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Original Article

Assessment of relationship between contrast-induced nephropathy and left ventricular myocardial performance index in patients at risk for nephropathy

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Abstract

Aim: Contrast induced nephropathy (CIN) is associated substantially with a risk of morbidity and mortality. The aim of this study was to assess the left ventricular myocardial performance assessed by 'Tei index' on the development of contrast induced nephropathy in patients underwent coronary angiography.
Material and Methods: Study population consist of patients who underwent coronary angiography and/or percutaneous coronary intervention and baseline creatinine level 1 mg/dl above and/or having diabetes mellitus. 51 patient were included the study. Patients divided into two groups as CIN developed or not. CIN was defined as %25 and/or 0.5 mg/dl increase in basal serum creatinine levels after 48-72 hours exposure to contrast media. Conventional and tissue Doppler echocardiography was performed in all patients prior to angiography. Tei index was calculated from tissue Doppler echocardiography data.
Results: Two groups were defined as CIN-developed group (n =13, 62.5 ± 6.8) and CIN-undeveloped (n=38, 62.4±9.6)group. Except gender, there is no difference in demographic characteristics between the study groups. Left ventricular (LV) systolic function such as ejection fraction and tissue Doppler imaging Sm and basic LV diastolic function (E/A, Em/Am, DT) parameters were found to be similar in both groups. Tissue Doppler-derived Tei index values did not differ significantly between the two groups (0.42 ± 0.09 vs 0.46 ± 0.12, p = 0.25).
Conclusion: The Tei index is inadequate for predicting the risk of developing nephropathy in patients at risk for contrast induced nephropathy with preserved ejection fraction.

Keywords: Contrast induced nephropathy; tei index; preserved ejection fraction.

INTRODUCTION

Contrast-induced nephropathy (CIN) is an important complication of interventional procedures after administrated of iodinated contrast media (1-3). The third most common cause of hospitalization induced acute renal injury is CIN representing about 12% of cases (4). Although CIN is generally thought to be reversible form of acute renal failure, it is associated with a longer hospital stay and increased rate of morbidity and mortality (1-3,5). The incidence of CIN after percutaneous coronary intervention (PCI) varies from 0 to 24% that mainly depends on the prevalence of associated risk factors (6-9). Patients with normal renal function have a fairly low incidence for CIN with 0-5% of range (10). But, CIN incidence increases as high as 12-27% in the case of impaired basal renal function (10,11). And, it can increase up to 50% in patients with diabetic nephropathy despite preventive measures such as use of low osmolar contrast media and adequate hydration (12).

Multiple risk factors that are described in the literature may contribute to the development of CIN. In addition, some risk scoring systems which predict the development of CIN have been developed by using these factors (13,14). These factors are mainly divided into two groups; patient- and procedure-related predictors. Important patient-related risk factors are reduced basal creatinine clearance (<60 ml/min) and the presence of diabetes, chronic heart failure, hypertension and peripheral vascular

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disease (13). Volume of contrast use is one of the most important procedure related risk factors (14). Although, the knowledge of all these factors and relevant preventive measures, CIN can still develop. Therefore, we need additional risk indicator(s).

Myocardial performance index (MPI) was firstly defined by Tei Chuwa. The most important advantage of MPI is the ability to evaluate systolic and diastolic functions together and simultaneous (15). In addition, it can reflect subclinical cardiac dysfunction. To best of our knowledge, there is no study evaluated the effect of MPI on the development CIN in patients undergoing coronary angiography. We have hypothesized that subclinical cardiac dysfunction evaluated by MPI may predict the development of CIN in subject at risk. Therefore, in this study, we aimed to assess the effect of left ventricular MPI on the development of CIN in patients underwent coronary angiography.

MATERIAL and METHODS

Study population

The study population was prospectively selected from patients underwent coronary angiography and percutaneous coronary intervention because of stable or unstable angina pectoris and/or non ST segment elevation myocardial infarction(NSTEMI) between October 2011 and July 2012. Patients with baseline creatinine level >1mg/dl and/or having diabetes mellitus were included the study. Exclusion criteria were the presence of prior heart surgery, congenital heart disease, a procedure administered contrast media for any causes within last one month, heart failure (ejection fraction <50%), heart block, atrial fibrillation, end stage renal disease history and refusal to participate the study. Study protocol was approved by the Regional Ethics Committee. A written informed consent was obtained from all patients. CIN was defined by an elevation of creatinine levels 0.5 mg/dl or 25% from baseline within 48-72 hours after contrast media exposure without confounding factors such as hypotension, urinary obstruction and nephrotoxic agents use (16). The patients group was were divided into 2 groups: CIN developed or CIN undeveloped.

Laboratory Parameters

Baseline and post-procedural laboratory parameters within 48-72 hours were obtained and recorded for all participants. Serum glucose, baseline and post-procedural creatinine, total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein and hemoglobin levels were measured. Total amount of contrast media and hydration were recorded for all patients. N-acetyl cysteine (NAC) use was also recorded if it was used.

Echocardiography

Echocardiographic assessment was made by commercially available GE Healthcare Vivid devices with 3s probes for all patients just after coronary angiography procedure. All patient-specific data such as diameter, wall thickness and volumes of left ventricle (LV) was recorded. LV ejection fraction (EF) was calculated by using the modified Simpson method. For the assessment of the pulse wave Doppler records, sample volume was placed at the tips of the mitral leaflets from the apical four chamber view. Transmitral early (E) and late (A) wave velocities and deceleration time (DT) were measured by recorded data. Tissue Doppler Imaging (TDI) was obtained with the sample volume placed at the medial and lateral corner of the mitral annulus from the apical four chamber view. Then, isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT), ejection time (ET), early diastolic mitral annular velocity (Em), late diastolic mitral annular velocity (Am), and peak systolic mitral annular velocity (S) were measured from TDI records at the same cardiac cycles. The mean velocities on TDI were calculated by averaging the velocities from the three cardiac cycles from the recorded data. IVCT is defined as the interval measured from the end of the late-diastolic mitral annular velocity pattern to the onset of the systolic mitral annular velocity pattern; IVRT is the interval measured from the end of the systolic mitral annular velocity pattern to the onset of the diastolic mitral annular velocity pattern and ET is the interval measured from the onset to the end of the systolic mitral annular velocity pattern on the same cardiac cycle.

MPI was assessed by TDI derived parameters. Briefly, it was calculated as the sum of isovolumetric contraction time (IVCT) and isovolumetric relaxation time (IVRT) divided by ejection time (ET) (17).

Statistical analysis

Statistical analyses were performed using the SPSS software (Version 14.0, SPSS, Inc., Chicago,IL). The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov) to assess normal distribution. Continuous variables were presented as mean±standart deviation. Categorical variables were showed as percentage value. Then, student t-test or Mann Whitney-U test was used to analyze continuous variables according to normal distribution status. The Chi-square test was used to analyze categorical variables. A p-value of less than 0.05 was considered to show a statistically significant result.

RESULTS

Basal characteristics of both groups are demonstrated in Table 1. Study population consisted of 51 patients: 13 patients who developed CIN and 38 patients without CIN. Overall incidence for the development of CIN was 25.49%. There was no significant difference between the two groups with regards to age, history of hypertension, diabetes mellitus, prior CAD, smoking status, baseline systolic and diastolic blood pressure level, body mass index and current use of medications such as ACE-inh., ARB, CCB and diuretics. Only female gender was more frequent in CIN developed group (p=0.021). Stable angina pectoris, unstable angina pectoris and/or NSTEMI frequencies were found to be similar in both groups.

Laboratory data and procedural parameters are demonstrated in Table 2. Blood samples collection time after coronary angiography was similar for both groups (p=0.16). Fasting serum glucose, total, low and high density cholesterol and hemoglobin levels were similar in both groups. Baseline creatinine levels were found to be higher in CIN undeveloped group (0.72±0.26 vs 1.1±0.31, respectively, p<0.001). However, post-procedure creatinine levels were found to be similar (0.99±0.3 vs 1.14±0.34, respectively, p=0.12). Creatinine increase ratio was significantly higher in CIN developed group (41.5±28.6 vs 5.7±12.1%, respectively p<0.001). Pre-procedural NAC use and total amount of hydration were found similar between groups. (p=1 and 0.16, respectively). Procedural contrast media amount was similar between groups (133.8±100.3 vs 120.3±112.1, respectively p=0.62).

Standard and M-mode echocardiographic data are demonstrated in Table 3. M-mode parameters such as LV systolic, interventricular septum, posterior wall and left atrium diameter were similar in both groups (p=0.27, 0.1, 0.13, 0.65, respectively). LV diastolic diameter were found to be higher in CIN undeveloped group (p=0.003). Left ventricular systolic and diastolic volume and ejection fraction were not significantly different between the groups (p = 0.3, 0.07, 0.49, respectively). E and A diastolic mitral filling velocities and E velocity deceleration time were not significantly different between groups (p = 0.94, 0.75, 0.11, respectively). E/A ratio found to be similar in both groups (p=0.71). TDI echocardiography data are demonstrated in Table 4. Sm, Em, Am, Em/Am and MPI were similar in both groups (p =0.4, 0.1, 0.085, 0.086, 0.025, respectively).

Table 1. Baseline characteristic data of all patients

		CIN (+) (n=13)	CIN (-) (n=38)	p-value
Age (years)		62.5±6.8	62.4±9.6	0.84
Female, n (%)		6 (46.2)	5 (13.2)	0.021
HT, n (%)		8 (61.5)	29 (76.3)	0.31
DM, n (%)		8 (61.5)	21 (55.3)	0.7
Prior CAD, n (%)		10 (76.9)	23 (60.5)	0.33
Tobacco use, n (%)		3 (23.1)	7 (18.4)	0.7
ACE-inh, n (%)		5 (38.5)	14(36.8)	1
ARB, n (%)		3 (23.1)	9 (23.7)	1
Diuretics, n (%)		4 (30.8)	10 (26.3)	0.73
CCB, n (%)		4 (30.8)	9 (23.7)	0.71
SBP (mmHg)		134.6±17.6	131.6±14.7	0.66
DBP (mmHg)		77.7±8	77.9±9	0.91
BMI (kg/m^2)		29.9±3.6	29.6±5.0	0.86
Admission diagnosis (%)	SAP	5 (%38.5)	20(%52.6)	0.65
	UAP	7(%53.8)	15(%39.5)	
	NSTEMI	1(%7.7)	3(%7.9)	

Abbreviations: ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker, BMI: Body mass index, CAD: Coronary artery disease, DBP: Diastolic blood pressure, DM: Diabetes mellitus, HT: Hypertension, NSTEMI: Non ST elevated myocardial infarction, SAP: Stable angina pectoris, SBP: Systolic blood pressure, UAP: Unstable angina pectoris,. Continuous data are shown as mean ± standard deviation, and categorical data are shown as percentages.

Table 2. Laboratory and procedural parameters in patients with CIN developed and undeveloped group

	CIN (+) (n=13)	CIN (-) (n=38)	p-value
Glucose (mg/dl)	173.3±88	112.6±34	0.13
Total cholesterol (mg/dl)	171±39	163±38.1	0.64
LDL-K (mg/dl)	124±45.4	111.9±35.8	0.48
HDL-K (mg/dl)	40±11.3	40.3±9.6	0.79
Triglyceride (mg/dl)	139.1±82.2	150.3±102.8	0.94
Hemoglobin (g/dl)	13.5±1.4	13.4±1.6	0.86
Baseline creatinine (mg/dl)	0.72±0.26	1.1±0,31	<0.001
Post procedural creatinine (mg/dl)	0.99±0.3	1.14±0.34	0.12
Creatinin increasing ratio (%)	41.5±28.6	5.7±12.1	<0.001
Hydration amount (L)	1.58±0.39	1.36±0.98	0.16
Contrast media amount (ml)	133.8±100.3	120.3±112.1	0.62
Blood samples collection time (hour)	76.8±15.7	70.7±17.8	0.16
NAC use, n (%)	1 (%7.7)	3 (%7.9)	1.0

Abbreviations: HDL: High density lipoprotein, LDL: Low density lipoprotein, NAC: N-Acetyl cysteine, Data are shown as mean ± standard deviation Continuous data are shown as mean ± standard deviation, and categorical data are shown as percentages (n=13, n=38 respectively).

Table 3. Standard and M-mode Echocardiographic values of all patients

	CIN (+) (n=13)	CIN (-) (n=38)	p-value
LVSD (mm)	29.1±3.7	30.5±3.7	0.27
LVDD (mm)	44.5±4.2	48.7±3.7	0.003
LVSV (ml)	33.5±7.5	37.0±11.7	0.3
LVDV (ml)	84.2±11.1	95.7±24.6	0.07
IVS (mm)	11.2±1	12±1.6	0.1
PW (mm)	10.5±1.3	11.1±1.2	0.13
Ejection Fraction (%)	60.4±5.3	61.5±5.3	0.49
LA (mm)	35.9±2.6	36.2±3.2	0.65
E (cm/s)	64.9±16.4	64.1±14	0.94
A (cm/s)	76.3±18.5	79.3±18	0.75
DT (ms)	233.8±47.9	251.6±46	0.11
E/A	0.9±0.3	0.8±0.3	0.71

Abbreviations: A: Late diastolic mitral filling velocity, DT: E velocity deceleration time, E: Early diastolic mitral filling velocity, IVS: Interventricular septum, LA: Left atrium, LVDD: Left ventricular diastolic diameter, LVDV: Left ventricular diastolic volume, LVSD: Left ventricular systolic diameter, LVSV: Left ventricular systolic volume, PW: Posterior wall.

Table 4. Tissue Doppler Echocardiographic imaging data of all patients

	CIN (+) (n=13)	CIN (-) (n=38)	p-value
Sm (cm/s)	7.3±1.5	7.8±2	0.4
Em (cm/s)	8±2.2	8.1±2.5	0.1
Am (cm/s)	10.3±3.2	10.3±2.6	0.85
Em/Am	0.9±0.4	0.8±0.3	0.86
DT	93.7±28.8	87.4±19.1	0.83
MPI	0.42±0.09	0.46±0.12	0.25
Ejection Fraction (%)	60.4±5.3	61.5±5.3	0.49
LA (mm)	35.9±2.6	36.2±3.2	0.65

Abbreviations: A: Late diastolic mitral annular wave, DT: E velocity deceleration time, Em: Early diastolic mitral annular wave, MPI: Myocardial performance index, Sm: Mitral annular systolic wave, Continuous data are shown as mean ± standard deviation.

DISCUSSION

In this study, a possible relationship between the development of CIN and MPI was firstly assessed in patients at risk for nephropathy who underwent coronary angiography or PCI. We could not find any difference for MPI between patients with CIN and those without.

During the last decade, coronary angiography and intervention procedures has significantly increased worldwide. In addition, the number of coronary intervention for more complex lesions such as bifurcation lesion and chronic total occlusion has spread that means contrast media use has rapidly increased. This situation increases the risk for the development of CIN, especially in patients at risk for nephropathy. Until today, patient and procedure related risk factors predicting the development of CIN were defined by previous studies. In our study, basal creatinine levels were higher in CIN undeveloped group than CIN developed group but creatinine increasing ratio was higher in CIN developed group. In both groups, the distribution of factors that may affect renal function values were balanced such as diabetes, hypertension and age. As is known, CIN is the rate of increase in creatinine rather than basal creatinine level which is important in the definition. The results obtained in our study support this definition.

The well-known risk factors for the development of CIN are the presence of low basal creatinine clearance (<60 ml/min), diabetes mellitus, chronic heart failure, hypertension and peripheral vascular disease and total amount of contrast media use (13). Although, these risk factors are taken into accounts at pre-procedural period, CIN can still develop. Thus, additional risk indicator(s) need to be identified to reduce the risk, further. By this study, we aimed to evaluate the effect of MPI on the development of CIN as a possible risk factor.

MPI which was firstly defined in 1995 by Tei C. offers the assessment of left ventricular systolic and diastolic function, simultaneously (15). As widely accepted, it calculated by sum of isovolumetric contraction and relaxation time divided by ejection time obtained from tissue Doppler imaging. One of the main advantages of MPI is its ability to demonstrate subclinical dysfunction in which turn reflects early myocardial dysfunction (17,18). This situation is especially important for symptomatic subjects without overt heart failure. Therefore, in this study, we basically hypothesized that subclinical dysfunction can be influential on the development of CIN. MPI may have prognostic significance in different clinical conditions. MPI has an important prognostic value in cardiovascular diseases such as coronary artery disease, heart failure, myocardial infarction and heart valve diseases and is a parameter that can be used in clinical follow-up (19). It has been shown that MPI can be a useful non-invasive follow-up parameter in heart failure patients after cardiac resynchronization therapy (19). MPI can show subclinical dysfunction of the myocardium in the early period, while standard echocardiography parameters are normal. Left ventricular systolic and diastolic functions, which are considered normal with standard echocardiographic parameters, were found to be impaired when evaluated with MPI in endocrinological diseases such as Cushing and primary hyperparathyroidism without structural heart disease (20,21). We aimed to evaluate MPI in patients who underwent coronary angiography and / or percutaneous coronary intervention and were at risk for CIN development. However, impaired LV function was a predictor of CIN development, but we concluded that MPI was not an early predictor of CIN development in patients with preserved ejection fraction.

A positive correlation between serum creatinine levels and MPI has been shown in diabetic patients with preserved left ventricular function without structural heart disease. MPI can also be a sensitive marker in the diagnosis of ventricular dysfunction in subclinical conditions such as without apparent renal function disorder (22). In another study, it was concluded that there was no relationship between MPI and GFR in hypertensive patients (23). In the light of abovementioned studies, we can say that the relationship between MPI and renal functions is not clear. As a result of our study, we concluded that MPI is not a predictor of CIN development in high-risk patients.

We could not find any difference for MPI between subjects with and without CIN in this study. A possible explanation of this situation may be that MPI may not have an effect on cardiac output. Thus, renal blood perfusion can be preserved in these patients. According to our results it can be said that MPI is not an influential factor for the development of CIN in subjects without overt hearth failure.

Limitations

The small sample size might have decreased the power of our study; hence it is possible that a higher number of patients might have differentiate the results. Number of patients who met the definition of CIN developed was very low, and that could have caused the Tei index values being statistically insignificant. Also our study had either CIN development risk factors or Tei index effecting factors well balanced. Therefore, this will increase our study strength.

CONCLUSION

Our results show that Tei index did not predict CIN development risk. It's reasonable to conclude that demographic and other risk factors well balanced groups increased our study strength. Results obtained in this preserved ejection fraction patient group might explain a possible cause of unrelated test results. Nevertheless, our results should be supported by additional clinical trials.

Competing interests: The authors declare that they have no competing interest.

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