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ORIGINAL ARTICLE

Attainment of Guideline-Directed Medical Treatment in Stable Ischemic Heart Disease Patients With and Without Chronic Kidney Disease

Efstratios Koutroumpakis[1] · Elvira O. Gosmanova[2,3] · Heather Stahura[4] · Stephanie Jou[4] · Rabah Alreshq[4] · Ashar Ata[5] · Mandeep S. Sidhu[4] · Edward Philbin[4] · William E. Boden[6,7] · Radmila Lyubarova[4]

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Abstract

Background Stable ischemic heart disease (SIHD) is prevalent in patients with chronic kidney disease (CKD); however, whether guideline-directed medical therapy (GDMT) is adequately implemented in patients with SIHD and CKD is unknown.

Hypothesis Use of GDMT and achievement of treatment targets would be higher in SIHD patients without CKD than in patients with CKD.

Methods This was a retrospective study of 563 consecutive patients with SIHD (mean age 67.8 years, 84% Caucasians, 40% females). CKD was defined as an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73m^2 using the four-variable MDRD Study equation. We examined the likelihood of achieving GDMT targets (prescription of high-intensity statins, antiplatelet agents, renin-angiotensin-aldosterone system inhibitors (RAASi), and low-density lipoprotein cholesterol levels < 70 mg/dL, blood pressure < 140/90 mmHg, and hemoglobin A1C < 7% if diabetes) in patients with ($n = 166$) and without CKD ($n = 397$).

Results Compared with the non-CKD group, CKD patients were significantly older (72 vs 66 years; $p < 0.001$), more commonly female (49 vs 36%; $p = 0.002$), had a higher prevalence of diabetes (46 vs 34%; $p = 0.004$), and left ventricular systolic ejection fraction (LVEF) < 40% (23 vs. 10%, $p < 0.001$). All GDMT goals were achieved in 26% and 24% of patients with and without CKD, respectively ($p = 0.712$). There were no between-group differences in achieving individual GDMT goals with the exception of RAASi (CKD vs non-CKD: adjusted risk ratio 0.73, 95% CI 0.62–0.87; $p < 0.001$).

Conclusions Attainment of GDMT goals in SIHD patients with CKD was similar to patients without CKD, with the exception of lower rates of RAASi use in the CKD group.

Keywords Guideline-directed medical treatment · Coronary artery disease · Stable ischemic heart disease · Chronic kidney disease · Angiotensin-converting enzyme inhibitors · Angiotensin receptor blockers · Renin-angiotensin-aldosterone system inhibitors · Statins

Introduction

There is a complex relationship between stable ischemic heart disease (SIHD) and chronic kidney disease (CKD). SIHD is highly prevalent in CKD patients and it has been reported that CKD patients have 2 to 16 times higher risk of developing a major adverse cardiovascular event compared with patients without CKD. [1–4] In addition, the presence of CKD has

✉ Radmila Lyubarova
lyubarr@amc.edu

1 Division of Cardiovascular Medicine, Department of Internal Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA

2 Division of Nephrology and Hypertension, Department of Medicine, Albany Medical College, Albany, NY, USA

3 Nephrology Section, Stratton VA Medical Center, Albany, NY, USA

4 Division of Cardiology, Department of Medicine, Albany Medical College, 43 New Scotland Avenue, A2 wing, Albany, NY 12208, USA

5 Department of General Surgery, Albany Medical College, Albany, NY, USA

6 Massachusetts Veterans Epidemiology, Research, and Informatics Center (MAVERIC), VA New England Healthcare System, Boston, MA, USA

7 Boston University School of Medicine, Boston, MA, USA

been independently associated with increased cardiovascular morbidity and mortality in SIHD patients, and especially in patients with concomitant DM [1, 5, 6]. The management of SIHD patients with concomitant CKD is often challenging due to concerns of medication-induced acute kidney injury, hyperkalemia, and increased medication intolerance with declining renal function [7]. Moreover, most clinical studies of patients with SIHD excluded patients with significant kidney dysfunction defined as estimated glomerular filtration rate (eGFR) of < 30 mL/min/1.73m^2 [7]. Nonetheless, optimal medical management is crucial for reduction in cardiovascular morbidity and mortality in the CKD population.

There is a paucity of data whether guideline-directed medical treatment (GDMT) is adequately implemented in SIHD patients with CKD, as compared with those without CKD. In this study, we evaluated the use of GDMT, including prescription of antiplatelet therapy, high-intensity statins, and renin-angiotensin-aldosterone system inhibitors (RAASi), as well as achievement of low-density lipoprotein cholesterol (LDLc) levels < 70 mg/dL, blood pressure (BP) < 140/90 mmHg, and hemoglobin A1C (A1C) < 7%, in SIHD patients with and without concomitant CKD.

Methods

Study Population and Data Collection

We conducted a single-center retrospective cross-sectional study including patients seen in the outpatient cardiology clinic of Albany Medical College and Albany Medical Center, Albany, NY. The study was approved by the Albany Medical College Institutional Review Board. A total of 614 consecutive patients who were seen in 2015 and had the 10th Revision of International Statistical Classification of Diseases (ICD-10) codes for SIHD (I25.10, I25.2, I25.810, I21, Z95.5, Z98.61) were identified. The diagnosis of SIHD was also confirmed during individual chart review. The information obtained from medical records included demographic and clinical characteristics, such as age, gender, race, insurance information, tobacco use, presence of diabetes mellitus (DM), hypertension (HTN), history of a prior acute myocardial infarction and myocardial revascularization, systolic and diastolic blood pressure, left ventricular ejection fraction (LVEF), use of lipid lowering drugs and their dosages, and antiplatelet and antihypertensive medications at the index visit. In addition, we obtained laboratory values for serum creatinine (SCr), LDLc, and A1C closest to the index visit and within 12 months. Allergies and adverse drug reactions to RAASi and statins were also collected.

Patients with unconfirmed SIHD diagnosis during chart review ($n = 18$), absent baseline SCr values ($n = 31$), and patients who had undergone kidney transplantation ($n = 2$) were excluded. A total of 563 patients were included in the final analyses.

Definitions

SIHD was defined as history of prior acute myocardial infarction, evidence of obstructive coronary artery disease on coronary angiography, prior myocardial revascularization with percutaneous coronary intervention (PCI), or coronary artery bypass graft surgery (CABG) or stress test positive for ischemia. CKD was defined as a baseline eGFR < 60 mL/min/1.73m^2 utilizing the four-variable MDRD Study formula (eGFR = 186 × serum Cr-1.154 × age-0.203 × 1.212 (if patient is black) × 0.742 (if female)) [8]. CKD stages were further defined based on baseline eGFR as following: CKD stage 3: eGFR 30–59 mL/min/1.73m^2, CKD stage 4: eGFR 15–29 mL/min/1.73m^2, CKD 5: eGFR < 15 mL/min/1.73m^2 or requirement of renal replacement therapy.

Outcomes

The primary outcome was the attainment of GDMT in SIHD patients with and without CKD based on the 2012 American College of Cardiology and American Heart Association (ACC/AHA) guidelines for the diagnosis and management of patients with SIHD [9]. Optimal medical treatment included use of high-intensity statin, at least a single antiplatelet agent, and the use of RAASi, including angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) in patients with at least one of the following comorbid conditions including HTN, DM, or LVEF < 40%. The antiplatelet agents recorded included aspirin, clopidogrel, prasugrel, or ticagrelor. The therapeutic goals that were assessed included achievement of LDLc < 70 mg/dL, BP < 140/90 mmHg, and HbA1C < 7% in patients with DM.

Statin Intensity

The statin intensity was defined according to the 2013 ACC/AHA guidelines on cholesterol treatment [10]. High-intensity statins included atorvastatin 40–80 mg daily and rosuvastatin 20–40 mg daily. Moderate-intensity statins included atorvastatin 10–20 mg daily, rosuvastatin 5–10 mg daily, pravastatin 40–80 mg daily, lovastatin 40 mg daily, simvastatin 20–40 mg daily, fluvastatin 40 mg twice daily, fluvastatin XL 80 mg daily, or pitavastatin 2–4 mg daily. Low-intensity statins included pravastatin 10–20 mg daily, lovastatin 20 mg daily, simvastatin 10 mg daily, fluvastatin 20–40 mg daily, or pitavastatin 1 mg daily.

Statistical Analysis

Continuous variables were presented as mean values ± standard deviation (SD) and were compared using the Student *t* test. Categorical variables were expressed as percentages and were compared using the chi-square test. Risk ratios (RR) with

95% confidence intervals (CI) were calculated utilizing univariate and multivariate logistic regression analysis. All potential confounders, such as age, gender, blood pressure, presence of DM, LVEF < 40%, and history of CABG were evaluated via multivariate analysis. A two-sided p value of less than 0.05 was considered statistically significant. All statistical analyses were performed using STATA 14 (StataCorp, College Station, TX).

Results

Demographics and Clinical Characteristics

Mean (SD) age for the entire study population ($N = 563$) was 67.8 (11.5) years. Eighty-four percent of patients were Caucasian, 40% were female, 72% had HTN, 37% had DM, 18% were current, and 46% were former smokers. A total of 77% of patients had previously undergone coronary revascularization. Fourteen percent of patients had LVEF < 40%. Additional demographics and clinical characteristics are presented in Table 1.

Among all patients with SIHD, 166 (29%) and 297 (71%) were with and without CKD, respectively. Patients with CKD were significantly older (71.7 vs 66.1 years; $p < 0.001$), more commonly female (49 vs 36%; $p = 0.002$), more frequently insured under Medicare (58 vs 48%; $p = 0.026$), had higher prevalence of DM (46 vs 34%; $p = 0.004$), had lower diastolic BP (DBP; 67.4 vs 72.6 mmHg; $p < 0.001$), had undergone more frequently CABG (39 vs 28%; $p = 0.016$), and had more often LVEF < 40% (23 vs 10%; $p < 0.001$). Comparison of the demographics and clinical characteristics between SIHD patients with and without CKD is presented in Table 1.

Achievement of Individual GDMT Goals

In the total cohort, 88% of patients were treated with any antiplatelet agents, 85% with statins, including 47% with a high-intensity statin. RAASi was prescribed in 68% of patients with SIHD and HTN, DM or LVEF < 40%. Overall, the BP goal (< 140/90 mmHg) was achieved in 81% of patients, while only 35% of the patients had an LDLc < 70 mg/dL. A1C of < 7% was achieved in 49% of diabetic patients.

When patients with CKD were compared with non-CKD patients, RAASi use was significantly lower in CKD patients (56 vs 74%; unadjusted risk ratio (RR) 0.76, 95% confidence interval (CI) 0.64–0.89, $p = 0.010$); Table 2). However, no significant difference was identified in antiplatelet agent and high-intensity statin use, or in the achievement of BP, LDLc, and A1C goals between the two groups (Table 2; Fig. 1). Adjustment for baseline characteristics did not alter the association of lower RAASi use in CKD patients (adjusted RR 0.73, 95% CI 0.62–0.87, $p < 0.001$), as compared with non-CKD patients.

Out of 166 patients with eGFR < 60 mL/min/1.73m^2, 71% were grouped in the CKD 3 group, 14% in CKD 4, and 14% in CKD 5 group. RAASi were used proportionally less with advancing CKD stages (in unadjusted and adjusted analyses; Table 3).

Number for GDMT Targets Attained Among CKD and Non-CKD Patients

Diabetic patients qualified for a total of six GDMT targets (use of antiplatelet, high-intensity statin, RAASi, goal BP, LDL, and A1C). Only 5% of the diabetic patients in our cohort achieved all six targets with no significant differences in the six GDMT target attainment between CKD and non-CKD patients ($p = 0.474$; Fig. 2). Patients with either history of HTN or LVEF < 40% but no history of DM, qualified for a total of five GDMT targets (use of antiplatelet, high-intensity statin, RAASi, goal BP, and LDL). All five goals were achieved by 11% of the qualified patients with no significant difference between CKD and non-CKD patients ($p = 1.0$; Fig. 2). The remaining patients (with no DM, HTN, or LVEF < 40%) qualified for a total of four targets. All four targets were achieved by 10% of patients and there was no significant difference between CKD and non-CKD patients ($p = 0.672$; Fig. 2).

Discussion

The present study was the first to evaluate the implementation of GDMT in patients with CKD. We demonstrated that the attainment of GDMT was similar in patients with and without CKD with the exception of lower rates of RAASi use in CKD patients. However, the overall achievement of GDMT was low irrespective of CKD with only 8% of patients reaching all GDMT targets based on appropriate indications. The use of antiplatelet agents and achievement of BP goals were among the highest. Despite the large number of patients receiving statins, only 47% were on high-intensity statins. Furthermore, only 2 out of 3 were receiving RAASi and about half of the patients with diabetes had achieved the A1C target of < 7%.

In addition to lower rates of RAASi use in CKD, we also found that RAASi use declined with CKD progression. This is perhaps not unexpected given progressive propensity for acute kidney injury and hyperkalemia with eGFR loss. Of note, we found that 56% of CKD patients with SIHD were receiving RAASi and this number is similar to 58% of RAASi use in CKD patients presented in the 2017 United States Renal Data System (USRDS) report [11]. No statistically significant differences were identified in prescription of antiplatelet agents

Table 1 Demographic and clinical characteristics of 563 patients with stable ischemic heart disease and with or without chronic kidney disease

	Total (*N* = 563)	Group without CKD (*N* = 397)	Group with CKD (*N* = 166)	*p* value*
Age mean (SD), years	67.8 (11.5)	66.1 (10.6)	71.7 (12.4)	< 0.001
Female gender, %	40	36	49	0.002
Race, %				0.283
Caucasian	84	83	86	
African-American	12	13	10	
Other	4	5	4	
BMI mean (SD), kg/m^2	30.0 (7.1)	30.1 (6.8)	29.7 (7.8)	0.490
Insurance, %				0.026
Private insurance	43	45	39	
Medicare	51	48	58	
Medicaid	5	6	1	
Uninsured	2	2	2	
Comorbidities				
Diabetes, %	37	34	46	0.004
Hypertension, %	72	72	71	0.866
SBP mean (SD), mmHg	127.3 (15.9)	128.0 (15.1)	125.6 (17.4)	0.106
DBP mean (SD), mmHg	71.1 (11.1)	72.6 (10.9)	67.4 (10.6)	< 0.001
LVEF < 40%, %	14	10	23	< 0.001
History of MI, %	36	35	37	0.558
PCI, %	47	49	42	0.126
CABG, %	31	28	39	0.016
Smoking status, *N* (%)				0.102
Current	101 (18)	79 (20)	22 (14)	
Past	255 (46)	181 (46)	74 (46)	
Never	196 (36)	130 (33)	66 (41)	
eGFR mean (SD), mL/min/1.73m^2	73.7 (30.5)	88.2 (22.1)	38.5 (16.0)	N/A
CKD stage, *N* (%)		N/A		
Stage 3	118 (21)		118 (71)	
Stage 4	24 (4)		24 (14)	
Stage 5	24 (4)		24 (14)	
Medications				
RAAS inhibitors, *N* (%)	349 (62)	260 (65)	89 (54)	0.010
ACEi, *N* (%)	251 (45)	192 (48)	59 (36)	0.005
ARB, *N* (%)	98 (17)	68 (17)	30 (18)	0.808
Any lipid lowering Rx, *N* (%)	494 (88)	349 (88)	145 (87)	0.853
Statin, *N* (%)	480 (85)	338 (85)	142 (86)	0.902
Statin intensity, *N* (%)				0.664
High	263 (47)	188 (47)	75 (45)	
Moderate	189 (34)	132 (33)	57 (34)	
Low	28 (5)	17 (4)	11 (7)	
Statin intolerance, *N* (%)	37 (7)	30 (8)	7 (4)	0.145
Any antiplatelet, *N* (%)	493 (88)	350 (88)	143 (86)	0.575
Aspirin, *N* (%)	459 (82)	331 (83)	128 (77)	0.095
Tot Chol mean (SD), mg/dL	158.7 (41.6)	159.8 (42.6)	156.1 (39.2)	0.382
LDL-C level, mean (SD), mg/dL	85.7 (34.0)	86.9 (34.7)	82.8 (32.2)	0.239
HDL level mean (SD), mg/dL	46.4 (15.0)	46.7 (15.1)	45.8 (14.9)	0.558
TGL level mean (SD), mg/dL	139.2 (95.4)	135.7 (89.1)	147.4 (108.5)	0.227

**p* value for comparisons between patients with and without CKD

N, number; *SD*, standard deviation; *eGFR*, estimated glomerular filtration rate; *RAAS inhibitors*, renin angiotensin aldosterone system inhibitors; *ACEi*, angiotensin converting enzyme inhibitors; *ARB*, angiotensin receptor blockers; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *LVEF*, left ventricular ejection fraction; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass grafting; *CKD*, chronic kidney disease

and high-intensity statin treatment or achievement of BP, LDL, and A1C goals between CKD and non-CKD patients.

The use of antiplatelet agents was 88%, which was one of the highest among GDMT goals in our study population. The benefit of antiplatelet therapy for secondary prevention has been evaluated in CKD patients. In a recent meta-analysis of 50 studies including more than 27,000 CKD patients of all stages, antiplatelet use for the secondary cardiovascular prevention was significantly associated with decreased fatal and non-fatal myocardial infarction [12]. No dose adjustment is required for the available antiplatelet agents in CKD patients [13]. The prospeCtive observational LongitudinAl RegIstry oF patients with stable coronary arterY disease (CLARIFY study) reported that among 22,000 patients, antiplatelet agents were used in 95% of patients but they were significantly less frequently used in CKD patients [14].

Table 2 Attainment of goal-directed therapeutic targets among patients with stable ischemic heart disease and with or without chronic kidney disease

	Group without CKD ($N = 397$)	Group with CKD ($N = 166$)	Unadjusted risk ratio (95% CI)	p value	Adjusted risk ratio (95% CI)	p value
Any antiplatelet, %	88	86	0.98 (0.91–1.04)	0.523	0.99 (0.91–1.07)	0.751
High intensity statin, %	47	45	0.95 (0.78–1.16)	0.640	0.99 (0.80–1.23)	0.938
LDLc < 70 mg/dL, %	34	38	1.13 (0.87–1.46)	0.367	0.89 (0.66–1.20)	0.445
BP < 140/90 mmHg, %	80	84	1.04 (0.96–1.13)	0.330	0.95 (0.87–1.04)	0.260
A1C < 7%, %	46	52	1.12 (0.83–1.51)	0.453	0.97 (0.73–1.36)	0.984
RAASi, %	74	56	0.76 (0.64–0.89)	0.001	0.72 (0.61–0.86)	< 0.001

CKD, chronic kidney disease; *LDLc*, low-density lipoprotein cholesterol; *BP*, blood pressure; *A1C*, hemoglobin A1C; *RAASi* renin angiotensin aldosterone system inhibitors; *eGFR*, estimated glomerular filtration rate. Analysis was adjusted for the following variables: age, gender, Medicare, history of CABG, diabetes mellitus, diastolic blood pressure, and ejection fraction less than 40%; *CI*, confidence interval. For risk ratios, CKD group served as a reference group

Contrary to our findings, a large study from Spain by Lahoz et al. including more than 7800 SIHD patients (the PREvención SEcundaria eN Atención Primaria; Secondary Prevention in Primary Care (PRESENAP study)) reported that patients with CKD were treated less frequently with antiplatelet therapy compared with non-CKD patients (77% vs. 82%) although that difference lost significance in the multivariate analysis [15].

The 2013 ACC/AHA guidelines recommend that treatment with high-intensity statin should be initiated or continued as first-line therapy in women and men ≤ 75 years of age who have clinical atherosclerotic cardiovascular disease (ASCVD), unless contraindicated [10]. Furthermore, in recognition of CKD being associated with significant cardiovascular morbidity and mortality, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend use of statins for primary and secondary cardiovascular disease prevention in non-dialysis dependent CKD patients aged 50 years and older or kidney transplant recipients, irrespective of underline etiology of CKD [16]. Additionally, statins are recommended even at a younger age (age > 18 years) for diabetic CKD patients and CKD patients with established CVD or 10-year CVD risk of > 10% [16]. De novo statin therapy failed to reduce cardiovascular events in dialysis-dependent CKD and is not advocated by current guidelines [17–19]. Nonetheless, statins initiated prior to dialysis should be continued based on observational data [20] and expert opinion [16]. Overall, reported rates of statin use ranged between 73% in a study by Kumbhani et al., and 97% in a study by Cordero et al [21, 22]. However; neither study reported the percentage of patients treated with high-intensity statin.

In a study from Japan, including 391 patients with CKD and coronary artery disease following percutaneous coronary intervention, statins were prescribed less frequently as the GFR decreased [5]. The CLARIFY study similarly reported that statins were used significantly less in CKD patients (82% vs 85%; $p < 0.001$) [14]. Our findings also suggest that although 85% of SIHD patients have been receiving a statin and less than half have been on the recommended high-intensity form, there was no difference in high-intensity statin

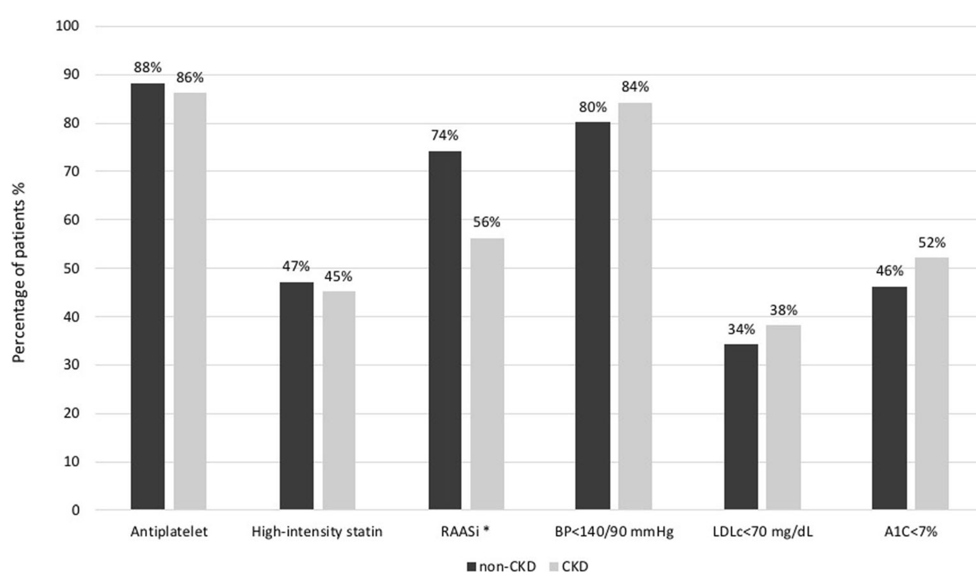

Fig. 1 Attainment of individual goal-directed medical therapy goals among patients with stable ischemic heart disease and with or without chronic kidney disease.*$p < 0.05$. RAASi, renin-angiotensin-aldosterone system inhibitors; BP, blood pressure; LDL-C, low density lipoprotein cholesterol; A1C, glycosylated hemoglobin; CKD, chronic kidney disease

Table 3 Use of renin-angiotensin aldosterone system inhibitors in different stages chronic kidney disease

	RAASi use, %	Unadjusted risk ratio (95% CI)	Adjusted risk ratio (95% CI)
No CKD ($N = 317$)	74	1.00 (Reference group)	1.00 (Reference group)
CKD stage3 ($N = 104$)	56	0.86 (0.74–1.01)	0.84 (0.71–1.01)
CKD stage 4 ($N = 20$)	46	0.75 (0.50–1.12)	0.75 (0.51–1.11)
CKD stage 5 ($N = 20$)	13	0.20 (0.07–0.58)	0.20 (0.07–1.57)
Trend p value	< 0.001		

CI, confidence interval; *CKD*, chronic kidney disease; *RAASi*, renin-angiotensin aldosterone system inhibitors; Analysis was adjusted for the following variables: age, gender, Medicare, history of CABG, diabetes mellitus, diastolic blood pressure, and ejection fraction less than 40%

use in patients with and without CKD. A low percentage of high-intensity statin use may be responsible for two thirds of the SIHD patients not achieving the LDL goal of < 70 mg/dL. Morrison et al. have proposed that the most common reason for long-term statin discontinuation in CKD patients is adverse reactions [23]. On the other hand, there are studies supporting that statins are safe to use long-term in CKD patients and they are associated with reduction in major adverse cardiovascular events [24]. In our cohort, there was no difference in statin therapy between SIHD patients with and without CKD. In terms of adverse reactions to statin therapy, 9% of SIHD patients did not tolerate any dose of statin but intolerance rates were similar between CKD and non-CKD groups. Our study supports that patients with CKD are treated with statins and tolerate them similarly to the non-CKD patients but the overall percentage of patients treated with the recommended high intensity statin is suboptimal.

The ACC/AHA guidelines for management of SIHD and HTN recommend RAASi treatment in all patients who also have HTN, DM, LVEF 40% or less, or CKD, unless contraindicated (Class IA indication) [9, 25]. ARBs are recommended over ACEi when ACEi are not tolerated [9].

In this study, we found that patients with clear indications for RAASi, such as patients with HTN, DM, or LVEF 40% or less had a higher use of RAASi at 68%. More importantly, the current study revealed CKD patients were less likely to receive RAASi compared with non-CKD patients and RAASi use declined with progressing stages of CKD. This is consistent with the CLARIFY study, which also reported that among 22,000 prospectively enrolled SIHD patients, ACEi use decreased with declining eGFR [14]. Increased awareness regarding RAASi use especially in SIHD patients with concomitant CKD is of great importance and every effort should be made to increase safe use of ACEi or ARBs.

Achievement of good BP control decreases the incidence of major cardiovascular events in SIHD patients and it is recommended by current guidelines [15, 25, 26]. Lahoz et al., in their study, reported a significantly lower percentage of SIHD patients with concomitant CKD achieving good BP control when compared with non-CKD patients [15]. When the cutoff of 140/90 was used, only 55% of CKD patients achieved the goal [15]. In contrary to the above, our study found that 81% of SIHD patients achieved the BP goal of 140/90 and there was no significant difference between CKD and non-CKD groups. We elected the BP goal of less than 140/90 mmHg as that was the recommended target by the national guidelines during the period that the study was contacted [9, 27]. However, the 2017 ACC/AHA guidelines recommend a BP target of < 130/80 mmHg for adults with confirmed hypertension and known cardiovascular disease, 10-year atherosclerotic cardiovascular disease event risk of 10% or higher or CKD. For adults with confirmed hypertension, but without additional markers of increased cardiovascular disease risk, a BP target of < 130/80 mmHg is recommended as reasonable [25]. Using the 130/80 target, rates of achieving optimal BP drop further and approach the 50% range.

Despite the widespread use of statins and their well-established benefit in SIHD patients with or without CKD, achievement of LDLc goals seems to be suboptimal in different reports. In two studies coming from Europe, optimal LDLc goals were achieved only in 15–20% of patients [28, 29]. Similarly, studies from North America in SIHD patients reported attainment of LDLc goal in the range of 12–18% [30, 31]. Lahoz et al. in their study reported a poor control of LDLc in both CKD and non-CKD groups, with 1 out of 4 SIHD patients achieving that goal. No significant difference was reported between CKD and non-CKD groups [15]. The LDLc target used in most of the above studies was 100 mg/dL. In our study, we elected to use the latest recommended by ACC guidelines LDLc goal (< 70 mg/dL), and even though lower, we still found slightly higher rates of LDLc goal achievement (35%). No significant difference was noted between the CKD and non-CKD groups. Despite the slightly better rates, achievement of LDLc goals remains low which might reflect the limited use of high-intensity statins in this population. Clinicians should make the effort to not only administer statin to SIHD patients but also optimize the dose for LDLc target achievement.

Reports on achievement of A1C goals in SIHD patients with concomitant DM and CKD are limited. In the PRESENAP study by Lahoz at al., diabetic patients with CKD achieved A1C goal less often than diabetics with normal GFR (44% vs 53%) [15]. In our study, although the percentages of diabetic patients achieving the A1C goal were in the

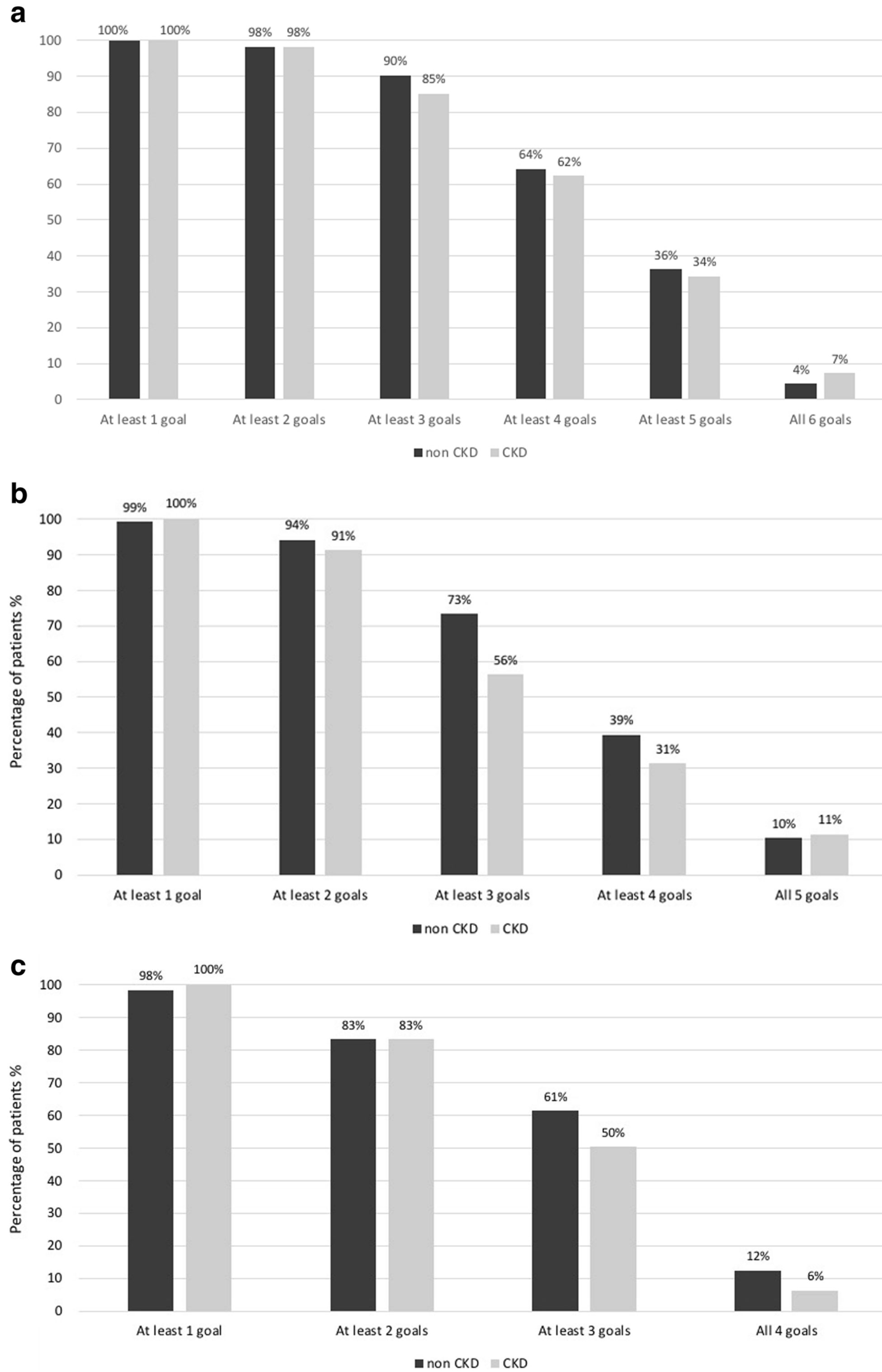

Fig. 2 Attainment of guideline-directed medical therapy targets in patients with stable ischemic heart disease with or without chronic kidney disease. **a** Attainment of GDMT in patients with SIHD and diabetes. **b** Attainment of GDMT in patients with SIHD and HTN and/or LVEF < 40% and no diabetes. **c** Attainment of GDMT in patients with SIHD and no diabetes, HTN, or LVEF < 40%. GDMT, goal-directed medical therapy; SIHD, stable ischemic heart disease; HTN, hypertension, LVEF; left ventricular ejection fraction, CKD; chronic kidney disease

same range as in the PRESENAP study (52% and 46%, respectively), no statistically significant difference between CKD and non-CKD patients was noted.

Achievement of optimal medical therapy goals for patients with SIHD in the USA as reported in population-based studies has been suboptimal. Results from the REGARDS Study (REasons for Geographic And Racial Differences in Stroke) showed that less than 1% of subjects achieved all 7 identified risk factor goals. On average, 4 out of 7 risk factor goals were achieved [32]. The risk factor goals used were those studied in the COURAGE trial [33]. In our study, although slightly different goals were used, the overall achievement of GDMT was low with only 8% of patients reaching all GDMT targets based on appropriate indications. This suggests that there is substantial opportunity for optimization of therapy of these individuals which could potentially improve their life expectancy. It is worth mentioning here that even in the clinical trial setting, like in COURAGE trial, GDMT targets were not achieved by all study subjects. Therefore, although it might be unrealistic to achieve complete adherence to GDMT for all patients, there is certainly a lot of room for improvement.

The current study was the first study to systematically assess individual and global GDMT goal achievement in patients with and without CKD. However, several limitations are needed to be acknowledged. This was a retrospective study from a single tertiary center and, therefore, inherited limitations of a retrospective analysis cannot be excluded. Additionally, we examined the attainment of six guideline-directed treatment targets, while other treatments, such as lifestyle modifications and influenza vaccination were not assessed due to limited information about these parameters. Although, the current guidelines recommend the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula for the calculation of eGFR [34]; the MDRD formula was applied in the current study as it was used for eGFR reporting in our institution at the time of this study conduction.

In conclusion, attainment of GDMT in SIHD patients with or without CKD was similar, with the exception of lower rates of RAASi use in CKD patients. Only a small percentage of patients reached all goals of GDMT based on their indications. Increased awareness and implementation of GDMT is of great importance in SIHD patients irrespective of presence of CKD.

Funding Own resources

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest. EEG and WEB are employees of the Department of Veterans affairs. Opinions expressed in this paper are those of the authors' and do not necessarily represent the opinion of the Department of Veterans Affairs. The results of this paper have not been published previously in whole or part.

Ethical Approval This article is based on retrospective patient chart review and does not contain any studies with human participants or animals performed by any of the authors. Our study was approved by the institutional review board of Albany Medical College.

References

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2003;139:137–47.
2. Schiffrin EL, Lipman ML, Mann JF. Chronic kidney disease: effects on the cardiovascular system. Circulation. 2007;116:85–97.
3. Mathew RO, Bangalore S, Lavelle MP, Pellikka PA, Sidhu MS, Boden WE, et al. Diagnosis and management of atherosclerotic cardiovascular disease in chronic kidney disease: a review. Kidney Int. 2017;91:797–807.
4. Mathew RO, Bangalore S, Sidhu MS, Fleg JL, Maddux FW. Increasing inclusion of patients with advanced chronic kidney disease in cardiovascular clinical trials. Kidney Int. 2018;93:787–8.
5. Kaneko H, Yajima J, Oikawa Y, Tanaka S, Fukamachi D, Suzuki S, et al. Effects of statin treatment in patients with coronary artery disease and chronic kidney disease. Heart Vessel. 2014;29:21–8.
6. Farkouh ME, Sidhu MS, Brooks MM, Vlachos H, Boden WE, Frye RL, et al. Impact of chronic kidney disease on outcomes of myocardial revascularization in patients with diabetes. J Am Coll Cardiol. 2019;73:400–11.
7. Marenzi G, Cosentino N, Guastoni C. How to balance risks and benefits in the management of CKD patients with coronary artery disease. J Nephrol. 2015;28:403–13.
8. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of diet in renal disease study group. Ann Intern Med. 1999;130:461–70.
9. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012;60:e44–e164.
10. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2889–934.
11. Saran R, Robinson B, Abbott KC, Agodoa LYC, Bhave N, Bragg-Gresham J, et al. US renal data system 2017 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis. 2018;71:A7.
12. Palmer SC, Di Micco L, Razavian M, Craig JC, Perkovic V, Pellegrini F, Jardine MJ, Webster AC, Zoungas S, Strippoli GF: Antiplatelet agents for chronic kidney disease. Cochrane Database Syst Rev 2013;Feb 28;(2):CD008834.
13. Agrawal H, Aggarwal K, Littrell R, Velagapudi P, Turagam MK, Mittal M, et al. Pharmacological and non pharmacological strategies in the management of coronary artery disease and chronic kidney disease. Curr Cardiol Rev. 2015;11:261–9.
14. Kalra PR, Garcia-Moll X, Zamorano J, Kalra PA, Fox KM, Ford I, et al. Impact of chronic kidney disease on use of evidence-based therapy in stable coronary artery disease: a prospective analysis of 22,272 patients. PLoS One. 2014;9:e102335.
15. Lahoz C, Mostaza JM, Mantilla MT, Taboada M, Tranche S, Lopez-Rodriguez I, et al. Achievement of therapeutic goals and utilization of evidence-based cardiovascular therapies in coronary heart disease patients with chronic kidney disease. Am J Cardiol. 2008;101:1098–102.
16. Wanner C, Tonelli M. KDIGO clinical practice guideline for lipid management in CKD: summary of recommendation statements and clinical approach to the patient. Kidney Int. 2014;85:1303–9.
17. Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson 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;377:2181–92.

18. Fellstrom BC, Jardine AG, Schmieder RE, Holdaas H, Bannister K, Beutler J, et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. N Engl J Med. 2009;360:1395–407.
19. Wanner C, Krane V, Marz W, Olschewski M, Mann JF, Ruf G, et al. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med. 2005;353:238–48.
20. Streja E, Gosmanova EO, Molnar MZ, Soohoo M, Moradi H, Potukuchi PK, et al. Association of continuation of statin therapy initiated before transition to chronic dialysis therapy with mortality after dialysis initiation. JAMA Netw Open. 2018;1:e182311.
21. Kumbhani DJ, Steg PG, Cannon CP, Eagle KA, Smith SC Jr, Hoffman E, et al. Adherence to secondary prevention medications and four-year outcomes in outpatients with atherosclerosis. Am J Med. 2013;126:693–700.e691.
22. Cordero A, Rodriguez Padial L, Batalla A, Lopez Barreiro L, Torres Calvo F, Castellano JM, Ruiz E, Bertomeu-Martinez V. Optimal pharmacological treatment and adherence to medication in secondary prevention of cardiovascular events in Spain: results from the CAPS study. Cardiovasc Ther 2017;35(2).
23. Morrison FJ, Zhang H, Skentzos S, Shubina M, Bentley-Lewis R, Turchin A. Reasons for discontinuation of lipid-lowering medications in patients with chronic kidney disease. Cardiorenal Med. 2014;4:225–33.
24. Huang H, Zeng C, Ma Y, Chen Y, Chen C, Liu C, et al. Effects of long-term statin therapy in coronary artery disease patients with or without chronic kidney disease. Dis Markers. 2015;2015:252564.
25. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71:e127–248.
26. Sarnak MJ, Greene T, Wang X, Beck G, Kusek JW, Collins AJ, et al. The effect of a lower target blood pressure on the progression of kidney disease: long-term follow-up of the modification of diet in renal disease study. Ann Intern Med. 2005;142:342–51.
27. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311:507–20.
28. Banegas JR, Vegazo O, Serrano P, Luengo E, Mantilla T, Fernandez R, et al. The gap between dyslipidemia control perceived by physicians and objective control patterns in Spain. Atherosclerosis. 2006;188:420–4.
29. Diamantopoulos EJ, Athyros VG, Yfanti GK, Migdalis EN, Elisaf M, Vardas PE, et al. The control of dyslipidemia in outpatient clinics in Greece (OLYMPIC) study. Angiology. 2005;56:731–41.
30. Mosca L, Merz NB, Blumenthal RS, Cziraky MJ, Fabunmi RP, Sarawate C, et al. Opportunity for intervention to achieve American Heart Association guidelines for optimal lipid levels in high-risk women in a managed care setting. Circulation. 2005;111:488–93.
31. Pearson TA, Laurora I, Chu H, Kafonek S. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Arch Intern Med. 2000;160:459–67.
32. Brown TM, Voeks JH, Bittner V, Brenner DA, Cushman M, Goff DC Jr, et al. Achievement of optimal medical therapy goals for U.S. adults with coronary artery disease: results from the REGARDS study (REasons for geographic and racial differences in stroke). J Am Coll Cardiol. 2014;63:1626–33.
33. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356:1503–16.
34. Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013;158:825–30.