Hypertension remains a major global public health burden, leading attributed cause of mortality worldwide [1]. Every 20/10-mm Hg increase in blood pressure (BP) is associated with a doubling of cardiovascular mortality [2,3]. Epidemiological studies have shown that awareness of this disease is low, with only half of hypertensives adequately treated to target BP levels [4–6]. Nowadays, out-of-office BP is an important adjuvant method to be associated with conventional office BP measurement, but this last one currently continues to be the most important tool for hypertension screening, diagnosis, and treatment. Office BP was enshrined over time. However, this method has important limitations, which have led to the increasingly frequent suggestion that 24-hour ambulatory blood pressure measurements (ABPM) play an important role in hypertension management [7]. Hypertension is defined as mean systolic BP levels ≥130 mm Hg and/or diastolic BP ≥80 mm Hg in 24-hour ABPM [7].

Sympathetic hyperactivity is well known to increase cardiovascular risk in chronic kidney disease (CKD) patients and is a hallmark of an essential hypertensive state that occurs early in the clinical course of the disease [8–10]. In both conditions, hypertension and kidney failure, the mechanisms of hyperadrenergic state are varied and include reflex and neurohumoral pathways [8,9,11]. In CKD, the sympathetic hyperactivity seems to be expressed at the earliest clinical stage of the disease, showing a direct relationship with the severity of the condition of renal impairment [12–15]. The interruption of sympathetic hyperactivity and feedback of the renin–angiotensin–aldosterone system cycle can at least partly be beneficial for this population. Based on these pathophysiological mechanisms, renal sympathetic denervation (RSD) in CKD and hypertensive patients may ameliorate renal function and blood pressure control. The aim of this prospective study was to compare the magnitude of the effects on renal function and blood pressure control in CKD and non-CKD patients with controlled hypertension (CHT) vs. uncontrolled hypertension (UHT).

We conducted a prospective, longitudinal study of 187 hypertensive subjects, being 60 CKD CHT, 48 CKD UHT, 37 non-CKD CHT, and 42 non-CKD UHT patients. The study was conducted in accordance with the Helsinki Declaration and approved by the local ethics committee. All patients gave written informed consent before inclusion. This study was conducted in the state of Rio de Janeiro, Brazil in the Hospital e Clínica São Gonçalo. Patients were recruited from June 2012 to January 2016 and were derived from the hospital and the public health network of the state county. Patients who had the combination of the following criteria were consecutively enrolled: (i) CHT: mean 24-hour ABPM ≥130/≥80 mm Hg; (ii) UHT: mean 24-hour ABPM ≥130/≥80 mm Hg despite treatment with non-pharmacological measures and use of at least three antihypertensive drugs (including a diuretic) on maximally tolerated doses or confirmed intolerance to medications; (iii) CKD: glomerular filtration rate estimated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation, eGFR [16], >60 mL/min/1.73 m² between 15 and 89 mL/min/1.73 m² (patients with eGFR >60 mL/min/1.73 m² were required to have microalbuminuria); (iv) non-CKD: glomerular filtration rate estimated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation, eGFR [16], >60 mL/min/1.73 m² (without microalbuminuria); (v) age from 18 to 80 years; and (vi) able to read, understand and sign the informed consent form, and attend clinic visits and exams. Patients with any of the following criteria were excluded: (i) pregnancy; (ii) valvular heart disease with significant adverse sequelae; (iii) myocardial infarction, unstable angina, stroke or transient ischemic attack within the previous six months; (iv) renovascular abnormalities; (v) psychiatric disease; (vi) allergy to ionic contrast; (vii) inability to be followed clinically after the procedure; and (viii) serious disease, which in the opinion of the investigator, may adversely affect the safety and/or efficacy of the participant or the study.

The 24-hour ABPM [17] and the renal sympathetic denervation are previously described [18] by our group.

The results were expressed as the mean and standard deviation (mean ± SD) of the mean in the case of normal distribution and as...
Table 1
General features of patients at baseline.

| Parameters                  | CKD CHT | CKD UHT | Non-CKD CHT | Non-CKD UHT | Overall P-value |
|-----------------------------|---------|---------|-------------|-------------|-----------------|
| n                           | 60      | 48      | 37          | 42          |                 |
| Age, years                  | 54.2 ± 11.3 | 57.5 ± 10.2 | 59.4 ± 15.7 | 61.0 ± 16.5 | 0.0657          |
| Body mass index, kg/m²      | 28.5 ± 6.3 | 26.8 ± 5.4 | 28.0 ± 6.4  | 27.3 ± 5.1  | 0.4672          |
| Male sex (%)                | 45 (72%) | 31 (65%) | 22 (59%)    | 28 (67%)    | 0.6561          |
| White ethnicity (%)         | 46 (77%) | 30 (63%) | 20 (54%)    | 30 (71%)    | 0.1033          |
| Atrial fibrillation (%)     | 22 (37%) | 14 (29%) | 14 (38%)    | 17 (40%)    | 0.7945          |
| Hypertension (%)            | 60 (100%)| 48 (100%)| 37 (100%)   | 42 (100%)   | 1.0000          |
| Type 2 diabetes mellitus (%)| 35 (58%) | 22 (46%) | 16 (43%)    | 21 (50%)    | 0.5328          |
| Hyperlipidemia (%)          | 40 (67%) | 30 (63%) | 24 (65%)    | 31 (74%)    | 0.4958          |
| Chronic kidney disease (%)  | 60 (100%)| 48 (100%)| 0 (0%)      | 0 (0%)      |                 |
| Creatinine, mg/dL           | 1.04 ± 0.32| 0.0017  | 0.86 ± 0.24 | 0.0002      | 0.5812          |
| eGFR, mL/min/1.73 m² (CKD-EPI)| 58.7 ± 24.8 | 55.7 ± 33.0 | 93.0 ± 10.0 | 82.1 ± 14.6 | <0.0001         |
| Albumin:creatinine ratio, mg/g| 88.2 ± 33.5 | 97.5 ± 30.6 | 14.5 ± 6.4  | 12.2 ± 6.5  | <0.0001         |

Values are expressed as Mean ± SD; ABPM, ambulatory blood pressure measurements; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CHT, controlled hypertension; DHP, dihydropyridine; eGFR, estimated glomerular filtration rate; RSD, renal sympathetic denervation; UHT, uncontrolled hypertension. Creatinine: *P < 0.05 for CKD CHT vs. non-CKD CHT, CKD CHT vs. non-CKD UHT, CKD UHT vs. non-CKD CHT, and CKD UHT vs. non-CKD UHT; eGFR and albumin:creatinine ratio: **P < 0.0001 for CKD CHT vs. non-CKD CHT, CKD CHT vs. non-CKD UHT, CKD UHT vs. non-CKD CHT, and CKD UHT vs. non-CKD UHT. CKD stages: †comparison between only CKD CHT and CKD UHT; Mean 24-hour ABPM: †P < 0.0001 for all comparisons, except for CKD CHT vs. non-CKD CHT.

Table 2
Parameters at 6th month after renal sympathetic denervation.

| Variable                  | CKD CHT 6th month | P-value CKD CHT vs. non-CKD CHT | CKD UHT 6th month | P-value CKD UHT vs. non-CKD UHT | Non-CKD CHT 6th month | P-value Non-CKD CHT vs. non-CKD UHT | Non-CKD UHT 6th month | P-value Non-CKD UHT vs. non-CKD CHT |
|---------------------------|-------------------|---------------------------------|------------------|---------------------------------|----------------------|-----------------------------------|----------------------|-----------------------------------|
| Mean 24-hour ABPM, mm Hg  |                   |                                 |                  |                                 |                      |                                   |                      |                                   |
| Systolic                  | 123.5 ± 6.2       | <0.0001                         | 158.6 ± 9.6      | <0.0001                         | 122.0 ± 4.3          | <0.0001                          | 143.4 ± 8.0          | <0.0001                          |
| Diastolic                 | 74.0 ± 4.7        | <0.0001                         | 110.6 ± 6.5      | <0.0001                         | 73.6 ± 5.4           | <0.0001                          | 102.3 ± 4.4          | <0.0001                          |

Values are presented as mean ± SD; ABPM, ambulatory blood pressure measurements; ACR, albumin:creatinine ratio; CKD, chronic kidney disease; CHT, controlled hypertension; eGFR, estimated glomerular filtration rate; UHT, uncontrolled hypertension.

Table 3
Variation (Δ) between groups at 6th month after renal sympathetic denervation.

| Comparisons                | CKD CHT vs. CKD UHT | CKD CHT vs. non-CKD CHT | CKD CHT vs. non-CKD UHT | Non-CKD CHT vs. non-CKD UHT | Non-CKD CHT vs. non-CKD CHT |
|----------------------------|---------------------|------------------------|--------------------------|-----------------------------|-----------------------------|
| Mean 24-hour ABPM, mm Hg   |                     |                        |                          |                             |                             |
| Systolic                   | −12.5               | <0.0001                | 0.2                      | 0.9995                      | −0.6                        | 0.9857                      | 12.7                  | −0.0001                         | 11.9                  | <0.0001                         | −0.8                  | 0.9763                         |
| Diastolic                  | −10.8               | <0.0001                | 1.5                      | 0.7971                      | −9.9                        | <0.0001                      | 12.3                  | −0.0001                         | 0.9                  | 0.5484                         | −11.4                 | <0.0001                         |
| Creatinine, mg/dL          | 0.18                | 0.006                 | 0.12                     | 0.0979                      | 0.08                        | 0.3784                      | −0.06                 | 0.6857                         | 0.10                  | 0.2273                         | −0.04                 | 0.8906                         |
| eGFR, mL/min/1.73 m² (CKD-EPI) | −13              | <0.0001               | −10.8                    | 0.0088                      | −4.1                        | 0.4709                      | 2.2                   | 0.8911                         | 8.9                  | 0.0164                         | 6.7                   | 0.1531                         |
| Albumin, mg/g              | 14                  | 0.0022                | 34.1                     | <0.0001                     | 36.6                        | <0.0001                     | 20.1                  | <0.0001                         | 22.6                  | <0.0001                         | 2.5                   | 0.5935                         |

Values are presented as variation (Δ) between means; ABPM, ambulatory blood pressure measurements; ACR, albumin:creatinine ratio; CKD, chronic kidney disease; CHT, controlled hypertension; eGFR, estimated glomerular filtration rate; UHT, uncontrolled hypertension.
The general features of the 187 hypertensive patients, divided into 60 CKD CHT, 48 CKD UHT, 37 non-CKD CHT, and 42 non-CKD UHT individuals are listed in Table 1. During the six months of follow-up, the changes in mean 24-hour ABPM, serum creatinine, eGFR and ACR are displayed in Table 2. The variation (Δ) between all the comparisons at the 6th month post RSD for all groups related to the parameters aforementioned and their respective P values are displayed in Table 3.

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Conflict of interest

None declared.

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