

# The correlation of neck circumference and insulin resistance in NAFLD patients

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**ABSTRACT – Background** – Insulin resistance, especially that induced by obesity, plays a central role in the development of non-alcoholic fatty liver disease. Although the evaluation of overweight patients is important, the nutritional assessment tools used in clinical practice have limitations. Neck circumference (NC), from this, becomes a viable and low-cost alternative, which seems to be related to the accumulation of fat in the hepatic tissue. **Objective** – To evaluate the association between NC and metabolic alterations in patients with non-alcoholic fatty liver disease. **Methods** – A cross-sectional study performed in 82 patients, of whom 76 underwent liver biopsy. We performed weight, height, abdominal circumference and NC measures. Values of NC  $\geq 42$  cm and  $\geq 36$  cm were considered as altered for men and women, respectively. Laboratory tests and liver biopsy result were collected in the participants' charts. We evaluated fasting blood glucose levels, insulin, glycosylated hemoglobin, triglycerides, total cholesterol, high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), ferritin, alkaline phosphatase, gamma glutamyltransferase, albumin, total bilirubin, direct bilirubin, glutamic-oxalacetic transaminase, glutamic-pyruvic transaminase and the HOMA-IR index. **Results** – We evaluated eighty-two patients. Patients with altered NC had increased body mass index ( $P=0.043$ ), abdominal circumference ( $P=0.007$ ), insulin ( $P=0.003$ ) and HOMA-IR ( $P=0.029$ ) when compared to those with adequate NC. NC was significantly correlated with reduced levels of high-density cholesterol (HDL-C) in men ( $r=-0.42$ ,  $P<0.05$ ), increased insulin levels in men and female ( $rs=0.47$ ;  $P<0.05$  and  $rs=0.51$ ;  $P<0.01$ , respectively), as well as higher HOMA-IR index both males ( $rs=0.49$ ;  $P<0.01$ ) and female ( $rs=0.30$ ;  $P<0.05$ ). There was no significant association between NC and liver outcomes ( $r=0.145$ ;  $P=0.36$ ). **Conclusion** – NC is associated with the HOMA-IR index in patients with non-alcoholic fatty liver disease. NC can be used in the screening of insulin resistance in these patients, considering that insulin resistance plays a key role in the progression of the disease.

**HEADINGS** – Abdominal fat. Insulin resistance. Non-alcoholic fatty liver disease. Nutritional and metabolic diseases. Overweight.

## INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) corresponds to the accumulation of more than 5% of fat in the hepatocyte in the absence of secondary causes such as excessive alcohol consumption and other liver diseases such as viral hepatitis, autoimmune disease, and metabolic and hereditary diseases affecting the liver<sup>(1)</sup>. The hepatic alteration of NAFLD presents a broad spectrum, occurring since the condition of hepatic steatosis to non-alcoholic steatohepatitis, liver cirrhosis and hepatocellular carcinoma<sup>(2)</sup>.

The prevalence of NAFLD is increasing at approximately the same rate as obesity<sup>(3)</sup>. The prevalence of NAFLD in general population has been estimated to be 25% whereas the global prevalence of non-alcoholic steatohepatitis (NASH) has been estimated to range from 3% to 5%<sup>(4-6)</sup>. The prevalence of NAFLD (based on ultrasound) for South America has been estimated at approximately 30.45%<sup>(6)</sup>, most studies reporting the prevalence were performed in Brazil<sup>(7)</sup>.

Considering the close relationship between NAFLD and overweight, the importance of tracking and evaluating this group of patients is evident. Although the nutritional evaluation of these in-

dividuals is fundamental, the conventionally used methods present limitations, being difficult to gauge body circumferences and skin folds; in addition, the efficacy of these methods is compromised by excess of adipose tissue.

In this context, neck circumference (NC) consists of a rapid, viable and low cost evaluation. The use of NC as an anthropometric indicator not influenced by variations in certain health conditions, that cause abdominal distension, for example, or by respiratory movements, reinforces the use of this measure as an indicator that provides consistent results to predict the deposition of subcutaneous fat<sup>(8)</sup> in the upper region of the body, and with the liver fat deposit, consequently, with NAFLD<sup>(8,9)</sup>.

Clinical practice demands criteria of easy applicability and reliability, making evaluation feasible to be reproduced. The main aim of our study was to evaluate the association between NC and metabolic alterations in patients with NAFLD. Were evaluated presence, absence, degree and activity of steatosis, steatohepatitis and fibrosis according to the outcome of liver biopsy and differences regarding biochemical and anthropometric variables in patients with adequate and altered NC.

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## METHODS

### Population and design

This is a cross-sectional study of 82 adult patients (older than 18 years) – of both sexes and race independent – with a diagnosis of NAFLD established through liver biopsy. The patients studied were accompanied in two outpatient clinics of a large hospital and in a clinic for the treatment of obesity, both located in the city of Porto Alegre, Rio Grande do Sul State, Brazil.

### Clinical data collection and anthropometric evaluation

Data collection occurred between May 2015 and December 2016. Through the review of medical records, information was collected regarding the clinical characteristics (sex and age), laboratory tests and the results of each patient's liver biopsy. The anthropometric evaluation was performed by trained and qualified nutritionists and included weight and height measurements for the calculation of body mass index (BMI), abdominal circumference (AC) and NC. To measure the weight, the subject was asked to stand and be barefoot in the center of the base of a calibrated digital scale Digipeso® (Digipeso S/A, Brazil), with capacity of up to 300 kg, wearing light clothes. The height was measured with the help of a stadiometer, the subject standing erect, barefoot, with the heels together and the arms extended at the side of the body. For the calculation of BMI, the following formula was used: weight (kg) / height (m)<sup>2</sup>.

The circumferences of the abdomen and neck were performed through an anthropometric tape, and the reading was performed and recorded in centimeters. The AC was measured with the patient standing in the narrowest part of the trunk, under the umbilical scar and at the end of a normal expiration. The circumference of the neck, in turn, was performed below the prominence of the larynx and perpendicular to the long axis of the neck, with the tape positioned at the same height at the front and at the back of the neck. The individual was asked to remain in an upright position, with proper posture and looking forward. The determination of the reference values for NC to be classified as adequate ( $\leq 42$  cm for men and  $\leq 36$  cm for women) and as altered ( $\geq 42$  cm for men and  $\geq 36$  cm for women) were based on the Lucas study<sup>(10)</sup> and collaborators.

In relation to the biochemical tests, results were obtained for: fasting glycemia, glycosylated hemoglobin, triglycerides, total cholesterol, high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), ferritin, alkaline phosphatase, gamma glutamyltransferase, albumin, total bilirubin, direct bilirubin, glutamic-oxalacetic transaminase, glutamic-pyruvic transaminase and insulin. For the classification of biochemical tests, the same cut-off points for men and women were used in all exams, except: ferritin (considered adequate when less than 322 ng/mL and 291 ng/mL in men and women, respectively) and gamma glutamyltransferase (considered appropriate when less than 73U/L and 38U/L in men and women, respectively). Insulin resistance was determined on the basis of the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index, calculated according to the formula: fasting insulin ( $\mu\text{U L}$ ) x fasting blood glucose (nmol/L) / 22.5. The methodology used for the analysis and interpretation of the results was defined according to the routine and protocol of the Hospital in which the scientific research was conducted. The glycosylated hemoglobin test was performed using the capillary electrophoresis technique through Capillarys 2 flex piercing device (Sebia). Insulin and ferritin were determined

based on chemiluminescence methodology using Architect i1000 (Abbott) and Centaur XPT (Siemens) equipment, respectively. Fasting glycemia, triglycerides, total cholesterol, HDL-C, established on the basis of Friedewald's formula, LDL-C, alkaline phosphatase, gamma glutamyltransferase, albumin, total and direct bilirubin, glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase were determined using the Advia 1800 equipment (Siemens).

As for the hepatic biopsy, patients were classified into the following groups: presence or absence of steatosis (mild, moderate, marked), presence or absence of steatohepatitis (mild, moderate, marked) or presence of fibrosis (classified as mild – 1A, 1B, 1C and 2 and accentuated – 3 and 4).

### Statistical analysis

In the statistical analysis, the quantitative variables were described by mean and standard deviation or median and interquartile range. Categorical variables were described by absolute and relative frequencies. To compare means, the t-student test was applied. In case of asymmetry, the Mann-Whitney test was used. In the comparison of proportions, Pearson's chi-square or Fisher's exact tests were applied. To evaluate the association between continuous variables, the Pearson correlation (symmetric distribution) or Spearman (asymmetric distribution) tests were used. The significance level adopted was 5% ( $P \leq 0.05$ ) and the analyzes were performed in the Statistical Package for the Social Sciences (SPSS) program, version 21.0.

### Approval on the Research Ethics Committee

This study is part of a project approved by the Research Ethics Committee of the *Irmandade Santa Casa de Misericórdia de Porto Alegre* and by the Committee of *Universidade Federal de Ciências da Saúde de Porto Alegre*, under the number 745.415. The evaluated patients agreed to participate in the study by signing the Informed Consent Term.

## RESULTS

We evaluated 82 patients, 55 (67%) of whom were women, and the mean age of the sample was  $41.7 \pm 13$  years. The mean body mass index was  $40.1 \pm 6.7$  kg/m<sup>2</sup>. There was a significant difference in the NC ( $P < 0.001$ ) between men and women. TABLE 1 shows the characteristics of the sample regarding sex distribution, mean age, anthropometric variables and severity of liver disease. For the classification of liver disease severity, the biopsy results of 76 patients were used, since 6 patients had no liver biopsy result available for consultation or did not undergo the examination. As for the severity of the liver disease, 49 (64.4%) patients presented progression of the disease to fibrosis.

Regarding the biochemical variables analyzed, there was a significant difference regarding the levels of HDL-C ( $P = 0.022$ ) and ferritin ( $P < 0.001$ ) between men and women. While 19.1% of the women had HDL-C above 60 mg/dL, no male individual had HDL-C value higher than the reference. Increased levels of ferritin ( $> 322$  ng/mL) were identified in 80% of males, while only 8.7% of female ferritin levels were above baseline ( $> 291$  ng/mL). Differences between men and women were also observed for glutamic oxalacetic transaminase levels ( $P = 0.046$ ) and glutamic pyruvic transaminase ( $P = 0.014$ ). Among males, 38.5% and 40% presented increased glutamic pyruvic transaminase and glutamic oxalacetic transaminase, respectively, compared to 10.9% and 15.6% in women.

**TABLE 1** Characterization of the studied sample regarding sex, age, anthropometry (body mass index, neck and abdominal circumference) and liver outcome according to liver biopsy.

Variables	Total	Men	Female	P value
<b>Gender – n (%)</b>	<b>82 (100)</b>	<b>27 (32)</b>	<b>55 (67)</b>	
Age (years) – mean and SD	41.7±13	42.2±12.5	41.5±13.5	0.829
BMI (kg/m <sup>2</sup> ) – mean and SD	40.1±6.7	38.8±6.6	40.8±6.8	0.204
NC (cm) – mean and SD	41.7±4.66	46.5±3.7	39.4±3.0	<0.001
AC (cm) – mean and SD	119.1±13.2	123.9±14.3	116.8±12.2	0.022
Absence of steatosis	02 (2.6)	0 (0)	02 (100)	
Exclusive steatosis (without NASH)	22 (28.9)	05 (22.7)	17 (77.2)	
Exclusive NASH (withouth fibrosis)	03 (3.9)	01 (33.3)	02 (66.6)	
NASH with progression to fibrosis	49 (64.4)	18 (36.7)	31 (63.2)	

SD: standard deviation; BMI: body mass index; NC: neck circumference; AC: abdominal circumference; NASH: non-alcoholic steatohepatitis.

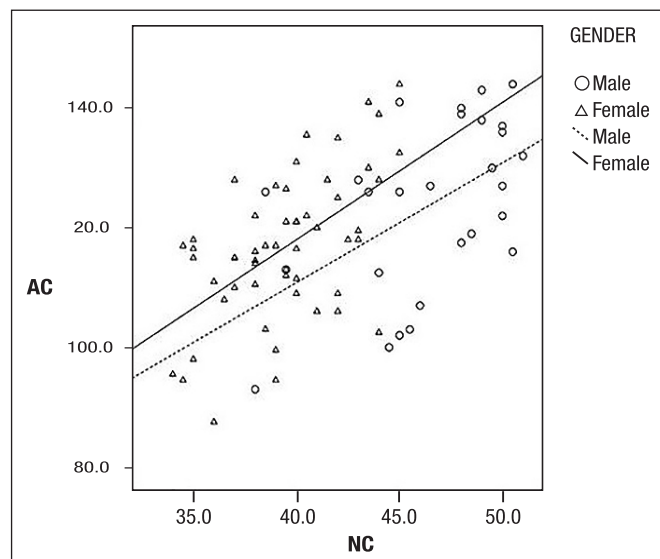
As can be seen in TABLE 2, there was no significant difference in the age of patients with adequate and altered neck circumference. Regarding the anthropometric evaluations, a significant difference was observed between the groups of patients with adequate NC and altered in relation to BMI, AC and HOMA-IR index.

**TABLE 2** Anthropometry and biochemical evaluation according to the circumference of the neck.

	NC Adequate 11 (13.4%)	NC Altered 71 (86.6%)	P value	Reference value
Age (years)	46.9±17.1	40.9±12.3	0.288	
Men – n (%)	3 (27.3)	24 (33.8)	1.000	
BMI (Kg/m <sup>2</sup> )	36.3±8.1	40.7±6.4	0.043	
AC (cm)	108.7±12.1	120.6±12.9	0.007	
Blood glucose (mg/dL)*	91 (87–127)	97 (87–119)	0.796	< 99
HbA1C (%)	5.35±0.40	5.79±0.75	0.250	< 7
TAG (mg/dL)*	132 (118–178)	149 (121–234)	0.302	< 150
TC (mg/dL)	191.1±38.9	194.9±36.5	0.749	< 200
HDL-C (mg/dL)	51.1±11.3	46.6±12.7	0.278	> 60
LDL-C (mg/dL)	106.4±34.5	116.3±34.8	0.456	< 130
Ferritin (ng/mL)*	105.9 (56.3–382.8)	171 (79.8–414.5)	0.390	Men <322 and Women <291
AF (U/L)*	93.5 (75.5–102.5)	78 (64–91)	0.162	< 130
GGT (U/L)*	32 (23–56)	35 (25–56)	0.076	Men <73 and Women <38
Albumine (g/dL)*	4.4±0.38	4.32±0.30	0.433	> 3.5
TB (mg/dL)*	0.60 (0.35–0.71)	0.50 (0.40–0.78)	0.841	< 1.2
DB (mg/dL)*	0.20 (0.10–0.26)	0.20 (0.10–0.30)	0.985	< 0.2
GOT (U/L)*	22 (20–31)	27 (21–35)	0.216	< 34
GPT (U/L)*	28 (21–38)	34 (21.5–47.5)	0.263	< 49
Insuline (µU/mL)*	12.9 (7.3–20.5)	23 (16.9–33.3)	0.003	< 25
HOMA-IR	3.38 (2.41–4.18)	6.79 (4.18–9.33)	0.029	

\* Values described in median (P25–P75). NC: neck circumference; BMI: body mass index; AC: abdominal circumference; HbA1C: glycosylated hemoglobin; TAG: triglycerides; TC: total cholesterol; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; AF: alkaline phosphatase; GGT: gammaglutamyltransferase; TB: total bilirubin; DB: direct bilirubin; GOT: glutamic oxalacetic transaminase; GPT: glutamic pyruvic transaminase.

In patients with adequate NC, the mean BMI was 36.3±8.1 kg/m<sup>2</sup>, whereas in the group of patients who presented altered NC, it was 40.7±6.4 kg/m<sup>2</sup> (P=0.043). Comparing the mean AC of the two analyzed groups, patients with altered NC had mean AC of 120.6±12.9 cm, being significantly higher (P=0.007) than patients with adequate NC, whose mean AC found was 108.7±12.1 cm. FIGURE 1 shows the relationship between AC and NC in both sexes in the studied sample (r=0.65, P<0.01).



**FIGURE 1.** Relationship between abdominal circumference (AC) and neck circumference (NC), in centimeters. (r=0.65, P<0.01).

Comparing the HOMA-IR index of patients with altered and adequate NC, it is observed that patients with altered NC presented higher insulin resistance (6.79) when compared to patients with lower NC (3.38), being  $P=0.029$ .

Regarding the biochemical variables, only insulin levels differed significantly between groups of patients with adequate and altered NC ( $P=0.003$ ). In the group of patients with adequate NC, the median relative to insulin levels was  $12.9 \mu\text{U/mL}$  ( $7.3\text{--}20.5 \mu\text{U/mL}$ ) compared to the group of patients with altered NC, whose median was  $23 \mu\text{U/mL}$  ( $16.9\text{--}33.3 \mu\text{U/mL}$ ). There was a correlation between the HOMA-IR index and the NC, and this correlation was positive, in which the higher the NC, the higher the insulin resistance ( $r=0.48$ ,  $P<0.01$ ).

Correlating the NC with biochemical variables, as shown in TABLE 3, it was identified an association between NC and a reduction in HDL-C levels only in males ( $r= -0.42$ ;  $P<0.05$ ) and a correlation with increased levels of insulin in both men ( $r=0.47$ ,  $P<0.05$ ) and women ( $r=0.51$ ,  $P<0.01$ ).

The severity of hepatic disease, categorized according to the degree of hepatic impairment assessed in liver biopsy, did not correlate with NC ( $r=0.14$ ,  $P=0.360$ ), but correlated with HOMA-IR ( $r=0.39$ ;  $P=0.006$ ).

TABLE 3 Correlation between neck circumference and biochemical tests.

Biochemical variables	NC Men	NC Female
Fasting glycemia	-0.37	0.15
HbA1C	-0.25	0.32
TAG	0.15	0.19
TC	0.11	-0.12
HDL-C	-0.42*	-0.05
LDL-C	0.22	-0.18
Ferritine	-0.01	0.22
AF	-0.13	-0.03
GGT	-0.25	0.11
Albumine	-0.30	-0.07
TB	-0.23	-0.06
DB	0.04	-0.06
GOT	-0.01	0.02
GPT	-0.11	-0.12
Insuline	0.47*	0.51**
HOMA IR	0.49**	0.30*

\* $P<0.05$ . \*\* $P<0.01$ . HbA1C: glycosylated hemoglobin; TAG: triglycerides; TC: total cholesterol; HDL-C: High Density LipoproteinCholesterol; LDL-C: low density lipoprotein cholesterol; AF: alkaline phosphatase ; GGT: gamma-glutamyltransferase; TB: total bilirubin; DB: direct bilirubin; GOT: glutamic oxalacetic transaminase; GPT: glutamic pyruvic transaminase.

## DISCUSSION

According to the liver biopsy in the sample studied, the NC was not able to predict the presence of steatosis and steatohepatitis. Despite this, it was identified that patients with altered NC presented, as expected, higher BMI and greater AC when compared to patients with adequate NC. The same was observed in the study

by Joshipura et al.<sup>(11)</sup>, which evaluated 1.206 hispanic patients free of comorbidities with a mean age of 50 years, and identified that patients with greater waist circumference and higher BMI were also those that presented greater NC, as well as lower levels of HDL-C ( $r= -0.23$ ;  $P<0.001$ ), corroborating the data of the present study in which a correlation was observed between NC and lower levels of HDL-C ( $r= -0.42$ ;  $P<0.05$ ) among males.

A study by Assyov and collaborators<sup>(12)</sup> evaluated 255 patients with severe obesity and a mean age of  $49\pm 12$  years. Among men, the study found that NC was positively correlated with insulin levels ( $r=0.368$ ;  $P<0.01$ ) and inversely correlated with HDL-C levels ( $r= -0.322$ ;  $P<0.01$ ), the same was observed in the present study. Among women, it was identified that a larger NC was positively correlated with higher insulin levels ( $r=0.263$ ;  $P<0.01$ ); there was, however, no correlation between NC measurement and HDL-C reduction, in keeping with the data observed in the present study, as shown in TABLE 3.

In order to evaluate the relationship between NC and NAFLD, a study by Hu et al.<sup>(9)</sup> evaluated 2.761 chinese and identified that patients with NAFLD with an alteration in glutamic pyruvic transaminase presented NC of  $38.94\pm 2.62$  cm and patients without alteration presented NC of  $37.21\pm 3.06$  cm.

These NC values were significantly higher when compared to other patients with other metabolic disorders (hypertension, diabetes mellitus, pre-diabetes, dyslipidemia, abdominal obesity, overweight and obesity, hyperuricemia and gout), whose mean NC was  $35.33\pm 3.03$  cm and also higher than in the control group, whose mean NC was  $32.60\pm 2.37$  ( $P<0.001$ ). In addition, there was a correlation between NC and HOMA-IR index in both men ( $r=0.250$ ;  $P<0.001$ ) and women ( $r=0.339$ ;  $P<0.001$ ).

A study by Li et al.<sup>(13)</sup> proposed to evaluate the relationship between NC and NAFLD in eutrophic patients ( $\text{BMI} \geq 18.5 \text{ kg/m}^2 - < 25 \text{ kg/m}^2$ ). For that, 2.668 patients with an average age of  $50.07\pm 14.09$  years old were studied. In both sexes, there was a significant correlation ( $P<0.01$ ) between NC and waist circumference, hip circumference, BMI, systolic and diastolic pressure, insulin, HOMA-IR, triglycerides and the glutamic oxalacetic transaminase (GOT) ( $P=0.05$  in the male sex and the  $<0.01$  in the female sex). A significant correlation ( $P<0.01$ ) between a higher NC and reduced levels of HDL-C was found in both men and women, corroborating in part with the findings of the present study, since a correlation was identified only between men. In addition, the study<sup>(13)</sup> pointed NC as an independent indicator for NAFLD in eutrophic men, but not in women. The authors justify this finding based on the fact that the female hormones may be a protective factor for the development of NAFLD and the fact that the number of female smokers was lower than the male smokers. Cigarette leads to oxidative stress, involved in the pathophysiology of NAFLD; however, the mechanism for the association between smoking and NAFLD has not yet been well elucidated.

Although the results of the present study did not identify a direct relationship between NC and NAFLD, it is suggested that the admeasurement of this measure can be used to distinguish patients who present insulin resistance, that plays a key role in the pathogenesis of NAFLD, of those who do not.

A cohort study<sup>(14)</sup> followed 2.623 patients over a 10-year period. The study identified that an increased NC had a negative impact on the development of type 2 diabetes mellitus (DM2). The study evaluated men and women. The risk of developing

DM2 was higher in the group of men with higher NC. Men with mean NC of  $40.3 \pm 1.1$  cm; 39.1–45.3 presented 1.74 times higher risk of developing DM2 in relation to men with lower NC, that is, mean NC of  $35.1 \pm 0.9$  cm; 31.8–3.2 cm. The same was observed among women. Women with higher NC (mean of  $35.2 \pm 0.4$  cm; 34.1–40.0 cm) presented 2.077 times more risk of developing type 2 diabetes mellitus than those with lower NC ( $30.7 \pm 0.8$  cm; 23.0–31.6 cm), being  $P < 0.05$ . At the end of the study, 632 (24.1%) patients developed type 2 diabetes mellitus. The incidence of the disease was higher in the group of patients with higher NC. The incidence of the disease was 17.6% in patients with lower NC x 36.0% in patients with higher NC.

A study by Cho et al.<sup>(14)</sup> identified a positive correlation between NC and triglyceride levels, that is, the higher the NC, the higher the triglyceride levels. On the other hand, there was a negative correlation between NC and HDL-C levels, and the higher the NC, the lower the HDL-C levels. Because triglyceride and HDL-C levels influence the reduction of insulin sensitivity<sup>(15)</sup>, these findings become of great importance.

In the present study, it was not possible to observe a direct relationship between NC and NAFLD. However, there was a relationship between NC and insulin resistance, a metabolic disorder that plays a key role in the development of NAFLD<sup>(16)</sup>.

In the presence of insulin resistance, the available glucose is not captured by the cells, causing hyperglycemia. As a consequence, fatty acids are mobilized from the hydrolysis of triglycerides in the adipose tissue, generating accumulation of these in the hepatic tissue. In addition, insulin resistance reduces hepatic glycogen stores and promotes gluconeogenesis in patients with NAFLD<sup>(17)</sup>, causing an uncontrolled production of hepatic glucose, which, together with decreased uptake by muscle and adipose tissue, contributes to hyperglycemia. Insulin resistance in muscle and adipose tissue are important components in the pathogenesis of NAFLD, due to the increased availability of circulating glucose and substrate to be accumulated in the form of lipid in the liver<sup>(18)</sup>. These events elucidate the crucial role of insulin resistance in the development of NAFLD<sup>(19,20)</sup>, in particular, insulin resistance induced by obesity<sup>(21)</sup>.

In our study, we identified a relationship between NC and biochemical markers related to NAFLD. In addition, we also identified the relationship between NC and higher AC and BMI. The findings regarding NC and anthropometric assessments are important since in overweight patients NC is an easier tool to perform when compared to AC and BMI measurement. Therefore, NC is a feasible evaluation to perform in clinical practice.

Although a direct relationship between NC and NAFLD was not identified, the progression of liver disease correlated with the HOMA-IR index, suggesting that it may be a more sensitive marker to indicate the progression of liver disease when compared to the circumference in the studied sample. Studies exploring this relationship between progression of liver disease, such as signaling pathways of cellular apoptosis, and insulin resistance remain scarce.

A study by Ferreira et al., which evaluated severely obese patients undergoing bariatric surgery, identified that hepatic cell apoptosis and insulin resistance increase the severity of liver disease in morbidly obese patients<sup>(22)</sup>.

Another study, developed by Amer et al., evaluated the results of the liver biopsy of 72 patients and observed a correlation between HOMA-IR index and the progression of liver disease. The increase in HOMA-IR index was significantly correlated ( $P = 0.0002$ ) with

the histological diagnosis of necro-inflammatory activity and fibrosis. That is, HOMA-IR gradually increased with the progression of liver disease to fibrosis ( $P = 0.0002$ )<sup>(23)</sup>.

Thus, although we have identified clear results in the present study regarding the importance of NC measurement in overweight patients, which refers to the deposition of subcutaneous fat in the upper region of the organism, showed related to metabolic changes, but not to the deposit of visceral fat.

Some limitations of the present study are related to the number of patients evaluated, that should be higher to have greater statistical strength and eventually to establish the best relation with NAFLD; the anthropometric evaluations were not performed by a single professional and, even done by very experienced professionals, it suffers from inter-rater variations.

Considering that NC is a promising nutritional assessment tool, especially for overweight patients, we should consider whether this measure is capable of replacing commonly used anthropometric assessments (BMI, waist circumference and skinfolds), or whether it would be a complementary measure to be added to the nutritional assessment. It should also be determined the best cut-off point that can characterize and classify NC in different populations and ethnicities along with their food consumption profiles and their anthropometric characteristics to be universally accepted.

## CONCLUSION

NC is a relatively new anthropometric evaluation, rarely used in clinical practice, easy to perform and with an excellent reproducibility.

We found a relationship between NC and metabolic alterations and insulin resistance in these patients. Patients with altered NC had higher levels of insulin when compared to patients with adequate NC, noting the role of metabolic alterations in the development of NAFLD. Despite this, we did not identify the relationship between NC and pathological abnormalities of NAFLD, that is, it was not possible to observe a direct relation between the altered NC and the presence of NAFLD in patients with overweight.

NC measurement should be used in routine clinical practice, because of its ease and reproducibility, especially in overweight patients, not only as a complementary measure but as a reliable valuation index. Further studies are suggested in order to establish the best relationship between NC and NAFLD and to determine a cut-off point for each population.

## Authors' contribution

Boemeke L: contributed in the elaboration of the research project, data collection, tabulation and data analysis and writing of the scientific article. Raimundo FV, Fernandes SA, Marroni CA: contributed in the elaboration of the research project, data analysis and writing of the scientific article. Bopp M, Leonhard LR: contributed to the design of the research project and data collection.

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**RESUMO – Contexto** – A resistência à insulina, em especial a induzida pela obesidade, desempenha papel central no desenvolvimento da doença hepática gordurosa não alcoólica (DHGNA). Embora seja importante a avaliação de pacientes com excesso de peso, as ferramentas de avaliação nutricional utilizadas na prática clínica apresentam limitações. A circunferência do pescoço, a partir disso, torna-se uma alternativa viável e de baixo custo, a qual parece estar relacionada ao acúmulo de gordura no tecido hepático. **Objetivo** – Avaliar a associação entre a circunferência do pescoço (CP) e as alterações metabólicas em pacientes com DHGNA. **Métodos** – Estudo transversal realizado em 82 pacientes, dos quais 76 foram submetidos à biópsia hepática. Foram realizadas as medidas de peso, altura, circunferência abdominal e CP. Valores de CP  $\geq 42$  cm e  $\geq 36$  cm foram considerados alterados para homens e mulheres, respectivamente. Os exames laboratoriais e o resultado da biópsia hepática foram coletados dos prontuários dos participantes. Foram avaliados os níveis glicêmicos em jejum, insulina, hemoglobina glicosilada, triglicerídeos, colesterol total, lipoproteína de alta densidade (HDL-C), lipoproteína de baixa densidade (LDL-C), ferritina, fosfatase alcalina, gama glutamiltransferase, albumina, bilirrubina total, bilirrubina direta, transaminase glutâmico-oxalacética, transaminase glutâmico-pirúvica e o índice HOMA-IR. **Resultados** – Foram avaliados 82 pacientes. Os pacientes com CP alterada apresentaram aumento do índice de massa corporal ( $P=0,043$ ), circunferência abdominal ( $P=0,007$ ), insulina ( $P=0,003$ ) e HOMA-IR ( $P=0,029$ ) quando comparados àqueles com CP adequada. A CP foi significativamente correlacionada com níveis reduzidos de colesterol de alta densidade (HDL-C) em homens ( $r=-0,42$ ,  $P<0,05$ ), aumento dos níveis de insulina em homens e mulheres ( $r_s=0,47$ ,  $P<0,05$  e  $r_s=0,51$ ;  $P<0,01$ , respectivamente), bem como maior índice HOMA-IR, tanto do sexo masculino ( $r_s=0,49$ ;  $P<0,01$ ) quanto do feminino ( $r_s=0,30$ ;  $P<0,05$ ). Não houve associação significativa entre CP e os desfechos hepáticos ( $r=0,145$ ,  $P=0,36$ ). **Conclusão** – A CP está associada com o índice HOMA-IR em pacientes com DHGNA. A CP pode ser utilizada no rastreamento da resistência à insulina nesses pacientes, considerando que a resistência à insulina desempenha um papel fundamental na progressão da doença.

**DESCRITORES** – Gordura abdominal. Resistência à insulina. Hepatopatia gordurosa não alcoólica. Doenças nutricionais e metabólicas. Sobrepeso.

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