RESEARCH ARTICLE

A Retrospective Study of the Perioperative Period Management of Joint Arthroplasty in Patients with Chronic Kidney Disease

Hongfu Jin, MB, Graduate Student[1,2], Miao He, MB, Graduate Student[1,2], Guang Yang, MB, Graduate Student[1,2], Wenqing Xie, MB, Graduate Student[1,2], Dengjie Yu, MB, Graduate Student[1,2], Hengzhen Li, MB, Graduate Student[1,2], Wenfeng Xiao, MD, Chief Physicians[1,2], Yusheng Li, MD, Chief Physicians[1,2]

[1]*Department of Orthopedics and* [2]*National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, Hunan, China*

Objective: With the rising prevalence of chronic kidney disease (CKD) and the increasing demand for joint arthroplasty, the management of CKD patients in the perioperative period of joint arthroplasty has become an issue worthy of attention for orthopedic surgeons. This study aimed to explore comprehensive perioperative period management strategies for CKD patients.

Methods: From March 2017 to August 2022, 62 patients who underwent joint arthroplasty in our hospital were included in a retrospective study, including 31 CKD patients (mean age 69.8 ± 13.4 years old) and 31 non-CKD patients (mean age 69.4 ± 14.2 years old). The outcome indicators were analyzed, including serum urea, serum creatinine, blood uric acid, hematocrit, and hemoglobin.

Results: All patients included in the retrospective study had an average preoperative preparation time of 4.3 ± 2.6 days and an average hospitalization time of 11.0 ± 7.3 days. There were no significant differences in the changes in the serum urea values between the preoperative and postoperative measurements in the CKD patients or in the serum creatinine values and blood uric acid values ($P > 0.05$). The hemoglobin value in postoperative measurements was lower than in preoperative measurements in the CKD patients ($P < 0.05$). The hematocrit value in postoperative measurements was lower than in preoperative measurements in the CKD patients ($P < 0.001$).

Conclusion: Patients with CKD have distinct characteristics compared to non-CKD patients, and they generally have a higher risk for postoperative complications and adverse events. Recognition of risk factors, suitable timing of surgery, the undertaking of protective strategies, and proper management of complications are vital for managing CKD patients in the perioperative period of joint arthroplasty.

Key words: Chronic kidney disease; Joint arthroplasty; Perioperative period; Renal function

Introduction

Chronic kidney disease (CKD) has been recognized as a significant public health issue worldwide and can significantly affect older people's quality of life (QoL). With the rising prevalence of CKD and the increasing demands for joint arthroplasty, managing CKD patients in the perioperative period of joint arthroplasty has become an issue worthy of attention. CKD patients are asymptomatic in the early stages, and renal insufficiency increases with its progression. CKD patients are in a high-risk state during the perioperative period, and adverse events can occur postoperatively. Age, male sex, and complications were all independent predictors

Address for correspondence Wenfeng Xiao and Yusheng Li, Department of Orthopedics, Xiangya Hospital, Central South University, Changsha 410008, Hunan, China. Email: xiaowenfeng@csu.edu.cn and liyusheng@csu.edu.cn
Hongfu Jin and Miao He have contributed equally to this work and share the first authorship.
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of postoperative creatinine elevation in CKD patients.[1] Studies have indicated, that compared with non-CKD patients, CKD patients showed worse health conditions and had higher rates of comorbidities and complications in the perioperative period of joint arthroplasty.[2,3] In addition, there have been studies showing that CKD/end-stage renal disease (ESRD) patients had a greater risk of postoperative surgical site infections and wound complications than non-CKD patients, especially CKD/ESRD patients receiving dialysis therapy.[4] All of these findings emphasize the importance of perioperative management strategies for CKD patients after joint arthroplasty.

CKD patients undergoing orthopedic procedures are at increased risk for prolonged morbidity and increased length of postoperative hospital stay.[5] Furthermore, a study showed that CKD is associated with an increased risk of urinary tract infections, myocardial infarction, and all-cause mortality after total knee arthroplasty (TKA).[6] A thorough understanding of the experience of the perioperative management of CKD patients is of great importance for orthopedic surgeons. The primary purpose of the perioperative evaluation and management of CKD patients is to control and reduce the risk factors that can lead to acute kidney injury (AKI). Practical strategies for renal protection are essential for protecting the kidneys from AKI. An increasing number of studies have begun in recent years to focus on perioperative optimization with special risk assessments, including cardiovascular and bleeding risk evaluations, hypertension management, and timing of dialysis.[4,5] Current clinical practice guidelines recommend early recognition and modification of the risk factors associated with CKD progression.[7] The prevention and control of bleeding in the perioperative period of joint arthroplasty are keys to reducing the risk of AKI. Meticulous intraoperative control of surgical trauma and bleeding is essential for preventing low hematocrit, hemoglobin, and blood pressure values after surgical procedures. The risk of postoperative complications can be decreased by reducing the risk of AKI. One study showed that patients with renal dysfunction did not have an increased risk of bleeding or an increased incidence of perioperative blood transfusions with a pragmatic blood-sparing protocol.[8] The purposes of our study were: (i) to analyze the changes in the perioperative indicators; (ii) to summarize the experience of the perioperative management of CKD patients; and (iii) to explore comprehensive perioperative period management strategies for patients with CKD.

Materials and Methods

Patients

The study was approved by the ethics committee of our hospital (No. 202204096) and was exempted by the review board, so informed consent was not required. Electronic medical records were used to collect relevant perioperative outcome variables.

The inclusion criteria were as follows: (i) adults aged ≥18 years old; (ii) diagnosed with CKD; (iii) having signs of joint replacement procedures; and (iv) undergoing joint replacement procedures in our hospital. The exclusion criteria were as follows: (i) severe anemia; (ii) complicated with multiple organ failure; (ii) having a severe bleeding tendency; and (iv) missing or incomplete treatment data.

This retrospective study included 62 patients undergoing total hip/knee/femoral head replacement in our hospital from March 2017 to August 2022. There were 31 CKD patients (14 patients with CKD I, one patient with CKD II, five patients with CKD III, one patient with CKD IV, and nine patients with CKD V) and 31 non-CKD patients. There were 25 patients who underwent THA, 23 patients who underwent FHR, and 14 patients who underwent TKA. Considering that we mainly studied the changes in clinical indicators in CKD patients, we divided the CKD patients into three groups, including the THA group ($n = 13$), the TKA group ($n = 8$) and the FHR group ($n = 10$). Thirty-one non-CKD patients were included in the comparative analysis, which included the THA group ($n = 12$), the TKA group ($n = 6$), and the FHR group ($n = 13$) (Fig. 1).

Management of Patients with Chronic Kidney Disease in the Perioperative Period

Preoperative Management

After admission, all patients were initially admitted for whole history taking and physical examinations and three routine examinations (routine blood examination, routine urine examination, and stool examination). The objective of preoperative examinations was a definitive diagnosis, including CKD stage and comorbid diagnoses. As a result, all CKD patients avoided inappropriate use of drugs with nephrotoxic effects and employed effective strategies for renal protection (Zhi Ling capsules, 2 grains, 3 times/day; coated aldehyde oxysarch capsules, 6 grains, 3 times/day; compound α-ketoacid tablets, 4 grains, 3 times/day).

The diet of CKD patients should conform to the principles of a low-salt, low-fat, and high-quality protein diet. Angiotensin convertase inhibitors (ACEIs), angiotensin receptor blockers (ARBs) or calcium channel blockers (CCBs) and other antihypertensive drugs were taken by the CKD patients with hypertension to keep blood pressure within physiologically tolerated ranges. For CKD patients with renal anemia, oral iron supplementation, such as chalybeate sucrose with or without folic acid tablets, was needed. For CKD patients requiring dialysis, intravenous iron supplementation was needed for those who suffered from iron deficiency. Recombinant human erythropoietin was used for subcutaneous injection (dose 3000 IU, subcutaneous injection, 3 times/week). A low-sugar diet and 24 h blood glucose monitoring were applied in the CKD patients with diabetes. According to the CKD stage, the appropriate hypoglycaemic drugs were chosen to control blood glucose levels. It was important for CKD patients with renal calculi to relieve complete or incomplete obstruction. The patients took tamsulosin 1 h before bedtime and were instructed to drink more water. CKD patients with a high serum potassium level

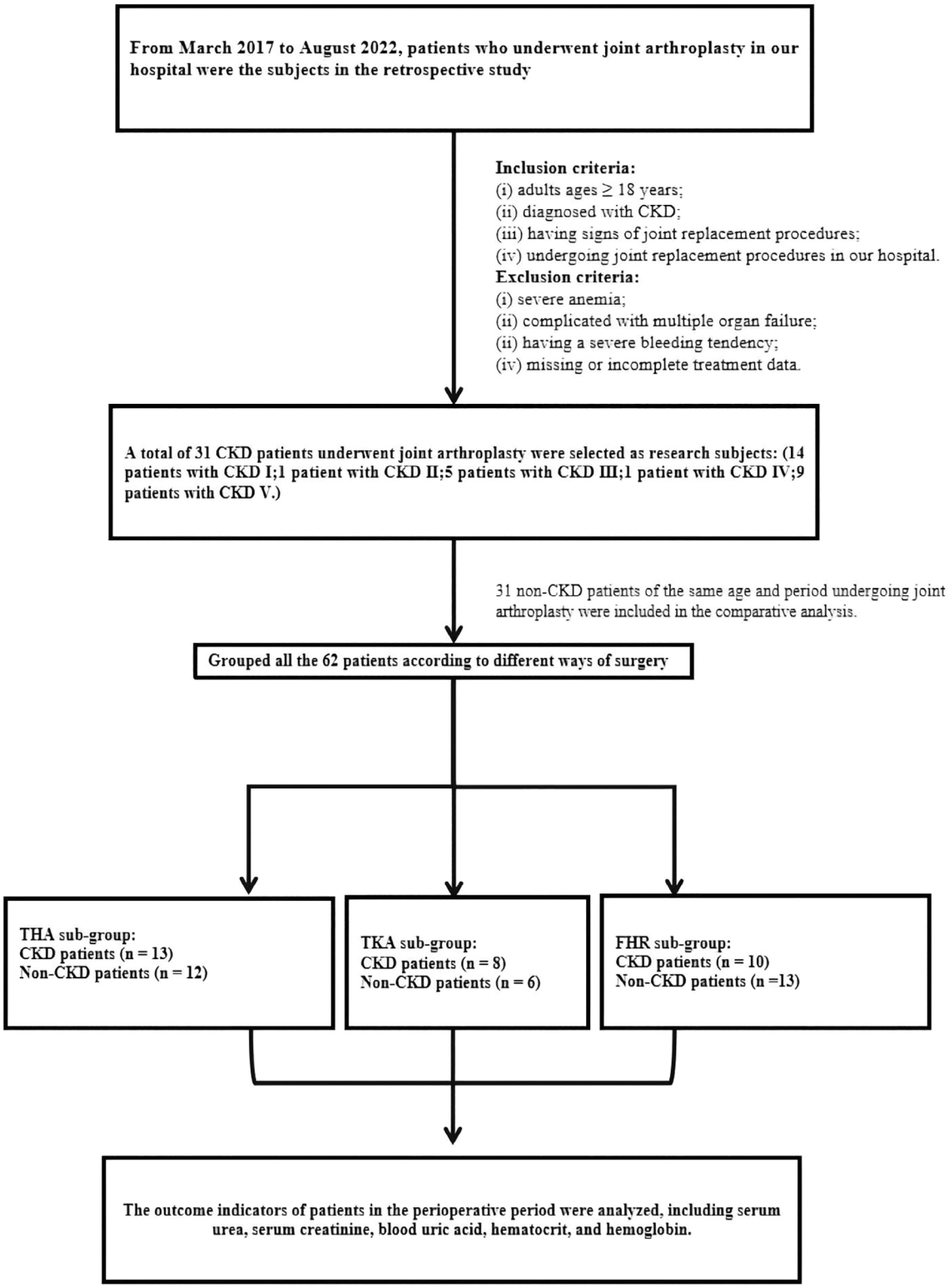

Fig. 1 Flow chart showing the of our study.

were treated with a diuretic. To maintain arterial blood gas homeostasis, sodium bicarbonate was applied based on arterial blood gases. CKD patients with inferior physical function were treated with dialysis.

For CKD patients with bone and mineral metabolism disorders, calcitriol soft capsules (0.25 μg, 1 time/day) were used to regulate bone metabolism and calcium-phosphorus homeostasis. Dynamic monitoring of parathyroid hormone (PTH), blood calcium, and phosphorus was also necessary. For patients with coronary heart disease (CHD), anticoagulant therapy with low molecular weight heparin (LMWH) was administered 12 h before surgery. Ventricular rate control by metoprolol was the primary treatment for CKD patients with atrial fibrillation (AF) and ventricular premature beats (VPBs). Dialysis treatments were used in CKD patients with azotaemia or uraemia. For CKD patients with gout, allopurinol (100 mg, 1 time/day), sodium bicarbonate tablets (0.3 g/piece, 3 times/day), or febuxostat (20 mg/piece, 1 time/day) was administered to control uric acid levels. A high dose of uric acid-lowering drugs and etoricoxib tablets (120 mg, 1 time/day) was used to treat acute gout attacks and relieve pain. Methylprednisolone (8–12 mg/d) was used to alleviate the pain of CKD patients with rheumatoid arthritis (RA). For CKD patients with Parkinson's disease, continuing to take anti-Parkinson's medication was necessary. Antibiotic-based treatment was the primary treatment approach for CKD patients with pulmonary infections.

Intraoperative Management

The surgical team performed the joint replacement procedure under g nerve block combined with general anesthesia. The patients undergoing TKA were in the supine position. Using the parapatellar medial approach, cutting of the joint capsule and cleaning of the synovium and osteophytes were included in the whole procedure. Osteotomy and removal of soft tissues were performed according to additional damage to the knee joint. The proximal tibial bone defect was repaired by tibial autografts and fixed with cement. A knee prosthesis with posterior cruciate substitution was used (Smith & Nephew, London, UK).

A lateral position and posterior-lateral approach were used for THA or FHR. The hip joint capsule was opened to remove the diseased femoral head. The acetabular and femoral head sides were processed to install the hip joint prosthesis. FHR was the transformation of the femoral head into an artificial femoral head replacement without the acetabulum. THA was the transformation of both the acetabulum and the femoral head. A classic plus bone-cemented hip prosthesis was used (Link, Hamburg, Germany).

Surgical stress results in CKD patients being at risk for developing renal dysfunction. The primary goals of managing the bleeding intraoperatively are avoiding hypotension, maintaining adequate renal perfusion and oxygenation, maintaining hemostasis while simultaneously smoothly keeping intravenous rehydration to prevent blood pressure fluctuations, and achieving the goal of blood pressure control. All CKD patients were infused to hold water and electrolyte balances during the intraoperative period. Vital signs were monitored during the procedure, and a laryngeal mask airway was used to achieve airway management. Anesthetic drugs were appropriately reduced in elderly patients with CKD.

Postoperative Management

After surgery, the following treatment measures were undertaken by CKD patients: real-time electrocardiogram (ECG) monitoring, oxygen uptake, anti-infection, and fluid management. The ECG monitoring system was used after joint arthroplasty. Postoperative oxygen was routinely administered to prevent hypoxaemia. Antibiotics were used to avoid postoperative infections. Postoperative fluid management was based on the patient's status and type of operation.

Outcome Measures

Serum Urea Measurement

Serum urea is one of the most common assays used in the clinical assessment of glomerular function. Automated enzyme-coupled assay was performed for the determination of serum urea values. Urease catalyzes the hydrolysis of urea to produce carbon dioxide and ammonia. Glutamate dehydrogenase catalyzes the interconversion of ammonia and α-ketoglutarate to produce glutamate. At the same time, the reduced form of coenzyme I transforms into the oxidized form of coenzyme I. The reduced form of coenzyme I has an absorption peak at 340 nm. Its absorbance is proportional to the content of urea in the sample. All serum urea values were obtained from the electronic medical records during the patients' hospitalization.

Creatinine Measurement

Serum creatinine concentrations reflect the glomerular filtration rate. The alkaline picrate assay (Jaffe) and the enzymatic assay were used to measure serum creatinine levels. All creatinine values were obtained from the electronic medical records during the patients' hospitalization.

Serum Uric Acid Measurement

Uric acid is excreted mainly by the kidneys, and the level of uric acid in serum is associated with the glomerular filtration rate. Uric acid is metabolized to allantoin and hydrogen peroxide (H_2O_2) by the enzyme uricase. Catalase enzyme catalysis of H_2O_2 creates 3,5-dichloro-2-hydroxybenzenesulfonic acid, and 4-aminoantipyrine forms red quinone compounds. The absorbance at a wavelength of 520 nm is proportional to the serum uric acid concentration. All serum uric acid values were obtained from the electronic medical records during the patients' hospitalization.

Hematocrit Measurement

Hematocrit determines the volume ratio of red blood cells in the blood. The quantitative anticoagulant blood was injected

into a Wen's ratio tube and centrifuged at a certain speed and time, providing the red blood cells and plasma deposition ratio of the volume per liter of red blood cells. All hematocrit data were obtained from the electronic medical records during the patients' hospitalization.

Hemoglobin Measurement

The cyanide methaemoglobin (HiCN) colorimetric method was used to measure hemoglobin. Blood hemoglobin, except for sulphide hemoglobin (s-Hb), can be oxidized to Hi by high potassium ferricyanide and can be combined with the CN domain to produce a stable brown-red complex HiCN. The maximum absorption peak of HiCN was 540 nm. The absorbance of HiCN at 540 nm can be directly proportional to the concentration in the solution. The hemoglobin concentration of the tested specimen could be obtained according to the measured absorbance. The blood cell analyzer automatically analyzed all of these steps. All hemoglobin data were obtained from the electronic medical records during the patients' hospitalization.

Statistical Analysis

Data analysis was conducted using IBM SPSS software version 26 (IBM, Armonk, NY, USA) and GraphPad Prism software version 9.3.1 (GraphPad Software Company, La Jolla, CA, USA). Quantitative data are shown as the mean ± standard deviation. Homoskedasticity (equal variances) was tested *via* the F test. All clinical indicator comparisons were performed between the preoperative and postoperative measurements using *t*-tests. Student's two-tailed *t*-test was used to compare the differences in admission pain scores among different groups. All statistical tests were two-tailed, and significance was considered at $P < 0.05$.

Results

General Information

There were 38 men (mean age was 74.2 ± 9.7 years old) and 24 women (mean age was 62.3 ± 15.9 years old). All of the patients included in the retrospective study had an average preoperative preparation time of 4.3 ± 2.6 days and an average hospitalization time of 11.0 ± 7.3 days. The combined diagnoses of the CKD patients included 14 patients with hypertension, nine patients with diabetes, seven patients with renal anemia, six patients with coronary heart disease, five patients with a history of cerebral hemorrhage or cerebral infarction, four patients with gout, three patients with bone and mineral metabolism disorders, and nine patients with hyperkalemia. The combined diagnoses of the non-CKD patients included nine patients with hypertension, one patient with diabetes, one patient with renal anemia, five patients with coronary heart disease, two patients with a history of cerebral hemorrhage or cerebral infarction, two patients with gout, and three patients with bone and mineral metabolism disorders. The comparison of the clinical parameters between the CKD patients and the non-CKD patients is shown in Table 1.

Clinical Indicator Assessments

Statistical methods were used to compare all clinical indicators between the preoperative and postoperative measurements 1 day after surgery. Figure 2 presents the serum urea values in the CKD patients and the non-CKD patients. The results showed that there were no significant differences in the changes in the serum urea values between the preoperative and postoperative measurements in the CKD patients ($P > 0.05$; Fig. 2A). The CKD patients in the THA and FHR subgroups had a larger serum urea value than the non-CKD patients in preoperative measurements ($P < 0.001$), as well as postoperative measurements, in the THA subgroup ($P < 0.01$) and the FHR subgroup ($P < 0.001$; Fig. 2B,C).

The changes in serum creatinine values in the CKD patients and the non-CKD patients are shown in Fig. 3. The results showed that there were no significant differences in the changes in the serum creatinine values between the preoperative and postoperative measurements in the CKD patients ($P > 0.05$; Fig. 3A). The CKD patients in the THA subgroup had a larger serum creatinine value than the non-CKD patients in preoperative measurements ($P < 0.01$). The CKD patients in the THA subgroup had a larger serum creatinine value than the non-CKD patients in postoperative

TABLE 1 Comparison of the clinical parameter between CKD patients and non-CKD patients

Parameter	CKD patients ($n = 31$)	Non-CKD patients ($n = 31$)	T value/χ^2 value	P value
Age (years)	69.8 ± 13.4	69.4 + 14.2	$t = 0.1178$	0.9067
Male (n, %)	16 (51.61%)	20 (64.52%)	$\chi^2 = 1.0598$	0.3033
Hip (n, %)	23 (92.31%)	25 (88.46%)	$\chi^2 = 0.3690$	0.5435
Hospitalization time (d)	11.7 ± 9.8	10.3 ± 3.0	$t = 0.7261$	0.4706
Preoperative preparation time (d)	4.0 ± 2.3	4.7 ± 2.9	$t = 0.7261$	0.3168
Intraoperative bleeding (ml)	189.0 ± 157.7	188.3 + 166.6	$t = 0.0169$	0.9866
Smoking number (n, %)	5 (16.13%)	6 (19.35%)	$\chi^2 = 0.1105$	0.7396
Drinking number (n, %)	4 (12.90%)	7 (22.58%)	$\chi^2 = 0.9947$	0.3186

Note: Quantitative data were shown as mean ± standard deviation or number of individuals (percentages); Abbreviations: CKD: chronic kidney disease.

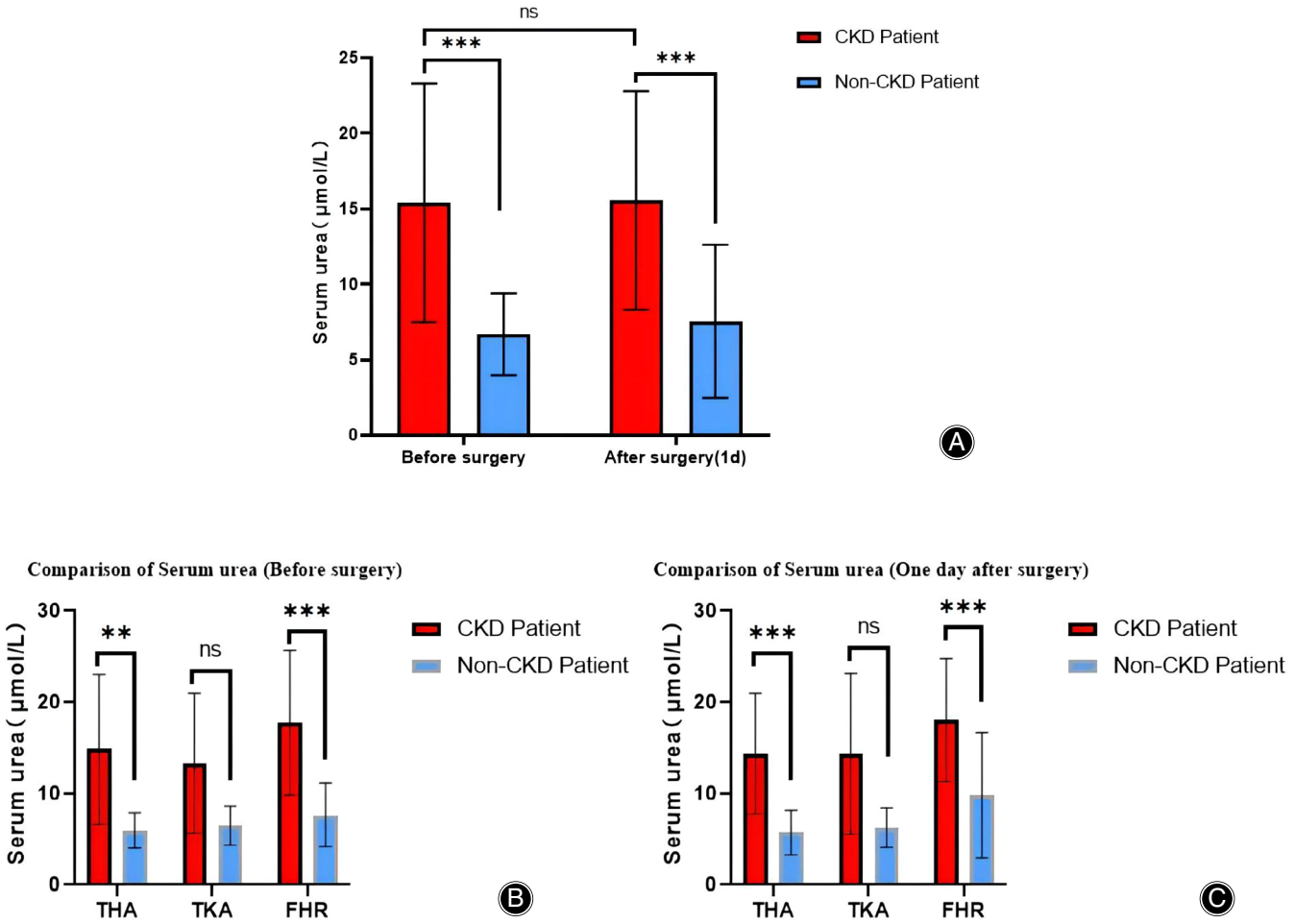

Fig. 2 The serum urea values of CKD patients compared to the non-CKD patients in the Perioperative Period. (A) Comparison of serum urea between the preoperative and postoperative measurements in CKD patients and non-CKD patients. (B) Comparison of serum urea values in the preoperative measurements among the subgroups (THA, TKA, and FHR); (B) Comparison of serum urea values in the postoperative measurements among the subgroups (THA, TKA, and FHR). *Notes*: ns: not significant; $^{**}P < 0.01$, $^{***}P < 0.001$.

measurements ($P < 0.001$), as did those in the FHR subgroup ($P < 0.0001$; Fig. 3B,C).

The results showed that there were no significant differences in the changes in the blood uric acid values between the preoperative and postoperative measurements in the CKD patients ($P > 0.05$). The blood uric acid value in CKD patients was larger than in non-CKD patients in the preoperative measurements ($P < 0.001$), as well as in postoperative measurements ($P < 0.0001$; Fig. 4A). The CKD patients in the THA subgroup had a larger serum urea value than the non-CKD patients in preoperative measurements ($P < 0.0001$), as well as in postoperative measurements in the THA subgroup ($P < 0.0001$; Fig. 4B,C).

Figure 5A shows the individual hemoglobin values in the CKD and non-CKD patients (each point represents the value of hemoglobin of an individual in the perioperative period). The results showed that there were no significant differences in the hemoglobin values between the CKD and non-CKD patients in the preoperative and postoperative measurements ($P > 0.05$). The hemoglobin value in postoperative measurements was lower than in preoperative measurements in the CKD patients ($P < 0.05$). No significant differences were found in the hemoglobin values between the preoperative and postoperative measurements in any of the subgroups of CKD and non-CKD patients ($P > 0.05$; Fig. 5B,C).

The results showed that there were no significant differences in the changes in the hematocrit values in the preoperative and postoperative measurements between the CKD and non-CKD patients ($P > 0.05$; Fig. 6A). The hematocrit value in postoperative measurements was lower than in preoperative measurements in the CKD patients ($P < 0.001$; Fig. 6B). The hematocrit value in the TKA subgroup of CKD patients was lower than in the TKA subgroup of non-CKD patients in postoperative measurements ($P < 0.01$; Fig. 6C).

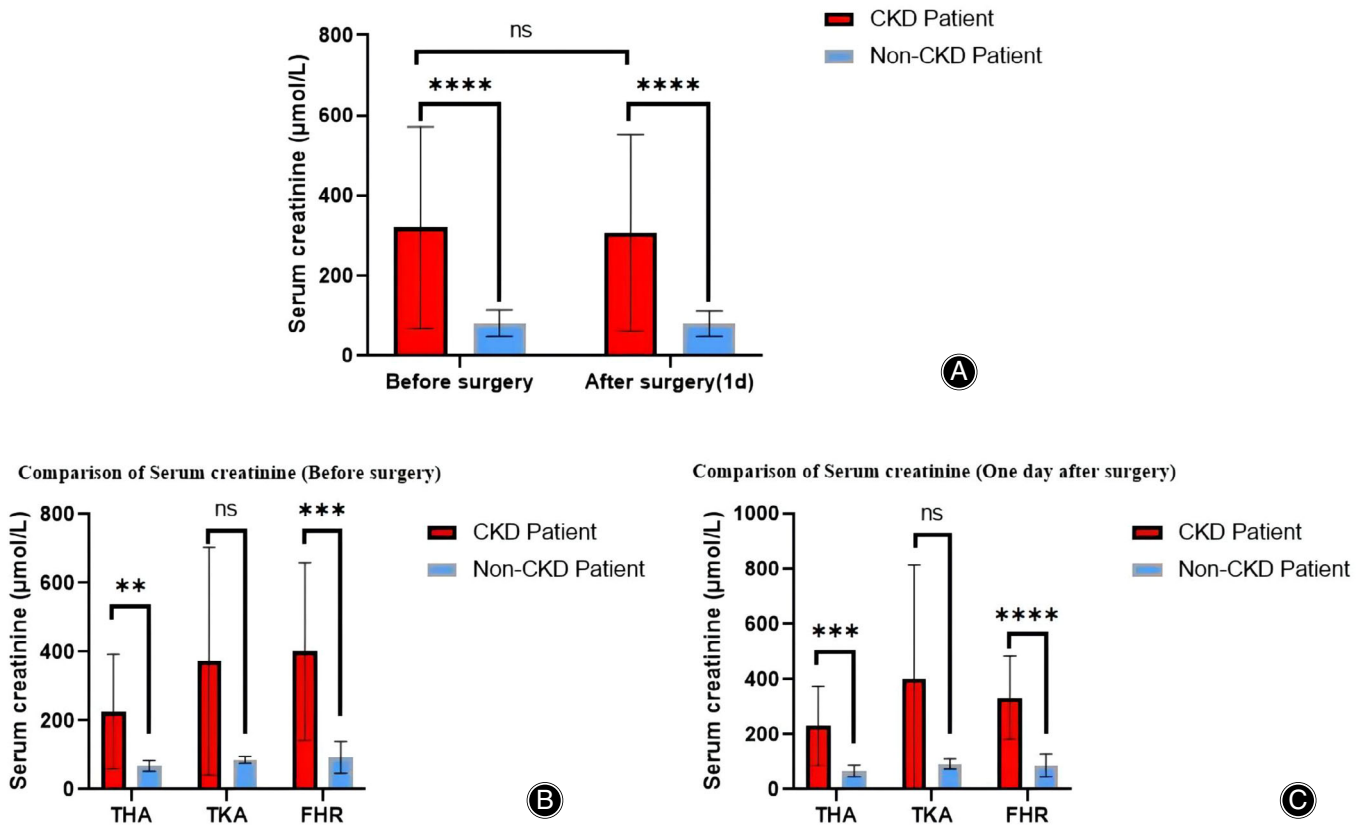

Fig. 3 The serum creatinine values of CKD patients compared to the non-CKD patients in the Perioperative Period. (A) Comparison of serum creatinine between the preoperative and postoperative measurements in CKD patients and non-CKD patients. (B) Comparison of serum creatinine values in the preoperative measurements among the subgroups (THA, TKA, and FHR); (B) Comparison of serum creatinine values in the postoperative measurements among the subgroups (THA, TKA, and FHR). *Notes*: ns: not significant; $^{**}P < 0.01$, $^{***}P < 0.001$.

Complications

There was one patient with mild liver dysfunction. Reduced glutathione tablets and pantoprazole were taken by the patient. One patient complained of dyspnoea and restlessness. Cedi-lanid was administered through intravenous injection to attain a strict rate-control target of resting heart rate. Aminophylline was taken by the patient through intravenous injection to induce bronchial relaxation. Sodium nitroprusside was also taken by the patient through intravenous administration. Furosemide was taken by the patient through intravenous administration to reduce volume overload. The patient with hypovolaemic shock received the following treatment measures: vital sign detection, fluid management, and elevated blood pressure. The patient with narcolepsy received the following treatment measures: anti-infection, aminophylline injected intravenously to relieve bronchospasm, and induced sputum using nebulized saline.

Discussion

Main Findings of the Study

Managing CKD patients in the perioperative period of joint arthroplasty has become an issue worthy of attention. There is an increasing prevalence of CKD worldwide. As a result, the demand for joint arthroplasty in CKD patients is also increasing. In our study, we summarized the characteristics of CKD compared to non-CKD patients, and they generally have higher risks of postoperative complications and adverse events. Recognition of risk factors, suitable timing of surgery, the undertaking protective strategies, and proper management of complications are vital for managing CKD patients in the perioperative period of joint arthroplasty.

Perioperative Characteristics of Patients with Chronic Kidney Disease Undergoing Joint Replacement

CKD patients undergoing joint replacement differ from hospice inpatients in some features, which demand special attention: (i) these patients are seniors; (ii) the complications are complex and multifactorial; (iii) there is a high risk of AKI during and after the procedure; and (iv) there is a high risk of postoperative infectious complications. With the increasing aging population and the larger prevalence of CKD, an increasing number of CKD patients have received joint replacement surgery in recent years.[9] Preventing and controlling bleeding in the perioperative period of joint

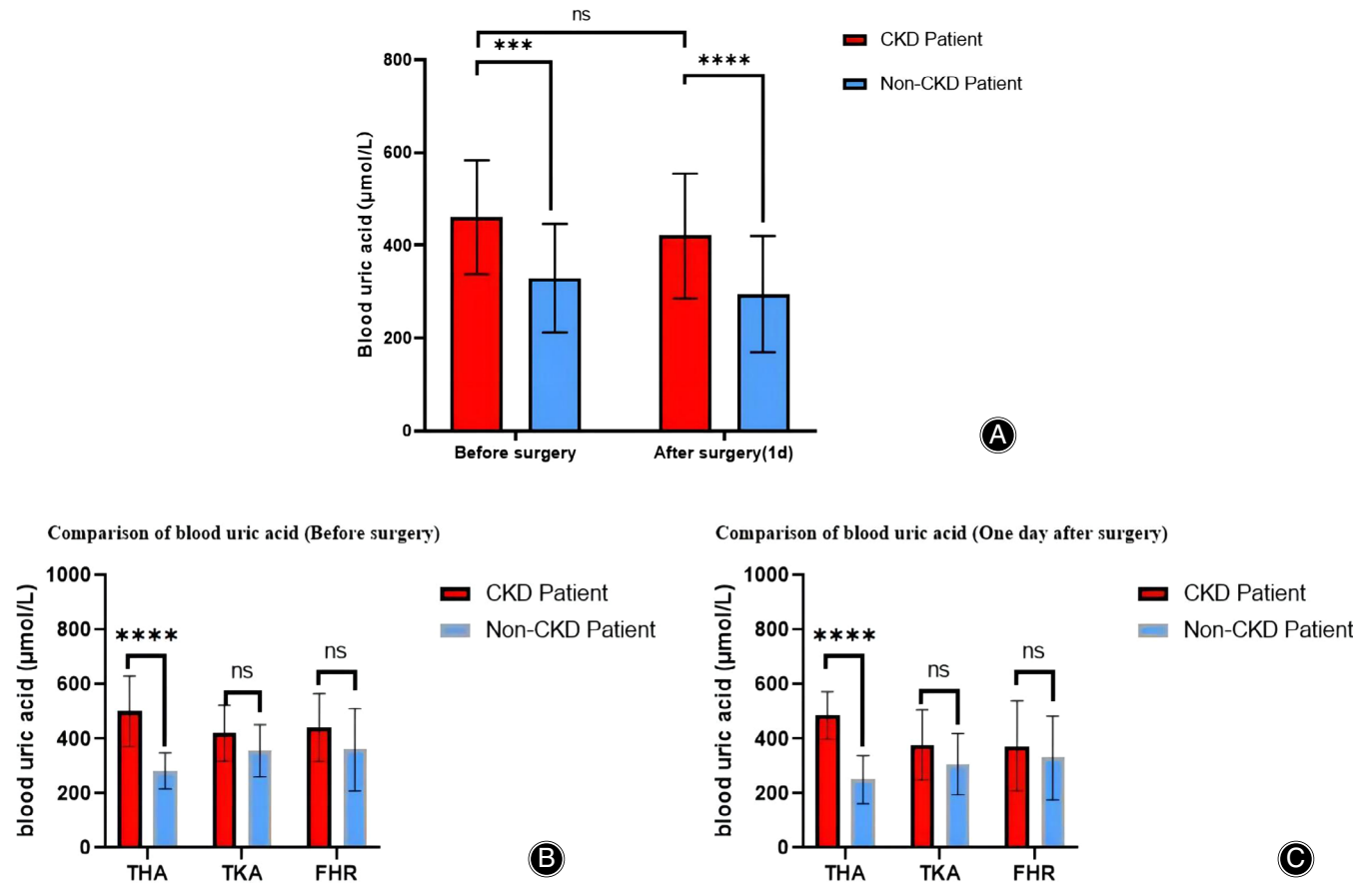

Fig. 4 The blood uric acid values of CKD patients compared to the non-CKD patients in the Perioperative Period. (A) Comparison of serum creatinine between the preoperative and postoperative measurements in CKD patients and non-CKD patients. (B) Comparison of serum creatinine values in the preoperative measurements among the subgroups (THA, TKA, and FHR); (B) Comparison of serum creatinine values in the postoperative measurements among the subgroups (THA, TKA, and FHR). *Notes*: ns: not significant; $^{**}P < 0.01$, $^{***}P < 0.001$.

arthroplasty are keys to reducing the risk of AKI. Meticulous intraoperative control of surgical trauma and bleeding is essential for preventing low hematocrit, hemoglobin, and blood pressure values after surgical procedures. The risk of postoperative complications can be decreased by reducing the risk of AKI. Various complications can develop after joint replacement, including postsurgical infection, AKI, cardiovascular events, and even death.[10] Studies have shown that the risk of preoperative AKI in CKD patients undergoing joint replacement was 6.2%, and male patients with preoperative comorbidities, such as diabetes, hypertension, and using vancomycin preoperatively, were associated with an increased risk of AKI.[11] The occurrence of AKI negatively impacts patient prognosis. In addition, AKI has adverse effects on immune function, which is widely considered the consequence of immune suppression. Compromised immune function renders CKD patients more vulnerable to pathogens. Studies have indicated that CKD patients with AKI have a significantly increased risk of infection and sepsis.[12] More than half of CKD patients who have AKI after surgery were mild or not severe cases, with good outcomes. However, 18% of CKD patients do not recover after surgery, and patients can remain symptomatic for a long time. Studies have shown that CKD is a significant risk factor for the progression of AKI.[13] Therefore, the prevention of AKI is essential for treating CKD patients during the perioperative period. The most frequent complications of CKD are hypertension, anemia, heart failure, electrolyte disturbances, acid–base imbalances, renal osteopathy, and infections.[14] Patients with CKD III, CKD IV, or CKD V are at higher risk for postoperative complications than other hospice inpatients or patients with CKD I or CKD II.[15] At the same time, patients admitted for CKD III, CKD IV, or CKD V are at high risk for readmission and mortality after discharge.[16] CKD patients are immunocompromised, making them more vulnerable to bacterial infections. Therefore, anti-infection treatment in the perioperative period of CKD patients is essential.[17] The preoperative and postoperative radiographic changes in Fig. 7 show that one patient achieved satisfactory surgical results after excellent perioperative management.

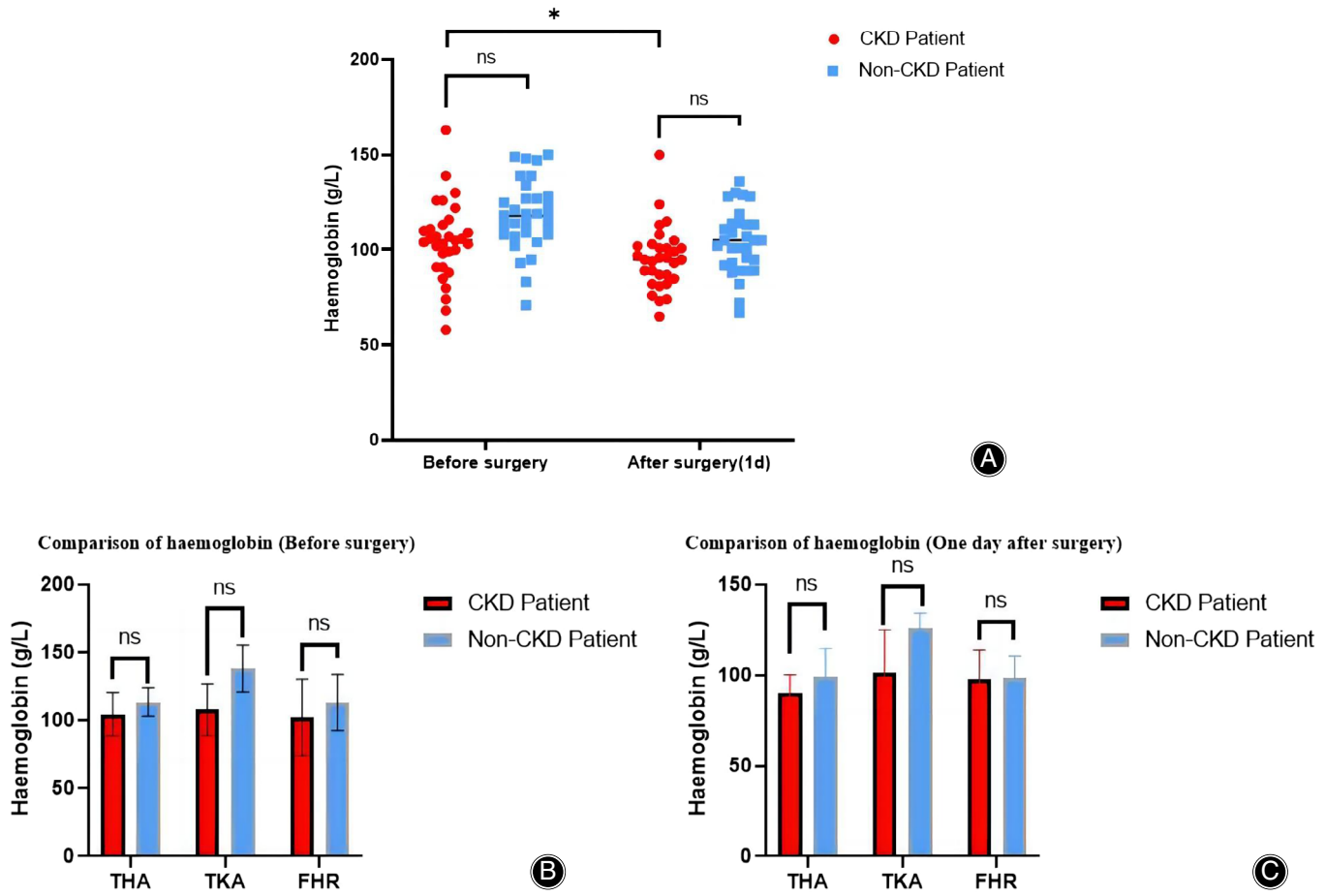

Fig. 5 The individual hemoglobin values of CKD patients compared to the non-CKD patients in the Perioperative Period. (A) Comparison of hemoglobin values between the preoperative and postoperative measurements in CKD patients and non-CKD patients. (B) Comparison of hemoglobin values in the preoperative measurements among the subgroups (THA, TKA, and FHR); (B) Comparison of hemoglobin values in the postoperative measurements among the subgroups (THA, TKA, and FHR). *Notes*: ns: not significant; *$P < 0.05$.

Perioperative Focus of Patients with Chronic Kidney Disease

Identifying Risk Factors

Early detection and identification of risk factors are the priority in managing CKD patients in the perioperative period of joint arthroplasty. The high costs of care, adverse outcomes, and increasing burden of ESRD make it a significant global public health issue. Therefore, it is essential to identify risk factors and prevent their progression to ESRD in the perioperative period. The effects of the perioperative treatment of these patients on the short- and long-term prognoses of patients undergoing surgery have been recognized as a health concern. A multidisciplinary assessment approach is required to reduce peri-anesthetic risks and improve perioperative outcomes for CKD patients. Traditional risk factors include aging, smoking, alcohol, and nephrotoxic drugs.[18] Risk factors for a poor outcome following surgery include renal anemia, bleeding, the burden of cardiovascular diseases (CVDs), and haemodynamic overload, which are more common in CKD patients. In addition, the risks associated with dialysis treatment are endemic to these patients.[19] Renal anemia, a common feature of CKD, is associated with adverse outcomes, such as decreased quality of life, hospitalization, cognitive impairment, and increased mortality. Clinical trials have shown an increased risk of complications related to erythropoiesis-stimulating agents (ESAs) used in CKD patients to treat anemia.[20] Many studies have shown that the serum urate concentration is an independent predictor of CKD incidents, such as arteriosclerosis, glomerular injury, and renal tubulointerstitial fibrosis.[21] Therefore, it is reasonable to regard a high serum urate concentration as a risk factor for CKD. Hypertension is not only a cause but also a consequence of CKD. The interaction between hypertension and CKD is complex and increases the risk of adverse cardiovascular outcomes.[22] Diabetic kidney disease is the primary cause of CKD and ESRD. Long-term high blood glucose levels will lead to glomerular hypertrophy,

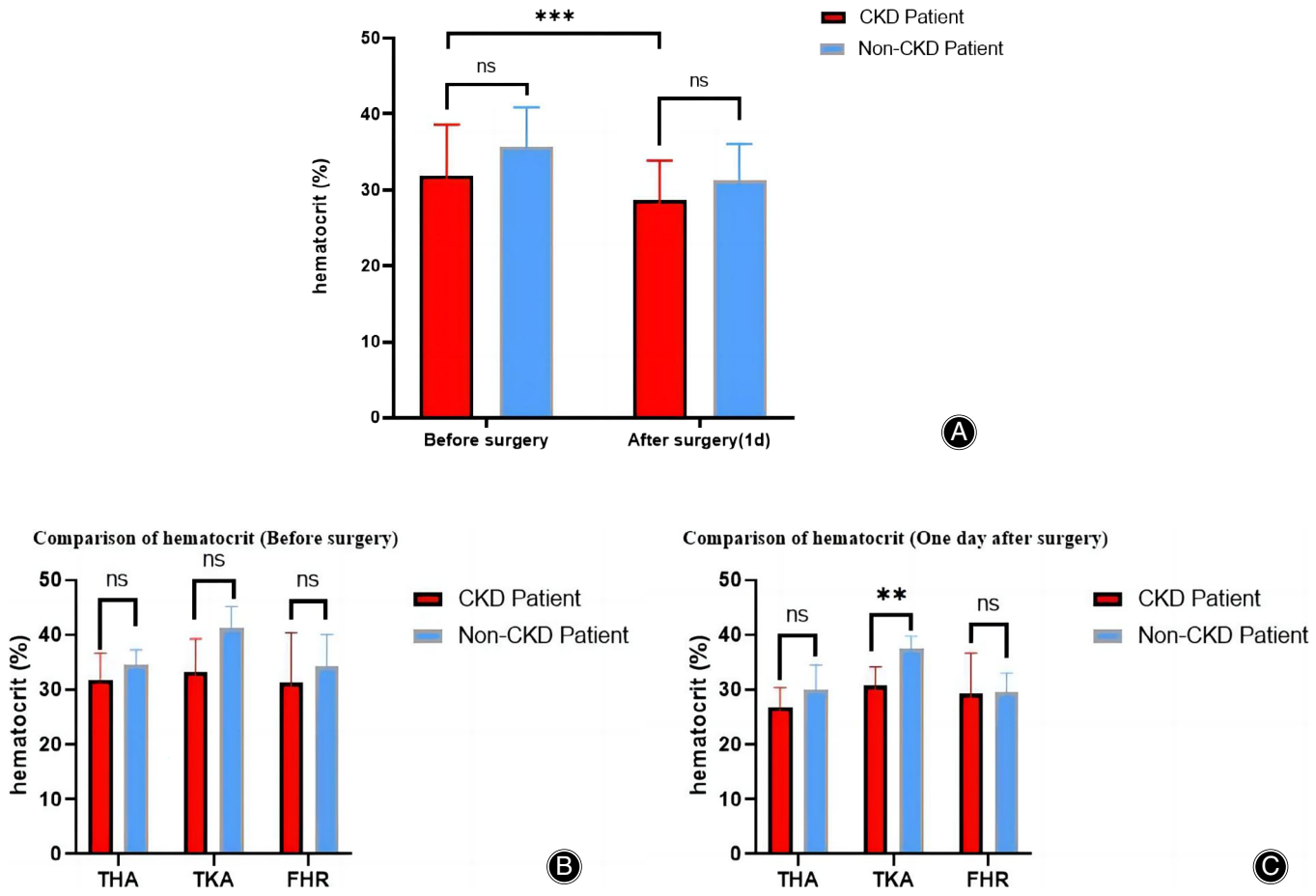

Fig. 6 The hematocrit values of CKD patients compared to the non-CKD patients in the Perioperative Period. (A) Comparison of hematocrit values between the preoperative and postoperative measurements in CKD patients and non-CKD patients. (B) Comparison of hematocrit values in the preoperative measurements among the subgroups (THA, TKA, and FHR); (B) Comparison of hematocrit values in the postoperative measurements among the subgroups (THA, TKA, and FHR). *Notes*: ns: not significant; $^{**}P < 0.01$, $^{***}P < 0.001$.

glomerulosclerosis, renal tubulointerstitial inflammation and fibrosis, and other renal pathological changes.[23] Many epidemiological studies have confirmed that CKD patients have a significantly increased risk of cardiovascular disease. The association was attenuated after adjustment for traditional cardiovascular risk factors. Impaired kidney function and elevated urinary albumin concentrations increase the risk of cardiovascular disease by 2–4 fold.[24] Advanced age, hypertension, diabetes, and dyslipidaemia in CKD patients undergoing joint replacement are high-risk factors for cardiovascular disease.[25]

Renal Protection Strategies

Considering the poor renal function of CKD patients, it is essential to protect residual renal function and undertake effective management measures against complications that can lead to loss of renal function during the perioperative period of joint replacement. Nutrition management of CKD patients is an essential component of renal protection strategies. High protein intake can lead to increased glomerular perfusion pressure and glomerular hyperfiltration, damaging the glomerular filtration barrier and improving the glomerular filtration rate and albuminuria. Dietary protein restriction is one of the significant components of therapy for CKD patients. CKD patients can benefit from a dietary protein intake (DPI) of <0.8 g/kg/day.[26] Nutrition management of CKD patients should be based on low-protein and individualized diets to ensure adequate protein and energy intake.[27] Ketoacid analogues of essential amino acids (KA/EAA) can be converted into their respective amino acids without providing additional nitrogen, and they can be used as an important nutritional supplement for CKD patients to improve their nutritional status. Studies have shown that a low-protein diet combined with KA/EAA supplementation can delay CKD progression.[26] Advanced age is typical in CKD patients who have multisystem pathology and receive multiple medications. CKD is significant in halting the drug use of patients. A substantial proportion of the circulating drugs is excreted *via* the kidneys. Improper drug selection can cause a rapid deterioration in kidney function.[28] During

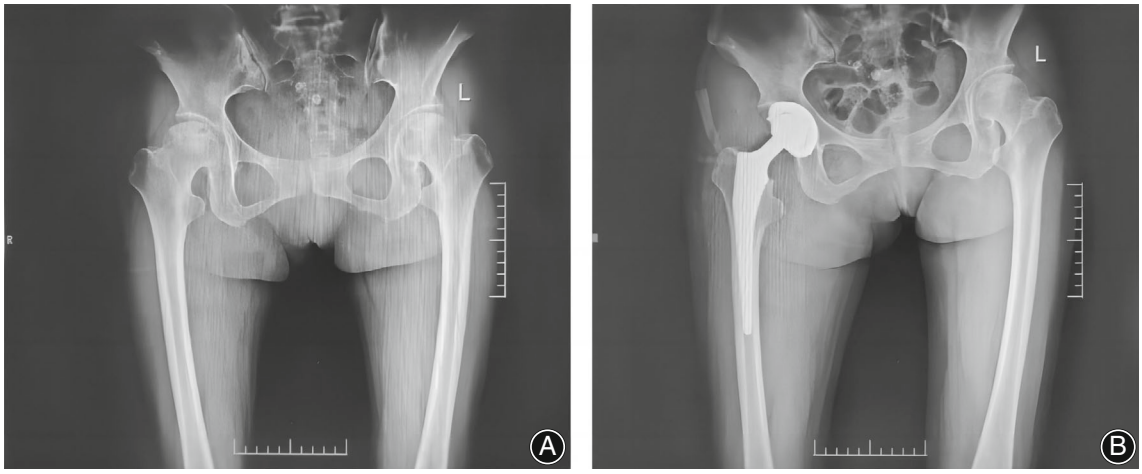

Fig. 7 The preoperative and postoperative radiographic changes in the hip joints of one elderly patient with CKD (Anteroposterior Pelvic Radiograph). (A) The femoral heads' bone mineral density (BMD) was inhomogeneous, and there were low-density zones under the articular surface. The lesion at the right is distinct compared with the left side. (B) The artificial joint was visible in the right hip joint with a good position and no radiological signs of implant loosening.

therapy for diabetes, hypertension, primary kidney diseases, or other diseases that can deteriorate kidney function, it is essential to avoid using nephrotoxic drugs in CKD patients. Considering that there are electrolyte imbalances and fluid overload in CKD patients, it is important to focus on the perioperative fluid management of CKD patients. Improper fluid management can be associated with an increased risk of adverse postoperative outcomes. Studies have shown that forced diuresis by fluid overload can compromise kidney function. Perioperative fluid management is a crucial element of perioperative care, and it is essential to maintain stable haemodynamics and sufficient organ perfusion. The renin-angiotensin-aldosterone system (RAAS) is pivotal to regulating and preserving renal function. The application of RAAS blockers could help to correct fluid imbalance.

Surgical Timing

According to the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, it is essential to evaluate the risks and benefits of renal replacement therapy (RRT) when renal function declines, reaching CKD V (GFR <15 ml/min·1.73 m^2).[29] Hemodialysis is necessary before joint replacement in patients with CKD V. However, dialysis-dependent patients are at a higher risk of adverse outcomes during and after surgery, so postdialysis surgical timing is a vital issue. Using anticoagulants in hemodialysis is crucial. Heparin is a widely used anticoagulant in clinical practice. Other alternative anticoagulants include low molecular weight heparin, direct thrombin inhibitors, heparin analogues, citrate, etc.[30] However, treatment with anticoagulants requires a constant balance between undertreatment and overtreatment to prevent premature clotting of the extracorporeal circuit or a high bleeding risk after dialysis. CKD can increase the risks of intraoperative and postoperative bleeding. Experts recommend heparin-free hemodialysis for CKD patients.[31] Studies have shown many local and systemic risk factors in dialysis-dependent patients undergoing joint replacement. Satisfactory results following these procedures can be achieved by the appropriate timing of surgical interventions.[32] Surgery is considered safe for patients on anticoagulant hemodialysis if the hematological indicators are in the tolerance range for surgery after a brief period (24–48 h). Surgery for patients with heparin-free hemodialysis is considered safe after 24 h if the hematological indicators are in the tolerance range for surgery after a brief period.[33] In conclusion, the coagulation function of patients after dialysis merits close attention. Avoiding a hypercoagulable state during the operative procedure is the criterion for surgical timing.[34] Dialysis can improve the tolerance of CKD patients to surgery by maintaining water and electrolyte balances and controlling metabolic waste products and toxins within tolerance levels.

Management of Perioperative Complications in Patients with Chronic Kidney Disease

Hypertension

Hypertension is both a cause and a consequence of CKD. Blood pressure usually increases as kidney function declines, and continued elevated blood pressure accelerates the progression of renal disease. Hypertension, occurring in more than 80% of CKD patients, leads to an increased risk of progression to ESRD and serious cardiovascular events, such as heart attacks and stroke. Studies have shown that the risk of cardiovascular death in CKD patients is greater than the risk of progressing to ESRD in CKD patients.[35] Perioperative blood pressure control is vital for CKD patients. However, there is no consensus on the optimal blood pressure target

for these patients in existing guidelines.[36] The blood pressure target for all CKD patients recommended by the National Kidney Foundation (NKF) clinical practice guidelines is 130/80 mm Hg.[37] The Japanese Society of Nephrology (JSN) and the Japanese Society of Hypertension (JSH) recommended in their respective guidelines that, for CKD patients with diabetes, the target levels of blood pressure are 130/80 mm Hg; for all nondiabetic CKD patients, it is strongly recommended that the target blood pressure level be 140/90 mm Hg.[38] Good blood pressure management could provide renal protection in CKD patients. In general, with progression of the CKD stage, the difficulty of blood pressure control gradually increases. Proper management of hypertension could provide protective effects on the kidneys for CKD patients.

Generally, blood pressure control problems gradually increase with CKD upstaging. International diagnosis and treatment guidelines recommend angiotensin-converting enzyme inhibitors (ACEIs) as the first-line standard treatment for such patients. ARBs could be an alternative to ACEIs if patients are intolerant to ACEIs or if these drugs are contraindicated. ACEIs and ARBs are RAAS inhibitors that are superior to other antihypertensive drugs in controlling blood pressure, decreasing urinary protein, and protecting renal function.[34] Studies have shown that ACEIs/ARBs can effectively prevent ESRD and cardiovascular events. However, it remains necessary to combine RAAS inhibitors with other antihypertensive drugs (such as calcium channel blockers, diuretics, etc.) to achieve optimal BP control.[39] The management of hypertension in dialysis-dependent CKD patients should focus on ambulatory blood pressure measurements and the use of long-acting antihypertensive drugs.[40] Close monitoring of blood pressure and adjusting of antihypertensive medications according to patients' conditions are essential for perioperative blood pressure control.

Anemia

Anemia, a common complication in CKD, has been confirmed to be associated with adverse outcomes. Anemia in CKD is typically normocytic, normochromic, and hyperproliferative. Deficiency of erythropoietin (EPO) and reduced erythropoiesis are the leading causes of CKD anemia.[41] Other causes include EPO resistance, iron deficiency, chronic inflammation, uraemic toxins, shortened-life RBCs, and vitamin deficiency (vitamin B12 or folic acid).[20] In dialysis-dependent CKD patients, hemodialysis can also cause blood loss and breakdown of RBCs. Therefore, perioperative management of anemia is an essential part of the health care of CKD patients. Erythropoiesis-stimulating agents (ESAs) and iron supplementation are the primary treatment measures for anemia in CKD.[42] Iron supplementation (oral or intravenous) is the standard first-line treatment for CKD anemia. At the same time, ESAs (IV and subcutaneous) are available for treating CKD anemia that cannot be corrected by iron supplementation alone. Hb <9 g/dl is often considered the intervention threshold for CKD anemia, and the target Hb range is 10–11 g/dl, consistent with recommendations of the US Food and Drug Administration (FDA).[43]

ESAs improve clinical outcomes in CKD patients. However, they have not been shown to reduce adverse effects. Trials have shown an increased risk of death, adverse cardiovascular events, and stroke when using ESAs for the treatment of anemia in CKD patients.[44] Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), which are new drugs to treat anemia in CKD patients, can promote the generation of endogenous EPO by inhibiting prolyl hydroxylase activity, leading to the production of hypoxia-inducible factor-α (HIF-α) in the liver and kidney. HIF-2α mainly controls EPO expression and iron-regulated genes. HIF-2α can directly upregulate the gene expression of iron transporters and indirectly inhibit the expression of hepcidin from promoting iron utilization.[45] One potential benefit of HIF-PHIs in treating renal anemia compared with ESAs is that Hb control targets can be achieved at lower EPO plasma levels. The increasing morbidity and mortality of cardiovascular disease patients treated with ESAs have been associated with supraphysiological levels of EPO in plasma.[46]

Hyperglycaemia

Diabetes, particularly type 2 diabetes mellitus (T2DM), is the primary cause of CKD and ESRD worldwide, resulting in nearly half of CKD patients requiring renal replacement therapy.[47] A retrospective cohort study showed a significant incidence of AKI in patients with diabetes compared to patients without diabetes.[48] For CKD patients with diabetes, establishing individualized glycaemic targets to maintain normal blood glucose levels during the perioperative period is of great significance. The risk of hypoglycaemia in patients with diabetic nephropathy (DN) increased when the GFR was <60 mL/min·1.73 m,[2] mainly caused by decreased clearance of hypoglycaemic drugs and downregulation of renal gluconeogenesis.[49] Therefore, choosing of hypoglycaemic drugs requires carefully weighing the risks and benefits for CKD patients. The dose of hypoglycaemic drugs should be adjusted for kidney function. Traditional hypoglycaemic drugs, such as metformin, remain suitable for these patients. Other hypoglycaemic drugs, such as dipeptidyl peptidase-4 (DPP-4) inhibitors, incretin analogues, and sodium-glucose cotransporter-2 (SGLT-2) inhibitors, have potential renal-protective effects independent of their impact on glycaemic control.[50] The Portuguese–Brazilian evidence-based guidelines for managing T2DM recommended hemoglobin A1c (HbA1c) <7% as the target for glycaemic control in non-pregnant adults. Higher HbA1c is recommended for frail and elderly patients or patients at higher risk for hypoglycaemia. When HbA1c is 6.5%–7.5%, diabetes mellitus diet therapy and metformin are the preferred choices for CKD patients; when HbA1c is 7.5%–9.0%, metformin, SGLT2 inhibitors and glucagon-like peptide receptor agonists (GLP-1RA) are recommended. The latest expert consensus of the Chinese Diabetes Association and the Chinese Endocrine Society recommends metformin as first-line treatment for patients with T2DM, cardiovascular atherosclerosis disease, or an extremely high risk of cardiovascular

events. For patients with T2DM and CKD, combination treatments should be based on individualized HbA1c targets. SGLT2 inhibitors are the preferred choice for these patients, and GLP-1RA can be considered when SGLT2 inhibitors are not contraindicated or are not tolerated.[51]

Hyperuricaemia

Hyperuricaemia and gout are common in CKD patients, and managing serum uric acid (SUA) levels in these patients during the perioperative period is a challenge. Uric acid (UA) is the final product of purine metabolism in the human body and is maintained through its production and excretory process. Two-thirds of SUA is excreted by the kidneys, and one-third is excreted by the gastrointestinal tract. Elevated SUA can be seen in CKD patients due to hypercatabolism, as well as reduced excretion of uric acid by the kidneys.[52] Gout is characterized by hyperuricaemia and the deposition of urate crystals in the joints, causing great pain to patients. Studies have shown that hyperuricaemia is an independent risk factor for the onset and progression of CKD.[53] The target level of SUA in patients with gout is <6 mg/dl (or in patients with tophaceous gout, <5 mg/dl).[54] UA is formed from nucleic acids either endogenously from cell breakdown or exogenously from the metabolism of food. Phosphoribosyl pyrophosphate synthetase (PRPS) and xanthine oxidase play essential roles in the generation of UA. Xanthine oxidase inhibitors, such as allopurinol or febuxostat, are the preferred choice for reducing SUA.[55] Allopurinol is an inhibitor of xanthine oxidase, which can prevent the oxidation of xanthine to UA. The use of allopurinol in CKD patients can increase the risk of metabolite accumulation. Therefore, it is widely recommended that CKD patients begin with a low dose of allopurinol and gradually increase to an effective dose.[56] Febuxostat, a non-purine-selective xanthine oxidase inhibitor, has been proven to safely and effectively reduce SUA, and it can be used as a substitute when allopurinol is not contraindicated or tolerated.[57] Other uric acid-lowering drugs include losartan, fenofibrate, and probenecid.[58] During the perioperative period of joint replacement, the renal function of CKD patients should be fully considered when selecting uric acid-lowering drugs.

Strengths of the Study

Our study was a retrospective study of CKD patients, summarizes the management experience, and provides advice for clinicians. All data were obtained from the patients' medical records during hospitalization. Identifying risk factors, developing renal protection strategies, pain grading management, and surgical timing are issues that require more emphasis in the perioperative period of joint arthroplasty. In addition, recommendations for the management of postoperative complications from clinical practice guidelines, such as the Japanese Society of Nephrology (JSN), the Japanese Society of Hypertension (JSH), the Portuguese–Brazilian evidence-based guidelines, the Chinese Diabetes Association, and the Chinese Endocrine Society, were also discussed.

Limitations

There are some limitations of our study that must be clarified. We acknowledge the small sample size of this study. A limitation to the methodology of our study was the lack of a cohort design, and future improvements in methods are necessary. The leading clinical indicators of renal function measures include glomerular filtration rate (GFR), serum creatinine, blood uric acid, β2-microglobulin (β2-MG), and so on. Blood creatinine is the most direct index of renal function and is influenced by a few other factors. We used serum creatinine and blood uric acid in previous clinical practice to quickly reflect the changes in renal function. In future studies, it might be beneficial to consider new indicators, such as GFR and creatinine clearance rate.

Conclusion

Patients with CKD have distinct characteristics compared to non-CKD patients, and they generally have a higher risk of postoperative complications and adverse events. Recognition of risk factors, suitable timing of surgery, undertaking of protective strategies, and reasonable management of complications are vital for managing CKD patients in the perioperative period of joint arthroplasty.

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Author Contributions

Hongfu Jin and Miao He wrote the manuscript and revised this manuscript. Guang Yang and Wenqing Xie prepared the Figures. Dengjie Yu and Hengzhen Li prepared the Table. Yusheng Li and Wenfeng Xiao conceptualized this research and decided on the content. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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