Heinz Völler | Anselm Gitt | Christina Jannowitz
Marthin Karoff | Barbara Karmann | David Pittrow
Rona Reibis | Steven Hildemann

Treatment patterns, risk factor control and functional capacity in patience with cardiovascular and chronic kidney disease in the cardiac rehabilitation setting

Suggested citation referring to the original publication:
European Journal of Preventive Cardiology 21(9) (2014)
DOI https://doi.org/10.1177/2047487313482285

European Journal of Preventive Cardiology

Original scientific paper

European Journal of Preventive Cardiology
2014, Vol. 21(9) 1125–1133

DOI: 10.1177/2047487313482285
ejpc.sagepub.com
SAGE

Treatment patterns, risk factor control and functional capacity in patients with cardiovascular and chronic kidney disease in the cardiac rehabilitation setting

Heinz Völler[1,2], Anselm Gitt[3], Christina Jannowitz[4], Marthin Karoff[5], Barbara Karmann[4], David Pittrow[6], Rona Reibis[1,7] and Steven Hildemann[4,8]

Abstract

Background: Chronic kidney disease (CKD) is a frequent comorbidity among elderly patients and those with cardiovascular disease. CKD carries prognostic relevance. We aimed to describe patient characteristics, risk factor management and control status of patients in cardiac rehabilitation (CR), differentiated by presence or absence of CKD.

Design and methods: Data from 92,071 inpatients with adequate information to calculate glomerular filtration rate (GFR) based on the Cockcroft–Gault formula were analyzed at the beginning and the end of a 3-week CR stay. CKD was defined as estimated GFR <60 ml/min/1.73 m^2.

Results: Compared with non-CKD patients, CKD patients were significantly older (72.0 versus 58.0 years) and more often had diabetes mellitus, arterial hypertension, and atherothrombotic manifestations (previous stroke, peripheral arterial disease), but fewer were current or previous smokers had a CHD family history. Exercise capacity was much lower in CKD (59 vs. 92 Watts). Fewer patients with CKD were treated with percutaneous coronary intervention (PCI), but more had coronary artery bypass graft (CABG) surgery.

Patients with CKD compared with non-CKD less frequently received statins, acetylsalicylic acid (ASA), clopidogrel, beta blockers, and angiotensin converting enzyme (ACE) inhibitors, and more frequently received angiotensin receptor blockers, insulin and oral anticoagulants. In CKD, mean low density lipoprotein cholesterol (LDL-C), total cholesterol, and high density lipoprotein cholesterol (HDL-C) were slightly higher at baseline, while triglycerides were substantially lower. This lipid pattern did not change at the discharge visit, but overall control rates for all described parameters (with the exception of HDL-C) were improved substantially. At discharge, systolic blood pressure (BP) was higher in CKD (124 versus 121 mmHg) and diastolic BP was lower (72 versus 74 mmHg). At discharge, 68.7% of CKD versus 71.9% of non-CKD patients had LDL-C <100 mg/dl. Physical fitness on exercise testing improved substantially in both groups. When the Modification of Diet in Renal Disease (MDRD) formula was used for CKD classification, there was no clinically relevant change in these results.

Conclusion: Within a short period of 3–4 weeks, CR led to substantial improvements in key risk factors such as lipid profile, blood pressure, and physical fitness for all patients, even if CKD was present.

[1]Department of Cardiology, Klinik am See, Rüdersdorf, Germany
[2]Center of Rehabilitation Research, University of Potsdam, Germany
[3]Institut für Herzinfarktforschung an der Universität Heidelberg, Germany
[4]Medical Affairs und Klinische Forschung, MSD Sharp & Dohme GmbH, Germany
[5]Klinik Königsfeld der Deutschen Rentenversicherung Westfalen in Ennepetal (NRW), Klinik der Universität Witten-Herdecke, Germany
[6]Institute for Clinical Pharmacology, Medical Faculty, Technical University of Dresden, Germany
[7]Cardiological Outpatient Clinic, Am Park Sanssouci, Potsdam, Germany
[8]Klinik für Kardiologie und Angiologie I, Universitäts-Herzzentrum Freiburg - Bad Krozingen, Germany

Corresponding author:
Heinz Völler, Universität Potsdam, Am Neuen Palais 10, Haus 12, D-14469 Potsdam, Germany.
Email: heinz.voeller@uni-potsdam.de

Keywords
Cardiac rehabilitation, registry, chronic kidney disease, glomerular filtration rate, dyslipidemia, control rates, risk factor, lipids

Received 9 October 2012; accepted 21 February 2013

Introduction

Chronic kidney disease (CKD) is a frequent condition in the community[1,2] and in the primary care setting,[3] in particular in elderly patients and those with cardiovascular disease. The association between CKD and cardiovascular morbidity and mortality has been well established in the general population and in cardiovascular patients.[4–6]

The National Kidney Foundation (NKF)[7] and the American Heart Association[8] have issued statements to consider CKD in cardiovascular risk stratification and treatment guidelines. The current European Guidelines on cardiovascular disease prevention in clinical practice (version 2012) also focus on CKD as disease with increased risk for cardiovascular disease.[9]

The glomerular filtration rate (GFR) is primarily used to assess renal function, as an estimated value of $<60\,ml/min/1.73\,m^2$ is an established threshold to define CKD.[9]

There is no routinely available method to measure GFR directly. Therefore, various methods to estimate GFR (eGFR) have been established, which all use creatinine and incorporate factors such as age, gender, muscle mass, and ethnicity. Usually, the formula of Cockcroft and Gault or of the Modification of Diet in Renal Disease (MDRD) is used.

Cardiac rehabilitation (CR) is a setting with a high prevalence of CKD patients.[10] CR is mainly offered to patients who have had an acute coronary syndrome event (ACS) such as myocardial infarction (MI) or unstable angina (UA), or those who have undergone coronary revascularization (percutaneous coronary intervention; PCI), or have coronary heart disease (CHD) [AU: please check definitions]. In Germany, CR is initiated after a hospital stay in which the acute phase of the event was treated or PCI was performed.[11] The goal of CR as part of a secondary prevention program is to modify coronary risk factors with physical exercise and conservative interventions, including fine-tuned drug therapy. Recent findings have confirmed that CR is associated with significant short-term and long-term survival advantages after cardiovascular (CV) hospitalizations.[12,13]

At present, data on cardiovascular patients in CR who have CKD as a comorbidity are sparse. Thus, we aimed to describe differences between patients with CKD and those without CKD (non-CKD) with regard to (1) patient characteristics including demographics, risk factors and comorbidities, (2) risk factor management including drug treatment, and (3) control status of risk factors. This paper presents a post-hoc analysis of the Transparency Registry to Objectify Guideline-Oriented Risk Factor Management (TROL), which is one of the largest contemporary CR registries.[14]

Methods

Design

TROL is a prospective non-interventional study (registry) performed from 2003 to 2010 under the auspices of the German Society for Prevention and Rehabilitation (DGPR) in cardiac rehabilitation centers in Germany.[14,15] The ethics committee of the Bavarian physician chamber approved the study, and all patients provided written informed consent. The present post-hoc analysis aggregates data from 92,071 patients who had a CR stay between 2003 and 2010 and for whom complete information to calculate GFR on the basis of the Cockcroft–Gault formula was available. Data were collected at the beginning of the CR period and at discharge, usually after 3 weeks.

Variables

As well as demographics (age, gender), information on education status, employment, insurance, and type of CR (ambulatory or hospital-based) were collected. Indications for CR included non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI), UA, aorto-coronary artery bypass graft (CABG), cardiac arrest, and other forms of CHD. Previously performed diagnostic measures comprised PCI, stenting, lysis therapy, implantable cardioverter defibrillator, and others. CV risk factors (diabetes mellitus, hyperlipoproteinemia, arterial hypertension, smoking, positive cardiac family history) and concomitant diseases (peripheral arterial disease (PAD), previous stroke) were documented. Particular focus was on measurements of laboratory parameters at entry and discharge: total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting blood glucose (FPG) and HbA_{1c} in diabetic patients. Further, systolic and diastolic blood pressure at entry

and discharge were noted, as were results of cardiopulmonary exercise testing (Watts). Medication use at entry and discharge was noted by drug class.

For the definition of CKD, the cutoff was set at an eGFR of $<60\,ml/min/1.73\,m^2$, as estimated using the Cockcroft–Gault equation: GFR = (140−age) * (weight in kg) * (0.85 if female) / (72 *serum creatinine in mg/dl). An ancillary analysis was performed using the MDRD formula, which also accounts for ethnicity.[16]

Statistical analysis

Data are presented as absolute numbers, percentages, or means with SD. The frequencies of categorical variables in populations were compared by chi square test. Continuous variables were compared by two-tailed Wilcoxon rank sum test. Percentages were calculated on the basis of patients with data for each respective parameter (i.e. no percentages for missing values provided). The analysis was performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Patient demographics and characteristics

Total cohort. A total of 92,071 patients with adequate information to calculate eGFR based on the Cockcroft–Gault equation were in the database. Of these patients, 35,197 (38.2%) had an eGFR $<60\,ml/min/1.73\,m^2$, defined as CKD. During the 8 years of observation in this analysis (2003 to 2010), 34–42% of patients met the CKD definition. The great majority of patients received CR in a hospital setting (97.9%). Mean duration of rehabilitation was 22 days.

Demographic and clinical characteristics are summarized in Table 1. The proportion of males in total was 72.4%, the average age 63.4 ± 11.6 years, and the mean body mass index (BMI) $28.1 \pm 4.6\,kg/m^2$. Due to the large sample size, statistically significant differences between the two subgroups were noted for *all* mentioned demographic and clinical characteristics. Patients with CKD were considerably older than those without CKD (72.0 versus 58.0 years) and had a lower BMI, while slightly more men were present (Table 2). Education level was generally lower in CKD patients.

Cardiovascular risk factors were highly prevalent in CKD patients, in particular lipid disorders (94.7%), diabetes mellitus (37.4%), arterial hypertension (89.3%), and former smoking (36.3%) or current smoking (7.9%). In addition to coronary artery disease, 15.8% of CKD patients also had vascular comorbidities such as PAD, and 11.5% had had a prior stroke event. Compared with patients without CKD, those with CKD more often had diabetes mellitus, hypertension, and atherothrombotic manifestations (PAD and stroke), but fewer were smokers and fewer had a CHD family history (Figure 1). While systolic blood pressure did not differ between groups at entry, diastolic blood pressure was lower in CKD. As per definition, mean creatinine was considerably higher in CKD (1.44 versus 0.95 mg/dl). Exercise capacity was much lower in CKD (59 vs. 92 Watt).

STEMI occurred less frequently (35.4% vs. 45.1%) in CKD than in non-CKD. In terms of cardiac

Table 1. Demographic and clinical factors in patients with and without CKD

Parameter	Total $n = 92071$	CKD $n = 35197$	No CKD $n = 56874$	p value[a]
Demographics				
Age, years	63.4 ± 11.6	72.0 ± 8.4	58.0 ± 9.9	<0.0001
Gender, male, %	72.4	54.0	83.8	<0.0001
Body mass index, kg/m^2	28.1 ± 4.6	26.5 ± 4.0	29.1 ± 4.7	<0.0001
Diagnosis for CR, %				
STEMI	41.4	35.4	45.1	<0.0001
NSTEMI	19.1	19.5	18.9	<0.05
Unstable Angina pectoris	19.0	20.3	18.2	<0.0001
Therapy in acute hospital, %				
PCI	56.8	48.3	42.1	<0.0001
Coronary bypass	45.8	51.8	42.0	<0.0001

[a]p values refer to the comparison between the two groups (chronic kidney disease (CKD) vs. no CKD) at entry.; CR: cardiac rehabilitation; NSTEMI: non-ST elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST elevation myocardial infarction.

Table 2. Drug treatment at entry and discharge

Parameter	Total $n=92071$		CKD $n=35197$		No CKD $n=56874$		p value[a]	
	Entry	Discharge	Entry	Discharge	Entry	Discharge	Entry	Discharge
Statins, any	77.3	90.1	71.0	87.4	81.2	91.7	<0.0001	<0.0001
CAI	5.4	40.0	4.6	40.1	6.0	40.0	<0.0001	0.65
ASA	85.0	84.8	79.8	79.1	88.2	88.4	<0.0001	<0.0001
ASA + Clopidogrel	45.0	40.8	26.0	32.3	50.5	46.1	<0.0001	<0.0001
Beta blocker	85.9	89.7	83.6	88.1	87.3	90.7	<0.0001	<0.0001
ACE inhibitor	70.9	73.6	69.0	71.5	72.1	74.8	<0.0001	<0.0001
ARB	10.1	13.5	11.8	15.7	9.1	12.2	<0.0001	<0.0001
Oral antidiabetic drug	11.5	12.7	12.5	13.7	10.9	12.1	<0.0001	<0.0001
Insulin	10.6	10.9	13.4	13.9	8.9	9.0	<0.0001	<0.0001

[a]p values refer to the comparison between the two groups (CKD vs. no CKD) at entry. All values are percentages.; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; ASA: acetylsalicylic acid; CAI: cholesterol absorption inhibitor; CKD: chronic kidney disease.

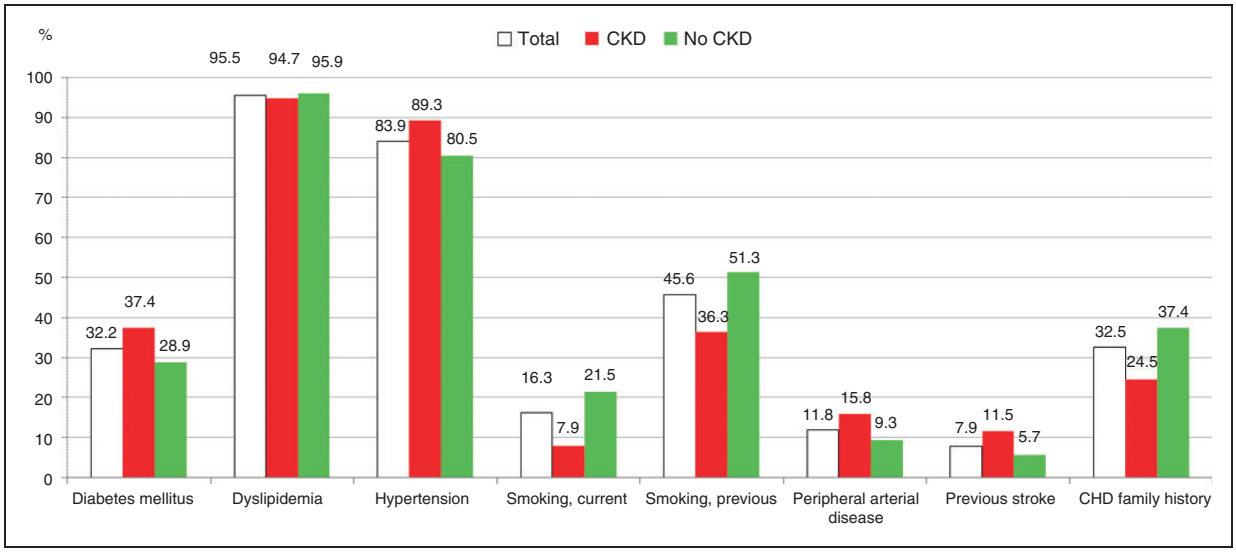

Figure 1. Comorbidities.
CHD: coronary heart disease; CKD: chronic kidney disease.

interventions, patients with CKD had received PCI less often, but CABG surgery more often.

Drug utilization. Drug treatment at entry and discharge in the total cohort, categorized by CKD status, is shown in Table 2 and Figure 2. The majority of CKD patients received a statin (71.0%) at entry, frequently simvastatin (49.2% of all CKD patients, at a mean dose of 27.7 ± 11.8 mg/d), atorvastatin (11.0%, mean dose 23.1 ± 13.8 mg/d) and fluvastatin (5.0%, mean dose 53.0 ± 22.7 mg/d). At the end of CR, the proportion of CKD patients on a statin had increased to 87.4%. The proportion of patients on simvastatin increased substantially, while use of all other statins decreased somewhat. However, the mean statin doses increased slightly for all statins used. Treatment rates with cholesterol absorption inhibitor (CAI) increased during the CR in CKD patients (from 4.6% to 40.1%). Acetylsalicylic acid (ASA) use remained nearly unchanged at a high level (79.1% at discharge), while clopidogrel alone or in combination with ASA decreased somewhat. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) were frequently used in CKD (71.5% and 15.7%, respectively, at discharge).

In the comparison between CKD and non-CKD, there were statistically highly significant differences for all drug classes between both patient groups (with the exception of fluvastatin and CAI at discharge).

Table 3. Parameters and treatment goal achievement at entry and discharge

	Total $n=92071$		CKD $n=35197$		No CKD $n=56874$		p value[a]	
Parameter	Entry	Discharge	Entry	Discharge	Entry	Discharge	Entry	Discharge
Renal parameters								
Creatinine (mg/dl)	1.1 ± 0.7	1.2 ± 0.8	1.4 ± 1.1	1.4 ± 1.1	1.0 ± 0.2	1.0 ± 0.3	<0.0001	<0.0001
Lipid parameters								
Total cholesterol (mg/dl)	189.5 ± 46.7	157.7 ± 35.5	191.4 ± 48.0	160.1 ± 36.9	188.3 ± 45.8	156.3 ± 34.6	<0.0001	<0.0001
LDL-C (mg/dl)	116.2 ± 37.7	88.8 ± 27.8	117.3 ± 38.6	90.3 ± 38.8	115.6 ± 37.1	88.2 ± 27.1	<0.0001	<0.0001
HDL-C (mg/dl)	43.5 ± 12.7	43.7 ± 11.8	45.2 ± 13.6	45.6 ± 12.8	42.5 ± 12.0	42.6 ± 11.1	<0.0001	<0.0001
Triglycerides (mg/dl)	159.5 ± 83.4	139.2 ± 69.5	153.0 ± 76.2	133.8 ± 62.4	163.4 ± 87.2	142.3 ± 73.1	<0.0001	<0.0001
Systolic/diastolic BP at entry and discharge (mmHg)	130.8 ± 20.2	122.6 ± 14.7	130.9 ± 20.9	124.1 ± 15.6	130.7 ± 19.8	121.6 ± 14.0	0.09	<0.0001
	77.3 ± 11.7	73.4 ± 9.3	74.9 ± 11.6	72.0 ± 9.6	78.9 ± 11.5	74.2 ± 9.0	<0.0001	<0.0001
HbA_{1c} (%)	6.5 ± 1.1		6.4 ± 1.1		6.6 ± 1.2		<0.0001	
Fasting blood glucose (mg/dl)	107.6 ± 31.8	104.7 ± 26.5	110.2 ± 34.0	106.6 ± 27.9	106.0 ± 30.2	103.4 ± 25.4	<0.0001	<0.0001
Max. exercise capacity (Watts)	80.6 ± 38.6	96.3 ± 39.9	58.7 ± 28.4	71.2 ± 30.0	91.9 ± 38.4	109.4 ± 38.1	<0.0001	<0.0001

[a]p values refer to the comparison between the two groups (CKD vs. no CKD) at entry and at discharge.; BP: blood pressure; CKD: chronic kidney disease; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol.; For HbA_{1c}, values refer to entry visit.

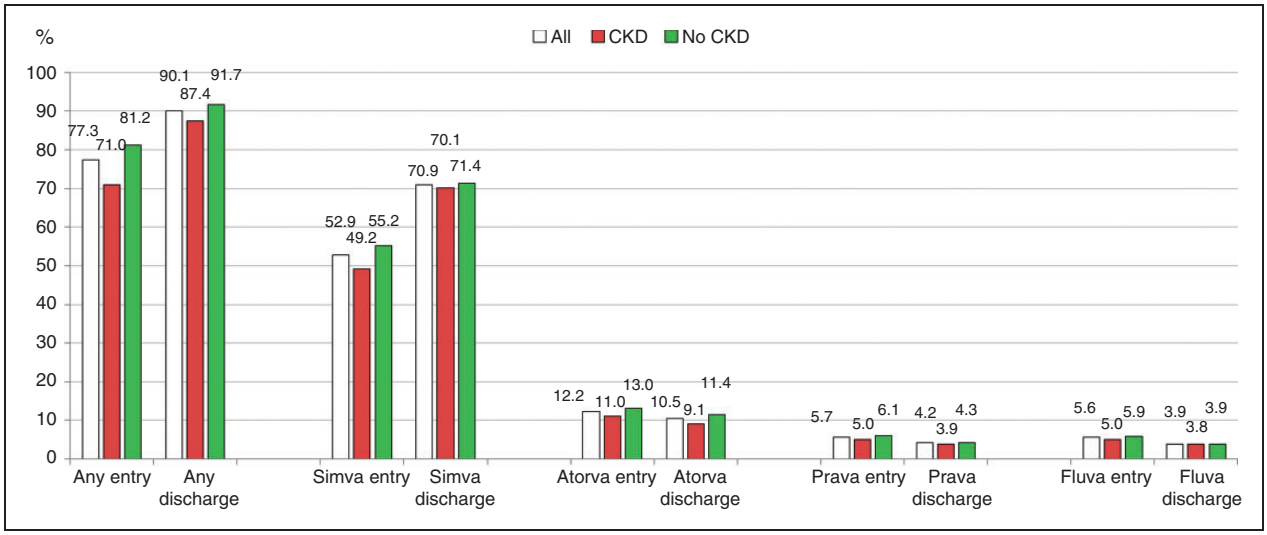

Figure 2. Statin use at entry and discharge.
Atorva: atorvastatin; CKD: chronic kidney disease; Fluva: fluvastatin; Prava: pravastatin; Simva: simvastatin.

To summarize major differences, statins overall were less frequently used in CKD. Further, patients with CKD less frequently received ASA, beta blockers, or ACE inhibitors (at entry and discharge for all named drugs). Conversely, ARBs, insulin and oral anticoagulant were used more frequently in CKD.

Target level attainment. Lipid levels, other surrogate parameters, and target level attainment at entry and at discharge are shown in Figure 3. In the total cohort at entry mean total cholesterol was 189.5 mg/dl, mean LDL-C 116.2 mg/dl, mean HDL-C 43.5 mg/dl, and mean TG 159.5 mg/dl. In patients with CKD, mean LDL-C, TC, and HDL-C were slightly higher at baseline, while TG was substantially lower. This pattern did not change at the discharge visit (Table 3).

Figure 4 displays control rates of various lipid parameters alone and in combination at entry and discharge, in the total cohort, and by subgroups. Overall, between entry and discharge, control rates of lipid parameters improved substantially, with the exception of HDL-C. The LDL-C goal (<100 mg/dl) was achieved at entry by 34.0% and at discharge by 70.7%, and control rates were similar in CKD and

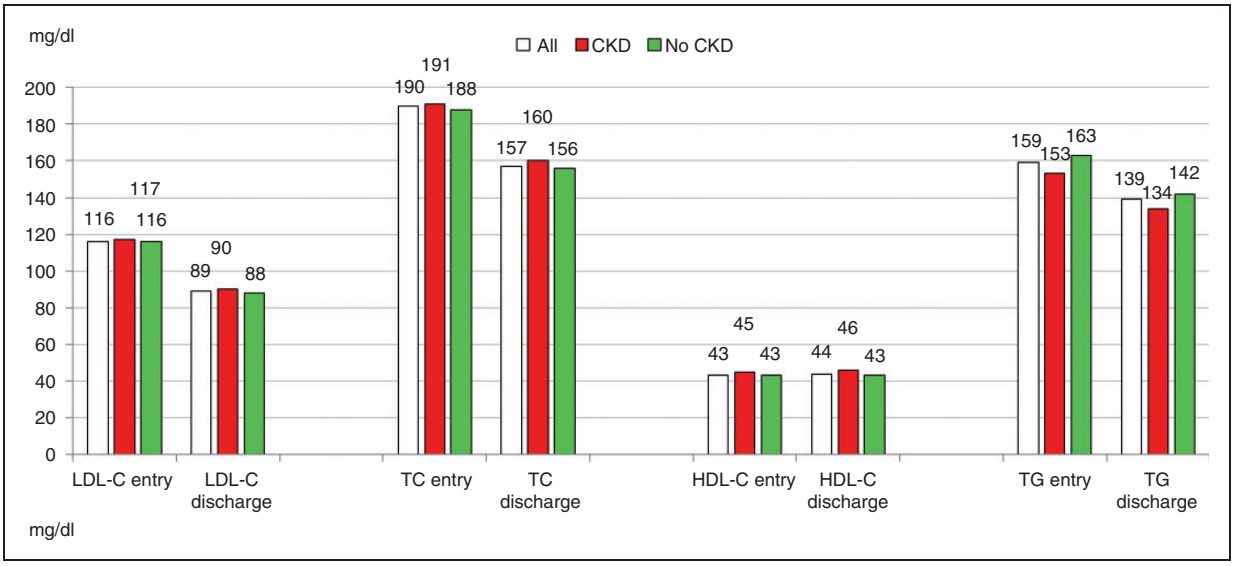

Figure 3. Absolute lipid values.
CKD: chronic kidney disease: HDL-C: high density lipoprotein; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.

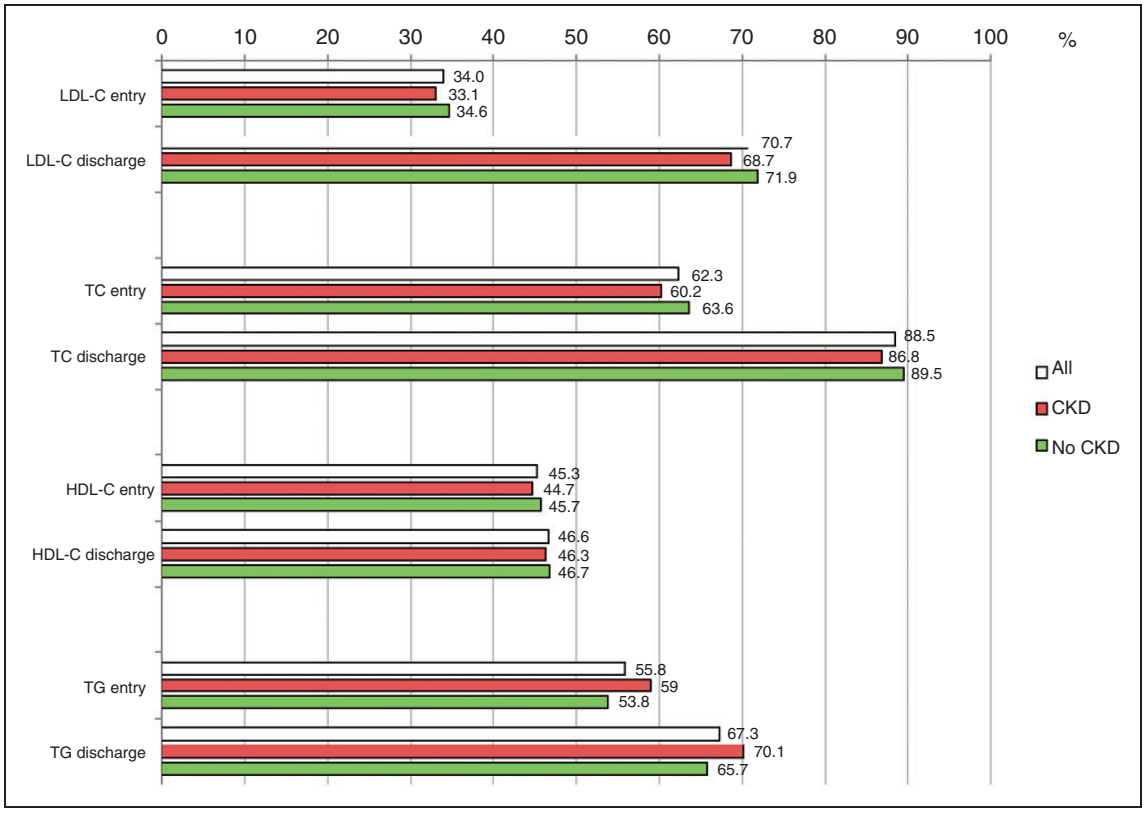

Figure 4. Lipid goal achievement.
LDL-C control was defined as <100 mg/dl. TC control was defined as <200 mg/dl. HDL-C control was defined as >50 mg/dl in females and >40 mg/dl in males. Triglycerides control was defined as <150 mg/dl.
CKD: chronic kidney disease: HDL-C: high density lipoprotein; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.

non-CKD patients. Fasting blood sugar remained higher in CKD patients (107 versus 103 mg/dl).

Overall, mean systolic and diastolic blood pressure decreased from 131/77 mmHg to 123/73 mm Hg. Systolic blood pressure was higher in CKD (124 versus 121 mm Hg) at discharge, but diastolic BP was lower (72 versus 74 mm Hg), both being in the normal range.

Mean exercise capacity was substantially lower in CKD compared with non-CKD also at discharge (71 versus 109 Watt).

Ancillary analysis using the MDRD formula. When the MDRD formula was used, there was no clinically relevant change in results. However, the proportion of patients with CKD was lower (26.5%), and, within the CKD group, patients with GFR <30 somewhat higher (20.2% versus 14.1%). Results of the MDRD analysis are not reported in detail here.

Discussion

The present analysis shows that patients with CKD, compared with those without CKD, (1) are highly prevalent and comorbid in the German CR setting (2), have a substantially reduced exercise capacity, (3) receive lipid lowering treatment in a similar fashion to other patients, and (4) seem to derive similar benefits from CR as patients without CKD, despite a short intervention period of about 3 weeks.

CKD definition

Many studies have documented that creatinine production varies substantially in individuals depending on gender, age, and ethnicity. In patients with established renal disease, the description of renal function based on equations to estimate GFR is undoubtedly more informative than the serum creatinine concentration alone.[17]

We used the cut-off of eGFR <60 ml/min/1.73 m^2 to differentiate between CKD and no CKD. This threshold, introduced in the Disease Outcomes Quality Initiative (K/DOQI) guidelines by the NKF in 2003,[18] is established to differentiate patients with normal function or mild renal impairment from those with moderate renal impairment (30–59 ml/min/1.73 m^2) or severe renal impairment (15–29 ml/min/1.73 m^2). It is applied in epidemiological research such as the National Health and Nutrition Examination Survey (NHANES),[19] and also by regulatory authorities in their guidelines for clinical development programs of new medicines.[20]

Comparative data in CR

Overall, our results are in line with a monocentric report by Venkataraman et al. on 376 patients who completed CR between 1996 and 2004. CKD was present in 115 (31%).[10] In that small study, patients with CKD were older, had more cardiac risk factors and comorbidities, and had lower functional capacity and perceived health status than patients without CKD. Both groups achieved significant improvements in diet scores, body weight, lipid profiles, 6-minute walk distances, physical activity level, perceived health status, and secondary prevention goals.[10]

Lipid modifying treatment

With regard to treatment of dyslipidemia , the approach adopted for adults with CKD by the NKF[18] closely parallels that recommended by the Adult Treatment Panel III (ATP III).[21] However, the NKF guidelines are limited to more severe stages of CKD (stage 4 CKD, i.e. <30 ml/min/1.73 m^2). Guidelines also highlight the possible effect of CKD on the pharmacokinetics of some statins (due to reduced excretion), not always for reduced kidney function per se but due to the lack of data; in patients with CKD in stages 4 or 5, statin doses should be reduced by approximately 50%.[22] Notably, there are very few data on the safety and efficacy of combination therapies in patients with CKD. As in our study, only a minority of patients (5% in the total cohort, 14% in the CKD cohort) had stage 5 CKD. The overall drug utilization pattern did not differ between CKD and non-CKD patients. Statins in terms of drugs and doses were rarely changed, but treatment rates with a CAI increased substantially during CR. This treatment approach is effective and safe, as the lowering of LDL-C with simvastatin 20 mg plus ezetimibe 10 mg daily reduced the incidence of major atherosclerotic events in a wide range of patients with advanced chronic kidney disease in the Study of Heart and Renal Protection.[23]

Control of risk factors

Despite the relatively short duration of CR stays, a substantial improvement in lipid parameters was achieved. In particular, triglycerides in the CKD group were reduced from 178 to 149 mg/dl, an effect that was much stronger than in the group without CKD. Both groups, independently of CKD status, benefited in terms of a notable blood pressure reduction and a reduction of fasting blood glucose at discharge compared with entry. If the lipid control rates as stipulated by the respective guidelines (e.g. LDL-C target <100 mg/dl) are taken into account, a substantial improvement after the CR stay was noted (with the exception of HDL-C). Nonetheless, there is further room for improvement of risk factors such as lipid values, HbA_{1c}, and blood pressure control rates.

Physicians in rehabilitation have limited time to initiate lifestyle modifications or drug treatment, and face the complexity of cardiovascular patients who often have concomitant diseases.[24]

Physical fitness

As an important finding in our study, exercise capacity was substantially lower in CKD patients than in non-CKD patients. Indeed, activity levels are reduced in CKD patients: in the NHANES III, inactivity was present in 13.5% of the non-CKD and in 28.0% of the CKD group (GFR <60, $p < 0.001$), and physical inactivity is associated with increased mortality in CKD and non-CKD populations.[25] Exercise is an important factor for improving aerobic capacity and reversing the metabolic risk factors, which may have important implications for exercise training in CR.[26] In both the Cardiovascular Health Study and NHANES III there was a clear association between physical activity and (decline of) GFR.[27,28] The available evidence on apparent, multiple, cardioprotective effects of exercise training supports its use as an adjunct component of a comprehensive treatment program for patients with predialysis CKD.[29]

Methodological aspects

While the registry is large and representative of the CR setting in Germany, bias is likely in terms of selection of centers (those voluntarily participating in a registry are more likely to have an interest and probably increased knowledge of the topic) and patients (participants may be more adherent to therapy compared with those declining). Missing or underreporting of characteristics may decrease robustness of results. However, in a subset of centers, data were verified in the context of monitoring visits. As this was a retrospective analysis, physicians were not aware of the condition of CKD, unless they diagnosed it themselves. As the awareness of CKD as a tool to stratify patient risk is low among caregivers and patients,[30,31] it is likely that the presence of the condition does not guide treatment decisions.

Conclusion

The present large-scale analysis provides insights into the characteristics, treatment, and risk factor control of CKD patients in the CR setting in Germany. Irrespective of whether or not CKD (assessed using the Cockcroft–Gault or MDRD formulas) was present, patients experienced substantial improvements in key CV risk factors such as lipid parameters, and physical activity training. Thus, patients both with and without CKD gain substantial and comparable benefit from participation in CR programs.

Conflict of interest

The registry was supported by MSD Sharp & Dohme GmbH, Munich-Haar, Germany. CJ, BK and SH are full-time employees of MSD. DP received consultancy fees from MSD. All authors are in the Steering Board or Scientific Board of the study. The authors declare no conflict of interest related to the registry.

References

1. Stevens LA, Viswanathan G and Weiner DE. Chronic kidney disease and end-stage renal disease in the elderly population: Current prevalence, future projections, and clinical significance. *Adv Chronic Kidney Dis* 2010; 17: 293–301.
2. Rothenbacher D, Klenk J, Denkinger M, et al. Prevalence and determinants of chronic kidney disease in community-dwelling elderly by various estimating equations. *BMC Public Health* 2012; 12: 343.
3. Van Pottelbergh G, Bartholomeeusen S, Buntinx F, et al. The prevalence of chronic kidney disease in a Flemish primary care morbidity register. *Age Ageing* 2012; 41: 231–233.
4. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351: 1296–1305.
5. Astor BC, Hallan SI, Miller ER 3rd, et al. Glomerular filtration rate, albuminuria, and risk of cardiovascular and all-cause mortality in the US population. *Am J Epidemiol* 2008; 167: 1226–1234.
6. Murphy CA, Robb SD, Weir RAP, et al. Declining renal function after myocardial infarction predicts poorer long-term outcome. *Eur J Cardiovasc Prev Rehab* 2010; 17: 181–186.
7. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. *Am J Kidney Dis* 2002; 39: S1-–S266.
8. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: A statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003; 108: 2154–2169.
9. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). *Eur J Prev Cardiol* 2012; 19: 585–667.
10. Venkataraman R, Sanderson B and Bittner V. Outcomes in patients with chronic kidney disease undergoing cardiac rehabilitation. *Am Heart J* 2005; 150: 1140–1146.
11. Karoff M, Held K and Bjarnason-Wehrens B. Cardiac rehabilitation in Germany. *Eur J Cardiovasc Prev Rehabil* 2007; 14: 18–27.
12. Junger C, Rauch B, Schneider S, et al. Effect of early short-term cardiac rehabilitation after acute ST-elevation

and non-ST-elevation myocardial infarction on 1-year mortality. *Curr Med Res Opin* 2010; 26: 803–811.
13. Alter DA, Oh PI and Chong A. Relationship between cardiac rehabilitation and survival after acute cardiac hospitalization within a universal health care system. *Eur J Cardiovasc Prev Rehabil* 2009; 16: 102–113.
14. Bestehorn K, Wegscheider K and Voller H. Contemporary trends in cardiac rehabilitation in Germany: Patient characteristics, drug treatment, and risk-factor management from 2000 to 2005. *Eur J Cardiovasc Prev Rehabil* 2008; 15: 312–318.
15. Völler H, Reibis R, Pittrow D, et al. Secondary prevention of diabetic patients with coronary artery disease in cardiac rehabilitation: Risk factors, treatment and target level attainment. *Curr Med Res Opin* 2009; 25: 879–890.
16. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* 2006; 145: 247–254.
17. Glassock RJ and Winearls C. Screening for CKD with eGFR: Doubts and dangers. *Clin J Am Soc Nephrol* 2008; 3: 1563–1568.
18. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Updated 2002. http://www.kidney.org/professionals/kdoqi/guidelines_ckd/toc.htm (accessed 2 December 2012).
19. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA* 2007; 298: 2038–2047.
20. Food and Drug Administration Center for Drug Evaluation and Research (CDER). Guidance for Industry Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling. Rockville, March 2010.
21. Cleeman JI, Grundy SM, Becker D, et al. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* 2001; 285: 2486–2497.
22. K/DOQI clinical practice guidelines for management of dyslipidemias in patients with kidney disease. *Am J Kidney Dis* 2003; 41: I–IV, S1–91.
23. Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): A randomised placebo-controlled trial. *Lancet* 2011; 377: 2181–2192.
24. Pittrow D, Kirch W, Bramlage P, et al. Patterns of antihypertensive drug utilization in primary care. *Eur J Clin Pharmacol* 2004; 60: 135–142.
25. Beddhu S, Baird BC, Zitterkoph J, et al. Physical activity and mortality in chronic kidney disease (NHANES III). *Clin J Am Soc Nephrol* 2009; 4: 1901–1906.
26. Tjonna AE, Lee SJ, Rognmo O, et al. Aerobic interval training versus continuous moderate exercise as a treatment for the metabolic syndrome: A pilot study. *Circulation* 2008; 118: 346–354.
27. Robinson-Cohen C, Katz R, Mozaffarian D, et al. Physical activity and rapid decline in kidney function among older adults. *Arch Intern Med* 2009; 169: 2116–2123.
28. Finkelstein J, Joshi A and Hise MK. Association of physical activity and renal function in subjects with and without metabolic syndrome: A review of the Third National Health and Nutrition Examination Survey (NHANES III). *Am J Kidney Dis* 2006; 48: 372–382.
29. Bronas UG. Exercise training and reduction of cardiovascular disease risk factors in patients with chronic kidney disease. *Adv Chronic Kidney Dis* 2009; 16: 449–458.
30. McClellan WM, Newsome BB, McClure LA, et al. Chronic kidney disease is often unrecognized among patients with coronary heart disease: The REGARDS Cohort Study. *Am J Nephrol* 2009; 29: 10–17.
31. Plantinga LC, Tuot DS and Powe NR. Awareness of chronic kidney disease among patients and providers. *Adv Chronic Kidney Dis* 2010; 17: 225–236.