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Transplant patient monitoring in the Democratic Republic of the Congo: a survival analysis of kidney transplant recipients abroad

Suivi en République démocratique du Congo des patients transplantés à l'étranger : analyse de la survie des transplantés rénaux

Clarysse Nsenga Nkondi, Jean-Robert Rissassy Makulo, Yannick Mayamba Nlandu, Yannick Mopango Engole, Vieux Momeme Mokoli, Justine Busanga Bukabau, Ernest Kiswaya Sumaili, Nazaire Mangani Nseka

Auteur correspondant
Clarysse Nsenga Nkondi, MD
Courriel : clarankondi@gmail.com
Service de Néphrologie, Cliniques Universitaires de Kinshasa, Université de Kinshasa, République démocratique du Congo

Résumé

Contexte & objectif. Bien que la transplantation rénale soit reconnue le meilleur traitement de l'insuffisance rénale chronique, elle n'est pas encore pratiquée en République démocratique du Congo (RDC). Ainsi, les patients sont orientés vers d'autres pays pour y être transplantés. Cependant, le devenir post-greffe rénale en RDC est très peu documenté. La présente étude visait à évaluer la survie des greffons rénaux et des patients greffés suivis à Kinshasa.

Méthodes. C'était une cohorte rétrospective et analytique ayant inclus des patients transplantés à l'étranger et suivi dans trois hôpitaux de Kinshasa/RDC, entre 2000 et 2020. La perte de la fonction du greffon a été définie par un débit de filtration glomérulaire estimé MDRD < 15 ml/minute/1,73 m^2 ou une reprise de la dialyse. L'analyse de survie a été décrite par la méthode de Kaplan Meier.

Résultats. Cinquante dossiers des patients ont été colligés. L'âge moyen à la transplantation était de 49,8 ± 14,3 ans. La majorité des patients était de sexe masculin (84 %). Ils étaient presque tous greffés en Inde (82 %) de donneurs vivants (96 %). Un patient sur cinq était diabétique. La survie du greffon à six mois, un et cinq ans était respectivement de 92, 83 et 63 %. *Conclusion***.** Malgré de nombreux défis, la prise en charge des patients transplantés à l'étranger et suivis en RDC est relativement satisfaisante. Les perspectives de pratique locale de la transplantation rénale et d'amélioration des plateaux techniques associés doivent être encouragées.

Mots-clés : Maladie rénale chronique, transplantation rénale, devenir, survie, République démocratique du Congo

Summary

Context and objective. The Democratic Republic of Congo (DRC) does not currently practice kidney transplantation, and patients are referred to other countries for transplantation. Furthermore, post-kidney transplant follow-up in the DRC is suboptimal and faces several challenges. The present study aimed to evaluate survival of kidney grafts and transplant recipients followed up in Kinshasa. *Methods.* This cohort retrospective study was conducted in three hospitals in Kinshasa/the DRC and included post-transplant patients selected between 2000 and 2020. Graft failure was defined as glomerular filtration rate < 15 ml/minute/1.73 m^2 or resumption of dialysis. *Results.* Only 50 patients were included. The mean age at transplantation was 49.8 ± 14.3 years. Most patients were male (84%) and received transplants in India (82%) from living donors (96%). One in five patients was diabetic. The six-month, one-, and five-year graft survival was 92, 83, and 63%, respectively. *Conclusion.* Despite several challenges, the care of patients transplanted abroad and followed up in the DRC is satisfactory. The prospects for practicing kidney transplantation locally and improving associated technical platforms must be encouraged.

Keywords: Chronic kidney disease, kidney transplant, outcome, survival, DRC

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Introduction

Chronic kidney disease (CKD) is a recognized major public health problem worldwide owing to its high prevalence, mortality, and the high cost of treatment by dialysis and transplantation (1-2). The increasing incidence of chronic non-communicable diseases (e.g., diabetes, obesity, hypertension), communicable diseases (such as malaria, HIV, and COVID-19), and the use of nephrotoxic drugs, particularly in developing countries, are major contributors to CKD (3).

In Kinshasa, the prevalence of CKD increased from 9.5% to 13.4% between 2006 and 2015 (4). Furthermore, among the 6,000 patients likely to be at the end stage of CKD in 2015, only around 180 were able to access renal replacement therapy (5). Dialysis, both peritoneal (PD) and hemodialysis (HD), has been carried out in Kinshasa for four decades. However, this treatment has well-known limits, justifying the interest in developing kidney transplantation to treat patients more effectively and reduce long-term treatment costs. The direct costs of hemodialysis in Kinshasa are estimated at $ 28,220 per year (6), which is equivalent to the cost of the curative surgical procedure (kidney transplantation) in some countries. Local medical teams select and prepare patients for kidney transplants, which are then carried out in other countries. Doctors then ensure post-transplant follow-up of patients who return to the DRC. However, this local monitoring of transplant recipients faces several challenges such as lack of regular contact with the surgeons who operated on the transplant recipients, lack of local sales of immunosuppressive drugs in a traceable pharmaceutical circuit, and difficulties in measuring the donor's specific anti-HLA antibodies (DSA). In addition, immunofluorescence assay can rarely be conducted in the pathology laboratory, and no current dosage of immunosuppressive drugs is available. In a context where DRC envisions having its own kidney transplant program, assessment of the current situation is critical to help identify key interventions to launch the program. The present study aims to describe the management of patients transplanted abroad and followed up in Kinshasa and to evaluate graft and patient survival.

Methods

Design, setting and period of study

We conducted a retrospective observational study in three hospitals in Kinshasa (Kinshasa University Hospital = KUH, Ngaliema Medical Center = NMC, and HJ Hospital) based on a historical cohort. Patients were selected between January 1st, 2000 and December 31st 2020.

Parameters of interest

The parameters of interest were sex, age at transplant, CKD etiology, country in which the transplant was carried out, type of transplant (with living or deceased donor), immunosuppressant treatment in Kinshasa, complications (including findings of kidney failure assessment on the graft, the examination carried out abroad), the duration before graft failure, hemodialysis resumption, and the patient's vital outcome. Graft failure was defined as GFR < 15 ml/min/1.73 m^2 or a resumption of dialysis.

Statistical analysis

Statistical analyses were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Comparisons between groups were performed using Student's t-test, Fisher's exact test, Mann-Whitney test, and chi-square test where appropriate. Kaplan–Meier curves were drawn for survival analyses using R software. We compared the survival of patients in the study with the survival of chronic hemodialysis patients from another study conducted in Kinshasa (7).

Ethical considerations

The study was approved by the Kinshasa School of Public Health Ethics Committee (ESP/CE/30/2020) and was conducted with strict confidentiality. Patients were not exposed to any particular risk or additional care during the study.

Results

The study included 50 patients. The mean age of the patients (men, 42; women, 8) at transplantation was 49.8 ± 14.3 years. Most patients had received transplants in India (82%), while those who received transplants in Europe

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and Africa represented 12% and 6%, respectively.

The kidney transplant was preceded by dialysis in 47 patients, and only 3 patients had benefited from pre-emptive transplantation.

Hemodialysis was the most used treatment before kidney transplant (37 patients vs. 10 patients for peritoneal dialysis). The median duration of dialysis before kidney transplant was 8 months [IQ $_{25,\ 75}$ 4 and 12 months], with extremes of 3 and 84 months. Other patient characteristics are described in Table 1.

Table 1. General characteristics of transplanted patients

	All (n=50)	Men (n=42)	Women (n=8)	p
Age at kidney transplantation, years	49.8 ± 14.3	51.5 ± 13.8	40.8 ± 14.5	0.051
Age < 20	1 (2)	1 (2)	0	0.622
Age 21-60	37 (74)	30 (71)	7 (88)	
Age > 60	12 (24)	11 (26	1 (13)	
Medical history				
Diabetes mellitus	14 (28)	13 (31)	1 (13)	0.274
Hypertension	42 (84)	37 (88)	5 (63)	0.105
Dyslipidemia	6 (12)	5 (12)	1 (13)	0.670
Stroke	1 (2)	1 (2)	0	0.840
HIV infection	1 (2)	0	1 (2)	0.160
HCV infection	6 (12)	5 (12)	1 (13)	0.703
HBV infection	2 (4)	2 (5)	0	0.622
Transfusion	7 (14)	5 (12)	2 (25)	0.310
Pregnancies	-	-	5 (63)	

Abreviations: HIV: human immunodeficiency virus HVC: hepatitis C virus HBV: hepatitis B virus
The results are expressed as mean and ± standard deviation or absolute frequency (%).

Living donors accounted for 96% of the transplants compared with only 4% for deceased donors. The immunosuppressive regimens received by patients are described in Table 2.

Table 2. Types of immunosuppressive therapy

Regimen	n (%)
Tacrolimus + MMF + CTCD	43 (86)
Tacrolimus + MMF + Everolimus + CTCD	1 (2)
Tacrolimus + azathioprine + CTCD	3 (6)
Everolimus + MMF +CTCD	1 (2)
Cyclosporine + MMF + CTCD	2 (4)

Abbreviations: CTCD: Corticosteroids; MMF: Mycophenolate mofetil.
The results are expressed in absolute frequency (%).

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The combination of tacrolimus + MMF + CTCD was the most used.

Patients were transferred abroad at least once a year (for follow-up assessment) or in case of proteinuria or unexplained renal failure, mainly because of the lack of local capacities to confirm the type of rejection or to optimally treat serious complications.

During the follow up, a total of 20 graft failures were reported. Figure 1 shows that graft failure was related mainly to chronic rejection (80%). Recurrence of nephropathy (1 case = 5%), graft pyelonephritis (1 case = 5%), and graft artery thrombosis (2 cases = 10%) have also been reported. The kidney biopsies were performed abroad.

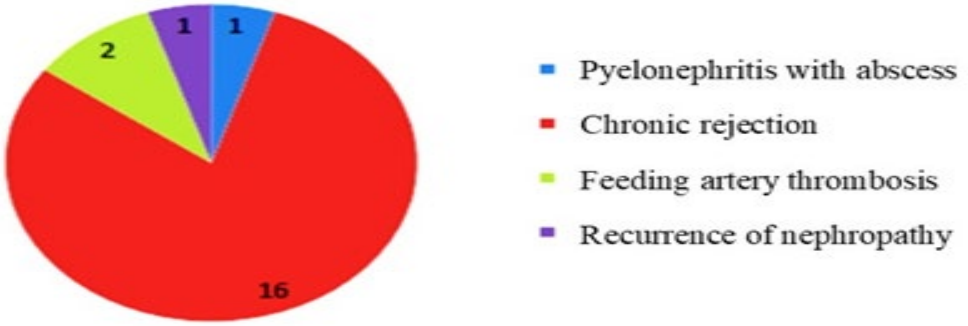

Figure 1. Causes of kidney graft failure

The incidence of graft failure over time is depicted in Table 3. The initial time corresponds to the start of post-kidney transplant follow-up in Kinshasa.

Table 3. Cumulative incidence of graft failure during the follow-up

Post-transplant follow-up duration	Cumulative number of graft failure	Number of functional grafts	Cumulative proportion of functional grafts (%)
1 month	1	49	98
6 months	4	46	92
12 months	8	38	83
60 months	13	22	63
120 months	19	5	21

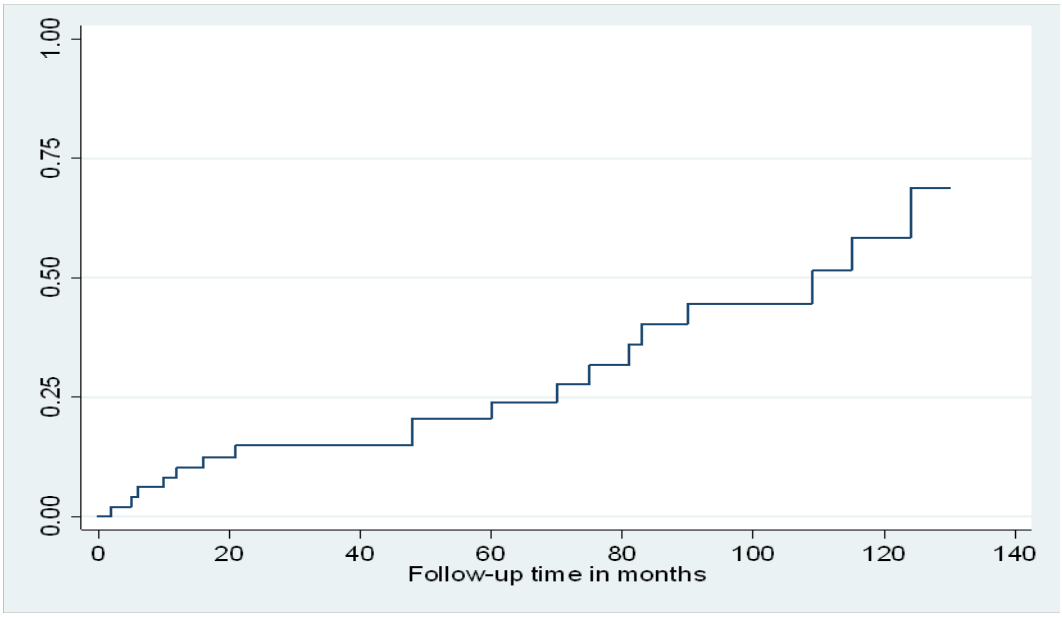

Figure 2. Incidence of graft failure during follow-up

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Over the 20-year study period, patients with graft failure (n=20) were readmitted for hemodialysis. None were treated with peritoneal dialysis.
Table 4 and Figure 3 report, respectively, the cumulative frequency of deaths and survival of transplant patients over time. In Figure 3, transplant recipients' survival was compared with that of hemodialysis patients in a study previously conducted in Kinshasa (7).

Table 4. Cumulative incidence of death during the follow-up period in Kinshasa

Post-transplant follow-up duration	Cumulative number of death	Living patients (%)
2 months	1	49 (98)
6 months	2	48 (96)
12 months	4	44 (92)
60 months	8	26 (76)
120 months	13	5 (28)

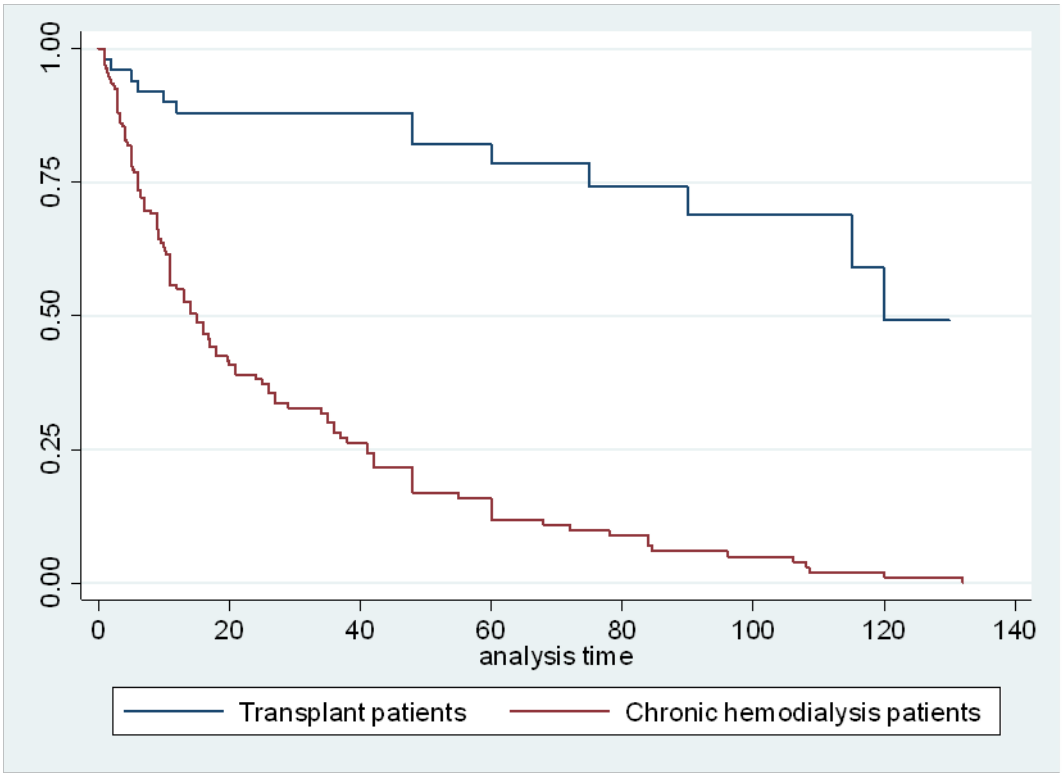

Figure 3. Incidence of deaths (data from hemodialysis patients from reference 7)

Discussion

The present study provides information on kidney transplant monitoring in Kinshasa—in particular, on the number of patients followed in the official circuit of hospitals, the complications observed, and the survival of both grafts and transplant patients in comparison with that of chronic hemodialysis patients. Only 50 patients were selected for the study period covering 20 years. This is primarily explained by the fact that transplanted patients generally do not return to the DRC, knowing that the local follow-up is suboptimal. Among transplant patients who return home after a transplant abroad, many do not consult hospitals. They generally contact their doctors abroad and consult Congolese doctors only when they experience complications. Furthermore, transplantation is unavailable for many Congolese and even African patients because the treatment usually comes with catastrophic costs due to out-of-pocket expenditures (1, 5, 8). Most patients (82 %) were transplanted in India. Indeed, since the 1990s, India has emerged as the world leader in "medical tourism". India has highly qualified doctors and advanced equipment. Additionally, treatments are approved by the World Health Organization (WHO) and the US Food and Drug

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Administration, and are much cheaper than in Western countries. For instance, a kidney transplant in India costs around US $13,000, compared with up to US $300,000 in the United States (9-11). The age at kidney transplant as well as the proportion of diabetic patients are within the range of studies carried out in other sub-Saharan African countries (11-13). The immunosuppressive treatment that the patients received corresponds to the most widely used regimen throughout the world.

Five-year follow-up showed that only 63% of grafts were functional. These data are similar to those of other African studies and partly reflect the limits of kidney transplant tourism (11-13). Better transplant results reported in Western studies and in South Africa, however, do show that the situation can be improved (14-16). In particular, it is necessary to improve the supply chain of immunosuppressive drugs, strengthen the capacities of laboratories (immunology, biochemistry, pathology, etc.), and the training of medical staff.

Patients with kidney graft failure are at high risk of mortality. Although this complication was found in 20 patients (40 %), patient survival overall was satisfactory, i.e., 76 % after five years of follow-up. All patients who had kidney graft failure resumed hemodialysis. This demonstrates that a good hemodialysis program is necessary in parallel with kidney transplant. Some studies suggest that the outcome of patients starting peritoneal dialysis after kidney graft failure is similar to those starting hemodialysis (17-18). Therefore, peritoneal dialysis can be regarded as an alternative treatment option for patients returning to dialysis after kidney graft failure. The data shown in Figure 3 underscore the advantage of kidney transplant over chronic hemodialysis. The downside in criticizing this result is that, in general, patients selected for kidney transplant are initially treated with hemodialysis. Moreover, hemodynamic stability is an important criterion for eligibility for transplant. Hemodialysis, however, is usually indicated in many patients with uremic syndrome, resulting in high mortality upon initiation. However, it is known that kidney transplantation is superior to dialysis in terms of survival, quality of life, and long-term cost benefit. It is therefore the ideal treatment for stage 5 of CKD (19- 20).

Our study certainly did not address all aspects related to renal transplant monitoring. However, it has the advantage of providing critical data on the current status of kidney transplants, including follow-up of transplant patients, while identifying areas that need improvement as pre-requisites to establishing a local kidney transplant program.

Conclusion

Although encouraging, the results regarding graft survival and kidney transplant recipients monitored in Kinshasa are inferior to those reported in Western literature. Efforts must be made to improve the identified weaknesses.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be viewed as a potential conflict of interest.

Author contributions

CNK, NMN, and JRM conceived, designed, and supervised the study. They had full access to data and drafted the first version of the manuscript. JRM performed statistical analysis. All authors revised the manuscript, approved the final submitted version for publication, and agreed to be accountable for all aspects of the work.

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Availability of data and materials

The datasets used and analyzed in this study are available from the corresponding author upon reasonable request.

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