Morbidity and treatment in patients with atrial fibrillation and chronic kidney disease

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Chronic kidney disease (CKD) is associated with increased cardiovascular morbidity and mortality but there are few studies available about atrial fibrillation, the most frequent arrhythmia in CKD, and the applied treatment. Based on the prospective German Competence NETwork on Atrial Fibrillation, data of 3138 patients with atrial fibrillation were analyzed and categorized by their estimated glomerular filtration rate (stages 1–3 and 4 plus 5). With advanced CKD, significantly more patients suffered from a more severe form of atrial fibrillation. Despite significantly higher $CHADS_2$ scores in advanced CKD, oral anticoagulation was not prescribed more frequently while antiarrhythmic drugs and catheter ablations were used significantly less often, in contrast to more pacemaker implantations. However, in multivariate hierarchical logistic regression analyses of in-hospital treatments and complications, only hemorrhages and pacemaker implantations turned out to be independently and significantly associated with higher CKD stages. This nationwide study shows that patients with CKD and atrial fibrillation suffer from a markedly higher comorbidity. Thus, while CKD patients have received cardioversions, ablations, antiarrhythmic, or anticoagulation drugs significantly less often in their history, current treatments were not different if adjusted for multiple comorbidities. This might indicate an improvement in the often reported therapeutic nihilism in CKD.

Kidney International advance online publication, 4 June 2014; doi:10.1038/ki.2014.195

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Received 31 May 2013; revised 28 March 2014; accepted 3 April 2014

KEYWORDS: atrial fibrillation; chronic kidney disease; comorbidity; undertreatment

During the past 10 years, chronic kidney disease (CKD) has been identified as a major risk factor for cardiovascular morbidity and mortality with rapidly increasing prevalence.[1] Regardless of whether healthy individuals of the general population,[2,3] patients with already known structural heart disease,[4–6] or after cardiac interventions[7–9] were analyzed, CKD markedly increased subsequent cardiovascular events in all of these cohorts.

Although atrial fibrillation (AF) is the most common arrhythmia in both the general population and in patients with CKD,[10–12] only few reports have addressed the impact of AF in these patients. The scarce data available on outcome indicate that AF in CKD is associated with a poor prognosis.[10,13] Furthermore, the value of standard therapies such as antiarrhythmic drugs and oral anticoagulation is uncertain, and should therefore be reevaluated for their risks and benefits in CKD.[10,14]

As such data on morbidity and treatment standards in CKD patients with AF are not only rare but also derived from small and mostly single-center studies, here we present data from the German AFNET (German Competence Network on Atrial Fibrillation) database, a large nationwide prospective registry.[15]

RESULTS

Patient enrollment

Between 16 February 2004 and 12 March 2010, a total of 13,349 patients were enrolled in 264 centers in the German-wide, prospective AFNET database. Of these, 106 of the 264 centers reported baseline creatinine values for a total of 3138 patients who represented the basis for this analysis (for

details on availability of creatinine and registry composition, see Supplementary Appendix and Supplementary Figure S1 online; characteristics and any differences between the patients with available creatinine values presented in this study compared with those without creatinine values who are not analyzed in this study are shown in detail in Supplementary Tables S1 and S2 online).

Patient characteristics at the time of enrollment into the database

Table 1 shows the distribution of patients among the four subgroups of varying kidney function. In the subgroup with CKD stages 4 and 5, a total of 11 patients were in chronic dialysis programs. The proportion of women increased with increasing severity of CKD (controls: 23.2%, CKD stage 2: 31.8%, CKD stage 3: 53.5%, CKD stages 4 and 5: 49.2%, $P<0.0001$).

With increasing severity of CKD, risk factors such as hypertension, hyperlipidemia, and diabetes, as well as comorbidities such as valvular heart disease, previous myocardial infarction, coronary bypass grafting, percutaneous coronary intervention, and valve replacement, were observed significantly more often in patients with impaired renal function (Table 1). Symptomatic heart failure (New York Heart Association (NYHA) III and NYHA IV) was also 2.5- to 4.1-fold more frequent in patients with severe CKD compared between the groups ($P<0.0001$ and $P<0.0001$, respectively).

The mean $CHADS_2$ (*C*ongestive Heart Failure, *H*ypertension, *A*ge, *D*iabetes, *S*troke) score increased from 1.1 in controls to 2.5 in CKD stages 4 and 5 ($P<0.0001$). An increasing prevalence of higher $CHADS_2$ scores was observed in more severe CKD: 31.1% of patients with normal estimated glomerular filtration rate (eGFR) compared with 7.8% of CKD stage 4 and 5 patients had a low risk for stroke according to the $CHADS_2$ score of <2, whereas the $CHADS_2$ score of $\geqslant 2$, which represents an indication for oral anticoagulation, was present in 28.8% of the controls compared with 78.5% in CKD stage 4 and 5 patients ($P<0.0001$, Table 2 and Figure 1).

Treatment received within 12 months before enrollment

At index presentation, paroxysmal AF was most frequent in the control group (48.7% vs. 35.6% in CKD stages 4 and 5, Table 2), whereas patients with CKD stage 3 and those with stages 4 and 5 were mostly affected by permanent AF (35.5% and 37.3% vs. 17.5% in controls, $P<0.0001$). In the 12

Table 1 | Patient characteristics at the time of enrollment

	Controls (eGFR >89 ml/min per 1.73 m^2)	CKD stage 2 (eGFR 60–89 ml/min per 1.73 m^2)	CKD stage 3 (eGFR 30–59 ml/min per 1.73 m^2)	CKD stages 4 and 5 (eGFR <30 ml/min per 1.73 m^2)	*P*-value of trend	*P*-value of trend w/o CKD stages 4 and 5
Patients, *n* (% of all)	577 (18.4)	1722 (54.9)	780 (24.9)	59 (1.9)		
Women, *n* (%)	134 (23.2)	547 (31.8)	417 (53.5)	29 (49.2)	**<0.0001**	**<0.0001**
Age, mean ± s.d., years	57.9 ± 11.9	64.1 ± 10.2	70.9 ± 8.1	72.2 ± 9.1	**<0.0001**	**<0.0001**
BMI, mean ± s.d., kg/m^2	27.6 ± 4.9	27.8 ± 4.5	28.0 ± 4.6	27.7 ± 4.4	0.8690	0.1661
Family history of CHD, *n* (%)	130 (29.9)	382 (32.7)	176 (35.8)	8 (24.2)	0.1520	0.0561
Arterial hypertension, *n* (%)	331 (57.4)	1110 (64.5)	622 (79.7)	42 (71.2)	**<0.0001**	**<0.0001**
Hyperlipidemia, *n* (%)	198 (37.9)	690 (43.1)	374 (52.4)	34 (63.0)	**<0.0001**	**<0.0001**
Diabetes, *n* (%)	61 (10.6)	283 (16.4)	227 (29.1)	24 (40.7)	**<0.0001**	**<0.0001**
Insulin-dependent diabetes, *n* (%)	20 (3.5)	81 (4.7)	74 (9.5)	11 (18.6)	**<0.0001**	**<0.0001**
Nonsmoking, n (%)	209 (36.2)	748 (43.4)	343 (44.0)	20 (33.9)	**0.0457**	**0.0076**
Valvular heart disease	178 (30.8)	651 (37.8)	426 (54.6)	35 (59.3)	**<0.0001**	**<0.0001**
Mitral valve insufficiency, *n* (%)	141 (24.4)	511 (29.7)	329 (42.2)	27 (45.8)	**<0.0001**	**<0.0001**
Mitral valve stenosis, *n* (%)	11 (1.9)	50 (2.9)	44 (5.6)	1 (1.7)	**<0.001**	**<0.0001**
Aortic valve insufficiency, *n* (%)	46 (8.0)	204 (11.8)	125 (16.0)	9 (15.3)	**<0.001**	**<0.0001**
Aortic valve stenosis, *n* (%)	34 (5.9)	136 (7.9)	105 (13.5)	11 (18.6)	**<0.0001**	**<0.0001**
Previous MI, *n* (%)	32 (5.6)	163 (9.7)	138 (18.2)	13 (22.4)	**<0.0001**	**<0.0001**
Previous bypass grafting, *n* (%)	9 (1.6)	49 (2.8)	57 (7.3)	5 (8.5)	**<0.0001**	**<0.0001**
Previous PCI, *n* (%)	44 (7.6)	201 (11.7)	121 (15.5)	14 (23.7)	**<0.0001**	**<0.0001**
Previous valve replacement, *n* (%)	9 (1.6)	36 (2.1)	40 (5.1)	4 (6.8)	**<0.0001**	**<0.0001**
Known cardiomyopathy, *n* (%)	37 (6.4)	131 (7.6)	100 (12.8)	9 (15.3)	**<0.0001**	**<0.0001**
Dilated cardiomyopathy, *n* (%)	22 (3.8)	71 (4.1)	49 (6.3)	2 (3.4)	**0.0490**	**0.0218**
Other cardiomyopathy, *n* (%)	4 (0.7)	34 (2.0)	26 (3.3)	6 (10.2)	**<0.0001**	**0.0007**
NYHA III, *n* (%)	58 (10.6)	269 (16.5)	190 (26.6)	15 (27.3)	**<0.0001**	**<0.0001**
NYHA IV, *n* (%)	10 (1.8)	46 (2.8)	42 (5.9)	4 (7.3)	**<0.0001**	**<0.0001**
COPD, *n* (%)	43 (7.5)	133 (7.8)	79 (10.3)	8 (14.0)	**0.0194**	0.0541
Hypothyreosis, *n* (%)	29 (5.1)	81 (4.8)	73 (9.7)	10 (17.5)	**<0.0001**	**0.0002**
Malignancies, *n* (%)	21 (3.7)	85 (5.0)	63 (8.2)	7 (11.9)	**<0.0001**	**0.0002**

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

The data for 'family history of CHD' were selected from noticeably less patients: controls, $n=435$; CKD stage 2, $n=1$ 169; CKD stage 3, $n=492$; and CKD stage 4 + 5, $n=33$.

The *P*-value of trend describes differences among all four CKD groups; *P*-value of trend w/o CKD stages 4 and 5 describes differences between the control group and CKD stage 2 and 3 group. Bold numbers indicate significant differences as described in Materials and Methods section.