

## REVIEW ARTICLE

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# Type 1 diabetes and body composition in youth: A systematic review

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## Summary

An increasing prevalence of overweight and obesity was reported in youth with type 1 diabetes, likely due to the intensive insulin treatment and/or an unhealthy lifestyle. Analyses of body composition may help describe the real increase in fat mass, which contributes to the diabetes-related cardio-metabolic risk. This systematic review evaluated the current literature on body composition assessments in youth with type 1 diabetes and the potential association with cardio-metabolic, functional, or behavioural risk factors. A systematic search of literature studies reporting assessments of body composition in youth with type 1 diabetes published until April 2018 was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Twenty-three articles with different study designs reported assessments of body composition. The following methods were used to assess body composition: computerized dual energy X-ray absorptiometry ( $n = 10$ ), bioelectrical impedance analysis ( $n = 8$ ), skinfold thickness measurement ( $n = 4$ ), and air displacement plethysmography ( $n = 1$ ). Higher fat mass values were found in youth with type 1 diabetes in seven of the 13 studies that included a healthy control group. Most studies investigating the association between body composition and cardio-metabolic risk factors showed that youth with higher fat mass levels had poor glycaemic control, dyslipidaemia, or higher blood pressure. Assessments of body composition may represent a useful clinical procedure to support decision-making in type 1 diabetes management. Further research is needed to standardize the assessment of body composition and develop a consensus guideline.

## KEYWORDS

body composition, fat-free mass, fat mass, systematic review, type 1 diabetes, youth

## 1 | INTRODUCTION

Paediatric obesity increased remarkably over the past 4 decades, and it is one of the most serious public health challenges in the 21<sup>st</sup> century.<sup>1</sup> Several studies also described an increasing prevalence of overweight in youth with type 1 diabetes.<sup>2–5</sup> Surprisingly, youth with type 1 diabetes may have a greater likelihood of overweight than their

peers without the disease.<sup>3,6</sup> The increased weight gain may be explained by the intensive insulin therapy,<sup>7</sup> a low amount of physical activity,<sup>8</sup> or unbalanced nutrition, which mainly focuses on carbohydrate counting rather than proper fat consumption.<sup>9–11</sup>

Youth with type 1 diabetes are more predisposed to cardio-metabolic risk factors,<sup>12</sup> such as hypertension, abnormal lipid profile, insulin resistance, vascular dysfunction, and inactivity, especially when

they are overweight or obese. Recently, aerobic fitness, as an indicator of physical activity levels, was inversely related to cardiovascular disease risk and all-cause mortality in T1D.<sup>13</sup> Fat accumulation, particularly in the abdominal region, favours the development of resistance to exogenous insulin, the so-called “double diabetes,”<sup>14</sup> which leads to additional cardiovascular complications in the long term.<sup>15,16</sup> Body mass index (BMI) is routinely used in clinical assessments of youth with type 1 diabetes, but it is not an accurate measure of adiposity. Analysis of body composition (BC) may be more helpful in evaluating the cardio-metabolic risks in these subjects.

BC may change at the onset and during the course of the disease. Although standards of medical care in diabetes do not recommend evaluations of BC,<sup>17</sup> analyses of fat mass and fat-free mass may provide useful information for the management of the disease.<sup>18</sup>

Therefore, the present systematic review critically appraised the literature on assessments of BC in youth with type 1 diabetes and its potential association with cardio-metabolic, functional, or behavioural risk factors.

## 2 | METHODS

### 2.1 | Search strategy

This systematic review was performed according to a published protocol<sup>19</sup> and applied the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in each phase<sup>20</sup> (Table 1). A wide and accurate search of four comprehensive medical databases was performed: PubMed, Web of Science, Scopus, and the Cochrane Library. All of the keywords were combined in the premeditated algorithm presented in Table S1 (Supporting Information). The search ended on 23 May 2018 and included no language limits. Manual searching (ie, reference lists and citation searching) of studies that satisfied the eligibility criteria was also performed.

### 2.2 | Study selection

Cross-sectional, longitudinal, case control, and intervention studies in clinical or nonclinical settings were included. Only articles that included children, adolescents, and young adults up to 20 years of age with type 1 diabetes and a duration longer than 1 year were considered eligible. All types of interventions were accepted for experimental studies. The hallmark of the included articles was an assessment of BC. However, papers were excluded when the methodology for BC evaluation was not specified. Studies that reported only height, weight, BMI, and waist or hip circumferences, or studies published only as abstracts or conference papers were not included in this systematic review. Initially, all of the retrieved articles were checked, and duplicates or the obviously irrelevant articles were excluded. Three reviewers (P.C., F.G., and G.F.) independently screened the remaining studies according to the relevance of the titles and abstracts. Full texts were obtained to determine the eligibility of doubtful cases, and any discrepancy was discussed until a decision

**TABLE 1** Patients, intervention, comparison, outcomes, and study design (PICOS) criteria for inclusion and exclusion of studies

Parameter	Criteria
<i>Participants</i>	Youth with type 1 diabetes, aged $\geq 20$ years, with diabetes duration $> 1$ year.
<i>Intervention</i>	Evaluation of body composition, excluding studies based only on body weight, body height, body mass index, and waist or hip circumference measurements.
<i>Comparison</i>	Not essential a comparison group. A comparison with other age-matched groups was considered, if reported in the study. Type 2 diabetes youth were not considered as control group.
<i>Outcomes</i>	<p>Main outcome: body composition characteristics (fat mass and fat free mass composition, fat mass distribution, hydration status) in youth with type 1 diabetes and main tools used.</p> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>- Differences in body composition between youth with type 1 diabetes and healthy peers</li> <li>- Association between body composition and glycaemic outcomes—glycated haemoglobin (HbA1c) or glycaemic variability by continuous blood glucose monitoring (CGM) and daily insulin dose.</li> <li>- Association between body composition and cardio-metabolic risk profile—measures comprising the metabolic syndrome components (blood pressure, triglycerides, high and low density lipoprotein) or liver steatosis or functional components (aerobic capacity, strength and flexibility).</li> </ul>
<i>Study design</i>	No limits about the study design.

was reached with 100% agreement of the reviewers. The full texts of the eligible articles were retrieved and included in the list of full-text manuscripts for data extraction.

### 2.3 | Data extraction and quality assessment

P.C., F.G., and G.F. extracted the general characteristics of the studies, such as the title, author, journal, year of publication, study design, and main purpose. The study populations were analysed for age, gender, sample size of youth with type 1 diabetes and controls, disease duration, and insulin treatments. Additional information, such as the percentage of overweight or obese youth, was reported. A rigorous analysis of the methods was used to assess BC and the relative values of BMI ( $\text{kg}/\text{m}^2$ ), fat mass, fat-free mass, and total body water, reported in kilograms or as a percentage of total body weight. Last, the analysis focused on the potential association between BC and cardio-metabolic, functional, or behavioural risk factors.

To perform a quality evaluation of the articles, the Downs and Black<sup>21</sup> checklist was used in the full or short form, according to the study design. Twenty-seven items were gathered in four different categories: reporting (10 items); external validity (three items); internal validity (bias: seven items, confounding: six items); and

power of the study (one item). Items related to the intervention (items 4, 8, 12-15, 19, 23, and 24) were excluded for observational studies, and items concerning the follow-up (items 9, 17, and 26) were not considered for cross-sectional studies. Therefore, the risk of bias was evaluated on 18 items for observational studies and 15 items for cross-sectional studies. The reviewers assigned a score of 1 for each quality item satisfied by the article, and a score of 0 was assigned for each lacking or undetectable feature. Studies were considered of high, medium, or low quality according to the tertiles of each maximum score. Three reviewers (P.C., F.G., and G.F.) independently performed quality assessments, and a fourth reviewer (G.V.) resolved disagreements.

### 3 | RESULTS

#### 3.1 | Description of the included studies

Of the 6648 records originally retrieved, 82 studies were eligible for full-text analysis after screening the titles and abstracts and removal of duplicates (Figure 1). Only 23 studies<sup>11,22-43</sup> met the inclusion criteria. Studies were excluded for the following main reasons: (a) missing quantitative data on BC, (b) abstracts or conference papers, (c) subjects >20 years, (d) duration of diabetes  $\leq 1$  year, and (e) studies performed on the same sample. The included studies were published between 2003 and 2017 and were performed in 12 countries. Half of the studies were performed in Europe. Ten studies were cross-sectional,<sup>22,25,28-30,35,37,38,41,43</sup> three studies were randomized clinical trials,<sup>23,24,40</sup> three studies were case-control studies,<sup>26,31,33</sup> two studies were experimental studies,<sup>39,42</sup> two studies were nonrandomized clinical trials,<sup>34,36</sup> two studies were uncontrolled clinical trials,<sup>11,27</sup> and one study had a mixed design (both case-control and longitudinal)<sup>32</sup> (Table 2). The following interventions were used: (a) physical training or exercise testing in six studies<sup>11,34,36,39,40,42</sup> for a minimum of 12 weeks to a maximum of 6 months; (b) nutritional programmes in two studies,<sup>24,27</sup> both for 18 months; and (c) a combined treatment

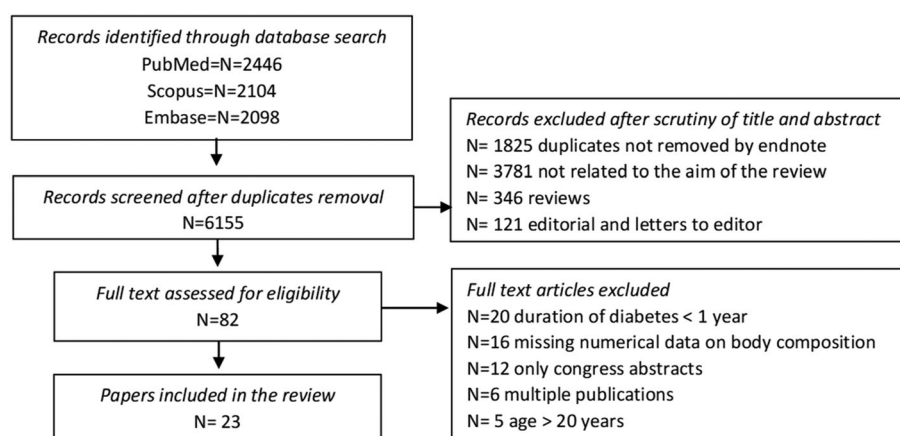
with metformin and insulin for 26 weeks in one study.<sup>23</sup> The main aim and findings of the studies are shown in Table 2. In six<sup>23,28,36,39,42,43</sup> of the 23 selected studies, the BC evaluation was not the primary aim but was included as a descriptive variable or considered a covariate in regression analyses.

#### 3.2 | Participants

The sample size varied between 10 and 427 youth with type 1 diabetes. Thirteen studies<sup>22,26,31-36,38,39,41-43</sup> presented a healthy control group with 10 to 87 youths. Six studies<sup>32,34,38-41</sup> enrolled only females, and one study<sup>36</sup> enrolled only males. The ages of youths with type 1 diabetes ranged from 2 to 20 years. Controls, when present, were age and gender matched. Diabetes duration was at least 1 year, which met the inclusion criteria, and the weighted arithmetic mean was 5.1 years. Multiple daily insulin injection was the treatment of choice in most studies, and continuous subcutaneous insulin infusion was used in four studies.<sup>24,25,27,28</sup> Mixed types of treatment (multiple daily injections or continuous subcutaneous insulin infusion or conventional treatment) were used in three studies,<sup>26,30,31</sup> and an insulin regimen was unspecified in five studies<sup>11,33,34,36,37</sup> (Table 3).

#### 3.3 | Body composition characteristics

Dual-energy X-ray absorptiometry was used in 10 studies.<sup>22-24,29,31,32,35,41-43</sup> One study used dual-energy X-ray absorptiometry and skin-fold thickness measurement.<sup>41</sup> Bioelectrical impedance analysis was used in eight studies.<sup>11,25-27,30,33,36,37</sup> Four studies used only skin-fold thickness measurement,<sup>34,38-40</sup> and one study<sup>28</sup> used air displacement plethysmography (Table 4). Eight studies<sup>22-24,29,30,33,40,43</sup> reported the percentage of overweight/obese subjects, but the overweight/obese population was selected as part of the study design in two studies.<sup>23,43</sup> Most studies were not generalizable because of the small sample size (19-45 cases) and/or missing information about enrolment procedures.<sup>22,29,33,40</sup> Two studies, with the largest sample



**FIGURE 1** Flow chart of study selection

**TABLE 2** Main characteristics of the included studies

Author-Year	Country	Study Design	Main Aim	Intervention	Duration	Main BC Findings
Abd El Dayem et al 2012 <sup>22</sup>	Egypt	CS	To estimate the influence of BC on blood pressure	-	-	AF is the only factor related to mean arterial blood pressure
Galli-Tsinopoulou et al 2009 <sup>33</sup>	Greece	Pilot CC	To assess BC and nutritional status and GC	-	-	No association between GC and nutrient intakes or anthropometric variables
Hassan et al 2014 <sup>37</sup>	Africa	CS	To compare growth and BC between controlled and uncontrolled T1D children	-	-	Controlled T1D children were susceptible to weight gain while uncontrolled children were more at risk of being underweight and short
Heyman et al 2007 <sup>39</sup>	France	Exp	To examine the glycaemic responses to an exhausting graded exercise	Exercise testing 1 session	-	Female adolescents with T1D displayed an altered sympathoadrenergic activity at rest and during intense exercise
Heyman et al 2007 <sup>40</sup>	France	RCT	To examine the effects of a physical training program on BC, leptin, and apolipoprotein profiles	Physical training 6 mo	-	An increase of PA in girls with T1D prevented the increases in FM and serum leptin
Heyman et al 2012 <sup>38</sup>	France	CS	To examine the relationship of PA or dietary composition with BC and IR	-	-	Low PA, television-watching, and total calorie intake were linked to higher adiposity measurements
Ingberg et al 2003 <sup>41</sup>	Sweden	CS	To compare BC between adolescents with T1D and healthy controls	-	-	AF was associated with poor GC and elevated blood lipids
Komatsu et al 2005 <sup>42</sup>	Brazil	Exp	To compare the aerobic exercise capacity between adolescents with T1D and healthy controls	Aerobic capacity testing one session	-	Adolescents with T1D showed a reduced aerobic exercising capacity compared with healthy peers matched for anthropometric conditions
Krishnan et al 2011 <sup>43</sup>	USA	CS	To examine the presence of CVRF in normal and overweight children	-	-	Diabetes status was not associated with an additional CVRF profile with respect to controls
Libman et al 2015 <sup>23</sup>	USA	RCT	To assess the efficacy and safety of metformin as an adjunct to insulin in overweight children	Metformin 26 wk	-	The addition of metformin to insulin did not improve GC while it was associated with less weight gain
Lipsky et al 2017 <sup>24</sup>	USA	RCT	To examine the associations between BC and CVRF	Behavioural nutrition intervention 18 mo	-	Excess adiposity was associated with increased CVRF
Maffei et al 2017 <sup>25</sup>	Italy	CS	To examine whether adiposity, diet, and GC were associated with an increase of CVRF	-	-	Adiposity and lipid-to-CHO intake ratio affected non-HDL cholesterol
Majewska et al 2014 <sup>26</sup>	Poland	CC	To evaluate the relationship between resistin serum concentrations and FM	-	-	Negative correlation between resistin levels and FM
Marigliano et al 2013 <sup>27</sup>	Italy	UCT	To explore the association CHOc and changes in GC, BC, and FM	Nutritional education program 18 mo	-	CHOc did not affect dietary habits, BC, and FM distribution
Metcalf et al 2014 <sup>28</sup>	USA	CS	To examine the associations between MVPA and hypoglycaemia	-	-	MVPA increased the risk of overnight and next-day hypoglycemia controlling for sex, FM%, aerobic capacity, and concurrent MVPA
Michaliszyn et al 2010 <sup>11</sup>	USA	Pilot UCT	To describe the associations between PA and changes in fitness and BC	Aerobic exercises 16 wk	-	Greater amounts of MVPA were associated with higher fitness and FFM
Mosso et al 2015 <sup>62</sup>	Chile	CS	To assess the relationships between dietary intake, BC, and GC	-	-	Girls with T1D had a FM% higher than the recommended value for age

(Continues)

TABLE 2 (Continued)

Author-Year	Country	Study Design	Main Aim	Intervention	Duration	Main BC Findings
Pietrzak <i>et al</i> 2009 <sup>30</sup>	Poland	CS	To estimate the influence of BC on blood pressure	-	-	There was an association between BMI and FM with blood pressure
Saki <i>et al</i> 2016 <sup>31</sup>	Iran	CC	To compare BC between adolescents with T1D and healthy peers	-	-	Higher FM and lower FFM in adolescents with T1D than healthy peers
Sarriblad <i>et al</i> 2007 <sup>32</sup>	Sweden	CC- L	To examine BC changes from late puberty to early adulthood	-	-	Increased FM in pubertal girls with T1D tended to persist in young adulthood
Sideraviciute <i>et al</i> 2006 <sup>34</sup>	Lithuania	NRCT	To evaluate the effect of long-term swimming program on BC	Swimming training	14 wk	Swimming training improved aerobic capacity and reduced FM in all the participants
Wierzbicka <i>et al</i> 2016 <sup>35</sup>	Poland	CS	To investigate vitamin D status and its association with BC	-	-	Low vitamin D levels were positively associated with poor GC and higher FM
Woo <i>et al</i> 2010 <sup>36</sup>	Korea	NRCT	To assess theeffect of a low-intensity exercise training on oxidative stress	Exercise training	12 wk	Low-intensity aerobic exercise did not change BC and was able to increase the antioxidant activity

Abbreviations: AF, abdominal fat; BC, body composition; BMI, body mass index; CC, case-control study; CH, cohort study; CHOC, carbohydrates counting; CVRF, cardiovascular risk factors; CS, cross sectional; Exp, experimental study; FFM, fat free mass; GC, glycometabolic control; FM, fat mass; HbA1c, glycated haemoglobin; IR, insulin resistance; L, longitudinal; MVPA, moderate vigorous physical activity; NRCT, nonrandomized clinical trial; PA, physical activity; RCT, randomized clinical trial; T1D, type 1 diabetes; UCT, uncontrolled clinical trial.

sizes (136 and 164 youth with type 1 diabetes, respectively) and a clear sampling design<sup>24,30</sup> reported an overweight prevalence of 20.6% and 22.7% and obesity prevalence of 11.8% and 4.9%, respectively.

The fat mass percentage in youth with type 1 diabetes ranged from 22.4 to 38.0 with dual-energy X-ray absorptiometry, excluding three studies<sup>29,32,41</sup> that reported data separately by gender. The highest values (fat mass percentages of 36 and 38) were found in two studies<sup>23,43</sup> that were specifically performed in overweight/obese subjects and in another study<sup>22</sup> (fat mass percentage 35.2) with a high prevalence (66.7%) of overweight/obese youth. The remaining four studies<sup>24,31,35,42</sup> were performed in normal weight youth (BMI ranged from 17.8 to 21.5 kg/m<sup>2</sup>), and the fat mass percentage ranged from 22.4 to 29.0. The fat mass percentage ranged from 15.0 to 24.5 for bioelectrical impedance analyses, excluding one study<sup>36</sup> that reported data only for males. The lowest values of 15.0 and 15.8 were found in two studies<sup>27,37</sup> that included younger populations. Skin-fold thickness measurements were performed only in females, who showed fat mass percentages from 30.9 to 40.2. The highest value was reported in a population with a mean BMI value of 26.3 kg/m<sup>2,41</sup>

### 3.4 | Body composition in youths with type 1 diabetes versus healthy controls

Five<sup>32,34,38,39,41</sup> of 13 studies reported that BMI was significantly higher in youths with type 1 diabetes than controls. One study<sup>33</sup> reported that the BMI Z-score was higher in youths with type 1 diabetes. The remaining studies did not report any significant differences. Seven<sup>22,31,32,34,38,39,41</sup> of 12 studies (one study was not included due to the lack of control group data) found significantly higher fat mass values (either as a percentage or absolute values) in the type 1 diabetes groups than that in controls. Four<sup>22,31,32,41</sup> of six studies used dual-energy X-ray absorptiometry, and four<sup>34,38,39,41</sup> of four studies used skin-fold thickness measurements. None of three studies used BIA, but one study used dual-energy X-ray absorptiometry and skin-fold thickness measurement.<sup>41</sup> Two studies<sup>28,29</sup> used air displacement plethysmography and dual-energy X-ray absorptiometry and reported higher fat mass values in females with type 1 diabetes than males. Data on fat-free mass were reported in 13 studies<sup>11,23,26,27,31-33,35,37-39,42,43</sup>; one study<sup>31</sup> showed lower values in adolescents with type 1 diabetes, and two studies<sup>33,38</sup> found higher values in the type 1 diabetes group than that in controls. Notably, these latter studies used the fat-free mass index normalized for height. For abdominal or truncal fat measured using dual-energy X-ray absorptiometry, one study<sup>22</sup> showed higher abdominal fat values, and two studies<sup>22,31</sup> found higher truncal fat in youths with type 1 diabetes than that in controls. One study<sup>38</sup> reported a higher waist/hip ratio in youths with type 1 diabetes than the ratio in controls. Another study<sup>43</sup> showed that normal weight diabetic subjects had higher fat mass percentages than normal weight nondiabetic subjects adjusted for age, gender and ethnicity ( $P < .05$ ).



**TABLE 3** Main characteristics of the population included in the studies

Author	Participants (Number) T1D Controls	Gender (M/F) T1D Controls	Age (years) T1D Controls	Diabetes Duration (y)	Insulin Treatment
<i>Abd El Dayem et al</i> <sup>22</sup>	45 30	NR	13.5 ± 3.1 NR	6.3 ± 3	MDI
<i>Galli-Tsinopoulou et al</i> <sup>33</sup>	24 24	(12/12) (12/12)	4-16 NR	3.7 ± 2.0	NR
<i>Hassan et al</i> <sup>37</sup>	427	(214/213)	6.7 ± 2.1 (2-10)	2.5 ± 1.5	NR
<i>Heyman et al</i> <sup>39</sup>	19 19	(0/19) (0/19)	15.9 ± 1.3 16.6 ± 1.1	7.3	MDI
<i>Heyman et al</i> <sup>40</sup>	16 (9 In-7 Nin)	(0/16)	16.3 ± 1.2 <sup>a</sup>	7.3 ± 4.4 <sup>a</sup>	MDI
<i>Heyman et al</i> <sup>38</sup>	19 19	(0/19) (0/19)	15.9 ± 1.3 16.6 ± 1.1	7.4 ± 4.5	MDI
<i>Ingberg et al</i> <sup>41</sup>	18 18	(0/18) (0-18)	17.3 ± 0.6 17.3 ± 0.6	9.3 ± 3.2	MDI
<i>Komatsu et al</i> <sup>42</sup>	72 46	(38/34) (26/20)	Range 9–20 Range 10–18	4.9 ± 3.6	MDI
<i>Krishnan et al</i> <sup>43</sup>	29 37	(19/10) (19/18)	16 ± 2.2 16.5 ± 2.4	>3	MDI
<i>Libman et al</i> <sup>23</sup>	140	(48/92)	15.3 ± 1.7 <sup>a</sup>	7.0 ± 3.3 <sup>a</sup>	MDI
<i>Lipsky et al</i> <sup>24</sup>	136 (66 In-70 Nin)	(57/69)	12.8 ± 2.6 <sup>a</sup>	6.0 ± 3.1 <sup>a</sup>	CSII
<i>Maffei et al</i> <sup>25</sup>	180	(90/90)	12.7 ± 3.3	5.8 ± 4.1	CSII
<i>Majewska et al</i> <sup>26</sup>	75 21	(30/46) (10/11)	12.5 ± 3.5 12.6 ± 2.7	4.9 ± 3.1	35 MDI, 21 CSII, 19 CONV
<i>Marigliano et al</i> <sup>27</sup>	25	(12/13)	10 ± 4.2 <sup>a</sup>	5.7 ± 3.2 <sup>a</sup>	CSII
<i>Metcalf et al</i> <sup>28</sup>	19	(10/9)	16.6 ± 1.9	≥1	CSII
<i>Michaliszyn et al</i> <sup>11</sup>	16	(10/6)	14.4 ± 1.6 <sup>a</sup>	5.6 ± 3.1 <sup>a</sup>	NR
<i>Mosso et al</i> <sup>29</sup>	30	(21/9)	15.2 ± 4.0	7.3 ± 4.3	MDI
<i>Pietrzak et al</i> <sup>30</sup>	164	(92/72)	14.8 ± 2.4	6.1 ± 4.2	96MDI, 68CSII
<i>Saki et al</i> <sup>31</sup>	87 87	(39/48) (39/48)	12.4 ± 4.2 12.4 ± 4.2	4.4 ± 2.8	45 MDI, 36 CONV, 6 Not specified
<i>Sarnblad et al</i> <sup>32</sup>	18 19	(0/18) (0/19)	17.5 ± 0.8 17.6 ± 0.8	9.8 ± 2.9	MDI
<i>Sideraviciute et al</i> <sup>34</sup>	19 28	(0/19) (0/28)	17.0 ± 0.4 <sup>a</sup> 16.9 ± 0.2	8.1 ± 0.9 <sup>a</sup>	NR
<i>Wierzbicka et al</i> <sup>35</sup>	60 40	(28/32) (20/20)	15.1 ± 1.9 15.6 ± 1.8	5.1 ± 3.9	MDI
<i>Woo et al</i> <sup>36</sup>	10 10	(10/0) (10/0)	11.2 ± 0.9 <sup>a</sup> 11.9 ± 1.9	3.9 ± 3.2 <sup>a</sup>	NR

<sup>a</sup>At recruitment.

Abbreviations: CONV, conventional insulin treatment; CSII, continuous subcutaneous insulin infusion; In, intervention group; MDI, multiple daily injections; Nin, not-intervention group; NR, not reported; T1D, type 1 diabetes.

### 3.5 | Body composition and cardio-metabolic, functional, or behavioural risk factors

Overall, seven studies<sup>22,24,25,30,38,41,43</sup> analysed the relationship between BC and cardio-metabolic, functional, or behavioural risk factors (Table 5). Two studies<sup>38,41</sup> reported a moderate-to-high

correlation between adiposity indices (waist-to-hip ratio and abdominal-to-leg ratio) and insulin dose, and one study<sup>41</sup> found that several adiposity indices (waist circumference, waist-to-hip ratio, abdominal-to-leg ratio, and abdominal fat) moderately correlated with glycated haemoglobin levels. Three studies<sup>22,24,30</sup> found a positive association between adiposity indices (fat mass percentage, abdominal

**TABLE 4** Main body composition characteristics of subjects included in the studies

Author	Techniques for BC Assessment	BMI (kg/m <sup>2</sup> )	T1D Controls	FM (%)	T1D Controls	FFM (%)	T1D Controls	AF or TF	T1D Controls
Abd El Dayem et al <sup>22</sup>	DXA	22.3 weighted mean		39.2 ± 6.4 22.5 ± 5.6 <sup>a</sup>		NR		AF% 17.9 ± 2 13 ± 5.1 <sup>a</sup> TF% 24.9 ± 4 21.6 ± 8.3 <sup>a</sup>	
Galli-Tsinopoulou et al <sup>33</sup>	BIA	20.2 ± 3.3 BMI z-score 0.8 ± 0.8 0.04 ± 1.4 <sup>a</sup>	18.8 ± 4.5	17.8 ± 7.6 21.3 ± 6.5		FFMI <sup>c</sup> (kg/m <sup>2</sup> ) 16.45 ± 2.9 14.5 ± 2.8 <sup>a</sup>		NR	
Hassan et al <sup>37</sup>	BIA	BMI z-score 0.63 ± 0.95		15.8 ± 9.9		84.1 ± 9.7		NR	
Heyman et al <sup>39</sup>	SFT	24.5 ± 0.5 21.3 ± 0.3 <sup>a</sup>		30.9 ± 5.8 24.3 ± 5.8 <sup>a</sup>		44.5 ± 4.3 (kg) 43.2 ± 5.1 (kg)		NR	
Heyman et al <sup>40</sup>	SFT	24.5 ± 4.6 <sup>c</sup> In 25.1 ± 3.9 <sup>c</sup> Nin		31.9 ± 6.2 <sup>c</sup> In 29.3 ± 5.4 <sup>c</sup> Nin unchanged in In and ↑ in Nin (P = .08) <sup>d</sup>		NR ↑ in In but not in Nin (P < .005) <sup>d</sup>		W/H (cm) 0.88 ± 0.04 <sup>a</sup> In 0.89 ± 0.07 <sup>a</sup> Nin	
Heyman et al <sup>38</sup>	SFT	24.6 ± 3.9 20.9 ± 2.8 <sup>a</sup>		30.9 ± 5.8 24.1 ± 6.0 <sup>a</sup>		FFMI <sup>c</sup> (kg/m <sup>2</sup> ) 16.8 ± 1.8 15.3 ± 2.0 <sup>a</sup>		W/H (cm) 0.89 ± 0.05 0.85 ± 0.03 <sup>a</sup>	
Ingberg et al <sup>41</sup>	SFT-DXA	26.3 ± 2.6 23.6 ± 3.8 <sup>a</sup>		40.2 ± 8.9 SFT 37.1 ± 5.5 DXA 29.1 ± 8.1 <sup>a</sup> SFT 32.1 ± 7.7 <sup>a</sup> DXA		NR		W/H (cm) 0.81 ± 0.08 0.79 ± 0.05 AF (kg) 1.5 ± 0.5 1.2 ± 0.6	
Komatsu et al <sup>42</sup>	DXA	21.5 ± 3.7 20.8 ± 2.8		22.4 ± 7.8 19.7 ± 7.2		41.2 ± 9.9 (kg) 45 ± 9.5 (kg)		NR	
Krishnan et al <sup>43</sup>	DXA	28.5 ± 3.6 OW 20.6 ± 2.0 NW 32.9 ± 5.6 OW 20.5 ± 1.5 NW		36.7 ± 2.7 OW 24.3 ± 1.7 NW 36.5 ± 1.7 OW 21.4 ± 1.6 NW		48.5 ± 2.0 (kg) 50.5 ± 1.5 (kg)		W/H (cm) 0.79 ± 0.02 0.79 ± 0.01	
Libman et al <sup>23</sup>	DXA	BMI z-score 1.6 (0.4) In 1.7 (0.3) Nin ↑ in Nin but not in In (P < .001) <sup>d</sup>		36 In 38 Nin ↑ in Nin but not in In (P < .04) <sup>d</sup>		47 In (kg) 44 Nin (kg)		NR	
Lipsky et al <sup>24</sup>	DXA	21.3 ± 4.2		25.9 ± 7.4 In 29.0 ± 8.2 Nin		NR		NR	
Maffei et al <sup>25</sup>	BIA	19.5 ± 3.1		18.5 ± 7.6		NR		WC (cm) 67.8 (8.6)	
Majewska et al <sup>26</sup>	BIA	NR		24.5 ± 7.9 23.2 ± 7.1		75.5 ± 8.0 76.6 ± 7.1		NR	

(Continues)

TABLE 4 (Continued)

Author	Techniques for BC Assessment	BMI (kg/m <sup>2</sup> )	T1D Controls	FM (%) T1D Controls	FFM (%) T1D Controls	AF or TF T1D Controls
Marigliano et al <sup>27</sup>	BIA	17.9 ± 2.4 B 19.3 ± 2.7 Fu		15.0 ± 6.8 B 17.0 ± 8.6 Fu	73.0 (25.0) B 73.1 (25.2) Fu	W/H 0.39 (0.1) B 0.40 (0.1) <sup>a</sup> Fu
Metcalf et al <sup>28</sup>	ADP	NR		19.2 ± 9.4 Males 26.2 ± 4.8 <sup>b</sup> Females	NR	NR
Michaliszyn et al <sup>11</sup>	BIA	NR		24.5 ± 9	75.5 ± 9.0	NR
Mosso et al <sup>29</sup>	DXA	21.4 ± 3.8		20.2 ± 1.9 Males 31.2 ± 8.7 <sup>b</sup> Females	NR	NR
Pietrzak et al <sup>30</sup>	BIA	21.5 ± 3.8		21.9 ± 7.1	NR	NR
Saki et al <sup>31</sup>	DXA	17.8 ± 3.2 17.5 ± 3		28.4 ± 5.8 23.4 ± 8.1 <sup>a</sup>	26.3 ± 10.3 (kg) 30.5 ± 10.3 <sup>a</sup> (kg)	TF% 23.7 ± 5.5 19.9 ± 7.8 <sup>a</sup>
Sarnblad et al <sup>32</sup>	DXA	26.4 ± 2.6 23.9 ± 3.7 <sup>a</sup>		27.5 ± 6.5(kg) 22.7 ± 8.4 <sup>a</sup> (kg)	41.6 ± 3.2 (kg) 40.3 ± 3.5 (kg)	NR
Sideraviciute et al <sup>34</sup>	SFT	23.3 ± 0.9 19.8 ± 0.4 <sup>a</sup>		34.8 ± 1.2 27.2 ± 1.0 <sup>a</sup>	NR	NR
Wierzbicka et al <sup>35</sup>	DXA	21.1 ± 3.4 21.7 ± 2.9		13.7 ± 7.4(kg) NR	42.8 ± 10.3 (kg) NR	NR
Woo et al <sup>36</sup>	BIA	19.6 ± 2.7 B 19.6 ± 3.1 Fu 19.0 ± 3.1 B 19.1 ± 3.4 Fu		12.4 ± 6.8 B 12.6 ± 7.2 Fu 11.4 ± 5.8 B 12.8 ± 6.9 Fu	NR	NR

<sup>a</sup>Significantly higher in youth with type 1 diabetes.

<sup>b</sup>Significantly higher in female.

<sup>c</sup>At recruitment.

<sup>d</sup>After intervention.

<sup>e</sup>(Calculated as fat-free weight [kg] divided by height squared [m<sup>2</sup>]).

Abbreviations: ADP, air displacement plethysmography; AF, abdominal fat; B, baseline; BC, body composition; BIA, bioelectrical impedance analysis; BMC, bone mineral content; BMD, bone mineral density; DXA, dual X-ray absorptiometry; BMI, body mass index; FFM, fat free mass index; FM, fat mass; Fu, follow-up; In, intervention group; MRS, magnetic resonance spectroscopy; Nin, not intervention group; NR, not reported; NW, normal-weight; OW, overweight; pQCT, peripheral quantitative computer tomography; SFT, skinfolds thickness; T1D, type 1 diabetes; TF, truncal fat; WC, waist circumference; W/H, waist-hip ratio.



**TABLE 5** Studies evaluating the association between body composition and cardio-metabolic, functional, or behavioural risk factors in type 1 diabetes

CARDIO-METABOLIC RISK FACTORS	
<b>Blood pressure</b>	<p>Abd El Dayem et al 2012<sup>22</sup> Positive association between percentage of abdominal fat and systolic blood pressure (<math>\beta = 8.6</math>, <math>P = .0001</math>) or diastolic blood pressure (<math>\beta = 2.7</math>, <math>P = .006</math>).</p> <p>Pietrzak et al 2009<sup>30</sup> Positive association between fat mass percentage and systolic blood pressure (<math>\beta = 0.23</math>, <math>P = .004</math>) or diastolic blood pressure (<math>\beta = 0.29</math>, <math>P &lt; .001</math>).</p> <p>Lipsky et al 2017<sup>24</sup> Positive association between fat mass percentage and systolic blood pressure (<math>\beta = 0.17</math>, <math>P = .001</math>) or diastolic blood pressure (<math>\beta = 0.1</math>, <math>P = .003</math>).</p> <p>Krishnan et al 2011<sup>43</sup> Positive association between truncal fat mass percentage and systolic blood pressure (<math>\beta = 0.17</math>, <math>P &lt; .001</math>) or diastolic blood pressure (<math>\beta = 0.11</math>, <math>P &lt; .001</math>).</p> <p>Krishnan et al 2011<sup>43</sup> Positive association between fat free mass and systolic blood pressure (<math>\beta = 0.3</math>, <math>P &lt; .05</math>).</p>
<b>Glycated haemoglobin</b>	<p>Ingberg et al 2003<sup>41</sup> Moderate correlation (<math>r = 0.51</math>–<math>0.69</math>, <math>P &lt; .05</math>–<math>P &lt; .005</math>) between several indices of abdominal fat (waist circumference, waist-hip ratio, abdominal to leg ratio, and abdominal fat based on dual X ray absorptiometry) and glycated haemoglobin</p>
<b>Insulin dose</b>	<p>Heyman et al 2012<sup>38</sup> Moderate correlation (<math>r = 0.66</math>, <math>P &lt; .01</math>) between waist-to-hip ratio and long-acting insulin dose</p> <p>Ingberg et al 2003<sup>41</sup> High correlation (<math>r = 0.78</math>, <math>P &lt; .005</math>) between abdominal to leg ratio by dual X ray absorptiometry and insulin dose.</p>
<b>Lipids</b>	<p>Ingberg et al 2003<sup>41</sup> Low to high correlation (<math>r = 0.49</math>–<math>0.71</math>, <math>P &lt; .05</math>–<math>P &lt; .01</math>) between several indices of abdominal fat (waist circumference, waist-hip ratio, abdominal to leg ratio, and abdominal fat based on dual X ray absorptiometry) and total cholesterol.</p> <p>Lipsky et al 2017<sup>24</sup> Moderate to high correlation (<math>r = 0.51</math>–<math>0.73</math>, <math>P &lt; .05</math>–<math>P &lt; .001</math>) between several indices of abdominal fat (waist-hip ratio, abdominal to leg ratio, and abdominal fat based on dual X ray absorptiometry) and triglycerides.</p> <p>Maffei et al 2017<sup>25</sup> Positive association between fat mass percentage and triglycerides, (<math>\beta = 0.02</math>, <math>P = .002</math>) or low density lipoprotein (<math>\beta = 0.01</math>, <math>P = .04</math>).</p> <p>Krishnan et al 2011<sup>43</sup> Positive association between truncal fat mass percentage and triglycerides (<math>\beta = 0.01</math>, <math>P = .006</math>), low density lipoprotein (<math>\beta = 0.11</math>, <math>P = .001</math>), and inverse association with high-density lipoprotein cholesterol (<math>\beta = -0.06</math>, <math>P = .04</math>).</p> <p>Krishnan et al 2011<sup>43</sup> Negligible correlation between fat mass percentage (<math>r = 0.27</math>, <math>P &lt; .01</math>) or waist-to-height ratio (<math>r = 0.16</math>, <math>P &lt; .05</math>) with nonhigh-density lipoprotein cholesterol.</p> <p>Krishnan et al 2011<sup>43</sup> Negative association between fat free mass and high-density lipoprotein cholesterol levels (<math>\beta = -0.4</math>, <math>P &lt; .05</math>).</p>
FUNCTIONAL RISK FACTORS	
	<p>Krishnan et al 2011<sup>43</sup> Positive association between total fat mass (<math>\beta = 0.1</math>; <math>P = .046</math>) or fat mass percentage (<math>\beta = 0.2</math>, <math>P = .046</math>) and large artery elasticity index.</p> <p>Krishnan et al 2011<sup>43</sup> Positive association between truncal fat mass (<math>\beta = 0.2</math>, <math>P &lt; .05</math>), fat free mass (<math>\beta = 0.1</math>, <math>P &lt; .05</math>), total fat mass (<math>\beta = 0.1</math>, <math>P &lt; .05</math>) and percent fat mass (<math>\beta = 0.1</math>, <math>P &lt; .05</math>), and small artery elasticity index.</p>
BEHAVIOURAL RISK FACTORS	
	<p>Heyman et al 2012<sup>38</sup> Low correlation between waist to-hip ratio and time spent doing club-organized activities (<math>r = -0.46</math>, <math>P &lt; .05</math>).</p> <p>Heyman et al 2012<sup>38</sup> Moderate correlation between body fat percentage and time spent in watching television/videos (<math>r = 0.60</math>, <math>P &lt; .01</math>).</p>

fat and truncal fat mass) and blood pressure levels, and one study<sup>43</sup> found a positive association between fat-free mass and systolic blood pressure. Four studies<sup>24,25,41,43</sup> found a positive association between several adiposity indices (fat mass percentage, abdominal fat, abdominal-to-leg ratio, waist circumference, waist-to-hip ratio, and waist-to-height ratio) and blood lipid levels (total cholesterol, nonhigh-density lipoprotein, low-density lipoprotein, and triglycerides). One study<sup>24</sup> found a negative association of high-density lipoprotein cholesterol with truncal fat mass percentage, and another study<sup>43</sup> found a negative association of high-density lipoprotein cholesterol with fat-free mass.

For the relationship between BC and functional risk factors, one study<sup>43</sup> reported a positive association between fat mass and the large artery elasticity index or between truncal fat mass, fat mass percentage and fat-free mass percentage, and the small artery elasticity index. In addition, two studies assessed aerobic capacity. One study demonstrated a reduced aerobic capacity in individuals with type 1 diabetes compared with healthy peers, matched for anthropometric conditions,<sup>42</sup> and the other study reported improvement in aerobic capacity and fat mass after a swim training programme.<sup>34</sup> However, no correlation analysis with BC was performed in these studies, and these results are not reported in Table 5.

Considering the relationship between BC and behavioural risk factors, one study<sup>38</sup> highlighted a low negative correlation between the time spent in club-organized activities and the waist-to-hip ratio, and a moderate positive correlation was found between the time spent watching television/videos and fat mass percentage.

### 3.6 | Quality of studies

The quality scores of the studies are shown in Table S2 (Supporting Information). Most of the studies had a medium quality. Two intervention studies had low quality, and four intervention studies, 11 cross-sectional, and one longitudinal study had medium quality. Three intervention studies and two cross-sectional studies had high quality.

## 4 | DISCUSSION

This systematic review appraised the evidence on BC and the distribution of fat mass and fat-free mass in youths with type 1 diabetes and assessed the differences with healthy peers and the relationships between BC and cardio-metabolic, functional, or behavioural risk factors. To the best of our knowledge, there are no published reviews on this issue in type 1 diabetes, but several studies were published in individuals with type 2 diabetes.<sup>44,45</sup>

Attention to BC in type 1 diabetes has grown over the past 15 years. The first studies were published in 2003, primarily in Europe. BC assessment was the main aim in most of these studies. Notably, the increasing trend of obesity in type 1 diabetes was documented in the same years.<sup>46</sup> Furthermore, the most commonly used treatment regimens in these studies were multiple daily injections or continuous subcutaneous insulin infusions, based on the effectiveness of

intensive therapy in reducing the long-term complications provided by the Diabetes Control and Complications Trial (DCCT).<sup>47</sup> This study also showed that the intensive glycaemic control must be weighed against the lipogenic effect of insulin.<sup>48,49</sup> The included studies were heterogeneous in several factors, such as study design, ethnicity, sample size, gender, BMI, and disease duration. To reduce variability due to the possible influence of insulinopenia on BC,<sup>50</sup> we only included youths with a diabetes duration longer than 1 year.

Dual-energy X-ray absorptiometry and bioelectrical impedance analysis were the most commonly used methods for BC assessment. Dual-energy X-ray absorptiometry is the gold standard method of measuring fat mass and fat-free mass.<sup>51</sup> However, the use of dual-energy X-ray absorptiometry is limited to the research context because of equipment cost, exposure to ionizing radiation, and lack of portability. Dual-energy X-ray absorptiometry is also useful for analysis of bone mineral density, but the studies selected in this review used this technique specifically to evaluate fat mass and fat-free mass, with the only exception being the paper by Sarnbald et al.<sup>32</sup> On the other hand, bioelectrical impedance analysis is a more practical, easy to perform, and noninvasive tool. However, hydration status may influence bioelectrical impedance analysis measurements, which may be compromised in type 1 diabetes.<sup>52</sup> To overcome this limitation, the phase angle may be used as an accurate index of nutritional status because it better reflects cellular health and intracellular and extracellular water, even in type 1 diabetes.<sup>53-55</sup> However, none of the studies included in this review reported the phase angle and only described the absolute and/or relative values of fat mass and fat-free mass. Our systematic review showed that other tools were less frequently used, such as skin-fold thickness measurements in only five studies.<sup>34,38-41</sup> This tool is inexpensive and noninvasive, but specific prediction equations from skin-fold thickness measurements must be developed in youths with type 1 diabetes. Indeed, the only skin-fold thickness-derived equation built in a paediatric population with type 1 diabetes had poor accuracy compared with dual-energy X-ray absorptiometry.<sup>56</sup> Last, air displacement plethysmography, which is a new, safe, and quick technique, was used in only one study.<sup>28</sup> However, hydration of fat-free mass may influence this tool similarly to bioelectrical impedance analysis.<sup>57</sup>

The two studies<sup>24,30</sup> with large sample sizes and clear sampling designs reported a prevalence of overweight and/or obesity in type 1 diabetes that was quite similar to the international SWEET registry.<sup>58</sup> Although BMI alone may be inadequate to predict future health problems, it is the most commonly used and simplest measurement to define overweight and obesity. However, BMI is not reliable in determining fat mass distribution,<sup>59</sup> and BC analysis is crucial for distinguishing fat mass from fat-free mass.<sup>60</sup> Almost all of the studies included in the present review expressed fat mass data as a percentage of body weight and fat-free mass in kg, which gives greater attention to fat mass than fat-free mass distribution.

Studies not supported by control groups are difficult to discuss and draw meaningful conclusions from. In studies with a gender-matched and age-matched control group, more than one-third reported higher BMI, and more than half found a higher fat mass in youths with type

1 diabetes compared with that of controls. Focusing on fat mass distribution, two studies reported higher abdominal or truncal fat percentages than controls, and four studies found higher waist-to-hip ratio values in youths with type 1 diabetes. Remarkably, despite the contribution of skeletal muscle to metabolic and general health, the effect of type 1 diabetes on skeletal muscle received less attention than fat mass. Only two studies<sup>33,38</sup> reported higher fat-free mass values in type 1 diabetes, and one study<sup>31</sup> highlighted higher values in the control group. Considering the anabolic effect of insulin,<sup>49</sup> studies of fat-free mass may provide useful details. Recent studies showed that individuals with type 1 diabetes presented structural and metabolic impairments in muscle mass,<sup>61</sup> decreased muscle function,<sup>62</sup> and low lean body mass associated with poor glycaemic control.<sup>63</sup> More studies are needed to understand whether the maintaining of skeletal muscle health contributes to a reduction of diabetic symptoms with systemic benefits and delayed diabetic complications.<sup>64,65</sup>

With regard to the health outcomes, the few studies that analysed the relationship between BC and various cardio-metabolic risk factors showed consistent associations between fat mass and high blood pressure or dyslipidaemia, which confirms the unhealthy effects of higher fat mass levels in type 1 diabetes.<sup>22,24,25,30,41,43</sup> For the other risk factors, other studies are needed to confirm the negative effects of fat mass on glycaemic control or functional parameters.

The limitations of this systematic review are the heterogeneity in study design, the small sample size, and the medium quality of most of the selected studies. Furthermore, meta-analyses or a quantitative summary were not feasible because the outcome data were scarce. Nevertheless, our review reports interesting findings and some new data, which may indicate novel directions for future research.

In conclusion, the attention to BC in youths with type 1 diabetes has increased in the last two decades. BMI revealed an increased prevalence of overweight/obesity in these subjects, but it was insufficient to describe the BC and distribution of fat mass and fat-free mass. The study of BC may help diabetologists and health professionals to optimize insulin therapy and address patients' diets and lifestyles. The tools widely used for BC assessment in youths with type 1 diabetes are dual-energy X-ray absorptiometry and bioelectrical impedance analysis. However, the lack of standardized cut-offs for BC parameters and the influence of diabetes control on hydration status remain obstacles to its use in routine clinical practice. No studies analysed the strengths and weaknesses of assessing BC during the course of the disease in youths. The determination of changes in BC requires further research using a valid and standardized assessment of BC that guarantees the reproducibility of the measurements to accurately address the dynamic changes in BC in the medium-term and long-term follow-up. Last, this review provides a new incentive for further studies aimed at understanding the best methodology for BC assessment in type 1 diabetes to develop future consensus guidelines.

## AUTHORS' CONTRIBUTIONS

P.C. and G.V. conceived and designed the study. F.G., G.F., and G.L. contributed to the design of the study. P.C. and G.F. performed the

search. P.C., F.G., and G.F. reviewed and extracted the data and performed quality ratings of the papers. P.C. and G.V. interpreted the results. P.C., G.F., and G.V. wrote the initial draft of the manuscript. All authors revised it for critically important content, read, and gave final approval of the version to be published.

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## CONFLICTS OF INTERESTS

The authors declare that they have no competing interests.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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