Introduction

Chronic kidney disease (CKD) is defined as having an abnormal kidney structure or function for three months or longer, which can be aggravated by the progression of disease and lead to irreversible kidney failure. It is a growing public health problem, with increasing morbidity and mortality in Brazil and worldwide. Cardiovascular disease (CVD) is commonly associated with CKD. These diseases have a significant impact on life expectancy. Individuals with CKD are more likely to die from CVD than to progress to end-stage renal disease. An important maker of this association is glomerular filtration rate (GFR), since GFR reduces the percentage of mortality and cardiovascular events increase. The main cause of kidney disease is diabetic nephropathy and hypertensive nephrosclerosis, both accelerated by smoking and dyslipidemia; thus, the higher risk of CVD among CKD patients is secondary to accumulation of risk factors. In addition, increased waist circumference (WC) and overweight further increases this risk, as these factors are associated with a greater likelihood of cardiovascular events.
In addition to anthropometric measurements, it is important to check some biochemical parameters, such as the lipid profile, uric acid levels, glycosylated hemoglobin (HbA1C) and blood glucose values, to prevent the progression of CKD and the risk of developing CVD.12

The Framingham Risk Score is a tool widely used for calculation of cardiovascular risk and estimation of the risk of developing CVD in ten years. It has been applied for risk stratification, making it possible to target specific groups of patients who will benefit from drug therapy as a form of primary intervention in CVD prevention.13,14

The aim of this study was to assess cardiovascular risk factors in patients with CKD under conservative treatment in a secondary care hospital.

Methods

This was an observational, cross-sectional study on the cardiovascular risk factors in CKD patients under conservative treatment. The inclusion criteria were patients with stages 3, 4 or 5 CKD, aged over 20 years, attending (i.e., not the first consultation) a secondary care center for chronic diseases in Juiz de Fora, Brazil. The exclusion criteria were presence of metabolic diseases, such as cancer, AIDS, chronic obstructive pulmonary disease, among others; amputation of a limb; use of a wheelchair; and use of a pacemaker.

For sample calculation, the population covered by the service (805,722), the prevalence of CKD stages 3 to 5 (10.6%), confidence limits of 5% and confidence interval of 95% were considered, yielding a sample of 146 individuals. This sample was calculated using the Epi Info software. Considering a loss of 15%, we chose to evaluate at least 169 individuals.

Socioeconomic data were collected through questionnaires, and nutritional status were evaluated by anthropometric measurements, bioelectrical impedance analysis, and biochemical tests. For physical activity level, those who reported at least 150 minutes of physical activity weekly were considered as physically active.17

Height was measured using a portable stadiometer, and weight was measured using a Tanita BC-553 Ironman® body composition monitor. Then, body mass index (BMI) was calculated and classified according to the World Health Organization (WHO)9 criteria for adults and the elderly.18

Body fat percentage (BF%) was measured using the Fresenius Medical Care body composition monitor, and classified according to Lohman and Champaign, 1992.19

WC was measured as the smallest circumference between the lowest rib and the iliac crest and classified according to the WHO criteria.9 Hip circumference was measured at the widest area of the hips at the greatest protuberance of the buttocks; the waist-hip ratio (WHR) was then calculated and classified according to the WHO.9

Regarding biochemical tests, fasting glycemia, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG), uric acid and HbA1C were evaluated, which were classified according to the reference values.20 For this, patients were asked to bring, on the day of the anthropometric assessment, the last tests performed within the last 90 days.

Blood pressure was measured using the auscultatory method, with an aneroid sphygmomanometer, properly calibrated. The values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were classified according to the 7th Brazilian Guideline for Hypertension.21

Glomerular filtration rate (GFR) was estimated by the CKD-EPI formula,22 and classified according to the KDIGO (2012) guidelines.1

The Framingham score was used to estimate the cardiovascular risk; the sum of scores was performed based on the variables: sex, age, smoking, diabetes mellitus, HDL-c, TC, SBP, DBP and then classified as low, medium and high risk of developing cardiovascular disease in the next ten years.23

Statistical analysis

First, an exploratory analysis was carried out to verify the integrity (coherence) of the data. Quantitative variables were analyzed for the presence of outliers and the Kolmogorov-Smirnov test was used to verify the normality of data distribution.

Descriptive analysis of the sample was carried out by sex. Continuous variables were expressed as mean ± standard deviation and compared using the unpaired Student’s t-test. The categorical variables, on the other hand, were described as absolute and relative frequencies, and compared, by sex and the Framingham score classification, using the Pearson’s chi-square test.
The SPSS version 20.0 software was used, and the level of significance adopted was 5%.

The study was approved by the research ethics committee of Juiz de Fora Federal University Teaching Hospital (submission number: 1.147.858).

**Results**

The sample consisted of 172 participants (57% male), with mean age of 68.85 ± 11.41 years, 80.2% were elderly.

Table 1 shows the general characteristics of the sample, including age, GFR, and anthropometric, biochemical and blood pressure data stratified by sex. Mean values of BMI, BF%, HDL-c, LDL-c and TC were higher in women, whereas WHR was higher in men. In both sexes, high mean values (above recommendations) were found for BMI, uric acid, fasting glucose and HbA1C for diabetics. Mean values of lipid parameters were within or close to the reference values for both sexes, as well as fasting blood glucose, HbA1C for non-diabetics, and SBP and DBP values.

The frequency of cardiovascular risk factors by sex is shown in Table 2. The frequency of diabetes mellitus (DM) and arterial hypertension was high in both men and women, and 50% of patients had both diseases. Most patients (51.5%) had CKD stage 3B, and most participants were physically inactive (62.2%). Smoking habit was more prevalent in males (15.3%) than in females (2.7%).

### Table 1 – General characteristics of chronic kidney disease patients under conservative treatment stratified by sex, Juiz de Fora, Brazil

| Characteristics                      | Female       | Male         | p1       |
|--------------------------------------|--------------|--------------|----------|
| Age (years)                          | 67.88 ± 12.84| 69.59 ± 10.20| 0.347    |
| GFR (ml/min/1.73m²)                  | 32.64±11.42  | 34.60±11.58  | 0.271    |
| BMI (kg/m²) Adults <60 years         | 31.33±7.12   | 30.57±6.59   | 0.756    |
| BMI (kg/m²) Adults ≥60 years         | 29.85±5.16   | 27.78±4.89   | 0.019    |
| Waist circumference (cm)             | 95.84±12.90  | 99.01±12.95  | 0.113    |
| WHR                                  | 0.90±0.07    | 0.96±0.08    | <0.001   |
| BF%                                  | 41.01±9.79   | 30.92±9.27   | <0.001   |
| Uric acid (mg/dL)                    | 7.85±5.33    | 7.22±1.54    | 0.363    |
| HDL-c (mg/dL)                        | 50.30±18.02  | 42.24±12.14  | 0.003    |
| LDL-c (mg/dL)                        | 109.61±45.83 | 91.13±31.47  | 0.008    |
| Total Cholesterol (mg/dL)            | 195.61±55.97 | 169.76±42.03 | 0.003    |
| Triglycerides (mg/dL)                | 179.63±104.11| 176.4±98.32  | 0.867    |
| Fasting Glucose Diabetics (mg/dL)    | 147.55±89.48 | 138.78±61.00 | 0.592    |
| Fasting Glucose Non-diabetics (mg/dL)| 102.31±28.95 | 98.81±15.32  | 0.527    |
| HbA1c Diabetics (%)                  | 7.67±1.77    | 7.80±1.97    | 0.753    |
| HbA1c Non-diabetics (%)              | 5.82±1.09    | 5.88±1.57    | 0.894    |
| SBP Hypertensive (mmHg)              | 135.06±20.34 | 136.81±24.39 | 0.642    |
| DBP Hypertensive (mmHg)              | 136.87±17.10 | 133.57±11.50 | 0.593    |
| SBP Non-hypertensive                 | 76.70±14.30  | 76.50±12.31  | 0.925    |
| DBP Non-hypertensive                 | 78.75±6.40   | 78.57±10.27  | 0.965    |

GFR: glomerular filtration rate; BMI: body mass index; WHR: waist-hip ratio; BF: body fat; HDL-c: high-density lipoprotein; LDL-c: low-density lipoprotein; HbA1c: glycated hemoglobin; SBP: systolic blood pressure; DBP: diastolic blood pressure

* Student’s t-test
| Variable                        | Female n(%) | Male n (%) | Total      | p value<sup>c</sup> |
|--------------------------------|-------------|------------|------------|---------------------|
| **Sample**                     |             |            |            |                     |
| < 60 years                     | 20 (27.0)   | 14 (14.3)  | 34 (19.8)  | 0.052               |
| ≥ 60 years                     | 54 (73.0)   | 84 (85.7)  | 138 (80.2) |                     |
| **Physical activity**          |             |            |            | 1.000               |
| > 150 minutes/week             | 28 (37.8)   | 37 (37.8)  | 65 (37.8)  |                     |
| < 150 minutes/week             | 46 (62.2)   | 61 (62.2)  | 107 (62.2) |                     |
| **Smoking**                    |             |            |            | 0.008               |
| Yes                            | 2 (2.7)     | 15 (15.3)  | 17 (9.9)   |                     |
| No                             | 72 (97.3)   | 83 (84.7)  | 155 (90.1) |                     |
| **Use of alcohol**             |             |            |            |                     |
| Yes                            | 6 (8.1)     | 16 (16.3)  | 22 (12.8)  | 0.166               |
| No                             | 68 (91.9)   | 82 (83.7)  | 150 (87.2) |                     |
| **SAH**                        |             |            |            | 0.646               |
| Present                        | 66 (89.2)   | 84 (85.7)  | 150 (87.2) |                     |
| Absent                         | 8 (10.8)    | 14 (14.3)  | 22 (12.8)  |                     |
| **DM**                         |             |            |            | 0.646               |
| Present                        | 38 (51.4)   | 54 (55.1)  | 92 (53.5)  |                     |
| Absent                         | 36 (48.6)   | 44 (44.9)  | 80 (46.5)  |                     |
| **SAH and DM**                 |             |            |            | 0.878               |
| Present                        | 36 (48.6)   | 50 (51.0)  | 86 (50.0)  |                     |
| Absent                         | 38 (51.4)   | 48 (49.0)  | 86 (50.0)  |                     |
| **CKD Stage**                  |             |            |            |                     |
| 3A                             | 9 (12.2)    | 17 (17.5)  | 26 (15.2)  |                     |
| 3B                             | 39 (52.7)   | 49 (50.5)  | 88 (51.5)  | 0.788               |
| 4                              | 21 (28.4)   | 26 (26.8)  | 47 (27.5)  |                     |
| 5                              | 5 (6.8)     | 5 (5.2)    | 10 (5.8)   |                     |
| **BMI Adults (Kg/m²)**         |             |            |            |                     |
| < 25                           | 3 (15.0)    | 3 (21.4)   | 6 (17.6)   | 0.672               |
| ≥25                            | 17 (85.0)   | 11 (78.6)  | 28 (82.4)  |                     |
| **BMI Elderly (Kg/m²)**        |             |            |            | 0.074               |
| < 27                           | 16 (29.6)   | 38 (45.8)  | 54 (39.4)  |                     |
| ≥27                            | 38 (70.4)   | 45 (54.2)  | 83 (60.6)  |                     |
| **WC (cm)**                    |             |            |            | < 0.001             |
| ♀ < 80; ♂ < 94                 | 6 (8.1)     | 35 (35.7)  | 41 (23.8)  |                     |
| ♀ ≥ 80; ♂ ≥ 94                 | 68 (91.9)   | 63 (64.3)  | 131 (76.2) |                     |
| **WHR (cm)**                   |             |            |            | < 0.001             |
| ♀ < 0.85; ♂ < 1.0              | 12 (16.2)   | 59 (60.2)  | 71 (41.3)  |                     |
| ♀ ≥ 0.85; ♂ ≥ 1.0              | 62 (83.8)   | 39 (39.8)  | 101 (58.7) |                     |
| ♀ < 27; ♂ < 17                 | 6 (8.1)     | 7 (7.3)    | 13 (7.6)   | 1.000               |
| ♀ ≥ 27; ♂ ≥ 17                 | 68 (91.9)   | 89 (92.7)  | 157 (92.4) |                     |
| **Body fat (%)**               |             |            |            |                     |
| ♀ < 27; ♂ < 17                 | 6 (8.1)     | 7 (7.3)    | 13 (7.6)   |                     |
| ♀ ≥ 27; ♂ ≥ 17                 | 68 (91.9)   | 89 (92.7)  | 157 (92.4) |                     |
| **Uric Acid (mg/dL)**          |             |            |            | 0.056               |
| ♀ < 6; ♂ < 7                   | 14 (18.9)   | 32 (32.7)  | 46 (26.7)  |                     |
| ♀ ≥ 6; ♂ ≥ 7                   | 60 (81.1)   | 66 (67.3)  | 126 (73.3) |                     |
| > 60                           | 43 (58.1)   | 43 (43.9)  | 86 (50.0)  | 0.090               |
| <40                            | 31 (41.9)   | 55 (56.1)  | 86 (50.0)  |                     |
| **LDL-c (mg/dL)**              |             |            |            | 0.129               |
| <160                           | 66 (89.2)   | 94 (95.9)  | 160 (93)   |                     |
| ≥160                           | 8 (10.8)    | 4 (4.1)    | 12 (7.0)   |                     |
Regarding the BMI classification, 82.4% of all the sample and 60.6% of the elderly were overweight. Elevated WC and WHR were highly prevalent among women (91.9% and 83.8%, respectively), and significantly higher than men (64.3% and 39.8%, respectively). Furthermore, a high BF% was found in 92.4% of the sample.

As for the risk of CVD, according to the Framingham score, 43% of the sample was at low risk, followed by 35.5% at medium risk and 21.5% at high risk of developing CVD in ten years.

The factors associated with cardiovascular risk, according to the Framingham score are shown in Table 3. It was verified that individuals with an income above the minimum wage and adults with a high BMI had a higher risk of developing CVD.

**Discussion**

The main cause of death in patients in stage 1 CKD is CVD, and the associated risks include traditional ones, such as old age, male gender, arterial hypertension, elevated LDL-c, reduced HDL-c, DM, smoking, sedentary lifestyle, and non-traditional ones such as decreased GRF, anemia, type of CKD, among others. Most of the sample was composed of male adults, older than 60 years. This finding can be justified by the fact that older adults are at relatively higher risk for developing CKD, due to physiological decrease in GFR and kidney injury secondary to aging and associated chronic disease, such as DM and hypertension. Moreover, according to Bregman, male sex is a non-modifiable risk factor for the progress of CKD.

Low income and low education, as observed in our study group (median per capita income of R$880.00 and incomplete elementary school in 66.3% of participants), are determining factors for the occurrence of CKD and must be analyzed for screening and monitoring of the disease.

In our study, the patients with CKD had a high prevalence of arterial hypertension (87.2%) and DM (53.5%), and 50% of them had both diseases concomitantly, which is a risk factor for CVD. Similar findings were
reported in a survey conducted by Pinho et al.,28 in a general medical clinic in São Paulo, in which 75.2% of CKD patients were hypertensive and 49.5% diabetic.

Our population (both hypertensive and non-hypertensive individuals) had high mean SBP and DBP values according to the reference values. This is a positive finding, since the control of hypertension is relevant to delay the progression of CKD and possibly the development of CVD.

Regarding smoking habit, it was more prevalent among men than women, as reported in a study carried out in São Paulo, Brazil, in which 36.4% of men were smokers. Smoking is one of the most important factors for acute myocardial infarction.29

The high prevalence of physical inactivity (62.2%) is worrying, since physical inactivity, added to other traditional cardiovascular risk factors, promotes accelerated atherosclerosis and early mortality.30 A high prevalence of physical inactivity (74%) was also identified in patients with CKD under conservative treatment by Fortes et al.31

Overweight in patients with CKD can increase renal plasma flow and intraglomerular pressure, which, in turn, increases cardiac output.31,32 Increased central adiposity demarcated by high WHR is associated with metabolic complications.9 In the present study, there was a prevalence of overweight of 82.4% in adults (<60 years old)

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### Table 3- Factors associated with cardiovascular risk, according to the Framingham score

| Variable                          | Framingham score classification | p value<sup>+</sup> |
|-----------------------------------|---------------------------------|--------------------|
|                                  | Low n (%) | Medium n (%) | High n (%) |
| Sample                           |           |              |            |
| Adults < 60 years old            | 14 (41.2) | 13 (38.2)   | 7 (20.6)   | 0.931     |
| Adults ≥ 60 years old            | 60 (43.5) | 48 (34.8)   | 30 (21.7)  |           |
| Income                           |           |              |            |
| Less than minimum wage           | 50 (47.6) | 40 (38.1)   | 15 (14.3)  | 0.015     |
| More than minimum wage           | 24 (35.8) | 21 (31.3)   | 22 (32.8)  |           |
| Education                        |           |              |            |
| Complete elementary school       | 17 (39.5) | 14 (32.6)   | 12 (27.9)  | 0.444     |
| Incomplete elementary school     | 57 (44.5) | 47 (36.7)   | 24 (18.8)  |           |
| Physical activity                |           |              |            |
| Yes (> 150 minutes/week)         | 27 (41.5) | 20 (30.8)   | 18 (27.7)  | 0.278     |
| No (< 150 minutes/week)          | 47 (43.9) | 41 (38.3)   | 19 (17.8)  |           |
| CKD stages                       |           |              |            |
| 3 A                              | 11 (42.3) | 9 (34.6)    | 6 (23.1)   |           |
| 3 B                              | 39 (44.3) | 32 (36.4)   | 17 (19.3)  | 0.990     |
| 4                                | 19 (40.4) | 17 (36.2)   | 11 (23.4)  |           |
| 5                                | 4 (40.0)  | 3 (30.0)    | 3 (30.0)   |           |
| BMI Adults < 60 years old (Kg/m²) |          |              |            |
| Appropriate                      | 5 (83.3)  | 0 (0.0)     | 1 (16.7)   | 0.050     |
| High                             | 9 (32.1)  | 13 (46.4)   | 6 (21.4)   |           |
| BMI Adults ≥ 60 years old (Kg/m²) |          |              |            |
| Appropriate                      | 26 (48.1) | 15 (27.8)   | 13 (24.1)  | 0.353     |
| High                             | 34 (41.0) | 33 (39.8)   | 16 (19.3)  |           |
| WC (cm)                          |           |              |            |
| ♀ < 80; ♂ < 94                   | 24 (58.5) | 10 (24.4)   | 7 (17.1)   | 0.068     |
| ♀ ≥ 80; ♂ ≥ 94                   | 50 (38.2) | 51 (38.9)   | 30 (22.9)  |           |
| WHR                              |           |              |            |
| ♀ < 0.85; ♂ < 1.0                | 37 (52.1) | 19 (26.8)   | 15 (21.1)  | 0.086     |
| ♀ ≥ 0.85; ♂ ≥ 1.0                | 37 (36.6) | 42 (41.6)   | 22 (21.8)  |           |
| BF (%)                           |           |              |            |
| ♀ < 27; ♂ < 17                   | 6 (8.1)   | 2 (3.3)     | 5 (14.3)   | 0.146     |
| ♀ ≥27; ♂ ≥17                     | 68 (91.9) | 59 (96.7)   | 30 (85.7)  |           |

<sup>CKD: chronic kidney disease; BMI: body mass index; WC: waist circumference; WHR: waist-hip ratio; BF: body fat; € Pearson’s Chi-square test.</sup>
and of 60.6% in the elderly (60 years old), and WHR values were higher in females, in agreement with a study carried out in Brusque, a city in Santa Catarina State, Brazil.23

BMI was high in both sexes and in all age groups and correlated with cardiovascular complications. However, BMI is considered a controversial marker, since it does not discriminate between the different components of the body (lean and fat mass) and does not describe the fat distribution (visceral fat and subcutaneous fat).6 For this reason, the use of WC is recommended, which has been suggested as a direct predictor of all-cause mortality from CVD.7 High values of WC was found in most patients (76.2%), with higher prevalence in women than men (p<0.001), similar to previously reported data.34

Alarming prevalence of increased BF% was found in men (92.7%) and women (91.9%). This fact draws attention, since excess body fat is associated with cardiovascular risk factors, such as metabolic syndrome, DM, hypertension, hypercholesterolemia and atherosclerosis.34

Dyslipidemia is common in CKD and its presence can contribute to increase cardiovascular risk,28 since elevated TG and reduced HDL-c are independent predictors of cardiometabolic episodes36. Regarding elevated LDL-c, data from the National Health and Nutrition Examination Survey (NHANES 1999-2006) demonstrated a 46% prevalence of this lipid alteration in adults with stages 1-2 CKD and 80% with CKD stages 3 and 4.37 Despite these findings, in the present study, the values of serum lipid parameters were within or close to the recommended values, similar to the results found in the study by Fortes et al.31

Regarding uric acid levels, these were above the recommended levels. It is known that hyperuricemia is highly prevalent in CKD; however, it is still unclear whether uric acid is merely a marker of comorbidities and kidney damage or whether it is a factor for cardiovascular outcomes.38 According to a cohort study by Wan-Chun Liu, which evaluated 3,749 patients with stages 3-5 CKD for three years, hyperuricemia is a risk factor for cardiovascular events in these patients.

The values found for fasting blood glucose and HbA1C were higher than recommended. According to Hage,4 the lack of glycemic control is associated with the progression of CKD and cardiovascular mortality. To prevent these outcomes, it is recommended to keep HbA1C at levels below 7.0% and postprandial glycemia below 140mg/dL for diabetics, and from 3.6 to 5.3% and less than 100mg/dL for non-diabetics.

In relation to GFR, it was shown that for each decrease of 10mL/min/1.73m in the GFR, there is a 10% increase in the relative risk of death or non-fatal cardiovascular complication.39 In the present study, patients were mostly in stage 3B, indicating that they should continue with nutritional monitoring and undergo treatment to prevent the progress to CKD stage 5 or even develop cardiovascular complications.

Regarding the 10-year cardiovascular risk estimated using the Framingham score, 43% of the sample was at low risk, 35.5% at medium risk and 21.5% at high risk. These results are similar to those reported by Cesarino.30 These findings can be used by health professionals to improve treatment adherence and develop strategies to the reduce risk and morbidity and mortality of CVD.

A limitation of the study is the fact that it is a cross-sectional study, which makes it impossible to infer that patients at cardiovascular risk will in fact develop CVD. However, despite its limitations, the relevance of the study lies in its originality and importance of the theme.

Assessing cardiovascular risk factors in patients with CKD is of paramount importance, since this condition is commonly comitant with many factors associated with an increased risk of cardiovascular diseases, such as older age, comorbidities like DM and hypertension, and overweight. Thus, a multidisciplinary approach is needed, to assist in the prevention and control of cardiovascular mortality in this population. since Adherence to healthy eating patterns is a protective factor for renal function, helping to prevent the development of chronic diseases, thereby improving the prognosis and favoring a better quality of life.

Conclusions

There was a high prevalence of cardiovascular risk factors in the population studied, such as physical inactivity, presence of comorbidities (hypertension and DM), increased BMI, WC, WHR and BF%, and elevated uric acid and high HbA1C levels. Nevertheless, 57% of the sample were at medium or high risk of developing CVD in 10 years, according to the Framingham score. Individuals with a per capita income above the minimum wage and high BMI had a higher 10-year risk of developing CVD.

Assessing cardiovascular risk factors in patients with CKD is important and allows guiding the conduct of health professionals to prevent mortality from cardiovascular causes.
Author contributions

Conception and design of the research: Pereira PML, Bastos MG, Candido APC. Acquisition of data: Oliveira CFM, Pereira PML, Soares IT, Monteiro MG. Analysis and interpretation of the data: Oliveira CFM, Pereira PML, Soares IT, Candido APC. Statistical analysis: Oliveira CFM, Pereira PML, Candido APC. Writing of the manuscript: Oliveira CFM, Pereira PML. Critical revision of the manuscript for intellectual content: Pereira PML, Soares IT, Monteiro MG, Bastos MG, Candido APC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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