Therapeutic Management in Patients with Renal Failure who Experience an Acute Coronary Syndrome

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Background and objectives: Prior reports have suggested that patients with impaired renal function receive less aggressive care after an acute coronary syndrome (ACS). The aim of this study was to determine whether this held true in a contemporary cohort, after thorough adjustment for cotreatments/comorbidities.

Design, setting, participants, & measurements: Patients who were admitted for an ACS in eight participating hospitals were stratified into three groups according to estimated creatinine clearance (CrC): less than 45 ml/min, 45 to 60 ml/min, and reference >60 ml/min.

Results: During hospitalization, uses of reperfusion therapy in tertiary care centers [difference between CrC ≤45 ml/min and reference group (Δ): 4%, 95% confidence interval (CI): (−13%, 21%)] and systemic anticoagulation [Δ: 0%, CI (−5%, 5%)] were similar in the three groups. Coronary angiography was performed less often in patients with lower CrC [Δ: −16%, CI: (−31%, −1%)]. At discharge, nearly all patients received either an antiplatelet agent or warfarin regardless of CrC [Δ: −1%, CI: (−3%, 1%)]. Discharge use of angiotensin converting enzyme (ACE) inhibitors or angiotensin-receptor blockers was comparable [Δ: 7%, CI: (−1%, 15%)]. β-blockers [Δ: −9%, CI: (−17%, −1%)] and lipid-lowering drugs (LLDs) [Δ: −7%, CI: (−13%, −1%)] were used less frequently in patients with lower CrC. In multivariate analyses, decreased CrC predicted lower coronary angiography and LLD use, but not lower β-blocker use at discharge.

Conclusions: These results suggest that in patients with ACS, the extent of undertreatment due to chronic kidney disease is less than reported previously, which is partially explained by more complete adjustment for cotreatments/comorbidities.

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Chronic kidney disease (CKD) is associated with an increased risk of cardiovascular events. Cardiovascular death in patients undergoing renal replacement therapy is at least 3.5 times that of the general population (1). The high prevalence of traditional risk factors for atherosclerosis undoubtedly contributes to the accelerated rate of cardiovascular disease (CVD) in patients with CKD (2,3). However, recent studies have shown that CKD remains associated with cardiovascular events and mortality (4), even after thorough adjustment for the presence of cardiovascular risk factors, suggesting that uremia *per se* is proatherogenic. In patients who survive an acute myocardial infarction (MI), the presence of CKD is associated with a higher rate of cardiovascular event recurrence and death (5,6). Hence, this population may be most likely to benefit from aggressive therapeutic strategies in the acute setting as well as cardioprotective drugs in the long term.

Observational studies have reported that patients with CKD who have acute MI are less likely to receive antiplatelet agents (7–9), heparin (7,9), β-blockers (8), and thrombolysis (8,9). Patients with CKD are also less likely to undergo coronary angiography in the acute setting (7,8,10). In patients who are discharged from the hospital after an acute coronary syndrome (ACS), the use of cardioprotective drugs seems to vary according to the level of kidney function. Generally, studies report lower use of aspirin (8,9,11), β-blockers (8,9,11), and lipid-lowering drugs (LLDs) (11) at discharge in patients with CKD. The mechanisms underlying these reported differences are unclear at the present time. They could reflect failure to aggressively treat a patient population that is deemed too sick to benefit from intervention. On the other hand, they could be due to a cluster of conditions or cotreatments associated with CKD that also contraindicate the use of some drugs or interventions. Finally, physicians may be fearful of worsening renal function in CKD patients by performing invasive interventions. Most previous reports recruited patients who experienced ACS in the mid-1990s, whereas a secular trend toward increased use of cardioprotective drugs has been demonstrated in recent years (12,13). Previous work on the topic has often come from large registries that may lack clinical information on some comorbidities and concomitant therapies (10,11).

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The primary aim of this study was to assess whether therapeutic management differs in patients who present with an ACS and also suffer from CKD independent of comorbidities or concomitant treatments. The secondary aim was of this study to understand the determinants at play in the explanation of any therapeutic differences observed.

Materials and Methods

Patients and Study Design

The prospective RISCA (acronym for Récurrence et Inflammation dans les Syndromes Coronariens Aigus) cohort study was conducted from 2000 to 2002 in eight Canadian hospital centers. The number of participating centers was limited to a balanced mix of community (n = 4) and tertiary (n = 4) centers to fully reflect the spectrum of practice patterns. All patients (n = 1210) hospitalized with an initial admission diagnosis of ACS [unstable angina (UA) or MI] were eligible if they were recruited within 24 h of the end of ischemic symptoms. The criteria used for the inclusion diagnoses of MI and UA, as well as a flow diagram of the number of patients approached, recruited, or excluded from this cohort study have been published previously (14). Clinical management was left to the discretion of treating physicians. The institutional review committee of each of the participating hospitals approved the study and all subjects gave written informed consent.

Data Collection

Clinical data collection including information on cardiovascular drug use was prospectively performed by trained research nurses at admission and at discharge from the hospital at each study site. Patients were followed-up at 1 mo after discharge (on-site visit) and 1 yr after discharge (detailed and structured phone contact) with systematic review of hospital files. Follow-up events were verified and centrally adjudicated. Loss to follow-up at 1 yr was minimal (0.3%).

Measurements

Because our study focused on physician's decisions regarding drug prescription, we chose to use the Cockcroft–Gault equation (15) to estimate creatinine clearance (CrC), as is generally recommended in this context (16). Patients were classified in three groups according to CrC [≤45 ml/min, 45 to 60 ml/min, and >60 ml/min (reference group)]. The main outcome criteria were reperfusion therapy by either thrombolysis or primary percutaneous coronary revascularization (PTCR) and use of heparin in the acute setting; coronary angiography during hospitalization for the ACS; and discharge prescription of aspirin and other antiplatelet agents, anticoagulants, β-blockers, LLDs, and angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs). Numerous clinical covariates were measured at baseline and are shown in Table 1. The baseline electrocardiogram (ECG) abnormalities recorded were ≥1-mm ST-segment elevation or depression or ≥1-mm T-wave inversion in at least two contiguous

Table 1. Baseline characteristics of patients at the time of hospital admission according to estimated CrC (n = 1078)

Characteristics	≤45 ml/min (n = 152)	45 to 60 ml/min (n = 198)	>60 ml/min (n = 728)
Age in years (SD)	75 (7)	70 (8)	58(10)[a]
Gender—male (%)	75 (49)	129 (65)	616(85)[b]
Previous coronary artery disease (%)	104 (68)	116 (59)	313(43)[b]
Previous vascular disease (%)	54 (36)	53 (27)	108(15)[b]
Previous congestive heart failure (%)	33 (22)	15 (8)	17(2)[b]
Hypertension (%)	120 (79)	113 (57)	312(43)[b]
Smoking status active (%)	20 (13)	51 (26)	265(36)[b]
Dyslipidemia (%)	106 (70)	128 (64)	431(59)[b]
Diabetes (%)	43 (28)	41 (21)	133(18)[b]
Chronic obstructive lung disease (%)	26 (17)	32 (16)	75(10)[b]
Mean GFR in ml/min (SD)	34 (7)	53 (4)	88(23)[a]
Mean body mass index in kg/m^2 (SD)	23 (4)	25 (4)	28(6)[a]
Median maximal CK (IQR[c])	161 (71 to 459)	252 (97 to 964)	356 (118 to 1143)[a]
Median cardiac troponin T (IQR)	0.19 (0.01 to 1.07)	0.45 (0.01 to 2.31)	0.42 (0.01 to 1.80)[a]
Abnormalities on baseline ECG (%)	87 (57)	119 (60)	413 (57)
Thrombolysis criteria on baseline ECG (%)	32 (21)	63 (32)	235(32)[b]
Diagnosis of MI (%)	69 (45)	117 (59)	449(62)[b]
Heart failure during hospitalization (%)	34 (22)	30 (15)	47(6)[b]
Use of antiplatelet agents before admission (%)	95 (63)	111 (56)	298(41)[b]
Use of warfarin before admission (%)	16 (10)	12 (6)	19(3)[b]
Use of β-blockers before admission (%)	69 (45)	78 (39)	219(30)[b]
Use of lipid-lowering agents before admission (%)	82 (54)	99 (50)	304(42)[b]
Use of ACE inhibitors/ARBs before admission (%)	66 (43)	65 (33)	183(25)[b]

[a]≤0.05 by Kruskall–Wallis test for a difference between the three groups.
[b]$P \leq 0.05$ by χ^2 for a difference between the three groups.
[c]IQR, interquartile range.

leads. We considered that patients were candidates for reperfusion therapy if they showed ≥1-mm ST-segment elevations in at least two leads on their baseline ECG. During hospitalization, heart failure was defined as significant dyspnea with oxygen desaturation requiring diuretics, characteristic chest x-ray, and presence of lung rales or medical notes indicating Killip class 3 or 4. Hemodynamic instability was defined as the use of intravenous amines for at least 24 h. Patients who had UA after a MI, heart failure, or hemodynamic instability were classified as high risk. Rehospitalization for UA, MI, and death were measured over a 1-yr follow-up.

Statistical Analyses

Approximately normally distributed variables are summarized using means and SD, and non-normally distributed variables are summarized using medians with interquartile ranges (25th and 75th percentiles). Categorical variables are summarized using proportions. χ^2 (for proportions) and Kruskall–Wallis (for non-normally distributed continuous variables) tests were used to detect differences in management between the three groups. Ninety-five percent confidence intervals (CIs) were used to estimate the differences in the proportion of use of drugs or interventions between patients with CrC ≤45 ml and the reference group. If crude between-group differences (by χ^2 or the 95% CI for the between-group difference) suggested variations in practice patterns according to renal function, we used logistic regression to estimate the independent association between CrC and outcome after adjustment for compelling indications and comorbidities. The effect of CrC on outcome was verified for linearity on the logit scale by visual inspection. CrC was used as a continuous variable in the regression when this assumption was met and was treated as a categorical variable otherwise. We performed stratified analyses by center type (community *versus* tertiary) to assess whether there was effect modification by center type in the relationship between renal function and use of reperfusion therapy and coronary angiography. We also tested for the significance of this interaction using a logistic regression model.

Results

Among the 1210 recruited participants, 1080 patients were discharged with a final diagnosis of MI or UA, and 1078 had an available creatinine measurement at baseline and were analyzed. In-hospital death occurred in six (0.01%) patients with an estimated CrC > 60 ml/min, in six (3%) subjects who had a CrC of 45 to 60 ml/min, and in six (5%) patients with a CrC ≤ 45 ml/min [odds ratio (OR): 6.69, 95% CI: 2.28 to 19.56 for the comparison between the lowest and highest CrC group]. Patients in the two CKD groups were more likely to be older, female, and to have a previous history of CVD and peripheral vascular disease, heart failure, hypertension, diabetes, and chronic obstructive pulmonary disease (COPD); however, they were less likely to be active smokers than subjects with a CrC > 60 ml/min. At the time of admission, they were also more likely to be taking antiplatelet agents, β-blockers, ACE inhibitors, ARBs, and LLDs (Table 1). Although the percentage of baseline abnormal ECGs was similar in patients with and without CKD, fewer patients in the most severe CKD group had ECG criteria for ST elevation MI (STEMI) or a discharge diagnosis of MI, consistent with their lower troponin and creatine kinase levels. Recurrent hospitalization for UA, MI, or death at 1 yr occurred in 129 (18%) patients with an estimated CrC > 60 ml/min, in 44 (22%) subjects who had a CrC of 45 to 60 ml/min, and in 54 (36%) of those with a CrC ≤ 45 ml/min (OR: 2.56, 95% CI: 1.75 to 3.75 for the comparison between the lowest and highest CrC group).

We studied therapeutic interventions associated with the treatment of ACS during the course of hospitalization in all eligible patients (n = 1078). Because of local differences in resources, use of reperfusion therapy (by primary PTCR or thrombolysis) may have varied. We observed that the use of reperfusion therapy in subjects who had the appropriate ECG criteria was similar across levels of renal function in tertiary care centers (CrC ≤ 45 ml/min: 84%, CrC 45 to 60 ml/min: 85%, and CrC > 60 ml/min: 80%; difference between the lowest and highest CrC group: +4%, 95% CI: −13%, 21%). It appeared to be lower in patients with CKD in community-based centers (CrC ≤ 45 ml/min: 46%, CrC 45 to 60 ml/min: 73%, and CrC > 60 ml/min: 68%; difference between the lowest and highest CrC group: −22%, 95% CI: −52%, 8%), but the CI was wide and included the null value. The interaction term between center type and renal function was NS (P = 0.18). Heparin use was similar in the three groups (CrC ≤ 45 ml/min: 91%, CrC 45 to 60 ml/min: 86%, and CrC > 60 ml/min: 91%; difference between the lowest and highest CrC group: 0%, 95% CI: −5%, 5%) (Table 2).

The use of coronary angiography was lower in subjects with impaired renal function (CrC ≤ 45 ml/min: 47%, CrC 45 to 60 ml/min: 55%, and CrC > 60 ml/min: 63%; difference between the lowest and highest CrC group: −16%, 95% CI: −31%, −1%). This was also true in patients classified as high risk (UA after a MI, heart failure, or hemodynamic instability) (CrC ≤ 45 ml/min: 62%, CrC 45 to 60 ml/min: 71%, and CrC > 60 ml/min: 87%; difference between the lowest and highest CrC group: −25%, 95% CI: −35%, −11%) (Table 3). When adjusted for patient age, gender, and diabetes, post-MI UA and hemodynamic instability or heart failure during hospitalization, lower estimated CrC (OR: 0.93 for a 10-ml/min decrease, 95% CI: 0.85 to 0.99) and lower left ventricular ejection fraction (LVEF) (OR: 0.89 for a 10% decrease, 95% CI: 0.79 to 0.99) were independently associated with lower use of coronary angiography (Table 4). In high-risk patients who had a CrC ≤ 60 ml/min, the composite end point of recurrent hospitalization for UA, MI, or death over the following year occurred in 36% of patients who had a coronary angiography during the index hospitalization and in 54% of those who did not (difference: −18%, 95% CI: −37%, 1%). Use of coronary angiography was lower in subjects with CKD regardless of center type.

We studied discharge medications in all of those who survived past their initial hospital stay (n = 1058). At the time of discharge, aspirin use was lower in patients with CKD (CrC ≤ 45 ml/min: 85%, CrC 45 to 60 ml/min: 91%, and CrC > 60 ml/min: 94%; difference between the lowest and highest CrC group: −9%, 95% CI: −15%, −3%). However, when the use of oral anticoagulation and other antiplatelet agents was considered, the observed between group differences disappeared completely (Table 5). Hence, nearly all patients received either an antiplatelet agent or warfarin at

Table 2. Use of reperfusion therapy, heparin, and oral anticoagulants in the acute management of ACS according to estimated CrC

Medication Use	≤45 ml/min (n = 152)	45 to 60 ml/min (n = 198)	>60 ml/min (n = 728)	Difference[a,c]
Thrombolysis or primary PTCR in candidates by ECG criteria[b] (%)	22 (69)	52 (83)	182 (77)	−8 (−24, 8)
tertiary care centers	16 (84)	41 (85)	142 (80)	4 (−13, 21)
community-based centers	6 (46)	11 (73)	40 (68)	−22 (−52, 8)
Heparin use—acute treatment of ACS (%)	138 (91)	171 (86)	663 (91)	0 (−5, 5)
Heparin use or already receiving warfarin—acute treatment of ACS (%)	143 (94)	172 (87)	664 (91)	3 (−1, 7)

[a]Reported differences are between subjects with a CrC ≤45 ml/min and the reference group (>60 ml/min) and are expressed in percent with a 95% CI.
[b]There were 330 subjects considered appropriate candidates for reperfusion therapy by ECG criteria (≥1-mm ST-segment elevation in two leads): 32 with a CrC ≤45 ml/min, 63 in the 45- to 60-ml/min category, and 235 with a CrC >60 ml/min.
[c]There were no significant between-group differences by χ^2.

Table 3. Use of coronary angiography during hospitalization according to estimated CrC

	≤45 ml/min (n = 152)	45 to 60 ml/min (n = 198)	>60 ml/min (n = 728)	Difference[a]
Coronary angiography, all patients (%)	71 (47)	108 (55)	458 (63)	−16 (−31, −1)[c]
Coronary angiography, high-risk patients[b] (%)	34 (62)	39 (71)	131 (87)	−25 (−39, −11)[c]

[a]Reported differences are between subjects with a CrC ≤45 ml/min and the reference group (>60 ml/min) and are expressed in percent with a 95% CI.
[b]There were 261 subjects considered at high risk (UA after a MI, heart failure, or hemodynamic instability): 55 with a CrC ≤45 ml/min, 55 in the 45- to 60-ml/min category, and 151 with a CrC >60 ml/min.
[c]$P \leq 0.05$ by χ^2 for a difference between the three groups.

Table 4. Factors affecting the prescription of coronary angiography[a]

Predictive Factors	Univariate OR (95% CI)	Multivariate OR (95% CI)
CrC (per 10-ml/min decrease)	0.91 (0.87 to 0.96)[b]	0.93 (0.85 to 0.99)[b]
Age (per 10-yr increase)	0.84 (0.76 to 0.93)[b]	1.00 (0.98 to 1.01)
Female gender	0.79 (0.59 to 1.04)	0.88 (0.64 to 1.21)
Diabetes	1.04 (0.77 to 1.41)	0.97 (0.70 to 1.36)
Post-MI UA	4.84 (3.15 to 7.45)[b]	5.38 (3.45 to 8.39)[b]
Heart failure or hemodynamic instability	1.50 (0.99 to 2.28)	2.02 (1.23 to 3.33)[b]
LVEF (per 10% decrease)	0.94 (0.85 to 1.04)	0.89 (0.79 to 0.99)[b]

[a]The multivariate model includes all variables listed in the table.
[b]$P \leq 0.05$.

discharge, regardless of renal function (CrC ≤ 45 ml/min: 99%, CrC 45 to 60 ml/min: 98%, and CrC > 60 ml/min: 100%; difference between the lowest and highest CrC group: −1%, 95% CI: −3%, 1%). We observed similar discharge prescription rates of ACE inhibitors or ARBs (CrC ≤ 45 ml/min: 65%, CrC 45 to 60 ml/min: 63%, and CrC > 60 ml/min: 58%; difference between the lowest and highest CrC group: 7%, 95% CI: −1%, 15%) across all levels of renal function.

β-blocker use at discharge was only lower in the most severe CKD group (CrC ≤ 45 ml/min: 74%, CrC 45 to 60 ml/min: 83%, and CrC > 60 ml/min: 83%; difference between the lowest and highest CrC group: −9%, 95% CI: −17%, −1%). To understand whether CKD *per se* explained this observation, we performed

Table 5. Discharge prescription rates of antiplatelet agents/anticoagulants, β-blockers, LLDs, and blockers of the renin-angiotensin system according to estimated CrC

Medication Use	≤45 ml/min (n = 144)	45 to 60 ml/min (n = 192)	>60 ml/min (n = 722)	Difference[a]
Aspirin (%)	123 (85)	175 (91)	678 (94)	−9 (−15, −3)[b]
Any antiplatelet agent (%)	130 (90)	179 (93)	705 (98)	−8 (−13, −3)[b]
Warfarin (%)	28 (19)	23 (12)	57 (8)	11 (4, 18)[b]
Any antiplatelet agent/warfarin (%)	143 (99)	189 (98)	719 (100)	−1 (−3, 1)
β-blockers (%)	107 (74)	160 (83)	599 (83)	−9 (−17, −1)[b]
LLDs (%)	105 (73)	140 (73)	579 (80)	−7 (−13, −1)[b]
ACE inhibitor/ARB (%)	94 (65)	122 (63)	421 (58)	7 (−1, 15)

[a]Reported differences are between subjects with a CrC ≤45 ml/min and the reference group (>60 ml/min) and are expressed in % with a 95% CI.
[b]$P \leq 0.05$ by χ^2 for a difference between the three groups.

multivariate analyses. Independent predictors of β-blocker use at discharge (Table 6) were a diagnosis of MI (OR: 1.76, 95% CI: 1.20 to 2.57), prior β-blocker use (OR: 7.41, 95% CI: 4.30 to 12.76), and lower LVEF (OR: 1.23 per 10% decrease, 95% CI: 1.05 to 1.45). Increased age (OR: 0.79 for a 10-yr increase, 95% CI: 0.65 to 0.96) and COPD (OR: 0.13, 95% CI: 0.08 to 0.20) were associated with lower discharge use of β-blockers, whereas CKD was not (OR: 0.84, 95% CI: 0.47 to 1.52) once potential confounding factors were taken into account.

LLDs were used less frequently in patients with CKD at discharge (CrC ≤ 45 ml/min: 73%, CrC 45 to 60 ml/min: 73%, and CrC > 60 ml/min: 80%; difference between the lowest and highest CrC group: −7%, 95% CI: −15%, −1%). In multivariate analysis, lower estimated CrC (OR: 0.91 for a 10-ml/min decrease, 95% CI: 0.88 to 0.99) remained independently associated with lower LLD prescription at discharge. Prior use of LLDs (OR: 19.98, 95% CI: 10.54 to 37.89) and history of dyslipidemia (OR: 1.87, 95% CI: 1.26 to 2.78) were the only other factors that predicted use of LLDs at discharge (Table 7).

Discussion

We performed a population-based, prospective cohort study in which we assessed whether practice patterns in terms of acute management of an ACS and secondary prevention varied with renal function. Several past studies have suggested that patients with CKD receive less aggressive therapies when they experience an ACS. Such differences in prescription patterns lead to questioning the appropriateness of management in the high-risk subset of patients with CKD. Indeed, it has been shown that in patients with chronic conditions, unrelated disorders are often undertreated (17). We wanted to elucidate whether observed differences reflected a certain form of therapeutic nihilism in patients with CKD (18), or other mechanisms such as confounding by comorbid conditions, co-medication, or fear of deteriorating renal function.

We observed that after accounting for co-medication and other confounders, most aspects of care were similar in CKD *versus* non-CKD patients who suffer an ACS. Coronary angiography and LLDs at discharge were used less frequently in CKD patients than in non-CKD patients. Although lower β-blocker use at discharge was observed in subjects with a CrC ≤ 45 ml/min, this was no longer the case when confounding factors were taken into account. In tertiary care centers, reperfusion therapy, whether by primary PTCR or thrombolysis, was attempted in a similar proportion of patients who had ECG criteria for thrombolysis regardless of renal function. The proportion of subjects who received heparin was also similar in patients with and without CKD. Although aspirin use was lower at discharge in patients with stage III to V renal failure compared with those with a CrC > 60 ml/min, when the use of

Table 6. Factors affecting discharge prescription of β-blockers[a]

Predictive Factors	Univariate OR (95% CI)	Multivariate OR (95% CI)
CrC (reference >60 ml/min)	1.00	1.00
45 to 60 ml/min	1.03 (0.67 to 1.57)	1.38 (0.80 to 2.38)
≤45 ml/min	0.59 (0.39 to 0.91)[b]	0.84 (0.47 to 1.52)
Age (per 10-yr increase)	0.78 (0.68 to 0.90)[b]	0.79 (0.65 to 0.96)[b]
Chronic obstructive lung disease	0.12 (0.08 to 0.18)[b]	0.13 (0.08 to 0.20)[b]
Discharge diagnosis of MI	1.44 (1.05 to 1.97)[b]	1.76 (1.20 to 2.57)[b]
LVEF (per 10% increase)	0.85 (0.74 to 0.98)[b]	0.81 (0.69 to 0.95)[b]
Use of β-blockers before admission	6.17 (3.72 to 10.20)[b]	7.41 (4.30 to 12.76)[b]

[a]The multivariate model includes all variables listed in the table.
[b]$P \leq 0.05$.

Table 7. Factors affecting discharge prescription of lipid-lowering agents[a]

Predictive Factors	Univariate OR (95% CI)	Multivariate OR (95% CI)
CrC (per 10-ml/min decrease)	0.91 (0.85 to 0.96)[b]	0.91 (0.88 to 0.99)[b]
Age (per 10-yr increase)	0.81 (0.71 to 0.92)[b]	0.85 (0.70 to 1.04)
Female gender	0.79 (0.57 to 1.10)	0.94 (0.63 to 1.42)
Diabetes	1.15 (0.79 to 1.67)	0.83 (0.53 to 1.32)
Previously known dyslipidemia	5.85 (4.26 to 8.05)[b]	1.87 (1.26 to 2.78)[b]
Discharge diagnosis of MI	0.83 (0.61 to 1.11)	1.45 (0.98 to 2.14)
Previous coronary disease	1.98 (1.47 to 2.67)[b]	0.69 (0.45 to 1.06)
Use of lipid-lowering agent before admission	5.85 (4.26 to 8.05)[b]	19.98 (10.54 to 37.89)[b]

[a]The multivariate model includes all variables listed in the table.
[b]$P \leq 0.05$.

other antiplatelet agents or warfarin was considered, nearly 100% of patients received either an antiplatelet or an antithrombotic agent regardless of renal function. Use of ACE inhibitors or ARBs was similar in the three groups.

The differences between our findings and those of previous studies can be explained by multiple factors. First, we considered co-medication to a greater extent than in prior reports. For instance, in a large Canadian cohort study of patients admitted with a diagnosis of ACS between 1997 and 1999 (11), discharge use of aspirin was lower in patients with stage III to V renal failure when compared with subjects with normal renal function, a finding that has also been reported by others (8,9). However, the use of other antiplatelet agents and warfarin was not taken into account in these studies. We believe that lower discharge use of aspirin does not necessarily represent undertreatment in our cohort, because when the use of other antiplatelet agents and warfarin is considered, coverage with one drug or the others is nearly 100%, regardless of renal function. Given the possibility of platelet dysfunction in CKD (19), the combined use of aspirin and warfarin may have untold risks and cannot be taken as the standard of care.

Second, there is a secular trend for increased use of cardioprotective drugs (13). Regardless of renal function, overall rates of cardioprotective drug use were indeed much higher in our cohort and in another recent report (7) compared with earlier ones (8,9). The differences in cardioprotective drug use at discharge between patient with and without CKD that were reported in the past (8,9) are less important in recent years, as we and others (7) have found. Furthermore, another recent study has demonstrated a secular trend for a disproportionate increase in β-blocker and statin use in CKD *versus* non-CKD patients over time after an ACS (20). This may reflect increased physician's awareness of the high cardiovascular risk experienced by subjects with CKD.

Third, in previous American studies, patients with CKD were older and more likely to be of African-American origin (8,21); this may account for some differences observed in relation to lower socioeconomic status. In our cohort, seven of the participating centers were located in the province of Quebec where drug insurance plans have been mandatory since 1997 for all residents. Hence, the likelihood of socioeconomic status confounding our results is much lower. Despite the fact that only small therapeutic differences were observed in our cohort, patients with CKD still had twice the rate of recurrence experienced by others. This reinforces the recent finding that even among patients who have revascularization and optimal medical therapy, CKD predicts a poor outcome after an ACS (5).

The lower use of coronary angiography in patients with CKD was observed even when only high-risk patients were considered. The fact that CKD remains associated with lower use of angiography after adjusting for comorbidities and compelling indications for intervention suggests that fear of worsening renal function deters clinicians from ordering this procedure. A clear conclusion on whether this is justified cannot be drawn from observational studies because of potential residual confounding. In our study, the 1-yr outcome in high-risk CKD patients who had a coronary angiography was slightly better than in those who did not. This finding may reflect a beneficial effect of intervention, but also channeling, in that the best patients are selected for intervention. However, a better outcome is reassuring, given the higher risk of contrast nephropathy in patients with CKD (22) and the relationship of the latter with mortality (23).

Some (9,21), but not all (7,24), studies have previously reported lower β-blocker use at discharge in subjects with CKD. The reasons underlying this observation are not clear at first glance, because this drug class is not nephrotoxic, has no strong effect on renal hemodynamics, and contains many compounds that have hepatic rather than renal metabolism (25). We observed lower use only in subjects with a CrC $\leq$ 45 ml/min. However, multivariate analysis showed that a constellation of confounding factors, and especially age, rather than CrC *per se*, explained this observation. Underuse of β-blockers in elderly patients has often been reported in the post-MI setting (26,27). In our study, increased age was an independent predictor of lower β-blocker use, even after adjusting for LVEF and COPD. However, in the absence of information on heart rate and BP, we cannot exclude that increased prevalence of bradycardia or hypotension in the elderly explained this observation.

Only one previous report (11) has shown lower use of LLDs in patients with CKD after an ACS. In our study, CrC was independently associated with use of LLDs at discharge.

Hence, our results suggest that CrC *per se*, or a factor that is intimately associated with it and was not measured in our study, is responsible for lower use in patients with CKD. For instance, because patients with CKD often exhibit high triglycerides and low HDL and LDL cholesterol (28), one may expect lower statin use in these patients. Furthermore, fibrates can cause a hemodynamic decrease in GFR (29) and are used with caution in patients with CKD. Physicians may also be more reluctant to prescribe lipid-lowering agents to a patient population in whom a clear benefit from these drugs has never been shown (30,31) and who often have polypharmacy, increasing the risk of drug interactions and side effects (32,33). Although many reasons can explain the differences we observed, physicians should keep in mind that subgroup analyses from randomized controlled trials clearly show a beneficial effect of statins in the prevention of future cardiovascular events in subjects with moderate kidney dysfunction (34,35). Furthermore, current guidelines (36) consider CKD as mandating secondary prevention lipid targets.

Our study has certain limitations. The number of patients with stage IV and V renal failure was relatively limited. Hence, an independent, moderate underuse of β-blockers in subjects with a CrC $\leq$ 45 ml/min and an interaction between center type and renal function on the use of reperfusion therapy cannot be excluded. None of the patients were undergoing renal replacement therapy, and our conclusions are not applicable to this group. We used baseline creatinine to estimate chronic CrC and GFR. However, our approach was similar to that used in other studies (8,11) and seems a reasonable option, given that measurements were performed on admission, before any procedure could lead to increased creatinine levels. Lipid profile measurements, information on drugs taken by patients but unrelated to cardiac management, and the type of lipid-lowering agent used were not recorded, which does not allow us to make a clear statement on the appropriateness of lipid management in patients with renal failure. Finally, information on the occurrence of contrast nephropathy or permanent impairment in renal function after angiography was not available.

In conclusion, we observed that after adjustment for comedication and other confounders, most aspects of care were similar in CKD *versus* non-CKD patients who suffer an ACS. In multivariate models, only coronary angiography and LLDs at discharge were used less frequently in CKD patients. These results suggest that the extent of undertreatment due to CKD *per se* is less than reported in previous studies, which is partially explained by evolving medical awareness as well as more complete adjustment for cotreatments and comorbidities.

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Disclosures

None.

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