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Original Research Article

Skeletal Muscle and Metabolic Risk in Overweight Adolescents. An Indicator of Premature Sarcopenic Obesity

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ABSTRACT

Purpose: This study aimed to investigate the association between relative SMM (%SMM) and metabolic outcomes in overweight adolescents, and analyze the prevalence of overweight adolescents with decreased levels %SMM, based on reference charts for youth.
Methods: Clinical records from 240 overweight adolescents (BMI ≥ p85), aged 10-17, were collected retrospectively. From those, a sub-sample of 45 was used to analyze overtime changes in %SMM, anthropometric, metabolic and PA outcomes.
Results: %SMM was negatively associated with all the anthropometric variables, relative BFM (%BFM) (p<.001) and with Triglycerides (p<.01), and positively associated with PA levels (p<.001). Overtime decrease in %SMM percentile, was associated with increased %BFM (F=18.3, p<.001) and CRP (F=5.54, p<.05), and decreased HDL-C (F=4.37, p<.05) and PA levels (F=6.54, p<.01).
56 patients (26.9%) were classified ≤p25 for %SMM, showing higher BMI z-score, waist circumference, %BFM (p<.001), insulin, HOMA-IR (p<.01), Total cholesterol (p<.05), LDL-C (p<.01), Triglycerides (p<.001) and CRP (p<.05); and lower HDL-C (p<.05) and PA (p<.001) levels.
Conclusions: Body composition assessment together with the use of a p25 cut-off for %SMM, may act as a prior assessment of metabolic risk in overweight adolescents. Overweight adolescents at p25 or below for %SMM, may experience a deleterious effect of the combination of decreased %SMM levels and obesity-related metabolic outcomes, similarly to what happens with sarcopenic obesity, thus should be identified as a priority target for PA intervention.

Keywords: Adolescent; Overweight; Body composition; Skeletal muscle mass; Metabolic risk; Sarcopenic obesity.

INTRODUCTION

Adolescent overweight is associated with a constellation of cardiovascular and metabolic disorders. [1] Among them, hyperinsulinemia and/or insulin resistance are of particular importance due to the alarming increase of type 2 diabetes in youth. [2]

Overweight is characterized by excessive fat accumulation in adipose tissue and other organs. Body mass index (BMI) is a measure of weight adjusted for height commonly used to assess overweight in adults. In youth BMI varies with age and sex, thus it should be compared to a reference-standard according to child/adolescent age and sex. Nevertheless, BMI z-score is not an objective measure for fatness assessment, since it does not differentiate overweight due to excess body fat mass (BFM) from overweight due to increased fat free-mass (FFM). [3]

Together with height, body weight and BFM, FFM increases across childhood and adolescence. [4] It has been suggested that changes in BFM are accompanied by changes in the FFM, usually in the same direction. [5] Thus, overweight adolescents may present higher levels of FFM than their non overweight peers. [6]

Skeletal muscle mass (SMM) is the largest portion of whole body FFM, and plays a key role in overall metabolic health, [7] in particular in glucose/insulin homeostasis. [8]

Although it has been suggested that overweight adolescents have higher levels of SMM than their non overweight peers, glucose/insulin metabolism is often impaired, even at younger ages. [9]

A possible explanation for this, may be the fact that many overweight adolescents have high levels of total SMM (kg) but not of relative SMM (%SMM), which can be associated with muscle mass dysfunction and may lead to a decrease in PA levels and overall functional capacity. [10] Indeed, overweight adolescents frequently report physical discomfort or pain during physical exercise, which in turn may lead to a perception of reduced athletic ability compared to their non overweight peers. [11]

It has been suggested that in the elderly obesity-mediated factors and pathways may aggravate sarcopenia and muscle functional capacity, through a local pro-inflammatory status. [12,13] The condition that combines sarcopenic and obesity states has been defined as sarcopenic obesity. [14] Although an endogenous loss in SMM has never been reported in youth, a loss in %SMM associated with increased time spent in sedentary behaviors and weight gain may be more common in adolescents than it was supposed to. Furthermore, overweight is associated with impaired metabolic health and pro-inflammatory status, even in youth. Based on this evidence, may we admit the presence of sarcopenic obesity in adolescents?

To the best of our knowledge, few studies have focused on the relevance of %SMM for metabolic health in overweight adolescents. The aim of this study was to investigate the association of %SMM levels with metabolic outcomes in overweight adolescents attending a Pediatric Outpatient Obesity Clinic. Additionally, we aimed to analyze the prevalence of overweight adolescents with decreased levels of %SMM, based on reference charts for youth.

MATERIALS AND METHODS

Participants

Clinical Data from 240 overweight adolescents (BMI ≥p85), aged 10-17, followed at the Pediatric Outpatient Obesity Clinic, Hospital de Santa Maria, Lisbon, Portugal, were collected retrospectively. From those, a sub-sample of 45 patients with complete clinical information in two time periods was used to analyze the changes in % SMM and in metabolic outcomes overtime. Exclusion criteria included: (i) patients with major pathologies (other than obesity or its related comorbidities), (ii) enrolled in pharmaceutical therapies, (iii) with mental disorders, and/or (v) with conditions leading to inability to perform regular PA.

This study was approved by the research ethics committee of the Faculty of Medicine of the University of Lisbon, Portugal (271/2016), and is in accordance with the 1964 Helsinki declaration and its later amendments.

Measurements

Anthropometric and body composition assessment

Height was assessed with a height stadiometer (SECA 217, Hamburg, Germany) in the Frankfurt plan, without shoes, with the participant back to the stadiometer, and after an expiratory phase. Height was registered to the nearest 0.1 cm.

Body weight and body composition were measured with a bioelectrical impedance scale (In Body 230, Seoul, Korea) to the nearest 0.1 kg, with the

subjects wearing as few clothes as possible, and without shoes or socks. %BFM and %SMM was calculated dividing the total BFM (kg) and SMM (kg) by body weight, respectively. Muscle-to-fat ratio (MFR) was calculated dividing total SMM for total BFM (kg). [15]

BMI was calculated dividing the body weight in kilograms by the square of height in meters [BMI= weight (kg)/height^2 (m)]. The BMI z-score was based on the World Health Organization data [BMI z-score= $[(BMI/M(t))^{L(t)}-1]/L(t)S(t)$].

Waist (WC) and hip circumferences (HipC) were assessed using a flexible anthropometric tape (SECA 203, Hamburg, Germany). WC was measured at the iliac crest level, with the subjects standing and at the end of a regular expiration (Cameron method), and HipC at the maximum protuberance of the buttocks.

Waist-to-Height ratio (WHtR) was calculated dividing the WC in centimeters by the height in centimeters [WHtR= WC (cm)/Height (cm)].

Clinical assessments

Pubertal status was assessed and categorized according to Tanner stages.

Resting blood pressure was measured using a digital sphygmomanometer (CAS 9302S, CAS Medical Systems, Branford, USA) in the right arm with an appropriate sized cuff, after five minutes of rest in the seating position. The measurement was performed three times and the average of the three measurements was recorded.

Biochemical analysis was performed in the laboratory of clinical pathology at the Clinic. Blood samples were collected after overnight fasting (12 hours) in the presence of one of the parents/ caregivers, and after a local application of a topical anesthesia patch (EMLA). Blood glucose levels were determined using hexokinase method, and insulin was assessed using a chemiluminescence immunoassay technique. Insulin sensitivity was derived by the homeostasis model assessment (HOMA-IR) method. Total cholesterol, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) were determined using enzymatic, GPO-trinder, and direct methods, respectively. Low-density lipoprotein cholesterol (LDL-C) was calculated from total cholesterol and HDL-C. [16] C-reactive protein (CRP) was determined using turbidimetric immunoassay (Siemens, ADVIA 2400, Newark, DE, USA).

Physical activity

PA levels were assessed by interview. Patients were questioned about their weekly regular structured (Physical Education classes and sports participation) and unstructured (e.g. soccer, basketball, cycling,) PA. Additionally, patients were questioned about the time spent in active transportation (walking or cycling for and from school). PA was registered in number of minutes per week (from Monday to Sunday). [17]

Statistical analysis

Data was analyzed using the IBM SPSS statistics (IBM SPSS statistics, version 21.0, IBM, New York, USA).

Chi-square and Independent sample t-test were used in order to analyze the differences between female and male patients. Since, there were no statistical significant differences between sexes regarding metabolic outcomes, female and male patients were analyzed together. The associations between %SMM and metabolic outcomes were analyzed using partial correlations controlling for age, sex, and Tanner stage. ANOVA and Independent Sample T-test procedures were used in the association analysis between %SMM percentiles and %SMM under or above p25, respectively. Overtime changes in %SMM percentiles and its association with changes in metabolic outcomes were analyzed with ANOVA.

A p value of <.05 was considered as statistical significant.

RESULTS

Cross-sectional analysis

A total of 240 clinical files were analyzed (52.1% females). Female and male patients differed from height, pubertal status, %BFM and %SMM, but did not differ from PA levels or from any metabolic outcome (Table 1).

Table 1. Patient's characteristics.

		Girls Mean (SD)	*n*	Boys Mean (SD)	*n*	*p* value	Total Mean (SD)	*n*
Age (months)		174 (27.7)	125	168 (24.6)	115	.082	171 (26)	240
Weight (kg)		81.0 (18.0)	125	84.3 (23.1)	115	.231	82.6 (20.6)	240
Height (cm)		158.3 (7.4)	125	163.2 (9.6)	115	<.000	160.6 (8.9)	240
BMI (kg/m^2)		32.11 (5.62)	125	31.25 (6.41)	115	.271	31.70 (6.01)	240
BMI z-score		2.69 (0.72)	125	2.83 (0.86)	115	.164	2.76 (.80)	240
WC (cm)		100.0 (11.8)	102	102.4 (14.6)	80	.224	101.1 (13.1)	182
HipC (cm)		110.3 (15.7)	87	107.3 (12.6)	72	.193	108.9 (14.4)	159
WHtR		.63 (0.07)	102	.62 (.07)	80	.445	.63 (.07)	182
Tanner stage	1	8 (6.7%)	119	13 (11.8%)	110	<.000[a]	21 (9.2%)	229
	2	8 (6.7%)		23 (20.9%)			31 (13.5%)	
	3	10 (8.4%)		20 (18.2%)			30 (13.1%)	
	4	16 (13.4%)		27 (24.5%)			43 (18.8%)	
	5	77 (64.7%)		27 (24.5%)			104 (45.4%)	
BFM (%)		44 (5.5)	104	39.7 (7.7)	105	<.000	41.8 (7.0)	208
SMM (%)		32.9 (7.4)	104	36.4 (9.6)	105	.004	34.7 (8.7)	208
SMM ≤p25		21 (20.2%)	104	35 (33.3%)	105	.035[a]	56 (26.9%)	208
SBP (mmHg)		119 (11)	120	116 (17)	114	.119	118 (14)	234
DBP (mmHg)		62 (10)	120	63 (10)	112	.287	61 (10)	232
Glucose (mg/dl)		84.4 (14.6)	122	85.5 (9.1)	115	.493	84.9 (12.2)	237
Insulin (µlU/ml)		22.9 (11.7)	121	20.3 (14.1)	106	.135	21.7 (12.9)	227
HOMA-IR		5.0 (3.0)	118	4.4 (3.8)	106	.246	4.7 (3.4)	224
Tot. C (mg/dl)		157.3 (34.5)	125	158.2 (29.0)	115	.824	157.8 (31.9)	240
LDL-C (mg/dl)		88.8 (23.9)	125	94.6 (25.1)	115	.073	91.5 (24.6)	240
HDL-C (mg/dl)		49.2 (12.1)	125	47.3 (10.6)	115	.200	48.3 (11.4)	240
TG (mg/dl)		86.9 (46.9)	125	89.3 (44.7)	114	.686	88.0 (45.7)	240
CRP (mg/dl)		.51 (.70)	58	.38 (.38)	55	.253	.45 (.57)	113
fT4 (pmol/l)		1.13 (.26)	118	1.12 (.17)	104	.791	1.12 (.22)	222
TSH (mlU/l)		2.16 (1.34)	119	2.23 (1.09)	102	.697	2.19 (1.22)	220
fT4/TSHR		1.19 (3.54)	118	.69 (.73)	101	.139	.96 (2.65)	219
TSH ≥4,0 (mlU/l)		13 (10.9%)	119	9 (8.8%)	102	.658[a]	22 (10%)	221
PA (min)		186 (106)	102	189 (116)	100	.847	188 (111)	202

Legend:
BMI- Body mass index;
BFM- Body fat mass;
CRP- C-Reactive protein;
DBP- Diastolic blood pressure;
fT4- Free-Thyroxine (T4);
fT4/TSHR- fT4/TSH ratio;
HDL-C- High-density lipoprotein cholesterol;
HipC- Hip circumference;
HOMA-IR- Insulin resistance;
LDL-C- Low-density lipoprotein cholesterol;
SBP- Systolic blood pressure;
SMM- Skeletal muscle mass;
TG- Triglycerides;
Tot.C- Total cholesterol;
TSH- Thyroid-stimulating hormone;
PA- Physical activity;
WC- Waist circumference;
WHtR- Waist-to-height ratio.
[a] – analysis performed with χ^2

%BFM was positively associated with all the anthropometric variables (BMI, BMI z-score, WC, HipC, WHtR) (p<.001) and with Insulin levels, HOMA-IR, TG, and CRP (p<.001). In addition, %BFM was negatively associated with PA levels. Conversely, %SMM was negatively associated with all the anthropometric variables, %BFM (p<.001) and with TG (p<.01), and positively associated with PA levels. Similarly to %SMM, MFR was negatively associated with all the anthropometric variables (p<.001) and positively associated with PA levels. Additionally, MFR was negatively associated with insulin levels (p<.01), HOMA-IR (p<.05) and TG (p<.01). Partial correlations are presented in Table 2.

Table 2. Associations between skeletal muscle mass, anthropometrics, body fat mass and metabolic outcomes.

	BMI	BMI z	WC	HipC	WHtR	%BFM	%SMM	MFR	SBP	DBP	Gluc.	Insulin	HOMA-IR	Tot.C	C-LDL	C-HDL	TG	CRP	TSH	fT4	fT4-TSHR	PA
BMI	1																					
BMI z	.990 §	1																				
WC	.831 §	.831 §	1																			
HipC	.705 §	.742 §	.630 §	1																		
WHtR	.837 §	.842 §	.939 §	.601 §	1																	
%BFM	.729 §	.742 §	.608 §	.497 §	.667 §	1																
%SMM	-.286 §	-.298 §	-.269 §	-.359 §	-.313 §	-.415 §	1															
MFR	-.379 §	-.387 §	-.320 §	-.333 §	-.342 §	-.708 §	.688 §	1														
SBP	.073	.065	.241 †	.202 *	.162 *	-.006	-.043	-.009	1													
DBP	.009	.014	-.034	.034	.008	.042	.008	.003	.417 §	1												
Gluc.	.150 *	.140 *	.148	.289 §	.171 *	.118	-.012	-.017	-.001	.021	1											
Insulin	.345 §	.312 §	.360 §	.304 §	.299 §	.342 §	-.107	-.187 †	.086	.021	.318 §	1										
HOMA-IR	.311 §	.281 §	.363 §	.409 §	.326 §	.351 §	-.102	-.177 *	.069	.003	.593 §	.934 §	1									
Tot.C	.034	.019	.144	.127	.103	.103	-.051	-.056	-.025	-.047	.092	.111	.105	1								
C-LDL	.035	.019	.020	.013	.002	.095	-.014	-.024	-.057	-.084	.126	.133	.137 *	.779 §	1							
C-HDL	-.114	-.107	-.069	-.108	-.061	-.125	.013	.026	.009	.052	-.029	-.202 †	-.184 †	.232 §	.090	1						
TG	.264 §	.238 §	.298 §	.256 †	.285 †	.258 §	-.190 †	-.192†	.075	.011	.045	.321 §	.095	.394 §	.193 †	-.286 §	1					
CRP	.574 §	.582 §	.337 §	.357 §	.394 §	.449 §	-.049	-.135	.038	-.010	.507 §	.179	.398 §	.117	.021	.031	.081	1				
TSH	.004	.005	-.084	-.069	-.066	.002	-.083	-.072	-.040	-.028	.082	.075	.095	.052	.016	.024	.204 †	.023	1			
fT4	-.036	-.012	-.122	-.044	-.126	.071	-.141	-.119	.013	-.063	-.014	-.119	-.107	-.085	-.090	-.090	-.063	.105	.022	1		
fT4-TSHR	-.068	-.060	.078	.051	.060	.037	-.051	-.031	.064	.078	-.002	.009	-.003	-.013	-.017	.003	-.021	-.039	-.299 §	.108	1	
PA	-.136	-.159 *	-.093	-.053	-.149	-.208 †	.379 §	.343 §	-.084	-.056	.035	-.056	-.030	.043	.097	.051	-.189 †	-.057	-.125	.053	.032	1

BMI- Body mass index; BFM- Body fat mass; CRP- C-Reactive protein; DBP- Diastolic blood pressure; fT4- Free-Thyroxine (T4); fT4/TSHR- fT4/TSH ratio; HDL-C- High-density lipoprotein cholesterol; HipC- Hip circumference; HOMA-IR- Insulin resistance assessment; LDL-C- Low-density lipoprotein cholesterol; SBP- Systolic blood pressure; SMM- Skeletal muscle mass; TG- Triglycerides; Tot.C- Total cholesterol; TSH- Thyroid-stimulating hormone; PA- Physical activity; WC- Waist circumference; WHtR- Waist-to-height ratio.
Partial correlations controlling for age, sex and tanner's stage.
* p<.05; † p<.01; § p<.001.

56 patients (26.9%) were classified as ≤p25 for %SMM, which was associated with increased BMI z-score, WC, %BFM (p<.001), insulin, HOMA-IR (p<.01), total cholesterol (p<.05), LDL-C (p<.01), TG (p<.001) and CRP (p<.05); and decreased HDL-C (p<.05) and PA (p<.001) levels. Associations with %SMM percentiles are presented in Table 3.

Overtime changes analysis

Time between assessments was in average of 12.1 (±2.1) months. The patients who decreased their %SMM percentile showed an increase in %BFM (F=18.3, p<.001) and CRP, (F=5.54, p<.05) and a decrease in HDL-C (F=4.37, p<.05) and PA levels (F=6.54, p<.01). Conversely, those who have preserved or increased their percentile showed a decrease in %BFM (F=18.3, p<.001) and CRP (F=5.54, p<.05), and an increase in HDL-C (F=4.37, p<.05) and PA levels (F=6.54, p<.01) (Table 4).

Table 3. Associations between skeletal muscle mass percentiles, anthropometrics, body fat mass and metabolic outcomes.

		BMI z	*p*	WC	*p*	%BFM	*p*	Gluc.	*p*	Insulin	*p*	HOMA-IR	*p*	Tot. C.	*p*	LDL-C	*p*	HDL-C	*p*	TG	*p*	CRP	*p*	PA	*p*
%SMM	p2	4.21	<.001	125.4	<.001	50.3	<.001	94.2	.125	30.89	<.01	7.54	<.001	173.5	.319	109.1	.209	42.9	.195	133.6	<.001	1.47	<.001	150.7	<.001
	(*n*=15)	(.88)		(15.0)		(2.9)		(36.1)		(14.7)		(5.00)		(36.2)		(11.5)		(29.7)		(64.7)		(1.48)		(141.0)	
	p9	3.55		108.2		49.2		86.0		28.21		5.86		161.5		92.7		48.7		103.9		1.06		126.4	
	(*n*=18)	(.83)		(11.0)		(2.9)		(6.0)		(18.8)		(3.58)		(21.9)		(11.4)		(21.9)		(53.5)		(1.18)		(80.1)	
	p25	3.14		108.3		47.3		83.5		21.75		4.43		162.3		96.8		44.9		99.3		0.40		157.2	
	(*n*=24)	(.72)		(12.4)		(3.3)		(6.2)		(12.4)		(2.35)		(33.6)		(8.0)		(31.1)		(46.3)		(.27)		(85.1)	
	p50	2.82		104.1		42.9		82.6		18.91		3.86		158.9		94.6		51.4		73.9		0.53		170.7	
	(*n*=29)	(.52)		(9.6)		(3.7)		(6.5)		(10.2)		(2.11)		(32.9)		(10.8)		(24.8)		(34.9)		(.39)		(105.2)	
	p75	2.52		102.0		40.0		83.2		17.14		3.53		154.8		89.2		48.9		83.2		0.39		202.3	
	(*n*=25)	(.47)		(8.3)		(4.3)		(6.2)		(7.4)		(1.53)		(22.5)		(11.6)		(21.9)		(35.1)		(.29)		(144.0)	
	p91	2.33		95.9		37.9		84.0		20.91		4.42		154.0		88.4		46.9		93.8		0.19		180.7	
	(*n*=29)	(.33)		(10.4)		(4.0)		(7.4)		(10.8)		(2.43)		(27.7)		(11.3)		(21.8)		(47.8)		(.18)		(109.4)	
	p98	2.33		96.7		37.4		84.4		22.08		4.67		154.1		87.2		49.6		86.9		0.25		174.6	
	(*n*=26)	(.35)		(8.5)		(4.7)		(9.0)		(11.5)		(2.74)		(30.0)		(8.5)		(26.8)		(37.7)		(.30)		(70.0)	
	>p98	2.51		96.2		38.2		84.4		19.51		4.17		152.2		90.6		49.3		64,7		0.44		263.6	
	(*n*=42)	(.77)		(13.9)		(9.2)		(7.8)		(11.0)		(2.48)		(25.1)		(11.8)		(21.9)		(26.5)		(.41)		(99.2)	
[a]%SMM >p25		2.52	<.001	98.6	<.001	39.3	<.001	83.8	.086	19.7	<.01	4.1	<.01	154.5	<.05	89.8	<.05	49.2	<.05	79.1	<.001	.365	<.05	203	<.001
(*n*=152)		(.58)		(11.1)		(6.4)		(7.4)		(10.3)		(2.3)		(27.3)		(23.4)		(11.7)		(37.3)		(.343)		(111.6)	
%SMM ≤p25		3.54		112.4		48.6		87.1		26.2		5.7		165.6		99.6		45.7		110.3		.788		145	
(*n*=57)		(.91)		(14.6)		(3.3)		(19.5)		(15.5)		(3.8)		(30.0)		(27.5)		(10.2)		(55.4)		(.983)		(101.5)	

Legend:
BMI- Body mass index; BFM- Body fat mass; CRP- C-Reactive protein; HDL-C- High-density lipoprotein cholesterol; HOMA-IR- Insulin resistance; LDL-C- Low-density lipoprotein cholesterol; SMM- Skeletal muscle mass; TG- Triglycerides; Tot.C- Total cholesterol; PA- Physical activity; WC- Waist circumference.
[a] – analysis performed with independent sample T-test.

Table 4. Overtime changes in skeletal muscle mass (%) percentiles and its association with changes in anthropometrics, body fat mass and metabolic outcomes.

		Δ BMI z	*p*	Δ WC	*p*	Δ %BFM	*p*	Δ Gluc.	*p*	Δ Insulin	*p*	Δ HOMA-IR	*p*	Δ Tot. C	*p*	Δ LDL-C	*p*	Δ HDL-C	*p*	Δ TG	*p*	Δ CRP	*p*	Δ PA	*p*
Δ %SMM	- p	.14	.592	6.0	.093	2.7	<.001	.21	.114	-3.71	.193	-.73	.104	-7.14	.260	-4.93	.686	-3.50	<.05	6.50	.559	.08	<.05	-60	<.01
	(*n*=14)	(.48)		(6.2)		(4.3)		(4.80)		(8.49)		(1.96)		(11.16)		(11.81)		(6.07)		(35.76)		(.18)		(116.3)	
	= p	-.07		-.3		-.7		-7.62		-22.10		-6.27		6.31		.46		5.15		3.69		-.39		38	
	(*n*=13)	(.24)		(7.7)		(1.0)		(12.4)		(50.96)		(12.79)		(30.34)		(24.89)		(10.50)		(25.07)		(.27)		(167.6)	
	+ p	-.01		-2.7		-4.7		-4.11		-3.15		-.76		.06		.17		1.33		-4.28		-.07		93	
	(*n*=18)	(.73)		(8.3)		(3.8)		(9.90)		(8.14)		(1.87)		(18.49)		(17.62)		(6.17)		(26.44)		(.13)		(71.6)	

BMI- Body mass index; BFM- Body fat mass; CRP- C-Reactive protein; HDL-C- High-density lipoprotein cholesterol; HOMA-IR- Insulin resistance assessment; LDL-C- Low-density lipoprotein cholesterol; SMM- Skeletal muscle mass; TG- Triglycerides; Tot.C- Total cholesterol; PA- Physical activity; WC- Waist circumference..

DISCUSSION

Adolescent overweight remains a major health concern worldwide [18] and is associated with a vast array of metabolic comorbidities. [1]

One of the aims of this study was to investigate the association of %SMM with metabolic health in the population under study. This is of particular relevance, since it is acknowledged that low levels of SMM are associated with adverse metabolic outcomes, [7] placing these overweight adolescents at a higher risk of early cardiovascular events. [19]

Similarly to the results reported by other authors, [20] in our study %BFM was positively associated with all the anthropometric and metabolic variables,

reflecting an adverse health condition. %SMM showed to be negatively associated with the same anthropometric variables, %BFM, and TG levels. The lack of association of %SMM with other metabolic outcomes could be due to the fact that %BFM may have a higher influence on metabolic health among overweight adolescents than %SMM. We decided to calculate MFR as suggested by McCarthy *et al.* [15] in order to overcome the %BFM confounding effect. MFR showed higher association levels with metabolic outcomes than SMM alone. However, it was only negatively associated with TG, insulin and insulin resistance (HOMA-IR).

Another explanation for the lack of statistical associations between %SMM and the metabolic outcomes may be the noticeable variation in %SMM in this population, as can be seen trough the standard deviations in %SMM (Table 1). Indeed, we can differentiate two types of overweight adolescents based on body composition: those with high levels of %BFM and low levels of %SMM, and those with both high levels of %BFM and high levels of %SMM.

Based on this, we aimed to analyze the prevalence of overweight adolescents with low levels of %SMM, based on reference charts for youth. [15]

In our study, 56 patients (26.9%) presented a %SMM ≤p25, which was associated with a higher BMI z-score, WC and %BFM, as well as with a worse metabolic profile (increased insulin levels, insulin resistance, LDL-C, TG and CRP, and decreased HDL-C). Furthermore, patients classified as ≤p25 for %SMM, reported in average 145 minutes/week of PA, which represents only 34.5% of the recommended weekly PA time, [21] corresponding to less 58 minutes/week than the patients with a %SMM >p25. Since it is widely recognized that PA is largely responsible for the variability in SMM and muscular fitness, [22] we may assume that the (low) PA levels of these patients were not enough to positively influence %SMM, negatively affecting their metabolic health. [23]

Kalinkovich *et al.* has suggested that adipose tissue inflammation (represented in this study by CRP levels), insulin resistance, and associated diminished fatty acid uptake and oxidation (observed by elevated blood fatty acid levels), may lead to an increased ectopically accumulation of lipids in the SMM (muscle lipid toxicity), which in turn may result in a decline of SMM, its function, and strength (12). On the other hand, decreased levels of PA associated with increased levels of sedentary time may lead to an impaired protein synthesis clustered to an increased protein breakdown and associated muscle atrophy. [24] The lack of PA may further negatively influence insulin sensitivity through the under regulation of GLUT-4. [24,25]

In line with the results of the cross-sectional analyzes, in the sub-sample of 45 patients, overtime changes (increase) in %SMM percentiles were associated with changes in %BFM, CRP in the opposite direction; and with changes in HDL-C in the same direction. The lack of statistical significance between overtime changes in %SMM and other metabolic variables may be due to the small sub-sample size.

Although other authors have used similar samples (in age and size) in order to analyze changes in anthropometric, metabolic and PA outcomes, [26-28] we consider that the small sub-sample size in this study is a limitation for this kind of analysis.

The retrospective design and cross-sectional analysis can be considered as two other limitations, since cross sectional studies do not allow for causal inferences. Among the strengths of this study are the considerable number of clinical records analyzed and the extent of the clinical analysis performed, additionally to the overtime analysis.

Another limitation could be the use of bioelectrical impedance for the assessment of body composition. Bioelectrical impedance cannot be

considered as a gold-standard, however, it is a cost-effective, non-invasive and reliable method, [29] that can be used in the clinical practice.

Besides these limitations, this study brings extra knowledge to the study of adolescent overweight. To the best of our knowledge there is scarce literature on the relationship between SMM levels and metabolic outcomes in overweight adolescents, and even less literature regarding the adverse impact of the combination of decreased %SMM and the overweight state. Although this study suggests that overweight adolescents may experience the deleterious impact of sarcopenic obesity, similarly to what happens with the elderly, further studies are needed in order to understand the pathophysiology and the mechanisms behind the combination of a decreased %SMM and obesity-related factors in youth.

CONCLUSION

This study suggests that body composition analysis through bioelectrical impedance, together with %SMM classification in percentiles, using the p25 cut-off, can act not only as a guidance for adequate lifestyle counseling (focused on PA, diet or both), but also as a prior assessment of overall metabolic risk in overweight adolescents.

This study also draws the attention to the possible existence of a sub-group of overweight adolescents with low levels of %SMM, which is associated with an adverse metabolic profile, and possibly associated with an impaired functional capacity [10] and perceived quality of life, [30] similarly to what happens with those elderly diagnosed with sarcopenic obesity. This particular group represents a priority for intervention, where PA promotion may play a major role.

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