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ORIGINAL RESEARCH

Considerations Regarding Anesthesia for Renal Transplantation

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ABSTRACT

Background : Renal transplantation is a complex surgical procedure requiring meticulous anesthetic planning to ensure patient safety and optimal graft function.

Methods: We conducted a retrospective analysis of anesthesia management from 65 cases of live renal transplants carried out between January 2017 and February 2023 at Dr. Sardjito Central General Hospital, Yogyakarta. Preoperative patient status, anesthesia management, and postoperative care of the subjects were assessed.

Result : Most patients had preoperative anemia, normal serum potassium, increased serum creatinine, and normal ejection fraction. Anesthesia management began since 24 hours before surgery, in which the patients were hospitalized, had peripheral IV access and fluid maintenance, and hemodialysis, followed by premedication 1 hour before surgery. Prior surgery, anesthesia induction and intubation were done, followed by maintenance of anesthesia and intaoperative monitoring. Postoperative care consisted of administration of analgesia and management of complications.

Conclusion: Optimization of preoperative status, proper anesthesia management, and good postoperative care are keys for a successful renal transplant program.

Keywords: Anesthesia; End-stage Renal Disease; Renal Transplant.

INTRODUCTION

A renal transplant often become the most effective treatment optiom for patient with end-stage renal disease. This procedure can significantly improve longevity and quality of life, allowing patients to resume normal activities.[1] However, the process is complex, requiring careful donor matching, lifelong immunosuppressive medications and ongoing medical care to prevent rejection and complications.[2]

Good organ viability in renal transplants results from donor management, allograft, and recipient. The short-term and long-term outcomes are affected by fluid therapy and perioperative medications.

Close intraoperative monitoring, optimization of intravascular fluid status to boost renal perfusion, and immediate electrolyte disorder correction (especially potassium) are the key to successful short-term and long-term kidney transplants.[3]

A retrospective analysis of 65 living renal transplant cases was done to identify the trend based on patient age, gender, end-stage renal disease (ESRD) etiology, anesthesia management, and patient outcome in our hospital.

METHODS

This study applied retrospective approach. Inclusion criteria were all adult renal transplant cases ((≥18 years) from January 2017 – February 2023 in Dr. Sardjito Central General Hospital, patients with incomplete medical record regarding anesthesia management were excluded. All medication usage and perioperative events were manually documented. Age, gender, chronic kidney disease etiology, preoperative status, and dialysis history were also recorded. Preoperative preparation, supporting examinations, details of anesthesia management, monitoring, and outcome were also recorded and included in the baseline data.

American Society of Anesthesiology (ASA) status from the renal donor was generally ASA I-II. Renal extraction from the donors was done through open nephrectomy dan laparoscopic nephrectomy with general anesthesia and controlled ventilation or epidural anesthesia. This study focused on the perioperative management of renal transplant patients.

RESULTS

A total of 65 subjects fulfilled the inclusion and exclusion criteria and included in the analysis. The average age

of the participants is 39.28 years, with a standard deviation of 12.83 years. The majority of the participants are male, as only 20.0% (n=13) are female. The average Body Mass Index (BMI) is 22.99, with a standard deviation of 4.51, and 12.3% (n=8) of the participants are classified as obese. Hypertension is prevalent in 95.4% (n=62) of the population, while 24.6% (n=16) have heart valve disease. More than half of the participants (55.4%, n=36) are living related donors. The average preoperative creatinine level is 4.70 (SD=1.61), and the average preoperative hemoglobin (Hb) level is 10.42 (SD=9.68). The average ischemic time is 85 minutes (SD=19), and the average duration of preoperative hemodialysis (HD) is 2.18 years (SD=1.91) (table 1).

Table 1. Subject characteristics

Variables	n	%
Age*		39.28±12.83
Sex: female	13	20.0%
BMI*		22.99±4.51
Obesity	8	12.3%
Hypertension	62	95.4%
Heart disease	16	24.6%
Living related donor	36	55.4%
Preoperative creatinine level*		4.70±1.61
Preoperative Hb level*		10.42±9.68
Ischemic time*		85±19
Preoperative HD duration*		2.18±1.91

*) presented as mean±SD; BMI = body mass index; HD = hemodyalisis

a. Preoperative status

Preoperative anemia was the most common finding. The mean hemoglobin was 9.2 ± 1.7 g/dL. Hemoglobin concentration < 8 g/dL was found in 9 patients (13.8). Iron supplementation was not given to patients before the transplant and 1 patient (1.5%) required a blood transfusion due to very low hemoglobin concentration (5.4 g/dL). Serum potassium concentration was within the normal range (3.6-4.7 mEq/L) with a mean of 4 mEq/L. Serum creatinine

concentration varied between 2.4-8.6 mg/dL with the mean of 4.69 mg/dL (Table 2).

Echocardiograms revealed left ventricular diastolic dysfunction in 8 patients (12.3%) with ejection fractions between 28-76%, with tricuspid regurgitation, and mitral regurgitation. An ejection fraction of 30-40% was reported in 6 patients. Ejection fraction below 30% was found in 2 patients before hemodialysis, but repeat echocardiograms post-hemodialysis showed an ejection fraction > 30%. There was only 1 patient (1.5%) with minimal pericardial effusion. In the chest x-ray examination, 2 patients (3%) had bilateral pleural effusion (Table 2).

Table 2. Preoperative status

Parameter	N (%) / mean ± SD
Hemoglobin (g/dL)	9.2±1.7
Hemoglobin < 8 g/dL	3 (15)
Serum potassium (g/dL)	4 ± 1.3
Serum creatinine	4.69±1.61
Diastolic dysfunction	8 (12.3)
Ejection fraction	
> 40%	51 (78)
30-40%	12 (19)
< 30%	2 (3)
Pericardial effusion	1 (1.5)
Bilateral pleural effusion	2 (3)
Anti-HLA antibody > 300 MFI	6 (9.2)

dL: deciliter; g: gram; HLA: Human Leukocyte Antigen; MFI: Mean Fluorence Intensity; N: number of patients; SD: standard deviation

Human Leukocyte Antigen (HLA) matching among donor and recipient tissues was conducted in all patients. HLA matching results exhibited Anti-HLA antibody > 300 MFI in 6 patients (9.2%) and preoperative plasmapheresis was conducted. Immunosuppressive drugs such as steroids (including methylprednisolone), tacrolimus, anti-lymphocyte globulin, and basiliximab were given to reduce the incidence of graft rejection.

b. Anesthesia management

General anesthesia with continuous epidural anesthesia was conducted in all cases. Hemodialysis was done in all recipients 24 hours before surgery to diminish the risk of volume overload, hyperkalemia, and massive bleeding. One day before surgery, patients were hospitalized in the intensive care unit (ICU) as the regular procedure in Dr. Sardjito Central General Hospital, which involved hemodynamic (blood pressure, electrocardiography, oxygen saturation, and temperature) monitoring, and immunosuppressive drugs administration. Antihypertensive drugs were continued until the day of the surgery. Premedication was given 1 hour before surgery, consisting of sedatives and the individual regular medication (Figure 1)

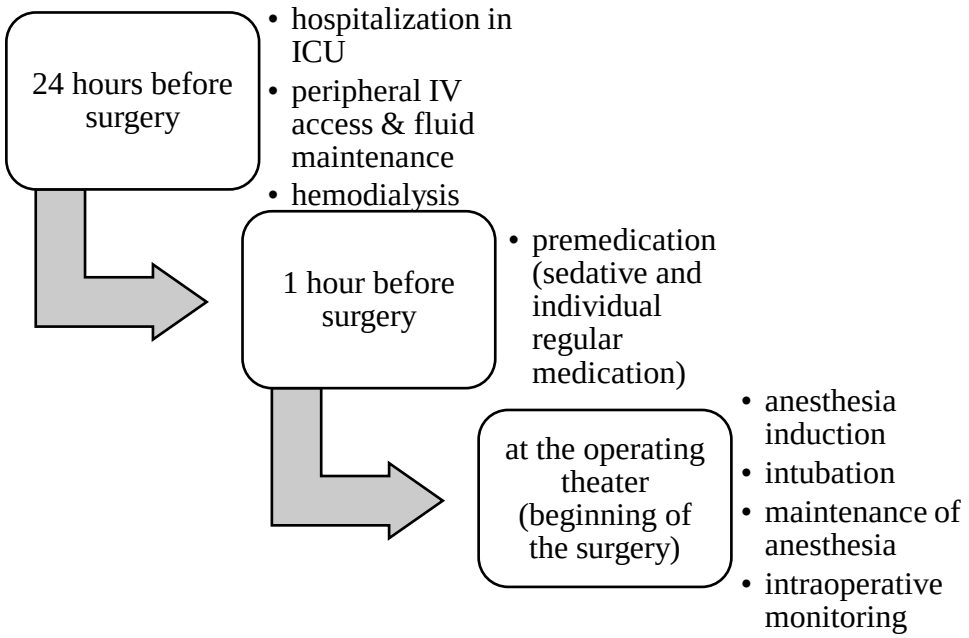

Figure 1. Anesthesia management
ICU: intensive care unit; IV: intravenous

Peripheral intravenous access was performed in the contralateral hand of the arteriovenous (AV) shunt on the night before surgery and maintenance fluid was given according to insensible water loss (IWL) calculation. Coinduction was carried out via midazolam 0.05 mg/kg BW and fentanyl 3 mcg/kg BW. Anesthesia induction was done using propofol (1-2 mg/kg BW) in 58 patients (89%), dexmedetomidine in 7 patients (11%), and fentanyl (2-4

mcg/kg BW) in all patients. Muscle relaxant choices included atracurium 0.5 mg/kg BW in 49 patients (75%), rocuronium 0,6 mg/kg BW in 15 patients (23.5), and vecuronium in 1 patient (1.5%). All patients were intubated and underwent controlled ventilation. Anesthesia maintenance throughout the surgery was carried out using Oxygen 50% with 1-2% sevoflurane supplementation and fresh gas flow of 2 L/min. Analgesia was retained with fentanyl 1-2 mcg/kg BW/hours or through a continuous epidural of 2-4 cc/hours bupivacaine/ropivacaine 0.25% with prior 10 ml bolus (target the T6-L2 vertebrae) and TAP block. Most patients were given the combination of colloid (gelofusine or BES) and crystalloid (normal saline) infusion. A 40 mg of furosemide injection was administered to all patients, and 4 patients were given mannitol and an additional dose of furosemide (Table 3).

Table 3. Anesthesia management and drugs

Management	Drugs	N (%)
Induction of anesthesia	Propofol (IV)	58 (89)
	Dexmedetomidine (IV)	7 (11)
Co-induction	Midazolam and fentanyl (IV)	All patients
Muscle relaxant	Atracurium	49 (75)
	Rocuronium	15 (23.5)
	Vecuronium	1 (1.5)
Maintenance of anesthesia	Oxygen 50% and sevoflurane 1-2%, fresh gas flow 2 L/min (inh)	All patients
Maintenance of analgesia	Fentanyl (IV) or Bupivacaine/ropivacaine 0.25% (IV and epidural dan TAP block)	All patients
Fluid management	Crystalloids only	15 (23.5)
	Combination of crystalloids and colloids	50 (76.5)
Diuretics	Furosemide only	61 (94)
	Combination of furosemide and mannitol	4 (6)
Vasopressors	Dobutamine and/or norepinephrine	34 (52.3)

Inh: inhalation; IV: intravenous; N: number of patients

Intraoperative monitoring such as heart rate, invasive blood pressure monitoring (artery line), oxygen saturation, central venous pressure (CVP), end-tidal carbon dioxide ($ETCO_2$), electrocardiogram, stroke volume variation, cardiac output (with Most Care® and ICON™) was conducted in most patients. CVP was installed in the left or right subclavian vein or right internal jugular vein (as opposed to the location of the AV shunt and relied on the presence/absence of a hemodialysis catheter). The hemodynamic parameters were recorded in the 15-minute interval. Dobutamine and/or norepinephrine 0.05 mcg/kg/minutes was administered to 34 patients (52.3%) (Table 3).

c. Postoperative care

The mean surgery duration was 6 hours (± 2.3 SD). At the end of the surgery, reverse muscle relaxants using intravenous neostigmine 0.05 mcg/kg and atropine sulfate 8 mcg/kg were given to patients with remaining muscle relaxant effects according to the train of four (TOF) monitor. All patients were extubated postoperatively in the operating theater and were transported to the ICU equipped with supplemental oxygen using a non-rebreathing mask and a minimally invasive monitor (Most Care®).

All patients were hospitalized postoperatively in the ICU. Intravenous analgesia (i.e fentanyl 1-2 mcg/kg BW), epidural analgesia (i.e bupivacaine/ropivacaine) and TAP block were administered in almost all patients (1 patient was not given epidural analgesia postoperatively due to the clot formation in the epidural catheter). Dialysis support was indicated in 2 patients during the postoperative period. Acute graft rejection was witnessed in 2 patients, both showed good clinical response to tacrolimus and plasmapheresis. Reexploration was performed in 1 patient due to the thrombus in the blood vessel proximal to the graft. Sixteen out of sixty five patients were given heparin before anastomosis, instigating massive bleeding during and after surgery which dictated leukodepleted PRC transfusion in 20 patients (30.7%) and fresh frozen plasma (FFP) transfusion in 2 patients (3%). The remaining patients were not given heparin before anastomosis, abolishing the need for either PRC or FFP transfusion. One patient died more than 3 months after surgery (Table 4).

Table 4. Postoperative care

Indication	Management	N (%)
Postoperative pain management; routine procedure	Intravenous and epidural analgesia	64 (98)
Acute graft rejection	Tacrolimus and plasmapheresis	2 (3)
Graft thrombosis	Reexploration	1 (1.5)
Massive bleeding	Leukodepleted PRC	10 (15.4)
	FFP	2 (3)
	None	53 (81.5)

FFP: fresh frozen plasma; PRC: packed red cell

DISCUSSION

Renal transplantation is the treatment of choice for patients with ESRD.[1,2] Despite important evolutions in renal transplant surgery, the risk of perioperative complications remained high. About 25% of all renal recipients suffer from the delayed function of the graft postoperatively and some of them still require renal replacement therapy which contributes to 40% of increased mortality. Majority of renal transplant recipients suffered from cardiovascular, hematology, respiratory, and metabolic problems secondary to the existing kidney failure. These factors complicated anesthesia management.[1,3]

Cardiovascular disease remains an essential factor in postoperative morbidity and mortality, particularly in patients over 50 years old.[2] The incidence of coronary artery disease in ESRD patients is 25%. If patients are added to the waitlist for organ transplantation for several years, before the donor organ is available, repeated cardiac evaluations are recommended, especially in patients with active cardiac disease such as unstable coronary syndrome, heart failure, significant arrhythmia, and severe valve disease. A 12-lead electrocardiography and echocardiography examination are recommended.[2,4] In one study entailing 22 hospitals, several most common preoperative examinations include echocardiography, cardiopulmonary exercise testing, lung function test, and stress echocardiography. One hospital (4,5%) routinely instructs a cardiovascular review before transplantation, while other hospitals only conduct cardiovascular reviews in patients over 50 years old, diabetic patients, or patients with underlying cardiovascular diseases.[5,6,7]

Other comorbidities which are associated with the end-stage renal

disease include hypertension and diabetes mellitus. Hypertension prevalence was 90% in patients with glomerular filtration below 30 ml/min. Hypertension is the cause as well as the consequence of chronic kidney failure. Hypertension exacerbated chronic kidney failure through the renin-angiotensin-aldosterone system and volume overload.[2,4] Diabetes mellitus was observed in 30% of patients requiring renal replacement therapy and could occur concomitantly with hypertension and cardiovascular disease, further enhancing the risk of stroke and myocardial infarction[2,4].

Metabolic acidosis is a common problem in a patient with ESRD. However, a large-scale retrospective study of more than 22,000 patients demonstrates a higher risk of delayed graft function in patients undergoing hemodialysis compared to CAPD. Routine usage of immediate hemodialysis before surgery is therefore not recommended, but it should be considered in patients with hyperkalemia due to potential potassium spikes during graft reperfusion.[2,6]

Most hospitals (63.6%) conduct preoperative dialysis on the recipients until their dry weight is achieved. Three hospitals (13.6%) set body weight post-dialysis 1-2 kg above the dry weight, while others do not specifically determine the target body weight before surgery.[5] In our study, all patients underwent preoperative dialysis to achieve their dry weight. Consequently, all patients had normal potassium levels and were not in the hypervolemic state preoperatively.[7]

ESRD patients are prone to infection due to uremia, comorbidities (such as hypertension, diabetes mellitus, and cardiovascular disease), infection from donors, and immunosuppressive drugs. As a result, broad-spectrum prophylactic antibiotics should be given before surgery, such as first-generation cephalosporin or vancomycin, and comorbidities should also be carefully controlled.[7]

ESRD patients generally have low albumin levels due to plasma volume expansion, albumin redistribution, exogenous loss (in peritoneal dialysis patients), and decreased synthesis of albumin. Hypoalbuminemia and uremia-induced blood-brain barrier amplify the fraction of over-the-counter medications. Hence, drug dosage adjustment is essential and the drugs are administered at titration

doses.[1,7] Induction choices of drugs including thiopentone, propofol, or etomidate. Succinylcholine should be used with caution because it can instigate hyperkalemia, particularly in patients with high initial potassium levels (>5 meq/l). Atracurium, cisatracurium, vecuronium, rocuronium, and mivacurium can be safely used, although rapid sequence intubation (RSI) may require appropriate modifications. Short-acting beta-blockers such as esmolol or short-acting opioids such as fentanyl or remifentanil are used to prevent elevated blood pressure and hemodynamic disorders during laryngoscopy.[3,7]

Isoflurane, sevoflurane, desflurane, or intravenous propofol are some options for the maintenance of anesthesia. However, isoflurane is considered the agent of choice because it is metabolized in small amounts. Analgesia can be preserved using fentanyl or remifentanil. Morphine should be used with caution because morphine-6-glucuronide, an active metabolite of morphine can cause respiratory depression.[3,7]

Perioperative fluid management is crucial to maintain sufficient intravascular volume and perfusion to the transplanted kidneys. After vascular unclamping, a large volume of blood enters directly into the transplanted kidney and there is a release of mediators from the kidney ischemic tissue. There is also an excessive loss of fluid during dialysis and perioperative fasting. All these predispose the patients to hypovolemia which may lead to acute tubular necrosis and graft dysfunction.[1,4,7]

Optimal perioperative fluid management can be achieved by maximizing graft function with aggressive fluid management (up to 30 ml/kg/h and central venous pressure > 15 mmHg) with particular attention to cardiac patients. The restrictive hydration regimen demonstrated by Gasperi et al with a CVP target of 7-9 mmHg is equally effective in maintaining graft patency (crystalloid 2400 ± 1000 ml, 15 m/kg/h). Some institutions recommend CVP as the parameter for fluid adequacy, with an increase of> 7 mm after the fluid bolus indicating the maximum intravascular volume. However, CVP and PAP are static markers of fluid responsiveness and therefore are generally less acceptable.[1,4,7]

The recommended fluid therapy of choice for a kidney transplant is

isotonic crystalloids such as ringer lactate, plasmalytes, and normal saline.[4,5] In our patients, 15 patients (75 %) patients got a combination of crystalloids (saline-based, non-potassium-containing fluids) and colloids (gelatin-based). Potura et al compared 0.9% saline with buffered balanced acetate crystalline fluid in patients undergoing kidney transplantation. They found no significant differences in the incidence of hyperkalemia in both groups and found a lower percentage of patients who needed inotropic in the crystalloid group. Hadimioglu et al concluded that among the crystalloids, plasmalyte provides the best metabolic profile.[4,5]

In other studies comparing Ringer lactate fluid and normal saline of 0.9% during kidney transplantation, researchers showed that patients who were given a lactic ringer solution had a lower incidence of hyperkalemia and acidosis. Saline infusion can cause acidosis due to dilution of the bicarbonate or hyperchloremia, lowering the strong ion difference. Metabolic acidosis of hyperchloremia triggers hyperkalemia by shifting potassium into the extracellular space. However, the volume of crystalloids used during surgery in those studies was approximately 3 liters.[1,5,6]

Colloids can also be used for volume replacement. In recent decades there has been a shift in clinical practice from the use of natural colloids to synthetic colloids. These colloids include natural colloids such as albumin and synthesis such as dextrans, gelatin, and others. However, the safety of gelatin and dextran has not been established, hence their usage should be done with caution.[4,5] There are also some concerns regarding the use of hydroxyethyl starch (HES) due to osmotic lesions, such as nephrosis shown in transplanted kidneys taken from deceased donors transfused with HES200/0.62.[1,6]

The timing of fluid administration is also crucial. Othman et al compared a CVP biphasic regimen of 5 mmHg in the pre-ischemic phase and 15 mmHg in the ischemic phase with a constant infusion of 10-15 ml/kg/h. They found better initial graft function with the biphasic regimen.[4,5]

In our study, intraoperative monitoring was conducted in most patients. Intraoperative monitoring is divided into the static method, such as transesophageal echocardiography

(TEE) and central venous pressure (CVP), and the dynamic method, such as systolic volume variation (SVV), pulse pressure variation (PPV), and systolic pressure variation (SVP). Dynamic measurements of patient fluid responsiveness are better predictors than static methods. SVV is a better predictor of fluid responsiveness in patients undergoing kidney transplantation compared to CVP, hence more commonly used. However, SVV usage is limited to mechanically ventilated patients.[4,1,7]

In our study, a 40 mg of furosemide injection was administered to all patients, and 4 patients were also given mannitol and an additional dose of furosemide. Mannitol has a protective effect on tubule cells of the transplanted kidney against ischemia and prompts the release of prostaglandin vasodilators on the kidneys, therefore accommodating the removal of free radicals. Mannitol is generally given at the time of anastomosis release in some hospitals, but the effect of mannitol on graft function is unclear. Furosemide can also lower kidney oxygen consumption by inhibiting Na-K ATPase in the thin loop of Henle, but its clinical effect on improving renal function has not been proven.[4]

General anesthesia is generally used for kidney transplants, although there are cases of kidney transplants performed under regional anesthesia.[1,3,7] All patients in our study had continuous epidural anesthesia and there were no major complications in our cases. However, Lauretti and Gabriela Rocha reported frequent complications of continuous epidural anesthesia such as respiration and rupture of renal anastomoses, which are caused by coughing, hiccups, and agitation. Endotracheal intubation or laryngeal mask airway is an alternative to maintain airway patency during continuous epidural anesthesia.[1,7]

Acute graft rejection was witnessed in 2 patients in our study, both showed good clinical response to tacrolimus, immunosuppressant, and plasmapheresis. The risk of acute rejection is the highest in the first week and several months after kidney transplantation. This risk can be lowered by prescribing rapid-acting and strong immunosuppressive drugs with minimal side effects (induction agents). The drugs of choice are antilimocyte antibodies (both polyclonal and monoclonal) and interleukin-2 receptor

antagonists with IL-2 antagonists mediated by cell proliferation. This induction strategy allows early steroid discontinuation and delayed initiation of calcineurin inhibitors when there are concerns of slow or delayed graft function.[2,8,9,10]

CONCLUSION

Improvements in anesthesia, surgical techniques, and immunosuppressive drugs enable patients to receive transplants that were deemed unsuitable at first. Optimization of preoperative status, proper anesthesia management, and good postoperative care with a solid collaboration of nephrologists, urological surgeons, and anesthesiologists are compulsory for the successful management of kidney transplant patients.

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