Inferior Vena Cava Collapsibility Index and the Risk of Contrast-Induced Nephropathy in Patients Undergoing Coronary Angiography

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ABSTRACT

Introduction: The present study aims to investigate the association between contrast-induced nephropathy (CIN) and inferior vena cava collapsibility index (IVC-CI) measured via echocardiography to estimate intravascular volume.

Patients and Methods: A total of 100 patients were referred to coronary angiography (CAG). On the day of admission, blood samples were collected, and an echocardiographic evaluation was performed to estimate IVC-CI immediately before CAG. IVC-CI ratios were stratified into three groups (low, mid, high) (<50%, 50-75%, >75%). Creatinine was assessed again at 48 hours following the CAG procedure. The difference between baseline serum creatinine and serum creatinine at 48 hours was calculated as ΔCrea while the difference in GFR was calculated as ΔGFR. Biochemical parameters and CIN ratios were compared between all groups.

Results: There were no differences across the groups in terms of procedural characteristics, preprocedural lab parameters, and concomitant medication. ΔCreatinine, ΔGFR, and the incidence of CIN were significantly higher in the high IVC-CI group.

Conclusion: Post-procedure incidence of CIN, ΔGFR, and Δcreatinine compared to the pre-procedure values were higher in the high IVC-CI group.

Key Words: Contrast induced nephropathy; inferior vena cava collapsibility index; coronary angiography

Koroner Anjiyografi Uygulanan Hastalarda İnferior Vena Kava Kollapsibilite İndeksi ve Kontrast Nefropati Riski

ÖZET

Giriş: Bu çalışmada, intravasküler hacmi tahmin etmek için ekokardiyografi ile ölçülen kontrast inferior vena kava kollapsibilite indeksi (IVC-CI) ile kontrast nefropati arasındaki ilişkiyi araştırmak amaçlanmıştır.

Hastalar ve Yöntem: Çalışmaya koroner anjiyografi (KAG) yapılan toplam 100 hasta dahil edildi. KAG'den hemen önce IVC-CI için ekokardiyografik değerlendirme yapıldı ve kan örnekleri alındı. IVC-CI oranları üç gruba ayrıldı (düşük, orta, yüksek) (<%50, %50-75, >%75). Kreatinin değerlerine, KAG sonrası 48 saat sonra tekrar bakıldı. Kırk sekizinci saatte bazal serum kreatinin ile serum kreatinin arasındaki fark ΔCrea, GFR'deki fark ΔGFR olarak hesaplandı. Biyokimyasal parametreler ve CIN oranları tüm gruplar arasında karşılaştırıldı.

Bulgular: Prosedürel özellikler, prosedür öncesi laboratuvar parametreleri ve kullanılan ilaçlar açısından gruplar arasında fark yoktu. Kırk üç hastada (%42.2) düşük IVC-CI, 32 hastada (%31.4) orta IVC-CI ve 27 hastada (%26.4) yüksek IVC-CI bulundu. Δkreatinin, ΔGFR ve CIN insidansı yüksek IVC-CI grubunda anlamlı olarak daha yüksekti.

Sonuç: İşlem sonrası CIN, ΔGFR ve Δkreatinin insidansı, yüksek IVC-CI grubunda işlem öncesi değerlere göre daha yüksekti.

Anahtar Kelimeler: Kontrast nefropati; vena cava inferior kollapsibilitesi; koroner anjiografi

INTRODUCTION

Contrast-induced nephropathy (CIN) is one of the most commonly seen complications of procedures that require the use of contrast agents[1,2]. Widespread use of diagnostic imaging and interventional procedures have increased the incidence of CIN, which is associated with acute renal failure, hemodialysis requirement, prolonged hospitalization, increased costs, and decreased short and long-term survival[1,3,4]. Periprocedural hydration is the only effective treatment that is strongly recommended in recent guidelines for the prevention of CIN[5,6].

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Inferior vena cava collapsibility index (IVC-CI) is a non-invasive method with an increasing trend of use and provides insight into the estimated intravascular volume[7,8]. Previous studies have shown that IVC-CI is a useful, non-invasive method to estimate intravascular volume that is associated with central venous pressure and right atrial pressure[8,9]. Hydration is the mainstay of preventing CIN as it reduces the contraction in renal vessels and urinary cast formation, thereby increasing renal blood flow[10,11]. The present study aims to investigate the association between CIN and IVC-CI measured via echocardiography to estimate intravascular volume.

PATIENTS and METHODS

A total of 117 patients referred to coronary angiography (CAG) due to suspected coronary artery disease at Kartal Koşuyolu Training and Research Hospital from January 2015 to November 2015 were enrolled in the study. Informed consent was obtained from all patients before the procedures and the study was approved by the local ethics committee. On the day of admission, an echocardiographic evaluation was performed to estimate IVC-CI immediately before CAG. Of these patients, 15 were excluded due to poor echocardiographic image quality. CIN was defined as an absolute ≥0.5 mg/dL or a relative ≥25% increase in serum creatinine level 48 hours after the procedure. Patients who had left ventricular ejection fraction (LVEF) <60%, moderate or severe valve disease, serum creatinine level ≥1.5 mg/dL, pulmonary hypertension, acute coronary syndrome, anemia, chronic liver disease or liver failure, history of coronary artery bypass grafting, percutaneous coronary intervention and heart valve surgery, peripheral artery disease (requiring peripheral angiography), contrast agent exposure within three months before the procedure, active infection, systemic inflammatory disease, malignancy, hypothyroidism or hyperthyroidism, those receiving N-acetylcysteine, theophylline, aminophylline, nonsteroidal anti-inflammatory drugs, vitamin supplements, antibiotics or steroids as well as patients with poor echocardiographic image quality were excluded from the study.

Echocardiographic Evaluation

Echocardiographic evaluation was performed with Vivid 6S (Vivid 6S Echocardiography; General Electric). Maximum and minimum IVC dimensions (IVCmax and IVCmin) were measured in the subcostal view, at 10 mm from the junction between IVC and the right atrium during quiet respiration using the M-mode. IVC-CI was calculated using the following formula:

$$\text{IVC-CI} = [(\text{IVCmax} - \text{IVCmin})/\text{IVCmax}] \times 100\%.$$

IVC-CI ratios were stratified into three groups (low, mid, high) (<50%, 50-75%, >75%).

Biochemical Measurements

Blood samples were collected on the day of admission before CAG (following 12 hours of fasting). Glucose, urea, creatinine, blood cell counts, and lipid profile were assessed using standard methods.

Creatinine was assessed again at 48 hours following the CAG procedure. Glomerular filtration rate (GFR) was calculated with the Cockcroft-Gault formula before CAG (baseline) and 48 hours after the procedure[12]. The difference between baseline serum creatinine and serum creatinine at 48 hours was calculated as ΔCrea while the difference in GFR was calculated as ΔGFR. Biochemical parameters were compared between all groups.

Coronary Angiography

Coronary angiography was routinely performed using the Judkins technique using six-French right and left heart catheters through the femoral approach. Quantitative coronary angiography (Siemens AcomQuantcor QCA, Erlangen, Germany) was performed by two experienced cardiologists who were blinded to the clinical background of the patients. All of the patients were given the same nonionic contrast agent (iohexol) and contrast doses were recorded. All patients received continuous intravenous saline infusion (0.9%) for 5 hours after CAG (1 mL per kilogram of body weight per hour).

Statistical Analysis

SPSS 23.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range, as appropriate. Categorical variables were expressed as percentages. The Kolmogorov Smirnov test was used to test the distribution normality of continuous variables. Group means for continuous variables were compared using the Student's t-test, the Mann-Whitney U test, ANOVA, or Kruskal-Wallis test, as appropriate. Categorical variables were compared using the Chi-square test. Tukey's honestly significant difference test was used for the post hoc analysis. A p-value of ≤0.05 was considered statistically significant.

RESULTS

Table 1 shows the baseline characteristics of the patient enrolled in the study. Among the 102 patients included in the study, the mean age was 36 ± 10 years and the ratio of male subjects was 39% (40 patients) with a prevalence of 52% (53 patients) for hypertension and 24% (25 patients) for diabetes mellitus and mean systolic and diastolic blood pressure values were 135 ± 11 and 88 ± 11 mmHg, respectively. Mean creatinine value was 0.7 ± 0.2 mg/dL, while mean GFR was 109 ± 31 mL/min/1.73 m^2. There were 45 patients (44%) receiving

Table 1. Baseline demographic and laboratory characteristics of the patients

	Patients (n= 102)
Age (years)	58 ± 10
Gender, n (male %)	40 (39)
Hypertension, n (%)	53 (52)
Diabetes Mellitus, n (%)	25 (24)
Current Smoking, n (%)	26 (25)
SBP (mmHg)	135 ± 11
DBP (mmHg)	88 ± 11
Laboratory	
White Blood Cells (μL)	6.3 ± 1.4
Hemoglobin (g/dL)	13 ± 1.1
Platelet (μL)	236 ± 53
Urea (mg/dL)	31 ± 7.3
Creatinine (mg/dL)	0.7 ± 0.2
GFR	109 ± 31
LDL (mg/dL)	115 ± 30
Fasting glucose (mg/dL)	115 ± 40
Sodium (mEq/L)	137 ± 1.8
Potassium (mEq/L)	3.9 ± 0.2
Drugs	
ß Blockers, n (%)	37 (36)
ACE or ARB	44 (43)
Statins	45 (44)
Calcium antagonists	45 (44)
Oral antidiabetics	25 (24)
Insulin	14 (14)

ACE: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, DBP: Diastolic blood pressure, SBP: Systolic blood pressure.

statin treatment and 25 (24%) patients were on oral antidiabetics. Low IVC-CI was found in 43 patients (42.2%), with mid IVC-CI in 32 patients (31.4%) and high IVC-CI in 27 (26.4%). CAG results revealed normal coronary arteries in 11 patients. Thirty patients underwent medical follow-up due to noncritical stenosis, 40 patients underwent percutaneous coronary stent implantation, and 21 patients underwent coronary artery bypass grafting.

Table 2 compares the patient characteristics of low, mid, and high IVC-CI groups. There was no difference in terms of baseline characteristics between the groups except for male gender and hypertension. The male gender was significantly more common in the moderate IVC-CI group while hypertension was significantly more prevalent in the low IVC-CI group. There were no differences across the groups in terms of procedural characteristics, preprocedural lab parameters, and concomitant medication. ΔCreatinine, ΔGFR, and the incidence of CIN were significantly higher in the high IVC-CI group.

DISCUSSION

The present study aims to investigate the association between CIN and IVC-CI measured via echocardiography to estimate intravascular volume. The number of patients who developed CIN was significantly higher in the high IVC-CI group compared to the others. Significantly higher ΔCrea and ΔGFR were noted in the high IVC-CI group versus the other groups.

CIN is a high-cost complication associated with increased mortality and morbidity rates[13]. Various mechanisms such as chronic kidney disease, concomitant hypotension, diabetes mellitus, exposure to a high-dose contrast agent, congestive heart failure, advanced age, and anemia have been suggested as etiological factors for CIN[14,15]. The pathophysiology of CIN is complex and multifactorial[16]. Chronic renal failure plays an essential role in CIN pathophysiology. A significant decrease in functional nephrons occurs together with the toxicity caused by the contrast agent[1,17]. Following transient vasodilation, the contrast agent causes adenosine-mediated vasoconstriction of endothelium as well as inhibiting nitric oxide-mediated vasodilation, thereby reducing renal blood flow, and resulting in medullary hypoxia, ischemic injury, and apoptosis in renal tubular cells[18,19]. The main aspect of CIN prevention is to distinguish the patients at high risk and provide appropriate periprocedural hydration treatment[20].

IVC-CI is a convenient and non-invasive method to estimate intravascular volume. In the present study, the incidence of CIN and the ΔCrea and ΔGFR values were significantly higher in the high IVC-CI group compared to the other groups. The smaller intravascular volume among high IVC-CI patients versus the other groups may have resulted in increased exposure to the contrast agent toxicity. The patients included in this study were relatively low-risk patients in terms of CIN (creatinine <1.5 mg/dL, without congestive heart failure). Since only patients undergoing CAG were included in the study, less contrast agent was used compared to patients undergoing percutaneous coronary intervention. However, a significant correlation was found between IVC-CI and CIN development even in this patient group. In addition to the previously defined predictors for CIN, identifying preprocedural IVC-CI may also be a useful, convenient method to determine the patients with CIN risk in clinical practice. In our study, the hypertension rate was found to be significantly high in the low IVC-CI group.

Table 2. Comparison of clinical and laboratory characteristics of all groups

	Low IVC-CI	Mid IVC-CI	High IVC-CI	p
	(n= 43)	(n= 32)	(n= 27)	
Age (years)	57 ± 11	60 ± 9	56 ± 8	0.22
Gender, n (male %)	10 (23)	17 (53)	13 (48)	**0.01**
Hypertension, n (%)	30 (69)	16 (50)	7 (25)	**<0.001**
Diabetes mellitus, n (%)	13 (30)	5 (15)	7 (25)	0.34
Current smoking, n (%)	9 (20)	8 (25)	9 (33)	0.50
SBP (mmHg)	137 ± 10	133 ± 13	137 ± 12	0.22
DBP (mmHg)	91 ± 11	86 ± 10	87 ± 10	0.12
Procedural characteristics				
Procedure time	19 ± 5	21 ± 5	20 ± 7	0.34
Contrast volume (mL)	59 ± 7	62 ± 7	59 ± 7	0.19
Laboratory				
Hemoglobin (g/dL)	12 ± 1.0	13 ± 1.1	13 ± 1.2	0.60
Platelet (μL)	224 ± 56	243 ± 48	245 ± 53	0.18
Fasting glucose (mg/dL)	114 ± 29	113 ± 53	117 ± 38	0.93
LDL (mg/dL)	111 ± 30	115 ± 29	121 ± 30	0.42
PreCreatinin	0.8 ± 0.2	0.8 ± 0.2	0.7 ± 0.1	0.32
PreGfr	106 ± 32	104 ± 28	118 ± 34	0.19
ΔCreatinin	0.03 ± 0.09	0.11 ± 0.14	0.32 ± 0.17	**<0.001**
ΔGfr	3.8 ± 8.9	10 ± 12	32 ± 29	**<0.001**
CIN, n (%)	1 (2)	3 (9)	6 (22)	**<0.001**
VCDmax	20.1 ± 3.6	20.3 ± 3.5	21.1 ± 2.7	0.119
VCDmin	14.2 ± 4.1	13.3 ± 3.9	13.1 ± 3.9	0.203
Drugs				
ß Blockers, n (%)	12 (28)	13 (40)	12 (44)	0.31
ACE or ARB	19 (44)	13 (41)	12 (44)	0.90
Statins	19 (44)	13 (41)	13 (48)	0.84
Calcium antagonists	19 (44)	15 (47)	11 (41)	0.89
OAD	13 (30)	5 (15)	7 (26)	0.32
Insulin	5 (12)	6 (19)	3 (11)	-

DBP: Diastolic blood pressure, SBP: Systolic blood pressure, OAD: Oral antidiabetics, VCDmax: Vena cava maximum diameter, VCDmin: Vena cava minimum diameter, ACE: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers.

This may be related to a higher volume load in hypertensive patients. Hypertension may play a protective role in the development of contrast nephropathy in patients without severe renal dysfunction. Periprocedural hydration is the only effective treatment that is strongly recommended to prevent CIN[5,6]. The mechanism of action of such treatment is multifactorial. CIN may be reduced by decreasing the contrast agent concentration via volume expansion with saline, by suppressing the renin-angiotensin-aldosterone system and through the down-regulation of tubuloglomerular feedback via contrast agent dilution in the tubular lumen[21-24]. There is no evidence-based and recommended method to determine the optimal ratio of fluid treatment in recent guidelines. Standard hydration therapy is administered to all patients. Serial IVC-CI measurements may help determine the ratio and adequacy of hydration in patients with chronic renal failure requiring hydration, who are at

high risk of CIN. This parameter may allow optimal treatment for patients with a greater need for hydration; however, further studies are warranted in this regard.

Study Limitations

Although the development of CIN is often determined 48 hours after the procedure, it may also occur in subsequent days. In the present study, evaluation was performed only at 48 hours although the follow-up could have been longer. IVC changes due to hydration could not be evaluated. The limited number of patients is another limitation of this study.

CONCLUSION

Post-procedure incidence of CIN, ΔGFR, and Δcreatinine compared to the pre-procedure values were higher in the high IVC-CI group. IVC-CI may be used as a parameter to show the adequacy of preprocedural hydration in the patient group at high risk; however, further studies are warranted in this regard.

Ethics Committee Approval: The approval for this study was obtained from Kartal Koşuyolu High Specialization Training and Research Hospital Ethics Committee (Decision no: 2021/10/528, Date: 24.08.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

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