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Hypertension in Renal Transplant Patients: A Prospective Descriptive and Analytical Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The prevalence of hypertension in kidney transplant patients is significant. The physiological circadian evolution of blood pressure (BP) shows a nocturnal decrease of 10 to 20%, called dipping rate. According to this dipping rate, several profiles have been determined, some of which were correlated with the occurrence of cardiovascular events. We set two main objectives for this study: to evaluate the prevalence of hypertension in kidney transplant patients and to determine the dipping rate of hypertensive transplant patients in our series, and its impact on albuminuria. 62 renal transplant patients were included in this study. They underwent 24-hour ambulatory blood pressure measurement (ABPM) with the Suntech AccuWin Pro device in a nephrology department. Arterial hypertension (AH) and dipper status were defined according to the 2018 European Society of Cardiology (ESC) recommendations. A Mann Whitney test assessed the impact of dipper status

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on albuminuria. The prevalence of hypertension was 52% in a population with a median age of 44 years; 67% of patients had albuminuria >30 mg/24 hours. 3% of hypertensive patients were dippers, 42% of patients were nondippers, and 6% of patients were reverse dippers. A correlation between albuminuria and reverse dipper profile was found with a p = 0.044. In renal transplant recipients, arterial hypertension is a major risk factor of graft loss. Blood pressure control in our population is suboptimal, especially in a population where the impact of nocturnal hypertension on markers of renal damage is well documented.

Keywords: Hypertension; kidney transplant; ambulatory blood pressure measurement; albuminuria.

1. INTRODUCTION

Hypertension is a major risk factor for cardiovascular disease, decline in renal function and all-cause mortality in patients with chronic kidney disease (CKD), and its prevalence is increasing in this population [1]. International guidelines consider ambulatory blood pressure measurement (ABPM) as the gold standard for the diagnosis and monitoring of hypertension in CKD patients [2,3]. It can be used to detect masked hypertension (HTNm) and white coat hypertension (HTNwc). It also has a prognostic effect on the occurrence of complications [4,5]. Finally, it allows assessment of variability (dipping), an independent risk factor for cardiovascular events and mortality in CKD patients [6].

Renal transplantation (RT) is the treatment of choice for end-stage chronic kidney disease (ESKD), providing a significant benefit in terms of quality and quantity of life compared with dialysis patients [7], although they still have a higher cardiovascular risk than the general population [8].

Despite the well-established value of ABPM in the diagnosis of hypertension in CKD patients [9,10], descriptive and comparative data on the blood pressure profile of RTs in the moroccan context remain scarce.

The aim of this study is twofold. Firstly, to assess the prevalence of the different blood pressure phenotypes in patients with CKD, and to point out the dipping pattern of hypertension patients.

2. MATERIALS AND METHODS

2.1 Study Design

This was a single-center prospective study conducted in the nephrology, dialysis and transplantation department of the Ibn Rochd University Hospital of Casablanca, from January to June 2022. During the routine consultation, anthropometric data were collected from patient registers. After consent and information of participants, a Suntech Accuwin Pro device was placed on the patient's arm for 24 hours. The device took measurements at 15-minute intervals during the day and every 30 minutes at night.

2.2 Inclusion Criteria

All kidney transplant patients with a graft age between 3 months and 10 years with a glomerular filtration rate (GFR) greater than 30ml/min/1,73m² were included.

2.3 Exclusion Criteria

Patients who have been hospitalized during the last 6 months were excluded. ABPM with less than 85% of measurements taken and missing biological data were also excluded.

2.4 Data Collection

A biological assessment was requested from each selected patient. It included an IDMS standardized creatinine enzyme assay with an estimate of glomerular filtration rate (GFRe) using the CKD-Epi formula, and a measurement of urinary creatinine clearance. A 24-hour urine collection with 24-hour albuminuria, lipid profile (total cholesterol, triglycerides, HDL and LDL cholesterol), glycated hemoglobin and a residual immunosuppression level were also requested.

2.5 Definitions and Classifications

HTN has been defined according to the ESC/ESH 2018 recommendations [11] as follows: BPo ≥ 140/90 mmHg or 24-hour ABPM ≥ 130/80 mmHg or the use of at least one antihypertensive drug. HTNwc was defined by a BPo ≥140/90 mmHg and 24-hour ABPM <130/80 mmHg while HTNm by a BPo < 140/90 mmHg and 24-hour ABPM ≥ 130/80 mmHg.

The dipping rate, expressed as a percentage, is calculated using the formula: (Daytime systolic blood pressure - Night-time systolic blood pressure / Daytime systolic blood pressure) x100. This calculation is used to define four profiles according to the ESH recommendations on the use of ABPM: *Dipper*: when the dipping rate is between 10 and 20%. *Non dipper*: when the dipping rate is between 0 and 10%. *Extreme dipper*: when the dipping rate exceeds 20%. *Reverse dipper*: when it is less than 0%.

Statistical analysis was carried out using STATA 15.1 software. The various biological and anthropometric parameters were compared using the Mann Whitney test to assess their correlation with the different blood pressure profiles.

3. RESULTS

62 patients were included in our study. Anthropometric and biological data are summarized in Tables 1 and 2.

The mean age was 43.6 ± 12 years, and 74% were male. Dialysis vintage before transplantation was 45.9 ± 47.5 months. Causal nephropathy was unknown in 65% of cases.

The mean age of the graft was 64 ± 52 months. Prevalence of hypertension at the time of office visit and ABPM was identical, at 51.61%. A discrepancy between ABPM and BPo was found in 26% of patients. 13% had HTNwc and 13% had HTNm.

Mean BPo was 144 ± 21/90 ± 18 mm Hg. On ABPM, global BP was 128 ± 14/78 ± 9 mmHg, daytime BP 129 ± 14/79 ± 9 mm Hg, nighttime BP 124 ± 16/72 ± 15 mmHg. 49% of individuals were compliant with their antihypertensive treatment.

With regard to dipper status, 80% of hypertensive patients were non-dippers, 13% were reverse dippers and 7% were dippers.

Regarding the analytical study, we found a correlation between albuminuria > 30 mg/24h and the reverse dipper profile. (*P*=.05)

Table 1. Patient characteristics

Patient characteristics	Value
Age (years)	43.6±12
Male (%)	74
Length of time on dialysis (months)	45.9 ± 47.5
Average age of the graft (months)	64 ± 52
Causal nephropathy (%)	
Unknown nephropathy	65
Diabetic nephropathy	23
IgA, Lupus, FSGS	7
Smoking	5
Diabetes mellitus	13
BMI (Kg/m²)	25
Cardiovascular events (%)	6.5
Calcineurin inhibitors (%)	97
Prednisone (%)	100
MMF (%)	100
Patients under anti hypertensive (%)	48
Number of anti hypertensive	1.3

Table 2. Biological data

Biological data	Value
Creatinine (mg/l)	12 ± 2,8
eGFR (ml/min/1,73 m²)	71,5 ± 16,4
Creatinine clearance (ml/min)	82,5 ± 27,5
Microalbuminuria (%)	67
Lipid profile	
LDL cholesterol	1,1 ± 0,3
HDL cholesterol	0,5 ± 0,1
Triglyceride	1,3 ± 0,7
HbA_1C	6,1 ± 1,5

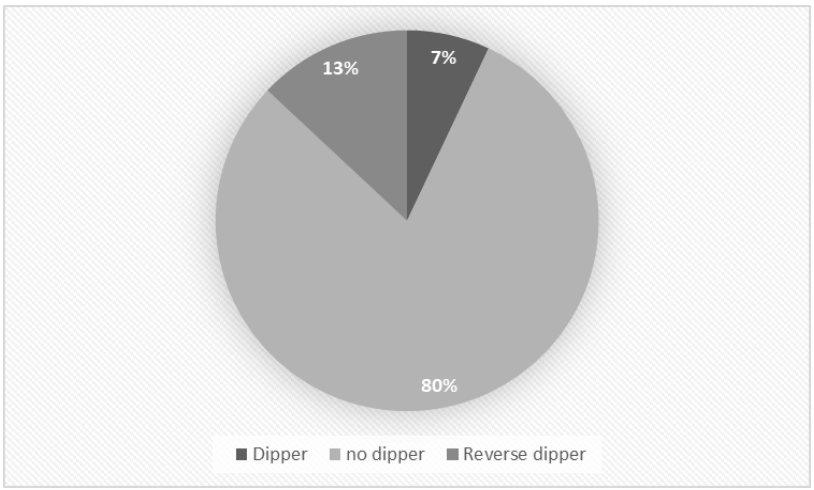

Fig. 1. Different patient dipper status

4. DISCUSSION

Hypertension is a major risk factor of CKD and its progression to end-stage renal disease. It is also a major non-immunological risk factor for graft loss [12].

This study held a threefold significance: First and foremost, it enabled us to assess the prevalence of HTN among patients with resistant HTN under our care, amounting to 51%. Secondly, it facilitated the detection of HTNwc and ruled out HTNm. Indeed, a discrepancy between BPo and ABPM was identified in 26% of patients, with an equal proportion of HTAm and HTNwc. Last but not least, it allowed the evaluation of the variability pattern of blood pressure, notably highlighting a correlation between the reverse dipper profile and the presence of microalbuminuria.

ABPM is increasingly used by nephrologists for the diagnosis of HTN, offering a deeper understanding of HTN's impact on CKD. Our HTN prevalence figures align with literature findings, reporting 60 to 80% HTN prevalence among renal transplant recipients [13].

Previous studies have demonstrated discrepancies between ABPM and BPo, establishing ABPM as superior to BPo in diagnosis, prognosis, prevention of target organ damage, and mortality [5]. Its significance is capital as it aids in detecting untreated HTN, particularly those free from medication. Such HTNm are associated with an increased cardiovascular risk [5]. Lingens et al. [14] found a 37% difference between the two measurement methods in a pediatric population of 27 transplant recipients. Similarly, Ahmed et al. [15] identified a HTNm rate of 58% and 3% HTNwc in an adult population of 98 patients. Kooman et al. [16] reported a HTNwc prevalence similar to our series, as 32% in a population of 36 renal transplant recipients had HTN.

The correlation between the dipping rate of BP and the presence of markers of renal impairment is not surprising. The Ohasama study [17] involving 843 normorenal patients from the general population underwent ABPM and were followed for 8.3 years to detect CKD incidence (positive proteinuria or estimated glomerular filtration rate [eGFR] < 60 ml/min/1.73m²). During follow-up, 220 patients developed CKD. Adjusted hazard ratios for CKD with an increase of one standard deviation in daytime and nighttime systolic BP were 1.13 [95% confidence interval (CI) 0.97–1.30] and 1.21 [95% CI 1.04–1.39], respectively. When nocturnal and diurnal systolic BP were mutually adjusted in the same model, only nocturnal systolic BP emerged as an independent predictor of CKD [17].

ABPM is increasingly used by nephrologists to diagnose HTN, providing a better understanding of the consequences of HTN on CKD. Our figures for the prevalence of hypertension are similar to those found in the literature, with 60 to 80% of hypertension in kidney transplant patients [13].

Previous studies have demonstrated discrepancies between ambulatory BP and office BP, and ABPM is currently considered superior to office BP measurements in terms of diagnosis, prognosis, prevention of target organ damage and mortality (5). Its value is all the greater in

that it can be used to detect undiagnosed hypertension in the practice, and a fortiori untreated hypertension. These hypertensives are associated with an increased cardiovascular risk [5]. Lingens et al. [14] also found a 37% difference between the two measurement methods, in a paediatric population of 27 transplanted children. Similarly, Ahmed et al. [15] found an HTNm rate of 58% and a HTNwc rate of 3% in an adult population of 98 patients. Kooman et al. [16] found a prevalence of hypertension similar to our series, i.e. 32% in a population of 36 kidney transplant patients.

The correlation between BP dipping rate and the presence of markers of renal damage is not surprising. In the Ohasama study [17], 843 patients from the general population without CKD underwent ABPM and were followed for 8.3 years to detect CKD (positive proteinuria or eGFR < 60 mlmin1.73m2). During follow-up, 220 patients developed CKD. The adjusted hazard ratios for CKD in a one standard deviation increase in daytime and nighttime SBP were 1.13 [95% confidence interval (CI) 0.97-1.30] and 1.21 [95% CI 1.04-1.39], respectively. When nighttime and daytime SBP was mutually adjusted into the same model, only nighttime BP was an independent predictor of CKD [17].

The AprODiTe [18] study looked at the blood pressure profile of patients with chronic renal failure. The non-dipper profile was predominant (34.5%), followed respectively by the dipper, reverse dipper and extreme dipper profiles. Reverse dippers had higher proteinuria than the other profiles, which supports the results found in our study. The dipper profile was associated with a reduced risk of mortality. A primary analysis of the ANBP2 clinical trial also found a close correlation between reverse dipper profiles and all-cause mortality, as well as cardiovascular mortality [19].

5. CONCLUSION

Thsi study highlights the prevalence of the different blood pressure phenotypes in patients with CKD, and to point out the dipping pattern of hypertension patients. ABPM is an effective diagnostic and therapeutic tool. It makes a major contribution to the diagnosis of HTNm, and can also be used to label mistakenly treated HTNwc. Hypertension deserves to be studied extensively in kidney transplant patients, given the fact that cardiovascular risk in this population is a cause of graft loss. The therapeutic benefit of ABPM is major in adjusting the type and timing of treatment according to dipper status, but still needs to be supported by clinical trials to assess its effectiveness in controlling blood pressure and improving survival in this population.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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