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Association between diagnostic imaging and biochemical markers: a possible tool for monitoring metabolic disorders

Danila Cianciosi[1], Yasmany Armas Diaz[1], Giuseppe Grosso[2], José L Quiles[3,4,5], Francesca Giampieri[1,4] and Maurizio Battino[1,4,6]

Metabolic syndrome (MetS), obesity, and diabetes mellitus (DM) are the most common metabolic disorders (MDs) in the world, characterized by abnormalities in body's metabolic processes. The typical diagnosis of MDs is usually executed by monitoring the levels of specific biochemical markers, but diagnostic imaging may provide valuable complementary information in MDs, offering advantages in diagnosis, target organ monitoring, follow-up, and development of new therapeutic approaches. The aim of this review is to summarize and discuss the studies published in the literature about the connection between images deriving from the diagnostic techniques and the key biochemical markers in the main MDs, in order to gain a comprehensive view of the different disorders.

Addresses
[1] Dipartimento di Scienze Cliniche Specialistiche e Odontostomatologiche - Università Politecnica delle Marche, Via Ranieri 65, Ancona 60130, Italy
[2] Department of Biomedical and Biotechnological Sciences, University of Catania, Catania, Italy
[3] Department of Physiology, Institute of Nutrition and Food Technology "José Mataix", Biomedical Research Center, University of Granada, Avda del Conocimiento s/n, Parque Tecnologico de la Salud, Armilla, Granada 18016, Spain
[4] Research Group on Foods, Nutritional Biochemistry and Health, Universidad Europea del Atlántico, Isabel Torres, 21, Santander 39011, Spain
[5] Research and Development Functional Food Centre (CIDAF), Health Science Technological Park, Avenida del, Conocimiento 37, Granada 18016, Spain
[6] International Joint Research Laboratory of Intelligent Agriculture and Agri-Products Processing, Jiangsu University, Zhenjiang 212013, China

Corresponding authors: Giampieri, Francesca (f.giampieri@univpm.it), Battino, Maurizio (m.a.battino@univpm.it)

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Introduction

Metabolic disorders (MDs) are different medical conditions characterized by abnormalities in body's metabolic process. In MDs, one or more of these metabolic processes may be impaired, leading to a wide range of symptoms and complications. MDs may involve disturbances in carbohydrate, lipid, protein, mineral, or nucleic acid metabolism. Metabolic syndrome (MetS), obesity, and diabetes mellitus (DM) are the most common widespread pathologies related with nutrition, that can affect both children and adults in developing and developed countries. They can be caused by inherited genetic defects, enzyme abnormalities, impairments in the transport of molecules, or other factors that interfere with normal metabolic pathways. These MDs can be congenital or can develop later in life due to environmental factors, diet, or other risk factors. MDs can affect several body systems and organs, including nervous, cardiovascular, and musculoskeletal systems, together with liver, pancreas, kidneys, and many others [1].

The typical diagnosis of MDs often involves laboratory tests to measure the levels of specific metabolites, the so-called biochemical markers, genetic analyses to identify genetic mutations, or functional tests to evaluate body's ability to carry out specific metabolic pathways [2]. Diagnostic imaging techniques, alongside biochemical marker monitoring, could provide valuable complementary information in MDs, offering numerous advantages in diagnosis, monitoring, follow-up, and development of new therapeutic approaches. Evaluating the association between imaging and biochemical markers can be extremely helpful in randomly identifying unexpected target organs, early detecting the severity or worsening of MDs, and measuring significant complications for subsequent treatment [3].

Computed tomography (CT), magnetic resonance (MR) imaging (MRI) or spectroscopy (MRS) X-rays, dual-energy X-ray (DXA), echocardiography, positron emission tomography, ultrasound (US), nuclear magnetic resonance, and single-photon emission computed tomography are the main potential diagnostic imaging techniques [4].

The aim of this review is to present the principal recent scientific articles, from the last 5 years about the

connection between images deriving from diagnostic techniques and the key biochemical markers in the main MDs with the aim of offering a complete overview and reinforce the concept that the combination of different medical information could be an excellent tool to provide a more complete and detailed view of these complex disorders.

The role of diet in metabolic disorders

An increased intake of energy-rich foods is considered a significant risk factor for the onset of MDs. Various studies have indeed demonstrated that the adoption of diets characterized by high consumption of sugars and/or fats can induce MetS, obesity, dyslipidemia, and insulin resistance [5].

The mechanisms underlying the pathogenesis are not yet fully understood, although, in recent years, the role of intestinal microbiota has emerged [6]. Overall, it has been observed that an unbalanced diet in terms of both quality and quantity, characterized by excessive consumption of ultraprocessed foods, sugary drinks, sweeteners, high-fat products, and a low intake of vegetables, fruits, cereals, and fish, can contribute to the development of chronic systemic inflammation that is the basis of MD pathogenesis. [7]. Diet plays a fundamental role not only in the onset but also in the management of MDs: in fact, the choice of specific foods and the control of dietary habits can positively impact the progression of these disorders [8].

In recent years, various observational and intervention clinical studies have been conducted to evaluate how different diets, primarily categorized as Western diet and Mediterranean Diet (MedD), can influence the onset, severity, and management of these MDs.

Among the most recent and significant studies related to MetS, in a clinical trial involving 70 adolescent girls (average age 14 years), the acute effect of MedD has been investigated for 12 weeks. The results showed that in the intervention group, there was a significant decrease in weight, body mass index (BMI), and waist circumference, as well as systolic blood pressure (SBP). Metabolic changes were also observed, including a reduction in fasting blood glucose, triglycerides (TG), low-density lipoprotein (LDL), and a significant increase in high-density lipoprotein (HDL). Additionally, a reduction in some inflammation markers, such as interleukin-6 and C-reactive protein (CRP), was noted [9]. Similarly, in another study involving 124 patients (with an average age of around 50 years) affected by MetS, the effects of the MedD or a standard low-fat diet for 12 months were measured on the key parameters of MetS, such as SBP and fasting plasma glucose, and HDL levels. The patients who followed the MedD showed a more significant improvement of these parameters [10]. Another clinical trial involving 70 obese women with MetS (aged 20–50 years) evaluated the effects of a low-carbohydrate diet (42–45% carbohydrates and 35–40% fats) followed for 3 months, against a standard weight-loss diet (52–55% carbohydrates and 25–30% fats), both with the same percentage of protein intake. The low-carbohydrate diet led to a more significant reduction in weight, BMI, waist circumference, and blood TG levels, as well as an increase in HDL levels compared with the other diet [11].

Regarding obesity, an interesting recent study investigated the effect of MedD compared with a regular diet in 82 subjects (average age 43 years) for 8 weeks. The results showed that in subjects who followed the MedD, there was a significant reduction in plasma cholesterol levels and a notable change in the intestinal microbiota composition, associated with a decrease in systemic inflammation and a reduction in insulin resistance and bile acid levels [12]. In general, there are various studies correlating the adherence to a healthy and balanced diet in obese subjects, showing that a significant intake of fruits and vegetables, such as the MedD suggests, improves many parameters associated with obesity, such as reduction of weight, BMI, and all biochemical markers associated with this condition [13]. A recent study, instead, compared the effect of the MedD alternated over time (8 weeks for each one) with a vegan diet in the same 62 obese subjects and observed that during the vegan diet period, there was a greater weight reduction and improvement in lipid concentration and insulin sensitivity [14].

The management of diabetes through diet is a crucial aspect in the care of this disease. A recent study compared the effects of a 12-week ketogenic diet and a MedD in 40 prediabetic and type-2 diabetes mellitus (T2DM) subjects. The results demonstrated that HbA1c levels decreased similarly in both diets, while the reduction in TG levels was greater in subjects who followed the ketogenic diet, along with lower levels of LDL and weight, and a more pronounced increase in HDL levels [15]. An interesting clinical trial conducted on 253 prediabetic adults aged 25–60 compared the effects of three different types of diets (MedD and two Chinese diets, one with a high intake of vegetables and another with low intake) for 6 months. A greater weight loss in subjects who followed both the MedD and the Chinese diet with a high plant intake, while no significant differences were found among the three groups regarding fasting blood glucose and insulin levels [16].

Metabolic syndrome

MetS is a complex condition involving multiple organs and systems: it is characterized by a combination of different risk factors, including abdominal obesity, hypertension, high blood sugar, high TG, and HDL

cholesterol levels [17]. It increases the likelihood of developing cardiovascular diseases (CVDs), T2DM, and other related conditions [17]. Diagnosis follows specific criteria from the International Diabetes Federation, requiring at least three risk factors, with central obesity being mandatory and two others published elsewhere [18]: diagnostic imaging techniques can aid in its diagnosis and follow-up [19].

One of the target organs of MetS is the cardiovascular system, since it is associated with an increased risk of atherosclerosis, hypertension, and coronary heart disease [20]. An interesting study evaluated the correlation between MetS and its classical blood biochemical markers with calcification of the abdominal aorta (AAC), which is usually asymptomatic and is discovered incidentally during imaging studies. This retrospective observational study included 2731 participants and evaluated AAC through DXA. A high correlation between the β-values of the AAC and HDL (odds ratio [OR]= 8.1, p = 0.047) was found [21]. Carotid intima media thickness (CIMT) is a measure used to assess the health of the carotid arteries, which is also associated with atherosclerosis processes with increased risk of CVDs and stroke or coronary heart disease. The measurement is often done through high-resolution US. In a recent study carried out on 862 adolescents, the increased CIMT (assessed by US) was closely correlated with a low amount of HDL (OR=2.98, p = 0.001) and with a high concentration of TG (OR=1.95, p = 0.051) in the blood. The predictive value of this relationship could help predict the risk of establishing MetS in adolescents with elevated CIMT values [22].

Adipose tissue plays a key role in MetS and is considered one of its target organs. Pathological changes in adipose tissue contribute to insulin resistance, inflammation, dyslipidemia, and other factors, increasing the risk of CVDs and T2DM. Understanding, evaluating, and managing adipose tissue are crucial in MetS prevention and treatment [23]. The assessment of abdominal periaortic fat and of the renal sinus fats could be similarly important in MetS. In a recent study, obese and nonobese subjects with and without a diagnosis of MetS underwent CT for the evaluation of these two components of visceral fat. The results showed a direct correlation between these fats and higher amounts of cholesterol, TG, as well as with aspartate aminotransferase (AST), alanine transaminase (ALT), and CRP [24]. In another observational study, intra-abdominal visceral fat was measured by US in 423 adolescents and was found to have a significant association with the diagnosis of MetS (p = 0.037), as well as with different biochemical parameters, such as low-plasma HDL (p = 0.034) and high TG levels (p = 0.012) [25].

MetS can have a significant impact also on liver health, being characterized by alterations in lipid and carbohydrate metabolism, which can adversely affect liver function. One of the most common hepatic manifestations of MetS is nonalcoholic fatty liver disease [26]. Three different liver quantitative parameters were analyzed from US images (n = 394 patients) and were compared with different biochemical parameters, resulting to be statistically correlated with high TG, LDL, ALT, and low HDL, giving a predictive meaning to this diagnostic imaging technique [27].

Moreover, MetS can increase the risk of developing pancreatic disorders such as pancreatitis and T2DM, since the accumulation of visceral fat can interfere with normal pancreatic function. The determination of pancreatic shear wave measurement (SWM) through US elastography, which allows to measure tissue stiffness, could be useful in the diagnosis of MetS [28]. In a study involving 125 patients with or without pancreatic steatosis, SWM was found to be positively correlated not only with high levels of pancreatic and hepatic steatosis, but also with the diagnosis of MetS and associated biochemical parameters, including TG levels (coefficient of correlation [cc]= 0.437, p = 0.000) [29].

Osteoarthritis is a degenerative joint disease that causes the deterioration of articular cartilage. Although it is primarily a joint disease, metabolic factors associated with MetS may contribute to the structural changes found in osteoarthritis [30]. Through MRI and X-ray, images were acquired in a study involving 435 participants for the evaluation of bone and cartilaginous structural abnormalities. Low HDL levels were associated with medial tibial loss (β = −0.21, confidence interval [CI]= 95%) and size of the spinal cord lesion (β = 1.65, CI=95%), which was also statistically associated with hypertriglyceridemia (β = 1.43, CI=95%) [31].

Table 1 summarizes the studies described above.

In conclusion, it can be stated that a broader future application of the combination of diagnostic imaging and biochemical parameters in patients with MetS could offer numerous advantages to both patients and physicians, albeit accompanied by some disadvantages. Specifically, for patients, this association may help to accurately identify MetS, enabling timely initiation of targeted personalized treatment. Early management of MetS helps to prevent or slow the development of serious complications such as T2DM, CVDs, and hypertension. The disadvantages for patients are the potential high economic costs and the fact that some diagnostic imaging tests may be uncomfortable or invasive.

For physicians, this association certainly leads to a more accurate and comprehensive diagnosis, along with specific monitoring, while one of the main disadvantages for medical personnel is undoubtedly the complexity, as

Table 1

Studies describing the association between imaging parameters and biochemical markers in people with MetS.

Subjects involved	Diagnostic imaging technique	Imaging parameters	Biochemical marker	Available statistical correlation values	Reference
2731 participants *(1343 males and 1388 females, mean age 58 years)*	DXA	AAC	HDL	OR= 8.1, p = 0.047	[21]
862 adolescents *(51.7% males and 48.3% females, mean age 18 years)*	US	CIMT	Low HDL TG	OR= 2.98, p = 0.001 OR= 1.95, p = 0.051	[22]
325 participants *(83 males and 242 females, mean age 41.2 years)*	CT	Abdominal periaortic fat Renal sinus fat	Cholesterol, TG, AS, ALT, and CRP	n.d. (positive correlation)	[24]
423 adolescents *(32.9% males and 67.1% females, mean age 16.1 years, from Brazil)*	US	Intra-abdominal visceral fat	Low HDL TG	p = 0.034 p = 0.012	[25]
394 patients *(151 males and 243 females, mean age 40.5 years)*	US	Three different liver quantitative parameters	TG, LDL, ALT, and low HDL	n.d. (positive correlation)	[27]
125 patients *(48 males and 77 females, mean age 43.38 years)*	US	Pancreatic SWM	TG	cc= 0.437, p = 0.000	[29]

DBP, diastolic blood pressure; n.d: not determined.

managing MetS requires a thorough understanding of its various manifestations, which often overlap with other conditions, necessitating interdisciplinary collaboration among physicians from different specialties.

Obesity

Obesity is an excessive accumulation of body fat compared with lean mass, caused by different factors such as excessive caloric intake, sedentary lifestyle, genetics, and environmental influences. At metabolic level, obesity can be characterized by a reduced sensitivity to insulin, that can lead to high blood sugar levels, T2DM, and other MDs [32]. The main biochemical markers to monitor obesity include lipid profile, CRP, glucose, insulin, leptin, and adiponectin. Obesity, too, can affect different organs, increasing the risk of developing several medical complications and conditions [33].

In obesity, adipose tissue is the main organ involved. The excessive accumulation of fat can occur in different areas of the body, especially in the abdomen, hips, and thighs [34]. In a study involving 167 volunteers, serum leptin levels were significantly correlated with subcutaneous (cc=0.823, p = 0.001), visceral (cc=0.703, p = 0.001), and abdominal fat (cc=0.831, p = 0.001) from images obtained through MRI [35]. Similarly, in a population of 76 volunteers, 13 of whom were obese, TG levels were found to be correlated with abdominal fat (r = 0.445, $p < 0.00$), visceral fat (r = 0.592, $p < 0.00$), and subcutaneous fat (r = 0.340, $p < 0.05$) measured with MRI and MRS. HDL levels were also correlated to these three types of fat showing indices of r = –0.453, r = –0.484, and r = –0.386 respectively, all with $p < 0.00$ [36].

Hepatic steatosis is also a crucial condition in obese subjects, a risk factor for the onset of non-alcoholic fatty liver disease especially in children and adolescents [37]. A high association between hepatic steatosis, diagnosed by US, and various biochemical markers, was observed in 177 children, 100 of whom were obese. Hepatic steatosis was found to be correlated with serum levels of HDL (OR=0.96, CI=95%), TG (OR=1.005, CI=95%), AST (OR=1.03, CI=95%), ALT (OR=1.03, CI=95%), and TG-glucose index (OR=4.047, CI=95%) [38].

Obesity is a significant risk factor for cardiovascular issues, such as atherosclerosis, heart failure, and excessive production of pro-inflammatory cytokine from adipose tissue [39]. In 319 obese subjects, a clear correlation was demonstrated between the left ventricular ejection fraction (LVEF), measured by echocardiography, and hypoadiponectinemia (r = 0.60, p = 0.001) [40]. Similarly, in 50 patients, a strong positive correlation was observed between chemerin and some cardiac parameters measured by echography and US, such as CIMT (r = 0.404, p = 0.050), systolic thickness of the media (r = 0.492,

$p = 0.015$), and diastolic thickness (r = 0.620, $p = 0.001$). These three parameters also showed a correlation with the ratio between chemerin/adiponectin with values of r = 0.447, $p = 0.025$ and r = 0.480, $p = 0.015$, respectively, for these two parameters [41].

Accumulating evidence demonstrates that there are some functions of the central nervous system that could be affected by obesity [42]. In this regard, a recent study involving 171 elderly participants found that cognitive functions in obese (specifically the volume of the hippocampus observed through MRI) were negatively associated with leptin levels (r = –2.60, $p = 0.045$) [43]. Similarly in an elderly population of 748 people, gray matter volume, observed by MRI, was negatively associated with some metabolic parameters, such as leptin, hemoglobin A_{1c} (HbA_{1c}), CRP, and BMI and positively with adiponectin (single statistical correlation data n.d) [44].

The studies described above are summarized in Table 2.

Based on the findings from the analyzed studies, the association between diagnostic imaging and biochemical parameters in obese patients offers advantages and disadvantages similar to those observed in MetS. Specifically, the combined use of this clinical information is significantly helpful in personalized treatment, as a better understanding of adipose tissue distribution along with the associated evaluation of biomarkers allows obese patients to receive personalized treatment for weight management and metabolic health improvement. Another advantage is the rapid assessment of possible complications, especially at the cardiovascular level, through the evaluation of visceral fat. Among the disadvantages for patients, there are the same ones mentioned in the paragraph on MetS. For physicians, once again, the most significant disadvantage is the need for a multidisciplinary approach to the combined evaluation of the obtained results.

Diabetes

DM is a MD characterized by hyperglycemia due to insulin production defects or insufficient action. DM types include type-1 diabetes mellitus (T1DM), T2DM, and gestational diabetes mellitus. There are several biochemical markers that are used to diagnose and monitor diabetes, including blood sugar, HbA_{1c}, and lipid profile. Diabetes can cause several long-term complications, including CVDs, kidney and pancreas disease, neuropathies, retinopathies, foot, dental and bone problems, and more. Adequate control of blood parameters, together with careful management of related risk factors, with the help of diagnostic imaging, could be essential to prevent or delay these complications [45].

People with diabetes have a higher incidence of CVDs than the general population [46]. In a study involving 50 patients with DM (< 60 years), two different parameters obtained through US images of carotid artery plaques and of its neovascularization were correlated with serum levels of HbA_{1c} (cc=0.565, $p = 0.000$; cc=0.563, $p < 0.001$; cc=0.472, $p < 0.005$) and blood glucose (cc 0.467, $p = 0.001$; cc=0.458, $p = 0.002$; cc=0.264, $p = 0.076$) [47].

Myocardial fibrosis is a cardiovascular complication that can occur in DM patients. In a study involving 84 T2DM patients, HbA_{1c} levels were predictive of this hypertrophic cardiomyopathy, being to be positively correlated with the severity of myocardial fibrosis assessed by cardiac MR (OR=2.00, $p = 0.014$) [48]. Again, at the myocardial level, a ventricular dyssynchrony status, monitored by echocardiography, was correlated with serum levels of HbA_{1c} (OR=2.21, $p < 0.05$) and CRP (OR=2.09, $p < 0.05$) in 91 patients with T2DM [49]. In a large study involving 1654 participants, 354 of whom were DM patients (type 1 and 2), the value of AAC obtained by DXA was positively correlated with the TG-glucose index (OR=1.08, $p = 0.127$) [50].

Excessive body fat is a risk factor for several MDs including diabetes [51]. One study observed that the thickness of intra-abdominal (peritoneal and subcutaneous) fat detected with US imaging could be a predictor of insulin resistance, since it turned out to be positively correlated in 399 participants to various serum biochemical parameters. Specifically, peritoneal fat thickness was found to be related to fasting serum insulin levels (cc=0.39, $p < 0.005$), TG (cc=0.21, $p < 0.005$), and HDL (cc=–0.30, $p < 0.005$). The thickness of skin fat was similarly correlated to the same previous parameters with the following values: cc= 0.27, $p < 0.005$, cc= 0.35, $p < 0.005$, and cc= –0.28, $p < 0.005$ and of LDL, respectively (cc=0.19, $p < 0.05$) [52]. Additionally, the volume of visceral adipose tissue, assessed by CT, in 75 women with prediabetes or T2DM (> 45 years), was found to be correlated with the levels of TG (cc=0.309, $p = 0.007$), HDL (cc=–0.335, $p = 0.003$), and fasting blood glucose (cc=0.292, $p = 0.011$) [53].

The main target organ of diabetes is the pancreas [54]. In a recent study involving 50 children with T1DM, pancreatic stiffness measured by US fibroscan correlated with % HbA_{1c} (r = 0.301, $p = 0.03$), fasting C-peptide levels (r = - 0.542, $p < 0.001$), LDL (r = 0.533, $p < 0.001$), and cholesterol (r = 0.596, $p < 0.001$) [55].

Diabetic nephropathy is a common complication of diabetes and a major cause of chronic kidney disease [56]. In a study involving 57 patients with T2DM, microstructural measures of the kidneys measured with MRI and expressed as the apparent diffusion coefficient were positively correlated with the levels of HbA_{1c} (r = 0.414, $p < 0.000$) and blood glucose (r = 0.417, $p < 0.000$) [57].

Table 2

Studies describing the association between imaging parameters and biochemical markers in people with obesity.

Subjects involved	Diagnostic imaging technique	Imaging parameters	Biochemical marker	Available statistical correlation values	Reference
167 volunteers *(83 males and 84 females, mean age 27.2 years, from Giordania)*	MRI	Subcutaneous adipose tissue	Leptin	cc= 0.823, p = 0.001	[35]
		Visceral adipose tissue	Leptin	cc= 0.703, p = 0.001	
		Abdominal adipose tissue	Leptin	cc= 0.831, p = 0.001	
76 volunteers *(29 males and 47 females, mean age 21.5 years, from Thailand)*	MRI/MRS	Abdominal adipose tissue	TG	r = 0.445, p < 0.00	[36]
			HDL	r = –0.453, p < 0.00	
		Visceral adipose tissue	TG	r = 0.592, p < 0.00	
			HDL	r = –0.484, p < 0.00	
		Subcutaneous adipose tissue	TG	r = 0.340, p < 0.05	
			HDL	r = –0.386, p < 0.00	
177 children *(111 males and 66 females, mean age 8.9 years from Mexico)*	US	Hepatic steatosis	HDL	OR= 0.96, CI= 95%	[38]
			TG	OR= 1.005, CI= 95%	
			AST	OR= 1.03, CI= 95%	
			ALT	OR= 1.03, CI= 95%	
			TG-glucose index	OR= 4.047, CI= 95%	
319 participants *(176 males and 143 females, mean age 38.8 years + 18 children males, mean age 58.4 years)*	Echocardiography	LVEF	Low adiponectin	r = 0.60, p = 0.001	[40]
50 patients *(68 males and 84% females, mean age 41.3 years)*	Echography/US	CIMT	Chemerin	r = 0.404, p = 0.050	[41]
			Chemerin/adiponectin	r = 0.447, p = 0.025	
		Systolic thickness of the media	Chemerin	r = 0.492, p = 0.015	
			Chemerin/adiponectin	r = 0.480, p = 0.015	
		Diastolic thickness	Chemerin	r = 0.620, p = 0.001	
			Chemerin/adiponectin	r = 0.480, p = 0.015	
171 elderly participants *(48 males and 123 females, mean age 74.3 years)*	MRI	Volume of the hippocampus	Leptin	r = –2.60, p = 0.045	[43]
748 elderly participants *(416 males and 332 females, mean age 68.4 years)*	MRI	Gray matter volume	Leptin, HbA_{1c}, CRP, and adiponectin	n.d. (negative correlation with leptin, HbA1c, and CRP) (positive correlation with adiponectin)	[44]

aPWV, aortic pulse wave velocity; RNFL, retinal nerve fiber layer.

Table 3

Studies describing the association between imaging parameters and biochemical markers in people with diabetes.

Subjects involved	Diagnostic imaging technique	Imaging parameters	Biochemical marker	Available statistical correlation values	Reference
50 patients with DM (1 & 2) *(5 males and 45 females, mean age 56.8 years)*	US	Carotid artery plaque parameter 1	HbA_{1c}	cc= 0.565, $p = 0.000$	[47]
			Blood glucose	cc 0.467, $p = 0.001$	
		Carotid artery plaque parameter 2	HbA_{1c}	cc= 0.563, $p < 0.001$	
			Blood glucose	cc= 0.458, $p = 0.002$	
		Neovascularization of the plaques	HbA_{1c}	cc= 0.472, $p < 0.005$	
			Blood glucose	cc= 0.264, $p = 0.076$	
84 T2DM patients *(33 males and 51 females, mean age 58.2 years)*	Cardiac MR	Myocardial fibrosis	HbA_{1c}	OR= 2.00, $p = 0.014$	[48]
91 T2DM patients *(53 males and 38 females, mean age 44.5 years)*	Echocardiography	LV dyssynchrony	HbA_{1c}	OR= 2.21, $p < 0.05$	[49]
			CRP	OR= 2.09, $p < 0.05$	
1654 participants (354 with DM type 1 or 2) *(690 males and 964 females, mean age 57.5 years)*	DXA	Value of AAC	TG-glucose index	OR= 1.08, $p = 0.127$	[50]
399 participants *(173 males and 226 females, mean age 36.7 years)*	US	Peritoneal fat thickness	Insulin	cc= 0.39, $p < 0.005$	[52]
			TG	cc= 0.21, $p < 0.005$	
			HDL	cc= −0.30, p < 0.005	
		Thickness of skin fat	Insulin	cc= 0.27, $p < 0.005$	
			TG	cc= 0.35, $p < 0.005$	
			HDL	cc= −0.28, $p < 0.005$	
			LDL	cc= 0.19, $p < 0.05$	
75 women with prediabetes or T2DM *(mean age 61 years)*	CT	Volume of visceral adipose tissue	TG	cc= 0.309, $p = 0.007$	[53]
			HDL	cc= −0.335, $p = 0.003$	
			Fasting blood glucose	cc= 0.292, $p = 0.011$	
50 children with T1DM *(22 males and 28 females, mean age 13 years)*	US fibroscan	Pancreatic stiffness	HbA_{1c}	r = 0.301, $p = 0.03$	[55]
			Fasting C-peptide	r = - 0.542, $p < 0.001$	
			LDL	r = 0.533, $p < 0.001$	
			Cholesterol	r = 0.596, $p < 0.001$	
57 T2DM patients *(30 males and 27 females, mean age 60.3 years)*	MRI	Apparent diffusion coefficient of the kidneys	HbA_{1c}	r = 0.414, $p < 0.000$	[57]
			Blood glucose	r = 0.417, $p < 0.000$	
614 T2DM patients *(55.5% males and 44.5% females, mean age 62.4 years)*	MRI	Gray matter volume	Blood glucose	$\beta = -0.053$, $p < 0.04$	[59]

LV, left ventricle.

Diabetes has been associated also with an increased risk of developing cognitive problems and dementia. People with diabetes may have a higher risk of cognitive decline, memory impairment, and problems in concentrating or performing complex mental tasks [58]. A study involving 614 patients with T2DM observed that gray matter volume, measured by MRI, was negatively associated with plasma glucose levels ($\beta = -0.053$, $p < 0.04$) [59].

The studies described above are summarized in Table 3.

In conclusion, regarding diabetes, the association between diagnostic imaging and biochemical parameters, in addition to the general advantages and disadvantages mentioned for other MDs, offers a significant advantage, especially for the patients, in preventing complications such as cardiac problems, neuropathies, and retinopathies.

Conclusions, limitations, and future remarks

MDs are a diverse and complex group of diseases affecting body's metabolic process. The severity, the age of onset, and target organs make diagnosis and management challenging. This review highlights that combining diagnostic imaging techniques with classic biochemical markers offers detailed information on affected organs, can detect complications early, prevent further damage, and aid in developing new therapies. The studies on MetS, obesity, and DM found significant correlation between parameters from various diagnostic imaging techniques and classic biochemical markers specific for these MDs. This provides a starting point to potentially standardize parameters for diagnosing, monitoring, and following up on MDs in the future.

In this field, the main limitations include

(i) variability in biochemical markers and images, affecting result accuracy: indeed, there is intraindividual variability, as an individual's biological response can vary over time, and the levels of certain biochemical markers can be influenced by various nonpathological factors. There is also interindividual variability: people may exhibit significant variations in their levels of biochemical markers due to genetic factors, age, lifestyle, and the presence of preexisting medical conditions. Diagnostic images can also be subjected to variability due to factors such as equipment quality, imaging technique, patient positioning, and operator expertise.

(ii) cost and complexity in conducting studies with both parameters: the management and interpretation of data from both types of tests require specialized personnel, such as laboratory technicians, radiologists, and highly qualified healthcare professionals. The training and compensation of this personnel contribute to the overall study costs. Additionally, coordinating the collection of biochemical samples, conducting diagnostic analyses, and integrating data require thorough planning and careful organization. The processing and analysis of data from various sources necessitate sophisticated computer platforms and can escalate data management costs.

(iii) small sample sizes may lack representativeness or statistical power: when sample sizes are small, there is a risk that the composition of the sample may not accurately reflect the diversity present in the reference population. This can compromise the representativeness of the obtained results. In smaller samples, random variability can have a significant impact. A limited number of participants can lead to results that are more susceptible to random effects, affecting the validity and generalizability of studies. The reduced sample size limits the statistical power of the study, that is, the ability to detect significant differences, if present. This can compromise the study's ability to draw robust and generalizable conclusions.

(iv) uncontrolled confounding effects in the study: confounding occurs when an external factor influences both the independent variable (biochemical markers and diagnostic analyses) and the dependent variable (study outcomes), generating a spurious or distorted association between them.

(v) noncausal relationships between markers and images may require further investigation: integrating detailed clinical data and information about the participants' health status can help distinguish between casual correlations and actual causal relationships.

(vi) publication bias may influence available literature: if studies with positive results are more likely to be published, the scientific literature may present a distorted and misleading picture of the actual association between biochemical markers and diagnostic analyses. This can lead to an overestimation of the real effect. The adoption of transparent research practices and the promotion of an open scientific culture are essential to reduce this type of bias.

Though few studies have focused on the correlation between imaging parameters and biochemical markers in MDs, it is a growing research field. Advancements in technology and artificial intelligence integration may drive more future research. This could enhance our understanding of MD pathogenesis and lead to new diagnostic and therapeutic approaches.

Data Availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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