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The Application Value of CRRT in the Treatment of Cardio-Renal Syndrome: A Meta Analysis

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Abstract

Objective: To evaluate the therapeutic effect of continuous renal replacement therapy (CRRT) combined with drug therapy and drug therapy alone on cardiorenal syndrome (CRS) by statistically comparing the efficacy of CRRT in the clinical treatment of CRS.

Method: Chinese databases (China National Knowledge Infrastructure, VIP Database, Wanfang Database) and English databases (PubMed, EmBase, The Cochrane Library, Web of Science) were searched for literature on continuous renal replacement therapy (CRRT) and the application of conventional drugs in cardiorenal syndrome (CRS) using computers. The search period was from the establishment of each database to September 1, 2023. By reading and screening the title, abstract, and full text, 10 articles that meet the inclusion criteria were finally included. Excel was used to summarize and integrate the data, and RevMan5.3 software was used for outcome indicator analysis.

Result: A total of 10 articles were included. Including 741 patients, including 369 patients in the continuous renal replacement therapy (CRRT) combined with drug treatment group and 372 patients in the internal medicine drug treatment group. 1. Cr: The decrease in CRRT group was higher than that in the internal medicine drug treatment group[MD=-58.73, 95%CI(-108.77, -8.69),P=0.02], (I^2=98%, P＜0.00001); 2. LVEF: The recovery of the CRRT group was better than that of the internal medicine drug treatment group [MD=5.93,95%CI(3.21, 8.65), P＜0.0001], (I^2=85%, P＜0.00001); 3. BUN: The CRRT group showed better reduction than the internal medicine drug treatment group[MD=-1.21, 95%CI(-1.75, -0.67), P＜0.0001], (I^2=93%, P＜0.00001); 4. UA: The decrease in CRRT group was higher than that in the internal medicine drug treatment group[MD=-95.05, 95%CI(-156.94, -33.16), P=0.003], (I^2=80%, P=0.002); 5. BNP: The reduction effect of CRRT group is better than that of internal medicine drug treatment group[MD=-474.92, 95%CI(-636.76, -313.09), P＜0.00001], (I^2=91%,P＜0.00001); 6. LVD: The CRRT group showed better reduction than the internal medicine drug treatment group[MD=-3.97, 95%CI(-6.75, -1.19), P=0.005], (I^2=0%, P=0.002); 7. Urine output: The CRRT group showed better recovery than the internal medicine drug treatment group[MD=87.91, 95%CI(38.09, 137.73), P=0.0005], (I^2=84%, P=0.002); 8. Classification of cardiac function: The downgrading effect of the CRRT group is better than that of the internal medicine drug treatment group[MD=-1.10, 95%CI(-1.43, -0.78), P＜0.00001], (I^2=76%, P=0.02); 9. GFR: The increase in CRRT group was better than that in the internal medicine drug treatment group[MD=21.36,95%CI(18.59, 24.13), P＜0.00001], (I^2=0%, P=0.73); 10.Ccr:The recovery of the CRRT group was better than that of the internal medicine drug treatment group[MD=7.68,95%CI(4.52, 10.83)P ＜ 0.00001](I^2=82%, P=0.02); 11.SV: There was no statistically significant difference between the CRRT group and the internal medicine treatment group[MD=2.35, 95%CI(-3.38, 8.07), P=0.42], (I^2=92%, P=0.0006); 12. CysC: There was no statistically significant difference between the CRRT group and the internal medicine treatment group[MD=-1.13, 95%CI(-2.41, 0.15), P=0.08], (I^2=95%, P=0.00001); 13. K+: There was no statistically significant difference between the CRRT group and the internal medicine treatment group[MD=-0.15, 95%CI(-0.31, 0.01), P=0.07], (I^2=0%, P=0.75).

Keywords: CRRT, continuous renal replacement therapy, Cardio-Renal Syndrome, meta-analysis

1. Introduction

In 2004, a meeting of the working group of the National Heart, Lung, and Blood Institute in the United States first mentioned "cardiorenal syndrome" and evaluated the interaction between the heart and kidneys[1]. Afterwards,

the consensus conference on cardiorenal syndrome (CRS) further clarified the definition and classification of CRS[2]. The conference defined CRS in a broad sense as a syndrome in which acute or chronic dysfunction of one organ in the cardiovascular and renal systems leads to acute or chronic functional impairment of another organ, and classified CRS into five subtypes based on different onset characteristics and pathological types.

CRS has a complex pathogenesis, and if not treated in a timely manner, it may cause multiple organ dysfunction and ultimately lead to death. Data shows that the mortality rate of CRS patients can be as high as 62% [3]. Due to the rational mutual influence between heart and kidney diseases[4], when one of the functions of the heart or kidneys is impaired, it will aggravate and affect each other, ultimately leading to a sharp deterioration of heart and kidney function. The use of internal medicine drugs such as vasodilators and diuretics for treatment can increase the risk of patients after treatment.

The definition of continuous renal replacement therapy (CRRT) is a therapeutic technique that replaces kidney function by continuously and slowly clearing water and solutes through extracorporeal circulation blood purification. Conventional hemodialysis is effective in clearing excess water, maintaining electrolyte balance, and removing toxins from the body. However, it also has a significant impact on hemodynamics, which can lead to serious complications such as kidney damage or hemodynamic instability[5]. CRRT is a treatment developed on the basis of intermittent hemodialysis, which can achieve slow and isotonic dehydration with minimal impact on hemodynamics[6, 7] .

Many scholars have conducted randomized controlled studies on the treatment of cardiorenal syndrome with CRRT, but the sample size of these studies is generally small and the quality of the research has not been systematically evaluated. In order to further obtain evidence of the efficacy of CRRT in the treatment of cardiorenal syndrome and provide evidence-based medicine for the clinical treatment of cardiorenal syndrome, this study conducts a meta-analysis of the existing published randomized controlled trials involving CRRT in the treatment of cardiorenal syndrome, and further evaluates the application value of CRRT in the treatment of cardiorenal syndrome.

2. Data and Methods

2.1 Inclusion and Exclusion Criteria for Literature

2.1.1Types of Research

The types of studies included are all randomized controlled trials (RCTs)

2.1.2 Research Object

The diagnostic criteria are in line with the expert consensus of the Acute Dialysis Quality Guidance Group: (1) age>18 years old; (2) The patient exhibits symptoms of circulatory overload such as pulmonary edema, peripheral edema, and elevated central venous pressure. (3) The patient has both cardiac dysfunction (grades II-IV) and renal dysfunction (glomerular filtration rate<125ml/min or elevated blood creatinine level>110umol/L)

2.1.3 Intervention Measures

The observation group received continuous renal replacement therapy (CRRT) combined with conventional medication treatment, while the control group received conventional internal medicine medication treatment. Compare the outcome indicators of two treatment methods and evaluate the treatment effect.

2.1.4 Observation Indicators

Observation indicators include: creatinine (Cr), left ventricular ejection fraction (LVEF), urea nitrogen (BUN), uric acid (UA), B-type natriuretic peptide (BNP), left ventricular diameter (LVD), urine output, cardiac function grading, glomerular filtration rate (GFR), creatinine clearance rate (Ccr), stroke volume (SV), cystatin C (CysC), and blood potassium (K+).

2.1.5 Exclusion Criteria

(1)The number of cases in each study group is less than 10. (2) Not a randomized controlled trial. (3) The experimental design is unreasonable. (4) Literature with incomplete experimental data or inability to extract data. (5) Select the most comprehensive or earliest published literature for repeated publications.

2.2 Literature Search

The Chinese and English literatures on the application of continuous renal replacement therapy (CRRT) and conventional drugs in cardiorenal syndrome (CRS) in Chinese databases (China National Knowledge Infrastructure, VIP database, Wanfang database) and English databases (PubMed, EmBase, The Cochrane Library, Web of science) were searched by computer. The retrieval time was from the establishment of each database to

September 1,2023. Chinese search terms included continuous renal replacement therapy, continuous venovenous hemodialysis, continuous venovenous hemofiltration, continuous venovenous hemodiafiltration, continuous blood purification, cardiorenal syndrome, renal heart syndrome, heart failure, acute kidney injury.English search terms included CRRT, Continuous Renal Replacement Therapy, CRRT Technique, CAVHD, CVVHDF, CVVHD, CVVH Technique, Cardio-Renal Syndrome, Cardio Renal Syndrome, Cardio-Renal Syndromes, Syndrome. Cardio-Renal, Heart failure, continuous blood purification, CBP. Expand the scope of literature search by searching for references involving literature.

2.3 Literature Screening and Data Extraction

To ensure the completeness and reliability of the included data, two evaluators will respectively read the titles, abstracts, and full texts of the literature, and decide whether to include the literature based on the inclusion and exclusion criteria. The results obtained by two evaluators need to be cross checked. If there are any differences in the results, they need to be resolved through joint discussion or seeking third-party opinions. Use Excel to organize data and extract literature information, including the first author of the literature, the type of study, the number of cases, the age and gender of the study subjects, intervention measures for the experimental and control groups, treatment courses, and various outcome indicators.

2.4 Risk Assessment of Bias in Included Literature

Conduct a systematic evaluation using the RCT bias risk assessment tool in Cochrane Systematic Reviewer's Handbook 5.1.0, which includes: ① generation of random sequences; ② Allocation hidden; ③ Whether to blind the research subjects and researchers; ④ Has the outcome indicator evaluator been blinded? ⑤ Whether the outcome indicators are complete; ⑥ Is there selective reporting? ⑦ Are there any other biases present.

2.5 Data Statistical Analysis

Perform statistical analysis using RevMan (ReviewManager, version 5.3). Use I^2 to represent the degree of heterogeneity in statistical data, with the specific formula being $I^2=100\% \times (Q-df)/Q$. When the heterogeneity of the data is small ($I^2<50\%$, $P>0.1$), a fixed effects model is used for data analysis. When data heterogeneity is significant ($I^2>50\%$, $P<0.1$), a random effects model is used for data analysis, followed by sensitivity analysis using a one by one exclusion method or only descriptive analysis.

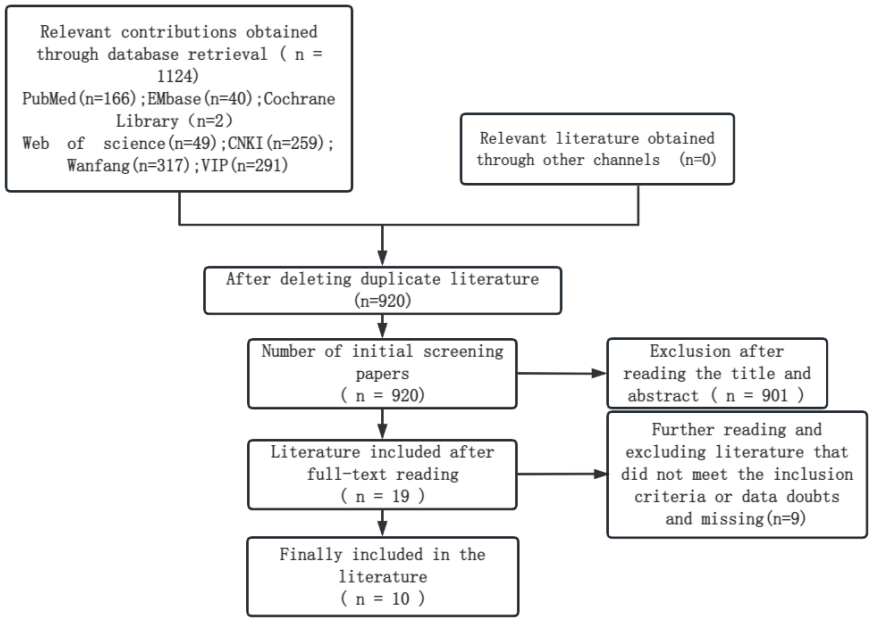

Figure 1. Literature screening process

3. Results

3.1 Literature Screening

A total of 1124 articles were retrieved from authoritative Chinese databases (Wanfang Database, CNKI, VIP Chinese Science and Technology Journal Database) and English databases (PubMed, EMBASE, Cochrane Library, etc.) both domestically and internationally. 204 duplicate articles were detected using NoteExpress software, and

after removal, 920 articles remained; Further eliminate 901 articles that do not meet the inclusion criteria by reading the remaining literature titles and abstracts; By conducting a detailed full-text reading of the remaining 19 articles, removing 9 articles, and finally including 10 articles, the outcome indicators involved were analyzed. The literature screening process is detailed in Figure 1.

3.2 Basic Characteristics of Literature

A total of 10 randomized controlled trials[8-17]were included, involving 741 patients with cardiorenal syndrome, all of which were studies comparing the efficacy of CRRT combined with internal medicine drug therapy and conventional drug therapy for cardiorenal syndrome. See Table 1.

Table 1. Basic characteristics of research

Eligible studies	number of samples	Gender (male / female)		Age		intervention measures		course of treatment	outcome index
	T/C	T	C	T	C	T	C		
Dinghong 2011[8]	26/29	14/12	18/11	55.4±9.84	57.5±11.57	Drug therapy combined with CRRT	drug	two Week	②⑧⑨
Yu Zeying 2017[9]	20/20	12/8	16/4	55.6±9.82	54.2±8.76	Drug therapy combined with CRRT	drug	NA	①②③⑤⑦
Shi Ying 2023[10]	34/34	19/15	20/14	61.13±4.65	60.27±4.12	Drug therapy combined with CRRT	drug	One Week	①②③⑤⑩⑪
Song Yuanshen 2022[11]	57/57	36/21	30/27	76.3±6.7	77.2±7.1	Drug therapy combined with CRRT	drug	One Week	①②③④⑤⑪⑫⑬
Yin Wei 2014[12]	19/19	NA	NA	NA	NA	Drug therapy combined with CRRT	drug	NA	①④⑬
Xu Heng 2016[13]	30/30	16/14	17/13	63.2±7.4	64.5±7.6	Drug therapy combined with CRRT	drug	One Week	①⑤⑧⑩
Zhu Yi 2014[14]	36/36	20/16	19/17	63.22±15.45	62.01±13.6	Drug therapy combined with CRRT	drug	One month	①②③④⑥⑦
Wu Zhifeng 2017[15]	65/65	32/33	33/32	48.67±1.53	46.58±2.42	Drug therapy combined with CRRT	drug	One month	①②③④⑥⑦⑫
Zhao Rui 2020[16]	30/30	19/11	18/12	56.08±8.63	55.42±9.71	Drug therapy combined with CRRT	drug	One Week	①②③⑥
Huo Feijiao 2012[17]	52/52	26/26	28/24	53.6±9.6	56.4±9.2	Drug therapy combined with CRRT	drug	NA	②⑧⑨

Note: T is the experimental group; c is the control group; nA means not mentioned; ① Creatinine (Cr) ② Left ventricular ejection fraction (LVEF) ③Blood urea nitrogen (BUN) ④Uric acid (UA) ⑤B-type natriuretic peptide (BNP) ⑥ Left ventricular diameter (LVD) ⑦Urine volume ⑧ Cardiac function classification ⑨ Glomerular filtration rate (GFR) ⑩ Creatinine clearance rate (Ccr) ⑪stroke volume (SV) ⑫cystatin C (CysC) ⑬serum potassium (K +)

3.3 Quality Assessment for Inclusion in the Study

Among the 10 studies included, one study used a random number table method[14], one study used a random ball tapping method[10], and six studies only reported the use of randomization but did not describe the specific methods [11-13, 15-17]. The bias risk assessment of each study is shown in Figure 2A and Figure 2B.

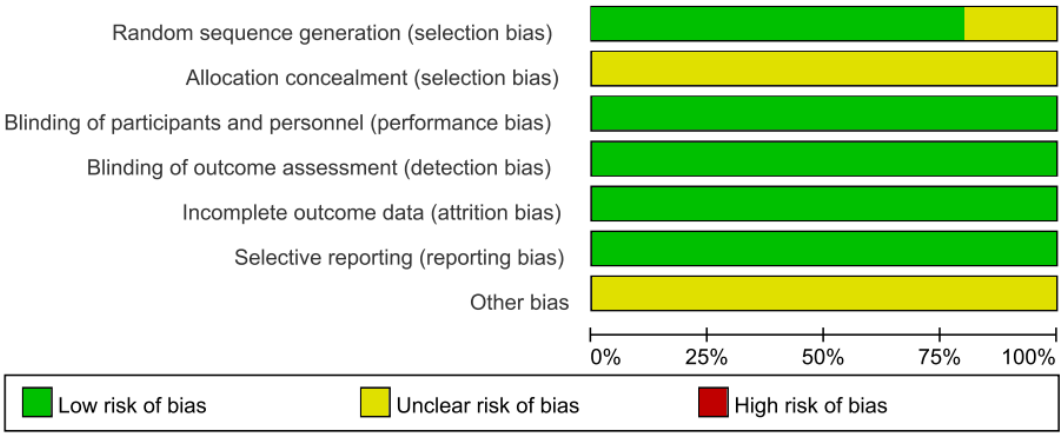

Figure 2A. Risk of bias analysis of included

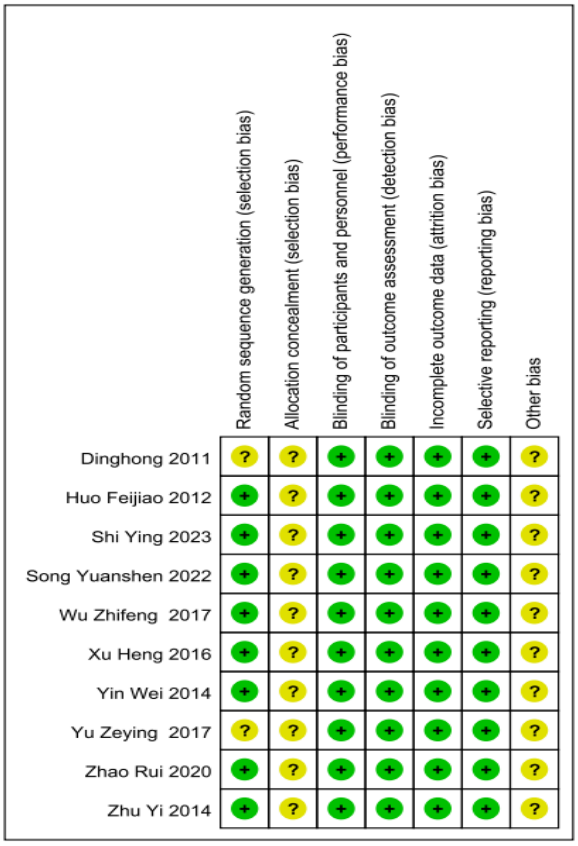

Figure 2B. Summary of risk of bias of included trials

3.4 Meta Analysis

3.4.1 Creatinine (Cr)

A total of 8 included articles compared the creatinine levels of patients in the observation group and the control group. After merging and analyzing the outcome indicators, the results showed that I ²=98%, P < 0.00001, Due to significant statistical heterogeneity, a random effects model was used for data analysis, and the results showed that the differences were statistically significant [MD=-58.73, 95% CI (-108.77, -8.69), P=0.02]. See Figure 3. This indicates that the combination therapy of CRRT and medication has a better effect on reducing creatinine than the internal medicine medication treatment group.

Eight studies involving creatinine were excluded one by one for sensitivity analysis. After eliminating Xu Heng 's study, the heterogeneity test results (I^2 = 57 %, P < 0.03), the effect size [MD = -29.85,95 % CI (-44.47, -15.24), P < 0.0001]. The results of the heterogeneity test (I^2 = 98 %, P < 0.00001), the effect size [MD = -65.15, 95 % CI (-127.28, -3.01), P = 0.04]. After excluding the study of Shi Ying, heterogeneity test results (I^2 = 97 %, P < 0.00001), effect size [MD = -66.13,95 % CI (-126.62, -5.64), P = 0.03]. After excluding Song Yuanshen 's research, the heterogeneity test results (I^2 = 98 %, P < 0.00001), the effect size [MD = -61.10,95 % CI (-119.49, -2.71), P = 0.04]. After eliminating Yin Wei 's research, the heterogeneity test results (I^2 = 98 %, P < 0.00001), the effect size [MD = -56.44, 95 % CI (-110.86, -2.02), P = 0.04]. After eliminating Zhu 's study, the heterogeneity test results (I^2 = 98 %, P < 0.00001), the effect size [MD = -63.13,95 % CI (-117.59, -8.66), P = 0.02]. After excluding Wu Zhifeng 's research, the heterogeneity test results (I^2 = 98 %, P < 0.00001), the effect size [MD = -63.49, 95 % CI (-119.18, -7.81), P = 0.03]. After excluding Zhao Rui 's study, heterogeneity test results (I^2 = 98 %, P < 0.00001), effect size [MD = -55.35, 95 % CI (-107.58, -3.11), P = 0.04]. After eliminating Xu Heng 's study, the heterogeneity was significantly reduced. Considering that it may be the cause of significant heterogeneity, we further read the original literature and believed that it may be related to the fact that the patient 's condition before treatment was more serious than other studies.

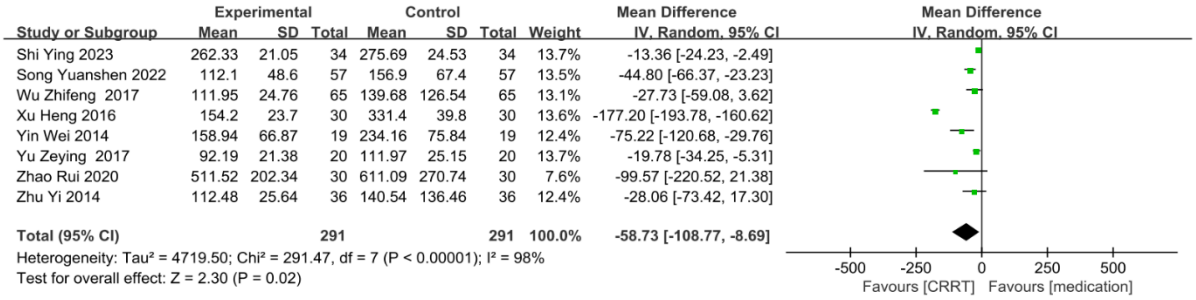

Figure 3. Meta-analysis of creatinine

3.4.2 Left ventricular ejection fraction (LVEF)

A total of 8 articles included in the literature compared the left ventricular ejection fraction of the observation group and the control group. After combining the outcome indicators, the results showed that I^2 = 85 %, P < 0.00001, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the analysis results showed that the difference was statistically significant [MD = 5.93,95 % CI (3.21,8.65), P < 0.0001]. See figure 4. It shows that the effect of CRRT combined with drug treatment group on LVEF recovery is better than that of medical drug treatment group.

Eight studies involving left ventricular ejection fraction were excluded one by one for sensitivity analysis. After eliminating the study of Huo Feijiao, the heterogeneity test results (I^2 = 81 %, P < 0.0001), the effect size [MD = 5.28, 95 % CI (2.51, 8.06), P = 0.0002]. After excluding Zhao Rui 's study, heterogeneity test results (I^2 = 86 %, P < 0.00001), effect size [MD = 5.46,95 % CI (2.45,8.46), P = 0.0004]. After excluding Wu Zhifeng 's research, the heterogeneity test results (I^2 = 87 %, P < 0.00001), the effect size [MD = 5.90,95 % CI (2.68, 9.12), P = 0.0003]. After excluding Zhu 's study, heterogeneity test results (I^2 = 87 %, P < 0.00001), effect size [MD = 5.78,95 % CI (2.75,8.82), P = 0.0002].After excluding Song Yuanshen 's research, the heterogeneity test results (I^2 = 75 %, P < 0.0006), the effect size [MD = 6.88,95 % CI (4.59,9.16), P < 0.00001]. After excluding Shi Ying 's study, heterogeneity test results (I^2 = 87 %, P < 0.00001), effect size [MD = 6.05,95 % CI (2.94,9.16), P = 0.0001]. After excluding Yu 's study, heterogeneity test results (I^2 = 84 %, P < 0.00001), effect size [MD = 6.64, 95 % CI (3.92,9.35), P < 0.00001]. After excluding the study of Dinghong, the heterogeneity test results (I^2 = 86 %, P <

0.00001), the effect size [MD = 5.47,95 % CI (2.46, 8.47), P = 0.0004]. After excluding the studies in turn, the heterogeneity still existed and did not affect the final results, indicating that the analysis results of the outcome indicators were robust and credible.

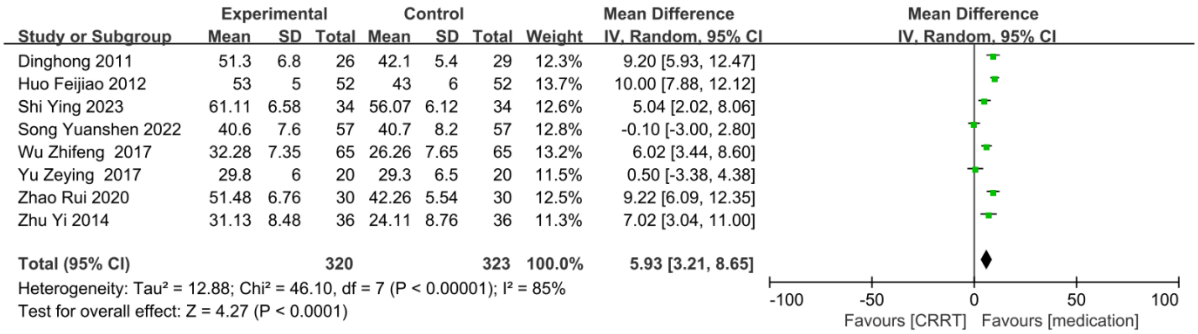

Figure 4. Meta-analysis of LVEF

3.4.3 Urea nitrogen (BUN)

A total of 6 articles included in the literature compared the urea nitrogen status of patients in the observation group and the control group. After combining the outcome indicators, the results showed that I^2 = 93 %, P < 0.00001, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the analysis results showed that the difference was statistically significant [MD = − 1.21, 95 % CI (− 1.75, − 0.67), P < 0.0001]. See Fig.5. It shows that the effect of CRRT combined with drug treatment group on reducing urea nitrogen is better than that of medical drug treatment group.

Six studies involving urea nitrogen were excluded one by one for sensitivity analysis. After excluding Zhao Rui 's study, heterogeneity test results (I^2 = 94 %, P < 0.00001), effect size [MD = -1.00, 95 % CI (-1.51, -0.49), P = 0.0001]. After excluding the study of Wu Zhifeng, the heterogeneity test results (I^2 = 95 %, P < 0.00001), the effect size [MD = -2.94,95 % CI (-5.20, -0.67), P = 0.01]; after excluding Zhu 's study, heterogeneity test results (I^2 = 95 %, P < 0.00001), effect size [MD = -2.95,95 % CI (-5.18, -0.72), P = 0.01]; after excluding the study of Song Yuanshen, heterogeneity test results (I^2 = 94 %, P < 0.00001), effect size [MD = -1.11,95 % CI (-1.64, -0.57), P < 0.0001]; After excluding Shi Ying 's research, the heterogeneity test results (I^2 = 92 %, P < 0.00001), the effect size [MD = -0.71,95 % CI (-1.19, -0.23), P = 0.003]; after excluding Yu 's study, heterogeneity test results (I^2 = 91 %, P < 0.00001), effect size [MD = -0.66,95 % CI (-1.12, -0.19), P = 0.005]; after eliminating the studies in turn, the heterogeneity still existed significantly, which did not affect the final results, indicating that the analysis results of the outcome indicators were robust and reliable.

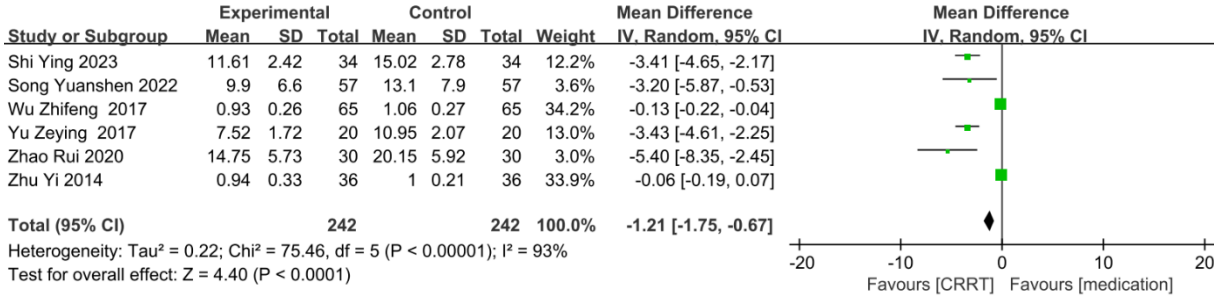

Figure 5. Meta-analysis of BUN

3.4.4 Uric acid (UA)

A total of 4 articles in the included literature compared the uric acid status of patients in the observation group and the control group. After combining the outcome indicators, the results showed that I^2 = 80 %, P = 0.002, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was statistically significant [MD = -95.05, 95 % CI (-156.94, -33.16), P = 0.003]. See Figure 6. It shows that the effect of CRRT combined with drug treatment group on reducing uric acid is better than that of medical drug treatment group.

Four studies involving uric acid were excluded one by one for sensitivity analysis. After eliminating Yin Wei 's research, the heterogeneity test results (I^2 = 0 %, P = 0.42), the effect size [MD = -68.30, 95 % CI (-92.20, -44.39), P = 0.00001]; after excluding Wu Zhifeng 's research, the heterogeneity test results (I^2 = 84 %, P = 0.002), the effect size [MD = -118.11, 95 % CI (-212.70, -23.52), P = 0.01]; after excluding Zhu 's study, heterogeneity test results (I^2 = 86 %, P = 0.0009), effect size [MD = -111.96, 95 % CI (-190.69, -33.23), P = 0.005]; After excluding Song Yuanshen's research, the heterogeneity test results (I^2 = 87 %, P = 0.0006), the effect size [MD = -108.62, 95 % CI (-220.88, 3.64), P = 0.06]. After removing Yin Wei 's study, the heterogeneity was significantly reduced, and the original literature was further read. It may be related to the significant difference between the treatment plan of the patients included in the study and the other three studies.

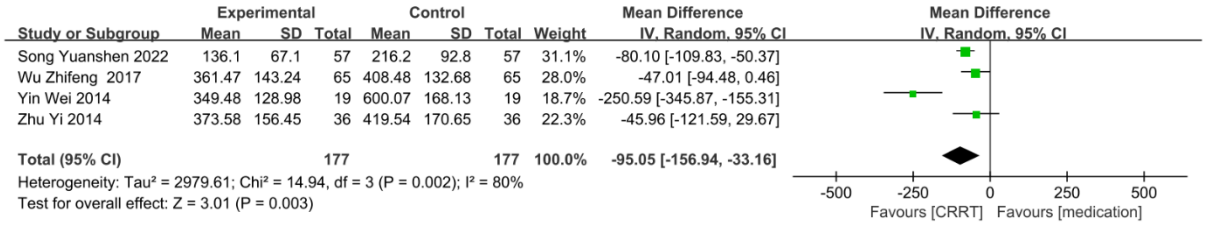

Figure 6. Meta-analysis of UA

3.4.5 B-Type Natriuretic Peptide (BNP)

A total of 4 articles included in the literature compared the B-type natriuretic peptide between the observation group and the control group. After analyzing the outcome indicators, the results showed that I^2 = 91 %, P < 0.00001, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was statistically significant [MD = -474.92, 95 % CI (-636.76, -313.09), P < 0.00001]. See Figure 7. It shows that the effect of CRRT combined with drug treatment group on reducing BNP is better than that of medical drug treatment group.

Four studies involving B-type natriuretic peptide were excluded one by one for sensitivity analysis. After excluding Song Yuanshen 's research, heterogeneity test results (I^2 = 31 %, P = 0.23), effect size [MD = -567.74,95 % CI (-630.90, -504.57), P < 0.00001]; after excluding Xu Heng 's study, the heterogeneity test results (I^2 = 77 %, P = 0.01), the effect size [MD = -413.73, 95 % CI (-584.70, -242.76), P < 0.00001]; after excluding Shi Ying 's research, the heterogeneity test results (I^2 = 94 %, P < 0.00001), the effect size [MD = -450.80,95 % CI (-703.17, -198.43), P = 0.0005]; the results of heterogeneity test (I^2 = 94 %, P < 0.00001), effect size [MD = − 480.24,95 % CI (− 644.72, − 315.77), P < 0.00001];After excluding the study of Song Yuanshen, the heterogeneity was significantly reduced. Considering that it may be the cause of significant heterogeneity, we further read the original text and believed that it may be caused by the difference between BNP and other three studies before treatment.

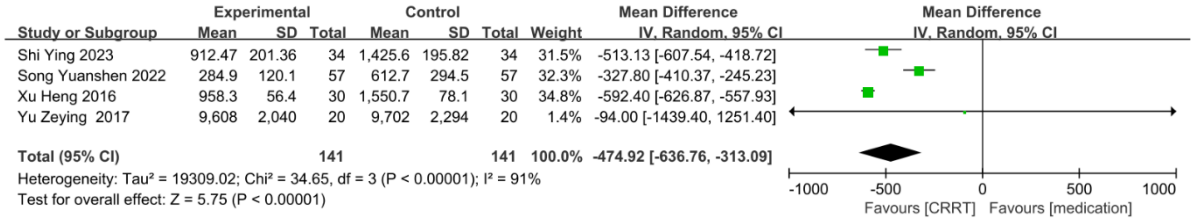

Figure 7, Meta-analysis of BNP

3.4.6 Left Ventricular Diameter (LVD)

A total of 3 articles in the included literature compared the left ventricular diameter of the observation group and the control group. After analyzing the outcome indicators, the results showed that I^2 = 0 %, P = 0.99, no heterogeneity, so the fixed effect model was used for data analysis. The analysis results showed that the difference was statistically significant [MD = -3.97,95 % CI (-6.75, -1.19), P = 0.005]. See figure 8. It shows that CRRT combined with drug therapy can significantly reduce LVD in patients with cardiorenal syndrome.

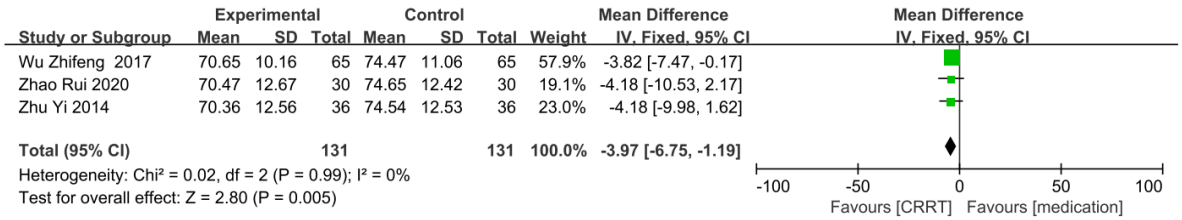

Figure 8. Meta-analysis of LVD

3.4.7 Urine Volume

A total of 3 articles in the included literature compared the urine volume of patients in the observation group and the control group. After analyzing the outcome indicators, the results showed that I^2 = 84 %, P < 0.002, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the analysis results showed that the difference was statistically significant [MD = 87.91,95 % CI (38.09,137.73), P = 0.0005]. See Figure 9. It shows that the effect of CRRT combined with drug treatment group on restoring urine volume is better than that of medical drug treatment group.

Three studies involving urine volume were excluded one by one for sensitivity analysis. After excluding Yu 's study, heterogeneity test results (I^2 = 0 %, P = 0.42), effect size [MD = 67.14, 95 % CI (53.28, 81.00), P < 0.00001]; after excluding Wu Zhifeng 's research, the heterogeneity test results (I^2 = 92 %, P = 0.0005), the effect size [MD = 186.56,95 % CI (-86.46, 459.57), P = 0.18]; after excluding Zhu 's study, heterogeneity test results (I^2 = 91 %, P = 0.0008), effect size [MD = 192.29, 95 % CI (-67.84,452.43), P = 0.15]; after excluding Yu Zeying 's study, the heterogeneity was significantly reduced. Considering that it may be the reason for the significant heterogeneity, we further read the original text and believed that the severity of the patients included in the study may be different from the other two studies, resulting in the difference in urine volume before treatment from the other two studies or different medical treatment regimens.

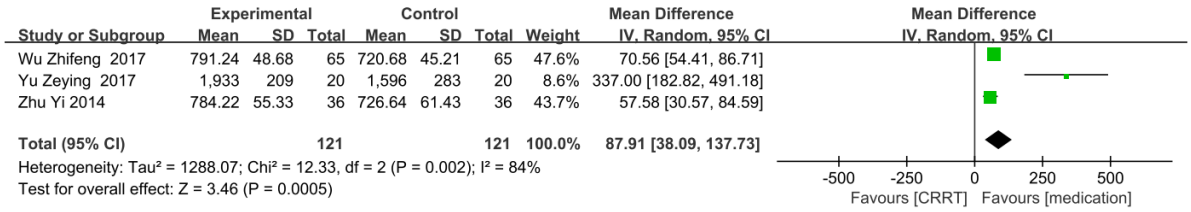

Figure 9. Meta-analysis of Urine volume

3.4.8 Cardiac Function Classification

A total of 3 articles included in the literature compared the cardiac function classification of patients in the observation group and the control group. After combining the outcome indicators, the results showed that I^2 = 76 %, P < 0.02, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was statistically significant [MD = -1.10,95 % CI (-1.43, -0.78), P < 0.00001]. See Figure.10. It shows that the effect of CRRT combined with drug treatment group on reducing cardiac function classification is better than that of medical drug treatment group.

Three studies involving cardiac function classification were excluded one by one for sensitivity analysis. After eliminating Xu Heng 's study, the heterogeneity test results (I^2 = 0 %, P = 0.63), the effect size [MD = -1.28,95 % CI (-1.45, -1.10), P < 0.00001]; after eliminating the study of Huo Feijiao, the heterogeneity test results (I^2 = 66 %, P = 0.09), the effect size [MD = -0.98, 95 % CI (-1.37, -0.59), P < 0.00001]; after excluding the study of Dinghong, the heterogeneity test results (I^2 = 88 %, P = 0.004), the effect size [MD = -1.06, 95 % CI (-1.55, -0.57), P < 0.0001]; after eliminating Xu Heng 's study, the heterogeneity was significantly reduced, considering that it may be the cause of significant heterogeneity. Further reading the original text, it is considered that the severity of the patients included in the study may be different from that of the other two researchers, resulting in higher cardiac function classification before treatment.

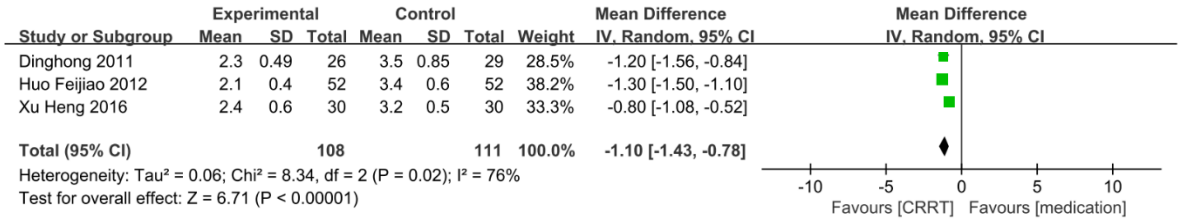

Figure 10. Meta-analysis of Cardiac function classification

3.4.9 Glomerular Filtration Rate (GFR)

A total of 2 articles in the included literature compared the glomerular filtration rate between the observation group and the control group. After analyzing the outcome indicators, the results showed that $I^2 = 0$ %, P = 0.73, and there was no heterogeneity. Therefore, the data analysis used a fixed effect model. The analysis results showed that the difference was statistically significant [MD = 21.36, 95 % CI (18.59, 24.13), P < 0.00001]. See Figure 11. It shows that the GFR recovery effect of CRRT combined with drug treatment group is better than that of medical drug treatment group.

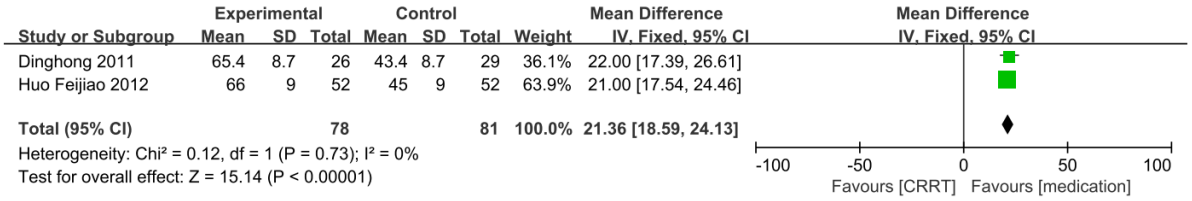

Figure 11. Meta-analysis of GFR

3.4.10 Creatinine Clearance Rate (Ccr)

A total of 2 articles included in the literature compared the creatinine clearance rate between the observation group and the control group. After combining the outcome indicators, the results showed that $I^2 = 82$ %, P = 0.02, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was statistically significant [MD = 7.68, 95 % CI (4.52, 10.83), P < 0.00001]. It shows that the recovery effect of Ccr in CRRT combined with drug treatment group is better than that in medical drug treatment group. See figure 12.

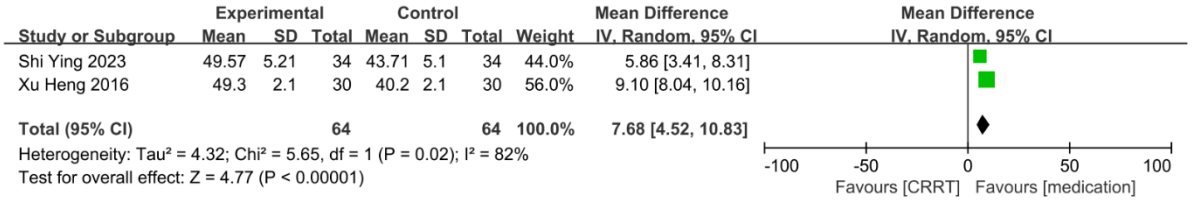

Figure 12. Meta-analysis of Ccr

3.4.11 Stroke Volume (SV)

A total of 2 articles included in the literature compared the stroke volume of patients in the observation group and the control group. After combining the outcome indicators, the results showed that $I^2 = 92$ %, P = 0.0006, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was not statistically significant [MD = 2.35, 95 % CI (-3.38, 8.07), P = 0.42]. The results showed that there was no significant difference in SV recovery between CRRT combined with drug treatment group and medical drug treatment group. See Figure 13.

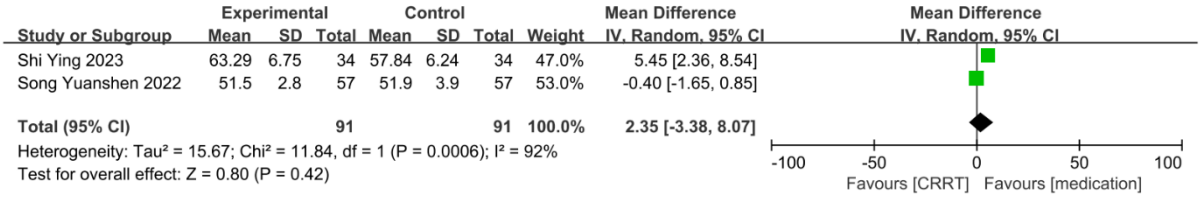

Figure 13. Meta-analysis of SV

3.4.12 Cystatin C (CysC)

A total of 2 articles were included in the literature to compare the cystatin C status of patients in the observation group and the control group. After analyzing the outcome indicators, the results showed that $I^2 = 95\ \%$, $P = 0.00001$, with significant statistical heterogeneity. Therefore, the data analysis used a random effect model, and the results showed that the difference was not statistically significant [MD = -1.13,95 % CI (-2.41, 0.15), P = 0.08]. It shows that the effect of CRRT combined with drug treatment group on reducing cystatin C is not significantly different from that of medical drug treatment group. See Figure 14.

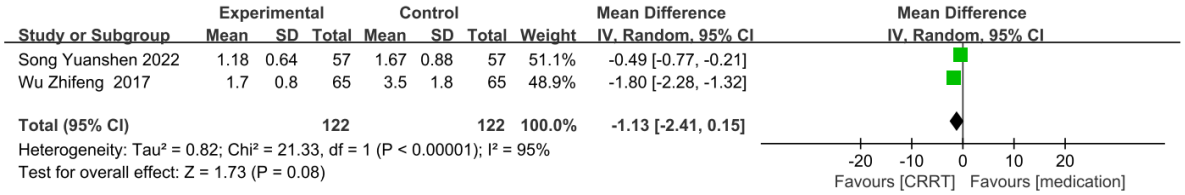

Figure 14. Meta-analysis of Cystatin C

3.4.13 Serum Potassium (K +)

A total of 2 articles included in the literature compared the serum potassium status of patients in the observation group and the control group. After combining the outcome indicators, the results showed that $I^2 = 0\ \%$, $P = 0.75$, no heterogeneity, so the data analysis used a fixed effect model, and the analysis results showed that the difference was not statistically significant [MD = -0.15, 95 % CI (-0.31, 0.01), P = 0.07]. See figure 15. It shows that the effect of CRRT combined with drug treatment group on reducing serum potassium is not significantly different from that of medical drug treatment group.

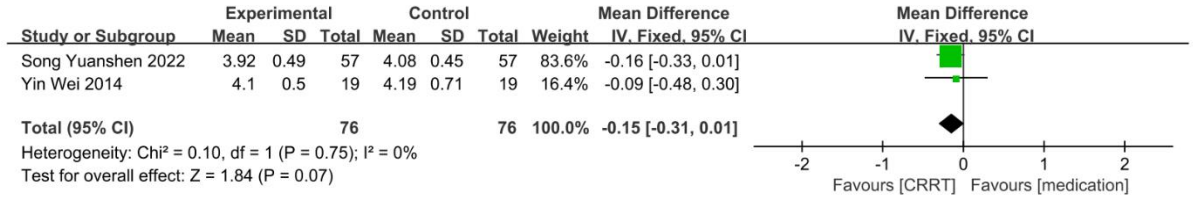

Figure 15. Meta-analysis of K+

3.5 Publication Bias Analysis

Because the number of studies involving the same outcome index in all included studies did not exceed 10, no funnel plot was made for publication bias analysis.

4. Discussions

4.1 Research Significance

The prevalence of chronic kidney disease (CKD), heart failure, and CRS continues to increase due to the accumulation of common risk factors such as population aging, hypertension, obesity, diabetes, and vascular diseases, as well as advances in drug treatment, procedures, and equipment for patients with heart failure[18-21].

In 2007, a report of 118465 patients with acute decompensated heart failure in the ACCISE database showed that[22], 9.0 % of patients had normal renal function on admission, while 27.4 % had mild renal insufficiency (GFR60mL / min · 1.73m to 89mL / min · 1.73m), and 43.5 % had moderate renal insufficiency (GFR30mL / min · 1.73m to 59mL / min · 1.73m). 13.1 % of patients had severe renal insufficiency (GFR 15-29 mL / min · 1.73m), and 7.0 % of patients had GFR less than 15 mL / min · 1.73m or were undergoing chronic dialysis. Other large databases show that the prevalence of cardiac or renal insufficiency increases the incidence of other diseases[23]. Studies have shown that the risk of death in patients with cardiorenal syndrome is three times that of patients with simple heart failure or simple chronic kidney disease[24]. Some researchers have found that the mechanism of cardiorenal syndrome includes excessive activation of sympathetic nervous system, increase of intra-abdominal pressure and central venous pressure, accumulation of uremic toxins, endothelial dysfunction, hemodynamic disorders, activation of inflammatory system and many other factors, which eventually lead to impaired cardiac and renal function and volume overload [25-28]. No matter what type of cardiorenal syndrome, although its course and pathogenesis are different, it will eventually lead to severe heart and kidney failure. Renal hypoperfusion and renal failure may be due to heart failure caused by decreased cardiac ejection capacity and decreased blood pressure; the formation or aggravation of heart failure may be caused by water and sodium retention, electrolyte disorders, toxins and inflammatory mediators accumulation caused by renal failure.Therefore, how to maintain the balance of body fluid, maintain the stability of circulation, correct the homeostasis of the internal environment and restore the function of heart and kidney is the key to the treatment of CRS, and the application of drugs to dilate blood vessels, diuresis, strong heart and other treatments can only temporarily relieve symptoms and cannot cure cardiorenal syndrome, and long-term use will bring a series of adverse reactions: On the one hand, diuresis to reduce fluid load is the cornerstone of the treatment of CRS, which can not only reduce systemic venous congestion, but also make neurohumoral regulation and inflammatory response tend to balance[29]. However, on the other hand, studies have shown that the use of large doses of strong diuretics may lead to diuretic resistance and prerenal renal damage[30-33], which limits the application of diuretics in the treatment of CRS.Positive inotropic drugs can improve left ventricular ejection fraction, improve cardiac function, and reduce circulating fluid retention, but digitalis drugs and other cardiac drugs can also cause kidney damage while improving cardiac function. Some scholars believe that RAAS system inhibitors (angiotensin enzyme inhibitors, angiotensin receptor antagonists, angiotensin receptor neprilysin inhibitors) can improve the prognosis of patients with heart failure, and can improve renal function[34]. However, other researchers have found that RAAS system inhibitors may cause damage to renal function and accelerate GFR reduction[35]. Therefore, there is a contradiction in the application of RAAS inhibitors in CRS patients with advanced renal dysfunction. In summary, drug therapy alone is often difficult to control the progression of CRS. This leads to the difficulty in the treatment of cardiorenal syndrome, and there is still no radical cure.

As a new type of therapy in recent years, continuous renal replacement therapy (CRRT) is widely used in clinical practice. The value of CRRT in the treatment of CRS patients is getting higher and higher, mainly to prevent complications, protect heart and kidney function, avoid aggravation of the disease and ensure the life safety of patients[36, 37]. This treatment method can greatly reduce the release of serum inflammatory mediators, reduce the level of inflammatory indicators, and improve the body's inflammatory state[38-40]. Some foreign RCT studies have shown that CRRT can quickly eliminate excess water in the body, effectively relieve circulatory overload, and has a better effect on diuretic-resistant CRS[41, 42].

The relative contraindications of CRRT are severe hypotension and obvious bleeding tendency, but there is no absolute contraindication. Timely CRRT can effectively alleviate the side effects of CRS caused by drug treatment, such as increased creatinine, decreased urine volume, and hemodynamic instability.

Based on the complex pathological mechanism of CRS, the poor effect of simple drug treatment and the side effects, CRRT treatment has its unique advantages. This meta-analysis aims to compare CRRT combined with drug treatment and simple medical drug treatment of CRS in reducing patients' creatinine, urea nitrogen, uric acid, improving ejection fraction, BNP and other aspects, to explore the difference in the efficacy of the two treatment effects, and then to evaluate the application value of CRRT in the treatment of cardiorenal syndrome, and to provide a theoretical basis for better clinical treatment of cardiorenal syndrome.

4.2 Research Conclusions

A total of 10 randomized controlled trials were included, involving 741 patients with cardiorenal syndrome. All of them involved the comparison between CRRT combined with medical drugs and simple drugs in the treatment of cardiorenal syndrome. Among them, 8 literatures reported Cr and LVEF, 6 literatures reported BUN, 4 literatures reported UA and BNP, 3 literatures reported LVD, urine volume and cardiac function classification, 2 literatures reported GFR, Ccr, SV, cystatin C and serum potassium. Meta-analysis showed that CRRT combined

with drug therapy had more advantages in reducing creatinine, urea nitrogen and uric acid, improving left ventricular ejection fraction, relieving heart failure and restoring urine volume than conventional drug therapy in the treatment of CRS. In summary, compared with medical treatment, CRRT is a more effective treatment for patients with cardiorenal syndrome.

4.3 Limitations of the Study

①The literature analyzed in this study is all Chinese literature, and the lack of foreign literature has a certain impact on the credibility of the conclusion. ②The number of documents and samples included in the study were small, and no allocation concealment and blind method were reported. ③The course of cardiorenal syndrome is long. This study did not follow up the subjects for a long time, so it is impossible to clarify the long-term therapeutic effect of continuous renal replacement therapy (CRRT) combined with drug therapy on cardiorenal syndrome. ④Most of the outcome indicators had significant heterogeneity. ⑤Because the number of studies containing the same outcome index in all included studies did not exceed 10, no funnel plot was made for publication bias analysis.

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