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Research Article

Peri-Procedural Clinical Characteristics and Short-Term Renal Outcomes of Metformin-Treated Patients with Type 2 Diabetes Mellitus Undergoing Coronary Angiography

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Abstract
Background: Patients with type 2 diabetes mellitus (T2DM) frequently undergo coronary angiography because of their increased cardiovascular risk. Periprocedural management of metformin remains important because of concerns about renal safety, contrast-associated acute kidney injury (CA-AKI), and lactic acidosis. ***Objective***: To describe the peri-procedural clinical characteristics and short-term renal outcomes of metformin-treated patients with T2DM undergoing coronary angiography and to examine the relationship between short-term serum creatinine change and selected clinical and procedural factors. ***Methods***: This prospective observational study was conducted at Azadi Cardiac Centre, Kirkuk, Iraq, from May 2022 to May 2024. One hundred adults with T2DM receiving metformin and undergoing coronary angiography were enrolled. Baseline demographic, clinical, and laboratory data were recorded before the procedure. Patients continued metformin throughout the peri-procedural period, low-osmolality contrast medium was used, and serum creatinine was remeasured 72 hours later. ***Results***: Hyperlipidemia (64%) and hypertension (55%) were the most common comorbidities. Mean serum creatinine increased slightly from 0.73±0.13mg/dL to 0.75±0.19mg/dL at 72 hours, but this change was not statistically significant (p=0.103). Only one patient developed post-procedural kidney injury and recovered with hydration and monitoring. No clinically evident lactic acidosis was observed. Creatinine change was not significantly associated with metformin dose, contrast volume, or left ventricular systolic function. ***Conclusions***: Short-term renal function remained generally stable in metformin-treated patients with T2DM undergoing coronary angiography. These findings support a cautious, individualized approach to peri-procedural metformin management in lower-risk patients.

Keywords: Acute kidney injury; Coronary angiography; Contrast media; Lactic acidosis; Metformin; T2DM.

الخصائص السريرية المحيطة بالإجراءات والنتائج الكلوية قصيرة الأمد للمرضى الذين عولجوا بالميتفورمين المصابين بداء السكري من النوع الثاني والذين يخضعون لتصوير الأوعية التاجية

الخلاصة
الخلفية: يخضع مرضى داء السكري من النوع الثاني بشكل متكرر لتصوير الأوعية التاجية بسبب زيادة خطر الإصابة بالقلب والأوعية الدموية. تظل متابعة استخدام الميتفورمين مهمة بسبب المخاوف المتعلقة بسلامة الكلى، وإصابات الكلى الحادة المرتبطة بالتباين (CA-AKI)، وحماض اللاكتيك. **الهدف**: وصف الخصائص السريرية حول الإجراء والنتائج الكلوية قصيرة المدى للمرضى الذين عولجوا بالميتفورمين المصابين بالسكري من النوع الثاني الذين يخضعون لتصوير الأوعية التاجية، وفحص العلاقة بين التغير قصير الأمد في الكرياتينين في المصل والعوامل السريرية والإجرائية المختارة. **الطرائق**: أجريت دراسة رصدية مستقبلية في مركز آزادي للقلب، كركوك، العراق، من مايو 2022 إلى مايو 2024. تم تسجيل مئة بالغ مصاب بالسكري من النوع الثاني يتلقون الميتفورمين وخضعوا لتصوير الأوعية التاجية. تم تسجيل بيانات ديموغرافية وسريرية ومخبرية أساسية قبل الإجراء. استمر المرضى في تناول الميتفورمين طوال فترة ما قبل الإجراء، وتم استخدام وسط تباين منخفض الأسمولية، وأعيد قياس كرياتينين المصل بعد 72 ساعة. **النتائج**: كان فرط الدهون (64٪) وارتفاع ضغط الدم (55٪) هما أكثر الأمراض المصاحبة شيوعا. ارتفع متوسط الكرياتينين في المصل قليلا من 0.73±0.13 إلى 0.75±0.19 ملغ/ديسيلتر بعد 72 ساعة؛ هذا التغير لم يكن ذا دلالة إحصائية. أصيب مريض واحد فقط بإصابة كلوية بعد الإجراء، وتعافى بالترطيب والمراقبة. لم يلاحظ وجود حماض لاكتيك واضح سريريا. لم يكن تغير الكرياتينين مرتبطا بشكل ملحوظ بجرعة الميتفورمين، حجم التباين، أو وظيفة الانقباض في البطين الأيسر. **الاستنتاجات**: ظلت وظيفة الكلى قصيرة المدى مستقرة بشكل عام لدى مرضى السكري من النوع الثاني الذين عولجوا بالميتفورمين الذين يخضعون لتصوير الأوعية التاجية. تدعم هذه النتائج نهجا حذرا وفرديا لمراقبة الميتفورمين في الفترة المحيطة بالإجراءات لدى المرضى الأقل خطورة.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major and growing global health problem and remains strongly associated with cardiovascular morbidity and mortality. Cardiovascular disease is a leading cause of adverse outcomes in patients with T2DM, and this high-risk profile frequently necessitates diagnostic evaluation for coronary artery disease, including coronary angiographic assessment in selected patients [1,2]. Coronary imaging and angiographic evaluation play an important role in the diagnosis and management of coronary artery disease in patients with diabetes and suspected ischemic heart disease [3,4]. Metformin remains the most widely used

first-line glucose-lowering therapy for T2DM because of its proven efficacy, favorable safety profile, low cost, and broad cardiometabolic utility [5]. Contemporary diabetes and kidney guidelines continue to support metformin use in appropriately selected patients, including many with chronic kidney disease, provided that renal function is monitored and treatment is individualized according to kidney function and overall clinical status [6,7]. The peri-procedural management of metformin becomes particularly important when iodinated contrast media are administered during coronary angiography. Historically, metformin was often withheld before or after contrast exposure because of concern that contrast-associated acute kidney injury might impair metformin clearance and increase the risk of lactic acidosis, especially in patients with renal dysfunction or other predisposing conditions [8,9]. However, more recent evidence has challenged the routine discontinuation strategy. Systematic reviews and meta-analyses have shown no convincing evidence that continuation of metformin in appropriately selected patients exposed to contrast media increases the risk of CA-AKI, clinically significant renal deterioration, or lactic acidosis [10,11]. In addition, the NO-STOP study found that continuation of metformin during invasive coronary angiography was not associated with a significant worsening of renal function or an important lactate-related safety signal in the studied population [12]. Appraisals of contemporary recommendations have also shown that current guidance increasingly favors a selective, risk-based approach based on renal function, the presence or absence of acute kidney injury, and the clinical setting, although some variability in recommendations still exists across guidelines [10,13]. Despite these advances, much of the published literature has focused mainly on the question of whether metformin should be continued or temporarily interrupted around contrast exposure [11,12,14]. Less attention has been given to the real-world peri-procedural clinical profile of metformin-treated patients with T2DM undergoing coronary angiography, particularly in regional practice settings where comorbidity burden, medication patterns, and procedural characteristics may differ from those reported in larger trials or pooled analyses. Therefore, the present study aimed to describe the peri-procedural characteristics and short-term renal outcomes of metformin-treated patients with T2DM undergoing coronary angiography, with particular emphasis on short-term serum creatinine change and its association with selected clinical and procedural factors.

METHODS

Study design and setting

This prospective, single-center observational study was conducted at Azadi Cardiac Centre, Kirkuk, Iraq, from May 2022 to May 2024. The study population consisted of adult patients with previously diagnosed type 2 diabetes mellitus who received metformin therapy and underwent coronary angiography during the study period.

Study population

A total of 100 patients were enrolled in the study. Eligible patients were consecutively enrolled during the study period if they were adults with previously diagnosed T2DM, were receiving metformin therapy before admission, and were scheduled for coronary angiography. Patients were excluded if baseline creatinine clearance was ≤30 mL/min, if they had acute kidney injury before the procedure, severe hemodynamic instability, cardiogenic shock, severe heart failure, or clinical conditions associated with major tissue hypoxia. No formal a priori sample size calculation was performed. The sample size was determined pragmatically based on the number of eligible metformin-treated patients with T2DM who underwent coronary angiography during the study period and met the study inclusion criteria.

Data collection

Baseline demographic, clinical, and laboratory data were recorded before coronary angiography. These included age, comorbidities, medication history, blood pressure, heart rate, oxygen saturation, metformin dose, contrast volume, left ventricular systolic function, and renal function assessment. Patients continued their usual metformin dose throughout the peri-procedural period. Coronary angiography was performed in the catheterization laboratory using a low-osmolality contrast medium. Serum creatinine was remeasured 72 hours after the procedure. Patients were also clinically monitored after the procedure for evidence of renal deterioration and for symptoms or signs suggestive of lactic acidosis. Because routine serum lactate measurement was not performed, lactic acidosis was assessed on a clinical basis only.

Variables and outcome measurement

The primary outcome was the short-term change in serum creatinine between baseline and 72 hours after coronary angiography. Post-procedural kidney injury was defined as an increase in serum creatinine of ≥0.3 mg/dL or ≥50% from baseline within 48-72 hours after contrast exposure. Secondary descriptive outcomes included the occurrence of post-procedural kidney injury and clinically evident lactic acidosis. Exploratory analyses were performed to determine whether the change in serum creatinine varied according to metformin dose (≤1 g/day, 1.1-1.9 g/day, and 2.0-2.5 g/day), contrast volume (30-100 mL *vs*. 100-250 mL), and left ventricular systolic function (good vs. impaired/fair).

Ethical approval

The study was approved by the Research Ethics Committee, College of Medicine, University of Kirkuk, Kirkuk, Iraq (approval No. 19B). Written informed consent for participation and publication was obtained from all patients before enrollment.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 25. Categorical variables were presented as numbers and percentages. Continuous variables were summarized as mean ± standard deviation and median when appropriate. Normality of continuous variables was assessed using the Shapiro-Wilk test. Because serum creatinine values and creatinine change were not normally distributed, nonparametric tests were used for inferential analyses. The Wilcoxon signed-rank test was used for paired comparison of baseline and 72-hour serum creatinine values. The Kruskal-Wallis test was used to compare creatinine change across metformin dose categories, while the Mann-Whitney U test was used for two-group comparisons according to contrast volume and left ventricular systolic function. A *p*-value of < 0.05 was considered statistically significant.

RESULTS

In Table 1, 100 metformin-treated patients with T2DM undergoing coronary angiography were included in the study. The age distribution showed that the largest subgroup was ≤50 years (29%), followed by >70 years (27%), 61-70 years (23%), and 51-60 years (21%). Hyperlipidemia (64%) and hypertension (55%) were the most common comorbidities.

Table 1: Baseline demographic, clinical, and medication characteristics of the study population (n=100)

Variable	n(%)
Age group (year)	
≤50	29(29)
51-60	21(21)
61-70	23(23)
>70	27(27)
Comorbidities	
Hypertension	55(55)
Hyperlipidemia	64(64)
Ischemic heart disease	34(34)
Impaired/fair LV systolic function	28(28)
Concomitant medications	
ACE inhibitors/ARBs	59(59)
Beta-blockers	44(44)
Statins	87(87)
SGLT2 inhibitors	65(65)
Anticoagulants	2(2.0)
Sulfonylureas	20(20)
Diuretics	55(55)
Proton pump inhibitors	49(49)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LV, left ventricular; SGLT2, sodium-glucose cotransporter-2.

Ischemic heart disease was documented in 34% of patients, while impaired/fair left ventricular systolic function was present in 28%. Regarding concomitant medications, statins were the most frequently used drugs (87%), followed by SGLT2 inhibitors (65%), ACE inhibitors/ARBs (59%), diuretics (55%), proton pump inhibitors (49%), beta-blockers (44%), sulfonylureas (20%), and anticoagulants (2%) (Table 1). Figure 1 illustrates the distribution of individual serum creatinine values before coronary angiography and at 72 hours after the procedure. The mean serum creatinine increased slightly from 0.73 ± 0.13 mg/dL at baseline to 0.75 ± 0.19 mg/dL at 72 hours, while the median value increased from 0.73 mg/dL to 0.74 mg/dL.

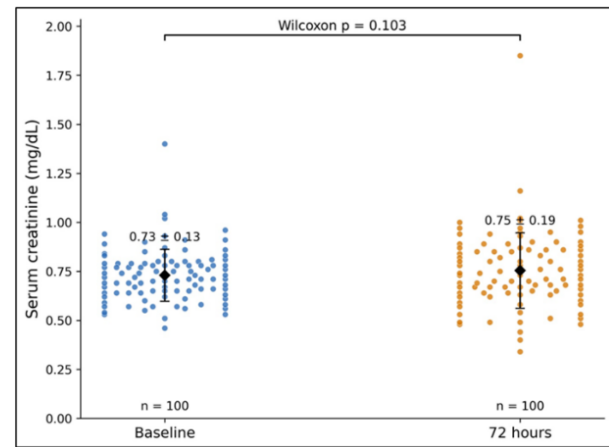

Figure 1: Serum creatinine before and 72 hours after coronary angiography.

This small increase was not statistically significant using the Wilcoxon signed-rank test (*p*= 0.103). Only one patient (1.0%) developed post-procedural kidney injury during follow-up. This patient was an elderly woman with a baseline serum creatinine of 1.4 mg/dL, and her renal function returned to baseline within 7 days after hydration and close monitoring. No clinically evident lactic acidosis was documented during follow-up. Exploratory analyses of serum creatinine change according to metformin dose, contrast volume, and LV systolic function are summarized in Table 2.

Table 2: Exploratory analysis of serum creatinine changes according to metformin dose, contrast volume, and left ventricular systolic function

Variable	n	Mean change (mg/dL)	Median change (mg/dL)	*p*-value
Metformin dose				
≤1 g/day	40	0.019±0.121	-0.005	
1.1-1.9 g/day	31	0.038±0.118	0.040	0.696*
2.0-2.5 g/day	29	0.018±0.154	0.000	
Contrast volume				
30-100 mL	55	0.043±0.131	0.040	0.109†
100-250 mL	45	0.001±0.125	-0.010	
LV systolic function				
Impaired/fair	28	0.024±0.122	0.035	0.842†
Good	72	0.024±0.133	-0.005	

Values are presented as median and mean±SD. * Kruskal-Wallis test. † Mann-Whitney U test.

There was no statistically significant difference in creatinine change among metformin dose categories (p= 0.696). Similarly, creatinine change did not differ significantly between patients who received 30-100 mL and those who received 100-250 mL of contrast medium (p= 0.109). No significant association was observed between creatinine change and LV systolic function (p= 0.842).

DISCUSSION

The peri-procedural management of metformin in patients with type 2 diabetes mellitus (T2DM) undergoing coronary angiography remains clinically important because these patients have a high burden of coronary artery disease and frequently require invasive cardiac evaluation while also being vulnerable to renal impairment and adverse cardiovascular outcomes [15,16]. For many years, routine interruption of metformin around contrast exposure was driven mainly by concern that contrast-associated acute kidney injury might reduce metformin clearance and increase the risk of lactic acidosis [8, 9, 17]. However, more recent evidence and guideline appraisals support a more selective, risk-based approach rather than automatic discontinuation in all patients [10,13,14]. The present study was designed to describe the peri-procedural profile and short-term renal outcomes of metformin-treated patients with T2DM undergoing coronary angiography in a real-world regional cardiac center. The main finding was that short-term renal function remained generally stable. Serum creatinine increased only slightly at 72 hours, from 0.73 ± 0.13 mg/dL to 0.75 ± 0.19 mg/dL, and this change was not statistically significant (p= 0.103). In addition, only one patient developed post-procedural kidney injury, and no clinically evident lactic acidosis was observed. Taken together, these findings suggest that continuation of metformin in clinically selected lower-risk patients undergoing coronary angiography was not associated with an obvious short-term safety signal in this cohort. These results are broadly consistent with the available literature. The NO-STOP trial reported that continuation of metformin during invasive coronary angiography was not associated with clinically important deterioration in renal function or excess lactate-related adverse effects [12]. Likewise, a randomized comparison by Shavadia *et al.* found no clinically meaningful increase in lactic acidosis risk with continuation compared with temporary interruption after coronary angiography or angioplasty [18]. In addition, systematic reviews and meta-analyses have generally found no convincing evidence that metformin continuation in appropriately selected patients exposed to contrast media increases the risk of contrast-associated acute kidney injury, significant renal deterioration, or lactic acidosis [11,15,19]. At the same time, the favorable short-term outcomes observed in this study should be interpreted cautiously. The study population represented a clinically selected lower-risk group with preserved baseline renal function, use of low-osmolality contrast medium, and routine peri-procedural monitoring. These characteristics reduce the likelihood of major renal or metabolic complications. Therefore, the present findings should not be interpreted as proof that metformin continuation is universally safe in all patients undergoing coronary angiography. Rather, they support the safety of an individualized approach in lower-risk patients. This interpretation is consistent with contemporary reviews showing that older age, chronic kidney disease, diabetes, heart failure, hypertension, myocardial infarction, anemia, and hemodynamic instability remain important determinants of contrast-associated acute kidney injury risk [20,21]. Another finding of the present study was the absence of a statistically significant association between short-term creatinine change and metformin dose, contrast volume, or left ventricular systolic function. Creatinine change did not differ significantly across metformin dose categories (p= 0.696), between contrast-volume groups (p= 0.109), or according to LV systolic function (p= 0.842). Although these findings may suggest that none of these factors exerted a major short-term effect within this cohort, the result should be interpreted carefully. The sample size was modest, only one clinically clear renal event occurred, and subgroup analyses were exploratory. So, the study was underpowered to detect small or moderate subgroup effects. In addition, the contrast-volume range was moderate rather than extreme, and even the impaired/fair LV subgroup was relatively limited in size. Thus, the absence of statistical significance should not be interpreted as proof of no biological effect, but rather as an indication that no clear signal was detectable within this selected cohort. This is in line with recent work suggesting that multifactorial risk-prediction approaches are more informative than isolated single variables when evaluating peri-procedural renal risk after coronary angiography or percutaneous coronary intervention [22,23]. The baseline profile of the study population also deserves attention. Hypertension, hyperlipidemia, ischemic heart disease, LV dysfunction, and frequent use of statins, ACE inhibitors/ARBs, diuretics, and SGLT2 inhibitors indicate that these were clinically complex cardiometabolic patients rather than low-comorbidity cases. This is relevant because peri-procedural decision-making in the catheterization laboratory is influenced by overall cardiovascular risk, renal reserve, hemodynamic status, and the urgency of intervention, not by metformin exposure alone. In this context, the present study provides practical local data that place metformin management within broader Cath-lab care rather than treating it as an isolated pharmacologic issue. The high prevalence of background cardiometabolic therapy is also noteworthy. In particular, the frequent use of SGLT2 inhibitors reflects contemporary diabetes management. Although the present study was not designed to evaluate treatment interactions, recent evidence suggests that

SGLT2 inhibitors may have potential renoprotective effects in patients undergoing coronary angiography or percutaneous coronary intervention, although the topic remains an evolving area rather than an established standard of care [24]. Future studies should examine whether background use of modern glucose-lowering agents modifies peri-procedural renal risk in patients continuing metformin. The current findings also reinforce the broader principle that prevention of contrast-associated acute kidney injury depends more on appropriate risk stratification, hydration, and contrast management than on routine discontinuation of metformin alone. Recent reviews continue to support isotonic hydration as a cornerstone of prevention, with growing interest in simplified or tailored hydration strategies in selected higher-risk patients [25]. From a practical standpoint, metformin management should therefore be considered within an overall renal-protection strategy rather than as a separate binary decision.

Study Limitations

Several limitations should be acknowledged. First, the study was a single-center observational study without a comparator group in whom metformin was withheld; therefore, the study cannot establish causality or directly compare metformin continuation with temporary discontinuation strategies. Second, the sample size was modest, and the subgroup analyses should be considered exploratory. Third, lactic acidosis was assessed clinically rather than through routine biochemical confirmation using serum lactate, bicarbonate, blood pH, or blood gas analysis. Therefore, the absence of clinically evident lactic acidosis should not be interpreted as excluding mild or subclinical biochemical abnormalities. Fourth, no multivariable regression model was performed, so the analyses identify associations rather than independent predictors. Fifth, follow-up was limited to 72 hours after coronary angiography; therefore, delayed renal impairment occurring beyond this period may not have been captured. Finally, because the cohort consisted of clinically selected patients with preserved baseline renal function, the findings should not be generalized to patients with severe chronic kidney disease, acute kidney injury, cardiogenic shock, severe heart failure, or major tissue hypoxia.

Conclusion

In metformin-treated patients with T2DM undergoing coronary angiography, short-term renal outcomes were generally favorable. Serum creatinine showed only a slight, non-significant increase at 72 hours; clinically documented post-procedural kidney injury was uncommon; and no clinically evident lactic acidosis was observed. Short-term creatinine variation was not significantly associated with metformin dose, contrast volume, or left ventricular systolic function. These findings support a cautious, individualized approach to peri-procedural metformin management in clinically selected lower-risk patients with preserved baseline renal function. However, the results should not be generalized to patients with advanced chronic kidney disease, acute kidney injury, hemodynamic instability, severe heart failure, cardiogenic shock, or major tissue hypoxia, in whom metformin interruption and closer biochemical monitoring may remain appropriate.

Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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