***Pediatric Exercise Science*, 2018, 30, 60-70**
https://doi.org/10.1123/pes.2016-0275

Human Kinetics
REVIEW

Effects of Exercise Training Alone on Depot-Specific Body Fat Stores in Youth: Review of Recent Literature

YoonMyung Kim
Yonsei University

The prevalence of childhood obesity has increased at an alarming rate. The increased obesity rate in pediatrics parallels the increased risks for developing metabolic abnormalities, such as insulin resistance, type 2 diabetes, and nonalcoholic fatty liver disease. In particular, the strong relationship between obesity and such health consequences is well explained by the excessive accumulation of depot-specific body adiposity, such as visceral adipose tissue, intrahepatic lipid content, intermuscular adipose tissue, and/or intramyocellular lipid content. Limited evidence suggests that both aerobic and resistance exercise alone, independent of weight loss, can be an effective therapeutic strategy for improving risk markers of metabolic abnormalities as well as inducing positive changes in depot-specific body adiposity in obese children and adolescents. However, the independent role of exercise alone (without calorie restriction) in body fat distribution is still unclear, and the results are less conclusive in pediatrics. In this brief review, the effects of aerobic and resistance exercise on depot-specific body adiposity changes in children and adolescents are discussed.

Keywords: childhood obesity, visceral, hepatic, intermuscular adipose tissue, intramyocellular lipid

Childhood obesity is an epidemic (45), and it is recognized as a leading health concern due to its strong associations with comorbid conditions, such as impaired glucose tolerance (57), metabolic syndrome (7), type 2 diabetes (T2DM) (29,48), and nonalcoholic fatty liver disease (NAFLD) (5,55), in children and adolescents. It is also well established that obese children and adolescents are more likely to remain obese as adults (66). Furthermore, tracking for such health outcomes from childhood into adulthood is more predominant in overweight and obese youth than their lean counterparts (21). Thus, early detection, prevention, and treatment for childhood obesity and obesity-related health risks are of importance.

There is a strong body of evidence supporting that a regional body fat distribution is one of the fundamental elements explaining the link between obesity and its related risks for metabolic abnormalities in pediatrics (1,10,40,64). As in adults (25,44,49,51), excessive accumulation of adiposity in the abdomen and liver is recognized as an independent risk factor for developing insulin resistance and T2DM in children and adolescents (1,64). In addition, limited evidence also demonstrates a significant relationship between intermuscular adipose tissue (IMAT) or intramyocellular lipid (IMCL) content within skeletal muscle and obesity-related health abnormalities in children and adolescents (40,64). These results clearly suggest that depot-specific body adipose tissue (AT) stores may modulate the degree of health risks in children and adolescents.

The current advances in imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), provide accurate and reproducible quantifications of specific fat depots, such as visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), hepatic lipid content, IMAT, and IMCL (26,30). Therefore, the use of these imaging techniques in clinical research settings allows to investigate and develop an effective prevention and treatment strategy for reductions in depot-specific body AT, which can further reduce the childhood obesity epidemic and its concomitant complications.

In adults, a strong body of evidence (8,14,22,32) suggests that regular exercise training (≥3 times/wk, 30–60 min/session) without weight loss or calorie restriction results in significant reductions in total and abdominal AT and improvements in metabolic profiles in obese men and women. Some studies also reported significant reductions in lipid content in liver and skeletal muscle through regular exercise training alone in adults (6,35,37); however, there is insufficient evidence to draw secure conclusions. Previous intervention studies in obese children and adolescents (12,38,39,53,56) have also shown some beneficial effects of regular exercise

Kim is with the University College, Center for Health and Wellness, Yonsei University, International Campus, Incheon, Korea. Address author correspondence to YoonMyung Kim at yoonkim@yonsei.ac.kr.

without calorie restriction on insulin resistance and specific body fat depots. However, at present, relatively few studies have assessed the independent role of regular excise alone, as an efficient therapeutic treatment tool for reductions in depot-specific body AT in pediatrics. Furthermore, the well-accepted exercise modality for concurrent reductions of AT particularly in obese children and adolescents has not been firmly established. Thus, this review focuses on the effect of exercise training alone on the depot-specific body fat changes, in particular, on the abdominal AT, hepatic lipid content, IMAT, and IMCL content in children and adolescents. In addition, available evidence demonstrating the best exercise modality that yields positive changes in depot-specific adiposity in obese children and adolescents is reviewed and presented.

Exercise Training and Abdominal Adiposity

A strong body of evidence from well-controlled randomized studies in adults (8,14,22,32,41,50,52) suggests that aerobic exercise without calorie restriction (in the absence of weight loss) is an effective treatment tool for reducing abdominal AT, particularly visceral AT, in nondieting obese men and women. So far, there have been 8 randomized controlled trials (Table 1) that examined the effects of aerobic exercise training alone on abdominal adiposity in children and adolescents. Owens et al (46) previously reported that, compared with the controls, a 4-month intense aerobic exercise training program (5 times/wk, 40 min/d, 70%–75% of maximal heart rate) was associated with a significant reduction in MRI-determined abdominal SAT (ASAT, −16.2 cm^3) and lower increase in VAT (1.3 cm^3) in young obese girls (7–11 y). In a later study by the same research group (3), moderate to vigorous school-based aerobic exercise program (daily activity, 80 min/d, >150 bpm) attenuated the age-associated increases in ASAT (65.2 cm^3 vs 130.0 cm^3) and VAT (0.8 cm^3 vs 16.1 cm^3) in obese girls (8–12 y) compared with the controls. A recent study by Davis et al (12) conducted with 222 overweight and obese children (7–11 y) showed that a 10–15-week aerobic exercise intervention (low dose: 5 d/wk, 20 min/session vs high dose: 5 d/wk, 40 min/session) without calorie restriction resulted in significant reductions in both ASAT (−23.7 cm^3 in high dose and −15.1 cm^3 in low dose) and VAT (−3.9 cm^3 in high dose and −2.8 cm^3 in low dose) in the intervention groups compared with the control group. In that study (12), despite somewhat greater improvements with high dose compared with low-dose exercise training, dose–response relationships between aerobic exercise and insulin resistance, fitness, and abdominal AT (except for ASAT) were not observed. Gutin et al (28) examined the effects of an 8-month intensive aerobic exercise training [5 d/wk, 55%–80% of peak oxygen uptake (VO_{2peak})] combined with lifestyle education on MRI-determined abdominal adiposity in overweight and obese adolescents (13–16 y). Compared with the lifestyle education group, significant reductions in VAT (−42.0 cm^3) and ASAT (−69.7 cm^3) were observed after the aerobic exercise training. However, low compliance rate (51%–56%) with the prescribed exercise regimens and no true control group impeded such results in that study (28).

Recently, Lee et al (38,39) conducted randomized controlled trials using whole-body MRI technique in sedentary obese male (38) and female (39) adolescents (12–18 y). In both studies (38,39), the attendance rates and the compliance to the prescribed exercise training were relatively high (>95%) during the 12-week intervention period, thereby providing a robust effect of exercise training alone on the abdominal adiposity in obese youth. Compared with the controls, a 3-month aerobic exercise training (3 times/wk, 60 min/session, 50%–75% of VO_{2peak}) without calorie restriction resulted in significant reductions in VAT [−0.1 kg in boys (38) and −15.7 cm^2 in girls (39)] and ASAT [−0.5 kg in boys (38)]. Such observations confirm and expand previous findings from other groups (3,12,28,46) and suggest that regular aerobic exercise alone can attenuate the accumulation of adiposity in the abdomen in overweight and obese male and female adolescents even without weight loss. In addition, in the study with obese boys (38), abdominal AT volume was derived using multislice MRI techniques, thereby providing a better understanding of abdominal AT changes in response to the intervention because the mobilization or presence of abdominal AT, particularly VAT, may not be uniform across the abdomen region in pediatrics (42).

Although aerobic exercise has been conventionally employed in the prevention and treatment for childhood obesity, overweight or obese youth might be bored or have physical discomforts with traditional forms of prolonged aerobic exercise (18). A growing body of evidence suggests that carefully supervised resistance training is safe and beneficial for improving muscular strength and body composition, so this training is recognized as an alternative exercise modality for the treatment of childhood obesity. In obese adults, similar to the effects of aerobic exercise training on abdominal AT, emerging evidence (11,31,33) also suggests beneficial and protective effects of resistance exercise training without calorie restriction on abdominal AT. However, only a few studies (13,38,39,59,61) have assessed the effects of resistance exercise on abdominal AT in overweight and obese youth (Table 2). Treuth et al (59) examined the effects of a 5-month resistance exercise training alone [3 times/wk, 20 min/session, >50% of 1 repetition maximum (RM), 2 sets, 12–15 repetitions (reps)] on total and abdominal AT, determined by CT technique, in prepubertal obese girls (7–10 y) and found significant increases in total AT (1.5 kg) and ASAT (16.1 cm^2); however, VAT did not increase in their study. These findings are in agreement with the current observations by van der Heijden et al (61), who demonstrated that no significant change in VAT (−3.0 cm^2)

Table 1 Aerobic Exercise Training and Abdominal Adiposity

References	Subjects	Age, y	Treatment	BW/BMI at baseline	Study period	Protocol	Δ BW/BMI	Δ VAT	Δ SAT	Abdominal AT measure
Nonrandomized controlled trials										
van der Heijden et al (62)	17 boys	15.1	Obese exercise	91.7 kg	12 wk	2 times/wk, 30 min/d, ≥70% of VO_{2peak}	–0.5 kg	–5.1 cm[2a]	No change	MRI
	12 girls		Lean exercise	57.2 kg			0.8 kg	No change	No change	
Randomized controlled trials										
Barbeau et al (3)	201 girls (black)	8–12	Control	20.9 kg/m[2]	10 mo	Daily after school program, 80 min/d, HR > 150 bpm	1.3 kg/m[2]	16.1 cm[3]	129.8 cm[3]	MRI
			Exercise	20.9 kg/m[2]			0.7 kg/m[2b]	0.8 cm[3b]	65.2 cm[3b]	
Davis et al (12)	94 boys	7–11	Control	26.3 kg/m[2]	10–15 wk	5 times/wk, HR > 150 bpm	NA	Mean difference vs control	Mean difference vs control	MRI
	128 girls		Low-dose exercise	25.9 kg/m[2]		Low dose: 20 min/d		–2.8 cm[3b]	–15.1 cm[3b]	
			High-dose exercise	25.6 kg/m[2]		High dose: 40 min/d		–3.9 cm[3b]	–23.7 cm[3b]	
Eliakim et al (16)	44 girls	15–17	Control	58.3 kg	5 wk	2 h daily aerobic activities	NA	0.2%	0.1%	MRI
			Exercise					0.3%	0.0%	
Eliakim et al (17)	44 boys	15–17	Control	66.2 kg	5 wk	5 times/wk, 2–2.5 h daily aerobic activities	0.6 kg	4.5%[a,b]	1.8%[a]	MRI
			Exercise	61.0 kg			0.8 kg	–0.2%	–1.8%[a,b]	
Gutin et al (28)	26 boys	13–16	LSE	94.8–100.2 kg	8 mo	5 times/wk, 250 kcal/session, 55%–80% of VO_{2peak}	NA	–11.0 cm[3]	40.4 cm[3]	MRI
	54 girls		LSE + exercise					–42.0 cm[3a]	–69.7 cm[3]	
Lee et al (38)	45 boys	12–18	Control	100.0 kg	3 mo	3 times/wk, 60 min/session, 50%–75% of VO_{2peak}	2.6 kg	0.2 kg	0.2 kg	MRI
			Exercise	106.5 kg			–0.04 kg[b]	–0.1 kg[a,b]	–0.5 kg[a,b]	
Lee et al (39)	44 girls	12–18	Control	93.3 kg	3 mo	3 times/wk, 60 min/session, 50%–75% of VO_{2peak}	0.1 kg	5.9 cm[2]	–2.9 cm[2]	MRI
			Exercise	88.9 kg			–1.3 kg	–15.7 cm[2b]	–7.8 cm[2]	
Owens et al (46)	25 boys	7–11	Control	56.9 kg	4 mo	5 times/wk, 40 min/y, 70%–75% MHR, HR > 150 bpm	2.0 kg[a]	20.9 cm[2a,b]	48.9 cm[2a]	MRI
	49 girls		Exercise	57.5 kg			1.1 kg[a]	1.3 cm[2]	–16.2 cm[2b]	

Abbreviations: AT, adipose tissue; BMI, body mass index; BW, body weight; HR, heart rate; LSE, life style education; MHR, maximum heart rate; MRI, magnetic resonance imaging; NA, not available; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue; VO_{2peak}, peak oxygen uptake.

[a]Significantly different from baseline within group, $P < .05$.

[b]Significantly different from the control group, $P < .05$.

Table 2 Resistance Exercise Training and Abdominal Adiposity

References	Subjects	Age, y	Treatment	BW at baseline (kg)	Study period	Protocol	Δ BW (kg)	Δ VAT	Δ SAT	Abdominal AT measure
Nonrandomized controlled trials										
Treuth et al (59)	22 girls	7–10	Control (lean)	29.1	5 mo	3 times/wk, >50% of 1 RM, 2 sets, 12–15 reps	2.9[a]	NA	NA	CT
			Exercise	46.6			4.0[a]	1.5 cm^2	16.1 cm^2[a]	
van der Heijden et al (61)	6 boys 6 girls	15.5	Exercise	97.0	12 wk	2 times/wk, 60 min/session, 50%–85% of 3 RM, 2–3 sets, 8–20 reps	2.6[a]	–3.0 cm^2	34.0 cm^2[a]	MRI
Randomized controlled trials										
Davis et al (13)	94 boys 128 girls	14–18	Control	94.4	10–15 wk	2 times/wk, 60–90 min/session, 30–45 min of aerobic exercise, 30–45 min of resistance exercise	NA	8%[a]	6%[a]	MRI
			Exercise	80.2				–10%[a,b]	–10%[a,b]	
			Exercise + MI	88.5				No change	No change	
Lee et al (38)	45 boys	12–18	Control	100.0	3 mo	3 times/wk, 60 min/session, >60% of 1 RM, 2 sets, 8–12 reps	2.6	0.2 kg	0.2 kg	MRI
			Exercise	97.7			–0.6[b]	–0.2 kg[a,b]	–0.4 kg[a,b]	
Lee et al (39)	44 girls	12–18	Control	93.3	3 mo	3 times/wk, 60 min/session, >60% of 1 RM, 2 sets, 8–12 reps	0.1	5.9 cm^2	–2.9 cm^2	MRI
			Exercise	97.1			–0.3	–4.5 cm^2	–14.4 cm^2	

Abbreviations: AT, adipose tissue; BW, body weight; CT, computed tomography; MI, motivational interview; MRI, magnetic resonance imaging; reps, repetitions; RM, repetition maximum; NA, not available; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.
[a]Significantly different from baseline within group, $P < .05$.
[b]Significantly different from the control group, $P < .05$.

occurs after a 12-week resistance exercise (2 times/wk, 60 min/session, 50%–85% of 3 RM, 2–3 sets, 8–20 reps using weight-lifting machine and free weight), but reported significant increase in ASAT (34.0 cm^2) in 12 postpubertal obese Hispanic adolescents. These observations suggest that, similar to the aerobic exercise training, regular resistance exercise may also attenuate the growth-related increases in abdominal AT, particularly VAT, but not ASAT in obese children and adolescents. So far, there have been 3 randomized controlled trials that examined the effects of resistance or combined (aerobic + resistance) exercise training alone on abdominal AT in the pediatric population. Davis et al (13) examined the effects of a 16-week circuit (aerobic + resistance exercise) training (2 times/wk, 60–90 min/session) with/without motivational interview (MI) on total and abdominal AT in 38 overweight and obese Latino adolescents (14–18 y). In that study (13), compared with the controls, the circuit training without MI resulted in significant reductions in both ASAT (−10%) and VAT (−10%). However, although identical exercise regimen was used, and similar improvements (ie, fitness levels and muscular strength levels) were observed in both training groups, no significant changes in abdominal AT were reported in the circuit training + MI group, suggesting no additional benefits on MI. These unexpected results may be partially explained by the subjects' difference in habitual physical activity during the intervention period in this study (13). The authors also noted that too frequent MI sessions (8 times) held proximately before or after the exercise sessions throughout the intervention period may hamper the beneficial effects of exercise. In addition, short-term intervention period (16 wk) may limit to provide some positive impact of MI, suggesting further research on long-term effects of MI or MI + CT. Although the observations from this study (13) suggest that circuit training with modest dose (2 times/wk) induces abdominal AT reductions along with the reduced risks for metabolic disease in obese adolescents, the effects of resistance exercise alone are still limited in overweight and obese pediatric population.

In the aforementioned randomized controlled studies by Lee et al (38,39), it was also aimed to compare the effects of a 3-month resistance exercise training alone (3 times/wk, 60 min/session, >60% of 1 RM, 2 sets, 8–12 reps using weight-lifting machine and free weight) without calorie restriction versus aerobic exercise on multislice MRI-determined abdominal AT in obese youth. As with aerobic exercise training, compared with the controls, significant reductions in VAT (−0.2 kg) and ASAT (−0.4 kg) were observed in response to resistance exercise in obese boys. However, in obese girls (39), the changes in single-slice determined VAT (−4.5 cm^2) and ASAT (−14.4 cm^2) through resistance exercise did not reach statistical significance compared with the controls (+5.9 cm^2 and −2.9 cm^2, respectively). Given the similar exercise protocols and methodologies applied in both studies (38,39), such gender differences in response to resistant exercise training are unclear. Perhaps, the gender differences in preferred exercise modality or baseline amount of abdominal AT may confound the results. Regardless, these observations provide evidence that resistance exercise training is an effective approach for reducing abdominal AT particularly for sedentary obese boys, whereas aerobic exercise training is a better exercise modality to reduce abdominal VAT for obese girls.

Exercise Training and Intrahepatic Adiposity

NAFLD is a growing health concern in children and adolescents (54,65,67) because it is strongly associated with childhood obesity and hepatic insulin resistance in pediatrics (67). NAFLD is more common in boys, early adolescence, and overweight and obese individuals (54,65). In addition, racial and ethnic disparities exist in the prevalence of NAFLD in children and adolescents, such that Hispanics (11.8%) have a higher prevalence of NAFLD compared with Asians (10.2%), whites (8.6%), and blacks (1.5%) (54). Although the pathogenesis by which NAFLD is an emerging metabolic risk in pediatrics is not fully understood, abdominal adiposity, particularly VAT, is considered as a major predictor (9,19). Visceral adipocytes are more metabolically active compared with subcutaneous adipocytes, thereby increasing free fatty acids secretion directly into the portal vein and liver (4,20,63). The influx of increased free fatty acids results in high accumulation of triglycerides within the liver, which leads to increases in hepatic gluconeogenesis and impaired insulin clearance (4,63).

In adults, emerging evidence (6,35,37) suggests that exercise training with/without weight loss plays an important role in the treatment of NAFLD, despite some controversy over the best exercise modality and the dose–response relationships. In children and adolescents, only a limited number of studies have evaluated the effectiveness of exercise training alone on NAFLD or intrahepatic lipid contents (Table 3). A recent study by van der Heijden et al (62) examined the effects of 12-week aerobic exercise training alone (4 times/wk, 30 min/session, >70% of VO_{2peak}) on insulin resistance and hepatic lipid content determined by the localized proton magnetic resonance spectroscopy (^{1}H-MRS) technique in 15 overweight/obese and 14 lean Latino adolescents. The intervention resulted in significant reductions in hepatic lipid content (−3.3%), VAT (−9.3%), and percent body fat (−1.0%) in the absence of weight changes, but not in their lean counterparts. These observations are in agreement with previous randomized controlled trials, resulting in significant reductions in ^{1}H-MRS-determined intrahepatic lipid content by 1.9% in boys (38) and 1.7% in girls (39) in response to a 3-month aerobic exercise training (3 times/wk, 60 min/session, 50%–75% of VO_{2peak}). In addition, it was observed that the change in VAT was significantly correlated with the corresponding change in intrahepatic

Table 3 Exercise Training and Lipid Content in the Liver and Skeletal Muscle

References	Subjects	Age, y	Treatment	BW at baseline	Study period	Protocol	Δ BW	Δ Liver fat	Δ IMAT	Δ IMCL	Lipid measure
Nonrandomized controlled trials											
van der Heijden et al (61)	6 boys 6 girls	15.5	RE	97.0 kg	12 wk	2 times/wk, 60 min/session, 2–3 sets, 8–20 reps	2.6 kg[a]	0.2%	NA	No change	[1]H-MRS
van der Heijden et al (62)	17 boys 12 girls	15.1	AE (obese) AE (lean)	91.7 kg 57.2 kg	12 wk	2 times/wk, 30 min/d, ≥70% of VO_{2peak}	−0.5 kg 0.8 kg	−3.3% No change	NA	No change No change	[1]H-MRS
Randomized controlled trials											
McCormack et al (43)	6 boys 15 girls	10–17	Control Exercise (AE + RE)	34.3 kg/m^2 39.1 kg/m^2	8 wk	3 times/wk, 60 min/session AE: 60%–80% of HRR for 35 min RE: Wii Fit for 25 min	−0.19 kg/m^2 0.36 kg/m^2	NA	NA	−22% 11%[b]	[1]H-MRS
Lee et al (38)	45 boys	12–18	Control	100.0 kg	3 mo	3 times/wk, 60 min/session	2.6 kg	0.9%	NA	0.7	[1]H-MRS
			AE	106.5 kg		AE: 50%–75% of VO_{2peak}	−0.3 kg	−1.9%[a,b]		1.0	
			RE	97.7 kg		RE: 2 sets, 8–12 reps	−0.6 kg[b]	−2.0%[a,b]		−0.05 (mmol/kg wet weight)	
Lee et al (39)	44 girls	12–18	Control	93.3 kg	3 mo	3 times/wk, 60 min/session	0.1 kg	0.8%	1.1 cm^2	NA	[1]H-MRS
			AE	88.9 kg		AE: 50%– 75% of VO_{2peak}	−1.3 kg	−1.7%[a,b]	−13.5 cm^2[a]		
			RE	97.1 kg		RE: 2 sets, 8–12 reps	−0.3 kg	−0.7%	−10.9 cm^2[a]		

Abbreviations: AE, aerobic exercise; BW, body weight; 1H-MRS, proton magnetic resonance spectroscopy; HRR, heart rate reserve; IMAT, intermuscular adipose tissue; IMCL, intramyocellular lipid; NA, not available; RE, resistance exercise; reps, repetitions; VO_{2peak}, peak oxygen uptake.

[a]Significantly different from baseline within group, $P < .05$.

[b]Significantly different from the control group, $P < .05$.

lipid content ($r = .72$) in boys (38), but not in girls (39). Although such different responses by gender are unclear, the dissimilar accumulation level of VAT or intrahepatic lipid content by gender may influence the strength of the relationships within AT in overweight and obese youth in this study (39).

With respect to resistance exercise training on hepatic lipid content, results are inconsistent due to differences in exercise regimens, gender, or ethnicity. Previously, van der Heijden et al (61) examined the effects of a 12-week resistance exercise training (2 times/wk, 30 min/session, 50%–85% of 3 RM, 2–3 sets, 8–20 reps using weight-lifting machine and free weight) on hepatic lipid content and insulin sensitivity in 12 obese Hispanic adolescents. The intervention resulted in significant improvements in hepatic insulin sensitivity, muscular strength, and lean body mass in the absence of weight change, but hepatic lipid content and VAT remained unchanged (61). Similarly, Davis et al (13) also reported no change in hepatic lipid content after circuit training (aerobic + resistance exercise, 2 times/wk, 60–90 min/session) in Hispanic adolescents. Based on such observations, van der Heijden et al (61) noted that, compared with resistance exercise, aerobic exercise mode may have extensive positive effects on reductions in hepatic lipid content in overweight and obese adolescents. By contrast, Lee et al (38) reported a significant reduction in intrahepatic lipid content (−2.0%) after a 3-month supervised resistance exercise training (3 times/wk, 60 min/session, >60% of 1 RM, 2 sets, 8–12 reps using weight-lifting machine and free weight) in obese adolescent boys. In addition, in that study (38), the magnitude of improvement in insulin sensitivity and reductions in VAT and intrahepatic lipid content were somewhat greater in response to resistance exercise versus aerobic exercise in obese boys. However, the later study with obese girls (39) conducted by the same research group did not observe significant changes in intrahepatic lipid and VAT in response to resistance exercise; however, significant changes were observed in response to aerobic exercise. Given the similar exercise regimens and methods to determine depot-specific adiposity in both studies (38,39), it is unclear about such gender differences. Although further studies are required to investigate such gender-related differences in response to resistance exercise, greater secretion levels in testosterone or perhaps also growth hormone may possibly induce more beneficial effects of resistance exercise on body fat distribution as well as skeletal muscle mass in adolescent boys versus girls.

Collectively, very little is known about the influence of resistance training alone (without a concomitant weight loss or calorie restriction) on NAFLD or hepatic lipid content, and results are inconsistent in children and adolescents. Based on the current knowledge, reductions in abdominal AT, particularly VAT with resistance exercise, seem to play a key role for inducing positive changes in hepatic lipid content in children and adolescents. However, more attention should be paid to resistance exercise as an alternative tool for reducing hepatic adiposity in children and adolescents.

Exercise Training and Intermuscular/Intramyocellular Adiposity

IMAT is located beneath the fascia and within the skeletal muscles, and IMCL are the lipid droplets within skeletal muscle cells (36). Quantification of these specific fat depots can be acquired by advanced imaging techniques, such as CT or MRI, which provide direct visualization of AT within skeletal muscles in vivo (26,30). Skeletal muscle plays an important role in regulation of glucose metabolism and fatty acid oxidation, thereby affecting the maintenance of normal glucose homeostasis (60). Goodpaster et al (27) previously reported that increased IMAT, determined by CT, is associated with lower insulin sensitivity in obese and T2DM adults. Consistent with the observation in adults, Lee et al (40) have reported that, independent of race, IMAT was significantly associated with lower insulin sensitivity in both black ($r = −.61$) and white ($r = −.64$) obese adolescents, even after accounting for Tanner stage.

In adults, limited evidence (8,15) suggests that aerobic exercise is associated with a significant reduction in IMAT. Some other studies also provide evidence that resistance exercise or combined exercise training without weight loss has a protective effect on the age-associated increase in IMAT in older adults. However, to the best of author's knowledge in youth, there is only one intervention study (39). In agreement with the observations from adult studies (15,23,34,58), a significant reduction in IMAT, determined by mid-thigh CT technique, was observed after a 3-month aerobic exercise (−13.5 cm^2, 3 times/wk, 60 min/session, 50%–75% of VO_{2peak}) or resistance exercise (−10.9 cm^2, 3 times/wk, 60 min/session, >60% of 1 RM, 2 sets, 8–12 reps) training in sedentary obese girls (12–18 y), suggesting beneficial effects of regular exercise alone for reducing IMAT (39).

However, it is of interest to note that the previous randomized controlled study with obese boys (38) found no significant change in IMCL, accessed using the ^{1}H-MRS technique, in response to either a 3-month aerobic or resistance exercise training despite significant improvements in body composition, insulin resistance, and insulin sensitivity. Similar results were reported in an earlier study by van der Heijden et al (62), wherein a 12-week of aerobic exercise did not exhibit IMCL changes in obese Hispanic adolescents. However, a recent study by McCormack et al (43) reported a significant increase in IMCL after the exercise training (3 times/wk, 60 min/session, aerobic exercise: 60%–80% of heart rate reserve for 35 min + resistance exercise: Wii Fit for 25 min) in obese children and adolescents (10–17 y). Furthermore, in that study (43), the increased IMCL was significantly associated with increased resting energy expenditure ($r = .78$) and decreased respiratory quotient ($r = -.70$), thereby inducing greater muscle lipid oxidative capacity. These results are in agreement with the previous observations in adults (47) demonstrating a significant increase in IMCL and oxidative capacity within skeletal muscle in response to a 12-week aerobic exercise training. In a cross-sectional study by Goodpaster et al (24), it was observed that exercise-trained subjects had significantly higher level of IMCL compared with the sedentary lean counterparts. However, a recent study by Bajpeyi et al (2) reported a 35% decrease in IMCL content in adults with T2DM after 10-day aerobic exercise training (60 min/d, 70% of VO_{2peak}), but reported no changes in lean or obese adults. These confounding results suggest that the alteration in IMCL content may have no fixed or standard response to exercise training, but it may be closely linked to the metabolic status of individuals.

Given the strong associations between the increased IMAT or IMCL content and obesity and insulin resistance, it is presumed that regular exercise training alone may result in a significant alteration in IMAT or IMCL. However, based on the observations from the limited studies, it is plausible that the changes in IMAT or IMCL in response to exercise training may not exhibit a consistent response, but rather depend on exercise protocols or individuals' heterogeneity (ie, age, gender, ethnicity, and metabolic status). In addition, it is worth noting that favorable alterations in oxidative capacity within muscle or insulin sensitivity may play a substantially more important role in reducing insulin resistance rather than the alterations in IMCL content. Moreover, it should be noted that although both CT and ^{1}H-MRS are safe and appropriate methods to determine lipid content within skeletal muscle in vivo, in general, IMAT is acquired by CT and IMCL is acquired by ^{1}H-MRS, suggesting that both techniques are different (ie, acquisition process, term definition, measuring location, and structures). Therefore, possible mechanisms that explain the changes in skeletal muscle lipid contents in response to exercise training may differ, which warrants further studies in pediatrics.

Summary

Metabolic abnormalities, such as insulin resistance, T2DM, and NAFLD, once considered a disease of adults, are strongly linked with the health consequences of obesity in children and adolescents. In particular, predominant accumulation of ectopic fat in the abdomen (VAT), liver (hepatic lipid), or skeletal muscle (IMAT or IMCL) is recognized to increase the risks for developing insulin resistance or decreasing insulin sensitivity in children and adolescents. Using the recent advances in imaging techniques, such as CT or MRI, a better understanding of body fat distribution and depot-specific body AT changes after preventive or therapeutic strategies targeted at reducing obesity and obesity-related health risks is possible in pediatric populations.

In adults, mounting evidence suggests that regular exercise alone (≥3 times/wk, 30–60 min/session) is beneficial to reduce total and abdominal AT and to reverse obesity-related health risks. Indeed, some studies also reported that regular exercise alone induced the increases in hepatic lipid as well as IMAT in obese adults although this is still controversial. Similarly, limited evidence in children and adolescents suggests that regular exercise training alone attenuated or reduced the growth-associated increases in abdominal AT, in particular on VAT, without weight loss or calorie restriction. However, the effect of regular exercise alone as a treatment strategy for NAFLD varies according to exercise mode, gender, and ethnicity, and it is unclear in children and adolescents, which warrants further investigation. The available, but very limited studies have reported that aerobic exercise training is effective to drive hepatic fat loss, independent of gender and ethnicity, in obese children and adolescents. With respect to resistance exercise training alone, a significant reduction in hepatic lipid content was observed only in obese boys, but not in girls. At present, the alterations of IMAT or IMCL through exercise training without calorie restriction have not been extensively clarified, thereby its effects are inconclusive in pediatrics.

Given the limited evidence regarding the independent role of exercise training alone in depot-specific body fat changes in youth, further investigations using imaging techniques are required. In addition, it is still unclear whether some beneficial observations from previous studies could be maintained over the long term in overweight and obese youth. However, considering the strong associations between obesity and obesity-related comorbidities in pediatrics, regular exercise alone should be recommended as an integral part of therapeutic strategies for reducing adiposity as well as insulin resistance for obese children and adolescents.

Acknowledgment

The author declares no conflict of interest.

References

1. Bacha F, Saad R, Gungor N, Janosky J, Arslanian SA. Obesity, regional fat distribution, and syndrome X in obese black versus white adolescents: race differential in diabetogenic and atherogenic risk factors. *J Clin Endocrinol Metab*. 2003;88(6):2534–40. PubMed doi:10.1210/jc.2002-021267
2. Bajpeyi S, Reed MA, Molskness S, et al. Effect of short-term exercise training on intramyocellular lipid content. *Appl Physiol Nutr Metab*. 2012;37(5):822–8. doi:10.1139/h2012-051
3. Barbeau P, Johnson MH, Howe CA, et al. Ten months of exercise improves general and visceral adiposity, bone, and fitness in black girls. *Obesity (Silver Spring)*. 2007;15(8):2077–85. doi:10.1038/oby.2007.247

4. Bjorntorp P. "Portal" adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. *Arteriosclerosis*. 1990;10(4):493–6. PubMed doi:10.1161/01.ATV.10.4.493
5. Bugianesi E, Zannoni C, Vanni E, Marzocchi R, Marchesini G. Non-alcoholic fatty liver and insulin resistance: a cause-effect relationship? *Dig Liver Dis*. 2004;36(3):165–73. PubMed doi:10.1016/j.dld.2003.12.008
6. Clark JM. Weight loss as a treatment for nonalcoholic fatty liver disease. *J Clin Gastroenterol*. 2006;40 Suppl 1:S39–43.
7. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. *Arch Pediatr Adolesc Med*. 2003;157(8):821–7. PubMed doi:10.1001/archpedi.157.8.821
8. Cuff DJ, Meneilly GS, Martin A, Ignaszewski A, Tildesley HD, Frohlich JJ. Effective exercise modality to reduce insulin resistance in women with type 2 diabetes. *Diabetes Care*. 2003;26(11):2977–82. PubMed doi:10.2337/diacare.26.11.2977
9. Damaso AR, do Prado WL, de Piano A, et al. Relationship between nonalcoholic fatty liver disease prevalence and visceral fat in obese adolescents. *Dig Liver Dis*. 2008;40(2):132–9. PubMed doi:10.1016/j.dld.2007.09.009
10. Daniels SR, Morrison JA, Sprecher DL, Khoury P, Kimball TR. Association of body fat distribution and cardiovascular risk factors in children and adolescents. *Circulation*. 1999;99(4):541–5. PubMed doi:10.1161/01.CIR.99.4.541
11. Davidson LE, Hudson R, Kilpatrick K, et al. Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. *Arch Intern Med*. 2009;169(2):122–31. PubMed doi:10.1001/archinternmed.2008.558
12. Davis CL, Pollock NK, Waller JL, et al. Exercise dose and diabetes risk in overweight and obese children: a randomized controlled trial. *JAMA*. 2012;308(11):1103–12. PubMed doi:10.1001/2012.jama.10762
13. Davis JN, Gyllenhammer LE, Vanni AA, et al. Startup circuit training program reduces metabolic risk in Latino adolescents. *Med Sci Sports Exerc*. 2011;43(11):2195–203. PubMed doi:10.1249/MSS.0b013e31821f5d4e
14. Duncan GE, Perri MG, Theriaque DW, Hutson AD, Eckel RH, Stacpoole PW. Exercise training, without weight loss, increases insulin sensitivity and postheparin plasma lipase activity in previously sedentary adults. *Diabetes Care*. 2003;26(3):557–62. PubMed doi:10.2337/diacare.26.3.557
15. Durheim MT, Slentz CA, Bateman LA, Mabe SK, Kraus WE. Relationships between exercise-induced reductions in thigh intermuscular adipose tissue, changes in lipoprotein particle size, and visceral adiposity. *Am J Physiol Endocrinol Metab*. 2008;295(2):E407–12. PubMed doi:10.1152/ajpendo.90397.2008
16. Eliakim A, Burke GS, Cooper DM. Fitness, fatness, and the effect of training assessed by magnetic resonance imaging and skinfold-thickness measurements in healthy adolescent females. *Am J Clin Nutr*. 1997;66(2):223–31. PubMed
17. Eliakim A, Makowski GS, Brasel JA, Cooper DM. Adiposity, lipid levels, and brief endurance training in nonobese adolescent males. *Int J Sports Med*. 2000;21(5):332–7. PubMed doi:10.1055/s-2000-3779
18. Faigenbaum AD, Kraemer WJ, Blimkie CJ, et al. Youth resistance training: updated position statement paper from the national strength and conditioning association. *J Strength Cond Res*. 2009;23 Suppl 5:S60–79. doi:10.1519/JSC.0b013e31819df407
19. Fishbein MH, Mogren C, Gleason T, Stevens WR. Relationship of hepatic steatosis to adipose tissue distribution in pediatric nonalcoholic fatty liver disease. *J Pediatr Gastroenterol Nutr*. 2006;42(1):83–8. PubMed
20. Freedland ES. Role of a critical visceral adipose tissue threshold (CVATT) in metabolic syndrome: implications for controlling dietary carbohydrates: a review. *Nutr Metab (Lond)*. 2004;1(1):12. doi:10.1186/1743-7075-1-12
21. Freedman DS, Khan LK, Dietz WH, Srinivasan SR, Berenson GS. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. *Pediatrics*. 2001;108(3):712–8. PubMed doi:10.1542/peds.108.3.712
22. Gan SK, Kriketos AD, Ellis BA, Thompson CH, Kraegen EW, Chisholm DJ. Changes in aerobic capacity and visceral fat but not myocyte lipid levels predict increased insulin action after exercise in overweight and obese men. *Diabetes Care*. 2003;26(6):1706–13. PubMed doi:10.2337/diacare.26.6.1706
23. Goodpaster BH, Chomentowski P, Ward BK, et al. Effects of physical activity on strength and skeletal muscle fat infiltration in older adults: a randomized controlled trial. *J Appl Physiol*. 2008;105(5):1498–503. PubMed doi:10.1152/japplphysiol.90425.2008
24. Goodpaster BH, He J, Watkins S, Kelley DE. Skeletal muscle lipid content and insulin resistance: evidence for a paradox in endurance-trained athletes. *J Clin Endocrinol Metab*. 2001;86(12):5755–61. PubMed doi:10.1210/jcem.86.12.8075
25. Goodpaster BH, Krishnaswami S, Harris TB, et al. Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. *Arch Intern Med*. 2005;165(7):777–83. PubMed doi:10.1001/archinte.165.7.777
26. Goodpaster BH, Thaete FL, Kelley DE. Composition of skeletal muscle evaluated with computed tomography. *Ann N Y Acad Sci*. 2000;904:18–24. PubMed doi:10.1111/j.1749-6632.2000.tb06416.x
27. Goodpaster BH, Thaete FL, Kelley DE. Thigh adipose tissue distribution is associated with insulin resistance in obesity and in type 2 diabetes mellitus. *Am J Clin Nutr*. 2000;71(4):885–92. PubMed
28. Gutin B, Barbeau P, Owens S, et al. Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *Am J Clin Nutr*. 2002;75(5):818–26. PubMed
29. Hannon TS, Rao G, Arslanian SA. Childhood obesity and type 2 diabetes mellitus. *Pediatrics*. 2005;116(2):473–80. PubMed doi:10.1542/peds.2004-2536

30. Heymsfield SB, Wang Z, Baumgartner RN, Ross R. Human body composition: advances in models and methods. *Annu Rev Nutr*. 1997;17:527–58. PubMed doi:10.1146/annurev.nutr.17.1.527
31. Ibanez J, Izquierdo M, Arguelles I, et al. Twice-weekly progressive resistance training decreases abdominal fat and improves insulin sensitivity in older men with type 2 diabetes. *Diabetes Care*. 2005;28(3):662–7. PubMed doi:10.2337/diacare.28.3.662
32. Irwin ML, Yasui Y, Ulrich CM, et al. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. *JAMA*. 2003;289(3):323–30. PubMed doi:10.1001/jama.289.3.323
33. Ishii T, Yamakita T, Sato T, Tanaka S, Fujii S. Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care*. 1998;21(8):1353–5. PubMed doi:10.2337/diacare.21.8.1353
34. Jacobs JL, Marcus RL, Morrell G, LaStayo P. Resistance exercise with older fallers: its impact on intermuscular adipose tissue. *Biomed Res Int*. 2014;2014:1–7. doi:10.1155/2014/398960
35. Johnson NA, Sachinwalla T, Walton DW, et al. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. *Hepatology*. 2009;50(4):1105–12. PubMed doi:10.1002/hep.23129
36. Kim J, Heshka S, Gallagher D, et al. Intermuscular adipose tissue-free skeletal muscle mass: estimation by dual-energy X-ray absorptiometry in adults. *J Appl Physiol*. 2004;97(2):655–60. PubMed doi:10.1152/japplphysiol.00260.2004
37. Kistler KD, Brunt EM, Clark JM, Diehl AM, Sallis JF, Schwimmer JB. Physical activity recommendations, exercise intensity, and histological severity of nonalcoholic fatty liver disease. *Am J Gastroenterol*. 2011;106(3):460–8. PubMed doi:10.1038/ajg.2010.488
38. Lee S, Bacha F, Hannon T, Kuk JL, Boesch C, Arslanian S. Effects of aerobic versus resistance exercise without caloric restriction on abdominal fat, intrahepatic lipid, and insulin sensitivity in obese adolescent boys: a randomized, controlled trial. *Diabetes*. 2012;61(11):2787–95. PubMed doi:10.2337/db12-0214
39. Lee S, Deldin AR, White D, et al. Aerobic exercise but not resistance exercise reduces intrahepatic lipid content and visceral fat and improves insulin sensitivity in obese adolescent girls: a randomized controlled trial. *Am J Physiol Endocrinol Metab*. 2013;305(10):E1222–9. PubMed doi:10.1152/ajpendo.00285.2013
40. Lee S, Guerra N, Arslanian S. Skeletal muscle lipid content and insulin sensitivity in black versus white obese adolescents: is there a race differential? *J Clin Endocrinol Metab*. 2010;95(5):2426–32. PubMed doi:10.1210/jc.2009-2175
41. Lee S, Kuk JL, Davidson LE, et al. Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without type 2 diabetes. *J Appl Physiol*. 2005;99(3):1220–5. PubMed doi:10.1152/japplphysiol.00053.2005
42. Lee S, Kuk JL, Kim Y, Arslanian SA. Measurement site of visceral adipose tissue and prediction of metabolic syndrome in youth. *Pediatr Diabetes*. 2011;12(3 pt 2):250–7. PubMed doi:10.1111/j.1399-5448.2010.00705.x
43. McCormack SE, McCarthy MA, Harrington SG, et al. Effects of exercise and lifestyle modification on fitness, insulin resistance, skeletal muscle oxidative phosphorylation and intramyocellular lipid content in obese children and adolescents. *Pediatr Obes*. 2014;9(4):281–91. PubMed doi:10.1111/j.2047-6310.2013.00180.x
44. Nguyen-Duy TB, Nichaman MZ, Church TS, Blair SN, Ross R. Visceral fat and liver fat are independent predictors of metabolic risk factors in men. *Am J Physiol Endocrinol Metab*. 2003;284(6):E1065–71. PubMed doi:10.1152/ajpendo.00442.2002
45. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;311(8):806–14. PubMed doi:10.1001/jama.2014.732
46. Owens S, Gutin B, Allison J, et al. Effect of physical training on total and visceral fat in obese children. *Med Sci Sports Exerc*. 1999;31(1):143–8. PubMed doi:10.1097/00005768-199901000-00022
47. Pruchnic R, Katsiaras A, He J, Kelley DE, Winters C, Goodpaster BH. Exercise training increases intramyocellular lipid and oxidative capacity in older adults. *Am J Physiol Endocrinol Metab*. 2004;287(5):E857–62. PubMed doi:10.1152/ajpendo.00459.2003
48. Rocchini AP. Childhood obesity and a diabetes epidemic. *N Engl J Med*. 2002;346(11):854–5. PubMed doi:10.1056/NEJM200203143461112
49. Ross R, Aru J, Freeman J, Hudson R, Janssen I. Abdominal adiposity and insulin resistance in obese men. *Am J Physiol Endocrinol Metab*. 2002;282(3):E657–63. PubMed doi:10.1152/ajpendo.00469.2001
50. Ross R, Dagnone D, Jones PJ, et al. Reduction in obesity and related comorbid conditions after diet-induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial. *Ann Intern Med*. 2000;133(2):92–103. PubMed doi:10.7326/0003-4819-133-2-200007180-00008
51. Ross R, Freeman J, Hudson R, Janssen I. Abdominal obesity, muscle composition, and insulin resistance in premenopausal women. *J Clin Endocrinol Metab*. 2002;87(11):5044–51. PubMed doi:10.1210/jc.2002-020570
52. Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. *Obes Res*. 2004;12(5):789–98. PubMed doi:10.1038/oby.2004.95
53. Savoye M, Shaw M, Dziura J, et al. Effects of a weight management program on body composition and metabolic parameters in overweight children: a randomized controlled trial. *JAMA*. 2007;297(24):2697–704. PubMed doi:10.1001/jama.297.24.2697
54. Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, Behling C. Prevalence of fatty liver in children and adolescents. *Pediatrics*. 2006;118(4):1388–93. PubMed doi:10.1542/peds.2006-1212
55. Schwimmer JB, Deutsch R, Rauch JB, Behling C, Newbury R, Lavine JE. Obesity, insulin resistance, and other

clinicopathological correlates of pediatric nonalcoholic fatty liver disease. *J Pediatr*. 2003;143(4):500–5. PubMed doi:10.1067/S0022-3476(03)00325-1

56. Shaibi GQ, Cruz ML, Ball GD, et al. Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. *Med Sci Sports Exerc*. 2006;38(7):1208–15. PubMed doi:10.1249/01.mss.0000227304.88406.0f
57. Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *N Engl J Med*. 2002;346(11):802–10. PubMed doi:10.1056/NEJMoa012578
58. Taaffe DR, Henwood TR, Nalls MA, Walker DG, Lang TF, Harris TB. Alterations in muscle attenuation following detraining and retraining in resistance-trained older adults. *Gerontology*. 2009;55(2):217–23. PubMed doi:10.1159/000182084
59. Treuth MS, Hunter GR, Figueroa-Colon R, Goran MI. Effects of strength training on intra-abdominal adipose tissue in obese prepubertal girls. *Med Sci Sports Exerc*. 1998;30(12):1738–43. PubMed doi:10.1097/00005768-199812000-00013
60. Turcotte LP, Fisher JS. Skeletal muscle insulin resistance: roles of fatty acid metabolism and exercise. *Phys Ther*. 2008;88(11):1279–96. PubMed doi:10.2522/ptj.20080018
61. van der Heijden GJ, Wang ZJ, Chu Z, et al. Strength exercise improves muscle mass and hepatic insulin sensitivity in obese youth. *Med Sci Sports Exerc*. 2010;42(11):1973–1980. PubMed doi:10.1249/MSS.0b013e3181df16d9
62. van der Heijden GJ, Wang ZJ, Chu ZD, et al. A 12-week aerobic exercise program reduces hepatic fat accumulation and insulin resistance in obese, Hispanic adolescents. *Obesity (Silver Spring)*. 2010;18(2):384–90. doi:10.1038/oby.2009.274
63. Wajchenberg BL, Giannella-Neto D, da Silva ME, Santos RF. Depot-specific hormonal characteristics of subcutaneous and visceral adipose tissue and their relation to the metabolic syndrome. *Horm Metab Res*. 2002;34(11–12):616–21. PubMed doi:10.1055/s-2002-38256
64. Weiss R, Dufour S, Taksali SE, et al. Prediabetes in obese youth: a syndrome of impaired glucose tolerance, severe insulin resistance, and altered myocellular and abdominal fat partitioning. *Lancet*. 2003;362(9388):951–7. PubMed doi:10.1016/S0140-6736(03)14364-4
65. Welsh JA, Karpen S, Vos MB. Increasing prevalence of nonalcoholic fatty liver disease among United States adolescents, 1988–1994 to 2007–2010. *J Pediatr*. 2013;162(3):496–500.e1. PubMed doi:10.1016/j.jpeds.2012.08.043
66. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med*. 1997;337(13):869–73. PubMed doi:10.1056/NEJM199709253371301
67. Wieckowska A, Feldstein AE. Nonalcoholic fatty liver disease in the pediatric population: a review. *Curr Opin Pediatr*. 2005;17(5):636–41. PubMed doi:10.1097/01.mop.0000172816.79637.c5