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Research Article

The Value of Preoperative Amino Terminal Pro Brain Natriuretic Peptide Levels in Showing Post-Operative Kidney Functions in Patients Having Undergone Coronary Artery Bypass Grafting Surgery

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Abstract

Objectives: Natriuretic peptides are proteins secreted by myocardium as a response to the volume and/or pressure load; especially B type Brain Natriuretic Peptide (BNP) has started to be used for the last two decades in issues such as mortality, morbidity after coronary artery surgery and estimation of major adverse cardiac issues, particularly heart failure. The purpose of this study is to research on the activity of BNP in predicting the risk of kidney failure after coronary artery bypass grafting.

Methods: In this study, 40 patients (33 males/7 females) whose ejection fraction was between 30% and 50% were prospectively examined. These patients were among ones having undergone coronary artery bypass grafting by using a cardiopulmonary machine. Blood was venously taken from patients preoperatively, on the second postoperative day and in the sixth postoperative month in order to examine BUN (blood urea nitrogen), creatinine and plasma NT-proBNP.

Results: It was observed that values of NT- proBNP examined preoperatively were negatively correlated with both creatinine clearances before the operation (CrCl pre-op) (p=0.031) and the values of creatinine clearance examined on the second postoperative day (CrCl 2. day) (p=0.014).

Conclusion: On the basis of our results, we are of the opinion that the preoperative BNP value might be a leading parameter in renal monitoring in the early phase after the operation and in the treatment plan. We need prospective studies with high numbers of patients in this aspect.

Keywords: Brain natriuretic peptide, acute kidney injury, creatinin clearence, cardiac surgery

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Natriuretic peptides are proteins secreted by myocardium as a response to the volume and/or pressure load; especially B type Natriuretic Peptide (BNP) has started to be frequently used during the last two decades particularly in the diagnosis of heart failure.[1–3] A lot of studies revealing the determinative activity of BNP in such issues as mortality, morbidity after coronary artery surgery, estimation of major adverse cardiac issues have been published.

One of the leading types of morbidity that is most frequently observed after the operation of coronary artery bypass grafting is acute renal failure (ARF) in the frequency of 25.9% and 24.9% on the basis of the criteria of AKIN (Acute Kidney in-

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jury network) and RIFLE (Risk/Injury/Failure/Loss/End-stage) although this changes on the basis of definition.[4,5] Secondary prerenal and tubulotoxic neph-ropathic pictures after operation appear before us in the clinic of acute renal failure in the postoperative stage. The fact that diabetes, hypertension and the common atherosclerosis bear a higher risk for pos-toperative renal failure has been revealed through a lot of studies.[6] However, there is no other labo-ratory test than correlated tests with renal function such as Creatinine clearance, Cystatin C, Neutrop-hil gelatinase associated lipocalin (N-GAL) that are used in preoperative estimation of postoperative renal functions and that might be used as a tool in risk grouping and that might deteriorate quickly. Risk identification systems such as Euroscore, parsonnet are away from fulfilling this purpose both because they are affected by renal functions and because they are focused on mortality.

A relationship between BNP and postoperative outcomes following off pump and on pump coronary artery bypass grafting was studied previously.[6] Kato et al.,[7] found a correlation between preoperative BNP and postoperative renal replacement therapy requirement.

The purpose of this study is to determine the role of BNP in the estimation of renal functions after coronary artery bypass grafting in coronary artery patients with an ejection fraction of between 30% and 50% and to determine the risk and to research on its correlation with creatinine clearance.

Methods

40 patients having undergone open heart surgery in our clinic, whose Left Ventricle Ejection Fraction (LVEF) was between 30% and 50% were included in our study. The Ethics Committee Approval (Istanbul University Institute of Cardiology Institutional Ethics Commitee) and informed consent were provided. 33 of the patients were male, 7 of them were female (K: 17.5%, E: 82.5%). The age average was 62.15±11.27 (min: 46, max: 77). The average creatinine value of the patients was 0.93±0.18 mg/dl; the patients with renal failure were excluded from the study. Levosimendan had started to be given to 9 of the patients (22.5%) in the preoperative stage according to decision of cardiovascular team. 19 of the patients were diabetic (47.5%), 12 of them were smokers (30%), 15 of them were hypertensive (37.5%). The rhythm of 11 of the patients before the operation was atrial fibrillation (27.5%). The demographic data of them are summarized in Table 1. Before the operation, on the 2. postoperative day and in the 6. postoperative month, blood was venously taken from the patients in order to examine BUN (blood urea nitrogen), creatinine and plasma NT-proBNP. Postoperative 2nd day was choosen for detection of early renal failure and predictive value of BNP and postoperative 6th month for late relationship. Samples for NT-proBNP were venously taken by using a cold vacutainer containing ethylene-tetra-acedic-acid after the patient got a rest of 30 minutes in a semi-lying position. In the subsequent stage, the samples were centrifuged for 20 minutes and their plasma was frozen at -80˚c until evaluation. Measurements of Plasma NT-proBNP were carried out with solid phase dual chemiluminescent immunometric assay IMMULITE 1000 TurboNT-proBNP kits. (Siemens Healthcare Diagnostic Products Ltd. UK. Catalog#: LSKNT1, manufactured under license from ROCHE Diagnostic GmbH).

Table 1. Demographic data (n=40)

	n	%
Female/Male	7/40	17.5
Age	62.15±8.44	
Pre-op EF	39.38±5.9	
Pre-op LVESD	43.5±7.25	
DM	19/40	47.5
Smoking	12/40	30
HT	15/40	37.5
AF (n)	11/40	27.5

AF; DM: Diabetes mellitus; HT: Hypertension; EF: Ejection functions; LVESD0 Left ventricle end systolic dimension.

Statistical Analysis

Statistical analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA) version 16.0. Continuous variables are given as mean±standard deviation and categorical variables as n and percentage values. Student t test, chi square test and mann whitney u test were used in comparison of variables. Pearson correlation analysis carried out between Creatinine Clearance and BNP values. P value <0.05 was accepted as significant.

Exclusion Criteria

Patients having undergone a cardiac surgical attempt before, patients with an ejection fraction of <30%, >50%, those with a serum creatinine value of >1.2 mg/dl (normal upper limit of measurement), those with experienced kidney disease, those with pulmonary embolism, those with history of pulmonary edema were excluded from the study.

Surgical Technique

All of the patients underwent the operation of coronary artery bypass grafting under cardiopulmonary bypass. For all of them, LITA (Left Internal Thoracic Artery) was used as grafting to left anterior descending coronary artery (LAD), vena safena magna was preferred in other arteries. Operative data is specified in Table 2.

Results

40 consecutive patients in total were included in the study. The average EUROSCORE in the patient group is 4.4±1.9; no hospital mortality was observed in examined cases.

Creatinine clearances of the patients showed significant change between the preoperative stage and the second postoperative day and the sixth postoperative month. ($p<0.05$) Average values and change are indicated in Table 3.

While the average preoperative BNP value was 1044.54±413.27 pg/ml, the value for the second postoperative day was 5010.05±1168, 43 pg/ml, the value for the sixth postoperative month was 1149.16 pg/ml. It was found that the preoperative value and the value for the second postoperative day was significantly different ($p<0.05$).

In the comparison between BNP values and creatinine clearance based on duration, a negative correlation between 2nd postoperative day CrCl and preoperative BNP value and preoperative CrCl was determined. In a similar way, a negatively significant correlation was found between BNP value on the second postoperative day and CrCl values of the second preoperative and postoperative days (Table 4). No relationship between preoperative NT-proBNP values and creatinine clearances of the sixth postoperative month was determined (p=0.151). In a similar way, there was also no relationship between NT-proBNP values examined on the second postoperative day and creatinine clearances of the sixth postoperative month (p=0.052). There was also no relationship between NT-proBNP values examined in the sixth postoperative month and creatinine clearances of the preoperative stage, of 2nd day and of 6th month (respectively p=0.060, p=0.507, p=0.174).

No relationship was found between pre-op EF values of patients (min: 30%, max: 50%, mean: %39.38±5.9), post-op EF values of them (min: 20%, max: 62%, mean: %42.95±9.7) and their creatinine clearances of preoperative stage, of second postoperative day and sixth postoperative month.

In a similar way, no statistical significance was determined between the pre-op Left Ventricle End Systolic Dimension (LVESD) (min: 29 mm, max: 59 mm, mean: 43.50±7.25 mm), post-op LVESD (min: 30 mm, max: 55 mm, mean: 40.37±6.882 mm) values and pre-op, post-op 2. day and post-up 6. month creatinine clearances. The average CBP duration was 135.375±35.08 min (min: 57 min, max: 198 min) and X clamp duration was averagely 67.27±23.72 min (min: 21 min, max: 111 min). Through these parameters examined, no relationship was determined between pre-op, post-op 2. day and post-op 6. month creatinine clearances.

A negatively powerful correlation was determined between post-op 2. day and 6. month creatinine clearances and the ages of the 40 patients examined in this study whose average age was 62.15±8.44 (respectively; $p<0.005$, $p<0.005$).

Also, the number of anastomoses and post-op 2. day and 6. month creatinine clearances were correlated with each other (respectively; p=0.016, p=0.012).

Table 2. Operative data

CPB (minute, dk)	135.375±35.08
X Clamp (minute, dk)	67.27±23.72
Number of anastomoses (n)	3.58±0.9

CPB.

Table 3. Average values of creatinine clearances

	Min	Max	Average	SD
CrCl pre-op	44.0	139.9	73.220	20.33
CrCl post-op 2nd day	29.3	104.6	63.587	17.20
CrCl post-op 6th month	43.3	124.0	67.975	16.95

CrCl

Table 4. Results of Pearson correlation analysis carried out between creatinine clearance and BNP values

	CrCl pre-op	CrCl post-op 2nd day	CrCl Post-op 6th day
BNP	r=-0.341	r=-0.384	r=-0.231
Pre-op	p=**0.031**	p=**0.014**	p=0.151
BNP	r=-0.332	r=-0.464	r=-0.310
Post-op 2nd day	p=**0.037**	p=**0.003**	p=0.052
BNP	r=-0.300	r=-0.108	r=-0.219
Post-op 6th month	p=0.060	p=0.507	p=0.174

BNP: Brain natriuretic peptide.

Discussion

Natriuretic peptides are most often used in the differential diagnosis of cardiac-originated dyspnea in practice; it has been benefited from in time in the diagnosis of many manifestations and monitoring of their prognosis.[9–14] From the standpoint of cardiac surgery, the close relationship of pre-op BNP values with postoperative stay-at-hospital duration, mortality and morbidity has been shown.[15] In this study, what was researched was the determinative quality of the pre-op measurement of BNP value in the estimation of early and late renal functions in the postoperative stage. The significant relationship of the measurements of BNP value carried out on the second preoperative and postoperative days with both preoperative Creatinine Clearance and second postoperative day Creatinine clearance value

was found. This data might make one think that preoperative BNP value might be a determinant for postoperative kidney functions and about the prognostic importance of the postoperative value.

Perhaps the most important problem encountered in the clinic after the operation in the field of cardiac surgery is acute kidney failure. The impact of acute kidney damage on both early and late mortality after heart surgery has been shown in a lot of studies.[15–19] While the frequency of acute kidney damage after heart surgery changes depending on definition, it is indicated between 12% and 48.5%.[16,20–24] Lassnigg et al.[19] have shown the relationship of an increase of 0.3 mg/dl in the serum creatinine value with increased morbidity and mortality. Apart from this, it is specified that in patients receiving postoperative renal replacement treatment, mortality reaches up to 25%.[25–27]

There are no criteria to be used for the purpose of determining in advance the risky patient group with organ failure observed so frequently, having an important impact on both morbidity and mortality. Various researchers have developed clinical scoring systems to be used in determining the postoperative risk of acute kidney damage. The scoring systems commonly used are Cleveland Scoring System, Mehta Scoring, Simplified Renal Index; Cleveland scoring comes to the fore in the comparison of Englberger and his/her team in terms of being the discriminative force.[28] In the model Pannu et al.[29] published, which is one of the risk identification systems released recently, congestive heart failure, Canadian angina scoring, proteinuira, hemoglobin, procedure, the urgency of the operation, the existence of diabetes and GFR value were found to be the independent risk factors. In the model of Che et al.,[30] risk determinants included in the system are age, hypertension, hyperuricemia, low postoperative cardiac capacity, cardiac surgery experienced before, prolonged duration of operation, postoperative central venous pressure. What both models have in common is that they are based on data that can easily be obtained and that they can be carried out just next to the patient. Both systems have a decisiveness that is equivalent to Cleveland Risk Scoring, the most often used model in the comparison of predictive values.[29,30]

Preoperative biochemical parameters have been used by a lot of researchers in predicting postoperative acute kidney damage after cardiac surgery. While there are a lot of new biomarkers, the parameters still most commonly used are serum creatinine value and glomerular filtration speed. The creatinine value is regarded as one of the most determinative factors in predicting mortality after cardiac surgery beyond the fact that it predicts acute renal failure. For this reason, it is one of the key elements of risk identification systems most commonly used.[31] Depending on the formula used, GFR may alter up to 48 hours before serum creatinine value in acute renal failure. If the GFR value is <60 before the value of creatinine changes, it is regarded as the phase of occult renal failure. The fact that the value of creatinine is affected by a lot of factors apart from renal functions, that it changes depending on age in addition to the fact that it is by itself insufficient in the occult stage, decreases its predictive value in comparison with GFR. The relationship of occult renal failure with mortality and morbidity after cardiac surgery has been demonstrated.[31] For this reason, our study was based on creatinine clearance whose creatinine value is closer to its GFR value.

During the last two decades, neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), kidney injury molecule-1 (KIM-1) tubular damage marker, cystatin C have started to be used as more successful markers than creatinine in predicting GFR. In predicting tubular damage, NGAL comes to the fore due to the fact that it acts quickly and that it is selective.[32]

IL-8 is among proinflammatory cytokines; it has been shown to act more quickly than creatinine in acute kidney damage. However, a consensus hasn't yet been reached related to its cut-off value and selectivity.[33]

KIM-1 bears a diagnostic value that is slower. Cystatin C must be adjusted in accordance with age, gender and race.[34,35]

When all this data is assessed, it is observed that the existing parameters and biomarkers yet to be routinised can be used more in the early diagnosis of postoperative renal failure, that they have no place in making preoperative predictions. Risk identification systems are assessors that are creatinine-value-based; they make one think that the existing preoperative failure is the strongest predictor in terms of postoperative failure.

What was aimed at in this study is not the early diagnosis of postoperative acute renal failure related to cardiac surgery, but to research on the significance of BNP value in determining the preoperatively risky patient group. In the results of our study, the preoperative BNP value was revealed to be successful in predicting the postoperative early-stage renal failure. Again it is observed that the early postoperative BNP value is related to the creatinine value in the sixth month.

The restrictive traits of the study are that the number of patients was low and depending on this, no grouping was made in terms of renal failure. But, in order to obtain a more homogenous group and to examine patients with increased risk, the patient group whose left ventricular ejection functions (EF) were between 30% and 50% was cho-

sen (min: 30%, max: 50%, mean: 39.37%). While BNP may change in a lot of diseases, it is possible that it will have a cut-off value by being assessed in terms of risk identification in bigger-scale studies.

In conclusion, acute kidney damage related to cardiac surgery is one of the most important reasons for postoperative morbidity and mortality. Predicting patients with high risk might enable precautions to be taken to be personalized and enable results to be more successful. There is the need for big-scale prospective studies in this issue.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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