Applied nutritional investigation

Waist-to-height ratio: An accurate anthropometric index of abdominal adiposity and a predictor of high HOMA-IR values in nondialyzed chronic kidney disease patients

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Abstract

Objective: Chronic kidney disease (CKD) is associated with metabolic disorders, including insulin resistance (IR), mainly when associated with obesity and characterized by high abdominal adiposity (AbAd). Anthropometric measures are recommended for assessing AbAd in clinical settings, but their accuracies need to be evaluated. The aim of this study was to evaluate the precision of different anthropometric measures of AbAd in patients with CKD. We also sought to determine the AbAd association with high homeostasis model assessment index of insulin resistance (HOMA-IR) values and the cutoff point for AbAd index to predict high HOMA-IR values.

Methods: A subset of clinically stable nondialyzed patients with CKD followed at a multidisciplinary outpatient clinic was enrolled in this cross-sectional study. The accuracy of the following anthropometric indices: waist circumference, waist-to-hip ratio, conicity index and waist-to-height ratio (WheiR) to assess AbAd, was evaluated using trunk fat, by dual x-ray absorptiometry (DXA), as a reference method. HOMA-IR was estimated to stratify patients in high and low HOMA-IR groups. The total area under the receiver-operating characteristic curves (AUC-ROC; sensitivity/specificity) was calculated: AbAd with high HOMA-IR values (95% confidence interval [CI]).

Results: We studied 134 patients (55% males; 54% overweight/obese, body mass index ≥ 25 kg/m², age 64.9 ± 12.5 y, estimated glomerular filtration rate 29.0 ± 12.7 mL/min). Among studied AbAd indices, WheiR was the only one to show correlation with DXA trunk fat after adjusting for confounders (P < 0.0001). Thus, WheiR was used to evaluate the association between AbAd with HOMA-IR values (r = 0.47; P < 0.0001). The cutoff point for WheiR as a predictor for high HOMA-IR values was 0.55 (AUC-ROC = 0.69 ± 0.05; 95% CI, 0.60–0.77; sensitivity/specificity, 68.9/61.9).

Conclusions: WheiR is recommended as an effective and precise anthropometric index to assess AbAd and to predict high HOMA-IR values in nondialyzed patients with CKD.

Introduction

The increasing prevalence of overweight and obesity is reaching global epidemic status [1]. Considerable evidence supports the role of obesity and abdominal fat depots in the pathogenesis and development of metabolic disorders and risk factors for chronic diseases [2,3]. Abdominal adiposity (AbAd) is now recognized as a better predictor of cardiovascular disease (CVD) risk than global adiposity [4,5]. Moreover, AbAd is itself a determinant of altered insulin sensitivity and insulin resistance (IR), which in turn is a condition associated with hypertension and dyslipidemia, and has been considered an
independent predictor of CVD in the general population [3,6–8]. Additionally, high total and central adiposity are related to an increased prevalence of diabetes mellitus, hypertension, and CVD [2,3,9], which are directly correlated to chronic kidney disease (CKD) [10,11].

CKD is a public health problem in the general population [12], and in early stages is associated with metabolic and clinical disorders including IR, dyslipidemia, and coronary heart disease. Patients with mild to moderate CKD are likely to present IR [13], which leads to nutritional, metabolic, and cardiovascular complications [14]. IR is recognized as a risk factor for CVD in nondialyzed patients with CKD [15–17].

Recent studies report that overweight and obesity are the most common nutritional conditions in nondialyzed patients with CKD that contribute to the high prevalence of IR and CVD [18–21]. Considering that CKD and obesity are associated with increased risk for CVD, it is feasible to hypothesize that when occurring together they may worsen the prognosis. Therefore, the early recognition of modifiable risk factors associated with CVD, such as AbAd and IR, may improve CKD prognosis and treatment approach [22,23].

The evaluation of body adiposity and AbAd deports counts with many useful methods. Among reliable and sophisticated methods are hydrostatic weighing, dual-energy x-ray absorptiometry (DXA), computed tomography, and magnetic resonance imaging. However, such methods are complex, time-consuming, and costly, hindering their use in clinical settings [24,25]. Alternative methods to overcome these barriers, based on anthropometric measures, are recommended, but their accuracies need to be evaluated. Waist circumference (WC) and waist-to-hip ratio (WHR) are the most commonly used anthropometric methods to assess AbAd in individuals and groups, showing high correlation with more sophisticated methods [26,27]. In patients with CKD, the evaluation of the accuracy of AbAd indexes are limited and mostly performed in dialysis settings [28–30]. More recently, the ratio between waist and height (Wheir) has been demonstrated as a better index associated with CKD compared with body mass index (BMI) [31].

The ability of BMI, WC, WHR, and Wheir to determine major CVD risk factors has largely been based on receiver-operating characteristic (ROC) curve analysis [32,33]. Wheir is strongly associated with different CVD risk factors in population-based studies conducted in China [34], Taiwan [35], and Brazil [36]. These studies identified the best cutoff points for Wheir as a discriminator for high coronary risk, suggesting its use in population studies. To our knowledge, there has been no report to date attempting to identify the most appropriate cutoff point of these indices of AbAd with discriminant capability for IR in nondialyzed patients with CKD. Therefore, studies focusing on this topic might improve evaluation of AbAd and might help to apply more effective therapeutic strategies to reduce obesity–associated morbidity and mortality in these patients.

Objectives

The aim of this study was to evaluate the correlation between anthropometric parameters, used in clinical settings to estimate AbAd, with trunk fat mass estimated by DXA, as reference method in nondialyzed patients with CKD. As a secondary objective, we determined the association between AbAd with homeostasis model assessment index of insulin resistance (HOMA-IR), glucose, and triglycerides (TG) values and the cutoff point for AbAd to predict high HOMA-IR values in these patients.

Methods and procedures

Study design and population selection

This is an observational, cross-sectional study. Clinically stable nondialyzed patients with CKD, older than age 18 y, with an estimated glomerular filtration rate (eGFR) < 60 ml/min, were enrolled between August 2008 and July 2010. Exclusion criteria included the presence of apparent edema, active malignant diseases, acute inflammation, and use of immunosuppressive drugs. The nutritional recommendations for all patients followed the international guidelines for CKD treatment [10,37]. These included protein (0.6–0.8 g/kg daily) and energy (25–35 kcal/kg daily) intake, according to the nutritional status, and also counseling to restrict the food rich in trans-fats and saturated fatty acids, sodium, and phosphorus. All patients were under regular treatment at the CKD multidisciplinary outpatient clinic at the university hospital by a renal dietitian. The nephrologist and dietitian carefully reviewed the patient medical records to determine the patients’ dietary intake. Informed consent was obtained from each patient prior to the procedures.

Of 350 patients being followed per year by the renal dietitian at the outpatient clinic, 134 met the inclusion criteria. The CKD baseline diseases were hypertension (55%), diabetes mellitus (10%), other causes (23%), and unknown etiology (10%). Treatment for hypertension included angiotensin-converting enzyme (76%), angiotensin receptor blockers (13%), β-blockers (34%), calcium channel blockers (36%), and diuretics (17%). Treatment for diabetes included metformin (84%) and insulin (16%). The protocol was approved by the ethical human research committee of the university hospital, and all patients gave written consent before entering in the study.

Protocol and data collection

Demographic, clinical/labatorial, anthropometric, and nutritional data were collected on a different day from that of the routine. Patients were advised to fast for 12 h before the assessment day and to wear light weight clothing. Anthropometric measurements were performed on the same day by two experienced renal dietitians, whereas the DXA procedure was performed by a trained technician.

Anthropometric measurements

Anthropometric measurements included body weight, height, tricep skinfold thickness (SKF), and circumferences (waist, hip, and arm). Body weight was measured to the nearest 0.1 kg with a balance-beam scale and height was measured with patients standing erect with their head in the Frankfort plane and recorded to the nearest 0.5 cm. These measures were used to determine BMI (kg/m²), and patients were classified according to BMI range intervals proposed by the World Health Organization [38] as normal BMI range between 18.5 and 25 kg/m² and overweight/obese as ≥ 25 kg/m².

SKF was measured on the left side of the body or the opposite side to the arteriovenous fistula, using a Lange skinfold caliper (Cambridge Instrument, Cambridge, MA, USA), according to standard techniques [25]. Circumferences were measured using a flexible plastic tape with a graduated scale. The mean of the three determinations was recorded. Arm circumference was measured after marking the halfway point between the acromion of the scapula and the olecranon of the ulna, with the patient standing and the arm relaxed and flexed 90 degrees [39]. The tape surrounded the arm at the midpoint and was adjusted to avoid compression of the skin. Midarm muscle circumference (MAMC, in cm) was calculated using the formula: arm circumference – (0.134 × triceps SKF [mm]). Standard midarm muscle circumferences (MAMC) were obtained using the National Health and Nutrition Examination Survey percentile distribution tables adapted previously [39], as recommended by the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative Nutrition Guidelines [37].

WC was measured at the umbilical level and hip circumference was measured over nonrestrictive underwear, lightweight pants, or skirts, at the level of the maximum extension of the buttocks posteriorly in a horizontal plane [40]. Abdominal adiposity was evaluated by WC (cm), WHR (WC; cm/hip circumference; cm), conicity index (Conicity = WC; m/0.109 × square root of weight; kg/height; m), by Wheir [WC; cm/height; cm], a novel index recently proposed to evaluate AbAd in CKD patients and associated with CKD prevalence [31].

Nutritional status and adiposity

Nutritional status was determined according to the criteria proposed by the International Society of Renal Nutrition and Metabolism (ISRN) [41]. These criteria recommend that at least three of the four categories [serum albumin < 3.8 g/100 ml; low body weight [BMI = 18.5 kg/m²] or low total body fat as a percentage of body weight; < 10%; muscle mass [MAMC < 90% of the 50th percentile]] low energy intake [< 25 kcal/kg daily] or low protein intake [< 0.6g/kg daily]) must be satisfied for protein–energy wasting diagnosis.

Food intake was evaluated by 3-d food records. Nutritional intake was calculated using a software program (NUTWIN; São Paulo-Brazil) containing the
nutrient database of the U.S. Department of Agriculture tables [42] and Brazilian food. Energy and protein intake were normalized by the desirable body weight as proposed by the ISRNM [41].

Total body fat mass percentage was determined by DXA. The percentage of adequacy for total body fat was accepted according to reference values previously reported [40]. The DXA was performed using a Lunar DPX Bone Densitometer scanner (Lunar Radiation, Madison, WI, USA) with the patient in the supine position. A rectilinear scan over the length of the body, beginning at the top of the patient’s head and moving downward toward the feet, was performed. The system allows scanning up to 205 lines and during the scan, the source shutter opens to emit an x-ray beam. Software calculates the grams of fat tissue, total and trunk fat mass percentage, grams of lean tissue and grams of bone mineral mass. The trunk fat mass percentage evaluated by DXA in this study was used as the reference method for AbAd evaluation, which also was assessed by the anthropometric parameters: WC, WHR, ConIndex, and WheiR.

Laboratorial parameters

Laboratory analysis was performed at the university hospital laboratories. Patients underwent blood sampling early in the morning, after overnight fasting to measure creatinine, urea, total cholesterol, potassium, phosphorus, and albumin. The eGFR was estimated by the CKD-EPI equation [30]. Fasting plasma glucose and insulin values were used for HOMA-IR estimation, which was calculated as follows: HOMA-IR = fasting insulin (μU/mL) x fasting plasma glucose (mmol/L)/22.5 [43]. Serum insulin levels were analyzed by human insulin-specific radioimmunoassay kit (Millipore, Billerica, MA, USA).

Statistical analyses

The results are expressed as mean ± SD. Comparison of continuous variables between men and women was performed by unpaired Student’s t test for normally distributed values, and skewed variables were log10 transformed to normalize. The Pearson’s correlation coefficient was performed to analyze the degree of association between two variables: trunk fat percentage by DXA with AbAd assessed by WC, WHR, ConIndex, and WheiR measurements; DXA trunk fat and WheiR with HOMA-IR, fasting glucose, and TG. The partial correlation coefficient was analyzed between these variables, after adjusting for sex, age, eGFR and BMI, as confounding factors. HOMA-IR median value of the whole group (1.3; 95% confidence interval [CI], 1.1–1.4) was used to stratify patients into two groups: HOMA-IR < 1.3 was defined as the high HOMA-IR group and ≥1.3 was the low HOMA-IR group. The logistic regression was performed using the International Diabetes Federation (IDF) cutoff points for WC [44] and WheiR cutoff points proposed in the present study to analyze the relationship between high AbAd (as independent variable) with high HOMA-IR values (as dependent variable). The cutoff points for the AbAd were determined by ROC curve analysis. The ROC curves are a graphical representation of the sensitivity (vertical axis) and specificity (horizontal axis) for various cutoff points that allow for identifying the best cutoff of a specific measure to predict an outcome. The total area under ROC curve analysis was used to determine the ROC cutoff points for WC. The ROC cutoff points for the AbAd were determined by ROC curve analysis. The ROC curves are a graphical representation of the sensitivity (vertical axis) and specificity (horizontal axis) for various cutoff points that allow for identifying the best cutoff of a specific measure to predict an outcome. The total area under the ROC curve (AUC-ROC) and confidence intervals also were determined. The resulting interpretations determined that the larger the AUC-ROC, the greater the discrimination power of the AbAd method to predict high HOMA-IR values. The lower limit of the confidence interval should not reach 0.50. All statistical analysis was performed with statistical package STATA/SE version 8.2 (Stata Corporation, College Station, TX, USA). Statistical significance was considered when P < 0.05.

Results

One hundred and thirty-four patients with CKD (55% men) were under regular treatment with nephrologists for 4.9 ± 3.2 y and with dietitians for 3.3 ± 2.0 y, respectively. Mean age was 64.9 ± 12.5 y and eGFR was 29.0 ± 12.7 ml/min. CKD stage distribution was as follows: 10.4% (n = 14) in stage 3a (eGFR = 50.05 ± 4.1), 35.8% (n = 48) in stage 3b (eGFR = 37.6 ± 4.08 ml/min), 35.8% (n = 48) in stage 4 (eGFR = 22.6 ± 4.4 ml/min), and 17.9% (n = 24) in stage 5 (eGFR = 11.7 ± 2.4 ml/min). Laboratory parameters were within the range proposed for this population, reflecting an adequate clinical control (Table 1). There were no malnourished patients, according to ISRNM criteria. On the other hand, according to BMI class, 54% (n = 72) presented overweight/obesity (Table 1) and 46% (n = 62) showed normal BMI values. The high HOMA-IR group (n = 66; 49.3%), as expected, showed HOMA-IR median value greater (1.77; 95% CI, 1.6–1.9) than the low

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<th>Table 1</th>
<th>Laboratory and nutritional parameters in nondialed patients with CKD</th>
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<tr>
<td><strong>Laboratory parameters</strong></td>
<td><strong>All (N = 134)</strong></td>
</tr>
<tr>
<td>eGFR (ml/min)</td>
<td>29.0 ± 12.7</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>82.5 ± 40.5</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.2 ± 1.4</td>
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<tr>
<td>Phosphorus (mg/dL)</td>
<td>3.9 ± 0.9</td>
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<tr>
<td>Potassium (mEq/L)</td>
<td>4.8 ± 0.6</td>
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<tr>
<td>Glucose (mg/dL)</td>
<td>97.0 ± 19.0</td>
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<tr>
<td>Triglycerides (mg/dL)</td>
<td>136.7 ± 67.1</td>
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<tr>
<td>Total cholesterol (mg/dL)</td>
<td>186.3 ± 42.2</td>
</tr>
<tr>
<td><strong>HOMA-IR</strong></td>
<td>1.47 ± 0.8</td>
</tr>
<tr>
<td><strong>Nutritional parameters</strong></td>
<td><strong>BMI (kg/m²)</strong></td>
</tr>
<tr>
<td></td>
<td>25.9 ± 4.4</td>
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BMI, body mass index; CKD, chronic kidney disease; DXA, dual x-ray absorptiometry; eGFR, estimated glomerular filtration rate; HOMA-IR, homeostasis model assessment of insulin resistance; MAMC adequacy (%), midarm muscle circumference adequacy expressed in % of the 50th percentile; TEI, total energy intake

HOMA-IR group (n = 68; 50.7%; 0.9; 95% CI, 0.8–1.0; P < 0.0001). Mean BMI, WheiR, and ConIndex values were not different between men and women. The WC and WHR mean values were higher in men than in women. Total body fat and trunk fat determined by DXA were higher in women than in men (Table 2).

The correlation between DXA trunk fat and AbAd, assessed by WheiR, was higher than the correlations between DXA trunk fat and WC, ConIndex, and WHR (Table 3). After adjusting for sex, age, and eGFR, DXA trunk fat correlation with WheiR was maintained. On the other hand, after adjusting for the same confounders, the correlation analysis between DXA trunk fat and WC, ConIndex, and WHR was altered. It is worth noting that the correlation between DXA trunk fat and AbAd assessed by WheiR was the only anthropometric index that remained significant even after adjusting for BMI, age, and eGFR (Table 3). Furthermore, the correlations between WheiR and sex (r = 0.10), as well as between ConIndex and sex (r = −0.15) were not significant (P > 0.05), whereas WC (r = −0.22) and WHR (r = −0.31) were significantly (P < 0.01) correlated with sex.

AbAd assessed by WheiR showed the most precise correlation with DXA trunk fat (considered the reference method). Thus, the association between AbAd and HOMA-IR was analyzed using this anthropometric index. The correlation coefficients between DXA trunk fat with HOMA-IR, serum glucose, and TG levels were

<table>
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<th>Table 2</th>
<th>Total and abdominal adiposity in nondialed patients with CKD (N = 134)</th>
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<tr>
<td><strong>Body adiposity Parameters</strong></td>
<td><strong>Men (n = 74; 56%)</strong></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.8 ± 4.1</td>
</tr>
<tr>
<td>Total body fat by DXA (%)</td>
<td>29.4 ± 6.4</td>
</tr>
<tr>
<td>Trunk fat by DXA (%)</td>
<td>33.5 ± 8.7</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>92.5 ± 10.9</td>
</tr>
<tr>
<td>WHR</td>
<td>0.97 ± 0.07</td>
</tr>
<tr>
<td>ConIndex</td>
<td>1.3 ± 0.07</td>
</tr>
<tr>
<td>WheiR</td>
<td>0.56 ± 0.07</td>
</tr>
</tbody>
</table>

BMI, body mass index; CKD, chronic kidney disease; ConIndex, concity index; DXA, dual x-ray absorptiometry; WC, waist circumference; WheiR, waist to height ratio; WHR, waist-to-hip ratio

1. Men versus women: t test; statistical significance: 1 P < 0.001 1 P < 0.0001.
similar to that observed between WheiR and these same parameters (Fig. 1).

Although WheiR was the best anthropometric index to assess AbAd and to predict high HOMA-IR values in the treatment of nondialyzed patients with CKD, the WheiR cutoff point for the outcome of high HOMA-IR was determined as 0.55. The related AUC-ROC curve, for all studied patients was 0.69 (95% CI, 0.60–0.77; *P* = 0.0001) (Fig. 2).

Among patients with WheiR ≥ 0.55 (n = 74), 64% presented high HOMA-IR values, whereas among those with WC above the IDF cutoff point (n = 86), 58% showed high HOMA-IR values. The adjusted odds ratio for high HOMA-IR values was 4.6 (95% CI, 2.0–10.6; *P* = 0.0002) in patients with high WheiR and 3.5 (95% CI, 1.5–8.6; *P* = 0.003) in patients with high WC.

 Patients with WheiR values < 0.55 (low AbAd group) showed lower values for nutritional and metabolic parameters than those in the high AbAd group (WheiR ≥ 0.55) (Table 4).

**Discussion**

In the present study, the precision of different anthropometric measures of AbAd was evaluated in nondialyzed patients...
with CKD, using DXA trunk fat depots as a reference method. The efficacy of AbAd indexes for predicting high HOMA-IR values also was determined.

The studied patients showed no protein–energy malnutrition; on the other hand, overweight/obesity was the prevalent condition, similar to the obesity epidemic worldwide, observed also in Brazil and Asian countries [45,46]. High body adiposity is associated with the development of chronic diseases [2,3,12,47] and AbAd is considered more specific in determining risk for the morbidities associated with obesity than total body fat [3,6]. In fact, high AbAd is suggested as the main focus for metabolic disorders in the general population [48], and is associated with progressive resistance to insulin, ultimately favoring hypertension, dyslipidemia, diabetes, and CVD, all of which are linked to CKD [7,8,47].

The precision of anthropometric measures for assessing abdominal fat depots and predicting risk for metabolic disorders has been the subject of some studies, most of which were conducted with healthy Caucasian individuals and which only evaluated WC and WHR [49–52]. So far, simple and inexpensive anthropometric measures, such as WC and its derivative indexes, have not been studied in nondialyzed CKD patients. A cross-sectional study conducted in Brazil showed poor correlation between WC and these parameters. The excessive AbAd is related to the deposition of fat in the viscera, which is strongly linked to cardiovascular risk factors [3,26,53].

The use of WC or WHR for assessing CVD risk factors is recommended; however, there is no consensus on which of them shows the most consistent association and predictive power [54]. The currently recommended thresholds for WC were defined based on Caucasians and it seems that different cutoff points are required for different ethnicities [26]. A large case–control prevalence study found that the WHR was associated with myocardial infarction in both men and women [4].

The present data showed that the best WheiR cutoff point for the outcome of high HOMA-IR value was 0.55 cm. The related AUC-ROC for all studied patients was 0.69 ± 0.05 (95% CI, 0.60–0.77; P = 0.0001; Fig. 2). The larger the AUC-ROC, the greater the discriminatory power of the indicator AbAd for the outcome (IR). The greater the AUC, the greater the discriminatory power of them for high HOMA-IR values. The confidence interval determines whether the predictive capacity of the indicator AbAd is not due to chance. The inferior limit of the confidence interval should not be <0.50 [55]. A population-based study conducted with Brazilian adults considered WheiR as a discriminator of abdominal obesity and elevated coronary risk [55], considering the best cutoff point for this purpose as 0.52 for men and 0.53 for women. Similar WheiR values often are used in Asians to evaluate AbAd [35]. The sensitivity and specificity observed in these studies were similar to our results [35,36,55]. Furthermore, the prevalence of the patients in the higher HOMA-IR group was greater when the WheiR cutoff point proposed in the present study was used than when the WC cutoff points proposed by IDF [2006] [44] reinforces our recommendation for the use of WheiR as an AbAd index.

To the best of our knowledge, this study is the first to investigate the accuracy of the most widely used anthropometric indices to assess AbAd, in nondialyzed patients with CKD. WheiR was considered the most effective index to assess AbAd, independent of BMI, was significantly correlated with DXA trunk fat,
even after adjustment for sex, age, and eGFR, and also showed no differences between sexes. This is an easy or low-cost alternative parameter for evaluating AbAd in clinical routine. WheiR also was positively associated with HOMA-IR value independent of confounding factors. Therefore, the WheiR cutoff point for estimating high HOMA-IR values was proposed as WheiR 0.55.

Conclusion

In conclusion, the present results show consistent evidence for the use of WheiR as an index for evaluating AbAd, in nondiabetic patients with CKD because of its particularly strong correlation with DXA trunk fat, independent of BMI and with no differences between men and women. The cutoff value for WheiR ≥ 0.55 was identified as a substantial predictor of high HOMA-IR values.

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References


