



Research Article

Eligibility to Renal Transplantation in Dakar's Chronic Hemodialysis Patients

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Abstract

Introduction: Renal Transplantation (RT) is the ideal treatment for patients with chronic end stage renal disease because it offers a better quality of life, survival and at a lower cost. To date, it is not yet practiced in Senegal. The purpose of our work was to evaluate eligibility for RT in chronic hemodialysis patients in the Dakar region.

Patients and Method: This was a cross-sectional, descriptive, analytical and multicenter study conducted over a 3-month period from March 31st to June 30th, 2017. It was performed in 4 hemodialysis centers in the Dakar region. Two hundred and thirty chronic hemodialysis patients for more than 6 months, consenting, were included in the study. Standard and extended eligibility criteria and contraindications were sought. The epidemiological, clinical, paraclinical and therapeutic parameters made it possible to determine patients with absolute and relative contraindications; those meeting the standard eligibility criteria and / or extended to the RT. These parameters also made it possible to determine the patients eligible for RT. The statistical tests of Khi 2 were used, the p was significant when it was less than 0.05.

Results: Fifty-two patients (22.61%) were eligible for RT. Stopping hemodialysis (100%) and improving quality of life (97.18%) were the main motivations for RT. The refusal to be transplanted among the 16 patients was statistically correlated at the age of at least 50 years ($p < 0.05$), at the retired status ($p = 0.0001$) and at the possibilities of financial autonomy ($p = 0.001$). The absence of donors was mainly due to the lack of maintenance on the subject with the family (88.14%). The male gender of the donors was noted in 128 cases (58.99%) and the average age of the donors was 45.46 years with the extremes of 20 and 72 years. Eligibility for RT was not related to occupation, financial independence ($p > 0.05$). Immunizing events were not statistically correlated with eligibility criteria or contraindications at RT ($p > 0.05$). Hemodialysis duration increased the risk of having absolute contraindications to RT ($p = 0.003$) and not relative contraindications. These absolute contraindications were most related to severe cardiovascular comorbidities in 27 cases (11.74%).

Conclusion: RT is possible in chronic hemodialysis patients in Dakar. More financial means are needed to make available the necessary explorations for examinations before, during and in the post-kidney transplant.

Keywords: Chronic Hemodialysis; Dakar; Eligibility; Renal Transplantation

Abbreviations

RT : Renal Transplantation
CKD : Chronic Kidney Disease

Introduction

Renal Transplantation (RT) is a medical surgical operation consisting of replacing a diseased kidney with a healthy kidney or transplant from a living donor or cadaver [1]. RT is the treatment of choice for terminal chronic renal failure because it offers a

better quality of life and survival at a lower cost [2]. In Africa, RT is carried out in the Maghreb countries and in few sub-Saharan countries. Most African countries are starting RT programs. Less than 1% of terminal renal failure patients in sub-Saharan Africa receive RT [3]. In West Africa the annual rate of RT is 50 per year, or 0.15 per million inhabitants for a population of 332 million. In Central Africa, it is 0.02 per million inhabitants [3,4]. Senegal has 13 hemodialysis centers for 592 patients noting that more than 600 patients are on waiting lists for their dialysis care. The law on RT has been passed since 2015 [5]; however, RT has not yet started in Senegal to date. That is why this work was initiated for the first time to study the eligibility conditions of Senegalese patients for renal transplantation.

Methodology

This was a cross-sectional, descriptive, analytical and multi-center study conducted over a 3-month period from March 31 to June 30, 2017 and performed in 4 hemodialysis centers in the Dakar region (HALD, HOGGY, ABC, CHD). All chronic hemodialysis patients for at least 6 months and who were at least 12 years old, were included. The studied parameters were socio-demographic in nature (age, gender, occupation, number of donors, possibilities of financial autonomy, type of care). Clinically, field, history and comorbidities, smoking, substance abuse, general condition, BMI, psychological status, degree of immunization (number of pregnancies, number of blood transfusions, previous RTs), vaccination status, pulse pressure, recurrent urinary tract infections, number of received femoral catheters and their insertion site, ENT and stomatologic examination.

Paraclinically, the following tests were performed: the Rhesus blood group and phenotyping, the hemoglobin level; the serum bank; hemostasis, fasting glucose, HbA1c, transaminases; viral serologies (hepatitis B, B, EBV, CMV), *Treponema pallidum* Hemagglutination Assay (TPHA) and Venereal Disease Research Laboratory (VDRL); intradermal tuberculin reaction (IDR), quantiferon, ECBU; complete calcium-phosphate assessment; PSA, Cervicovaginal Smear (CVS); chest x-ray, mammography; ECG, echocardiography looking for severe cardiovascular comorbidity; retrograde Urethrocytography (UCR), uro-CT looking for significant residual post-micturition, malformative uropathy; Doppler ultrasound of ilio-femoral vessels and Oesophago-Gastro-Duodenoscopy (OGD). Eligibility was assessed by finding absolute and relative contraindications and according to standard eligibility criteria for RT and extended ones (presence of at least one immunizing event).

The standard eligibility criteria used in the study were: MRC 5D hemodialysis for more than 6 months; informed consent before RT; clear absence of risk of recurrence of renal pathology on the graft evaluated according to the initial nephropathy and the clinical and paraclinical investigations results; smoking cessation

≥ 1 month, <30 packs / year; the absence of intravenous drug use of illegal drugs ≥ 6 months; the absence of active addiction and / or active alcoholism; psychological evaluation; no major cardiovascular history without MI or unstable angina pectoris; absence of abnormalities on the Doppler ultrasound of the ilio-femoral vessels that may hinder the survival of the graft; HIV infection with undetectable viral load <50 copies/ml for at least the past 6 months with or without Highly Active Antiretroviral Therapy (HAART) and a CD4 count $> 200 / \mu\text{l} \geq 6$ last months; absence of Hepatitis C Virus (HCV) and / or severe Hepatitis B Virus (HBV) infections; absence of latent cancer; absence of active systemic infections; absence of any condition with a life expectancy <2 years; cancer treated curatively; absence of severe and irreversible extra-renal diseases; adherence to unalterable treatment; medically controlled psychiatric illness; the target Hemoglobin (Hb) level.

Retained absolute contraindications: patient's refusal; age over 85 years; cancer or hematological malignancy which is not in remission; severe cardio-vascular comorbidities; severe respiratory comorbidities; acute unstabilized or unfollowed chronic psychiatric disorders, alcohol dependence or addiction to hard drugs without a withdrawal plan; evolved proven dementia; obesity with a Body Mass Index (BMI) greater than $50 \text{ kg} / \text{m}^2$; the decision not to initiate a replacement therapy, uncontrolled Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Hepatitis D Virus (HDV) and HIV infections. Relative contraindications were related to: cancer treated curatively (the waiting time being based on the type of cancer); psychiatric condition and infections. These parameters were used to determine which patients met the standard eligibility criteria and extended to RT. A p less than 0.05 was considered statistically significant. Therapeutically, the existence of antihypertensive, anti-anemic, mineral-bone disorders treatments, the treatment of hyperparathyroidism by Para Thyroidectomy (PTx) were studied.

In univariate analysis, the mean, median, mode, minimum and maximum standard deviation for quantitative variables, and proportions for qualitative variables were studied. In bivariate analysis, the intersection between the clinical data and the other variables of the eligibility criteria for RT was considered significant when p was less than 0.05. In multivariate analysis, we crossed-examined clinical and paraclinical data as well as the contraindications and eligibility criteria for RT. The p was statistically significant when it was less than 0.05. The analysis of the data was done using Sphinx Plus2 and Epi Info software, English versions 3.5.1 and SPSS 15.0.

Results

Out of 272 patients who participated in the study, 230 were included (84.56%). There were 118 men and 112 women, hence a sex ratio of 1.05. The mean age was 50.83 ± 14.35 years [12 and 90 years]. Ninety-three patients (40.40%) were unemployed

due to the hemodialysis constraints. One hundred and eighty-four patients (80%) were married; 208 (90.4%) were Muslim and 22 were Christian (9.6%). Sixteen patients (7%) refused to be transplanted; the lack of motivation was linked to: the feeling of well-being in dialysis (47.06%), the minimum age requirement of at least 50 years (41.18%), the fact that it was necessary to favor young people (17.65%) and the possibilities of financial autonomy related to RT (11.76%). The main motivations for being renally transplanted were to stop dialysis (100%) and improve the quality of life (97.18%). The absence of a donor was noted in 118 patients (51.3%). The reasons for the lack of donors were that the patient “should talk to the family”, “it must come from them”, “I do not want to involve them”, reluctance, religion and refusal in the family in respectively 88.14% (n = 104); 8.47% (n = 10); 16.10% (n = 19); 8.47% (n = 10); 4.24% (n = 5) and 0% of cases. The relationship with the donor was 1st degree (36%), 2nd degree (46%), 3rd degree (14%) and unrelated (4%). The male gender of the donors was noted in 128 cases (58.99%) and the average age of the donors was 45.46 years with the extremes of 20 and 72 years.

There were 50% (n = 10) husbands and 50% wives as donors. Initial nephropathy was respectively vascular (48.26%), glomerular (13.48%), chronic tubulointerstitial (8.26%) and hereditary (4.78%). The risk of recurrence of initial nephropathy was noted in 14.8% of cases. The mean time between the diagnosis of Chronic Kidney Disease (CKD) and dialysis was 13.92 ± 33.24 months [0 and 300 months]. The mean duration of hemodialysis was 49.08 ± 36.24 months [+ 6 months and 204 months]. It was noted that 75.7% were receiving hemodialysis under right femoral catheter and 130 patients (56.5%) under left femoral catheter. Secondary and tertiary hyperparathyroidism were observed in 23.91% and 1.74% (4) patients, respectively. PTx was performed in 8 patients (3.48%). Six patients (2.61%) had a medically stabilized depressive state; 2 patients (0.87%) were weaned drug addicts and 49 patients (21.30%) were smokers and weaned. Alcohol consumption was noted in 12 patients (5.22%) and weaned in 100% of cases.

Comorbidities were represented by the metabolic syndrome, hypertension, history of stroke, diabetes, moderate and severe heart diseases in respectively 27 (11.74%), 206 (89.57%), 5 (2, 17%), 27 (11.74%), 140 (60.87%) and 21 cases (9.13%). Cardiovascular complications were represented by: hypertension (114 cases, i.e. 49.57%), hypertrophic heart disease (117 cases, 50.87%), valvular (48 cases, 20.87%), ischemic (29 cases, 12.61%). CMDs were hypokinetic in 8 cases (3.48%) and hyperkinetic in 2 cases (0.87%). There were 6 calcifications: 3 valvular (1.30%) and 3 vascular (1.30%). Hypertension was uncontrolled in 149 cases (64.78%). Mean pulse pressure was 61.78 ± 18.01 mmHg with the extremes of -10 and +110 mmHg; it was greater than 60 mmHg in 56.6% of patients and reached 110 mmHg in 3 patients. The general condition was classified WHO 3 in 5 patients (2.17%). One hundred and sixty-six patients (72.2%) were anuric; Residual

diuresis was noted in 27.83% of cases.

Overweight patients accounted for 18.3%; we noted 3 cases (1.3%) of severe obesity. In 65.7% of cases the patients had a normal weight. The blood group was O in 131 (56.96%) and AB in 6 (2.61%) cases. The serum was retained in 88 patients (38.26%). Cross-match and HLA typing were not yet done in patients. The average hemoglobin level was 8.92 ± 1.98 g/dl [4.90 and 14.00 g/dl]. Fifty-six patients (24.35%) had a target hemoglobin level. Two hundred and twenty-one patients (96.09%) had at least one immunizing event that was related to blood transfusions in 217 patients (98.19%), to pregnancies in 4 cases (1.81%) and the association pregnancy and blood transfusion was noted in 83 cases (37.56%). In terms of infection, 10.43% (n = 24) had a chronic carriage of HBsAg and 6 (2.61%) cases HCV; no patient was HIV-positive; 17 (7.83%) cases had a history of pulmonary and extra-pulmonary tuberculosis. There were 3 suspected cases of neoplasia including one case of squamous cell carcinoma of the oral lower lip that was treated with radiotherapy.

Absolute contraindications to RT were noted in 48 patients (21.72%). They were related to severe cardiovascular comorbidities in 27 cases (11.74%), severe respiratory comorbidities in 2 cases (0.87%), unstabilized psychiatric disorders and drug addiction with no possibility of withdrawal in 1 case (0, 40%) respectively. There were 16 cases (7.00%) of refusals and in 1 case (0.43%) a patient older than 85 years. One hundred and forty-six (63.48%) patients had relative contraindications (Table 1). The risk of recurrence of initial nephropathy was noted in 65 cases (28.26%); loss of autonomy in 6 cases (2.61%).

Relative Contraindications	Headcount	Percentage
Heart failure	67	29.10%
Risk of recurrence of initial renal disease	65	28.30%
Chronic infection	26	11.30%
Diabetes + myocardial infarction (MI)	8	3.50%
Thromboembolic risk factors	7	3.00%
Autonomy loss	6	2.60%
Diabetes + peripheral vascular diseases	4	1.70%
Diabetes + smoking	3	1.30%
Hepatic insufficiency	3	1.30%
Extensive vascular calcifications	3	1.30%
Peripheral Vascular Disease + Stroke (CVA)	2	0.90%
Stabilized psychiatric illness	2	0.90%

Moderate respiratory insufficiency	2	0.90%
Genitourinary tract malformations	2	0.90%
Diabetes + Stroke (CVA)	1	0.40%
Stroke (CVA) + smoking	1	0.40%
BMI between 35-50 Kg / m ²	1	0.40%
History of cancer	1	0.40%

Systemic amyloidosis	1	0.40%
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Table 1: Distribution of patients according to relative contraindications.

Regarding the eligibility criteria, informed consent was obtained in 216 (93.91%) patients. Fifty-two patients (22.61%) were eligible for RT. The psychological evaluation was done in 6 patients (2.61%). The distribution of patients according to the number of standard eligibility criteria is shown in (Figure 1).

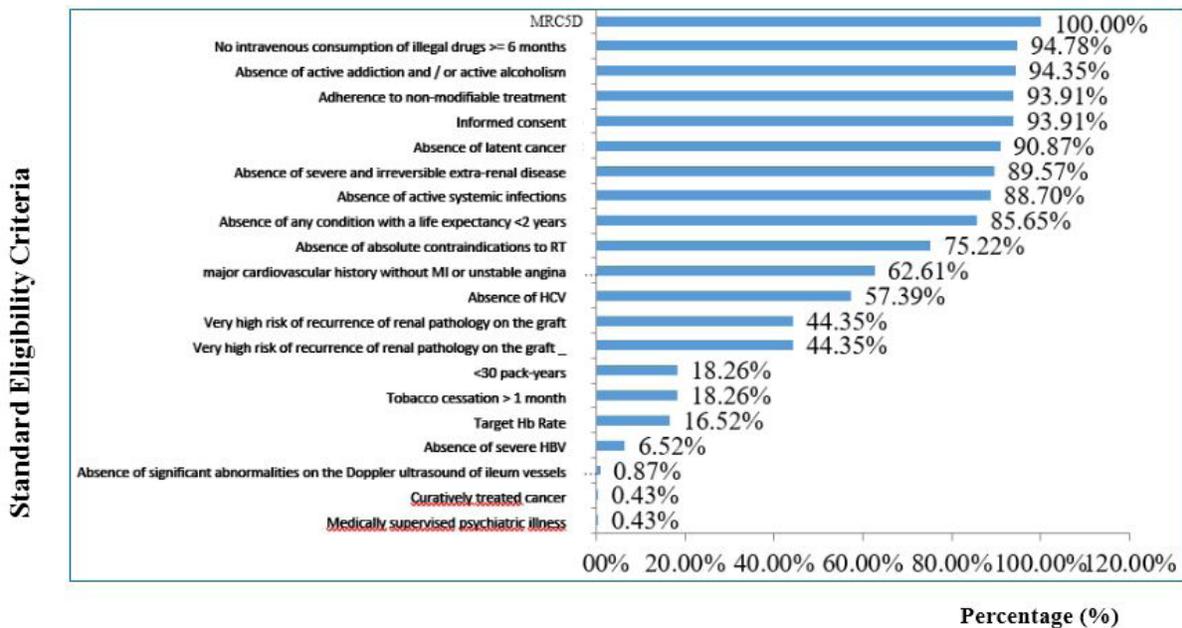


Figure 1: Distribution of patients according to the number of standard eligibility criteria

Extended eligibility criteria were noted in 221 patients (96.09%); these were patients with at least one hyperimmune event. In 9 and 29 patients respectively, the absolute and relative contraindications could not be specified as a result of lack of paraclinical investigations. In bivariate analysis, there was a statistically significant correlation between the refusal to be transplanted and the minimum age limit of 50 years, the retiree status ($p = 0.000$), the potential for financial autonomy ($p = 0.001$). Patients who refused to be transplanted included 43.8% ($n = 7$) men and 56.2% ($n = 9$) women. The refusal was not statistically related to gender ($p = 0.531$), religion ($p = 0.64$), hemodialysis center ($p > 0.05$), or hemodialysis duration ($p = 0.199$).

In multivariate analysis, absolute contraindications were

correlated with the eligibility criteria for RT ($p < 0.05$). (Table 2) The duration in hemodialysis was correlated with absolute contraindications ($p = 0.003$). Regarding relative contraindications, there were correlations with the high risk of recurrence of initial nephropathy ($p = 0.000$), active systemic infection ($p = 0.017$) and absolute contraindications ($p = 0.001$). The potential for financial autonomy had no impact on the absolute contraindications ($p = 0.163$) or the relative contraindications ($p = 0.964$); however, there was a correlation between the potential for financial autonomy, informed consent ($p = 0.048$), and the absence of addiction or alcoholism ($p = 0.000$). There was no statistically significant relationship between hyper-immunization and the eligibility criteria for or contraindications to RT ($p > 0.05$).

Absolute Contraindications						
		Yes		No		P
		Headcount	%	Headcount	%	
Standard Eligibility Criteria	Informed consent	36	75	172	99.4	0.001
	High risk of recurrence	17	35.4	84	48.6	0.106
	Smoking cessation <1 month and <30PA	13	27.1	28	16.2	0.086
	Absence of IV drug use	36	75	173	100	0.0001
	Absence of drug addiction, alcoholism	36	75	172	99.4	0.0001
	Major cardiovascular history without MI	33	68.8	105	60,7	0.308
	Absence of significant abnormalities on Doppler ultrasound of ilio-femoral vessels	0	0	2	1,2	0.454
	Absence of HCV	22	45.8	109	63	0.032
	Absence of severe HBV	3	6.3	11	6.4	0.978
	Absence of latent cancer	34	70.8	167	96.5	0.0001
	Absence of systemic infection	33	68.8	164	94.8	0.0001
	Absence of any condition with a life expectancy of less than 2 years	28	58.3	162	93.6	0.0001
	Treated cancer	0	0	1	0.6	0.598
	Absence of severe and irreversible extra-renal disease	32	66.7	166	96	0.0001
	Adherence to non-modifiable treatment	36	75	171	98.8	0.0001
	Medically controlled psychiatric illness	1	2.1	0	0	0.057
Target Hb Rate	6	12.5	32	18.5	0.33	

Table 2: Relationship between Standard eligibility criteria and Absolute contraindications.

Discussion

Fifty-two patients in our group were eligible for RT. The factors associated with this eligibility were related to the absence of absolute contraindications to RT, the RT standard and expanded eligibility criteria. Even if the socio-economic status of our patients did not influence the eligibility for RT ($p > 0.05$), however, the possibilities of financial independence were statistically correlated with the refusal ($p = 0.001$). On the contrary, in Morocco, Toufik MJ [6] observed that 79% of cases of patient's refusals of RT were related to financial inability. We noted in our results and those of the literature that respectively 91.30%; 97.29 [7] and 95% [8] of chronic hemodialysis patients had already heard of RT. The main motivations for RT in our group were identical to those found by [7], as well as [8]. The patients-donor's relationship was usually a 2nd degree one (62.38%), contrary to literature data reporting a predominance of affective donors [9]. The absence of donors can be explained by the reluctance of the patient to discuss RT with

those around him for fear of blaming himself in case of failure or complications inherent to RT; but this is also the responsibility of the nursing staff, especially the treating physician [10].

The prevalence of viral infections varies depending on the dialysis center and regions [11]. In the absence of active infection, patients can have a transplant and the curative treatment can be performed after RT. [12,13] showed the efficacy of antiviral treatment in patients with HCV who are eligible for RT. Only 38 of our patients (16.52%) had a target Hb rate, unlike the results of [14] where the target Hb level was noted in 40.3% of RT waiting list patients and in 27.9% of non-registered patients. This low target Hb level can be explained by the high cost of Erythropoiesis Stimulating Agents (ESAs) which our patients cannot afford paying due to financial constraints. These financial constraints force patients to use blood transfusion to normalize their Hb level. All the immunizing events mentioned in the methodology above are not a formal contraindication to RT, even though they entail

an additional cost associated with the de-immunization programs [15]. More than 50% of our patients had a cardiovascular disease including 12.6% related to severe cardiovascular comorbidities responsible for absolute contraindications. Our results differ from those of [14] with 85.8% of patients with cardiovascular diseases of whom 44.8% were not enrolled and 41% on RT waiting list. These differences in the number of eligible patients in our respective studies are explained by the lack of paraclinical investigations.

Absolute contraindications were noted in 48 patients (21.72%). The rate of refusal to have a RT is lower in chronic hemodialysis patients in countries where RT has not yet started, that is to say 7% in our group and 11% in Mauritania [7], unlike in countries where this activity is being practiced (79%, 21.69%, one-third) [6,8,16]. These differences can be explained by the level of knowledge of investigations constraints and possible complications related to RT, as perceived by our different populations. Our patient's eligibility was not statistically related to the number ($p > 0.05$) of eligibility criteria but to their nature ($p < 0.05$). None of our patients have been rejected for active consumption of tobacco and / or illicit drugs; unlike the results of Sandhu GS et al. [17] showing a significant rejection of patients due to the use of illicit substances with a risk ratio of 0.39 ($P < 0.001$). Our study showed a statistically significant correlation between the potential for financial autonomy and certain eligibility criteria for RT, including informed consent, absence of drug addiction or alcoholism ($p < 0.05$).

Schold JD, et al. [18] showed that advanced age and low financial income were associated with the lowest enrollment on RT waiting list. Sandhu GS et al. in the USA [19] reached the same conclusions; indeed, patients with a fixed professional activity (working full-time) are more likely to be placed on the waiting list (RR 2.24, $p < 0.001$), unlike the unemployed. Only 52 patients (22.61%) in our study had no contraindications. We did not note any correlations between our patients' eligibility for RT and the profession ($p > 0.05$), the potential for financial autonomy ($p = 0.769$) or hyper-immunization ($p = 0.332$). Hemodialysis duration influenced the eligibility for RT in patients with HCV infection ($p = 0.000$), those lacking a target Hg level ($p = 0.019$) and those with absolute contraindications ($p = 0.025$).

Conclusion

RT is the treatment of choice for chronic kidney patients at the dialysis stage. It is not yet practiced in Senegal. In Africa, RT access in 2015 was 0.01-4.9 / million population, except for Egypt having more interesting data with 15.0-24.9 / million inhabitants. Chronic kidney patient's demand for transplantation is frequent regardless of their care center. RT studies in French-speaking Sub-Saharan Africa have focused on the perception of kidney donation and potential donors (Senegal), the RT feasibility (Mali, Mauritania), the demand for renal transplantation in

chronic hemodialysis patients (Côte d'Ivoire) and access to kidney transplant (Chad). To date, in this part of Sub-Saharan Africa, no study has been conducted on chronic hemodialysis patients' eligibility for RT. The demand for RT is a reality expressed by hemodialysis patients; care management should be shared at both the diagnostic and therapeutic level to increase the patient's eligibility for RT. The limitations of this study are the difficulty in establishing a dialogue with certain patients, the absence of certain paraclinical investigations and certain initial undocumented nephropathies

Conflict of Interest

The authors do not declare any conflict of interest.

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