Myosteatosis and Type 2 Diabetes Mellitus

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ABSTRACT

Myosteatosis refers to the infiltration of fat into skeletal muscle tissue, being influenced by factors such as advanced age and overweight, which increase the inability of adipocytes to store lipids. This condition not only alters the structure of the muscle but is also associated with endocrinological imbalances such as insulin resistance (IR) and hyperinsulinemia, increasing the risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular diseases. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are effective methods for measuring myosteatosis, identifying areas of fat accumulation that may indicate specific regional patterns. This review aimed to evaluate the main evidence that associates myosteatosis with T2DM, compiling the epidemiological data already available on the subject and the main gaps in the literature. Ten observational studies were selected, from different regions of the world, which showed a relationship between myosteatosis and a higher incidence of T2DM, as well as IR, worse glycemic status, increased inflammatory mediators and a tendency to coronary artery disease. In conclusion, myosteatosis and T2DM are conditions with a relevant relationship and that have significant implications for public health, requiring greater standardization of myosteatosis assessment methods and interventional studies that address potential therapeutic strategies for this condition.

KEYWORDS

Diabetes Mellitus, Type 2; myosteatosis; myoskeletal lipid infiltration

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Received: 5 March 2025
Accepted: 9 August 2025
Published online: 6 October 2025

Acta Medica (Hradec Králové) 2025; 68(2): 37–44
https://doi.org/10.14712/18059694.2025.17

INTRODUCTION

Sarcopenia can be defined as a progressive and generalized disorder of skeletal muscle, where there is a gradual loss of strength and functionality, being more frequent in the elderly, but it can occur in younger individuals. Sarcopenia is diagnosed when low muscle strength is observed in addition to low muscle quantity or quality. When low physical performance is also observed, sarcopenia is considered severe (1). The assessment of muscle quantity is well established, but muscle quality is not yet fully explored, and there is no consensus on its assessment methods (1, 2). The deposition of pathological fat in muscle tissue, known as myosteatosis, compromises the quality of skeletal muscle and appears to lead to a faster loss of strength than of muscle mass, characterizing an important parameter of loss of muscle quality (2, 3). Recent data suggests that overweight, obesity, and advanced age imply the occurrence of myosteatosis, and that its occurrence culminates in reduced functionality, muscle strength, and individual mobility (4, 5).

Type 2 Diabetes Mellitus (T2DM) is a chronic and complex metabolic disorder characterized by elevated glycemic levels due to mechanisms of increased insulin resistance (IR), associated with hyperinsulinemia and, in later stages, failure in the production and secretion of insulin by the pancreas (6). Its prevalence is recognizably associated with being overweight and obese, advanced age, and unhealthy lifestyle habits, such as sedentary behavior, high caloric intake and poor nutritional quality (6). The occurrence of T2DM can lead to chronic complications associated with micro and macroangiopathy, such as diabetic retinopathy, diabetic kidney disease, and diabetic neuropathy, in addition to being associated with cardiovascular complications (6).

Although not yet fully understood, there appears to be an association between myosteatosis and T2DM as part of the increased ectopic fat distribution. The volume of adipose infiltration in skeletal muscle is significantly higher in individuals with T2DM than in normoglycemic individuals (7). Furthermore, even in individuals without diabetes, the accumulation of fat in the trunk skeletal muscle appears to be associated with an increase in IR (8). Still, it is possible that the occurrence of myosteatosis in patients with T2DM is an independent risk factor for unfavorable outcomes, such as coronary artery calcification and acute coronary syndrome (9).

Despite the amount of studies regarding the relationship between myosteatosis and T2DM still being small, some data points to a possible connection between the two conditions, which seem to share common risk factors and present a synergistic effect in terms of morbidity and mortality (10). With this in mind, the present study sought to conduct an integrative review, with the aim of demonstrating the association between myosteatosis and T2DM or changes in glucose metabolism that contribute to the development of T2DM.

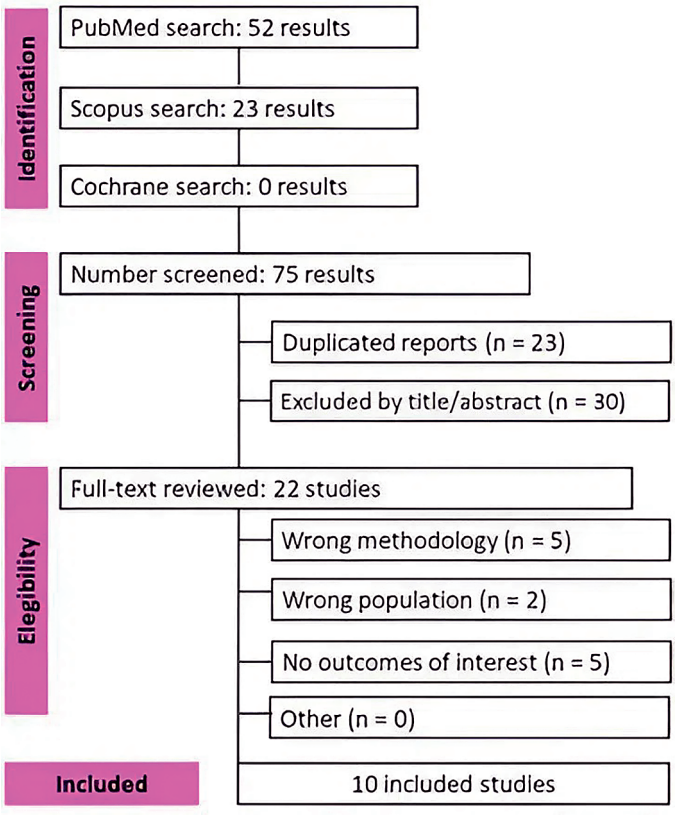


Fig. 1 Flowchart of the critical selection of articles conducted according to the recommendations of the PRISMA protocol.

MATERIALS AND METHODS

The present study is an integrative literature review, which is based on a research method grounded in the systematic synthesis of various studies and allows for the establishment of specific conclusions about a given topic (11). To guide this study with greater precision, the following guiding question was established: What is the association between myosteatosis and T2DM?

From this, the electronic research was conducted during the last three quarters of 2024. For the search, the following databases were consulted: PubMed (National Library of Medicine and National Institute of Health), Scopus, Biblioteca Virtual em Saúde (BVS), SciELO (Scientific Electronic Library Online), Cochrane Collaboration and ClinicalTrials. The inclusion criteria and filters used were articles related to the topic, studies that were not reviews or case reports and that were available in full text in the aforementioned databases. The exclusion criteria were duplicate articles, and studies on animals.

For the prospecting of the articles, the following descriptors were used: "type 2 diabetes mellitus", "non insulin dependent diabetes mellitus", "myosteatosis" and "myocellular lipid". In all databases, the combination – "(type 2 diabetes mellitus) OR (non insulin dependent diabetes mellitus) AND (myosteatosis) OR (myocellular lipid)" – was applied. In conclusion, the search was conducted by two independent reviewers and the analysis of agreement between observers was performed using the Kappa test (K) through the BioStatistics app V.1.1.0 and calculated according to the categorical method (12). The value found was K = 0.853 (almost perfect agreement).

Tab. 1 Baseline characteristics of the populations of the 10 selected studies and main findings related to glycemic status, myosteatosis and their measurement methods.

Author	Sample	ST	SP	MAP (years)	CR	MMM	Findings on glycemic status and myosteatosis
YAMAZAKI, H.; TAUCHI, S.; MACHANN, Y.; *et al. 2022*[8]	1073	Cohort study	Men and women	48	Germany and Japan	CT and MRI	AHR for incident T2DM in patients with trunk myosteatosis: 1.95 (95% CI 1.07–3.54).
KIM, E. H.; KIM, H.; LEE, M. J.; *et al. 2022*[13]	20986	Retrospective study	Men and women	54.5	South Korea	CT	Lower chances of T2DM (75% in men and 68% in women when comparing 1st and 4th quartiles) in individuals with greater muscle area with normal attenuation.
LIU, F. P.; GUO, M. J.; YANG, Q.; *et al. 2024*[9]	652	Cross-sectional Study	Men and women (with T2DM)	55.95	China	CT based on Martin's Criteria	Increased risk of coronary artery calcification in individuals with T2DM who had myosteatosis (OR = 2.381, P = 0.003).
MILJKOVIC, I.; KUIPERS, A. L.; CVEJKUS, R.; *et al. 2016*[14]	1515	Cohort study	Men	56.9	Caribbean	CT	Intermuscular fat was independently associated with a higher incidence of T2DM (OR per 1-SD increase in intermuscular fat = 1.29; 95% CI = 1.08–1.53).
MILJKOVIC, I.; CAULEY, J. A.; WANG, P. Y.; *et al. 2013*[15]	393	Cross-sectional Study	Men	74.3	United States	CT	Myosteatosis (greater infiltration of intermuscular adipose tissue in the abdominal muscles and psoas) was associated with higher glycemic levels, greater insulin resistance and hyperinsulinemia in elderly people without T2DM (in regression analyses adjusted for age, height, muscle volume, and study site, all P < 0.003).
MILJKOVIC, I.; KUIPERS, A. L.; CVEJKUS, R.; *et al. 2020*[16]	718	Cross-sectional study derived from prospective cohort	Men	64	Trinidad and Tobago	CT	Association between T2DM and liver and skeletal muscle adiposity in non-obese men, independently of visceral adiposity (in regression analyses adjusted for sociodemographic and lifestyle factors, all P < 0.05).
MILJKOVIC, I.; KUIPERS, A. L.; KAMMERER, C. M.; *et al. 2011*[17]	471	Cross-sectional study	Men and women	43	Trinidad and Tobago	CT	Markers of inflammation have been associated with myosteatosis, as well as greater insulin resistance and hypersinsulinemia – for example, higher levels of C-reactive protein correlated with lower muscle density (r = −0.10, P < 0.05), hyperinsulinemia (r = 0.12, P < 0.05), and higher HOMA-IR (r = 0.17, P < 0.01).
HUANG, Y.; YAN, J.; ZHU, H.; *et al. 2023*[18]	130	Prospective study with cohort	Men and Women	52.02	United States	MRI	Greater muscle fat infiltration (assessed by proton density fat fraction of intermuscular adipose tissue and intramuscular fat of thigh muscles) and worse muscle function (assessed by peak torque and total work of thigh muscles) in patients with T2DM compared to a control group (all with p < 0.05 in independent sample t-test).
KIEFER, L. S.; FABIAN, J.; ROS-PLESZCZ, S.; *et al. 2018*[10]	349	Retrospective study	Men and women	56	Europe*	MRI	Abdominal myosteatosis (proton density fat fraction) was significantly higher in individuals with T2DM and prediabetes compared to controls (13.1% (IQR 10.5–16.6%); 11.1% (IQR 8.9–15.0%) and 10.1% (IQR 7.5–13.3%), respectively; p < 0.001).
KIEFER, L. S.; FABIAN, J.; ROS-PLESZCZ, S.; *et al. 2021*[7]	337	Cohort study	Men and women	56	Germany	MRI	Individuals with T2DM and pre-diabetes had significantly higher amounts of intramyocellular (prediabetes: β: 0.76, 95% CI: 0.28–1.24, P = 0.002; T2DM: β: 1.56, 95% CI: 0.66–2.47, P < 0.001) and extramyocellular lipids (prediabetes: β: 1.54, 95% CI: 0.56–2.51, P = 0.002; T2DM: β: 2.15, 95% CI: 1.33–2.96, P < 0.001) than normoglycemic individuals.

Legend: AHR: Adjusted hazard ratio; CI: Confidence interval; CR: Country of Realization; CT: Computed Tomography; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; IQR: Interquartile Range; MAP: Middle Age of Patients; MMM: Measurement Method of Myosteatosis; MR: Magnetic Ressonance Imaging; OR: Odds Ratio; SD: Standard Deviation; SP: Sex of Patients; ST: Study Type; T2DM: Type 2 Diabetes Mellitus.
* Various countries around Europe.

RESULTS

A summary of the selection process can be seen below (figure 1). In total, 10 articles with various methodologies were selected for the extraction of results.

According to the selected articles (table 1), seven studies evaluated the muscle fat index through computed tomography (CT) (8, 9, 13–17), while four studies did so through magnetic resonance imaging (MRI) (7, 8, 10, 18), with one of them including both measurement methods (8). However, only one study evaluated infiltration according to Martin's criteria (attenuation of skeletal muscle (ASM) < 33 HU with body mass index (BMI) ≥ 25 kg/m² or ASM < 41 HU with BMI < 25 kg/m²) (9). Furthermore, the demographic and clinical characteristics of the patients were not considered as parameters for better evaluation and consideration of the lipid indices found. Besides, there was a great sociodemographic variability, both about the country of conduct and the general characteristics of the populations. The studies were conducted on different continents, without following a well-founded evaluation parameter for the level of lipid infiltration, including individuals without T2DM or other comorbidities in some of them.The study by Yamazaki et al. (2022) (8) explored fat distribution patterns, assessed by CT, and their relationship with the future development of T2DM. The study revealed that central fat distribution, particularly in the abdomen and muscles, was strongly associated with increased risk of diabetes, highlighting the importance of monitoring body fat in different regions to predict diabetes risk. Consistent findings were observed in the study by Kiefer et al. (2018) (10), where abdominal myosteatosis, seen on MRI, was higher in individuals with T2DM and prediabetes.

Other studies have also shown an association between myosteatosis and T2DM. Kim et al (2022) (13) found that normal muscle attenuation seen on CT reduced the chances of T2DM in a South Korean population. A cohort study with a Caribbean population showed a higher incidence of T2DM in those with myosteatosis (14). In Germany, intramyocellular and extramyocellular lipid infiltration was greater in men and women with T2DM or prediabetes than in those with normal glycemia (7). Furthermore, decreased muscle strength in patients with T2DM was associated with the presence of myosteatosis in studies that performed CT (15) and MRI (18).

The interrelationship between myosteatosis and changes in glucose metabolism is reinforced by studies that indicate that people without diabetes with greater fat deposition in skeletal muscle have lower insulin sensitivity (15, 17). A cross-sectional study with elderly Americans without T2DM demonstrated an association between myosteatosis, confirmed by CT, and greater IR and hyperinsulinemia (15). Another cross-sectional study with younger patients, developed by the same research group, showed an association between higher levels of inflammation markers, especially C-reactive protein (CRP), with adipose infiltration in the muscle, hyperinsulinemia, and IR (17).

The role of ectopic fat in the context of metabolic syndrome and T2DM can be corroborated by the findings of Mijkovic et al. (2020) (16), where there was an association between T2DM and the presence of muscle and liver adiposity in non-obese men, suggesting that myosteatosis may contribute to increased metabolic risk independently of abdominal fat. The findings of Liu et al. (2024) (9) show that in patients with T2DM the presence of myosteatosis was associated with a higher risk of coronary artery calcification, suggesting that this muscle alteration may emerge as a new risk factor for atherosclerosis in T2DM.

DISCUSSION

1. CONCEPT OF MYOSTEATOSIS

The term myosteatosis describes a condition characterized by fat infiltration in muscle tissue (4). Its main risk factors are advanced age and overweight, as both culminate in the exhaustion of the adipocytes' capacity to store lipids, so that these molecules begin to accumulate in other tissues, then being considered ectopic fat (8).

Myosteatosis can now be recognized as a clinical condition distinct from sarcopenia, originating not only from adipose tissue saturation but also from several other mechanisms. Adipogenic conversion of multipotent stem cells (through conditions such as muscle injury or increased glucocorticoid levels) and increased bone marrow adipogenesis (in situations such as prolonged bed rest, sex steroid deficiency, and altered leptin signaling) may also affect fat deposition in muscle (19).

Once considered inert, it is now known that adipose tissue has important metabolic and inflammatory capacity, and, in this way, it is understood that its accumulation in other tissues is related to several endocrinological disorders, such as decreased insulin sensitivity, hyperinsulinemia, and increased risk for the development of T2DM (4, 8).

2. MEASUREMENT METHODS

There are three types of lipid accumulation in muscle tissue that, together, are classified as myosteatosis: (a) intermuscular adipose tissue, that is, the clustering of fat below the muscle fascia and between muscle groups; (b) intramuscular adipose tissue, that is, the presence of lipid concentrates within a muscle group; and (c) intramyocellular lipids, the accumulation of fat droplets within muscle cells (2,3).

The first two forms of myosteatosis mentioned above (intermuscular adipose tissue and intramuscular adipose tissue) are the easiest to measure, with CT and MRI being the two main methods used. These exams allow for the precise and non-invasive quantification of intramuscular lipid content and the identification of specific regional patterns of fat accumulation, providing an understanding of the underlying pathophysiological mechanisms (2, 3).

Tissue density on CT can be quantified in a standardized manner using the Hounsfield unit (HU), identifying fatty infiltration by the presence of hypodense areas within the muscle. Healthy muscle presents attenuation of +30 to +150 HU, while the presence of intramyocellular lipid may present attenuation compatible with a muscle

area of low attenuation, from −29 HU to +29 HU. Intermuscular and intramuscular adipose tissue can be represented as areas of density between −30 HU and −190 HU (20). A cross-sectional analysis of 20,664 healthy adults proposed to define diagnostic cutoff points for myosteatosis, using muscle indices measured by CT at the L3 vertebra level. The ratio between the normal attenuation muscle area and the total muscle area stood out as a potentially useful index for evaluating myosteatosis, using a T-score < −2.0 as the cutoff point (21).

MRI can evaluate myosteatosis by means of the proton density fat fraction (PDFF) in T1-weighted images, suppressing the water signal. Through spectroscopy, MRI also provides measurement of intramyocellular and extramyocellular lipid contents, based on the differences in frequencies after the excitation of hydrogen nuclei (22).

CT was widely used to measure myosteatosis in the studies included in this review and is notable for its ability to visualize and quantify intermuscular and visceral fat. Some studies have used CT to assess the relationship between muscle fat and metabolic conditions (9, 13, 14). Although CT is effective in identifying hypodense areas that indicate fat, it may be less accurate in differentiating the site of fat deposition compared to MRI (2, 3). Other studies have used MRI for a detailed assessment of myosteatosis, and it is particularly useful in differentiating between intramyocellular and extramyocellular fat (7, 10, 18). Combined methods using CT and MRI have also been employed to obtain a comprehensive view of myosteatosis (8).

Quantitative ultrasound has also been studied as an imaging modality to assess myosteatosis, however, greater difficulty in standardization and the impossibility of distinguishing intramuscular and intermuscular fat are factors that hinder its implementation (3). Ultrasound was not used in any of the studies selected for this review.

3. PATHOPHYSIOLOGY OF MYOSTEATOSIS IN T2DM

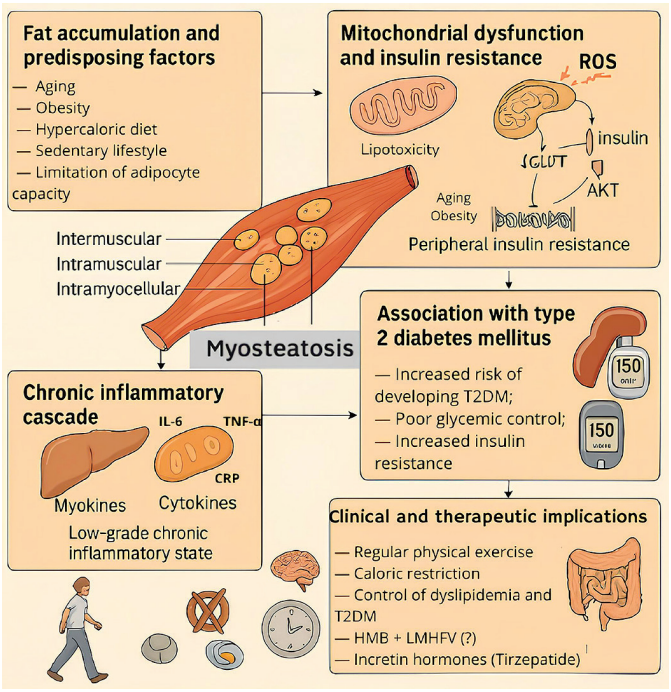
Ectopic fat is found in organs such as the liver, pancreas, kidneys, heart and skeletal muscle and is associated with a pathological response in adipocyte physiology, where several genetic and environmental factors lead to inflammatory dysfunction of adipocytes and limit their ability to store fat. This leads to a redirection of lipids to peripheral tissues, leading to ectopic fat deposition (23, 24). Hypercaloric diets and hyperinsulinemia cause IR and contribute to the accumulation of fat in central organs in the pathophysiology of diabetes, such as the pancreas, liver and skeletal muscle, potentiating IR in hepatic receptors and causing impairment in pancreatic insulin secretion. This contributes to hyperglycemia and the development of T2DM (23–25).

Therefore, although not completely understood, there is a relationship between the occurrence of myosteatosis and T2DM. Individuals with T2DM have a higher amount of fat infiltrated in various muscle tissues, especially in the abdominal muscles and thigh muscles (7).

Although T2DM and myosteatosis share risk factors such as advanced age, sedentary lifestyle, and high-calorie diet, there seems to be a relationship not merely of association between the two nosological entities, but rather of causality and consequence. This is due to the fact that fat infiltration into the muscle enables the onset of a pathological triad in that tissue, composed of IR, inflammation, and contractile dysfunction (15, 16). Additionally, it has been demonstrated that greater amounts of myosteatosis are strongly associated with increased IR. The reason for this is that the accumulation of intramuscular fat impairs glucose uptake and disrupts insulin signaling. Studies using CT and MRI have consistently shown that individuals with higher myosteatosis, even when matched for visceral or total body fat, exhibit reduced muscle quality, diminished insulin sensitivity and higher Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) levels. In other words, the greater the degree of myosteatosis, the higher the risk of IR and related metabolic dysfunction (15).

Another factor contributing to the occurrence of myosteatosis in patients with T2DM is the inflammatory role of adipose tissue in individuals with metabolic syndrome and obesity, particularly concerning the increased secretion of adipokines, which is directly linked to inflammation and increased IR, thereby creating a reciprocal relationship between the two conditions (1). One of the studies selected in this review demonstrated that elevated circulating inflammatory markers, including CRP, interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), are closely linked to increased ectopic fat deposition in skeletal muscle, which in turn contributes to a state of persistent, low-grade inflammation. This inflammation impairs insulin receptor signaling pathways, decreasing glucose uptake by myocytes. To compensate for the reduced insulin sensitivity, pancreatic β-cells increase insulin

Fig. 2 Infographic on the relationship between myosteatosis and insulin resistance, inflammation and diabetes diabetes mellitus.



Legend: CRP: C-reactive protein; HMB: β-hydroxy β-methylbutyrate supplementation; IL-6: interleukin-6; LMHF: low-magnitude high-frequency vibration treatment; ROS: Reactive oxygen species; T2DM: Type 2 diabetes mellitus; TNF-α: tumor necrosis factor-alpha.

secretion, resulting in hyperinsulinemia. This compensatory hyperinsulinemic state further IR, thus accelerating the progression to type 2 diabetes mellitus. These findings highlight the pivotal role of inflammatory processes, inflammatory markers, and intramuscular adiposity in the pathogenesis of metabolic dysfunction and IR (17).

Figure 2 compiles the main mechanisms that link myosteatosis with IR and T2DM.

4. MYOSTEATOSIS AND INSULIN RESISTANCE IN PEOPLE WITHOUT DIABETES

The association between myosteatosis and IR in people without diabetes is mainly observed in elderly populations (15), but signs of inflammation and hyperinsulinemia are also present in younger people with larger amounts of intramuscular fat or subclinical adiposity (17).

In a cross-sectional study by Miljkovic et al. (2013) of 393 elderly men with T2DM, CT revealed that larger volumes of intermuscular fat were associated with IR, regardless of visceral fat, subcutaneous fat, or BMI (15). In a younger population, individuals without T2DM but with intramuscular fat infiltration had significantly higher levels of CRP, insulinemia, and IR, even in the absence of obesity and overt hyperglycemia (17). In a longitudinal cohort of 1,515 Afro-Caribbean men initially without T2DM, the progression of intermuscular fat was an independent predictor of T2DM development during a six-year follow-up (14). For each one-standard deviation increase in intermuscular fat, the risk of conversion to T2DM increased by 29% (OR 1.29; 95% CI: 1.08–1.53), even after adjusting for BMI and abdominal adiposity (14).

These results, consistent across different age groups and ethnic groups, indicate that myosteatosis may act as an important marker of IR and cardiometabolic risk, even in individuals with normal blood glucose levels and independently of central obesity and BMI.

5. MYOSTEATOSIS AND LIVER FAT

The accumulation of ectopic fat deposits in muscles is not only associated with T2DM and IR, but also with overall metabolic health and ectopic fat deposition at other sites. A higher proportion of good-quality muscle is strongly associated with lower risks of non-alcoholic fatty liver disease (NAFLD), as assessed by ultrasound, and liver fibrosis, as determined by the NAFLD fibrosis score and the Fibrosis-4 index. Furthermore, muscle fat content, rather than muscle mass, has been reported to be strongly and independently associated with non-alcoholic steatohepatitis (NASH) in patients with greater degrees of obesity. Collectively, these findings suggest that myosteatosis may serve as a valuable diagnostic and prognostic marker in NAFLD, a hypothesis that warrants confirmation through prospective studies (2).

6. OBSERVATIONAL STUDIES

All 10 studies selected in this review are observational, including prospective and retrospective cohorts and cross-sectional studies (Table A1). The included studies demonstrate that myosteatosis is associated with various metabolic conditions, such as obesity, IR, metabolic syndrome, cardiovascular diseases and T2DM, in addition to directly compromising muscle functionality. Greater degrees of myosteatosis was directly correlated to a decrease in muscle functionality, as shown by lower peak torque, lower total work of thigh muscles, incident mobility disability and gait speed decline in patients with myosteatosis when compared to a healthy control group (5, 18).

In studies that do not directly evaluate T2DM, evidence already suggested the harmful effect of myosteatosis. A subanalysis of the Age, Gene/Environment Susceptibility (AGES) – Reykjavik Study evaluated muscle outcomes in elderly men and women, observing that thigh myosteatosis was associated with decreased strength, slower gait and decreased survival, but no mortality relationship was observed in the same study, with calf myosteatosis. Furthermore, muscle mass loss is not uniform, and slow-twitch type I fibers are less affected than fast-twitch fibers (26).

These results reinforce that myosteatosis should be considered for metabolic and cardiovascular care, although there are still many gaps regarding the pattern of involvement and the impact on cardiovascular outcomes.

7. INTERVENTIONAL STUDIES

Therapeutic interventions to reduce myosteatosis in populations with altered glycemic status have been proposed, but not yet implemented in experimental studies. Some strategies, such as dietary changes, encouragement of physical activity, and the use of lipid-lowering medications, have shown potential to reduce intramuscular lipid accumulation and improve muscle function in individuals with myosteatosis (2–4). However, there are no studies evaluating the long-term efficacy of these interventions and their effects on the progression of associated metabolic diseases.

Despite the limitations of the currently available data regarding the impact of lifestyle on myosteatosis, there are several indications of the benefits of exercise and dietary approaches (22, 27). Consumption of a high-fat and high-fructose diet is associated with myosteatosis, especially in animal models (22, 28, 29). Implementing a calorie-restricted diet shows favorable changes in muscle composition (22, 27). The reduction of intermuscular adipose tissue has been shown to be greater when induced by exercise compared with calorie restriction alone (30). Similarly, a hypocaloric diet, when combined with aerobic exercise, may be more effective than exercise alone in reducing low-density muscle and improving glycemic status (31). A recent systematic review and meta-analysis demonstrated that exercise was able to reduce lipid infiltration in skeletal muscle and increase the muscle attenuation coefficient (32). Benefits of the combined implementation of diet and exercise are also observed in individuals with T2DM, which raises the expectation of a combined improvement in myosteatosis and dysglycemia (20, 25).

An ongoing study aims to evaluate the combined effect of low-magnitude high-frequency vibration treatment and β-hydroxy β-methylbutyrate supplementation on

myosteatosis (33), based on an animal study that showed positive results (34).

The conduct of interventional studies on myosteatosis faces significant challenges due to the absence of standardized classification criteria for this condition. The standardization of criteria is crucial considering that myosteatosis can vary widely in terms of location, severity, and functional impact, which makes it difficult to compare and generalize results between different studies. Furthermore, the variation in diagnostic methods and the definition of inclusion and exclusion criteria can lead to inconsistent and sometimes contradictory results (35–37).

In view of this, a review study highlighted the need to develop robust and universally accepted criteria for the classification of myosteatosis, in order to allow a more accurate assessment of the effectiveness of therapeutic interventions. The lack of consensus on these definitions prevents the construction of a solid evidence base, essential for the development of effective clinical guidelines and for the advancement of knowledge in this area (36).

New drugs used in the treatment of T2DM and obesity, such as tirzepatide, may perhaps provide improvement in myosteatosis, given their results in the redistribution of body fat, with a reduction in ectopic fat (38).

8. THE RELEVANCE OF ASSESSING MYOSTEATOSIS

Despite the clear association between adiposopathy and T2DM, specific data on myosteatosis and changes in glycemic status gain relevance due to the direct pathophysiological relationship with T2DM and the apparently early contractile dysfunction that myosteatosis can cause (15, 16). The loss of muscle quality due to fat infiltration generates an early reduction in strength, apparently before leading to loss of muscle quantity, so there are prospects that the assessment of myosteatosis will gain visibility in the context of the assessment of sarcopenia and clinical practice (2, 3). Data from Mijkovic et al. (2020) (16) indicate that myosteatosis is associated with T2DM independently of abdominal fat. Therefore, the assessment of ectopic fat, especially that deposited in skeletal muscle, has been shown to have an important metabolic role, so that looking only at abdominal and peripheral fat may no longer be entirely sufficient.

The improvement of assessment techniques and the standardization of diagnostic criteria bring expectations of a greater and more useful approach to myosteatosis in the clinical management of patients with T2DM or at risk of developing it.

CONCLUSIONS

Myosteatosis represents a field of research with significant implications for public health. Observational studies have enriched the understanding of this pathology with regard to associated metabolic diseases and the tests used to quantify muscle fat accumulation. However, there is no standardization among the methods of measuring myosteatosis. Furthermore, for the conduction of the studies, it is necessary to take into account the demographic variations.

Therefore, there is a need for more research to establish standardized diagnostic criteria for myosteatosis and to define the pathophysiological mechanisms of this muscle disorder in the context of T2DM and other metabolic changes. Similarly, more intervention studies will be needed that address therapeutic strategies for these patients with muscle metabolic changes in a standardized way, aiming to establish the role and effectiveness of each intervention in managing these patients.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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