Prognostic Value of Pre-operative Plasma NT-proBNP Combined With Creatinine in Early Outcomes After Adult Cardiac Valve Surgery

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Research Article

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Abstract

Objective To assess to prognostic value of pre-operative plasma NT-proBNP combined with creatinine in early outcomes after adult cardiac valve surgery.

Methods A total of 125 patients who underwent cardiac valve surgery in the first affiliated hospital of nanchang university between October *2016* and *October 2018* were retrospectively reviewed. including age, gender, weight, height, pre-operative plasma creatinine, preoperative plasma NT-proBNP, number of valves involved, pre-operative EF and early postoperative outcomes. The independent pre-operative factors that have a significant impact on early post-operative outcomes after adult cardiac valve surgery were investigated. Prognostic value in early outcomes after adult cardiac valve surgery was analyzed by ROC curve analysis.

Results preoperative plasma creatinine, preoperative plasma NT-proBNP and the number of valves involved in the complication group were significantly higher than that in non-complication group;BMI and pre-operative EF in the complication group was lower than that in the non-complication group ,with a statistically significant difference(P<0.05). Factors having P-value < 0.15 in the bivariable logistic regression model were entered into a multivariable logistic regression model. The multivariate logistic regression analysis indicated that the preoperative plasma creatinine, preoperative plasma NT-proBNP,BMI and the number of valves involved were correlated with the early postoperative outcomes, and the differences were statistically significant (P < 0.05). *ROC* curve analysis was used to explore the predictive performance. Results in ROC curve analysis, the AUC for the preoperative plasma NT-proBNP was 0.806 (95% CI 0.712□0.900□P<0.00). Logistic regression model found that the predictive value increased after adding the pre-operative plasma creatinine.the joint prediction AUC was 0.843, the sensitivity and specificity were 85.0%, 72.4% respectively.

Conclusion The elevated NT-proBNP and creatinine levels were independently correlated with the early post-operative outcomes, were two promising prognostic predictors for predicting the worse clinical outcomes . The pre-operative plasma NT-proBNP and the plasma creatinine combination was determined to help identify high-risk patients and make appropriate clinical decisions.

Introduction

With the development of cardiac surgery,the surgical success rate have been greatly improving.But patients undergoing cardiac surgery often suffer from postoperative complications such as low cardiac output syndrome,hypoxemia,cardiac arrhythmias,multiple organ functional failure and paravalvular valve leak,leading to secondary operations,lengthier hospital stays and recovery times,or even death[1].Therefore, clinical efficacy arouse increasing attentions after cardiac valve surgery. WANG Y,et al [2] reported that preoperative risk factors including age and cardiac function classification are related to the postoperative complications after heart valve replacement.most studies have demonstrated that postoperative complications after heart valve replacement can be predict by echocardiographic indexes

including the left ventricular end-diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD)[3]. But the methods of determining normal heart function ,such as echocardiography,radionuclide Cardioplegia, and invasive left ventricular angiography exist some defects.Brain natriuretic peptide(BNP) is an important peptide hormone synthesized and secreted by ventricular muscle,which has important value in the diagnosis and treatment of cardiac insufficiency,coronary heart disease and other cardiovascular diseases[4]. N-terminal B-type natriuretic peptide (NTproBNP) is formed by reverse transcription,translation and enzyme digestion of BNP gene.Compared with BNP,NT-proBNP has a longer biological half-life in human body than BNP,and the plasma concentration is relatively higher(about 15-20times of BNP).Therefore,it becomes a sensitive and specific mark for diagnosing congestive heart failure[5].Clinical studies have shown that plasma BNP has important clinical significance in predicting the long-term prognosis of patients with myocardial infrarction[6–7].In recent years,some scholars have found that perioperative NT-proBNP has important predictive value for the prognosis of coronary artery bypass grafting,and the increased plasma concentration of NT-proBNP indicaties poor prognosis[8–9].Li Chunzhi et al.[10] showed that plasma NT-proBNP has a good predictive value for malignant arrhythmia in patients with valvular heart disease.However, because NT-proBNP in the body is mainly excreted through the kidney, it is easily affected by the kidney function of patients.Therefore, the clinical value of NT-proBNP in diagnosing heart failure is questioned.so this study explores the predictive value of preoperative NT-proBNP combined with creatinine on the early prognosis of adult patients undergoing heart valve surgery,and provides theoretical basis for it as an evaluation index to predict the early outcomes after adult heart valve surgery.

Materials And Methods

1.1 patient population

A total of 125 patients who underwent cardiac valve surgery in the first affiliated hospital of nanchang university between October *2016* and *October 2018* were retrospectively reviewed,including 52 males and 73females.The age ranged from 31 to 74 years,and they were divided in two groups:20 cases in the complication group and 105 cases in the non-complication group.Inclusion criteria:(1)cardiac valvular disease has been diagnosed before incharge,and cardiac valve surgery has been performed;(2)NYHAI~IV;(3)the plasma concentration of creatinine and NT-proBNP has been detected before surgery;(4) Echocardiography has been done before operation.Exclusion criteria:(1)emergency;(2)acute myocardial infarction;(3)patients with renal failure and regular dialysis. The study was approved by Ethics Committee of the first affiliated hospital of Nanchang University,all methods were carried out in accordance with relevant guidelines and regulations,and informed consent was obtained from all subjects.

1.2 methods

Retrospective cohort study.Clinical data of patients were collected,including age, gender, weight, height, pre-operative plasma creatinine, preoperative plasma NT-proBNP, number of valves involved, pre-operative EF and early postoperative outcomes. Early postoperative outcomes refer to the patient’s prognosis at

discharge,including postoperative complications and death.Postoperative complications include low cardiac output syndrome,hypoxemia,cardiac arrhythmias,pulmonary infection and multiple organ dysfunction syndrome.

1.3 Statistics

Data were analysed using SPSS® Statistics version 22.0. Descriptive statistics were calculated as mean values and standard deviations for normally distributed continuous variables, medians and quartiles for continuous variables with non-normal distribution and absolute numbers and percentages for dichotomous variables. Comparisons of continuous variables between groups were made by unpaired Student's t-tests or the Mann-Whitney U test, depending on their distribution, and dichotomous variables were compared using the chi-square or Fisher's exact test. Univariable and multivariable regression analysis was used to study the association. All independent covariates with $p < 0.15$ in univariable regression analyses were included in multivariable regression analysis. ROC curve of plasma NT-proBNP predicting postoperative complications was drawn,and combined with preoperative plasma creatinine to predict the risk of postoperative complications.A two-sided p-value <0.05 was considered statistically significant.

Results

2.1 Comparison of baseline data between the complication group and the non-complication group

pre-operative plasma creatinine, preoperative plasma NT-proBNP and the numbers of valves involved in the complication group was significantly higher than that in non-complication group;BMI and pre-operative EF in the complication group was lower than that in the non-complication group ,with a statistically significant difference(P<0.05).The differences of age and gender between two groups were no statistically significant (P>0.05,Table 1).

2.2 Logistic regression analysis

Factors having P-value < 0.15 in the bivariable logistic regression model were entered into a multivariable logistic regression model. The multivariate logistic regression analysis indicated that the pre-operative plasma creatinine, preoperative plasma NT-proBNP,BMI and the number of valves involved were correlated with the early postoperative outcomes, and the differences were statistically significant (P < 0.05,Table 2).

2.3 Receiver operating characteristic (*ROC*) curve analysis

ROC curve analysis was used to explore the predictive performance. Results in ROC curve analysis, the area under the curves (AUC) for the preoperative plasma NT-proBNP was 0.806 (95% CI 0.712–0.900)，the sensitivity and specificity of plasma NT-proBNP in predicting postoperative early complications were 70.0% and 78.1%(P<0.00,Table 3 and Figure 1). ROC curve analysis showed that the sensitivity and specificity of plasma creatinine were 80.0% and 64.8%,and the area under ROC curve was 0.786(95% CI

0.674□0.898□P<0.00).Logistic regression model found that the predictive value increased after adding the pre-operative plasma creatinine.the joint prediction under the ROC curve of AUC was 0.843(95% CI 0.759□0.928□P<0.00), the sensitivity and specificity were 85.0% and 72.4% ,respectively(Table 3 and Figure 2).

Discussion

In 2001,the European Society of Cardiovascular Diseases first proposed the use of plasma BNP to assist in the diagnosis of chronic heart failure.Since then,a large number of studies have also verified the role of BNP/NT-proBNP in the diagnosis,evaluation and prognosis in heart failure.Later,it has been found that there is a certain relationship with the prognosis of patitents undergoing cardiac surgery under cardiopulmonary bypass[12-14]. NT-proBNP has a long biological half-life and a higher concentration in blood.Therefore,it becomes a sensitive and specific mark for diagnosing congestive heart failure[5].However,due to the excretion of NT-proBNP in the body mainly through the kidney, it is easily affected by the kidney function of patients.Therefore, the clinical value of NT-proBNP in diagnosing heart failure is questioned[11].Plasma creatinine level is the most representative index of renal function.so in this study, NT-proBNP combined with creatinine predicts the early outcomes of patitents undergoing cardiac surgery under cardiopulmonary bypass.

In this study, the factors that may affect the early postoperative outcomes were analyzed by univariate analysis.The result showed that BMI,NT-proBNP,EF,plasma creatinine and the number of valves involved may be related to the early outcomes of patients undergoing heart valve surgery.In order to further explore the relationship between statistically significant factors in the above univariate analysis and the early outcomes,and to analyze the degree of its influence.,this study adopted multivariate logistics regression,including the factors such as BMI,NT-proBNP,plasma creatinine,EF and the number of valves involved. The univariate result of age suggests there is no significant difference between two groups in the study (P=0.14).but some studies showed the age of onset is a risk factor for the prognosis of patients undergoing cardiac surgery with cardiopulmonary bypass.Therefore,age are entered into the multivariable logistic regression model.The results of regression analysis showed that plasma creatinine,NT-proBNP and the number of valves involved were independent risk factors for early postoperative complications.But this results suggest that BMI may be a protective factor for the early outcomes after heart valve surgery(B=-0.374,P=0.012).The reason for this phenomenon may be that most of patients included in this study are patients with rheumatic heart disease,who have a long onset time and have poor physical quality,resulting in low body weight.The median BMI in the complication group is 19.4(18.4,21.9),which is significantly lower than that in the non-complication group.The result is consistent with that of Eun-heenah et al[15].However, the differences of age and EF between two groups were no statistically significant . Presumably it is because Chinese patients with valvular heart disease often wait for obvious clinical discomfort and poor cardiac function before hospital treatment,and emergency surgery is excluded in the study.As a result,the difference of EF and age between the two groups is weakened.Gender is no significant statistical difference between the two groups in this study.One study [16]have found that gender can change the direct relationship between NT-proBNP and age,thus weakening the influence of age.Finally,regression analysis suggested that plasma creatinine ,NT-

proBNP and the number of valves involved were probably related to the early postoperative outcomes,but as an evaluation index of early postoperative prognosis,futher analysis was needed.Therefore,in this study,ROC curve was used to analyze the predictive value of plasma NT-proBNP and creatinine on postoperative complications.The results showed that AUC of NT-proBNP is 0.806,and its sensitivity and specificity are 70.0% and 78.1%,respectively.Logistic regression model found that the predictive value increased after adding the pre-operative plasma creatinine.the joint prediction under the ROC curve of AUC was 0.843(95% CI 0.759□0.928), the sensitivity and specificity were 85.0% and 72.4% ,which indicates that preoperative NT - proBNP combined with serum creatinine has a good predictive ability for early postoperative prognosis , and is expected to be used as an index for predicting early postoperative prognosis in patients undergoing cardiac valve surgery with cardiopulmonary bypass.

However,the sample size in this study is small, and it is a single center,retrospective cohort study, which cannot completely eliminate the potential confounding factors and selection bias,and does not include all the influencing factors,such as blood volume,nutritional
status,the duration of CPB and ICU stay, usage of vasoactive agent, fluid intake and output,etc,which may affect the final conclusion.

In conclusion, the elevated NT-proBNP and creatinine levels were independently correlated with the early post-operative outcomes, were two promising prognostic predictors for
predicting the worse clinical outcomes . The preoperative plasma NT-proBNP and the plasma creatinine combination was determined to help identify high- risk patients and make appropriate clinical decisions.

Declarations

Author contributions

Tianyuan Li and Hanjun Cao designed the study.All author analyzed data,wrote and approved the manuscript.

Competing Interests

The authors have declared that no competing interests exist.

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Tables

Table 1 Comparison of baseline data between the complication group and the non-complication group

Variable	Complications		Statistics	P value
	Yes	No		
Age(yrs)	57.6±2.1	56.7±0.8	2.16	0.14
Male(%)	9(45)	42(40)	0.17	0.68
BMI(kg/m^2)	19.4(18.4,21.9)	22.0(19.8,24.1)	-2.99	0.003
EF(%)	50.0(46.2,56.0)	56.0(51.0,58.0)	-2.82	0.005
Number of valves involved(%)				
1	0(0)	2(1.9)		
2	10(50)	78(74)	-2.42	0.016
3	10(50)	25(24.1)		
Creatinine (umol/l)	110(58.5,153,5)	76(63.0,93.5)	-4.28	<0.00
NT-proBNP (pg/ml)	3924 (2447.0,5726.7)	1022 (603.5,1901.5)	-5.19	<0.00

Values are mean ±SD or median(Q1,Q3) ; Statistics:T ,Z or c^2;BMI:body mass index;NT-proBNP: N-terminal B-type natriuretic peptide;EF: ejection fraction

Table 2 Logistic regression analysis of factors

Variable	B	S.E.	Wald	Sig.	Exp(B)	95%C.I.for EXP(B)	
						Lower	Upper
Creatinine	0.021	0.010	4.279	0.39	1.022	1.001	1.042
Numbers of lesion valve							
1	-	-	>10	0.00	-	-	-
2	3.65E+11	>10	>10	0.00	-	-	-
3	3.65+11	>10	>10	0.00	-	-	-
EF	-0.047	0.078	0.357	0.55	0.954	0.818	1.113
NT-proBNP	0.00	0.00	4.952	0.026	1.000	1.000	1.001
BMI	-0.374	0.150	6.244	0.012	0.688	0.513	0.922
Age(1)	0.993	0.709	1.959	0.162	2.698	0.672	10.830

C.I: confidence interval;Age(1):³60 yrs

Table 3 *ROC* curve analysis of plasma NT-proBNP and creatinine

Variable	AUC	Sensitivity	Specificity	Youden's index	P value
Creatinine	0.786	0.80	0.648	0.448	0.00
NT-proBNP	0.806	0.70	0.781	0.481	0.00
Creatinine +NT-proBNP	0.843	0.85	0.724	0.574	0.00

ROC:Receiver operating characteristic ;AUC: area under the curves

Figures

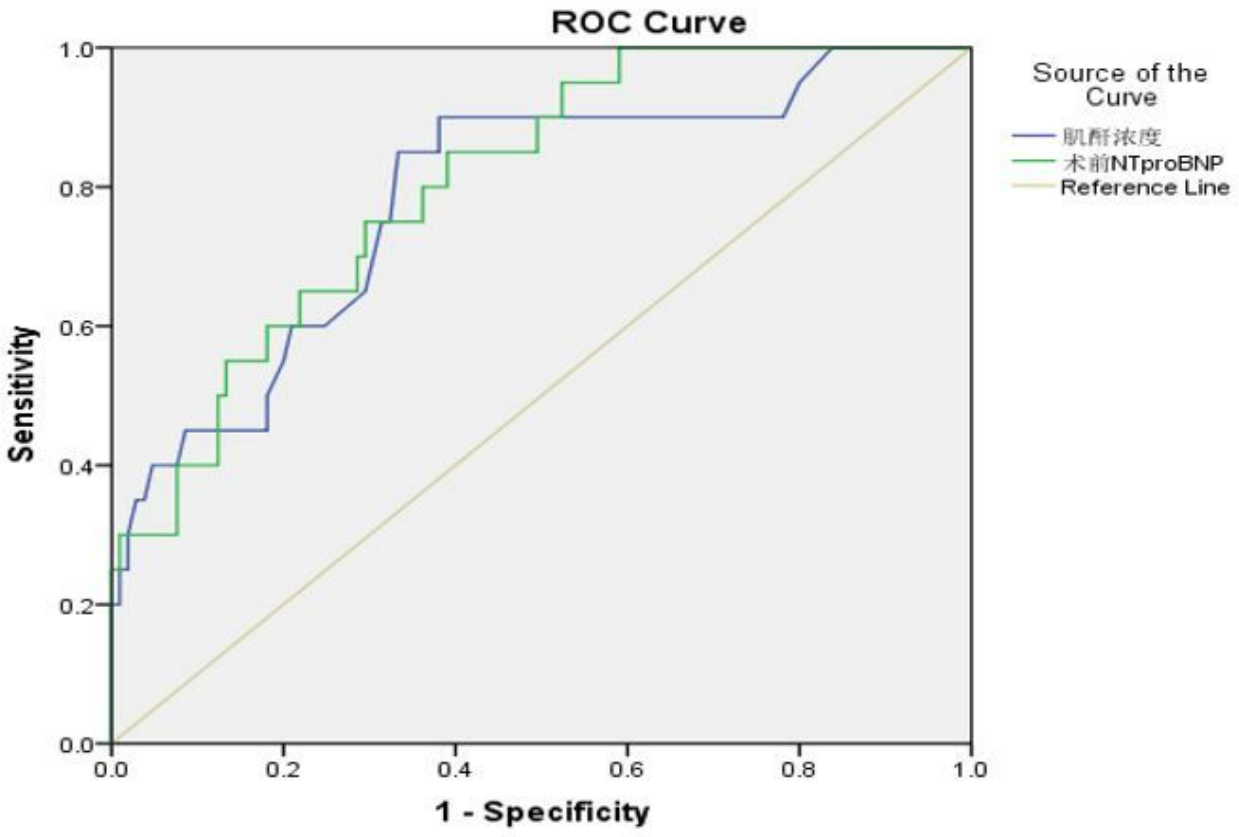

Figure 1

ROC curve analysis of plasma NT-proBNP and creatinine

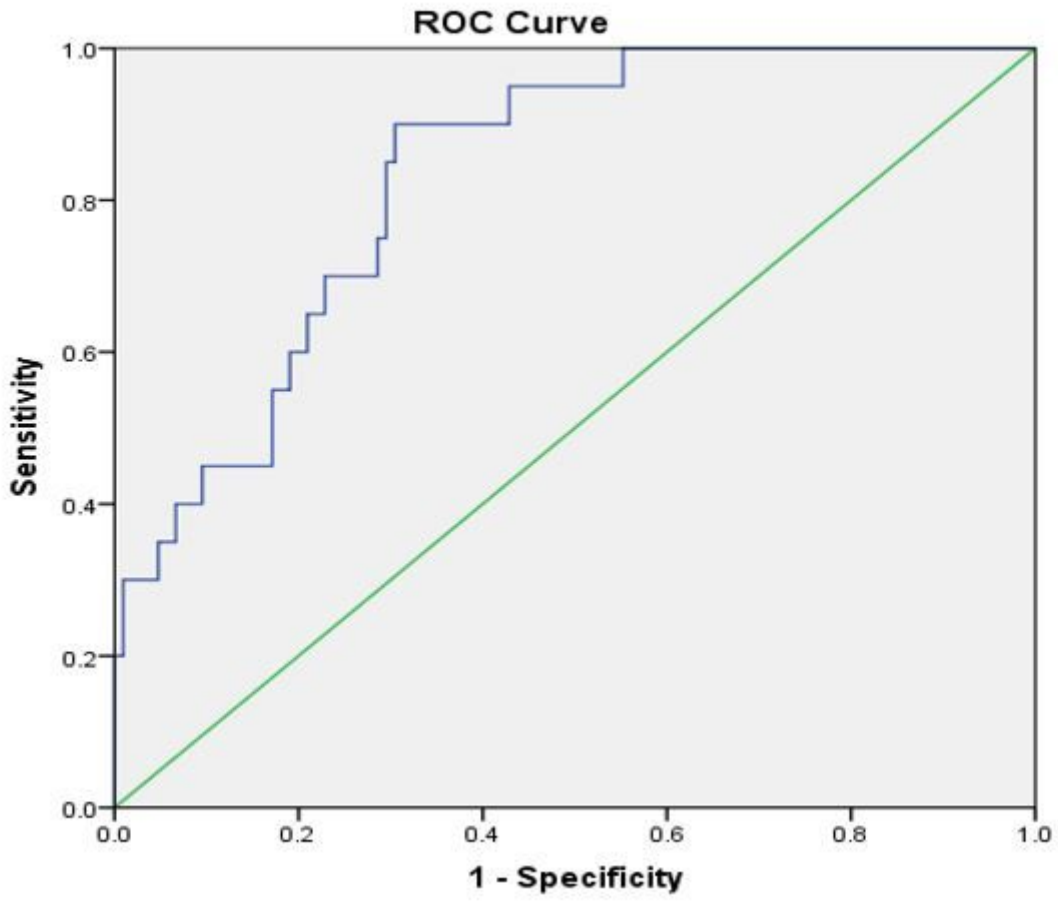

Figure 2

ROC curve analysis of plasma NT-proBNP combined with creatinine