The Impact of Serum Osmolarity on Contrast-Induced Nephropathy in Patients with ST-Segment Elevation Myocardial Infarction

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ABSTRACT

Introduction: Contrast-induced nephropathy (CIN) is one of the most important causes for increased mortality rates in ST-segment elevation myocardial infarction (STEMI) patients. In our study, we aimed to investigate the impact of serum osmolarity on CIN in patients with STMEI who were undergoing percutaneous coronary intervention.

Patients and Methods: A total of 163 consecutive patients with STEMI were enrolled in this study. The patients were divided into two groups; patients without CIN were assigned to group 1 and patients with CIN were assigned to group 2. The baseline clinical, laboratory and demographic features, including the serum osmolarity, were compared for both groups.

Results: A total of 144 patients without CIN comprised group 1, while 22 patients with CIN comprised group 2. The serum osmolarity level [289.06 (284.75-292.39), 291.71 (289.69-295.72); p= 0.004] was higher in patients with CIN. Additionally, age (OR: 1.097, CI: 1.033-1.164; p= 0.002) and serum osmolarity (OR:1.117, CI: 1.008-1.238; p= 0.035) were found to be independent predictors of CIN.

Conclusion: Higher serum osmolarity is related with CIN in STEMI patients who are undergoing percutaneous coronary intervention. This could cause increased adverse clinical outcomes, even if the underlying coronary artery disease is treated successfully.

Key Words: Contrast-induced nephropathy; serum osmolarity; STEMI

ST Elevasyonlu Miyokart İnfarktüsü Hastalarında Serum Ozmolaritesinin Kontrast Nefropatisi Üzerine Etkisi

ÖZET

Giriş: Kontrast ilişkili nefropati (KİN) ST elevasyonlu miyokart infarktüsü (STEMİ) hastalarında artmış mortalitenin en önemli nedenlerinden birisidir. Çalışmamızda perkütan koroner girişim uygulanan STEMİ hastalarında serum ozmolaritesinin KİN üzerine etkisini incelemeyi amaçladık.

Hastalar ve Yöntem: STEMİ olan 163 ardışık hasta çalışmaya dahil edildi. Ardından hastalar KİN gelişmeyen grup 1 ve gelişen grup 2 olarak ikiye ayrıldı. Bazal klinik, serum ozmolaritesini içeren laboratuvar ve demografik özellikler her iki grupta karşılaştırıldı.

Bulgular: Yüz kırk dört KİN olmayan hasta grup 1, yirmi iki KİN olan hasta grup 2 olarak alındı. Serum ozmolaritesi KİN gelişen hastalarda daha yüksek saptandı [289.06 (284.75-292.39), 291.71 (289.69-295.72); p= 0.004]. Ayrıca yaş (OR: 1.097, CI: 1.033-1.164; p= 0.002) ve serum ozmolaritesi (OR: 1.117, CI: 1.008-1.238; p= 0.035) KİN'in bağımsız öngördürücüleri olarak saptandı.

Sonuç: Artmış serum ozmolaritesi perkütan koroner girişim uygulanan STEMİ hastalarında KİN ile ilişkilidir. Bu ilişki koroner arter hastalığı tedavi edilse bile artmış kötü klinik sonlanımlardan sorumlu olabilir.

Anahtar Kelimeler: Kontrast nefropatisi, serum ozmolaritesi, ST elevasyonlu miyokart infarktüsü

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of morbidity and mortality worldwide[1]. Alongside this, ST-segment elevation myocardial infarction (STEMI) has the worst prognosis within the CAD spectrum. The complications of STEMI are important factors for determining long-term adverse clinical outcomes. Contrast-induced nephropathy (CIN) is one of the most important causes of poor prognosis in STEMI patients[2]. Its incidence ranges from 2% in the general population to > 50% in a variety of high-risk patients[3]. CIN is found to be related with increased complication rates, such as increased mortality[2]. Therefore, parameters that could be associated with progression or prevention to CIN are of great clinical interest.

Serum osmolarity is defined as a marker of serum concentration[4]. It is normally maintained within a narrow range of 275-295 mOsm/L. In previous studies, it was associated with adverse outcomes and mortality in patients with CAD or heart failure[5,6]. However, to the best of our knowledge, the prognostic value of serum osmolarity in patients with STEMI has not been studied yet. In our study, we aimed to investigate the impact of serum osmolarity on CIN in patients with STEMI who were undergoing percutaneous coronary intervention (PCI).

PATIENTS and METHODS

Study Population

This retrospective observational study was conducted at a single tertiary centre. A total of 228 consecutive patients with STEMI who were undergoing PCI from January 2018 to January 2019 were enrolled in this study. Patients with a history of coronary artery bypass grafting surgery, autoimmune or inflammatory diseases, end-stage renal insufficiency and exposure to a contrast medium within the last 1 month were excluded from the study. Patients receiving nephrotoxic medications after performing coronary angiography were also excluded from the study.

Baseline clinical and laboratory variables before performing coronary angiography and echocardiographic parameters were obtained from the hospital database. A 12-lead surface ECG was performed for all subjects before performing coronary angiography. The study was approved by the local ethics committee.

Patients with typical chest pain for more than 20 minutes and ST-segment elevation in at least two contagious leads were observed with the following cut-off points: ≥ 0.2 mV in men aged < 40 years old; ≥ 0.25 mV in men aged < 40 years old or ≥ 0.15 mV in women in leads V2-V3 and/or ≥ 0.1 mV in the other leads. When indicated, posterior (V7-V9) and right (V3R-V4R) derivations were also obtained. The cut-off points were 0.05 mV for V7-9 (≥ 0.1 mV in men < 40 years old) and ≥ 0.05 mV for V3R and V4R (≥ 0.1 mV in men < 30 years old). Additionally, there was no alternative aetiology for CIN[7].

Biochemical Analysis

CIN was defined as impairment of renal function. The diagnostic criteria for CIN was as follows: (a) a relative increase of at least 25% or (b) an absolute increase of at least 0.5 mg/dL in serum creatinine levels from the baseline levels within 72 hours. After establishing there criteria, the patients were divided into two groups; patients without CIN as group 1 and patients with CIN as group 2. Serum osmolarity was calculated using a formula: (2 x sodium) + (BUN/2.8) + (glucose/18)[8].

Statistical Analysis

Statistical analysis was done using the computer software Statistical Package for Social Sciences (SPSS, IBM Corp, Armonk, NY, USA). The Pearson chi-square analysis or Fisher's exact test were performed to determine categorical variables, while the Kolmogorov-Simirnov test was used to analyse the normal distribution. The data with normal distribution was expressed as 'mean ± standard deviation (SD)' and data without normal distribution was expressed as 'median (1^{st} and 3^{rd} percentiles)'. The notation 'n (%)' was used to denote categorical variables. The Mann-Whitney U test was used for comparing quantitative variables without normal distribution and the Student's t-test was used for comparing the means between two groups with normal distribution. Univariate and multivariate logistic regression analyses were used to detect the independent predictors of CIN. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 163 patients were enrolled in this study, of which 144 patients without CIN comprised group 1, while 22 patients with CIN comprised group 2. In the entire study group, the incidence of CIN was 13.4% (22 patients). The baseline clinical, demographic and laboratory variables of the whole group is demonstrated in Table 1. There were no statistical significant differences in the smoking status, hypertension, hyperlipidaemia, peripheral arterial disease, chronic obstructive pulmonary disease, medication usage, glucose, sodium, potassium, high density lipoprotein cholesterol, triglyceride, leukocyte and thrombocyte levels, culprit lesions, ejection fraction, contrast volume and Syntax score between the two groups. The mean age of patients with CIN was higher than the mean age of patients without CIN (51.8 ± 10.5, 64.0 ± 10.6; p< 0.001). The female gender [9.2% (13), 31.8% (7); p= 0.008] and the presence of diabetes mellitus [14.9% (21), 36.4% (8); p= 0.021] were also higher in group 2. While creatinine [0.80 (0.72-0.93), 1.04

Table 1. Baseline clinical, demographic and laboratory variables of patients with and without CIN

	Patients without CIN (n= 141)	Patients with CIN (n= 22)	p
Age	51.8 ± 10.5	64.0 ± 10.6	**< 0.001**
Gender (female) % (n)	9.2 (13)	31.8 (7)	**0.008**
Smoking % (n)	53.2 (75)	40.9 (9)	0.284
HT % (n)	31.2 (44)	36.4 (8)	0.629
HL % (n)	17.7 (25)	13.6 (3)	0.453
DM % (n)	14.9 (21)	36.4 (8)	**0.021**
PAD % (n)	5.0 (7)	0.0 (0)	0.355
COPD % (n)	3.5 (5)	4.5 (1)	0.587
Medication % (n)			
Beta-blocker	1.4 (2)	4.5 (1)	0.355
ACEI or ARB	17.0 (24)	18.2 (4)	0.547
CCB	6.4 (9)	18.2 (4)	0.078
Statin	18.4 (26)	18.2 (4)	0.621
Creatinine (mg/dL)	0.80 (0.72-0.93)	1.04 (0.79-1.24)	**0.004**
BUN (mg/dL)	14 (12-17)	18 (14-23)	**0.002**
Glucose (mg/dL)	124 (104-163)	143 (118-173)	0.104
Sodium (mmol/L)	138 (135-140)	139 (136-140)	0.198
Potassium (mmol/L)	4.5 (4.2-4.7)	4.4 (4.0-4.8)	0.473
Total cholesterol (mg/dL)	204.5 ± 42.5	178.8 ± 39.9	**0.009**
LDL cholesterol (mg/dL)	124.5 ± 37.6	104.0 ± 33.7	**0.017**
HDL cholesterol (mg/dL)	40.5 ± 9.2	40.9 ± 10.7	0.865
Triglyceride (mg/dL)	184 (121-260)	159 (105-213)	0.252
Haemoglobin (g/dL)	15.3 (14.1-16.0)	14.1 (13.0-15.0)	**0.005**
Leukocyte × $10^3/mm^3$	12.52 ± 3.29	12.62 ± 3.33	0.904
Thrombocyte × $10^3/mm^3$	263 (228-325)	271.5 (224-344)	0.944
Culprit lesion % (n)			0.393
LAD	51.1 (72)	36.4 (8)	
CXA	11.3 (16)	18.2 (4)	
RCA	37.6 (53)	45.5 (10)	
Ejection fraction (%)	50.0 (45-55)	47.5 (40-55)	0.138
Contrast volume (mL)	120 (100-200)	150 (100-200)	0.063
Serum osmolarity (mOsmol/L)	289.06 (284.75-292.39)	291.71 (289.69-295.72)	**0.004**
SYNTAX score	15.0 (10.5-20.5)	16.3 (11.5-24.0)	0.520

ACEI: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, BUN: Blood urea nitrogen, CCB: Calcium channel blocker, CIN: Contrast-induced nephropathy, COPD: Chronic obstructive pulmonary disease, CXA: Circumflex, DM: Diabetes mellitus, HDL: High density lipoprotein, HL: Hyperlipidemia, HT: Hypertension, LAD: Left anterior descending, LDL: Low density lipoprotein, PAD: Peripheral arterial disease, RCA: Right coronary artery.

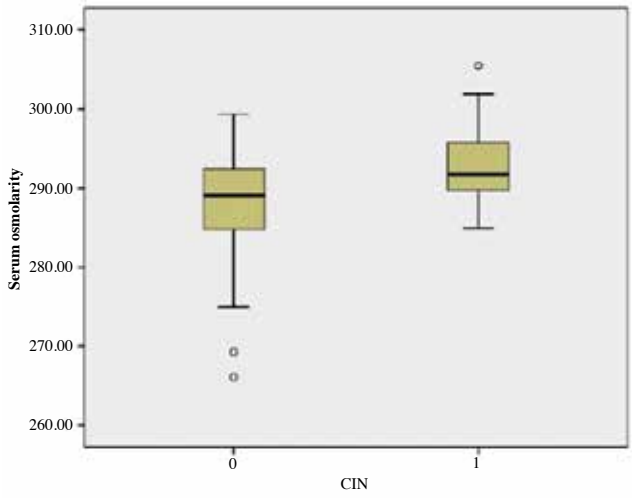

Figure 1. Comparison of serum osmolarity in patients with and without CIN. CIN: Contrast-induced nephropathy.

(0.79-1.24); p= 0.004], blood urea nitrogen [14 (12-17), 18 (14-23); p= 0.002] and serum osmolarity levels [289.06 (284.75-292.39), 291.71 (289.69-295.72); p= 0.004] were higher in patients with CIN (Figure 1), total cholesterol (204.5 ± 42.5, 178.8 ± 39.9; p= 0.009) low density lipoprotein cholesterol (124.5 ± 37.6, 104.0 ± 33.7; p= 0.017), and haemoglobin levels [15.3 (14.1-16.0), 14.1 (13.0-15.0); p= 0.005] were lower in patients with CIN with statistical significance.

Univariate and multivariate logistic regression analyses were performed to detect independent predictors of CIN. Age (OR: 1.097, CI: 1.033-1.164; p= 0.002) and serum osmolarity (OR: 1.117, CI: 1.008-1.238; p= 0.035) were found to be independent predictors of CIN (Table 2).

DISCUSSION

In our study, we demonstrated that serum osmolarity was associated with CIN in patients with STEMI who had undergone PCI. Additionally, higher serum osmolarity and older age were found to be independent predictors of CIN.

Acute kidney injury after undergoing PCI is one of the most important causes of increased adverse clinical outcomes in STEMI patients[2]. Contrast media that causes an impairment in renal function is known as CIN[9]. CIN is defined as a relative increase of at least 25% or an absolute increase of at least 0.5 mg/dL in serum creatinine levels from the baseline levels within 72 hours after performing coronary angiography. The incidence of CIN ranges from 2% in the general population to 50% in high-risk patients such as those with DM, chronic kidney disease, heart failure, anaemia and hypotension[3]. CIN rarely requires acute dialysis treatment and generally improves within 7 days[10]. In previous studies, it has been demonstrated that CIN can be related with short- and long-term complications, such as increased mortality rates[2,9]. In the Harmonising Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) study subgroup analysis, in post-PCI STEMI patients, CIN was found to be related with increased 30-day and 3-year mortality rates[2]. This is why CIN-linked variables are of great interest.

The balance of hydration and serum electrolyte levels are of important for assessing the prevalence of cardiovascular diseases in several different populations. Patients with CAD and heart failure can be especially sensitive to volume changes. Serum osmolarity, which is proportional to the number of particles per litre of solution, is an indicator of the osmolar concentration of serum[4]. In the presence of hyperosmolarity, dehydration affects renal function due to the activation of the renin-angiotensin and vasopressin systems. This results in the increase of tubular concentration and provides convenience of contrast media that is linked to kidney injury due to hyperfiltration and albuminuria[11-13]. Additionally, hyperosmolarity causes increased inflammation via increasing epithelial cell-linked apoptosis and decreasing macrophage apoptosis, besides inducing pro-inflammatory cytokine responses[14-17]. Finally, hyperosmolarity can activate a variety of pathways, including the central sympathetic nervous system

Table 2. Univariate and multivariate logistic regression analyses to determine the independent predictors of CIN

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI (Lower-Upper)	p	Odds ratio	95% CI (Lower-Upper)	p
Age	1.109	1.057-1.163	**< 0.001**	1.097	1.033-1.164	**0.002**
Gender (female)	0.218	0.075-0.630	**0.005**	0.355	0.069-1.826	0.215
DM	0.306	0.114-0.820	**0.018**	0.574	0.178-1.854	0.353
Haemoglobin	0.653	0.480-0.888	**0.007**	1.235	0.744-2.048	0.414
Serum osmolarity	1.160	1.054-1.276	**0.002**	1.117	1.008-1.238	**0.035**

CIN: Contrast-induced nephropathy, DM: Diabetes mellitus.

and the polyol (aldose reductase) pathway, which can lead to intrarenal fructose generation and tubular injury[18]. In the light of foregoing data, the baseline hyperosmolarity can cause acute kidney injury after contrast media exposure. In a previous study, a 5 mOsm/L change in serum osmolarity was associated with a 24% increased risk of kidney disease[19]. This was supported by our study, as we proved the association between hyperosmolarity and CIN in STEMI patients after PCI. Additionally, hyperosmolarity and dehydration are prognostic determinants in several populations. Hyperosmolarity particularly predicts poor prognosis in patients with CAD and heart failure[5,6]. Are´valo-Lorido JC et al. demonstrated that higher osmolarity had a relative risk of 1.02 for mortality in heart failure patients[5]. Briongos Figuero et al. also revealed that hyperosmolarity was an independent predictor of increased mortality rates in patients with acute coronary syndrome[6]. Hyperosmolarity linked to impaired renal function could be one of the most important underlying mechanisms of increased adverse clinical outcomes in patients with cardiovascular diseases. Thus, serum osmolarity measurement in high-risk populations can detect sensitive populations and treat them as early as possible. However, large-scale studies are needed for future investigations.

CONCLUSION

Higher serum osmolarity is related with CIN in STEMI patients who are undergoing PCI. This could cause increased adverse clinical outcomes, even if the underlying CAD is treated successfully.

STUDY LIMITATIONS

The relatively small sample size was the main limitation of our study. Its retrospective nature was another limitation. Due to this, the hyperosmolarity or the CIN-linked outcomes of adverse cardiovascular diseases were not mentioned in the study. Additionally, the lack of the data on the long-term follow-up was another important limitation.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: SK, HA
Analysis/Interpretation: SK, HA
Data Acquisition: SK, HA
Writting: SK, HA
Critical Revision: SK, HA
Final Approval: SK, HA

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