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FREQUENCY OF CONTRAST NEPHROPATHY AND DETERMINATION OF THE RISK GROUPS IN PATIENTS UNDERGOING CORONARY ANGIOGRAPHY

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Introduction

Coronary angiography is an invasive diagnosis method which is accepted as a golden standart both to diagnose coronary heart diseases and to guide the treatment nowadays. It has a vital significance to realize the complications occurring during the procedure or in the post-process term and to determine on the treatment as soon as possible in case of necessity for coronary angiography. It is possible to see contrast induced nephropathy (CIN) because of the involved contrast media after the process. The most important possible non-idiosyncrasic reaction is contrast induced nephropathy after using contrast media through a intravascular way [1]. Nephropathy, which develops as a result of the increase in the serum creatinine without considering the need for a clinical symptom or hemodialysis, is defined as contrast induced nephropath [2].

In many institutions, the risk analysis is not applied to the patients and there is not a consistent practice for CIN. It is known that the serum creatinine value is not checked before the procedure and 48 hours after the implementation regularly in the patients given contrast media. If the risky patients for CIN are detected via attentive clues and preventing

procedures are standartized and made effective, an important opportunity is gained to decrease the rate of mortality and morbidity. It is detected in a research taking place in a radiology clinic that only 20% of the patients and approximately 60% of the patients in the condition of diabetes which is a high risk for CIN were checked for the serum creatinine value before the contrast media procedure. And it indicates that many patients who have high risk are not detected before the procedure. It is possible to detect this risky group at least by asking some simple questions and laboratory practice and to follow-up them after the procedure. A slight increase in the serum creatinine level may increase the patient's mortality and mobility. Detecting the risky patients and fulfilling profilactic treatment (e.g prehydration) will decrease the possible problems [3-6].

We have aimed to make a research for the risk factors of CIN in the patients undergoing coronary angiography and the ones in the intensive care unit with the diagnosis of acute coronary syndrome; to classify the patients according to their risk factors and to detect the frequency of the CIN. Consequently, the patients who have a risk for CIN will be

detected by using risk scoring tables and the susceptibility to take the protective measures will be increased by applying protective treatment (acute renal failure, the need for dialysis, staying in hospital and increase in mortality).

Material and method

93 patients who lined in TC Başbakanlık Bezm-i Alem Valide Sultan Vakıf Gureba Hospital Coronary Intensive Care Unit (KYBÜ) with the diagnosis of acute coronary syndrome between November 2008 and 2009 were involved in our study. The diabetic, the ones in cardiogenic shock and who have crucial renal and hepatic failures, the ones who did not apply us for the urea and creatinine measurement on the third day of the procedure were not involved in the study. The analysis of the patients were taken by considering the risk factors. The level of glucose, urea, creatinine, uric acid, hemoglobin A1c, C-reactive protein; liver function tests, thyroid function tests, lipid profile, estimated glomerular filtration speed (eGFR), full urinalysis, hemogram were checked and the level of urea and creatinin were measured on the third day. Whether they took thrombotic treatment after the acute coronary syndrome, they smoke, were diagnosed as hypertension or diabetes mellitus (DM) or not were recorded. Cardiac failure was searched, the ones who have a background of Class-3 and Class-4 according to the New York Heart Committee and/or pulmonary edema experience were involved in scoring. According to the World Health Organisation (WHO) criteria, the level of hematocrit is accepted as anemic in men <39% and in women <36%. Estimated glomerular filtration speed was calculated via MDRD formula. In the light of these findings, the patients were classified according to the risk scoring table prepared by Mehran and his colleagues. The frequency of the patients who have low, middle and high risk in the whole patient group were detected. On the third day of the coronary angiography, the level of urea and creatinine were measured and the frequency and the percentage of the contrast nephropathy development were estimated. The one who developed contrast nephropathy were sent to nephrology polyclinic and their follow-ups were done here. Under the light of the findings, the influence of gender, diabetes, anemia, the level of eGFR, smoking, urea level above 50 mg, creatinine level above 1mg/dl, cholesterol-LDL-triglyceride level, age above 75 were studied. The meaningful data was shown in the tables.

This study was approved by Bezm-i Alem Valide Sultan Vakıf Gureba Hospital Local Ethic Board. Each patient was informed about the study and their approvals were taken with their signatures. For descriptive statics, average deviation \pm (mini-

mum and maximum values) and cardinal numbers (percentage); for group comparisons, Students t, Mann-Whitney U, Fisher exact tests and ki-kare tests were used. Besides, Odd's ratio (OR) and 95% confidence interval (95% CI) values were estimated. Statistical analysis was made with SPSS for Windows 12.0 programme and if the p value is below 0.05, it is accepted as meaningful statistically.

Findings

It was detected that 93 patients included into the study consisted of 51 males (54.8%), 42 females (45.2%); 22 patients suffering from contrast induced nephropathy (CIN) consisted of 13 males (59.15), 9 females (40.9%). It is found out that the gender does not have a meaningful influence on CIN development statistically ($p=0.831$) (table 1). The age average is estimated as 62.51 ± 10.81 (37-90). The age average in the cases with contrast nephropathy is 69.05 ± 10.30 and in the contrary case the age average is 60.48 ± 10.20 ($p=0.001$). It is seen that 66.7% of the patients who are above 75 and 19.0% of the patients who are 75 and below 75 suffered from CIN ($p=0.005$). Diabetes mellitus (DM) was found in 44 patients (47.3%) and 15 of these patients (34.1%) had CIN. 49 patients (52.7%) were not diagnosed with diabetes and CIN was detected in 7 of them (14.3%) ($p=0.046$). Anemia was detected in 43 patients (46.2%) and CIN developed in 17 of these patients (39.5%). Anemia is not determined in 50 patients (53.8%) and CIN developed in 5 (10%) of these patients ($p=0.01$). The eGFR level of the patients were measured and it was seen that the result was 40-60 ml/min/1.73 m² in 13 (14%) patients. CIN was found in 5 (38.5%) of these patients ($p=0.316$). The average creatinine level of the involved patients were detected as 0.85 ± 0.21 (0.5-1.4). In the cases developing CIN, the level was found as 0.82 ± 0.26 and in the contrary cases the level was found as 0.86 ± 0.19 ($p=0.165$). There were 19 patients (20.4%) whose creatinine levels were above 1 mg/dl and six of them (31.6%) developed CIN. There were 74 patients (79.6%) whose creatinine levels were under 1 mg/dl and 16 of them (21.6%) developed CIN ($p=0.543$). The average urea measurement level of the patients was 40.34 ± 14.84 (18-78) and this number was 40.45 ± 14.57 in the patients who developed CIN, 40.31 ± 15.03 in the ones who did not develop CIN ($p=0.867$). Of 22 (23.7%) patients whose urea level was above 50 mg, six of them (27.3%) developed CIN.

Of 71 patients (76.3%), 16 of them (22.5%) developed CIN ($p=0.865$). With regard to smoking, it was found that 63 patients (67.7%) had a habit of smoking and 30 patients (32.3%) did not. In both of the groups, 11 patients (17.5%; 36.7%) developed CIN ($p=0.076$) (table 1).

Table 1

The influence of risk factors on the development of contrast induced nephropathy

CIN n (%)	Available	Not available	P	OR	% 95 CI
Gender					
Females	33 (%78.6)	9 (%21.4)	0.831	0.797	0.302-2.102
Males	38 (%74.5)	13 (%25.5)			
Age					
75 and below 75	68 (%81.0)	16 (%19.0)	0.005	8.50	1.917-37.680
Above 75	3 (%33.3)	6 (%66.7)			
Diabetes Mellitus					
Not available	42 (%85.7)	7 (%14.3)	0.046	3.103	1.125-8.558
Available	29 (%65.9)	15 (%34.1)			
Anemia					
Not available	45 (%90.0)	5 (%10.0)	0.001	5.885	1.942-17.818
Available	26 (%60.5)	17 (%39.5)			
eGFR					
0	63 (%78.8)	17 (%21.3)	0.316	2.316	0.671-0.7997
2	8 (%61.5)	5 (%38.5)			
Creatinine					
1 mg/dl and below	58 (%78.4)	16 (%21.6)	0.543	1.673	0.549-5.100
1 mg/dl and above	13 (%68.4)	6 (%31.6)			
Urea					
50 ml and below	55 (%77.5)	16 (%22.5)	0.865	1.289	0.433-3.838
50 ml and above	16 (%72.7)	6 (%27.3)			
Smoking					
Not available	19 (%63.3)	11 (%36.7)	0.076	0.365	0.136-0.981
Available	52 (%82.5)	11 (%17.5)			
Total	71 (%76.3)	22 (%23.7)			

The average biochemical values of the patients were detected as cholesterol 186.9 ± 46.702 (100-364), LDL 117.83 ± 47.094 (45-391), triglyceride 128.19 ± 68.463 (35-398), uric acid 5.617 ± 1.71 (2.3-9.9). The average of the CIN developed patients and the non-developed ones and their p values were shown in table 2. It is discovered that the level of cholesterol, LDL, triglyceride and uric acid do not have an influence on the development of CIN. Estimating the risk level of the patients, risk scoring table of Mehran and his colleagues was used [11]. The risk groups and the percentage of the CIN development were shown in table 3. As seen via these findings, CIN development in low risk group is 12.3%, in middle risk group is 38.70% and in high risk group is 60%. Considering all of the patients, CIN was seen in the rate of 23.7%.

Table 2

The influence of cholesterol, LDL, triglyceride, uric acid levels on contrast induced nephropathy (CIN)

	CIN	N	Average	Standard deviation	P
Cholesterol	Not available	71	185.06	43.30	0.632
	Available	22	192.86	57.06	
LDL	Not available	71	116.73	48.89	0.418
	Available	22	121.36	41.57	
Triglyceride	Not available	71	123.39	61.32	0.464
	Available	22	143.68	87.57	
Uric Acid	Not available	71	5.55	1.72	0.483
	Available	22	5.82	1.67	

N – number of the people, **LDL** – low density lipoprotein.

Table-3

The percentage of patients' risk groups and development of contrast induced nephropathy (CIN)

		CIN n (%)	
		Not available	Available
Risk level	Low	50 (%87.7)	7 (%12.3)
	Middle	19 (%61.3)	12 (%38.7)
	High	2 (%40.0)	3 (%60.0)
Total		71 (%76.3)	22 (%23.7)

Discussion

Contrast induced nephropathy is the common third reason of acute renal failure which acquired in hospital setting [1, 2, 7]. The patients who have a high risk of contrast induced nephropathy are either the one who have renal function disorders or diabetes or congestive heart failure. The other risk factors are growing old (>75), being a female, dehydration, anemia and using too much contrast media.

Preexisting renal function disorder and diabetes are accepted as the most significant risk factors. Due to the synergic influence of these two factors, nephropathic patients with diabetes mellitus constitute the most risky group [1, 6, 8-10]. In a study made by Parfrey and his colleagues, it is found out that the CIN incidence in non-diabetic normal renal functioning patients is 2%, it is 7% in the patients with type DM 1 and not having a renal failure, and it is 50% in patients who have type 1 DM and renal failure [4]. 15 (34.1%) of the 44 diabetic patients were found to develop CIN and it was found meaningful p:0.046. Previous renal failure is a certain reason of CIN. In a study made by Chen and his colleagues, CIN incidence was found meaningfully higher in a group of which creatinine level is abnormal (serum creatinine ≥ 1.5 mg/dl) than the group which had a normal level (37.68%, 6.25%, p<0.001) [8]. In the study, a big difference could not be found considering the CIN development among the patients whose creatinine level were 0.5-1 and 1-1.5. In many studies, it was indicated

that the development of incidence of CIN increased in the patients who were above 75. Besides, it was seen that CIN developed in the 66.7 % of the patients who were above 75 (p:0.005).

The role of gender on CIN is controversial. Studies yield different results [6,10]. A meaningful difference could not be found between the males and female patients (p:0.83). In a study on 9726 patients undergoing to percutaneous coronary intervention made by Mehran and his colleagues, 21% of the anemic patients developed CIN [11]. 17 of the 43 anemic patients (39.5%) developed CIN (p:0.001). The relation between smoking and CIN was looked for, but a meaningful relation could not be found (p:0.076). Moreover, the relation between levels of urea, creatinine, cholesterol, LDL, triglyceride, uric acid and KMN was studied, but a meaningful relation could not be found similarly.

The primary approach to prevent nephropathy resulted from contrast media is to observe patients' present features systematically and scoring the risk grades. Risk scoring systems were suggested to foresee frequency of CIN development after percutaneous coronary intervention (PCI).

Lisstro F. and colleagues classified CIN risk development as low, middle and high risk groups [12]. Mehran and his colleagues identified eight independent risk predictors according to the risk scoring system based on the prospective data gained from 9726 patients undergoing PCI.

There was detected a linear relation between the total number of these risk factors and CIN frequency (şekil-1) [11]. CIN developed in 7 of 57 low risk patients (12.3%), 12 of 31 middle risk patients (38.7%) and 3 of 5 high risk patients. Totally, 22 out of 93 patients (23.7%) developed CIN. Looking at Mehran and his colleagues' study, it is seen that CIN developed in the rate of 7.5% in low risk group, 14% in middle risk group, 26.1% in high risk group and 57.3% in very high risk group.

In total, 13.1% of the patients developed CIN. The angiography was given to the patients in the out-patient services where they had been sent to. In spite of the suggestion, no protective procedure was applied to the patients before or after the procedure.

Whereas Mueller and his colleagues detected a CIN frequency of 0.6% in a group which was hydrated with isotonic liquid, they found the CIN frequency as 2.7% in a group which was given semi-isotonic liquid in a study made with 1620 patients [13]. Hydrating the patients to prevent the development of CIN is definitely necessary.

In a study, it was found that the mortality in hospital is 22% with the patients developing CIN [14].

The same measurement is 21.4% after using contrast media in a different study made by Marenzi and his colleagues (15). Permanent hemodialysis rate may increase to 12% with the high risk patients.

As a result of the study on 1826 patients undergoing to percutaneous intervention made by McCullough and his colleagues, the frequency of CIN requiring hemodialysis is <1%, and in hospital mortality is 35.7%, survival for two years is 18% [1]. This rate with the patients who did not develop CIN is just 1.4%. The mortality rate in the first and fifth years of the patients who developed contrast induced nephropathy and left the hospital alive are 12.1% and 44.6%. Although these rates do not directly reflect the prognosis resulted from using contrast media, it should be considered that preventing the development of contrast induced nephropathy, which is an important element for the development of acute renal failure, is a significant factor to heal the prognosis.

Conclusion

CIN is one of the most important reasons of acute renal failure developing in a hospital setting. Radiologic applications which do not require contrast media should be given priority at the first place, especially with the highest risk patients who suffer from renal failure (serum kreatinin >1.5 mg/dl). If using contrast media is absolutely necessary, then, nephrotoxic medicine has to be suspended, losing water and salt should be avoided and low dose osmolar non-ionic contrast media should be preferred.

Liquid treatment, the most valid and presently approved method used to prevent contrast induced nephropathy is a prophylactic procedure which is used very often since it is easy and cheap. CIN can be mostly prevented by enlarging the volume through giving 0.45% saline infusion – the urine level should be minimum 75 ml/min – 12 hours before the procedure and maintaining it for 12-24 hours after the procedure to the high risk patients undergoing the procedure requiring high dose contrast media such as patients who have previously known renal failure, old patients, having dehydration problem and having multiple risk factors in particular. Renal functions of the high risk patients have to be monitored after the contrast procedure for 48-72 hours. Since incidence rate is low, the patients who do not have risk factors do not have to be monitored. The first thing to be done is to scoring the risk in order to determine the high risk patients in the process of preventing the development of CIN and treatment.

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