

**HAART-associated
changes in body fat
distribution are
detectable in HIV-infected
children even in the
absence of clinical
evidence of lipodystrophy**

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Background

Lipodystrophy and metabolic abnormalities are poorly described in HAART-treated HIV-infected children.

Combined use of dual-energy X-ray Absorptiometry (DXA) and magnetic resonance imaging (MRI) allow a precise estimate of regional body composition and intraabdominal adipose tissue (IAT).

As body composition shows a great variation in growing children with age, gender, pubertal status and a possible association with obesity, a case-control study may minimise inter-individual variability.

Methods

Subjects

Body composition was assessed in 6 HAART-treated vertically HIV-infected children with lipodystrophy (LD^+) and in 28 without lipodystrophy (LD^-) and in the same number of age-, sex- and BMI-matched healthy controls (defined as HC^+ and HC^- respectively).

Lipid, glucose and insulin levels were assessed in all 34 HAART-treated children.

Anthropometric measurements

Body weight was measured to the nearest 0.1 kg on a balance beam scale (Seca, Hamburg, Germany) and height was measured to the nearest millimeter using a wall-mounted stadiometer (Holtain Ltd., Crosswell, U.K.). Body mass index (BMI) was then calculated as weight on height² (kg/m²).

Evaluation of body composition by DXA

Whole body composition was assessed by Dual-energy X-ray Absorptiometry (DXA) (Lunar DPX-L[®], Lunar Radiation Corp., Madison, WI), equipped with pediatric software (version 1.5 e). Body fat was expressed in kilograms; lean mass was expressed

in kilograms; the ratio between fat and lean mass was then calculated as a percentage. Total BMC was expressed as a percentage of lean mass. Three-compartment analyses were performed in the arms, trunk and legs.

Evaluation of visceral fat content by MRI

Intraabdominal fat content was measured by MRI. Patients were imaged on a Philips Gyroscan ACS-NT 1.5 T (Philips Medical Systems, Best., The Netherlands). The slice passing through the umbilicus (at the fourth lumbar vertebra) was reported as a valid predictor of total abdominal fat in men and women. A manual trackball with visual

control was used to limit adipose tissue areas. Intra-abdominal adipose tissue (IAT) area was expressed in square centimeters.

Results

LD⁺ and **LD⁻** were similar for: months of previous exposure to NRTIs (45.5 vs 39.5) and months on HAART (39.3 vs 39.1), CD4⁺/ul (1227 vs 936), % of pts with HIV-RNA < 50 copies/ml (100 vs 96.4) (Table 1).

Metabolic evaluation showed: hypertriglyceridemia (> 140 mg/dl) in 18/34 (51%), hypercholesterolemia in 18/34, elevated LDL-cholesterol in 6/34 (19%),

elevated insulin (> 20 uU/ml) in 6/34 (19%) and OMA index > 4 in 6/34 (19%) children.

Analysis of body composition is shown in Table 2. Lean mass in LD^+ and in LD^- children was similar to that observed in their controls. Fat mass was lower in LD^- children as compared to their HCS ($p=0.03$); fat mass was lower, but not significantly, also in LD^+ children as compared to their pair matched HCS . The percentage ratio between fat and lean mass was lower both in LD^+ and LD^- children than in their HCS ($p=0.005$).

Analysis of regional body composition is shown in Fig. 1 and in Fig. 2.

Fig 1. Fat trunk/Fat total ratio is increased: 0.54 LD^+ vs 0.38 HC^+ ($p=0.001$) and 0.47 LD^- vs 0.35 HC^- ($p<0.0001$);

Fig 2. Fat limbs/Fat total ratio is reduced: 0.37 LD^+ vs 0.55 HC^+ ($p<0.0001$) and 0.44 LD^- vs 0.56 HC^- ($p=0.009$).

LD^+ showed higher Fat trunk/Fat total ($p=0.04$) and lower Fat limbs/Fat total ratios ($p=0.009$) than LD^- .

Analysis of visceral adipose tissue by MRI is shown in Table 3. MRI was performed in all 6 LD^+ , in 10 out of 28 LD^- and in 16 HC.

The mean IAT content was 77 cm² (range 26-120) in LD⁺, 19 cm² (range 7-45) in LD⁻ and 21 (range 7-31) in HC. Thus LD⁺ showed an higher IAT content than both LD⁻ (p<0.0003) and HC (p<0.0001).

Conclusions

HAART-treated children showed frequent metabolic abnormalities.

Increased central fat and peripheral lipomatrophy are distinctive features of all HAART-treated children.

Changes in body fat composition are detectable by DXA even in the absence of signs of lipodystrophy.

Only children with lipodystrophy show true central obesity.

Table 1

Clinical and immunologic characteristics of
HAART-treated vertically HIV-infected children
with (**LD⁺**) and without (**LD⁻**) lipodystrophy

	LD⁺ (n=6)	LD⁻ (n=28)
CDC clinical stage		
N + A	2/6	11/28
B + C	4/6	17/28
CDC immunologic stage		
1 + 2	5/6	20/28
3	1/6	8/28
Previous NRTIs exposure (mos)		
Mean (DS)	45.5 (36)	39.5 (29)
range	0-90	0-99
NNRTs + PI exposure (mos)		
Mean (DS)	39.3 (4.1)	39.1 (6.4)
range	32-40	18-46
Children on:		
IDV	4/6	17/28
NFV	0/6	5/28
RTV	2/6	6/28
CD4 cells (/mm³) mean (DS)	1227 (870)	936 (303)
CD4 cells (%) mean (DS)	32 (9.5)	30.6 (6.7)
HIV-RNA < 50 cp/ml	6/6	27/28

Table 2

Body composition characteristics of HAART-treated vertically HIV-infected children and of their paired-matched healthy controls

	LD⁺ (n=6)	LD⁻ (n=28)	HC⁺ (n=6)	HC⁻ (n=28)
Lean mass (Kg) Mean (SD)	28.9 (7.7)	30.3 (11.6)	27.8 (6.8)	31.6 (11.1)
			┌────────── p = 0.03 ─────────┐	
Fat mass (Kg) Mean (SD)	8.2 (4.0)	6.6 (3.2)	11.8 (6.2)	9.3 (4.4)
			┌────────── p = 0.005 ─────────┐	
			┌────────── p=0.005 ─────────┐	
Fat mass/Lean mass (%) Mean (SD)	28.2 (9.0)	23.5 (9.3)	41.7 (15.5)	31.2 (13.6)

Table 3

Intra-abdominal adipose tissue content (IAT) in

LD⁺, **LD⁻** and **HC**

p < 0.0003
p < 0.0001

	LD⁺ n=6	LD⁻ n=11	HC n=15
IAT (cm²)			
mean (SD)	77 (36)	19 (12)	21 (10)
range	26 - 120	7 - 45	7 - 31

Fig. 1

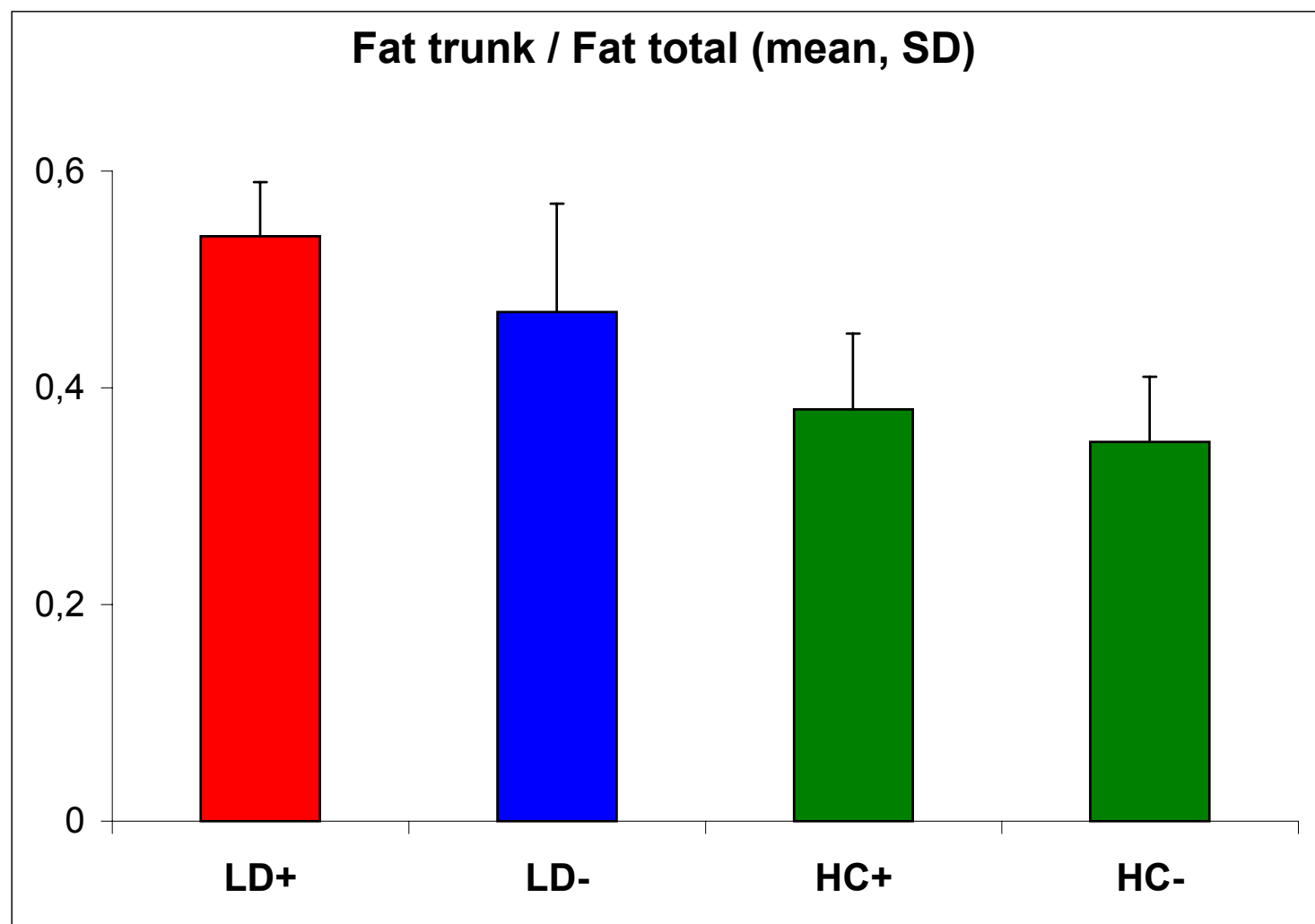


Fig. 2

