Supplementary Table S1. PICO spreadsheet.

Author / Year	Study type	Blinding	N	Characteristic	Age (years)	Sex	Intervention	Outcome
Abd El-Mottaleb et al. (2019) [25]	Cross-sectional	Not applicable	86	Myocardial infarction group (MI = 33); Myocardial infarction with heart failure group (MIHF = 33) ; Control group (CG = 20).	CG = 54,15; MI = 57,67; MIHF = 57.24	Not informed	Anthropometric parameters, serum levels of irisin, serum levels of adipokines, blood pressure, lipid profile, heart rate per min and ventricular ejection fraction were analyzed in all groups	Lower risk levels of irisin in MI and MIHF compared to control; Concentration of irisin inversely related to cardiac biomarkers (troponin-I, CK-MB), with TNF-alpha, LDL and triglycerides; Positively related to HDL and left ventricular ejection fractions in MI and MIHF.
Agh et al. (2017) [44]	Intervention	double-blind	45	Intervention group (IG = 24); Control group (CG = 21). Present> 50% stenosis in at least one major coronary artery.	IG = 55; CG = 57.76.	100% M	CG received 4 capsules / day of edible paraffin gel; IG received 4 capsules / day of omega-3 (720mg EPA and 480mg DHA). Both groups should consume two capsules at lunch and two at dinner, for 8 weeks.	Omega-3 supplementation reduced LDL levels, C-reactive protein levels. IG showed higher levels of irisin
Anaszewicz et al. (2019) [21]	Cross-sectional	Not applicable	245	Patients with atrial fibrillation (AF = 80) Control group with no history of atrial fibrillation (CG = 165)	FA = 69.5; CG = 69.2	FA = 41% M, 59% F GC = 88% M, 12% F	Analysis of levels of leptin, ADP, TNF-alpha, irisin and nutritional parameters by BIA.	Elevated leptin levels increase the risk of AF; Mild correlation between higher levels of adiponectin and reduced risk of AF; Relationship between irisin levels and reduced risk of AF
Aronis et al. (2015) [39]	Case-control and prospective cohort	Not applicable	349	A case-control study selected 88 patients diagnosed with acute coronary syndrome (ACS) and 158 healthy patients (C). In the cohort study, 103 patients were selected who underwent percutaneous coronary intervention and were followed for 12 months from admission, without other comorbidities.	Case-control: case = 67.2; control = 65.6 / Cohort: 63.6	Case-control: 100% M; Cohort: 81.5% M, 18.5% F.	Evaluation of anthropometric variables, insulin and glucose levels, levels of irisin and lipid profile. In the case-control study, the participants' serum leptin level was also analyzed. Both studies aimed to analyze the relationship between irisin levels and the worsening of cardiovascular diseases.	Case-control study: Correlation between the levels of irisin and leptin, however, there were no significant correlations with other variables analyzed. Cohort study: Relationship between levels of irisin in patients who underwent percutaneous coronary intervention.
Belviranli et al. (2016) [24]	Cross-sectional	Not applicable	20	Obese women (OW = 10); Control women with normal weight (NWW = 10)	OW = 34; NWW = 28.	100% F	Analysis and comparison of anthropometric measurements, plasma irisin level and insulin resistance markers (glucose, insulin and HOMA-IR)	Negative correlation between BMI and irisin level; Negative correlation of levels of irisin and insulin and HOMA-IR.
Bonfante et al. (2017) [23]	Cross-sectional	Not applicable	20	High irisin group (HIG = 11); Small irisin group (SIG = 9)	HIG = 49.09; SIG = 48	100% M	Analysis of biochemical markers (lipid profile, glycated hemoglobin, HOMA-IR), the risk of developing DM2, serum levels of adipokines, irisin and anthropometry.	Obese people with a higher concentration of irisin have a better metabolic profile, less risk of developing DM2 and lower levels of lipopolysaccharides (LPS).
Campolo et al. (2020) [33]	Cross-sectional	Not applicable	60	The participants had grade I or II obesity.	59	48.3% M, 51.7% F.	Evaluation of cardiovascular risk factors, anthropometric parameters, lipid profile, HOMA, regarding the level of physical activity and levels of irisin.	Women had higher values of irisin than men; Direct relationship between the levels of irisin and insulin resistance, in both genders, but they present gender-related differences when related to anthropometry, body composition and the metabolic condition of the participant. Irisin levels are also related to markers of visceral adiposity in men, but not in women.
Deng (2016) [27]	Cross-sectional	Not applicable	564	Coronary Artery Disease Group (CAD = 350); Healthy control group (CG = 214).	CAD = 60.33; CG = 59.3	CG = 55.1% M, 44.9% F; CAD = 54.3% M, 45.7% F.	Analysis of the serum level of irisin. In the CAD group, the coronary atherosclerosis index was evaluated.	Lower serum irisin concentration in CAD compared to CG. Negative correlation of the level of irisin with the ACI in the ACD group.
El-Lebedy et al. (2018) [22]	Cross-sectional	Not applicable	205	Type 2 Diabetes Group (DM2 = 68); Type 2 Diabetes + Cardiovascular disease group (DM2 + CVD = 68); Healthy control group (CG = 70)	DM2 = 51.6; DM2 + CVD = 55.6 anos; CG = 53.1	DM2 = 38% M, 62% F; DM2 + CVD = 36% M, 64% F; CG = 33% M, 67% F	Analysis of biochemical markers (lipid profile, glycated hemoglobin, HOMA-IR) and serum levels of irisin and vaspine.	Relationship between plasma vaspine levels and incidence in the DM2 + CVD group; Lower level of irisin in the DM2 group compared to CG and DM2 + CVD
Emanuele et al. (2014) [26]	Cross-sectional	Not applicable	437	Healthy centenarians (HC = 79); 178 were non-diabetics who suffered from myocardial infarction (MI) Healthy volunteers (HV = 180).	HC = 102; MI = 33.5 anos; HV = 33 anos	55.6% M, 44.4% F	Analysis of irisin concentration and odds ratio.	Higher levels of irisin in HC followed by HV and MI.
Hou et al. (2015) [32]	Cross-sectional	Not applicable	81	Obesity group (OB = 41) Eutrophic group as control (GE = 40)	OB = 33; GE = 31	OB = 48.7% M, 51.2% F; GE = 47.5% M, 52.5% F	Evaluation of anthropometry, lipid profile and endothelial function.	Group OB (non-diabetic and non-hypertensive) showed lower values of irisin than the individuals in the GE.
Hsieh et al. (2018) [43]	Cohort	Not applicable	399	Patients who suffered myocardial infarction due to ST segment elevation (STEMI) were selected. Within the cohort study, an analysis was made of a subgroup (72 participants) who underwent percutaneous intervention, who were analyzed for levels of irisin 6 times (0h, 8h, 16h, 3d, 7d, 28d). All participants were followed for 3 years.	58	56.9% M, 43.1 F	Patients were followed up for 3 years, evaluating the STEMI outcomes and the relationship between the participants' levels of irisin and these outcomes. Within this group, a subgroup of 72 participants was created, who underwent percutaneous coronary intervention, who were evaluated for levels of irisin in the moment after PCI.	Association between high risks levels of irisin and rates of cardiovascular events in patients who had previous STEMI. Over the 3-year follow-up, patients who had more high-risk levels also experienced some cardiovascular events. The patients in the subgroup showed a significant reduction in the level of irisin after STEMI with PCI, for up to 3 days after the event, but between 7 and 28 days of analysis there was no significant change.
Huerta et al. (2015) [46]	Intervention	double-blind	73	Participants were overweight or obese women, with no associated comorbidities. All received nutritional intervention (orientation to a diet restricted in energy aiming at weight reduction), there was the intervention divided between the groups: (1) control, received a placebo; (2) EPA - intervention; (3) alpha lipoic acid - intervention; (4) EPA + alpha lipoic acid. All groups underwent the intervention for 10 weeks	38,5	100% F	Nutritional intervention according to each group	Reduction of irisin levels (between baseline and the end of the intervention), due to a restrictive and low-calorie diet. Relationship between fasting irisin and fasting glucose, however, even with sudden changes in glucose and / or insulin levels, there was no change in irisin, Oral supplementation with alpha lipoic acid capsules and EPA had no effect in reducing irisin.
Kalkan et al. (2018) [19]	Cross-sectional	Not applicable	86	Heart failure patients with reduced ejection fraction. Cardiac cachexia group (GCC; n = 44) Control group without cachexia (CG; n = 42)	GCC = 65 GC = 61	GCC = 61.4% M, 38.6% F GC = 64.3% M, 35.7% F	Analysis of adropin and irisin and other laboratory parameters	Higher serum levels of adropin and irisin in the GCC compared to the GC; inverse association between irisin and BMI
Khorasani et al. (2019) [30]	Case-control	Not applicable	60	Voluntary participants - diabetic and divided into: Diabetic group (DM = 30) Diabetic patients group with cardiovascular disease (DM + CVD = 30)	DM = 54.5; DM + CVD = 57.7	DM = 30% M, 70% F; DM + CVD = 43.3% M, 56,7% F	Analysis of cardiovascular markers, lipid profile, HOMA, insulin, glycated hemoglobin and serum levels of irisin.	Lower level of irisin in the DM + CVD group compared to the DM group. High levels of irisin in relation to BMI, and more Low risks according to the time of diagnosis of diabetes and age. Positive relationship between irisin levels and insulin levels and inversely associated with LDL values in diabetics.
Ko et al. (2016) [38]	Cross-sectional	Not applicable	196	Patients were overweight or obese	46	49% M, 51% F	Evaluation of anthropometric variables, dietary patterns, dietary quality, risk markers of cardiometabolic diseases (leptin, ICAM, c-reactive protein) and levels of irisin	The DASH and AHEI-10 diets showed scores inversely related to body weight, BMI, body fat, waist circumference and C-reactive protein. DASH scores were found to be related to irisin levels. Values of leptin, ICAM and C- reactive protein are directly related to a less healthy diet (rich in CHO, alcohol and fats).
Liu et al. (2016) [45]	Intervention	Not applicable	89	Diabetic group (T2D = 51), where patients were newly diagnosed (last 3 months) and still did not receive any antidiabetic medication. Control group (C = 38) was formed by non-diabetic obese participants.	C = 44.58; T2D = 4393	C = 50% M, 50% F; T2D = 54.9% M, 45.1% F	T2D group, recently diagnosed with DM2, started treatment with exenatide. All participants were assessed for levels of irisin, lipid profile, and insulin-related variables.	Obese patients newly diagnosed with DM2 had significantly lower irisin values. Furthermore, in these patients, irisin showed an inverse correlation with BMI, fasting glucose, and glycated hemoglobin. The use of the drug (exenatide) showed an improvement in patients, helping to regulate the metabolism, increasing the levels of irisin, and maintaining the inverse correlation, reducing the values of fasting glucose and glycated hemoglobin.

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Panagiotou et al. (2014) [47]	Cross-sectional	Not applicable	39	Participants were selected from a parallel study and were expected to have diabetes or two cardiovascular risk factors. 3 clippings of the parallel study were made (with the same participants, 3 moments - baseline, 3 months, and 6 months)	64	64% M, 36% F	Evaluation of body variables, lipid profile, levels of irisin and ominitin-1; Correlation analysis between hormones and CVD risks was performed	There were no correlations between irisin and ominitin-1 and markers of insulin resistance, BMI, blood pressure.
Saadeldin et al. (2018) [29]	Case-control	Not applicable	69	Healthy control group (CG = 8); Type 2 diabetes group + Atherosclerosis (DM2 + TA = 39); DM2 group (DM2 = 22)	CG = 45.53; DM+TA = 49.95; DM2 = 47.59	100% F	Analysis of cardiovascular risk markers, lipid profile, glycated hemoglobin, HOMA-IR, blood pressure, irisin, and sclerostin levels.	Relationship between sclerotin and irisin in all groups.
Sahin-Efe et al. (2018) [34]	Cross-sectional and prospective case-control	Not applicable	263	A cross-sectional study recruited 111 obese and 105 non-obese individuals. Of this total, 4 groups were formed: Non-obese (NOB = 73); Non-obese diabetics (NOBDM = 38); Obese (OB = 41); Diabetic obese (OBDM = 64). 40 case-control studies were selected: Diabetics (DM = 40); Control group (C = 140)	NOB = 69.5, NOBDM = 66.9, OB = 69.4, OBDM = 67.7 / Case-control DM = 70.1; C = 70.0	100% M	Assessment of anthropometry, lipid profile, fasting glucose, levels of irisin and leptin.	There were no differences or significant reduction in irisin levels, contrary to the findings of other articles. It is concluded that irisin would not be involved with the risks of CVD and the onset of diabetes.
Sanchis-Gomar and Perez-Quilis (2014) [11]	Cross-sectional	Not applicable	153	153 patients were selected for the study, these were divided into 5 groups: Control (C = 20); Obese morbid with atherogenic dyslipidemia (MOAD = 34); Obese obese without atherogenesis (MO = 35) ia; Non-diabetic or overweight (NOD = 30); Diabetic obese (OD = 34).	C = 53.1, MOAD = 40.97, MO = 41.12, NOD = 64.24, OD = 61.65	C = 55% M, 45% F, MOAD = 38.2% M, 61.8% F, MO = 26.6% M, 71.4% F, NOD = 56.7% M, 43.3% F, OD = 34.3% M, 64.7% F	Evaluation of anthropometric variables, HOMA, lipid profile, and levels of irisin.	In this study, no correlations were found between levels of irisin and BMI, nor significant differences between levels of irisin between groups.
Sesti et al. (2014) [35]	Cross-sectional	Not applicable	192	The study group was composed of 192 non-diabetic participants and with no history of cardiovascular disease. One of the parents of all participants should present a diagnosis of DM2. Participants were drawn from a cohort of the European project EUGENE2	39	52.6% M, 47.4% F	Evaluation of anthropometric variables, lipid profile, insulin dosage variables, and the average thickness of the carotid artery (as a risk marker for atherosclerosis).	Positive correlation between levels of irisin and BMI and body fat. The older you are, the lower your irisin levels. Irisin levels were inversely proportional to insulin sensitivity, even adjusting the data by age and sex. There was no significant difference between the values presented between the sexes.
Shen et al. (2017) [28]	Cohort	Not applicable	161	Patients with acute heart failure with High irisine (HI = 69); Low irisin (LI = 92).	HI = 62; LI = 56	HI =51.7% M, 49.3% F; LI = 71.7% M, 28.3% F	Analysis of cardiovascular risk markers, levels of irisin, and the relationship of irisin to markers and outcomes.	1-year follow-up with the death of 42 participants. Death patients had higher levels of irisin than those who completed the study suggesting death risk markers. No relationship between irisin and other markers of comorbidities.
Shi et al. (2016) [37]	Cross-sectional	Not applicable	1115	The study is based on the baseline of a cohort study, where the participants are adults and obese without other comorbidities. Of the 1115 patients selected to participate in this study, 448 had no insulin resistance (NRI) and 667 had insulin resistance (IR)	NRI = 52.8; IR = 53.4	31.3% M, 68.7% F	Evaluation of anthropometric variables, lipid profile, HOMA, glycated hemoglobin, and irisin levels.	The IR group also showed higher values of adiposity than the NRIs, in addition, they presented a reduction in the levels of irisin.
Shoukry. et al. (2016) [42]	Cross-sectional	Not applicable	300	Participants were divided into 2 large groups: Individuals with DM2 and without DM2 (n = 150 in each). The group without DM2 was subdivided into 3 groups according to their BMI: normal weight (BMI 18.5-24.9 kg / m² - n = 31); overweight (BMI 25-29.9 kg / m² - n = 42); and obese (BMI ≥ 30 kg / m² - n = 76).	DM2= 47.34; normal weight = 45.1; overweight = 47.4; obese = 46.9	DM2 = 55.3% M, 44.7% F; normal weight = 58.1% M, 41.9% F; overweight = 58.1% M, 41.9% F; obese = 55.3% M./44.7% F	Anthropometric assessment, body composition and biochemical parameters such as plasma levels of irisin, complete lipid and glycemic profile, GFR, urea and creatinine.	Higher irisin levels in the control group (without DM2). In this group, obese individuals had higher levels of serum irisin compared to the group with low-risk weight. The obese in the control group had the IR markers higher than those of lower weight.
Silvestrini et al. (2019) [40]	Cross-sectional	Not applicable	40	Forty patients were selected who underwent cardiac failure, diagnosed early. These participants were divided into two groups: Group that suffered heart failure and had a reduction in ejection (HFeEF = 18); Group that suffered heart failure and maintained ejection preserved (HFpEF = 22)	HFeEF = 69.2; HFpEF = 75.7	HFeEF = 83.3% M, 16.7% F; HFpEF = 63.6% M, 36.4% F	Analysis of irisin levels and correlation with total antioxidant activity.	Negative (but very weak) correlation between irisin levels and total antioxidant activity in the HFpEF group. Correlation between levels of irisin and patients in the HFpEF group when compared to the other group.
Stengel et al. (2013) [41]	Cross-sectional	Not applicable	40	Patients were divided into 5 groups of 8 individuals in each: Anorexia nervosa (BMI less than / equal to 17.5 kg / m²); normal weight (BMI between 18.5-25Kg / m²); Obesity (30-40Kg / m²); Obesity (40-50Kg / m²); Obesity (greater than 50 kg / m²).	Anorexia = 26.1; normal weight = 48.5; Obesity (30-40Kg / m²) = 48.3; Obesity (40-50Kg / m²) = 47.3; obesity (greater than 50 kg / m²) = 45.9	50% M, 50% F	Analysis of body composition (BIA) and plasma levels of irisin, albumin, proteins, ghrelin, cortisol, TSH, glucose, insulin, and CRP.	Higher levels of irisin in obese patients compared to individuals with anorexia and normal weight. The level of irisin also demonstrated a positive relationship with the percentage of fat.
Tang et al. (2019) [31]	Cross-sectional	Not applicable	524	524 participants without diabetes, where BMI data were separated into groups. Eutrophic group (EUT = 230); Overweight / obesity group (SOB = 294).	EUT = 56.74; SOB = 57.14	Not informed	Evaluation of anthropometric markers, biochemical markers, lipid profile, irisin levels.	Individuals in the SOB group had lower levels of irisin. Irisine levels also showed a negative relationship with fasting HOMA and insulin values.
Vamvini et al. (2013) [20]	Cross-sectional	Not applicable	164	Cyprus Metabolism study selection (n = 150) Analysis of irisin and FNDC5 expression (n = 14)	Health group = 18.48; Obese group = 53.14	Health group = 100% F; Obese group = 57.14% M, 45.86% F	Serum analysis of irisin, phospholitin, activin A and myostatin and analysis of the expression of the precursor genes of these myosins.	Correlation between myosins among themselves and between genes among themselves in health group; Correlation between FNDC5 mRNA expression and phospholitin mRNA in obese group
Tu et al. (2018) [36]	Longitudinal	Not applicable	1530	The subjects were the first with acute ischemic stroke to be hospitalized patients in three Chinese stroke centers (Beijing, Weifang and Wuhan) during the period from January 2015 to December 2016.	66	52% M, 48 % F	BMI, cardiovascular risk factors (hypertension, DM, hypercholesterolemia, being a smoker, family history of ischemic stroke) and serum levels of total cholesterol, triglycerides, CRP, glycemia, homocysteine, HDL and irisin were evaluated. The National Institutes of Health Stroke Scale (NIHSS); TOAST (stroke subtype); and magnetic resonance. HOMA was also calculated.	Primary outcome: functional outcome of patients after 6 months of stroke. It was observed that the levels of irisin in patients with poor functional outcomes were significantly lower than those with good functional outcomes. Secondary outcome: death from any cause over the 6-month follow-up. It was observed that the levels of irisin were significantly higher in patients who survived than in patients who died.

Source: Own autorship