 German hospitals [10,11].

Since our hospital is one of the hospitals delivering data to the national DRG institute, we have access to very precise data to evaluate the impact of different stages of CKD on the in-hospital costs of patients with significant CHD

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requiring revascularization by percutaneous coronary intervention (PCI).

Subjects and methods

Patients

All consecutive patients who underwent a PCI procedure at our department from 1 January 2002 to 31 December 2002 were retrospectively identified from our data management system. The database contained information on the indication for the intervention as well as patient characteristics including potential risk factors. Data not available online, for concomitant diseases and drug use, were retrieved from the medical records. During the above period, all patients admitted to our institution for elective or emergency PCI were consecutively included in the analysis.

Renal function

Serum creatinine values determined by the Jaffe method (standardized by isotope-dilution mass spectrometry, ID-MS) were retrieved from the computer database of the Institute of Clinical Chemistry. Only values that were determined 1–3 days *before* the procedure were considered for analyses (missing values in five patients). To estimate the glomerular filtration rate (GFR), the simplified *Modification of Diet in Renal Disease* (MDRD) equation was used [4,12]:

$$eGFR(\text{ml}/\text{min}/1.73\text{m}^2) = 186 \times (\text{creatinine, mg}/\text{dl})^{-1.154} \times (\text{age, years})^{-0.203} (\times 0.742 \text{ in women}).$$

Based upon these results, the patients were then classified into five stages of CKD in accordance with the classification of the National Kidney Foundation [12]. Since only 22 patients were in stage 4 and 11 patients were in stage 5, these were analysed together in an aggregated group.

Interventional procedures

PCIs were performed using arterial access from the femoral or brachial arteries. The coronary segment, the type of coronary stenosis dilated and angiographic success were classified in accordance with the revised classification of the ACC/AHA guidelines [13]. Angiographic success after PCI was assumed if a residual stenosis in the vessel diameter of <30% could be achieved [13]. Left ventricular ejection fraction was assessed from the pre-PCI angiogram and determined from 30° right anterior oblique projections. Drug eluting stents (DES) were not available in Germany at the time of the analysis.

Definition of cardiovascular risk factors

Cardiovascular risk factors for PCI were assessed at presentation and were defined as follows: history of smoking was defined if patients had smoked within the last 10 years; hypertension if blood pressure >140/90 mmHg had been documented; hyperlipidaemia if total cholesterol or triglycerides levels were >200 mg/dl or levels of lipoprotein(a) >20 mg/dl; family history of cardiovascular disease

if stroke, myocardial infarction or a coronary intervention had occurred in a first-degree relative; diabetes was assumed if the patients required a specific diet or took oral antidiabetic medication or received insulin.

Cost calculations

Patient-level in-hospital costing data were derived from the hospital cost accounting and were available for all patients included in the analysis. All cost calculations refer to the hospitalization cost for the in-hospital stay necessary for the index PCI. The costing followed the principle of full cost accounting including actual direct costs and hospital overhead costs. A bottom-up approach for the cost calculation was performed including patient-specific utilization factors for calculating medical and nursing staff costs were taken into consideration. Furthermore, individual items of patient consumption were assessed for each single case including blood components, antibiotics, antimycotics, thrombolysis or glycoprotein IIb/IIIa inhibitors, amount of contrast media and all catheter material including balloons and stents. The costing methodology corresponded with the guidelines of the *German National DRG Costing Study* [14]. Thus, our data as one of 140 German hospitals were included in this nationwide DRG census that is conducted annually to calculate the German DRG system representing the basis for hospital reimbursement in the entire country.

Statistics

Differences between the four subgroups were analysed by the ANOVA *F*-test for continuous variables, and the chi-square test for categorical parameters. Parameters with skewed distribution were compared by the Kruskal–Wallis test. Univariate analyses of parameters associated with costs were performed by logistic regression. Furthermore, multivariate analyses using linear logistic regression models were performed and adjusted for confounding factors.

For all tests, *P*-values < 0.05 were taken as significant. All statistical analyses were performed with SPSS 14.0 for Windows.

Results

In 2002, a total of 770 patients consecutively underwent PCI at our institution. Current (1–3 days old) creatinine values before catheterization were not available in five patients; therefore, all subsequent analyses are based on the data of 765 patients.

Basic clinical and laboratory characteristics of the population are summarized in Table 1. The proportion of women, smokers, diabetics and patients with previous PCI increased significantly with advanced stages of CKD.

Cardiac and angiographic characteristics, as well as in-hospital outcomes, are summarized in Table 2. The proportion of patients with acute coronary syndromes was not higher with advanced stages of CKD, but multi-vessel disease was significantly more frequent in the subgroups with reduced estimated GFR.

With regard to in-hospital outcome (Table 2), the length of in-hospital stay and the rate of in-hospital deaths

Table 1. Baseline characteristics

	CKD stage 1	CKD stage 2	CKD stage 3	CKD stages 4 and 5	P-value
	(eGFR > 89 ml/min)	(eGFR 60–89 ml/min)	(eGFR 30–59 ml/min)	(eGFR < 30 ml/min)	
Patients, <i>n</i> (% women)	171 (12)	316 (19)	245 (39)	33 (36)	<0.001
Age, mean ± SD (years)	55 ± 9	65 ± 8	72 ± 8	70 ± 11	<0.001
Diabetes, <i>n</i> (% of column)	35 (21)	85 (27)	83 (34)	14 (42)	0.006
Smoking, <i>n</i> (%)	97 (57)	117 (39)	61 (25)	5 (16)	<0.001
Hypertension, <i>n</i> (%)	128 (75)	223 (73)	188 (22)	26 (79)	0.56
Previous MI, <i>n</i> (%)	29 (19)	58 (22)	159 (24)	9 (32)	0.75
Previous PCI, <i>n</i> (%)	36 (25)	85 (32)	48 (24)	9 (31)	<0.001
Previous bypass grafting, <i>n</i> (%)	13 (9)	50 (19)	44 (22)	5 (18)	0.12
Previous stroke, <i>n</i> (%)	1 (0.6)	11 (3.5)	8 (3.3)	3 (9.1)	0.048
eGFR, mean ± SD (ml/min)	108 ± 18	74 ± 9	49 ± 9	20 ± 8	<0.001
LDL cholesterol, mean ± SD (mg/dl)	116 ± 42	109 ± 39	109 ± 39	101 ± 40	0.27
HDL cholesterol, mean ± SD (mg/dl)	45 ± 9	51 ± 22	52 ± 15	45 ± 13	0.004
Triglycerides, median (range) (mg/dl)	140 (16–523)	116 (28–1507)	119 (32–791)	156 (60–501)	0.003
Lipoprotein(a), median (range) (mg/dl)	28 (4–278)	58 (0–215)	36 (0–185)	17 (1–182)	0.66
ACE-inhibitors, <i>n</i> (%)	115 (79)	197 (75)	138 (70)	14 (52)	0.021
AT1-blockers, <i>n</i> (%)	6 (4)	21 (8)	22 (11)	4 (11)	0.44
Statins, <i>n</i> (%)	131 (91)	242 (92)	168 (85)	21 (77)	<0.001

ACE indicates angiotensin-converting enzyme; AT1, angiotensin 1 receptor; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PCI, percutaneous coronary intervention. Differences between the subgroups were tested by the ANOVA *F*-test for continuous variables (except those marked by * that were compared by the non-parametrical Kruskal–Wallis test), and the chi-square-test for dichotomous or categorical parameters.

Table 2. In-hospital treatment and outcome

	CKD stage 1	CKD stage 2	CKD stage 3	CKD stages 4 and 5	P-value
	(eGFR > 89 ml/min)	(eGFR 60–89 ml/min)	(eGFR 30–59 ml/min)	(eGFR < 30 ml/min)	
Patients, <i>n</i> (% women)	171 (12)	316 (19)	245 (39)	33 (36)	<0.001
STEMI, <i>n</i> (%)	43 (30)	80 (30)	50 (25)	10 (35)	0.35
non-STEMI, <i>n</i> (%)	16 (11)	28 (11)	16 (8)	2 (7)	
CHD with one diseased vessel, <i>n</i> (%)	64 (37)	98 (31)	59 (24)	3 (8)	<0.001
two diseased vessels, <i>n</i> (%)	56 (33)	106 (34)	66 (27)	15 (45)	
three diseased vessels, <i>n</i> (%)	41 (30)	102 (35)	120 (49)	15 (45)	
Left ventricular function—normal	74 (43)	149 (47)	103 (42)	10 (30)	0.041
Moderately reduced	85 (50)	140 (44)	112 (46)	15 (46)	
Severely reduced	12 (7)	27 (9)	30 (12)	8 (24)	
Dilatation of one segment, <i>n</i> (%)	120 (70)	201 (63)	149 (61)	17 (52)	0.23
Of two segments, <i>n</i> (%)	37 (22)	90 (29)	73 (30)	14 (42)	
Of ≥3 segments, <i>n</i> (%)	14 (8)	25 (8)	23 (9)	2 (3)	
Use of GpIIb/IIIa-inhibitors, <i>n</i> (%)	19 (11.1)	29 (9.2)	24 (9.8)	4 (12.1)	0.96
In-hospital stay (days), mean ± SD	3.3 ± 2.4	4.2 ± 3.7	5.8 ± 7.3	11.5 ± 17.5	<0.001
In-hospital death, <i>n</i> (%)	0	1 (0.4)	3 (1.5)	2 (6.9)	0.003
In-hospital infarction, <i>n</i> (%)	2 (1.4)	2 (0.8)	4 (2.0)	0	0.61
Re-do PCI, <i>n</i> (%)	0	4 (1.5)	8 (4.0)	2 (7.1)	0.042
Intensive care treatment, <i>n</i> (%)	32 (19)	53 (17)	42 (17)	11 (33)	<0.001
Days in the ICU, mean (95% CI)	1.2 (1.0–1.5)	1.9 (1.5–2.2)	2.3 (1.3–3.3)	8.6 (0–18.5)	
In-hospital bleeding, <i>n</i> (%)	6 (4.1)	10 (3.8)	13 (6.5)	2 (7.1)	0.52

EF indicates left ventricular ejection fraction; CHD, coronary heart disease; GpIIb/IIIa, glycoprotein IIb/IIIa; PCI, percutaneous coronary intervention; ICU, intensive care unit; STEMI, ST-segment elevation myocardial infarction. Differences between the subgroups were tested by the ANOVA *F*-test for continuous variables and the chi-square-test for dichotomous or categorical parameters.

increased significantly with higher stages of CKD. While the proportion of patients with CKD who required treatment in the intensive care unit (ICU) was not higher, those patients with CKD who had to be treated in the ICU remained there significantly longer.

Predictors of in-hospital costs

The average in-hospital costs for this cohort of patients with CHD and PCI were €3885 (median €2829; range €908–67 307). Univariate analyses of predictors for in-hospital costs by logistic regression models are presented in Table 3. As expected, higher age showed a trend to higher

costs; however, these differences were not significant regardless of whether four classes of age (as in Table 3) or only three classes (<50 years, 50–75 years, >75 years; data not shown, *P* = 0.4) were analysed.

To identify whether eGFR was an independent predictor of in-hospital costs, a multivariate analysis using a logistic regression model was performed. This was adjusted for a number of clinically important, potentially confounding factors (Table 4). However, eGFR remained even after adjustment as an independent predictor of in-hospital costs; in detail, each loss of 1 ml/min in the eGFR was associated with an increase of €18 in expenses.

Table 3. Univariate analyses of predictors of in-hospital costs

Factor	Category	Mean costs (95% CI) (€)	P-value
Age (years)	<50	3319 (2741–3898)	0.4
	50–65	3862 (3214–4509)	
	66–75	3852 (3457–4247)	
	>75	4300 (3743–4857)	
Gender	Men	3948 (3568–4327)	0.5
	Women	3702 (3359–4046)	
Diabetes	No	3640 (3424–3856)	0.01
	Yes	4495 (3609–5381)	
History of smoking	No	4272 (3831–4714)	0.001
	Yes	3253 (2934–3571)	
Admission status	STEMI	4916 (3959–5874)	0.011
	Non-STEMI	3735 (3009–4461)	
	UAP	3534 (2916–4152)	
	Elective	3625 (3288–3963)	
Number of diseased coronary vessels	1	3321 (2931–3711)	< 0.0001
	2	3446 (3114–3777)	
	3	4659 (4019–5300)	
LV-function/impairment	Normal	3087(2857–3316)	< 0.0001
	Moderately	4124 (3608–4640)	
	Severely	6072 (4774–7369)	
Number of dilated segments	1	3523 (3186–3860)	0.006
	2	4427 (3721–5133)	
eGFR (ml/min)	≥3	4804 (4180–5429)	< 0.0001
	>89	2926 (2684–3167)	
	60–89	3466 (3197–3736)	
	30–59	4208 (3730–4687)	
	<30	9687 (4729–14 645)	
ACE-inhibitors	No	4437 (3370–5504)	0.056
	Yes	3734 (3492–3976)	
Statins	No	3720 (2956–4485)	0.7
	Yes	3901 (3583–4219)	

ACE indicates angiotensin-converting enzyme; eGFR, estimated glomerular filtration rate; STEMI, ST-segment elevation myocardial infarction; UAP, unstable angina pectoris. All analyses were performed by the ANOVA *F*-test.

Table 4. Multivariate analysis of predictors of in-hospital costs

Parameter	β , €	95% CI	P-value
eGFR (ml/min)	–18	–23 to –13	< 0.0001
<i>Adjusted for</i>			
Diabetes present	245	129 to 360	< 0.0001
Age (years)	–25	–39 to –12	< 0.0001
Male gender	289	28 to 549	0.03
No acute coronary syndrome	–129	–214 to –44	0.003
Left ventricular function	244	73 to 415	0.005
No history of smoking	–322	–560 to –84	0.008
Number of diseased vessels	98	–38 to 235	0.16
Number of dilated segments, <i>n</i>	–80	–246 to 86	0.34
(Constant)	3450	2207 to 4692	–

eGFR indicates estimated glomerular filtration rate. Multivariate analysis was performed by linear logistic regression.

The association of different stages of CKD (based on the eGFR) and in-hospital costs are displayed in Figure 1. Thus, in the univariate analysis as well as in the multivariate analysis adjusted for confounding factors (see Table 4 and the legend to Figure 1) the stages of CKD were significant predictors of in-hospital costs.

Discussion

The prevalence of CKD is rising dramatically [1,2,3,4] and has been predicted to become ‘a global challenge’ [5].

With this increase in the prevalence of this chronic disease, a marked increase in overall health care costs has to be expected. This was confirmed meanwhile by a few reports evaluating the ambulatory and hospitalization costs in patients with end-stage renal disease, e.g. for medical attendance; for drugs like ACE-inhibitors, diuretics and erythropoietin; and for chronic renal replacement therapies [2,15,16]. All these cost analyses referred only to patients with end-stage renal failure that in fact represent only a very small subgroup (~2%) of the large CKD population [12], and are moreover only in part identical with patients in CKD stage 5. However, there are no data available on

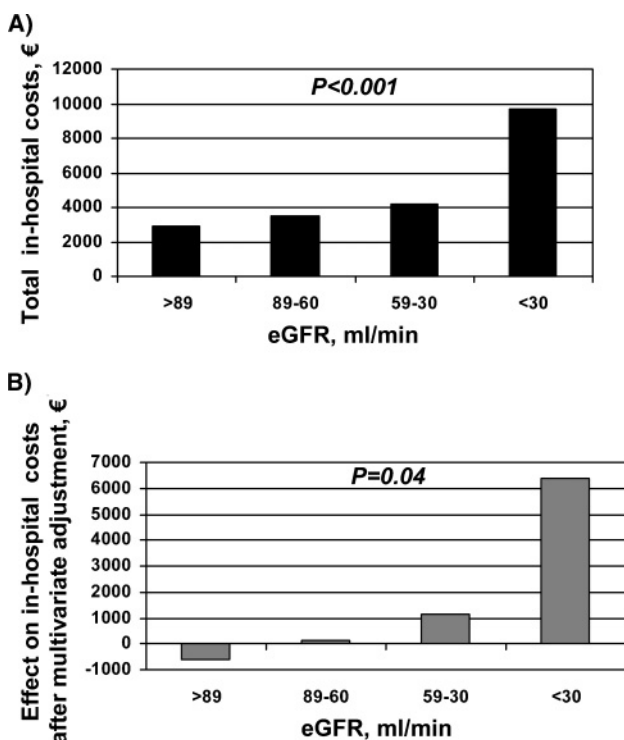


Fig. 1. The impact of different stages of CKD on total in-hospital costs. Panel (A) displays the unadjusted average costs for the distinct stages of CKD calculated from univariate analyses by the ANOVA *F*-test. This demonstrates the continuous and marked increase in costs with each step of CKD. Panel (B) visualizes the impact of different stages of CKD on in-hospital costs after multivariate logistic regression analyses, adjusted for age, gender, diabetes, number of diseased coronary vessels, number of dilated segments, smoking, acute coronary syndromes and left ventricular function. Thus, even after adjustment for the other confounding factors, CKD had a significant and independent impact on in-hospital costs, with a decrease in CKD stage 1 while all other stages of CKD were associated with an increase in costs.

the impact of stages 2 to 4 on expenses. Furthermore, the impact of CKD on indirect costs, e.g. for the treatment of CHD, which is a very frequent comorbidity and the major cause for morbidity and mortality in CKD, has not been assessed previously.

Previous analyses had already identified multi-vessel disease, acute coronary syndromes, left ventricular impairment, peripheral occlusive disease and diabetes to be significant predictors of in-hospital costs for the treatment of patients with CHD [17,18,19,20]. Our present analyses additionally found that CKD was a significant and major predictor of in-hospital costs. The distribution of patients in the distinct CKD stages is not identical to other reports, which [12] is probably due to the fact that we assessed not the general population but consecutive patients with significant CHD who underwent PCI. Univariate analyses showed that there was a significant and marked stepwise rise in in-hospital costs depending on the stage of CKD as defined by the *National Kidney Foundation*. Treating patients with CKD stage 4 or 5 consumed two- to threefold higher resources than, for instance, treating patients with ST-elevation myocardial infarctions, severely reduced left ventricular function or diabetes (Table 3 and Figure 1A).

Moreover, this marked impact of CKD on costs could also be seen after adjustment for relevant comorbidities such as age, diabetes, left ventricular function and others (see Table 4 and Figure 1B). This demonstrates that not the comorbidities of CKD but other inherent factors were associated with higher expenses.

Despite this clear and marked association of advanced stages of CKD with higher in-hospital costs, CKD is at present not taken into account by any of the current health care systems even if they are based on DRGs or other approaches for hospital reimbursement. Some DRG systems (e.g. Australia, Germany, Switzerland) include so-called *patient comorbidity and complexity level* (PCCL) scores. However, suffering from CKD solely is not sufficient to reach a higher PCCL score. In all cases, other comorbidities such as chronic heart failure, diabetes and severe infections must also be present in combination to reach a higher PCCL score and thereby to be grouped in a DRG with higher revenues. Moreover, only few DRGs do, at present, include the PCCL score as a split criterion. Therefore, even if multimorbidity including CKD is present, this leads, only in a small number of cases, to a higher reimbursement for the hospitals.

In summary, our analyses found CKD to be a significant and independent predictor of markedly higher in-hospital costs treating patients with significant CHD by PCI. Patients with CKD stages 4 and 5 consumed the highest resources of all subgroups and cost predictors evaluated in this study. Although these data could not necessarily be transferred to other cohorts with CKD and CHD (e.g. those with conservative treatment or those undergoing coronary bypass surgery), it might be reasonable to expect that comparable assessments in such patient cohorts will find similar results. Since the presence of CKD is not taken into account as a confounding factor by any of the health care systems in the western countries, those hospitals that treat a higher proportion of patients with CKD (usually academic hospitals or larger centres) have markedly higher expenses that are not covered by adequate revenues. The price that has to be paid for CKD will in the future be further augmented by the climbing prevalence of the ‘global challenge’ that is CKD.

Conflict of interest statement. There is no conflict of interest or any interest to be disclosed for all authors.

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