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The Protective Effect of Recombinant Human Brain Natriuretic Peptide on Acute Kidney Injury after Liver Transplantation

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Abstract

Background: To investigate the protective effect of recombinant human Brain Natriuretic Peptide (rhBNP) on Acute Renal Injury (AKI) after liver transplantation.

Methods: A retrospective cohort study was analyzed by collecting clinical and epidemiological data of 136 patients who underwent liver transplantation from March 2018 to December 2020. Patients were divided into rhBNP group (88 cases) and non-rhBNP group (48 cases) according to whether they were treated with rhBNP after the operation. The changes of liver and renal function after operation and the difference of clinical prognosis were studied.

Results: Patients (50.0%) in non-rhBNP group had a significantly higher incidence of AKI than those (31.8%) in rhBNP group (P=0.04), especially the AKI stage I. Average levels of serum creatinine within seven days were significantly lower in the rhBNP group than that in the non-rhBNP group (P=0.01). The rate of postoperative CRRT did not differ significantly between the two groups. However, the use of furosemide was significantly greater in the non-rhBNP group (P<0.001). The in-hospital mortality rate after liver transplantation was 18.2% in the rhBNP group and 22.9% in the non-rhBNP group. The mean length of Intensive Care Unit (ICU) stay in the rhBNP group was 2.9 ± 5.0 days, significantly shorter than the 6.4 ± 16.2 days in the non-rhBNP group (P=0.02). There were significant differences in the survival distributions of patients after liver transplantation with AKI versus non-AKI (P<0.001) by Kaplan-Meier curve analysis.

Conclusion: The application of rhBNP in patients after liver transplantation could reduce kidney injury, reduce the risk of postoperative AKI, increased urine volume after surgery, decrease the length of stay in ICU and improve the clinical prognosis of patients. It provided a new path for the clinical prevention and treatment of AKI after liver transplantation.

Keywords: rhBNP; Acute kidney injury; Liver transplantation; ICU

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Introduction

The kidney injury is one of the most common complications after liver transplantation, which has a significant impact on the recipient's quality of life and long-term survival, and is one of the main causes of death after orthotopic liver transplantation [1-4]. The incidence of acute kidney injury has been reported to vary between 17% and 95% after orthotopic liver transplantation, with an average incidence of 60.0% [5]. The proportion of patients requiring Renal Replacement Therapy (RRT) immediately after liver transplantation was as high as 8.0%~17.1%, which seriously affected the function of transplanted organs, resulting in prolonged postoperative hospital stay, prolonged mechanical ventilation, increased incidence of infection and increased treatment costs [6]. Therefore, prevention and treatment of AKI after liver transplantation was of great clinical significance in improving the short-term and long-term prognosis after liver transplantation. Previous studies have defined multiple criteria for AKI after organ transplantation, leading to great differences in the reported incidence of AKI [7,8]. In 2012, the Kidney Disease Improving Global Guidelines (KDIGO) Clinical Practice Guidelines standardized and unified the classification and

diagnostic criteria of AKI after liver transplantation [9]. It provided us a welcome and timely synthesis of the evidence base to support the management of AKI [9,10]. This study analyzed AKI after liver transplantation based on the above guideline. At present, few studies have reported a drug that can specifically prevent or treat AKI. Brain Natriuretic Peptide (BNP) was first extracted from pig brain tissue by a Japanese study team [11]. BNP belonged to the natriuretic peptide family and was primarily secreted by cardiomyocytes in the ventricles under volume or pressure overload conditions [12]. Studies on BNP have focused on its role in the diagnosis and treatment of heart failure, improvement of cardiac function and prognosis, and improvement of cardiac remodeling, while few studies have reported its value in the prevention and treatment of AKI after liver transplantation [13,14]. Recombinant human Brain Natriuretic Peptide (rhBNP) was the natural blockers of Renin-Angiotensin-Aldosterone System (RAAS) [15]. However, it was not clear whether rhBNP could protect kidney against damage. There have been a few reports on the impact of rhBNP on AKI, but the results were ambiguous [16]. Therefore, influence of rhBNP on AKI needs to be further researched and clarified. Based on the above evidence, we observed the effect of rhBNP on the changes of liver and renal function and clinical prognosis after liver transplantation. The results of this study could provide a reference for the clinical application of rhBNP in the treatment of AKI after liver transplantation.

Methods

Study design and patients

We recruited 136 patients who underwent liver transplantation in the First Affiliated Hospital of Nanjing Medical University between May 2018 and December 2020 in Jiangsu Province, China, and described in detail the clinical efficacy of rhBNP in these patients. The research was approved by the institutional ethics board of the First Affiliated Hospital of Nanjing Medical University. This study is a retrospective observational study, and informed consent is not available to all patients. The preoperative and postoperative clinical data of the included patients were retrieved using the teaching hospital's central electronic record system to identify cases with all of the following characteristics: Liver transplantation performed between May 2018 and December 2020; adult patients (age ≥ 18 years); and complete medical history and laboratory results during hospitalization. Patients with uremia or chronic renal failure before operation and those who died during or within 24 h after the liver transplantation operation were excluded. The characteristics of each case were collected from the electronic medical records database by the first author. A retrospective cohort study design was employed. The epidemiological characteristics, clinical characteristics and laboratory findings of liver transplantation patients, as well as the incidence of postoperative AKI and the use of rhBNP were analyzed. The rhBNP and non-rhBNP subgroups were compared to identify the clinical effect of rhBNP on postoperative AKI. Most of the characteristics of our cohort of patients after liver transplantation are shown in Table 1.

Procedures

Information recorded included demographics [including age, sex and Body Mass Index (BMI)], underlying diseases, complications, Model for End stage Liver Disease (MELD) score [17], laboratory findings (levels of serum creatinine, alanine aminotransferase and aspartate aminotransferase) and clinical features (urine volume and time of an hepatic period) prior to and during treatment. Treatment variables included the use of rhBNP, the use of diuretic, and the application of Continuous Renal Replacement Therapy (CRRT). Clinical outcomes consisted of in-hospital mortality, length of ICU stay, total length of hospital stay and the incidence of AKI. If the records were missing or needed to be clarified, we obtained the data through direct communication with the attending physicians and other health care providers. The data was reviewed by a trained team of physicians. In this study, orthotopic liver transplantation was used in most cases. After surgery, all patients were transferred to ICU and maintained sedation for 3 h. After confirmation of hemodynamic stability, sedation was then stopped and the trachea was extubated. After being transferred to ICU after surgery, the observation group was given continuous pumping of rhBNP at the concentrations of 10 μg/mL with the dose of 0.01 μg/kg/min maintained no less than 48 h in addition to routine treatment. The control group received no continuous pumping of rhBNP and received only routine treatment. According to the above treatment methods, the clinical data of 136 patients were divided into two groups for comparison to evaluate the clinical effect of rhBNP on AKI.

Definition of postoperative AKI

Early AKI after liver transplantation was determined according to the Renal Disease: Improving Global Outcomes (KDIGO) criteria [9]. Maximum serum Creatinine (sCr) levels were measured in the first week after surgery and compared with preoperative baseline levels [18]. AKI could be diagnosed by meeting any of the following criteria: The increase of sCr level during 48 h ≥ 26.5 μmol/L (≥ 0.3 mg/dL) or the sCr level increased to 1.5 times the base value within seven days or the urine volume <0.5 mL/kg/h for six hours. The severity of AKI was divided into the following categories [18]: The AKI stage I was a 1.5 to 1.9 times increase in the level of sCr from baseline or an increase of ≥ 26.5 μmol/L (≥ 0.3 mg/dL) compared with the baseline; AKI stage II was the level of sCr 2.0 to 2.9 times the baseline; AKI stage III was the level of sCr 3.0 times the baseline or an increase of ≥ 353.6 μmol/L (≥ 4.0 mg/dL) or the application of Renal Replacement Therapy (RRT).

Statistical analysis

Continuous variables were compared with the Student t test (for normally distributed variables) or the Mann-Whitney U test (for non-normally distributed variables). Categorical variables were evaluated with the χ^2 or 2-tailed Fisher exact test. Results are expressed as mean ± standard deviation (SD) or median (range; continuous variables) or as percentages of the group from which they were derived (categorical variables). Two-tailed tests were used to determine statistical significance; a value of *P* less than 0.05 was considered significant [19,20]. Survival distribution functions were estimated using the Kaplan-Meier method; nonparametric (log-rank and Wilcoxon) tests were used to compare survival functions in different groups. All statistical analyses were performed with the SPSS, version 20.0.

Results

Demographic and baseline characteristics

Of the 234 patients who underwent liver transplantation in our hospital between May 2018 and December 2020, 136 cases (88 cases from rhBNP group and 48 cases from non-rhBNP group) met the criteria for inclusion in this study. The main demographics and clinical characteristics of patients with rhBNP and non-rhBNP subgroups are shown in Table 1. There was no significant difference in gender and age distribution between patients with rhBNP and non-rhBNP. In the rhBNP group, 65 (78.4%) were man; the median age of the patients

Table 1: The demographic and clinical features of the 136 patients before liver transplantation.

Characteristics	Patients		*P* value
	rhBNP group (n=88)	Non-rhBNP group (n=48)	
Male sex	69 (78.4)	43 (89.6)	0.10
Age, yrs, median (range)	52 (20-72)	53 (18-78)	0.88
BMI, kg/m², mean ± SD	23.51±3.3	23.18 ± 3.6	0.90
MELD score on admission, median (range)	17 (4-58)	19 (5-74)	0.06
Etiology			
Hepatic malignant tumors	41 (46.6)	22 (45.8)	0.93
Hepatitis B	12 (13.6)	11 (22.9)	0.17
Hepatitis C	4 (4.5)	2 (4.2)	0.92
Autoimmune	4 (4.5)	1 (2.1)	0.47
Primary biliary	5 (5.7)	2 (4.2)	0.70
Nodular	13 (14.8)	4 (8.3)	0.28
Alcohol	3 (3.4)	2 (4.2)	0.82
Drug & Toxin	3 (3.4)	2 (4.2)	0.82
Wilson disease	2 (2.3)	1 (2.1)	0.94
Congenital biliary atresia	1 (1.1)	1 (2.1)	0.66
Underlying diseases			
Hypertension	37 (42.0)	19 (39.6)	0.78
Diabetes	12 (13.6)	5 (10.4)	0.59
Autoimmune disease	4 (4.5)	2 (4.2)	0.92
Laboratory index			
Hematocrit, %, normal range 40-50, mean ± SD	30 ± 4	31 ± 3	0.16
White blood cell count, ×10⁹/L, normal range 4-10, mean ± SD	4.3 ± 1.9	4.6 ± 2.1	0.37
Platelet count, ×10⁹/L, normal range 100-300, mean ± SD	65 ± 40	62 ± 35	0.29
ALT, U/L, normal range 9-50, mean ± SD	135 ± 46	126 ± 58	0.69
AST U/L, normal range 15-40	108 ± 34	97 ± 42t	0.79
Albumin, g/L, normal range 40-50, mean ± SD	31 ± 3.3	28 ± 3.3	0.19
sCr, μmol/L, normal range 44-133, mean ± SD	65.3 ± 15.6	61.3 ± 13.2	0.16

Data are expressed as number (%) unless otherwise specified.
Abbreviations: ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BMI: Body Mass Index; MELD: Model for End Stage Liver Disease; rhBNP: Recombinant Human Brain Natriuretic Peptide; sCr: Serum Creatinine; SD: Standard Deviation

was 52 years (range, 20 to 72); the mean BMI of the patients was 23.51 ± 3.3 kg/m²; the median MELD score at admission was 17 (range, 4 to 58). There were 43 (89.6%) males in the control group, with an average BMI of 23.18 ± 3.6 kg/m², a median age of 53 years (range 18 to 78) and a median MELD score of 19 (range 5 to 74) points. In both groups, hepatic malignant tumor (46% and 45.8%) was the most common etiology of liver transplantation, followed by hepatitis, including hepatitis B and hepatitis C, whereas congenital biliary atresia and Wilson disease were rare. In the rhBNP group, 37 patients (42.0%) had hypertension and 12 patients (13.6%) had diabetes; in the control group, 19 (39.6%) had hypertension and 5 (10.4%) had diabetes. There was no statistically significant difference between the two groups in the underlying diseases. Preoperative mean levels of albumin, hematocrit and platelet count for these patients were lower than the normal value. The average levels of alanine aminotransferase and aspartate aminotransferase in both groups were above the normal range. Preoperative serum creatinine levels were in the normal range in both groups, and there was no statistical significance between the two groups.

Postoperative changes in liver and kidney function

The time of a hepatic period was similar between the two groups, and there was no significantly statistical difference between the two groups in the time of a hepatic period during liver transplantation (*P*=0.17). According to the KDIGO criteria, a total of 52 patients (38.2%) developed AKI immediately after liver transplantation in Table 2. The severity of AKI stage was as follows: 19 cases (14.0%) in stage I, 21 cases (15.4%) in stage II, and 12 cases (8.8%) in stage III. Patients in non-rhBNP group had a greater incidence of AKI than those in rhBNP group (*P*=0.04). Further comparison of the differences in each stage of AKI showed that the incidence of AKI stage I in the rhBNP group was significantly lower than that in the non-rhBNP group (*P*=0.03). The levels of alanine aminotransferase and aspartate aminotransferase significantly increased from the preoperative phase to the after liver transplantation phase in both groups. However, no differences in postoperative levels of alanine aminotransferase and aspartate aminotransferase were observed between the rhBNP and non-rhBNP groups. Average levels of serum creatinine within seven days were significantly lower in the rhBNP group than that in the non-rhBNP group (*P*=0.01); the mean urine volume per hour on the

Table 2: The clinical characteristics of the rhBNP versus non-rhBNP subgroups after liver transplantation.

Characteristics	Patients		*P* value
	rhBNP group (n=88)	Non-rhBNP group (n=48)	
Time of anhepatic period, minutes, mean ± SD	62.4 ± 20.8	66.6 ± 20.7	0.17
Urine volume, mL/h, mean ± SD			
The first day	75 ± 40	70 ± 40	0.43
The second day	102 ± 47	98 ± 43	0.64
The third day	106 ± 50	95 ± 41	0.02
Laboratory index			
sCr, μmol/L, normal range 44-133, mean ± SD			
Within first 48 hrs	90.2 ± 79.2	92.9 ± 65.2	0.48
Within 7 days	109.8 ± 125.1	141.6 ± 141.1	0.01
ALT, U/L, normal range 9-50, mean ± SD	2098.3 ± 2465.7	2119.5 ± 2378.2	0.70
AST, U/L, normal range 15-40, mean ± SD	2040.7 ± 2283.1	2572.1 ± 2720.8	0.69
Incidence of AKI	28 (31.8)	24 (50.0)	0.04
AKI stage			
I	8 (9.1)	11 (22.9)	0.03
II	13 (14.7)	8 (16.7)	0.77
III	7 (8.0)	5 (10.4)	0.63
Treatment			
The use of Furosemide	66 (75.0)	47 (97.9)	<0.001
The dose of Furosemide, mg, median (range)	30 (0-540)	60 (0-2880)	<0.001
Continuous renal replacement therapy	13 (14.8)	7 (14.6)	0.72
Outcomes			
Death	16 (18.2)	11 (22.9)	0.51
Length of ICU stay, days, mean ± SD	2.9 ± 5.0	6.4 ± 16.2	0.02
Total length of stay, days, mean ± SD	28.4 ± 12.7	33.9 ± 31.7	0.97

Data are expressed as number (%) unless otherwise specified.
Abbreviations: AKI: Acute Kidney Injury; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ICU: intensive care unit; rhBNP: Recombinant Human Brain Natriuretic Peptide; sCr: Serum Creatinine; SD: Standard Deviation

third day after surgery was higher in the rhBNP group (*P*=0.02).

Treatment and outcomes

The rate of postoperative CRRT did not differ significantly between the two groups. However, there were 66 patients (75.0%) in the rhBNP group and 47 patients (97.9%) in the non-rhBNP group who were given furosemide after surgery. Hence, the use of furosemide was significantly greater in the non-rhBNP group (*P*<0.001). The in-hospital mortality rate after liver transplantation was 18.2% (16/88) in the rhBNP group and 22.9% (11/48) in the non-rhBNP group, respectively, with no statistically significant difference between the above two groups. Similarly, there was no significantly statistical difference in total length of stay between the two groups. However, the mean length of ICU stay in the rhBNP group was 2.9 ± 5.0 days, significantly shorter than the 6.4 ± 16.2 days in the non-rhBNP group (*P*=0.02). The influence of the occurrence of AKI after liver transplantation on the Kaplan-Meier curve during hospitalization was further analyzed. Survival distributions were significantly different in patients after liver transplantation with AKI versus non-AKI (Figure 1).

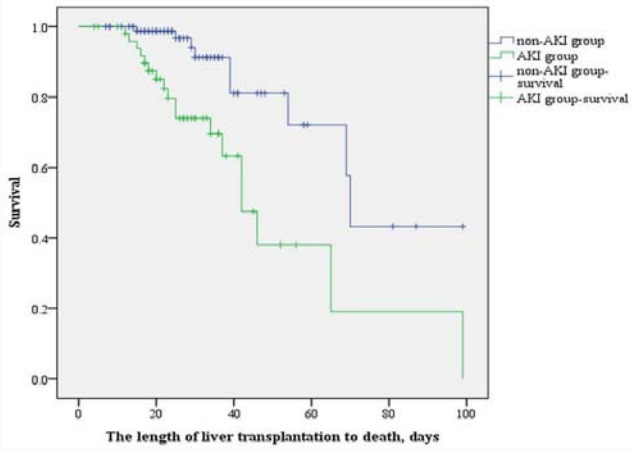

Figure 1: Kaplan-Meier curves showed the influence of the occurrence of acute kideny injury on in-hospital mortalityof patients after liver transplantation (*P*<0.001).

Discussion

Liver transplantation has become one of the most effective methods for the treatment of end-stage liver diseases and acute liver failure [21]. In recent years, with the maturity of organ transplantation technology, the success rate of liver transplantation had significantly increased, but the incidence of perioperative organ injury was still high, among which AKI was a common complication after liver transplantation and an important factor affecting the prognosis of

patients [22,23]. It had been reported that the incidence of AKI after orthotopic liver transplantation was 5%~94% [5]. In recent years, the incidence of AKI after liver transplantation in China was 4%~20%, which was different from that in other countries [24]. This may be due to different diagnostic criteria for acute kidney injury used in previous studies, including the RIFLE or AKIN criteria, leading to a large difference in the reported incidence of AKI. In this study, AKI after liver transplantation was diagnosed and graded based on the KDIGO criteria [9], instead of the RIFLE or the AKIN classification. The results showed that of the 136 patients, 52 patients developed AKI after surgery, with an incidence rate of 38.2%, among which the incidence rate of AKI was 31.8% in the rhBNP group, significantly lower than the 50.0% in the non-rhBNP group, especially the AKI stage I. It has been demonstrated that the use of rhBNP after liver transplantation can reduce the risk of AKI in patients. Liver transplantation was characterized by large trauma and long operation time, and the mechanism of postoperative AKI was complex. In addition to the age of the recipients, preoperative MELD scores, the levels of serum creatinine before surgery, the levels of serum albumin and other related basic situation, the occurrence of AKI was associated with the application of drugs resulted in kidney injure, the cold ischemia time of donor liver, the complexity of surgical procedures, the renal ischemia-reperfusion injury, and the triggering of cascades of inflammatory response, neuroendocrine response and excessive activation of Renin-Angiotensin-Aldosterone System (RAAS). At present, the inflammatory response and over-activation of RAAS have attracted much attention [25]. The BNP was a natriuretic peptide hormone that was released in large quantities from the ventricles during ventricular hypertrophy, increased ventricular wall pressure, or volume overload. Previous studies had shown that it could regulate vascular tension, regulate fat metabolism, improve the volume load, increase glomerular filtration rate and promote the excretion of water and sodium, thus restraining RAAS activity [26,27]. The main components of rhBNP had the same activity as BNP, which could decrease pre load and post load of heart, reduce pulmonary artery pressure, increase cardiac minute output, inhibit the RASS activity and increase the urine volume [16,28]. It could also promote the production of Nitric Oxide (NO) to regulate the body's inflammatory response [28]. Therefore, it has been theoretically proved that rhBNP can prevent and control the occurrence and progression of AKI after liver transplantation. In this study, we analyzed the preventive and therapeutic effect of rhBNP on AKI after liver transplantation, and found that compared with the non-rhBNP group, the patients in the rhBNP group had significantly increased urine volume on the third day after surgery, the reduced use of diuretics and decreased the levels of serum creatinine within one week after surgery. The results suggested that rhBNP could reduce renal injury of patients and the incidence of AKI after liver transplantation. Some studies had reported that the mortality rate of patients with AKI after orthotopic liver transplantation was high, with the mortality rate of 35%~45% in one year [29]. In consequence, we further studied the prognostic effect of rhBNP on patients, and found that there was no significant difference in in-hospital mortality rate between the two groups, but the length of stay in ICU of patients in the rhBNP group was significantly lower than that in the non-rhBNP group. At the same time, we also analyzed the effect of AKI on the survival curve of these patients, and proved that survival distributions were significantly different in patients after liver transplantation with AKI versus non-AKI. We hope that our findings can provide some reference experience and theoretical basis for the global community to treat and prevent the AKI cases after liver transplantation. Our study has several limitations. In the first place, it was a retrospective study, and some important data may have been omitted. Secondly, it was a single-center study, with a lack of homogeneity in the etiologies of liver transplantation, and the sample size was limited. Moreover, in our study, primary clinical outcomes of AKI cases after liver transplantation were confined to the changes of serum creatinine and urine volume within 7 days after surgery; other clinical outcomes beyond the postoperative period were not analyzed. Finally, the specific role and pathophysiological mechanism of the rhBNP in the prevention and treatment of AKI still need to be confirmed by later studies. The data in this study provided preliminary guidance for the optimal treatment of AKI patients after liver transplantation. Further studies with larger sample sizes are needed to confirm the results.

Conclusion

The use of rhBNP after liver transplantation was beneficial to reduce the risk of postoperative AKI, increased urine volume after surgery, decrease the length of stay in ICU and improve the clinical prognosis of patients after liver transplantation.

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References

1. Kim WR, Lake JR, Smith JM, Skeans MA, Schladt DP, Edwards EB, , et al. OPTN/SRTR 2013 annual data report: liver. Am J Transplant. 2015;15:1-28.
2. Wang H, Jiang W, Zhou Z, Long J, Li W, Fan ST. Liver transplantation in mainland China: The overview of CLTR 2011 annual scientific report. Hepatobiliary Surg Nutr. 2013;2(4):188-97.
3. Watt KD, Pedersen RA, Kremers WK, Heimbach JK, Charlton MR. Evolution of causes and risk factors for mortality post-liver transplant: Results of the NIDDK long-term follow-up study. Am J Transplant. 2010;10(6):1420-7.
4. Levitsky J, O'Leary JG, Asrani S, Sharma P, Fung J, Wiseman A, et al. Protecting the kidney in liver transplant recipients: Practice-based recommendations from the American Society of Transplantation Liver and Intestine Community of Practice. Am J Transplant. 2016;16(9):2532-44.
5. Rossi AP, Vella JP. Acute kidney disease after liver and heart transplantation. Transplantation. 2016;100(3):506-14.
6. Lewandowska L, Matuszkiewicz-Rowinska J. Acute kidney injury after procedures of orthotopic liver transplantation. Ann Transplant. 2011;16(2):103-8.
7. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute dialysis quality initiative w: Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004;8(4):R204-12.
8. Feldkamp T, Bienholz A, Paul A, Saner FH. Renal damage after liver transplantation. Biosci Rep. 2020;40(1):BSR20191187.
9. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-84.
10. Walther CP, Podoll AS, Finkel KW. Summary of clinical practice guidelines for acute kidney injury. Hosp Pract (1995). 2014;42(1):7-14.
11. Cao X, Xia HY, Zhang T, Qi LC, Zhang BY, Cui R, et al. Protective effect of lyophilized recombinant human brain natriuretic peptide on renal

ischemia/reperfusion injury in mice. Genet Mol Res. 2015;14(4):13300-11.

12. Grewal J, McKelvie RS, Persson H, Tait P, Carlsson J, Swedberg K, et al. Usefulness of N-terminal pro-brain natriuretic Peptide and brain natriuretic peptide to predict cardiovascular outcomes in patients with heart failure and preserved left ventricular ejection fraction. Am J Cardiol. 2008;102(6):733-7.

13. Babur Guler G, Karaahmet T, Tigen K. Myocardial fibrosis detected by cardiac magnetic resonance imaging in heart failure: Impact on remodeling, diastolic function and BNP levels. Anadolu Kardiyol Derg. 2011;11(1):71-6.

14. Phelan D, Watson C, Martos R, Collier P, Patle A, Donnelly S, et al. Modest elevation in BNP in asymptomatic hypertensive patients reflects sub-clinical cardiac remodeling, inflammation and extracellular matrix changes. PLoS One. 2012;7(11):e49259.

15. Yang H, Song Z, Jin H, Cui Y, Hou M, Gao Y. Protective effect of rhBNP on intestinal injury in the canine models of sepsis. Int Immunopharmacol. 2014;19(2):262-6.

16. Li N, Jin HX, Song Z, Bai CZ, Cui Y, Gao Y. Protective effect of recombinant human brain natriuretic peptide on acute renal injury induced by endotoxin in canines. Cell Biochem Biophys. 2014;70(2):1317-24.

17. Zhang JY, Zhang FK, Wang BE, Jia JD, Zhang ST. [The prognostic value of end-stage liver disease model in liver cirrhosis]. Zhonghua Nei Ke Za Zhi. 2005;44(11):822-4.

18. Chae MS, Park H, Choi HJ, Park M, Chung HS, Hong SH, et al. Role of serum levels of intraoperative brain natriuretic peptide for predicting acute kidney injury in living donor liver transplantation. PLoS One. 2018;13(12):e0209164.

19. Weiwei W, Ting J, Weihong Z, Chunyu L, Jun C, Dandan X, et al. Predictors of mortality in bloodstream infections caused by multidrug-resistant gram-negative bacteria: 4 years of collection. Am J Infect Control. 2017;45(1):59-64.

20. Weiwei W, Yin Y, Xia S, Xin Z, Ping L, Quan C, et al. The Value of plasma-based MicroRNAs as diagnostic biomarkers for ovarian cancer. Am J Med Sci. 2019;358(4):256-67.

21. Lv H, Wei X, Yi X, Liu J, Lu P, Zhou M, et al. High-dose ulinastatin to prevent late-onset acute renal failure after orthotopic liver transplantation. Ren Fail. 2020;42(1):137-45.

22. Simei Z, Jiguang M, Rui A, Lin L, Jianpeng L, Zeping F, et al.. Effect of cumulative fluid balance on acute kidney injury and patient outcomes after orthotopic liver transplantation: A retrospective cohort study. Nephrology (Carlton). 2020;25(9):700-7.

23. Kazuaki T, Claudia L, Felicia K, Antonio R, Anna J, Bo-Göran E, et al. Association of post-reperfusion syndrome and ischemia-reperfusion injury with acute kidney injury after liver transplantation. Acta Anaesthesiol Scand. 2020;64(6):742-50.

24. Zongyi Y, Baifeng L, Funian Z, Hao L, Xin W. Risk factors of acute kidney injury after orthotopic liver transplantation in China. Sci Rep. 2017;7:41555.

25. Barreto AG, Daher EF, Silva Junior GB, Garcia JH, Magalhaes CB, Lima JM, et al. Risk factors for acute kidney injury and 30-day mortality after liver transplantation. Ann Hepatol. 2015;14(5):688-94.

26. Menzorov MV, Shutov AM, Midlenko VI, Larionova NV, Morozova IV, Akulova OV. [Value of N-terminal pro brain natriuretic peptide in predicting acute kidney injury in patients with acute decompensated chronic heart failure]. Ter Arkh. 2017;89(3):78-84.

27. Mitaka C, Ohnuma T, Murayama T, Kunimoto F, Nagashima M, Takei T, et al. Effects of low-dose atrial natriuretic peptide infusion on cardiac surgery-associated acute kidney injury: A multicenter randomized controlled trial. J Crit Care. 2017;38:253-8.

28. Murray P. Brain natriuretic peptide therapy to prevent acute kidney injury after cardiac surgery. Am J Kidney Dis. 2008;51(1):5-9.

29. Barri YM, Sanchez EQ, Jennings LW, Melton LB, Hays S, Levy MF, et al. Acute kidney injury following liver transplantation: definition and outcome. Liver Transpl. 2009;15(5):475-83.