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Possibilities of Azilsartan Medoxomil for Preparation for Planned Percutaneous Coronary Intervention in Patients With Type 2 Diabetes Mellitus

Aim	To evaluate the efficacy and safety of azilsartan medoxomil for preoperative preparation and improving the long-term prognosis of elective percutaneous coronary intervention (PCI) in patients with ischemic heart disease (IHD), arterial hypertension (AH), and type 2 diabetes mellitus (DM).
Material and methods	The study sample included patients with type 2 DM referred for elective PCI who had poor blood pressure (BP) control according to 24-hour BP monitoring (24-BPM) (mean daily systolic BP ≥130 mmHg, mean daily diastolic BP ≥80 mmHg). The data were collected from 2018 through 2020. A total of 75 patients was included and distributed by simple randomization into two groups: group 1 (main, n=37) received azilsartan medoxomil as an antihypertensive drug at a dose of 40 mg/day (previously prescribed angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ARB) were discontinued); group 2 (control, n=38) continued on their previous antihypertensive therapy. The follow-up period was 6 months. During each of 5 consecutive follow-up visits, the patient was examined, 24-BPM was recorded, and urinary markers of renal dysfunction (glomerular filtration rate, GFR; neutrophil gelatinase-associated lipocalin, NGAL; urine albumin-creatinine ratio, UACR; kidney injury molecule, KIM-1; and interleukin-18, IL-18) were measured.
Results	During the azilsartan treatment, GFR decreased by 7.4%, while in the control group, it decreased by 18.9% ($p<0.001$). For 6 months of follow-up, no changes in the NGAL concentration were found in the main group, while the NGAL concentration in the control group increased by 12.9%. With azilsartan, there was a decrease in the urinary concentration of IL-18 (16.9%), while in patients of the control group, IL-18 increased (7.14%). Proteinuria progressed in both groups, which was expectable given the presence of DM; however, in patients receiving azilsartan, the UACR value increased by 37.5%, while in patients of the control group, it increased by 96.15%. These differences were statistically significant. No statistically significant differences were found in the concentrations of cystatin C and KIM-1.
Conclusion	This study demonstrated two important facts: the possibility for diagnosing contrast-induced acute kidney injury (CI-AKI) using new, more sensitive markers of kidney damage, which is important for assessing the effectiveness of prevention, and the possibility of using ARBs, in particular azilsartan, for the prevention of CI-AKI in patients with IHD in combination with AH and DM.

Keywords	Percutaneous coronary intervention; type 2 diabetes mellitus; acute kidney injury; preoperative therapy; long-term prognosis
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Introduction

Numerous studies have demonstrated a robust correlation between arterial hypertension (AH) and chronic kidney disease (CKD) [1, 2]. The presence of atherosclerosis, coronary heart disease (CHD), and diabetes mellitus (DM) significantly increases the probability of detecting CKD [3, 4] or developing contrast-induced acute kidney injury (CI-AKI).

It has been shown that a reduction in renal function associated with the onset of CKD exasperates the progression of pre-existing manifestations of AH and CHD and significantly elevates the risk of developing further cardiovascular complications [5]. The pathogenic relationship between atherosclerosis, AH, DM, and CKD is manifested by the progression of endothelial dysfunction and increased stiffness of the vascular wall. The presence of CKD in patients with CHD, AH, and DM is a key factor in determining the choice and doses of drug therapy used for secondary prevention. It is important to consider that the presence of CKD impedes the utilization of certain diagnostic and therapeutic interventions. For instance, the utilization of contrast agents in X-ray, computed tomography,

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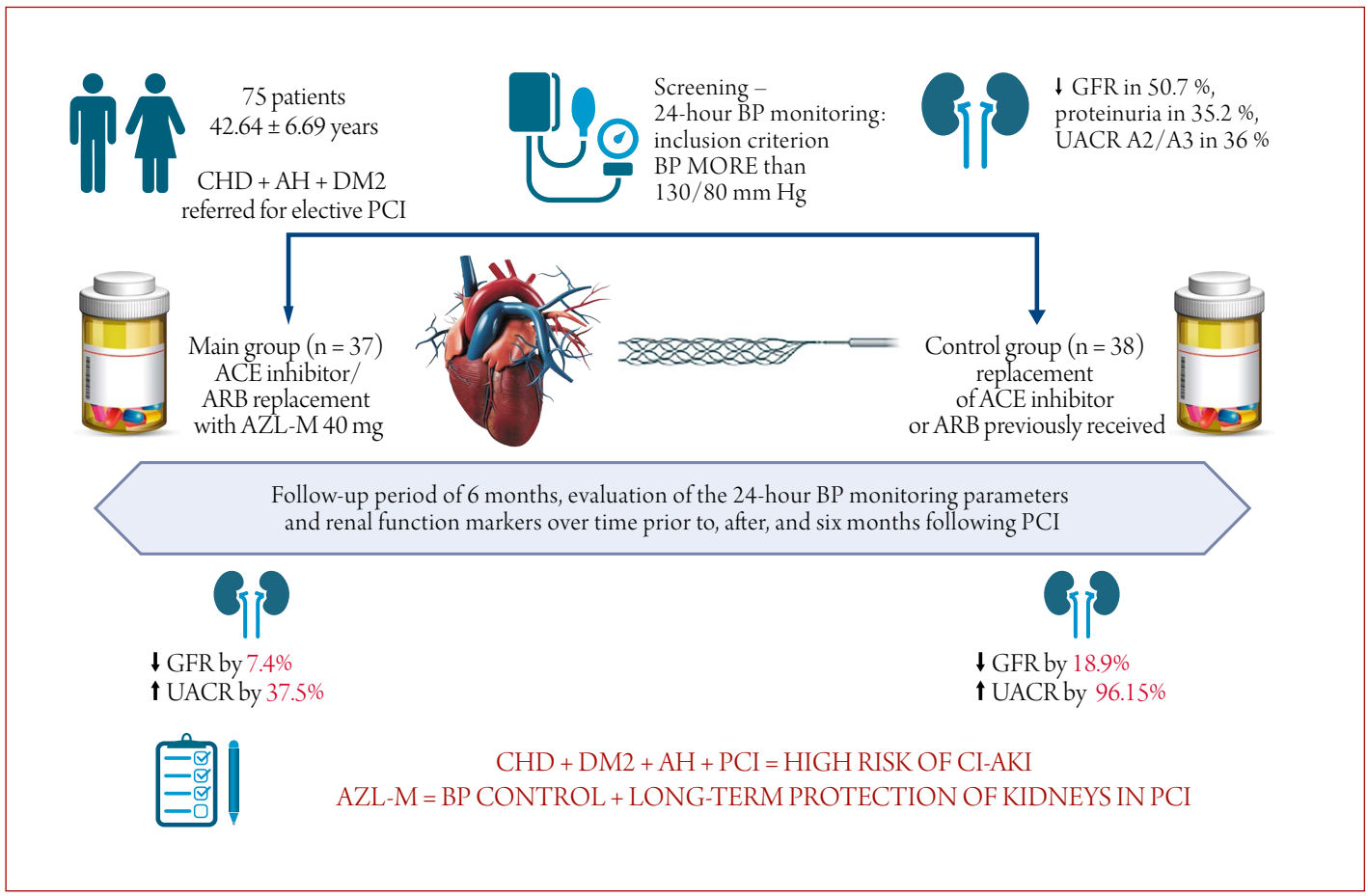
Central illustration. Possibilities of Azilsartan Medoxomil for Preparation for Planned Percutaneous Coronary Intervention in Patients With Type 2 Diabetes Mellitus



and magnetic resonance imaging is considerably constrained by their nephrotoxicity [6, 7]. The incidence of CI-AKI following angiography has been reported to range from 10% to 40% and increase with more sever baseline renal failure and left ventricular dysfunction [3].

The presence of CKD can be identified based on two markers: a reduction in the glomerular filtration rate (GFR), as determined by the CKD-EPI formula, and the presence of albuminuria of more than 30 mg, defined by the albumin-to-creatinine ratio in a morning urine sample over a period of at least three months. These indicators are also used to ascertain the stage of the disease and serve as prognostic markers [2]. It has been revealed that the identification of even a moderate reduction in GFR or relatively mild albuminuria/proteinuria, irrespective of each other and other risk factors for the emergence of cardiovascular complications, is associated with an elevated risk of cardiovascular diseases and their complications, as well as total mortality [8]. Nevertheless, a significant number of patients lack a documented diagnosis of CKD, despite the presence of diagnostic criteria.

The angiotensin II receptor blocker (ARB) azilsartan medoxomil has been demonstrated to be an efficacious agent for the reduction of blood pressure (BP) and has also been shown to possess a number of pleiotropic effects, including nephroprotection. The data substantiate the use of the drug as a tool to reduce the risk of CI-AKI during elective percutaneous coronary interventions (PCI), as it has been demonstrated to normalize BP variability and have a favorable impact on renal function.

Furthermore, the efficacy of the drug has been investigated in a subgroup of patients with DM. The 12 week study included patients with a prior diagnosis of type 2 DM and AH who had BP greater than 140/90 mm Hg despite the administration of antihypertensive therapy. At inclusion in the study, azilsartan 40 mg was substituted for a previously used angiotensin-converting enzyme (ACE) inhibitor or ARB. After 12 weeks of therapy, 25 (83.0%) patients achieved target BP < 140/85 mm Hg. In 11 (37%) patients, the dose of azilsartan medoxomil was increased to 80 mg after a six-week period. Following a 12-week period, a significant reduction in clinical peripheral and central BP was observed. The mean daytime peripheral BP decreased by 22/9 mm Hg, while the central BP exhibited a reduction of 18/13 mm Hg; the mean nighttime BP demonstrated a decrease of 24/9 mm Hg and 19/10 mm Hg, respectively. A statistically significant reduction in daytime and nighttime variability of systolic blood pressure (SBP) was observed, with a decrease from 15 ± 4 mm Hg to 10 ± 3 mm Hg

and from 11 ± 3 mm Hg to 8 ± 2 mm Hg, respectively. Similarly, there was a statistically significant decline in pulse wave velocity, from 10.2 ± 2.3 m/s to 9.5 ± 2.2 m/s, and in augmentation index, which decreased statistically significantly from 24.6 ± 8.6% to 13 ±7.0%. All differences shown were statistically significant ($p < 0.05$). The daily SBP index demonstrated improvement in 53.0% of cases undergoing azilsartan medoxomil therapy [9].

Objective

The objective of this study was to evaluate the efficacy and safety of azilsartan medoxomil as a tool for preoperative preparation and improvement of the long-term prognosis of elective percutaneous coronary intervention (PCI) in patients with coronary heart disease (CHD), acute heart failure (AH), and type 2 diabetes mellitus (DM).

Material and Methods

A total of 75 patients with type 2 DM who were referred for elective PCI were included in the study. Inclusion criteria: patients with a prior diagnosis of type 2 DM, indications for elective PCI, and inadequate BP control as evidenced by ambulatory BP monitoring (mean SBP ≥130 mm Hg, mean diastolic blood pressure (DBP) ≥ 80 mm Hg). Exclusion criteria: age over 75 years; decompensated chronic heart failure; a history of heart valve replacement or the presence of a heart valve defect requiring correction; acute coronary syndrome in the index hospitalization; exacerbation of comorbidities, information about intolerance to azilsartan medoxomil.

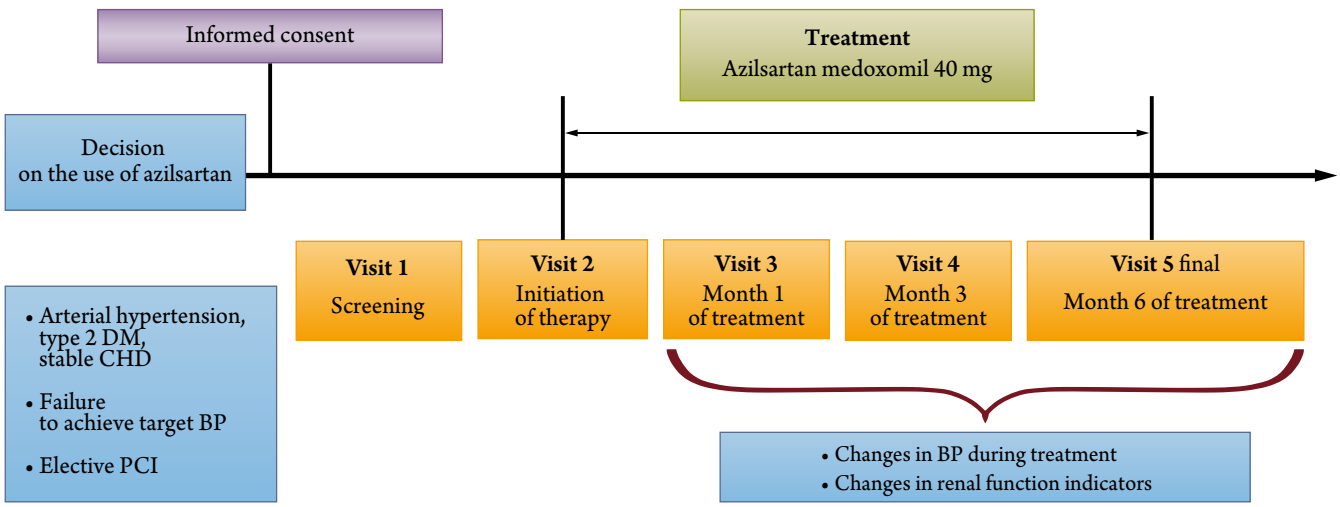
The material was collected between 2018 and 2020. The study protocol was approved by the Ethics Committee of the Research Institute of Cardiovascular Disease Complex Problems (Minutes no. 7, dated April 26, 2018). All patients provided written voluntary informed consent to participate in the study.

The sample was divided into two groups using a simple randomization method. Group 1 (the treatment group; n = 37) received azilsartan medoxomil at a dose of 40 mg/day as an antihypertensive agent (previously administered ACE inhibitors or ARBs were discontinued), while Group 2 (the control group; n = 38) continued to take hypotensive therapy prescribed earlier.

All 75 patients included in the study received statins, dual antiplatelet therapy, beta-blockers, ACE inhibitors, or ARBs after hospital discharge. At baseline, 26 of the 75 patients were taking ARBs. The ratio remained unaltered in the control group following patient randomization: 30% of the subjects received ARBs, while 70% were administered ACE inhibitors.

The follow-up period was 6 months. A total of five consecutive visits were conducted, each comprising a comprehensive patient examination, ambulatory BP monitoring, and the assessment of urine markers of renal dysfunction, including GFR, neutrophil gelatinase-associated lipocalin (NGAL), urine albumin-creatinine ratio (UACR), kidney injury molecule 1 (KIM-1), and interleukin 18 (IL-18) (Figure 1). Ambulatory BP monitoring was conducted using a BPLab device (Petr Telegin, Nizhny Novgorod, Russia). The ambulatory BP monitoring data were deemed valid if at least 20 daytime and 7 nighttime measurements were performed at each visit. The mean values of the 24-hour, daytime (07:00–23:00), and nighttime (23:00–07:00) BP were calculated. Patients were classified according to the

Figure 1. Study design



The concentration of IL-18 in urine was determined by enzyme-linked immunosorbent assay (ELISA) using reagents provided by eBioscience (Bender MedSystems, Austria). The KIM-1 was quantified by enzyme immunoassay using reagents manufactured by RnD Systems (USA). The concentration of lipocalin-2/NGAL was determined by enzyme immunoassay (reagents manufactured by BioVendor, Czech Republic).

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Table 1. Characteristics of patients (n = 75)

Parameter	Value
Mean age, years (M ± SD)	52.64 ± 6.96
Male, n (%)	45 (60.0)
BMI, kg/m2 (M ± SD)	32.65 ± 4.89
Smoking, n (%)	8 (10.66)
PICS, n (%)	44 (58.66)
History of PCI/CABG, n (%)	46 (61.33)
CVA/TIA, n (%)	5 (6.66)
Atrial fibrillation, n (%)	13 (17.33)
SYNTAX score, M ± SD	11.8 ± 9.62
Creatinine, μmol/L (M ± SD)	59.46 ± 24.8
GFR, mL/min/1.73 m2 (M ± SD)	82.81 ± 21.05
TC, mmol/L (M ± SD)	3.81 ± 1.78
LDL cholesterol, mmol/L (M ± SD)	2.8 ± 1.34
Glycated hemoglobin, % (M ± SD)	7.92 ± 1.66

BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CVA, cerebrovascular accident; TIA, transient ischemic attack; GFR, glomerular filtration rate; TC, total cholesterol; LDL, low-density lipoprotein.

2014 European practice guidelines for ambulatory blood pressure monitoring ambulatory BP monitoring as follows: those with a physiologic nocturnal decline (10.0–20.0%; dipper, D), a reduced nocturnal decline (0–10.0%; reduced dipper, RD), a severe nocturnal decline (> 20.0%; extreme dipper, ED), or no nocturnal decline (< 0; non-dipper, ND) from mean daytime BP.

Table 2. Characteristics of patients in the main and control groups one month prior to percutaneous coronary intervention

Parameter	Treatment group (n = 37)	Control group (n = 38)
Mean age, years (M ± SD)	53.14 ± 7.01	52.11 ± 6.96
Male, n (%)	22 (59.45)	23 (60.52)
BMI, kg/m2 (M ± SD)	31.85 ± 5.82	33.19 ± 4.57
Smoking, n (%)	4 (10.81)	4 (10.52)
PICS, n (%)	22 (59.45)	22 (57.89)
History of PCI/CABG, n (%)	24 (64.86)	22 (57.89)
CVA/TIA, n (%)	3 (8.1)	2 (5.26)
Atrial fibrillation, n (%)	7 (18.91)	6 (15.78)
SYNTAX score, M ± SD	10.4 ± 8.37	11.7 ± 7.19
Creatinine, μmol/L (M ± SD)	62.42 ± 25.1	59.46 ± 24.8
GFR, mL/min/1.73 m2 (M ± SD)	84.61 ± 19.35	82.81 ± 21.05
TC, mmol/L (M ± SD)	4.15 ± 1.68	3.98 ± 1.74
LDL cholesterol, mmol/L (M ± SD)	2.76 ± 1.03	2.68 ± 1.28
Glycated hemoglobin, % (M ± SD)	7.87 ± 1.49	7.91 ± 1.62

BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CVA, cerebrovascular accident; TIA, transient ischemic attack; GFR, glomerular filtration rate; TC, total cholesterol; LDL, low-density lipoprotein.

The concentration of urine albumin was determined by enzyme-linked immunosorbent assay. The urine creatinine levels were determined by the Jaffe method. The results were automatically calculated on a Konelab biochemical analyzer using a calibration curve. The UACR ratio was calculated using the online calculator at https://www.omnicalculator.com/health/acr. A diagnostic threshold of 30 mg/g (creatinine 3 mg/mol) is typically employed. The KDIGO criteria were employed for the evaluation of albuminuria in the classification of CKD. Table 1 presents an overview of the patient characteristics.

The patients included in this study exhibited a high incidence of CKD. The prevalence of high and very high proteinuria was 35.2% among all patients, and a baseline decrease in GFR was observed in 50.7%. The UACR A1 was less than 30 mg/day in 48 (64%) patients, the UACR A2 and UACR A3 were present in 2 (34.0%) and 2 (2.0%) patients, respectively. Therefore, patients with stable CHD accompanied by AH and DM initially exhibited a considerable risk of CI-AKI prior to PCI.

The statistical processing of the obtained data was conducted using the Statistica 8.0 (StatSoft, Inc., USA) and IBM SPSS Statistics 21.0 (SPSS Inc., USA) software programs. The data were subjected to standard methods of descriptive statistical analysis. The relative values are presented as percentages, while the quantitative values are presented as the arithmetic means and standard deviations (M ± SD) or the medians and interquartile ranges (Me [Q1; Q3]). In the case of normal distribution, a Student's t-test was employed for comparison. In instances where the data did not adhere to a normal distribution, two independent groups were evaluated using the Mann-Whitney U-test. For data sets comprising three or more independent groups, the Kruskal-Wallis rank analysis of variance was employed, followed by a pairwise comparison of groups using the Mann-Whitney test. Pearson's method was employed for the analysis of differences in frequencies. In two independent groups, Fisher's exact test with a two-sided confidence interval and Yates' chi-squared test were utilized. The observed differences were deemed to be statistically significant at $p < 0.05$.

Results

The baseline characteristics of the patient groups studied are presented in Table 2. No differences were observed between the patient groups with regard to their clinical, anamnestic, laboratory parameters, 24-hour BP monitoring data, or the therapies they received ($p > 0.05$ for all parameters).

Table 3. Changes in renal function markers observed in patients in the main and control groups prior to and following percutaneous coronary intervention

Parameter	Group	1 month prior to PCI	Prior to PCI	Following PCI
Creatinine, μmol/L	Treatment	62.42 ± 25.10	61.12 ± 19.81	64.57 ± 20.15
	Control	59.46 ± 24.82	62.42 ± 21.71	65.48 ± 18.74
	p	0.614	0.790	0.842
GFR, mL/min/1.73 m²	Treatment	84.61 ± 19.35	86.11 ± 20.05	83.91 ± 18.42
	Control	82.81 ± 21.05	79.54 ± 18.01	76.61 ± 17.35
	p	0.705	< 0.001	< 0.001
NGAL, mg/mL	Treatment	12.05 ± 2.05	11.17 ± 1.35	40.66 ± 6.18
	Control	14.01 ± 2.23	15.84 ± 2.04	60.92 ± 7.81
	p	0.272	< 0.001	< 0.001
IL-18, pg/mL	Treatment	123.56 ± 41.91	125.54 ± 15.11	124.71 ± 58.96
	Control	114.42 ± 49.29	113.46 ± 13.66	112.5 ± 41.61
	p	0.397	0.302	0.309
KIM-1, mg/mL	Treatment	2.73 ± 0.29	2.93 ± 0.69	2.68 ± 0.49
	Control	3.21 ± 0.88	3.10 ± 0.78	3.19 ± 1.65
	p	0.239	0.713	0.305
UACR, mg/g	Treatment	39.56 ± 2.38	35.20 ± 9.88	40.76 ± 6.41
	Control	40.92 ± 7.38	40.76 ± 6.41	52.12 ± 5.11
	p	0.772	< 0.001	< 0.001
Cystatin C, mg/L	Treatment	2.05 ± 0.61	1.91 ± 0.64	2.32 ± 0.22
	Control	1.95 ± 0.35	1.89 ± 0.71	2.24 ± 0.98
	p	0.566	0.899	0.734

The data are expressed as the mean and the standard deviation (M ± SD). PCI, percutaneous coronary intervention; GFR, glomerular filtration rate; NGAL, neutrophil gelatinase-associated lipocalin; IL, interleukin; KIM, kidney injury molecule; UACR, urine albumin-creatinine ratio.

Renal function indices were evaluated at the time of inclusion (one month prior to the elective procedure), prior to the radiographic contrast intervention, and within 48 hours thereafter. The data are presented in Table 3.

No statistically significant alterations were identified in the evaluation of conventional markers of renal dysfunction. For instance, plasma creatinine and calculated GFR demonstrated minimal alterations. The control group exhibited a 4.8% increase in creatinine levels, while the azilsartan group demonstrated a 4.9% increase. Additionally, GFR decreased by 3.7% and 3.4%, respectively.

However, the evaluation of novel biomarkers for AKI resulted in disparate findings. For example, within 48 hours following PCI, there was a 3.6-fold increase in NGAL concentration in the azilsartan group and a 4-fold increase in the control group. Furthermore, it was observed that during the early postoperative period, there was a notable elevation in proteinuria levels in the treatment group by 14% and in the control group by 30% compared to the baseline levels. The concentrations of IL-18 and KIM-1 remained unaltered in both groups.

The findings indicated that, irrespective of the selected biomarker and the employed calculation method, renal function declined following PCI. The identified phenomenon is well-documented and has been attributed to the effects of a contrast agent damaging renal and vascular endothelium, neurohumoral activation, and inflammation.

Additionally, the alterations in the concentrations of renal function markers were evaluated at successive visits over a six-month follow-up period.

A moderate increase in serum creatinine concentration was observed in patients during the six-month period following PCI, accompanied by a consistent decrease in GFR (Table 4).

Table 4. Changes in renal function markers observed in patients in the main and control groups over a 6-month period following percutaneous coronary intervention

Parameters of kidney function	Group	In 1 months	In 3 months	In 6 months
Creatinine, μmol/L	Treatment	66.17 ± 22.05	68.27 ± 20.15	72.21 ± 19.85
	Control	72.14 ± 23.04	81.03 ± 19.04	88.64 ± 25.27
	p	< 0.001	< 0.001	< 0.001
GFR, mL/min/1.73 m²	Treatment	81.71 ± 19.32	80.65 ± 18.42	75.24 ± 20.02
	Control	74.66 ± 17.08	65.25 ± 16.34	60.01 ± 19.55
	p	< 0.001	< 0.001	< 0.001
NGAL, mg/mL	Treatment	39.96 ± 25.81	40.26 ± 22.11	38.12 ± 18.71
	Control	62.72 ± 47.01	64.14 ± 52.26	70.04 ± 48.75
	p	< 0.001	< 0.001	< 0.001
IL-18, pg/mL	Treatment	124.71 ± 41.91	114.82 ± 36.25	103.08 ± 48.17
	Control	112.52 ± 41.61	118.45 ± 46.01	120.54 ± 43.12
	p	< 0.001	< 0.001	< 0.001
KIM-1, mg/mL	Treatment	2.69 ± 2.44	3.01 ± 2.49	3.11 ± 2.58
	Control	3.19 ± 1.65	3.24 ± 1.72	3.28 ± 1.82
	p	> 0.05	> 0.05	> 0.05
UACR, mg/g	Treatment	40.76 ± 16.41	51.68 ± 20.47	55.18 ± 22.15
	Control	52.12 ± 15.11	73.51 ± 25.43	102.95 ± 47.14
	p	< 0.001	< 0.001	< 0.001
Cystatin C, mg/L	Treatment	2.32 ± 1.04	2.08 ± 1.21	2.58 ± 0.98
	Control	2.34 ± 1.08	2.24 ± 0.98	2.54 ± 0.76
	p	> 0.05	> 0.05	> 0.05

The data are expressed as the mean and the standard deviation (M ± SD). PCI, percutaneous coronary intervention; GFR, glomerular filtration rate; NGAL, neutrophil gelatinase-associated lipocalin; IL, interleukin; KIM, kidney injury molecule; UACR, urine albumin-creatinine ratio.

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Table 5. Changes in indices of 24-hour blood pressure monitoring in the study groups, Me [Q25; Q75]

Parameter	AZL-M, main group, visit 1 (1 month prior to PCI)	Control, visit 1 (1 month prior to PCI)	AZL-M, main group, visit 2 (1 month following PCI)	Control, visit 2 (after 1 month)	AZL-M, main group, visit 4 (3 month following PCI)	Control, visit 4 (after 3 months)	AZL-M, main group, visit 5 (after 6 months)	Control, visit 5 (after 6 month)
Mean daytime SBP, mm Hg	144.37 [109; 178]	145.43 [108; 177]	132.7 [107; 184]	132.3 [108; 167]	122.54 [105; 175]	134.5 [101; 144]	137.04 [108; 160]	139.14 [105; 135]
Mean daytime DBP, mm Hg	80.39 [64; 98]	81.62 [69; 100]	75.39 [61; 89]	76.2 [66; 99]	74.5 [59; 110]	70.33 [66; 77]	75.33 [62; 94]	68.33 [62; 79]
Hypertension time index, daytime SBP, %	54.41 [0; 100.0]	60.1 [0; 100.0]	33.15 [1; 100.0]	39 [1; 89.0]	27.57 [0; 99.0]	41.17 [2; 48.0]	29.67 [0; 89.0]	42.83 [3; 58.0]
Hypertension time index, daytime DBP, %	29.78 [0; 82.0]	33.81 [69; 100.0]	16.42 [0; 65.0]	19.9 [0; 60.0]	21.61 [0; 93.0]	26.2 [5; 55.0]	16.63 [0; 62.0]	21.17 [1; 29.0]
Mean nighttime SBP, mm Hg	141.57 [104; 191]	142 [97; 190]	128.18 [103; 171]	126.5 [100; 170]	129.04 [99; 174]	132.5 [100; 150]	109.09 [100; 153]	115.83 [100; 139]
Mean nighttime DBP, mm Hg	76.21 [60; 94]	77.14 [60; 93]	70.7 [54; 88]	71.6 [60; 91]	71.96 [55; 107]	72.5 [63; 87]	70.39 [60; 88]	70 [67; 80]
Hypertension time index, nighttime SBP, %	66.75 [0; 100.0]	60.81 [0; 100.0]	45.24 [0; 100.0]	50.9 [0; 100.0]	40.37 [0; 100.0]	48.33 [2; 50.0]	33.83 [0; 100.0]	38.67 [0; 54.0]
Hypertension time index, nighttime DBP, %	49.26 [0; 100.0]	47.71 [0; 93.0]	33.18 [0; 90.0]	55.1 [2; 68.0]	31.85 [0; 100.0]	32.8 [5; 50.0]	31.35 [0; 90.0]	38.67 [0; 54.0]

AZL-M, azilsartan medoxomil (main group); SBP, systolic blood pressure; DBP, diastolic blood pressure.

GFR exhibited a reduction of 7.4% in the azilsartan group and decreased by 18.9% in the control group ($p < 0.001$). Over the course of the six-month follow-up period, no change in NGAL concentration was observed in the main group, whereas the mean value in the control group exhibited an increase of 12.9%. In patients who received azilsartan, there was a reduction in IL-18 concentration in urine by 16.9%, while the IL-18 level increased by 7.14% in the control group. The progression of proteinuria occurred in both groups, which is to be expected in view of the presence of type 2 DM. However, in patients treated with azilsartan, the mean UACR value increased by 37.5%, while in the control group, it increased by 96.15%. The discrepancies outlined are statistically significant. No notable discrepancies were identified with regard to cystatin C and KIM-1.

The mean 24-hour BP values in the main and control groups demonstrated consistent alterations over the six-month follow-up period (Table 5).

Discussion

Prior research has demonstrated that patients with CHD and DM face a greater risk of developing CI-AKI [10].

The present study employed the established criteria for CI-AKI, which are based on the evaluation of a serum creatinine increase (26.5 μmol/L) within 48 hours or an increase of 1.5 times the baseline) [11]. A comparison of standard markers of renal impairment in patients with stable forms of CHD over the periprocedural period revealed no statistically significant differences in creatinine levels or GFR, which was calculated based on blood creatinine before the procedure and on day 2 after PCI. The mean GFR prior to PCI was 80.05 ± 21.18 mL/min/1.73 m^2, while the mean GFR post-procedure was 77.37 ± 17.05 mL/min/1.73 m^2. Accordingly, the treatment group presented no cases of AKI when the common markers were evaluated.

As indicated in the literature [10], the incidence of CI-AKI is 5% in inpatients and 2% in outpatients. However, there are also data that report higher values for this indicator, reaching up to 20%.

Although the gold standard for assessing CI-AKI is the change in blood creatinine concentration, there is growing evidence that this method is not sufficiently sensitive and may have a delayed response in the development of CI-AKI.

The prevention of CI-AKI has been a topic of discussion for an extended period. While not all proposed methods have been demonstrated to be efficacious, the preprocedural use of therapies that are intended for other purposes, such as statins, ACE inhibitors, and ARBs, has been shown to offer a clear benefit. It is postulated that the utilization of ARBs is more effective than ACE inhibitors in the prevention and correction of AKI subsequent to major cardiovascular surgery [12].

Conclusion

The results of this study demonstrated two key findings. Firstly, it is possible to diagnose contrast-induced acute kidney injury using novel, more sensitive markers of kidney

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impairment. This is an important prerequisite for assessing the efficacy of preventive measures. Secondly, angiotensin II receptor blockers, in particular azilsartan medoxomil, can be used to prevent contrast-induced acute kidney injury in patients with stable ischemic heart disease associated with arterial hypertension and diabetes mellitus.

Statistical data analysis was performed with the support of AO Nizhfarm.

The authors declared no conflict of interest.

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