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Optimizing Subsequent CARdiovascular Medication Reintroduction in the Intensive Care Unit

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Abstract

Importance: Hospital admission for a critical illness episode creates communication breakpoints and can lead to medication discrepancies during hospital stays. Due to the patient's underlying condition and the care setting, chronic medications such as cardiovascular medication are often held, discontinued, or changed to alternative administration routes. Unfortunately, data on the optimal timing of cardiovascular drug reinitiation among intensive care unit (ICU) survivors are lacking.

Objective: The primary objective of this study was to describe the prevalence of chronic cardiovascular medication taken before hospital admission and discontinued at ICU discharge and hospital discharge for critically ill patients. A secondary objective was to assess factors associated with medication discontinuation.

Design setting and participants: We conducted a multicentered retrospective cohort study at 2 tertiary academic hospitals in Canada. All adult patients taking cardiovascular medication before ICU admission and surviving to hospital discharge between April 1, 2016, and April 1, 2017, were eligible.

Main outcomes and measures: The main outcome of the study was the discontinuation of cardiovascular medication prescribed before ICU admission. The outcome was assessed through participants' chart review.

Results: We included 352 patients with a median age of 71.0 years. A total of 155 patients (44.03%) had at least 1 cardiovascular medication discontinued during their stay. Our adjusted model uncovered 3 factors associated with cardiovascular medication discontinuation: male sex (odds ratio [OR] = 0.564, 95% confidence interval [CI] = 0.346-0.919), number of cardiovascular medications taken preadmission (OR = 1.669, 95% CI = 1.003-2.777 for 2 medications and OR = 3.170, 95% CI = 1.325-7.583), and the use of vasopressors (OR = 1.770, 95% CI = 1.045-2.997).

Conclusion: Our study uncovered that cardiovascular medication discontinuation for ICU patients is frequent, especially for renin-angiotensin system (RAS) blockers. Data from our study could be used to reinforce site-specific protocols of medication reconciliation and optimization, as well as inform future protocols aimed at RAS blocker reinitiation follow-up.

Abrege

Importance de cette étude L'admission à l'hôpital pour un épisode de maladie grave crée des ruptures de communication et peut entraîner des écarts dans la médication pendant le séjour à l'hôpital. Il arrive souvent, selon l'état sous-jacent du patient et l'environnement de soins, que les médicaments destinés à traiter des maladies chroniques, comme les médicaments cardiovasculaires, soient poursuivis, cessés ou administrés par d'autres voies. On manque malheureusement de données sur le moment optimal pour la reprise du traitement cardiovasculaire chez les survivants des unités de soins intensifs (USI).

Objectifs: L'objectif principal était de décrire la prévalence de l'arrêt, à la sortie de l'USI et de l'hôpital, des médicaments pris par les patients gravement malades pour traiter les maladies cardiovasculaires chroniques avant leur admission. Un objectif secondaire était d'évaluer les facteurs associés à l'arrêt du traitement.

Conception, sujets et cadre de l'étude: Nous avons mené une étude de cohorte rétrospective multicentrique dans deux hôpitaux universitaires tertiaires canadiens. Étaient admissibles tous les patients adultes qui prenaient des médicaments cardiovasculaires avant leur admission à l'USI entre le 1er avril 2016 et le 1er avril 2017 et qui avaient survécu jusqu'à leur sortie de l'hôpital.

Mesures et principaux critères d'intérêt: Le principal critère d'intérêt était l'arrêt du traitement cardiovasculaire prescrit avant l'admission à l'USI. Ce critère a été établi par l'examen des dossiers des sujets.

Résultats: Nous avons inclus 352 patients (âge médian : 71,0 ans) desquels 155 (44 %) avaient vu au moins un de leurs médicaments pour traiter une maladie cardiovasculaire cessé pendant leur séjour. Notre modèle corrigé a révélé trois

facteurs associés à l'arrêt du traitement cardiovasculaire : être de sexe masculin (rapport de cotes [RC] : 0,564; IC95 % : 0,346-0,919), le nombre de médicaments cardiovasculaires pris avant l'admission (RC : 1,669; IC95 % : 1,003-2,777 pour deux médicaments, et RC : 3,170; IC95 % : 1,325-7,583) et l'utilisation de vasopresseurs (RC : 1,770; IC95 % : 1,045-2,997).
Conclusion : Notre étude a révélé que l'arrêt du traitement contre les maladies cardiovasculaires chroniques, en particulier les inhibiteurs du SRA, est fréquent chez les patients hospitalisés aux soins intensifs. Les données de notre étude pourraient servir à renforcer les protocoles de bilan de médication et d'optimisation propre à chaque site de même que pour éclairer les futurs protocoles visant à assurer le suivi de la réinitiation des inhibiteurs du SRA.

Keywords
renin-angiotensin system inhibitors, cardiovascular medication, medication reconciliation

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Key Points

Question: Determine the prevalence of chronic cardiovascular medication discontinuation for intensive care unit (ICU) patients and the factors causing it.

Findings: We uncovered that RAS blockers tend to be more discontinued than other cardiovascular medication classes. Moreover, this discontinuation was associated with the number of medications prescribed previous to hospital admission and the use of vasopressors.

Meanings: Data from this study data might be used in future interventional studies aiming at optimizing medication management and reconciliation for ICU patients.

Introduction

As the population ages and life expectancy increases, a significant proportion of older adults (≥65 years old) live with multimorbidities.[1,2] Consequently, the prevalence of polypharmacy (≥5 chronic medications) is rising.[3] In Canada, approximately two-thirds of community-dwelling elders use more than 5 chronic medications daily.[4]

Hospital admission for an acute illness episode creates communication breakpoints and can lead to medication discrepancies during hospital stays.[5] They occur most when patients transition from one healthcare setting to another.[6,7] Patients admitted to an intensive care unit (ICU) are at higher risk of medication discontinuation and discrepancies.[8,9] Due to the patient's underlying condition and the care setting, chronic medications such as cardiovascular medication are often held, discontinued, or changed. Even when the patient's status improves, ongoing organ failures developed during ICU stay might preclude physicians from restarting discontinued medications on ICU discharge. Past studies have shown that statins and antiplatelet medications were more often discontinued in patients transitioning through the ICU than in patients staying on the ward.[8,9] Discontinuing chronic therapies, such as cardiovascular medications, can lead to decompensation requiring emergency department visits and even rehospitalization.[10-12]

Strong evidence exists about the adverse effects of discontinuation of cardiovascular drugs, especially renin-angiotensin system (RAS) blockers. In heart failure patients, it was associated with a 40% increase in the risk of 30-day readmissions and a 35% increase in the risk of 1-year mortality.[13] These effects were observed within a few weeks after discontinuation.[12] Considering that 34% of Canadian older adults take RAS blockers regularly[14] and with more than 230 000 ICU admissions yearly in Canada,[15] a substantial number of patients are at risk of complications due to RAS blocker discontinuation. Patient renal function might be an important factor in determining RAS blocker reinitiation. In a recent retrospective study, cardiovascular medications represented 15% of all medication errors on ICU discharge, with the use of renal replacement therapy (RRT) being a significant risk factor (adjusted odds ratio [OR] = 2.93, 95% confidence interval [CI] =1.42-6.07).[9] Unfortunately, data on the optimal timing of cardiovascular drug reinitiation among ICU survivors are lacking.

To understand the problem at hand, we need to better define the paths of cardiac chronic medications used for patients transitioning through the ICU, determine breakpoints in care transition, and understand patient and hospital factors involved. Therefore, we undertook a retrospective cohort study evaluating chronic medication transitions for critically ill patients. The primary objective of this study was to describe the prevalence of chronic cardiovascular medication taken on hospital admission and discontinued at hospital discharge, with secondary objectives aimed at assessing factors associated with discontinuation.

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Method

Study Population

This study, titled as *Optimisation de la réintroduction de la médication cardiovasculaire aux soins intensifs (OSCAR-ICU): une étude Retrospective*, was approved by the *comité d'éthique du CIUSS Est-de-l'Île de Montréal (CÉR-CEMTL)*, project number 2019-1812, on March 20, 2020. Informed consent was waived by the said committee, and we followed procedure according to the ethical standard. We conducted a retrospective cohort study at 2 tertiary academic hospitals in Canada: Maisonneuve-Rosemont Hospital (in Montreal, Quebec) and Mount Sinai Hospital (in Toronto, Ontario). All adult ICU patients taking cardiovascular medications before hospital admission between April 1, 2016, and April 1, 2017 were eligible if they were discharged from both the ICU and the hospital. Only the first hospital visit containing an ICU admission was considered for patients with multiple hospitalizations during the study time frame. We excluded patients transferred from and to a long-term care facility, palliative care unit, or another hospital. For these patients, discontinuation of cardiovascular medications might be warranted considering their health status.

Data Collection

Cardiovascular medication was defined as any of the following: angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), β-blockers (BB), and calcium channel blockers (CCB). Both ACEi and ARB were considered RAS blockers for the purpose of this study. We classified medications using the Anatomic Therapeutic Chemical (ATC) Classification System.[16] We collected cardiovascular medication before hospital admission through chart review and a medication list provided by the patient's local pharmacy or a medication history completed by a pharmacist. We extracted all in-hospital medication data through the electronic pharmacy record used for all in-hospital prescriptions. We retrieved cardiovascular medication at discharge from the pharmacy discharge summary note or a discharge summary that included discharge medication reconciliations. We used pharmacy discharge summaries as clinical pharmacists are responsible for medication reconciliation. Medications prescribed on hospital discharge day were not counted as in-hospital reinitiation. These reinitiations are generally due to physicians or pharmacists simply reconciling patients' medication lists and were standardized in both participating hospitals. Medication discontinuation was defined as any chronic medication taken by the patient before hospital admission and not taken by the patient at ICU discharge and hospital discharge. A change for another medication in the same therapeutic class or a dosage change was not deemed a discontinuation.

We collected other data directly from hospital electronic medical records. The baseline information extracted included patient demographics, comorbidities and renal function, primary diagnosis, admission type (medical, elective surgery, emergency surgery), length of hospital and ICU stays, relevant laboratory values, and clinical variables for the Sequential Organ Failure Assessment (SOFA) score in the first 48 hours of ICU admission. We also collected the use of vasopressor support, the presence and the severity of acute kidney injury (AKI) during ICU stay, RRT, and invasive mechanical ventilation. We also retrieved the following hospital-level variables from the medical record: type of ward transfer, hospital discharge location, and renal function at discharge.

Acute kidney injury was defined using the Kidney Disease Improving Global Outcome (KDIGO) definition published in 2012.[17] For feasibility reasons, we only used serum creatinine (SCr) levels for staging AKI severity. Urine output is not collected for hospitalized patients unless prescribed; therefore, this variable was often absent and was only available for patients where AKI was suspected. Past studies have also shown a similar prevalence of AKI and predictive value for mortality using serum creatinine or urine output.[18]

Outcomes

Our primary outcome was the proportion of patients discharged from the hospital with at least 1 cardiovascular medication discontinued. Our secondary outcome was to assess factors associated with cardiovascular medication discontinuation.

Statistical Analysis

We divided patients taking cardiovascular drugs before admission into 2 groups based on whether they had their medications reinitiated at hospital discharge. We also studied patients discharged with ACEi or ARB reinitiation compared with no reinitiation. We used descriptive statistics to describe medication pathways during hospital stays. Continuous variables are presented as means with standard deviations (SD) or medians with interquartile range (IQR) for skewed distributions after assessing normal distribution using the Shapiro-Wilk test. Categorical variables were expressed as proportions. We compared continuous variables with the t test and Wilcoxon rank sum test, and categorical variables with the χ^2 test.

We used multivariable logistic regression to examine the association between baseline characteristics and cardiovascular medication discontinuation at discharge. Patients without drug discontinuation were used as the reference. We chose a priori covariates if they were potentially associated with medication discrepancies, including the following: age, sex, comorbidities, number of cardiovascular medications at

home, hospital-level variables (length of stay, type of ward transfer, serum creatinine level at discharge), and critical illness severity (SOFA score, use of vasopressor or mechanical ventilation, AKI, RRT). As a subgroup analysis, we examined specifically factors associated with RAS blocker discontinuation such as sex, sCr levels, presence of AKI, and preexisting comorbidities. Statistical analyses were conducted using SPSS version 25.

Results

We included 352 consecutive survivors (295 from Maisonneuve-Rosemont Hospital and 58 from Mount Sinai) hospital. A total of 155 (43.9%) patients had at least 1 cardiovascular medication discontinued. The median (IQR) age was 71.0 years (58.5-83.5) and 40.5% (N = 143) of our cohort were female. According to the hospital medical record, high blood pressure (87.7%, n = 308) and diabetes (34.6%, n = 122) were the most prevalent comorbidities. Among the 352 survivors, 69.6% (n = 245) were on ACEi or ARB, 48.6% (n = 171) were on BB, and 46.1% (n = 148) were on CCB before admission. Medical admissions represented 48.9% (N = 172) of our cohort, followed by elective surgery at 27.0% (N = 95) and emergency surgery at 23.9% (N = 84). During their ICU stay, 127 patients (36.0%) required vasopressors, 141 patients (39.0%) received invasive mechanical ventilation, and 13 (3.70%) started RRT (Table 1).

Patients with cardiovascular medication discontinuation were more likely to be men (67.7% vs 53.0%, $P = .005$), had a higher baseline SCr level (85.0 vs 75.0 mmol/L, $P < .001$), and used more cardiovascular therapies, especially ACEi and ARB (21.00% vs 15.00% taking 3 cardiovascular medications) (all $P < .001$). Also, patients with cardiovascular medication discontinuation were characterized by a greater need for vasopressors (44.5% vs 28.00%, $P = .003$) and RRT (7.700% vs 0.500%, $P = .001$) (see Table 1). These tendencies were similar when looking at patients taking RAS blockers (see Table 3). Chronic cardiovascular medication reinitiation during hospitalization is shown in Table 2. RAS blockers were reinitiated for only 40.8% of the patients at ICU discharge, while CCB and BB were reinitiated for 55.4% of patients and 63.2% of patients, respectively. On hospital discharge, RAS blockers were reinitiated in only 51.4% of patients.

Our adjusted model uncovered 3 independent factors associated with cardiovascular medication discontinuation: male sex (OR = 0.564, 95% CI = 0.346-0.919), taking more than 1 cardiovascular medication on preadmission (OR = 1.67, 95% CI = 1.003-2.78 for 2 medications and OR = 3.17, 95% CI =1.33-7.58 for 3 medications), and the use of vasopressors (OR = 1.77, 95% CI = 1.05-3.00) (see Table 4). In addition, 3 variables were associated with RAS blockers' discontinuation: AKI during ICU (OR = 3.82, 95% CI = 1.99-7.32) and SCr levels at hospital discharge (OR = 1.007, 95% CI = 1.001-1.012). By contrast, suffering from heart failure as a comorbidity decreased by 61% this risk (OR = 0.39, 95% CI = 0.176-0.853) (see Table 5).

Discussion

We uncovered that a significant proportion of cardiovascular medications were discontinued at hospital discharge, especially RAS blockers (48.6%). Our data showed that 155 (43.9%) patients had at least 1 cardiovascular medication discontinuation. These numbers are slightly higher than those from an Ontario study[19] looking at medication discontinuation from 5 drug classes (ie, gastric acid-suppressing drugs, statins, antiplatelet and anticoagulants, respiratory inhalers and levothyroxine) following ICU hospitalization; however, these medications often do not necessitate an adjustment for ongoing AKI or hypotension. Moreover, when looking specifically at RAS blockers, an Albertan retrospective study found that nearly a quarter of non-ICU hospitalized patients saw their RAS blockers discontinued 6 months after hospital discharge.[20] By contrast, our data found that 59.2% of ICU patients taking RAS blockers did not reinitiate their medication at ICU discharge, and 48.6% did not reinitiate them at hospital discharge. Our numbers are in line with recent work demonstrating that ICU patients tend to see more medication discontinuation than general hospital patients.[8] Moreover, the Alberta study looked at discontinuation 6 months after discharge, while our work focused on discontinuation at ICU and hospital discharges only. The absence of follow-up after hospital discharge explains our higher numbers, as some patients might have their medication reinitiated during a follow-up visit with their primary care physicians.

Our adjusted model found the number of medications prior to admission and the use of vasopressors significantly increased the odds of discontinuation of cardiovascular medications. These results are akin to those found in the literature. A systematic review aiming at identifying predictors of unintentional medication discrepancies during preadmission showed that the number of medications, and the medication class were factors strongly affecting the risk of discontinuation.[21] Although we did not evaluate the appropriateness of the medication discontinuation, ICU and hospital discharge highlight important moments for medication reconciliation, taking into account patients' baseline illness, their residual organic function, and their indications for potentially hazardous medications such as antihypertensive agents. The use of medication reconciliation has already shown important reductions in medication errors, especially in patients transferring from an ICU to a medical ward or step-down unit.[22] Our data, therefore, highlight the potential absence of return to baseline health before hospital discharge and propose the question of the appropriateness of medication discontinuation during medical visit time points, such as ICU or hospital admission.

Table 1. Baseline Characteristics.

Characteristic	Full cohort (N = 353)	All cardiovascular drug represcribed at hospital discharge (n = 198)	One or more cardiovascular drug discontinued at hospital discharge (n = 155)
Age, years (IQR)	71 (12.5)	71.0 (13.4)	71.0 (11.4)
Female sex, no. (%)	143 (40.5)	93 (47.0)	50 (32.3)
Source of admission to hospital, no. (%)			
Home	328 (92.9)	189 (95.5)	139 (89.7)
Another hospital	24 (6.8)	8 (4.0)	16 (10.3)
Length of stay, days (IQR)			
Hospital	13 (18.8)	11 (18)	17 (19)
ICU	2 (5.6)	2 (6)	2.0 (4)
Preexisting medical comorbidities, no. (%)			
HTN	308 (87.3)	170 (85.9)	138 (89.0)
CAD	122 (34.6)	65 (32.8)	57 (36.8)
Heart Failure	62 (17.6)	35 (17.7)	27 (17.4)
Diabetes	167 (47.3)	86 (43.4)	81 (52.3)
CKD	109 (30.9)	54 (27.3)	55 (35.5)
Baseline creatinine level[a] (mmol/L), median (IQR)	80 (46.7)	75.0 (43.8)	85.0 (49.0)
Cardiovascular therapies before admission, no. (%)			
ACE inhibitor/ARB	245 (69.4)	121 (61.1)	124 (80.0)
β-blocker	171 (52.1)	98 (54.1)	73 (49.7)
Calcium channel blocker	148 (46.1)	78 (45.4)	70 (47.0)
Number of cardiovascular therapies before admission, no. (%)			
1	178 (50.4)	114 (57.6)	64 (41.3)
2	139 (39.4)	69 (34.9)	70 (45.2)
3	36 (10.2)	15 (7.6)	21 (13.6)
Cardiovascular therapies discontinued, median (IQR)	0 (0.7)	n/a	1.0 (0.5)
Type of admission, no. (%)			
Elective surgery	95 (27.0)	59 (30.0)	236 (23.4)
Emergency surgery	84 (23.9)	41 (20.8)	43 (27.9)
Medical	172 (48.9)	97 (49.2)	75 (48.7)
Medical or pharmacist consultant on surgical ward, no. (%)			
Presence	126 (71.6)	75 (76.5)	51 (67.1)
Absence	48 (27.3)	23 (23.5)	25 (38.9)
SOFA, median (IQR)	4 (3.30)	4 (3.10)	5 (3.70)
Vasopressors, no. (%)	127 (36.0)	57 (28.8)	69 (44.5)
Mechanical ventilation, no. (%)	141 (39.0)	71 (35.9)	70 (45.2)
Acute kidney injury, no.(%)	129 (36.5)	55 (29.0)	74 (48.1)
Renal replacement therapy[b], no.(%)	13 (3.70)	1 (0.5)	12 (7.70)

Note. ACE = angiotensin converting enzyme; ARB = angiotensin receptor blockers; HTN = hypertension; CAD = coronary artery disease; CKD = chronic kidney disease; ICU = intensive care unit; IQR = interquartile range; SOFA = Sepsis-related Organ Failure Assessment.
[a]Baseline creatinine level: end-stage renal disease excluded.
[b]Renal replacement therapy: patients on chronic hemodialysis excluded.

Table 2. Medication Reinitiation During Hospitalization.

Cardiovascular therapies	Preadmission medication	Medication at ICU discharge	Medication at hospital discharge
ACEi & ARB, no. (%)	245 (100)	100 (40.8)	126 (51.4)
BB, no. (%)	171 (100)	108 (63.2)	138 (80.7)
CCB, no. (%)	148 (100)	82 (55.4)	98 (66.2)

Note. ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; BB = β-blockers; CCB = calcium channel blockers; ICU = intensive care unit.

Table 3. RAS Blockers Patients' Characteristics.

Characteristic	ACEi & ARB reinitiation (n = 137)	ACEi & ARB not reinitiated (n = 108)
Age, median (IQR)	71 (12.2)	71 (11.3)
Female sex, no. (%)	63 (46.0)	32 (29.6)
Length of stay, days (IQR)		
Hospital	9 (17.8)	18 (20.9)
ICU	2 (7.00)	2 (4.80)
Preexisting comorbidities, no. (%)		
HTN	127 (92.7)	98 (90.7)
CAD	40 (29.2)	41 (37.8)
Heart failure	28 (20.4)	18 (16.7)
Diabetes	64 (46.7)	57 (52.8)
CKD	34 (24.8)	39 (36.1)
Baseline creatinine level[a] (mmol/L). median (IQR)	74 (38.5)	85 (48.3)
SOFA, median (IQR)	4 (3.10)	5 (3.20)
Vasopressors, no. (%)	35 (25.5)	47 (43.5)
Mechanical ventilation, no. (%)	46 (33.6)	44 (40.7)
Acute kidney injury[a], no. (%)	26 (19.0)	56 (51.9)
Stage of acute kidney injury in ICU, median (IQR)	1 (0.500)	1 (1.00)
Renal replacement therapy[b], no. (%)	0 (0)	9 (8.30)
Discharge creatinine level (mmol/L)[a], median (IQR)	68 (36.9)	97 (87.6)

Note. ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blockers; HTN = hypertension; CAD = coronary artery disease; CKD = chronic kidney disease; ICU = intensive care unit; IQR = interquartile range.
[a]Baseline creatinine level: end-stage renal disease excluded.
[b]Renal replacement therapy: patients on chronic hemodialysis excluded.

Table 4. Factors Associated With Cardiovascular Medication Discontinuation.

Variable	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	*P* value
Age	1.011 (0.994-1.029)	1.005 (0.985-1.025)	.649
Sex			
Female	Reference	Reference	Reference
Male	1.86 (1.20-2.88)	0.564 (0.346-0.919)	.021
Number of cardiovascular medications before admission			
1	Reference	Reference	Reference
2	1.81 (1.15-2.84)	1.669 (1.003-2.78)	.0490
3	2.49 (1.20-5.17)	3.17 (1.33-7.58)	.0100
Type of ward transfer			
Surgical	Reference	Reference	
Medical	1.013 (0.665-1.54)	0.898 (0.552-1.46)	.664
Vasopressors	1.94 (1.25-3.008)	1.77 (1.05-3.00)	.034
Mechanical ventilation	1.47 (0.959-2.26)	1.195 (0.726-1.96)	.484
Acute kidney injury	2.38 (1.53-3.69)	1.525 (0.909-2.56)	.095
Serum creatinine level at discharge (mmol/L)	1.005 (1.001-1.008)	1.002 (0.998-1.006)	.373

Note. CI = confidence interval.

An important subset of the population for which cardiovascular medication discontinuation could be hazardous are patients with heart failure and/or chronic kidney disease (CKD). In both populations, the use of RAS blockers has been shown to be cardioprotective and nephroprotective on disease progression and even mortality.[23-25] Our adjusted model found a significant association between AKI during ICU stay and RAS blocker discontinuation. Interestingly, these factors did not significantly affect other cardiovascular medication discontinuation, such as CCB and BB. This highlights the fact that despite being important in disease modification processes, RAS blockers might require special

Table 5. Factors Associated With RAS Blockers Discontinuation.

Variable	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	*P* value
Age	1.013 (0.991-1.036)	1.002 (0.976-1.03)	.884
Sex			
Female	Reference	Reference	Reference
Male	2.002 (1.19-3.44)	1.73 (0.940-3.18)	.212
Preexisting comorbidities			
HTN	0.772 (0.309-1.927)	0.741 (0.262-2.092)	.570
CAD	1.484 (0.869-2.535)	1.442 (0.785-2.643)	.240
Heart failure	0.982 (0.565-1.71)	0.387 (0.176-0.853)	.020
Diabetes	1.275 (0.769-2.11)	1.004 (0.566-1.78)	.990
CKD	1.712 (0.986-2.97)	1.426 (0.764-2.66)	.260
Vasopressors	2.25 (1.31-3.86)	1.778 (0.912-3.47)	.124
Mechanical ventilation	1.36 (0.807-2.29)	0.992 (0.528-1.86)	.588
Serum creatinine level at discharge (mmol/L)	1.005 (1.001-1.008)	1.007 (1.001-1.01)	.024
Acute kidney injury	4.60 (2.60-8.13)	3.82 (1.99-7.32)	<.001
No AKI	Reference	Reference	Reference
AKI stage 1	2.885 (1.507-5.52)	2.631 (1.253-5.524)	.011
AKI stage 2	2.423 (0.706-8.31)	2.153 (0.588-7.885)	.247
AKI stage 3	40.385 (5.274-309.243)	29.915 (3.815-234.582)	.001

Note. HTN = hypertension; CAD = coronary arterial disease; CKD = chronic kidney disease.

monitoring compared with other cardiovascular medications, with respect to their risk of AKI in acute settings.[26] In addition, we found that patients with heart failure had a decreased risk of RAS blockers discontinuation. These findings align with our recent Delphi study[27] where clinicians determined that AKI and its severity, and RAS blocker indication were important factors influencing their decision on RAS blocker reinitiation. The clinicians indicated that RAS blockers should be reinitiated early and at a lower glomerular filtration rate for heart failure patients compared with other patients. This decision might be explained by RAS blockers' known benefits for patients with heart failure, namely, a decrease in mortality.[25] Yet, in practice, clinicians will tend to reinitiate BBs and CCBs before RAS blockers as indicated by the Delphi panel due to their risk of worsening kidney function.[27] Specifically concerning ICU hospitalization, the use of RAS blockers following AKI was associated with a decrease in progression toward CKD and a decrease in mortality.[20,24,28] The ASSESS-AKI trial determined the prognostic importance of post-AKI proteinuria in the risk of progression toward CKD and the authors emphasize assessing proteinuria during posthospitalization follow-up.[29] They mention the incomplete perception of accurate kidney function post-AKI using sCr alone. They advance proteinuria as an adjunct tool to sCr values to guide clinicians and pharmacists in risk factor modification as well as medication optimization. Our study develops on this potential opportunity in identifying patients for whom prehospitalization cardiovascular medications are not reinitiated at discharge, potentially depriving them of benefits on morbidity and mortality. Our study is the first Canadian study to examine cardiovascular medication discontinuation in the ICU population. It is among the few studies addressing cardiovascular medication throughout the full hospitalization stay, from ICU admission to hospital discharge, and examining intrahospital causes of discontinuation. It encompassed data on 2 university hospitals from the 2 most populated Canadian provinces.

Limitations

Despite our efforts, this study has some limitations. First, we do not know whether medications were reinitiated after hospital discharge, which might decrease the number of discontinued medications and therefore might drift our ORs toward the null variable. However, in-hospital reinitiation is preferred to allow proper monitoring of sCr levels and serum potassium levels. Moreover, we did not differentiate between intentional and nonintentional discontinuation, which can be impacted by the covariables we used, such as renal function, and the appropriateness of discontinuation or replacement of these medications. Yet, all our patients had chronic cardiovascular medication indication and none were dialysis-dependent upon discharge. In addition, mineralocorticoid receptor antagonists were not evaluated in our study, but are medications currently used in heart failure populations. We did not look at other medications, such as benzodiazepines, which might affect the management of cardiovascular medications. Finally, we could only assess medication prescribing but not patient compliance.

Conclusion

Our study uncovered that cardiovascular medication discontinuation for ICU patients is frequent, especially for RAS blockers. Although acute hospitalization remains an important time point for medication reconciliation and reevaluation, it could be deleterious to specific patient populations to remain without cardiovascular therapies like RAS blockers. Data from our study could be used to reinforce site-specific protocols of medication reconciliation and optimization, as well as inform future protocols aimed at RAS blocker reinitiation follow-up. In addition, our data could serve to design a quality improvement study on medication resumption out of ICU.

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References

1. United Nations. World population ageing 2015. http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf. Published 2019. Accessed August 19, 2024.
2. Salive ME. Multimorbidity in older adults. *Epidemiol Rev*. 2013;35:75-83. doi:10.1093/epirev/mxs009.
3. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf*. 2014;13(1):57-65. doi:10.1517/14740338.2013.827660.
4. Vogel L. Two-thirds of seniors in long-term care take 10 or more drugs: CIHI. *CMAJ*. 2014;186(9):E309. doi:10.1503/cmaj.109-4797.
5. Bonaudo M, Martorana M, Dimonte V, et al. Medication discrepancies across multiple care transitions: a retrospective longitudinal cohort study in Italy. *PLoS ONE*. 2018;13(1):e0191028. doi:10.1371/journal.pone.0191028.
6. Stitt DM, Elliott DP, Thompson SN. Medication discrepancies identified at time of hospital discharge in a geriatric population. *Am J Geriatr Pharmacother*. 2011;9(4):234-240. doi:10.1016/j.amjopharm.2011.06.002.
7. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies at the time of hospital admission. *Arch Intern Med*. 2005;165(4):424-429. doi:10.1001/archinte.165.4.424.
8. Bell CM, Brener SS, Gunraj N, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA*. 2011;306(8):840-847. doi:10.1001/jama.2011.1206.
9. Tully AP, Hammond DA, Li C, Jarrell AS, Kruer RM. Evaluation of medication errors at the transition of care from an ICU to non-ICU location. *Crit Care Med*. 2019;47(4):543-549. doi:10.1097/ccm.0000000000003633.
10. Blanco M, Nombela F, Castellanos M, et al. Statin treatment withdrawal in ischemic stroke: a controlled randomized study. *Neurology*. 2007;69(9):904-910. doi:10.1212/01.wnl.0000269789.09277.47.
11. Sung JJ, Lau JY, Ching JY, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. *Ann Intern Med*. 2010;152(1):1-9. doi:10.7326/0003-4819-152-1-201001050-00179.
12. Howland RH. Potential adverse effects of discontinuing psychotropic drugs: part 2: antidepressant drugs. *J Psychosoc Nurs Ment Health Serv*. 2010;48(7):9-12. doi:10.3928/02793695-20100527-98.
13. Gilstrap LG, Fonarow GC, Desai AS, et al. Initiation, continuation, or withdrawal of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and outcomes in patients hospitalized with heart failure with reduced ejection fraction. *J Am Heart Assoc*. 2017;6(2):e004675. doi:10.1161/jaha.116.004675.
14. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. *Cochrane Database Syst Rev*. 2023;1(1):CD008986. doi:10.1002/14651858.CD008986.pub3.
15. Canadian Institute for Health Information. Care in Canadian ICUs. https://secure.cihi.ca/free_products/ICU_Report_EN.pdf. Published 2016. Accessed August 19, 2024.
16. World Health Organization. The anatomical therapeutic chemical classification system with defined daily doses (ATC/DDD) 2015. https://www.who.int/teams/health-product-and-policy-standards/inn/atc-ddd#:~:text=The%20ATC%2FDDD%20system%20is,improve%20quality%20of%20drug%20use. Published 2019. Accessed August 19, 2024.
17. Group KDIGOKAKIW. KDIGO Clinical practice guideline for acute kidney injury. https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf (Report No., Contract No. 1). March, 2012.
18. Xiong J, Tang X, Hu Z, Nie L, Wang Y, Zhao J. The RIFLE versus AKIN classification for incidence and mortality of acute kidney injury in critical ill patients: a meta-analysis. *Sci Rep*. 2015;5:17917. doi:10.1038/srep17917.
19. Bell CM, Rahimi-Darabad P, Orner AI. Discontinuity of chronic medications in patients discharged from the intensive care unit. *J Gen Intern Med*. 2006;21(9):937-941. doi:10.1111/j.1525-1497.2006.00499.x.
20. Brar S, Ye F, James MT, Hemmelgarn B, Klarenbach S, Pannu N. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with outcomes after acute kidney injury. *JAMA Intern Med*. 2018;178(12):1681-1690. doi:10.1001/jamainternmed.2018.4749.
21. Hias J, Van der Linden L, Spriet I, et al. Predictors for unintentional medication reconciliation discrepancies in preadmission medication: a systematic review. *Eur J Clin Pharmacol*. 2017;73(11):1355-1377. doi:10.1007/s00228-017-2308-1.
22. Pronovost P, Weast B, Schwarz M, et al. Medication reconciliation: a practical tool to reduce the risk of medication errors. *J Crit Care*. 2003;18(4):201-205. doi:10.1016/j.jcrc.2003.10.001.

23. Balamuthusamy S, Srinivasan L, Verma M, et al. Renin angiotensin system blockade and cardiovascular outcomes in patients with chronic kidney disease and proteinuria: a meta-analysis. *Am Heart J*. 2008;155(5):791-805. doi:10.1016/j.ahj.2008.01.031.
24. Gayat E, Hollinger A, Cariou A, et al. Impact of angiotensin-converting enzyme inhibitors or receptor blockers on post-ICU discharge outcome in patients with acute kidney injury. *Intensive Care Med*. 2018;44(5):598-605. doi:10.1007/s00134-018-5160-6.
25. Zhang Y, He D, Zhang W, et al. ACE inhibitor benefit to kidney and cardiovascular outcomes for patients with non-dialysis chronic kidney disease stages 3-5: a network meta-analysis of randomised clinical trials. *Drugs*. 2020;80(8):797-811. doi:10.1007/s40265-020-01290-3.
26. Joannidis M, Druml W, Forni LG, et al. Prevention of acute kidney injury and protection of renal function in the intensive care unit: update 2017: expert opinion of the Working Group on Prevention, AKI section, European Society of Intensive Care Medicine. *Intensive Care Med*. 2017;43(6):730-749. doi:10.1007/s00134-017-4832-y.
27. Dahel H, Lafrance J-P, Patenaude M, et al. Determining factors influencing RAS inhibitors re-initiation in ICU: a modified Delphi method. *Can J Kidney Health Dis*. 2022;9:1-10. doi:10.1177/20543581221112266.
28. Chou YH, Huang TM, Pan SY, et al. Renin-angiotensin system inhibitor is associated with lower risk of ensuing chronic kidney disease after functional recovery from acute kidney injury. *Sci Rep*. 2017;7:46518. doi:10.1038/srep46518.
29. Hsu CY, Chinchilli VM, Coca S, et al. Post-acute kidney injury proteinuria and subsequent kidney disease progression: the Assessment, Serial Evaluation, And Subsequent Sequelae In Acute Kidney Injury (ASSESS-AKI) study. *JAMA Intern Med*. 2020;180(3):402-410. doi:10.1001/jamainternmed.2019.6390.