# Cardiovascular and Neurologic Complications in Kidney Transplant Recipients: A Focused Appraisal of Symptoms

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ABSTRACT

Background and Objective. After a kidney transplantation, all efforts are focused on graft function. However, cardiovascular and neurologic complications might lead to decreased quality of life and shortened life expectancy. Early recognition of related symptoms might be critical to successfully manage these complications.

Methods and Patients. We retrospectively reviewed the medical records of patients who had undergone kidney transplantation in a tertiary center between January 2014 and December 2017. Demographic data and past medical history were systematically gathered. Symptoms related to cardiac or neurologic disorders and final diagnoses were recorded.

Results. One hundred eighty-six patients were evaluated by a cardiologist or a neurologist in the early post-operative period or long-term follow-up. Chest pain (n = 17; 9.1%) and palpitations (n = 13; 7.0%) were the most prevalent symptoms. Coronary artery disease was diagnosed in 70.6% (n = 12) of the patients presenting with chest pain. All of the patients were treated successfully, with either antianginal drugs or percutaneous angioplasty. Atrial fibrillation was diagnosed in 53.9% (n = 7) of the patients presenting with palpitations. Headache was the most prevalent chronic neurologic symptom (n = 16; 8.6%). Transient ischemic attack occured in 7 patients (3.8%) and 5 (2.7%) patients experienced ischemic stroke.

Conclusion. Kidney transplantation is associated with short- and long-term cardiac and neurologic complications. Our findings underscore the crucial role of questioning symptoms that might be related to severe disorders. Asymptomatic patients with high risk factors must also be under scope. Attending physicians should have a low threshold for referring these patients to cardiologists and neurologists.

KIDNEY transplantation is the only current definitive treatment for patients with end-stage renal disease. Modern immunosuppression protocols, better chemoprophylaxis against infections, and effective management of the post-transplantation period for complications have enabled lower rejection rates and significantly better prognoses for this particular group of patients [1]. Surgical techniques and intensive care conditions have also improved tremendously. Consequently, developing strategies for long-term follow-up has become crucial. Chronic kidney disease is associated with cardiovascular disease, stroke, and death [2]. Likewise, cardiovascular events are the leading causes of death among kidney transplant recipients [3]. Increased prevalence of atherosclerotic risk factors and prolonged effects of chronic kidney disease have been reported to be related with these complications [4]. Many different algorithms for pretransplant cardiac evaluation have been reported [5]. Furthermore, systemic complications after kidney transplantation

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have been widely investigated. However, no uniform approach has been established during long-term follow-up concerning cardiac and neurologic conditions. Data regarding presentation of the clinical picture and symptomatology in this particular group of patients are scarce. In this study we aimed to evaluate the frequency and types of cardiac and neurologic symptoms and complications in the early post-operative period and in long-term follow-up in kidney transplant recipients.

## METHODS

We retrospectively reviewed all the electronic medical records of 776 patients who had undergone kidney transplantation between January 20014 and December 2017 in Akdeniz University, Faculty of Medicine, General Surgery Department. Patients aged ≥16 years who were evaluated by a consultant physician in either the cardiology or neurology departments during the early post-operative period and over the long term after kidney transplantation were included in the study. The early post-operative period was defined as the time between the transplantation and 30 days post-operatively. In the literature it is common to define "long-term" as a follow-up period of 6 months or greater and "intermediate-term" as 1 to 6 months after kidney transplantation. However, we defined long-term as a follow-up period of 30 days or more to avoid any confusion when describing the symptomatology and complications.

All of the patients who died during the whole follow-up after transplantation were included in the study. Subjects were excluded if their follow-up period was less than 30 days or their available information was inadequate. Hospital charts included all clinically relevant parameters that had been captured at any time interval during the follow-up. Due to the retrospective design of the study, no exact regular visit intervals could be defined. Visit schedules were determined by the physician's judgement and the patients' health status. Demographic data and past medical history were systematically gathered, including age, sex, date of transplantation, etiology of initial renal failure, history of atherosclerotic risk factors, and cardiac and neurologic diseases. Records of the preoperative assessments of the patients were also evaluated. In our department, preoperative assessment of any patient undergoing noncardiac surgery is performed according to European Society of Cardiology and European Society of Anaesthesiology Guidelines on non-cardiac surgery [6]. Routine evaluation is conducted via a thorough physical examination and 12-lead electrocardiography. Exercise electrocardiography or myocardial perfusion scintigraphy are used for detection of myocardial ischemia, if indicated. According to current guidelines, routine transthoracic echocardiography is not recommended in patients undergoing intermediate- or low-risk surgery. Because left ventricular systolic dysfunction, moderate-to-severe mitral regurgitation, and increased aortic valve gradients are associated with major cardiac events, transthoracic echocardiography was performed if such conditions were suspected. Echocardiographic indices, left ventricular ejection fractions, and results of the coronary angiograms, if present, were recorded. Data regarding carotid Doppler ultrasonography was lacking, as it was not part of the routine preoperative assessment. Symptoms related to cardiac or neurologic disorders and the final diagnoses were recorded. When many symptoms were reported, only the principal symptom was taken into account.

The study was performed in compliance with the Declaration of Helsinki, and the study protocol was approved by the Akdeniz University School of Medicine Ethics Committee. As per the institutional review board guidelines, patients' personal and confidential information was obtained only after the local committee approvals of Akdeniz University had been obtained. As approved by the Akdeniz University School of Medicine Ethics Committee, individual patient informed consent was exempted, because the personal information was encrypted.

## STATISTICAL ANALYSES

Statistical analysis was carried out using SPSS 18 software (SPSS Inc, Chicago, Ill, United States). Continuous data were characterized by mean ± standard deviation and median. Categorical data were characterized by number and percentage. The significances of the differences between continuous variables were tested using the Student *t*-test for parametric variables and the Mann-Whitney U test for nonparametric variables. $\chi^2$ was used for categorical comparisons of nominal values. The level of significance was set at .05.

## RESULTS

Of 776 patients who underwent kidney transplantation in our tertiary center between January 2014 and December 2017, 186 patients (129 male; 69.4%) were evaluated by a cardiologist (n = 139; 74.7%) or a neurologist (n = 95; 51.1%) in the early post-operative period or as part of long-term follow-up. The mean age was 47.5 ± 13.1. Comorbidities such as hypertension (n = 143; 76.9%), diabetes mellitus (n = 57; 30.7%), and hyperlipidemia (n = 67; 36.0%) were highly prevalent. Transthoracic echocardiography was performed in 82.8% (n = 154) of the patients. Mean left ventricular ejection fraction was 60.7% ± 6.5%. Coronary angiography was performed in 50 (26.9%) of the patients preoperatively. The number of coronary angiograms performed over 60 years of age (n = 34) was 11 (32.4%). Considering past medical history and previous coronary angiograms along with preoperative angiograms, coronary artery disease was also highly prevalent (n = 68; 36.6%).

### Cardiac Symptoms Which Necessitated Cardiology Consultation

Chest pain was the most common complaint which required consultation (n = 17; 9.1%). The final diagnosis was noncardiac chest pain in 5 (29.4%) of these patients. Coronary artery disease was diagnosed in 12 (70.6%) of the patients. Seven (58.3%) of these patients with a diagnosis of coronary artery disease were treated medically. Elective stent implantation was performed in 2 patients (1.1%); 2 other patients (1.1%) had percutaneous coronary intervention due to acute coronary syndrome. None of the patients had any hemodynamical compromise due to acute coronary syndrome during the early post-operative period or long-term follow up. All patients were all discharged from the hospital without complications. One patient underwent successful elective coronary artery bypass surgery.

Palpitation was the second most frequent cardiac symptom (n = 13; 7.0%). Postoperative atrial fibrillation occured in 5 patients, whereas 2 patients had atrial tachycardia. During the long-term follow-up, late occurence of new-onset atrial fibrillation was observed in 2 patients and 1 patient experienced atrial tachycardia paroxysm. In 3 patients, persistent palpitation symptoms were observed due to sinus tachycardia; no underlying cause was identified in these patients. Beta blockers or calcium channel blockers were initiated to control heart rate or to alleviate symptoms.

Eight patients (4.3%) were admitted to cardiology outpatient clinics with symptoms associated with syncopal episodes. The final diagnosis was reflex syncope in all of these patients. Of the 14 patients who had shortness of breath, 7 (3.8%) had acute pulmonary thromboembolism, 5 of which occurred during the early postoperative period. One patient had lower extremity arterial thromboembolism 7 months after the transplantation.

### Neurologic Symptoms That Necessitated Neurology Consultation

Headache was the most prevalent neurologic symptom (n = 10; 5.4%) which required neurologic consultation in the early postoperative period. Six transplant patients complaining of headache were referred to outpatient clinics during long-term follow-up. None of the patients had any definitive etiology for headache. Symptoms were transient in all of the patients. In 1 patient the provisional diagnosis was posterior reversible encephalopathy syndrome (PRES) due to severe headache, elevated blood pressure, and confusional state; however, the symptoms subsided in about half an hour. The neurologic exam along with both cranial tomography and magnetic resonance imaging (MRI) were normal. One patient died 8 months after kidney transplantation. The etiology was an "uncontrolled" hypertensive crisis that ended in a lethal intraparenchymal hemorrhage.

Transient ischemic attack occured in 7 (3.8%) patients, whereas 5 (2.7%) experienced ischemic stroke. Early postoperative seizures occured in 4 patients and 1 patient required admission to the intensive care unit due to super refractory status epilepticus.

Because MRI is the most useful diagnostic investigation in early detection of brain injury including cerebrovascular diseases, it was performed on all patients presenting with any neurologic symptom. Final diagnoses and the causes of exitus in the study population are demonstrated in Tables 1 and 2, respectively.

Demographic and clinical characteristics, including age, sex, etiology of chronic kidney disease, cardiovascular risk factors, time period between the onset of symptoms and date of transplantation, and daily dose of immunosuppresive drugs at the onset of symptoms were compared between the patients with cardiac and neurologic symptoms. There was no statistically significant difference between the groups (Table 3).

## DISCUSSION

The prevalence of cardiovascular disease is remarkably high in kidney transplantation recipients [3,4,7]. However, data regarding the presentation of cardiac and neurologic symptoms during the early post-operative period and long-term follow-up are scarce. Recognizing symptoms accurately is the first step in establishing a uniform approach to evaluate and manage cardiac and neurologic diseases in kidney transplant recipients. The rationale of our retrospective observational study was to determine the early post-operative and long-term cardiac and neurologic symptoms and complications encountered after kidney transplantation.

According to our data, chest pain was the most frequent cardiac symptom causing referral to cardiologists after kidney transplantation. In about two-thirds of the patients with chest pain, coronary heart disease was identified; in the remaining one-third, the cause was noncardiac. In the majority of the patients (63.6%), relief of anginal symptoms was achieved by antianginal treatment. Attending physicians did not choose to perform coronary angiography, as the risk of cardiac events determined by stress testing were low or intermediate. This follow-up strategy is concordant with the guidelines of the American College of Cardiology and American Heart Association for the diagnosis and management of patients with stable ischemic heart disease and with the guidelines of European Society of Cardiology on the management of stable coronary artery disease and myocardial revascularization, respectively [8–10]. During follow-up visits, the medically treated patients experienced no major adverse cardiac events. As a consequence, when pain relief is achieved with medical treatment and the extent of cardiac ischemia cannot be found with stress testing, medical treatment rather than coronary angiography could be kept in mind as a treatment option, which would avoid the potential risks of contrast nephropathy. Elective coronary stent placement in 2 patients with stable angina cases and primary percutaneus balloon angioplasty in 2 patients with acute coronary syndrome were performed without any major complications. None of the patients had any hemodynamic compromise and they were all discharged from the hospital without any complications. In our center, preoperative evaluations for solid organ transplantations are made in compliance with current guidelines [6]. Successful management of these patients during late-term follow-up might be proof of the appropriateness of these guidelines. Furthermore, these satisfactory results might be attributed to the favourable effects of renal transplantation. In a recent nationwide population-based study, Liao et al. demonstrated higher survival rates and delayed occurrence of major adverse cardiac events in Taiwanese patients with end-stage renal disease who received renal transplantation [11]. They hypothesized that renal transplantation might have decreased vascular inflammation or damage. An earlier retrospective study using healthcare databases in Ontario published results supporting the findings of Liao

**Table 1. Final Diagnoses in the Study Population**

| Cardiac Disease | | | Neurologic Disease | | |
|---|---|---|---|---|---|
| Final Diagnosis | Early | Late | Final Diagnosis | Early | Late |
| Stable coronary artery disease | | 5 | Headache | 10 | 6 |
| Unstable angina pectoris | | 5 | Ischemic stroke | 1 | 4 |
| Non-ST elevation MI | 1 | 1 | Transient ischemic stroke | 2 | 5 |
| Noncardiac chest pain | 2 | 3 | Intracranial hemorrhage | | 1 |
| Atrial fibrillation | 5 | 2 | Postoperative seizure | 4 | |
| Atrial tachycardia | 2 | 1 | Status epilepticus | 1 | |
| Sinus tachycardia | 1 | 2 | Central pontine demyelination | 1 | |
| Reflex syncope | | 8 | Metabolic encephalopathy | 2 | |
| Cardiac arrest | 1 | 1 | Hypoxic/ischemic injury | 1 | 1 |
| Respiratory arrest | 1 | | | | |
| Pericarditis | 1 | | | | |
| Infective endocarditis | | 1 | | | |
| Deep venous thrombosis | | 2 | | | |
| Pulmonary embolism | 5 | 2 | | | |
| Postoperative hypertension | 1 | | | | |
| Lower extremity embolism | | 1 | | | |

Abbreviations: Early, early post-operative period; Late, late-term follow-up; MI, myocardial infarction.

et al. They reported that the incidence of death or major cardiovascular event has remained stable over a 3-year period, despite renal transplantation recipients being older and having more comorbidities [12].

Coronary event was diagnosed in 6.5% (n = 12) of the study population. Our findings are in line with evidence from studies reporting high cardiovascular event rates (annual: 3.5%-7%) in kidney transplant recipients [13–15]. We also demonstrated a high incidence (70.6%) of coronary heart diseases in renal transplant recipients presenting with chest pain. However, to the best of our knowledge, there is no study primarily questioning chest pain in this particular group of patients. Considering the high rates of cardiovascular events, attending physicians must be aware of the signs and symptoms of coronary heart disease. The threshold for referring these patients to cardiologists for stress tests such as the treadmill test or myocardial perfusion scintigraphy must be low to identify extensive ischemia jeopardizing myocardium.

Palpitation was the second most frequent cardiac symptom. In 7 patients (53.9% of the patients with palpitations), atrial fibrillation was identified. When $CHA_2DS_2$-VASc (congestive heart failure, hypertension, age $\geq$65 years, diabetes, history of transient ischemic attack or stroke, vascular disease, female sex) score is equal or higher than 1, European Society of Cardiology recommends administration of oral anticoagulation in patients with atrial fibrillation, irrespective of being paroxysmal or persistent [16]. In our patient population 82.2% of the patients had either hypertension, diabetes, or vascular disease which means a $CHA_2DS_2$-VASc score equal or higher than 1. It is well-established that initiation of oral anticoagulation reduces the risk of ischemic stroke by 30%-50% [16]. Therefore, it is crucial to be aware of the occurrence of atrial fibrillation both during the postoperative period and long-term follow-up. Hence, primary prevention of ischemic stroke might be possible in this high-risk population. Large-scale cohort studies have demonstrated that having palpitations was associated with increased atrial fibrillation risk in the general population [17]. In our study, atrial fibrillation was found in more than half of the patients who were referred to a cardiologist after complaining of palpitation. Our findings highlight the importance of questioning the occurrence of palpitations after kidney transplantation. However, a high

**Table 2. The Causes of Exitus in the Study Population**

| Patient No. | Age (y)/Sex | Date of Tx | Date of Exitus | Reason of Exitus |
|---|---|---|---|---|
| 3 | 59/F | May 2015 | February 2017 | Rectus sheath hematoma |
| 26 | 31/M | July 2017 | January 2018 | Sepsis |
| 45 | 23/F | December 2015 | February 2016 | Sepsis |
| 47 | 55/M | February 2017 | March 2017 | Acute respiratory distress |
| 49 | 55/M | January 2017 | September 2017 | Intracranial hemorrhage |
| 56 | 54/M | August 2014 | April 2018 | Acute respiratory distress |
| 62 | 47/F | September 2015 | June 2018 | Found dead at home |
| 131 | 48/F | August 2015 | September 2015 | Hypotensive shock |
| 145 | 62/M | September 2014 | May 2015 | Resistant pneumonia |
| 167 | 44/M | November 2015 | February 2016 | Sepsis |

Abbreviations: Early, early post-operative period; F, female; Late, late-term follow-up; M, male; Tx, transplant.

**Table 3. Comparison of Demograhic and Clinical Characteristics of the Patients With Cardiac and Neurologic Symptoms**

| | Px With Cardiac Symptoms (n = 54) | Px With Neurologic Symptoms (n = 39) | *P* Value |
|---|---|---|---|
| Age (y) | 47.4 ± 12.5 | 45.5 ± 13.1 | .48 |
| Sex (male, n [%]) | 39 (72.2) | 28 (71.8) | .96 |
| Etiology of CKD | | | .64 |
| HTN, n (%) | 21 (38.9) | 17 (43.6) | |
| DMN, n (%) | 9 (16.7) | 6 (15.4) | |
| VUR, n (%) | 3 (5.7) | 1 (2.7) | |
| FSGS, n (%) | 3 (5.7) | 0 (0) | |
| FMF, n (%) | 1 (1.9) | 3 (7.7) | |
| PKD, n (%) | 3 (5.7) | 1 (2.7) | |
| Kidney stone, n (%) | 1 (1.9) | 1 (2.7) | |
| Unknown, n (%) | 13 (24.1) | 10 (25.6) | |
| Donor (cadaver) | 11 (20.4) | 11 (28.9) | .46 |
| CV risk factors | | | |
| HT, n (%) | 35 (64.8) | 30 (76.9) | .26 |
| DM, n (%) | 15 (27.8) | 9 (23.1) | .64 |
| HL, n (%) | 19 (35.2) | 10 (25.6) | .37 |
| CAD, n (%) | 14 (25.9) | 8 (20.5) | .63 |
| LV EF* | 61.3 ± 4.5 (61) | 62.7 ± 2.5 (63.5) | .42 |
| Onset*,† (days) | 329 ± 358.5 (199) | 302.3 ± 306.9 (183) | .67 |
| Drugs‡ | | | |
| Tacrolimus, n (%) | 49 (90.7) | 36 (92.3) | .79 |
| Tacrolimus, dose (mg) | 8.4 ± 4.6 | 8.9 ± 3.7 | .44 |
| MMF, n (%) | 36 (66.7) | 24 (61.5) | .66 |
| MMF, dose (mg) | 1875 ± 325 | 1979 ± 102 | .20 |
| MA, n (%) | 8 (14.8) | 8 (20.5) | .58 |
| MA, dose (mg) | 1329 ± 270 | 1440 ± 217 | .10 |
| Everolimus, n (%) | 5 (9.3) | 0 (0) | .07 |
| Everolimus, dose (mg) | 2.9 ± 1.1 | - | - |
| Cyclosporine, n (%) | 4 (7.4) | 2 (5.1) | .66 |
| Cyclosporine, dose (mg) | 300 ± 108 | 225 ± 35 | .34 |

Abbreviations: CAD, coronary artery disease; CKD, chronic kidney disease; CV, cardiovascular; DM, diabetes mellitus; DMN, diabetic nephropathy; dose, dosage in mg/day; FMF, familial Mediterranean fever; FSGS, focal segmental glomerulosclerosis; HL, hyperlipidemia; HT, hypertension; HTN, hypertensive nephropathy; LV EF, left ventricular ejection fraction; MA, mycophenolic acid; MMF, mycophenolate mofetil; PKD, polycystic kidney disease; Px, patients; SD, standard deviation; VUR, vesicoureteral reflux.

*Mean ± SD (median).

†Time period between the onset of symptoms and date of transplantation.

‡Immunosuppressive drugs and their daily doses at the onset of symptoms.

percentage of the patients might be asymptomatic despite having atrial fibrillation paroxysms. A lack of palpitations has been reported to be associated with increased in-hospital mortality [18]. Although the underlying mechanisms are unclear, underuse of oral anticoagulants in asymptomatic patients might be a major issue. Careful auscultation of the heart and performing 12-lead electrocardiography are therefore essential, as well as questioning palpitations in patients with kidney transplantation to identify silent atrial fibrillation paroxysms.

Reflex syncope has a characteristic bimodal age distribution which makes 2 peaks, one in the second and the other in the seventh decades of the life [19]. In our patient population, the median age of initiation of syncopal episodes was 51 years (minimum 22, maximum 68). This average age is lower than the expected second peak. This finding could be attributed to the early involvement of the autonomic nervous system due to the long-term effects of chronic uremic syndrome. However, this mechanism may not be the only explanation, as none of the patients reported any history of syncope before kidney transplantatation. The reason for the initiation of syncopal attacks after kidney transplantation needs to be elucidated. Routine immunosuppression regimen after kidney transplantation consisted of prednisone, mycophenolate mofetil, tacrolimus/everolimus, or cyclosporine in our patient population. As there are no reports mentioning any syncopal episodes related to any of these agents in the literature, it might be inconvenient to hypothesize such a relevancy. Given our present findings we can not explain the reason for the onset of syncope episodes after the transplantation.

Carotid and intracranial atherosclerosis are among the leading causes of ischemic stroke and transient ischemic attack worldwide [20,21]. Cerebrovascular events occur commonly in patients with chronic kidney disease due to concomitant risk factors such as hypertension, diabetes, and hyperlipidemia [22]. Risk factors for cerebrovascular disease after renal transplantation are age, arrhythmias, and hypercoagulable states. The incidence of stroke after kidney transplant is 5%-10% [23,24]. In our patient population this

percentage was 7%, which is concordant with the current literature. Although none of the patients with cerebrovascular accidents had atrial fibrillation at the time of index event, presence of paroxysmal atrial fibrillation could not be totally ruled out. Atrial fibrillation paroxysms are frequently asymptomatic and stroke might be the first manifestation of this arrhythmia. The detection of potential atrial fibrillation paroxysms is thus very important, because it is well-demonstrated that secondary prevention with oral anticoagulants effectively reduces the recurrence risk of ischemic stoke, which has a remarkably worse prognosis [16]. However, there is no consensus on the best methodology for screening silent paroxysms of atrial fibrillation. Patient education, pulse-palpation, periodic 12-lead-electrocardiographic monitoring, and electrocardiographic-Holter/event-Holter monitoring are among the most available options.

Whereas the first month after transplantation is dominated by infections related to the surgical procedure, including urinary tract infection and line infection, the period between the first and the sixth months is associated with the highest levels of immunosuppression and thus the greatest risk of opportunistic infections [25]. In our study population, sepsis was the cause of death in 3 (1.6%) patients. Considering central nerve system complications such as new-onset headache, unexplained fever, altered mental status, and focal neurologic signs, performing an MRI is imperative [26]. In these patients, every diagnostic test, including lumbar puncture, should be planned in case there is a suspicion of infection [27]. In our patient population, the number of patients presenting with new-onset headache was 16 (8.6%). However, in this group of patients none of them had fever, altered level of consciousness, or any laboratory findings suggesting infection. Therefore, we did not perform lumbar puncture in any of these patients.

Neurologic symptoms might be obscure exclusively in the first few weeks of immunosuppressive treatments, including headache, tremor, paraesthesia, and mood changes. It is important to be aware of the fact that calcineurin inhibitors might cause serious neurotoxic effects [26]. Tacrolimus was the most commonly used immunosuppressive agent in our study. Tacrolimus has a narrow therapeutic window and serum concentration has to be monitored closely [28]. PRES is amongst the most serious complications of tacrolimus [26,29,30]. The relationship between of PRES and tacrolimus should therefore always be kept in mind. Recent literature has suggested that PRES can cause permanent neurologic deficits if misdiagnosed. Despite the fact that other calcineurin inhibitors can also lead to PRES, tacrolimus has the highest risk and may result in PRES, even when administered within the therapeutic range [26,31]. In these cases, clinicians must recognize the symptoms and reduce or withdraw the immunosuppressive therapy in order to prevent permanent impairment. The sine qua non for the treatment of PRES are monitoring and replacing the electrolytes (mainly magnesium), treating high blood pressure (which may not be present in every case), and supportive therapy [32]. In our study population, only 1 patient was suspected to have PRES, and this diagnosis was ruled out with a normal MRI and transient symptoms.

Another commonly encountered neurologic complication amongst renal recipients is encephalopathy. Encephalopathy is defined as altered awareness and is typically seen within the first 30 days after transplantation. In the absence of radiologic evidence for structural lesions, renal rejection, hypoxic/ischemic injury, and nonconvulsive seizures/convulsive status epilepticus, clinicans must rule out encephalopathy in patients after renal transplantation [26,29,30]. In this subgroup of patients, electroencephalography and detailed blood sample analyses are crucial to elucidate the etiology. In our patient population there were 3 cases with signs and symptoms consistent with encephalopathy. All of these patients were treated successfully by correcting electrolyte and/or acid-base abnormalities.

Seizure is another important symptom and complication encountered in patients with renal transplantation. Although the etiology is generally immunosupressant treatment, both central nerve system and peripheric infections, metabolic dearrangements, and cerebrovascular diseaes (ischemic or hemorrhagic) should be explored in detail [33,34]. In our patient population, 5 patients (2.7%) experienced seizures. One of these patients suffered from superrefractory status epilepticus after transplantation. He was on antiepileptic treatment before transplantation. He had been diagnosed with epilepsy at 14 years of age. The etiology of epilepsy in this patient was a prior insult associated with a traffic accident and a brain injury. This patient was admitted to intensive care and medicated properly; his seizures were controlled only after intensive parenteral medications.

There was no statistically significant difference between the patients with cardiac and neurologic symptoms regarding baseline characteristics or immunosuppresive drugs used after transplantation. However, the single-center retrospective nature of the study and the small number of observed events preclude definite conclusions concerning etiopathogenesis underlying these 2 groups of symptoms. We do not routinely administer a quality of life questionnaire after transplantations in our department. As a consequence, the lack of data regarding the physical activity status of our patient population after transplantation is a limitation of our study.

In conclusion, after improvements in the success rates of kidney transplantation, early post-operative and long-term follow-up of recipients gained importance. Early diagnosis of cardiac and neurologic conditions is challenging due to the diversity of symptoms and wide array of complications. Our findings underscore the crucial role of questioning the symptoms that might be related to severe disorders. Asymptomatic patients with high risk factors must also be monitored carefully. Attending physicians should have a low threshold for referring these patients to cardiologists and neurologists. This strategy will enable them to perform early preventive measures and provide optimal medical treatment and interventions.

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