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Association of “metabolic dysfunction-associated steatotic pancreas disease” (MASPD) and insulin resistance

Luís Jesuino de Oliveira **ANDRADE**¹, Gabriela Correia Matos de **OLIVEIRA**², Alcina Maria Vinhaes **BITTENCOURT**³, Gustavo Magno **BAPTISTA**⁴, Catharina Peixoto **SILVA**⁵ and Luís Matos de **OLIVEIRA**⁵

¹ Departamento de Saúde Universidade Estadual de Santa Cruz, Ilhéus, BA, Brasil. ² Programa Saúde da Família, Salvador, BA, Brasil. ³ Faculdade de Medicina Universidade Federal da Bahia, Salvador, BA, Brasil. ⁴ Clínica Médica e de Pneumologia, Itabuna, BA, Brasil. ⁵ Escola Bahiana de Medicina e Saúde Pública, Salvador, BA, Brasil.

HIGHLIGHTS

- Metabolic dysfunction-associated steatotic pancreas disease (MASPD) is a recent discovery in the world of metabolic disorders, and its potential connection to insulin resistance (IR) has sparked significant interest.
- Pancreatic steatosis, a defining characteristic of MASPD, may disrupt the delicate balance of the pancreas, potentially hindering its ability to secrete insulin effectively.
- The relationship between MASPD and IR is increasingly important for comprehending the pathophysiology of both conditions and may have clinical implications in their prevention and management.
- Research suggests a two-way street between MASPD and IR.

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Corresponding author: Luís Jesuino de Oliveira Andrade. E-mail: luis_jesuino@yahoo.com.br

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ABSTRACT – Background – To investigate the association between metabolic dysfunction-associated steatotic pancreas disease (MASPD) and insulin resistance (IR). **Methods** – This cross-sectional study involved 157 participants diagnosed with MASPD based on ultrasonography criteria. Baseline demographic data were collected, including age, gender, and body mass index. Serum levels of fasting glucose, insulin, lipid profile (including total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), glycated hemoglobin and insulin were measured using standardized laboratory techniques. Abdominal ultrasonography was performed on all participants using convex transducer (frequency range, 3,5 MHz) by experienced radiologist blinded to the clinical data. The association between MASPD and IR was assessed using logistic regression analysis, adjusting for potential confounders. Statistical significance was set at a *P*-value <0.05. **Results** – The logistic regression analysis was performed to verify whether MASPD was a risk factor for IR. After adjusting for gender and age, the results demonstrate a significant correlation between MASPD and markers of IR. TyG index: OR (95%IC) 5.72 (1.90–16.00), *P* 0.021, and HOMA –IR: OR (95%IC) 6.20 (2.1–22.00) *P* 0.037. **Conclusion** – This study presents a description of MASPD and its association with IR indices. Our findings demonstrate a significant correlation between MASPD and markers of IR. These results suggest that MASPD may contribute to the development of insulin resistance and further highlight the importance of pancreatic health in metabolic disorders.

Keywords – Metabolic dysfunction; pancreatic steatosis; MASPD; insulin resistance.

INTRODUCTION

Metabolic dysfunction-associated steatotic pancreas disease (MASPD) is not yet a term or condition described in the medical literature. The MASPD is a relatively new and emerging condition that has garnered significant attention in the field of metabolic disorders. This disease is characterized by pancreatic fat infiltration in the absence of chronic pancreatitis⁽¹⁾. Although the exact pathogenesis of MASPD remains unclear, there is growing evidence suggesting an association between MASPD and insulin resistance (IR)^(2,3).

IR is a key feature of various metabolic disorders, including type 2 diabetes mellitus, metabolic syndrome, and non-alcoholic fatty liver disease. It is characterized by impaired insulin signaling and reduced glucose uptake in insulin target tissues such⁽⁴⁾.

The prevalence of MASPD appears to be on the rise, mirroring the global epidemic of obesity and type 2 diabetes mellitus⁽⁵⁾. As a consequence, understanding the association between MASPD and IR has become increasingly important for a better comprehension of the pathophysiology of both conditions. Moreover, identifying this relationship may have clinical implications in the prevention and management of MASPD and its associated metabolic comorbidities.

The pancreas plays an important role in glucose homeostasis through the secretion of insulin and other hormones involved in the regulation of glucose metabolism. Any alteration in pancreatic function can have profound effects on glucose control and metabolic processes. Emerging evidence suggests that pancreatic steatosis, a hallmark feature of MASPD, may disrupt the normal pancreatic function, leading to impaired insulin secretion^(6,7).

There is a growing body of evidence suggesting a bidirectional relationship between MASPD and IR⁽⁸⁾. However, the precise mechanisms underlying this association remain incompletely understood, necessitating further investigation.

Despite the growing interest in understanding the relationship between MASPD and IR, there is a paucity of research investigating the precise mechanisms underlying this association. Moreover, the clinical implications of this association remain poorly defined. Thus, the objective of this research is

to investigate the association between MASPD and IR and explore the potential mechanisms that may contribute to this relationship.

METHODS

Study design and participants

This cross-sectional study involved 157 participants diagnosed with MASPD based on ultrasonography criteria. The study protocol was approved by the Ethics Committee.

Clinical and laboratory assessments

Baseline demographic data were collected, including age, gender, and body mass index. Fasting blood samples were obtained from each participant for laboratory assessments. Serum levels of fasting glucose, insulin, lipid profile (including total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), glycated hemoglobin and insulin were measured using standardized laboratory techniques.

Assessment of insulin resistance

IR was assessed using the triglyceride glucose index (TyG index) and homeostasis model assessment of insulin resistance (HOMA-IR). The TyG index was determined as $\text{Ln} [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$, and it is expressed on a logarithmic scale⁽⁹⁾. The benchmark for identifying IR is established at a TyG index value of 4.49. The HOMA-IR index was derived using the following formula: $(\text{Fasting insulin in } \mu\text{U/mL} \times \text{fasting glucose in mg/dL}) / 415$ ⁽¹⁰⁾. In accordance with earlier research, an HOMA-IR index ≥ 3.4 indicates IR, which represents the optimal threshold for predicting the development of diabetes mellitus and aligns with the hyperglycemic-hyperinsulinemic clamp method.

Pancreatic imaging

Abdominal ultrasonography was performed on all participants using a convex transducer (frequency range, 3.5 MHz) by experienced radiologists blinded to the clinical data. Pancreatic steatosis was assessed based on the presence and severity of hyperechogenicity in comparison to the liver parenchyma. The severity of pancreatic steatosis was graded as absent,

mild (Grade I), moderate (Grade II), or severe (Grade III), according to predefined criteria.

Statistical analysis

Descriptive statistics were presented as mean $\pm$ standard deviation (SD) or median (interquartile range) for continuous variables, and percentages for categorical variables. The association between MASPD and IR was assessed using logistic regression analysis, adjusting for potential confounders. Statistical significance was set at a *P*-value of less than 0.05.

Ethical considerations

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The study protocol The National Commission for Research Ethics (CONEP - Brazil) was approved by CONEP - Brazil, and written informed consent was obtained from all participants prior to their inclusion in the study. Confidentiality of personal information was strictly maintained throughout the study, and all data were analyzed and reported in an aggregated and anonymized manner.

RESULTS

A comprehensive assessment was conducted on a total of 157 specimens, comprising of 126 (63.0%) females and 74 (37.0%) males, who had an average age of 46.56 ± 18.98 years. IR was detected in 64 individuals (32.0%) based on the HOMA-IR index and in 132 individuals (66.0%) based on the TyG index. The HOMA-IR and TyG index demonstrated distinct patterns within the samples under evaluation. The summarized demographic features can be found in TABLE 1 and TABLE 2.

TABLE 1. Parameters of graded MASPD.

MASPD	Male	Female
Normal	21 (13.37%)	49 (31.21%)
Mild	15 (9.55%)	33 (21.01%)
Moderate	10 (6.36%)	15 (9.55%)
Severe	12 (7.64%)	2 (1.27%)

MASPD: metabolic dysfunction-associated steatotic pancreas disease.

TABLE 2. Demographic and biochemical characteristics.

Gender	Male: 58 (36.9%) Female: 99 (63.1%)
HbA1c	12.06 $\pm$ 9.12
Insulin	5.78 $\pm$ 0.91
Fasting glucose	82.29 $\pm$ 17.91
Average blood glucose estimated by HbA1c	106.90 $\pm$ 23.24
Triglycerides	144.84 $\pm$ 66.63
HOMA-IR	3.13 $\pm$ 2.74
TyG index	4.64 $\pm$ 0.30

The logistic regression analysis was performed to verify whether IR was a risk factor for MASPD. After adjusting for gender and age, the results are shown in TABLE 3.

TABLE 3. Logistic analysis of MASPD risk factors.

Variables	^a OR (95%CI)	P value
TyG index	5.72 (1.90–16.00)	0.021
HOMA-IR	6.20 (2.1–22.00)	0.037

^aAdjusted for gender and age. TyG index: triglyceride glucose index; HOMA-IR: homeostasis model assessment of insulin resistance.

In our study, we employed the ultrasonographic method to evaluate the degree of pancreatic fat infiltration and utilized the ultrasonographic fatty pancreas score (UFPS) to classify the severity of pancreatic fat infiltration (FIGURE 1).

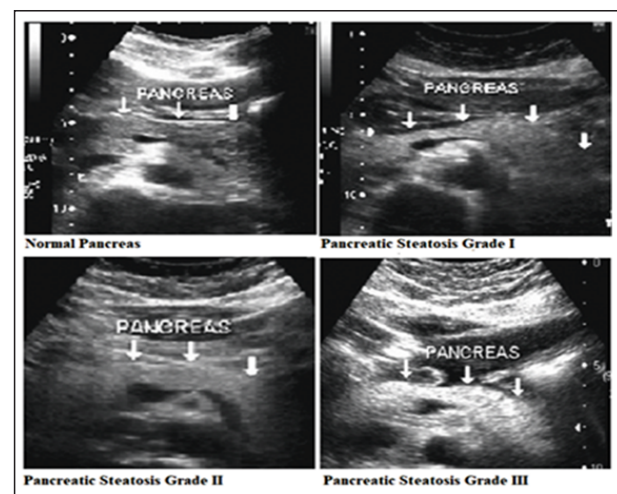


FIGURE 1. The severity of pancreatic steatosis.

DISCUSSION

In this study, we demonstrated that the TyG index and HOMA-IR levels serve as significant risk factors for the development of MASPD. Our analysis revealed a strong correlation between these metabolic indices and the pathogenesis of the disease, providing critical insights into the underlying mechanisms and potential therapeutic targets for this increasingly prevalent condition.

The MASPD is a complex disorder characterized by pancreatic steatosis⁽¹¹⁾. Despite its clinical importance, the risk factors contributing to MASPD remain poorly understood. In recent years, the TyG index and HOMA-IR have emerged as potential predictors of metabolic dysfunction and IR in various metabolic diseases⁽¹²⁾. Building upon this knowledge, this study aimed to investigate the association between the TyG index, HOMA-IR levels, and the risk of developing MASPD. By elucidating the role of these metabolic markers in MASPD pathogenesis, our findings may provide a foundation for early detection, risk stratification, and targeted interventions to mitigate the progression and complications of this pancreatic disorder.

The assessment of IR is crucial in clinical practice, and while the HOMA-IR index has been widely used as a reliable marker, and the TyG index has emerged as a promising alternative^(13,14). HOMA-IR, calculated from fasting insulin and glucose levels, provides an established measure of insulin sensitivity, but it may underestimate IR in certain populations due to its reliance on fasting insulin levels⁽¹⁵⁾. In contrast, the TyG index, derived from fasting triglycerides and glucose concentrations, offers a simple and practical surrogate for IR assessment, demonstrating associations with metabolic risk⁽¹⁶⁾. However, both indices have limitations, such as variability in cutoff values and sensitivity to changes in lipid and glycemic profiles, warranting cautious interpretation in clinical settings⁽¹⁷⁾. Overall, the combined use of HOMA-IR and TyG index enhances the precision of IR evaluation⁽¹⁸⁾.

The relationship between the TyG index and HOMA-IR with MASPD has been underexplored, despite evidence of the role of these indices in the pathophysiology of metabolic disorders such as NASH. Studies have shown that both an increase in the TyG index and HOMA-IR are associated with the

development of NASH, suggesting the importance of these markers in the assessment of hepatic steatosis^(19,20). However, few studies have investigated the potential association between these indices and MASPD. Therefore, our research aimed to evaluate the relationship between the TyG and HOMA-IR indices with the degrees of MASPD, demonstrating a significant association between them.

Ultrasonographic diagnosis of pancreatic fat infiltration involves the assessment of echogenicity and texture of the pancreatic parenchyma. Various grading systems have been proposed to classify the severity of pancreatic steatosis based on ultrasound findings. The UFPS assesses the degree of pancreatic fat infiltration based on the echogenicity of the pancreas compared to the liver and kidney⁽²¹⁾. In our study, we employed the ultrasonographic method to evaluate the degree of pancreatic fat infiltration and utilized the UFPS to classify the severity of pancreatic fat infiltration.

Thus, we are providing a description of the potential mechanisms linking IR and MASPD, along with the concurrent elevation of triglycerides, glucose, and insulin levels. IR, characterized by impaired insulin signaling and decreased glucose uptake in target tissues, may lead to increased lipolysis in adipose tissue, resulting in elevated circulating free fatty acids⁽²²⁾. These free fatty acids are then taken up by the liver and pancreas, leading to increased triglyceride accumulation within these organs^(23,24). Simultaneously, IR disrupts the normal regulation of glucose uptake and metabolism, resulting in hyperglycemia and compensatory hyperinsulinemia. The combination of elevated triglycerides, glucose, and insulin levels contributes to an environment conducive to the development of MASPD.

CONCLUSION

This study presents a description of MASPD and its association with IR indices. Our findings demonstrate a significant correlation between MASPD and markers of IR. These results suggest that MASPD may contribute to the development of IR and further highlight the importance of pancreatic health in metabolic disorders. Further investigations are warranted to elucidate the underlying mechanisms

and potential therapeutic strategies targeting MASPD and its impact on IR.

Authors' contribution

Andrade LJO and Oliveira LM: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, visualization, writing – original draft, writing – review & editing. Oliveira GCM: Conceptualization, data curation, formal analysis, methodology, validation, visualization, writing – original draft, Writing – review & editing. Bittencourt AMV and Baptista

GM: Data curation, formal analysis, methodology, validation, visualization. Silva CP: Data curation, formal analysis, investigation, methodology, validation, visualization.

Orcid

Luís J de Oliveira Andrade: 0000-0002-7714-0330.
Gabriela C Matos de Oliveira: 0000-0002-3447-3143.
Alcina M Vinhaes Bittencourt: 0000-0003-0506-9210.
Gustavo Magno Baptista: 0000-0001-8462-1098.
Catharina Peixoto Silva: 0009-0002-7702-9154.
Luís Matos de Oliveira: 0000-0003-4854-6910.

Andrade LJO, Oliveira GCM, Bittencourt AMV, Baptista GM, Silva CP, Oliveira LM. Associação de "doença esteatótica pancreática associada à disfunção metabólica" (MASPD) e resistência à insulina. *Arq Gastroenterol*. 2024;61:e24070.

RESUMO – Contexto – Investigar a associação entre a doença esteatótica pancreática associada à disfunção metabólica (DEPADM) e a resistência à insulina (RI) e explorar os possíveis mecanismos que podem contribuir para essa relação. **Métodos** – Este estudo transversal envolveu 157 participantes diagnosticados com DEPADM com base em critérios de ultrassonografia. Foram coletados dados demográficos de base, incluindo idade, gênero e índice de massa corporal. Os níveis séricos de glicose em jejum, insulina, perfil lipídico (incluindo colesterol total, triglicerídeos, colesterol de lipoproteína de alta densidade e colesterol de lipoproteína de baixa densidade), hemoglobina glicada e insulina foram medidos usando técnicas laboratoriais padronizadas. A ultrassonografia abdominal foi realizada em todos os participantes usando um transdutor convexo (frequência de 3,5 MHz) por um radiologista experiente e cego para os dados clínicos. A associação entre DEPADM e RI foi avaliada por meio de análise de regressão logística, com ajuste para possíveis fatores de confusão. A significância estatística foi definida como um valor de $P < 0,05$. **Resultados** – A análise de regressão logística foi realizada para verificar se a DEPADM era um fator de risco para RI. Após o ajuste para gênero e idade, os resultados demonstraram uma correlação significativa entre a DEPADM e os marcadores de RI. Índice TyG: OR (95%CI) 5,72 (1,90 - 16,00), $P 0,021$, e HOMA -IR: OR (95%CI) 6,20 (2,1–22,00) $P 0,037$. **Conclusão** – Este estudo apresenta uma descrição da DEPADM e sua associação com os índices de RI. Nossos achados demonstram uma correlação significativa entre o DEPADM e os marcadores de RI. Esses resultados sugerem que a DEPADM pode contribuir para o desenvolvimento da RI e destacam ainda mais a importância da saúde pancreática nos distúrbios metabólicos.

Palavras-chave – Disfunção metabólica; esteatose pancreática; DEPADM; resistência à insulina.

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