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Critical Care Management Following Kidney Transplant. A Single Center Experience

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ABSTRACT

Introduction: *Kidney transplant recipients have several co-morbidities which further complicates the surgical procedure and peri-operative recovery. Therefore, extensive pre-operative evaluation is performed on end-stage renal disease patients to assess their physical fitness for kidney transplant. Close hemodynamic monitoring during kidney transplant is performed to avoid intra- and post-operative complications. We aimed to review our clinical experience in managing kidney transplant recipients and evaluated their immediate post-operative outcomes. We aim to assess which patients can potentially avoid intensive care (ICU) management following kidney transplant.*

Methods: *A consecutive series of 100 patients who underwent kidney transplantation were reviewed. All demographic data including patient age, body mass index (BMI), and American Society of Anesthesiologists (ASA) scores were collected. Co-morbidities were reviewed on all patients. All patient's post-operative course was evaluated. All patients who were admitted to intensive care units were reviewed. Patients were divided into two groups for comparison, Group A (ICU care) and Group B (standard surgical floor care).*

Results*: 54 patients required intensive care admission (Group A). The mean age of patients was 54 years and BMI was 30.1 (Group A). There were 38 (70%) male and 16 (30%) female patients who required ICU care after kidney transplant. ASA score was III for 41 (76%) and IV for 13 (24%) of Group A patients. The indications for ICU admission were hypertensive urgency [n=31 (57%)], hypotension [n=12 (22%)], respiratory failure [n=3 (5%)], diabetic ketoacidosis [n=3 (5%)], hemodynamic monitoring [n=3 (5%)], hyperkalemia [n=1 (2%)], and arrhythmia [n=1 (2%)]. The mean SICU stay was 2.1 (range 1-6) days. All 54 patients required insertion of an arterial line for hemodynamic monitoring.*

Conclusions: *A routine critical care admission is not required after kidney transplant. The majority of patients who required admission for ICU care were for management of post-operative hypertension. Optimal peri-operative hypertension management can help to avoid potential intensive care requirements. This can avoid excessive cost and lead to better utilization of intensive care resources.*

Keywords

Kidney Transplant, Intensive Care Unit (ICU), Cardiopulmonary Comorbidities, Renal Disease.

Introduction

Kidney transplant patients, due to their co-morbidities and complex surgical procedure are pre-disposed to being admitted to the intensive care unit (ICU) [1]. The reasons for ICU admission are

manifold, with the most common immediate post-operative reason being cardiopulmonary irregularities, requiring ICU management and monitoring [1]. When including patients that were admitted later in the course post-kidney transplant, sepsis precedes as the leading cause for ICU admission followed by cardiovascular disease [2].

Risk factors associated with higher rates of ICU admissions include older age, increased body mass index (BMI), pre-transplant dialysis, cardiopulmonary comorbidities, higher American Society of Anesthesiologist (ASA) score, and deceased donor transplantation [3,4]. Polypharmacy and possible adverse drug interactions also remains a concern, particularly within the first post-operative week [5]. Immunosuppressants have significant impact on cardiac co-morbidity and gastrointestinal side effects [5,6]. When treating kidney transplant recipients peri-operatively, a holistic approach in the management of each patient as well as the complications and vulnerabilities faced by this patient cohort can help formulate effective approaches for treatment and management [7].

A study by El-Agroudy et al., found that ICU admissions were related to increased graft loss ($p = 0.022$) and a reduction in the 5-year and 10-year survival ($p = 0.031$) of kidney transplant patients [8]. Higher mortality rates were seen in association with longer ICU stays, mechanical ventilation and vasopressor support.

Our study to assess the management of immediate post-operative kidney transplant ICU admissions seen in our clinical practice, the indications for such admissions and our recommendations for ICU admissions in this patient cohort.

Methods

The study was conducted at Augusta University Medical Center, Augusta, Georgia, USA. Full research authorization was obtained from the research review board (2294849-1). Data collection was initiated following the approval of the study. Data was collected from a consecutive series of patients who underwent both deceased donor (DDKT) and living donor kidney transplant (LDKT). All kidney transplant recipients were listed on United Network of Organ Sharing (UNOS, 700 N 4th St Richmond, VA 23219) national list. All DDKT recipients who underwent kidney transplant received organ offers from national organ matching scheme coordinated by UNOS. Adult patients with ages of ≥ 18 years were included in the study.

We collected all demographic data which included patient's age, gender, race, co-morbidities and body mass index. Patients were divided into two groups based on the status of admission after kidney transplant (Group A: ICU admission, Group B: Surgical floor admission). All pre-transplant co-morbidities were collected for all patients. Each patient's duration of total inpatient stay, management in the intensive care unit and subsequent follow-up were recorded. All peri-operative complications were also reviewed.

Data Analysis

All data was collected on a standardized excel sheet with the data stored at the central human resource box drive of the Augusta University. The IBM SPSS Statistics version 29 (IBM, NY, USA) software was used to analyze continuous and discrete data variables.

The student's t-test (p-value < 0.05) was used to compare the demographic characteristics between the two groups.

Results

A total of 100 patients were included in the study. 54 patients were identified who required intensive care admission following kidney transplant (Group A). 46 patients were admitted to the standard surgical floor for post-operative care.

The mean calculated age range for all patients in the study was 53.4 years (range 26 to 75 years) (Table 1). There was no difference between the mean age (p=0.57) of patients in Group A (Mean=54, 30 to 74 years) when compared to Group B (Mean=52.6, range 26 to 75 years) (Table 1). The mean BMI for all patients in the study was 29.4 kg/m^2 (range 17 to 40 kg/m^2). There was no difference in the BMI (p=0.17) between the patient Group A (mean=30.1 kg/m^2, range 17 to 40 kg/m^2) and Group B (mean=28 kg/m^2, range 17 to 40 kg/m^2).

Table 1: General demographic details of two groups of patients.

	Group A (ICU) N=56	**Group B (Non-ICU) N=44**	***p* - value**
Age (mean no of years)	54.0	52.56	0.57
Body mass index (Kg/m^2)	30.1	28	0.17
Gender			
Male	38	27	
Female	16	19	0.22
Race			
Black	42	35	
Caucasian	8	8	
Hispanic	3	2	
Asian	1	1	
Cause of End stage renal disease			
Hypertension	20	19	
Diabetes Mellitus	19	11	
Focal Segmental glomerulosclerosis	3	4	
Previous Transplant	3	4	
Autoimmune Nephropathies	7	4	0.76
Polycystic kidney disease	2	2	
ASA score			
3	41	34	
4	13	12	0.81

On further sub-group analysis there was no difference identified in the gender distribution (p=0.22), race, co-morbidities (p=0.76) and American Society of Anesthesiologists (ASA) score (p=0.81)

between the two groups. In Group A, ASA score was III for 41 (76%) and IV for 13 (24%) of patients. Kidney donor profile index (KDPI, p = 0.20), cold time (p=0.63) and the regional blocks used for both groups of are enumerated in Table 2.

Table 2: Table details the cold ischemia time, kidney donor profile index (KDPI) and the number of patients who received regional anesthesia before kidney transplant.

	Group A (n=56)	Group B (N=44)	P - Value
KDPI	54 (range= 4- 99%)	45 (range= 2 to 96%)	0.20
Cold ischemia time (hours)	20 (range= 9 to 34)	19.3 (range= 9 to 33)	0.63
Regional Blocks	26	24	

The indications for ICU admission (Table 3) included hypertensive urgency [n=31 (57%)], hypotension [n=12 (22%)], respiratory failure [n=3 (5%)], diabetic ketoacidosis [n=3 (5%)], hemodynamic monitoring [n=3 (5%)], hyperkalemia [n=1 (2%)], and arrhythmia [n=1 (2%)]. The mean SICU stay was 2.1 (range 1-6) days. All 54 patients required insertion of an arterial line for hemodynamic monitoring.

Table 3: Detail of indications for intensive care admission post kidney transplant.

Indications for SICU admission	N=56 (%)
Hypertension	31 (57%)
Hypotension	12 (22%)
Respiratory failure	3 (5%)
Ketoacidosis	3 (5%)
Hyperkalemia	1 (2%)
Hemodynamic monitoring	3 (5%)
Cardiac arrhythmias	1 (2%)

Discussion

Protocols for ICU admission post kidney transplant vary between institutes. Most common reason for ICU admission post-kidney transplant is monitoring in a safe and supervised environment, however this justification for ICU admission is no longer as prevalent. A substantial decrease in the rate of ICU admissions post-kidney transplants has been seen in the last 20 years, and it is thought to be in-part due to advancements in surgical technique, immunosuppressive therapy, and post-operative infection prophylaxis [9].

However, there are several well-documented indications for post-operative ICU admission, including significant cardiovascular disease as being a leading cause of mortality in kidney transplant patients [10]. In our study, 57% of patients admitted to the ICU were treated for hypertension management. This matches data that reports half of all kidney recipients have hypertension (HTN), although this number increased to up to 90% when calcineurin-inhibitors were initiated [11].

There is recurrent and persistent HTN seen in post-kidney transplant patients. Calcineurin-inhibitors such as cyclosporine and tacrolimus effect the sodium-chloride co-transporter in the nephron, as well as on the relative levels of the vasoactive substances nitroxide and endothelin, contributing to the development of HTN [12]. Dose-dependent corticosteroids are also a well-known cause of HTN, with their mechanism of action related to increasing the sensitivity of vasoconstrictors such as angiotensin II and norepinephrine, as well as inducing sodium and water retention [13]. Other risk factors for post-transplant HTN include previous essential HTN (which can be seen in 80-90% of end-stage renal disease (ESRD) patients), renal artery stenosis in the transplanted kidney, acute rejection, chronic malfunction and native kidney disease [14].

Significant cost is linked with peri-operative management of patients requiring ICU care post-kidney transplant. A Brazilian study on 81 kidney transplant patients, Barreto et al calculated that a total of $327,336 was spent on in-patient stay and ICU services alone [15-17].

Extra focus on pre-operative management of HTN can significantly impact peri-operative outcome. A regular nephrologist review and optimization in the dialysis center can significantly reduce pre-op HTN which can significantly help peri-operative management of HTN. Patient should receive regular pre-operative HTN medicines as dictated and then can be initially managed post-operative with anti-HTN medicines boluses upto 4 to 6 hours after completion of surgery. The oral anti-HTN medicines can be initiated orally at 4 to 6 hours after extubation [18]. A large majority of patients who were admitted to ICU for management of HTN could have potentially avoided the ICU admission with intense peri-operative blood pressure management. Also a longitudinal analysis of kidney transplant recipients who maintain their systolic blood pressure (BP) < 140mmHg were found to have better 3-year survival [11]. With lifestyle modifications, anti-hypertensive medication such as β-blockers, calcium-channel blockers, angiotension-converting enzyme inhibitors, angiotensin receptor blockers, and diuretics have all been shown to curtail BP in kidney transplant recipients [19,20].

Cardiovascular diseases commonly seen in kidney transplant recipients include coronary artery disease, heart failure, arrhythmias, and pulmonary HTN [21]. In a study by Abrol et al., with 1525 kidney transplant recipients, 17.4% of kidney transplant patients required ICU admission. The two leading reasons for admission were hypotension (n = 87) and arrhythmias (n = 83) [22]. Comparatively, 22% of our ICU patients were admitted for hypotension (n=12) and 2% (n=1) for arrhythmia. All patients with hypotension (systolic BP < 90 mm of Hg) were treated with intravenous pressor support. The mean duration for pressor support was 11 hours and were titrated down and stopped. The arrythmia was due to new onset of atrial fibrillation with negative work-up for cardiac injury. Intra-operative hypotension is affiliated with acute kidney injury (AKI) and delayed graft rejection (DGR), resulting in inferior kidney outcomes [23]. In a study on simultaneous pancreas and kidney transplant by Aziz et al., 12% of transplant patients were found to have hypotension >6 months post-operative,

yet graft outcomes did not significantly differ in the hypotension group compared to the hypertensive and normotensive groups [24]. Atrial fibrillation is the most common arrhythmia to develop in CKD, and can be seen in 7% of kidney transplant recipients within 3 years of surgery [10,21]. Peri-operative optimization, accurate management of fluid balance, acid-base status and intra-operative anesthesia management can help to reduce the risk of new onset atrial fibrillation.

Pulmonary complications likely warrant ICU admission post kidney transplant, most often due to acute respiratory failure (ARF). ARF, seen in 5% of the ICU patients in our study, was caused by cardiogenic pulmonary edema (PE), or acute respiratory distress syndrome (ARDS) [25-29]. Several viruses and bacteria have been identified to cause eerily onset of pneumonia post-kidney transplant [27,30]. In a study examining the causes of ARF, Ulas et al reports cardiogenic PE (44%) following bacterial pneumonia (56%) as the second most common cause of ARF in post kidney transplant patients [31]. The pathophysiology of cardiogenic PE involves the left heart, where elevated left ventricular filling pressures effect the hydrostatic pressure gradient, which effectuates pulmonary HTN [32]. ARDS can also cause ARF [33].

Due to several peri-operative factors, electrolyte and acid-base disturbances are often seen post kidney transplant [34]. Hyperkalemia, hypomagnasemia, hyperparathydoidism leading to hypercalcemia and hypophosphatemia and metabolic acidosis are amongst the most commonly occurring disturbances [34,35]. Our study identified 2% of ICU admissions were due to diabetic ketoacidosis (DKA) and 5% due to hyperkalemia. A case report on an African-American kidney transplant recipient describes the development of DKA 4 months post-operative, despite the absence of traditional risk factors [36]. Tacrolimus, more than cyclosporine, is found to be associated with the development of both type 1 and type 2 diabetes mellitus in kidney transplant patients and DKA as a sequential complication. This risk of progression to DKA in the short term (<90 days form kidney transplant) is significantly related to the amount of tacrolimus prescribed at discharge, as well as a patient's ethnicity and body mass index (BMI) [37]. The hyperkalemia were initially managed medically followed by dialysis. Peri-operative metabolic changes can alter acid-base balance and diabetes mellitus as a complication of solid organ transplant have been well documented. Medications are often the culprit behind the development of hyperkalemia, particularly calcineurin-inhibitors and antihypertensives [38]. We routinely prescribe potassium binding agents in the peri-transplant period to avoid development of post-operative hyperkalemia.

Although our study did not identify any patients who were admitted to the ICU due to sepsis. Many studies have reported sepsis as a factor for ICU admissions in both the early and late post kidney transplant period [2]. In a study by Bige et al examining graft function in kidney recipients admitted to the ICU for sepsis or septic shock, sepsis-related organ failure (SOFA) score on day 1 was found to be associated with impaired graft function and mortality with in first 90 days [40].

Conclusion

Post kidney transplant ICU admissions can be due to multiple causes, although the role of intensive care in the treatment and management of kidney transplant recipients has been decreasing in the last 2 decades [9]. Our single-center practice found hypertensive urgency to the most common indication for ICU admission, which parallels the findings in other studies that list cardiopulmonary disturbances as the primary reason for ICU admissions in this patient population [11]. Although intensive care services are necessary in appropriate patients, we do not recommend its routine use for post-operative kidney transplant patient management. Other studies have shown ICU stays are associated with acute kidney injury, poor graft function and increased patient morbidity [8,9]. In regards to post transplant hypertension, strictly implementing a medication adherence regime has been shown to effectively control blood pressure and improve graft function [20]. The effective management of hypertension improves long-term patient survival and reduces the financial burden on the healthcare system [11,18].

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