Longitudinal body composition assessment in healthy term-born infants until 2 years of age using ADP and DXA with vacuum cushion

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ABSTRACT

Objectives Accelerated gain in fat mass (FM) in early life increases the risk for adult diseases. Longitudinal data on infant body composition are crucial for clinical and research use, but very difficult to obtain due to limited measurement tools and unsuccessful measurements between age 6–24 months. We compared FM% by dual-energy X-ray absorptiometry (DXA), with cushion to reduce movement artifacts, with FM% by air-displacement plethysmography (ADP) and evaluated the reliability of this cushion during DXA by comparing FM% with and without cushion. Subsequently, we constructed sex-specific longitudinal body composition charts from 1–24 months.

Methods In 692 healthy, term-born infants (Sophia Pluto Cohort), FM% was measured by ADP from 1–6 months and DXA with cushion from 6–24 months. At 6 months, FM% was measured in triplicate by ADP and DXA with and without cushion (n=278), later on in smaller numbers.

Results At 6 months, mean FM% by DXA with cushion was 24.1 and by ADP 25.0, mean difference of 0.9% (Bland–Altman p=0.321, no proportional bias). Mean FM% by DXA without cushion was 12.5% higher compared to ADP (Bland–Altman p<0.001). DXA without cushion showed higher mean FM% compared to DXA with cushion (+11.6%, p<0.001) at 6 months. Longitudinally, FM% increased between 1–6 months and decreased from 6–24 months (both p<0.001).

Conclusions In infants, DXA scan with cushion limits movement artifacts and shows reliable FM%, comparable to ADP. This allowed us to construct longitudinal body composition charts until 24 months. Our study shows that FM% increases from 1–6 months and gradually declines until 24 months.

INTRODUCTION

The first 1000 days window, from conception until 24 months, is an important period for body and brain development and hence an optimal time for early obesity prevention (1). Determining sex-specific changes in longitudinal body composition, i.e., fat mass (FM) and fat-free mass (FFM), during this period is crucial for clinical and research use, but challenging due to movement artifacts when infants become older and stronger and to the limited measurement tools between the age of 6 months and 2 years.

Earlier studies focused mainly on longitudinal anthropometric outcomes, such as weight-for-length, body mass index, and skinfolds as a proxy for infant adiposity (2). We and others demonstrated that rapid weight gain in infancy, and specifically in the first 3 months, was strongly associated with determinants of cardiovascular disease, type 2 diabetes, and overweight in early adulthood (3-6). It is essential to obtain longitudinal data on body composition in early life, as we previously showed that infants with similar weight and weight-for-length standard deviation scores (SDS) might have different fat mass percentage (FM%) (7).

Nowadays, methods exist to assess detailed body composition in infants (8). Techniques to determine body composition by the multi-component model for quantifying fat, water, mineral, and protein or by magnetic resonance imaging have been applied in infancy and childhood (9-11). However, these methods are laborious, expensive, and cannot be applied routinely in larger study settings. Air-displacement plethysmography (ADP) is a noninvasive, fast, and accurate technique for measuring longitudinal body composition in infants from birth until the upper limit of 8 kg (PEA POD) (12-15) and from ~2–3 years onward (BOD POD, pediatric option) (16), but there are no ADP systems for children between 6 months and 2 years (12, 17).

Dual-energy X-ray absorptiometry (DXA) is an alternative measurement technique (15, 18-20), but reference values exist only from age 4 years onward (21). Also, it has been reported that DXA overestimates FM (22). DXA has good reproducibility in infants in case of a successful scan (18), but successful measurements are extremely difficult to obtain in infants due to movement artifacts (8, 22, 23). Unsuccessful scans are reported in newborns up to 69% (19, 24), which could be higher when infants become older and stronger. The use of a vacuum cushion prevents movement in infants during DXA, but the effect on body composition measurement was unknown.

Two studies compared ADP and DXA in infancy, with conflicting results and performed in small populations (23, 25). Since both have different measurement techniques, it is important to determine whether measurements are comparable at the transition point at

age 6 months. Combining measurements of ADP and DXA would allow the construction of longitudinal data on body composition during the first 2 years of life, which is essential for the clinical and research use.

We hypothesized that infant body composition measured by DXA with vacuum cushion would be comparable with ADP measurements at the age of 6 months, because DXA measurements with vacuum cushion provide more reliable FM%, due to less movement artifacts, compared to DXA measurements without vacuum cushion. Consecutively, we wanted to construct sex-specific longitudinal body composition charts from age 1 until 24 months, based on our large group of healthy, term-born boys and girls.

MATERIALS AND METHODS

Study settings and subjects

The study population consisted of 692 healthy, term-born infants, participating in the Sophia Pluto Study, a birth cohort study in Rotterdam area (The Netherlands; Supplemental Fig. 1). Between January 2013 and October 2018, infants were recruited to obtain detailed data on body composition and growth during early life. The Medical Ethics Committee of Erasmus Medical Center approved the Sophia Pluto Study (MEC-2012-164) and parental written informed consent was obtained (13). All participants fulfilled the following inclusion criteria: term born (≥37 weeks of gestation), age < 28 days, uncomplicated neonatal period without signs of severe asphyxia (defined as an Apgar score < 3 after 5 min), sepsis, or long-term complication of respiratory ventilation. Infants were excluded if they had known congenital or postnatal diseases, confirmed intrauterine infection, maternal use of corticosteroids during pregnancy, or a significant maternal medical condition that could interfere with the study results.

Data collection and measurements

Outpatient clinic visits were scheduled at the age of 1, 3, 6, 9, 12, 18, and 24 months (Table 1). Pregnancy and birth data were obtained from midwife and hospital records. Measurements were performed by trained staff.

Anthropometrics

Weight was measured to the nearest 5 g by using an electronic infant scale (SECA 717, Hamburg, Germany). Length was measured twice by two-person technique to the nearest 0.1 cm using an infantometer (SECA 416) and head circumference was measured twice as the widest frontal–occipital circumference, to the nearest 0.1 cm using a measuring tape (SECA 201).

Table 1. Clinical characteristics.

	Gender	1 month	3 months	6 months	9 months	12 months	18 months	24 months
N	Total	692	617	550	505	473	396	346
	M	375	342	300	281	260	225	200
	F	317	275	250	224	213	171	146
Weight (kg)	M	4.42 [4.03 – 4.77]	6.19 [5.81 – 6.72]	7.90 [7.39 – 8.55]	9.15 [8.51 – 9.81]	9.98 [9.20 – 10.76]	11.48 [10.53 – 12.30]	12.83 [11.70 – 13.80]
	F	4.08 [3.67 – 4.42]	5.72 [5.20 – 6.18]	7.33 [6.83 – 7.87]	8.44 [7.83 – 9.06]	9.35 [8.74 – 9.99]	10.80 [10.10 – 11.46]	12.06 [11.30 – 12.85]
Length (cm)	M	55.0 [53.6 – 56.5]	62.2 [60.5 – 63.5]	69.0 [67.0 – 70.5]	73.2 [71.9 – 74.9]	77.0 [75.0 – 79.0]	83.9 [81.5 – 86.0]	90.0 [87.5 – 91.9]
	F	54.0 [52.4 – 55.3]	60.5 [59.0 – 61.5]	67.0 [65.5 – 68.4]	71.3 [69.6 – 72.6]	75.0 [73.5 – 76.5]	82.0 [79.8 – 83.4]	88.0 [85.9 – 90.0]
Head circum-ference (cm)	M	37.5 [36.5 – 38.2]	40.5 [40.0 – 41.3]	43.5 [42.7 – 44.3]	45.3 [44.5 – 46.2]	46.3 [45.5 – 47.2]	48.0 [47.0 – 48.5]	48.6 [47.5 – 49.8]
	F	36.4 [35.7 – 37.2]	39.5 [38.6 – 40.2]	42.0 [41.5 – 43.0]	44.0 [43.2 – 44.5]	45.0 [44.2 – 45.5]	46.3 [45.5 – 47.0]	47.5 [46.5 – 48.0]

Data expressed as median [IQR] for male and female.

Body composition measurements

Until the age of 6 months, body composition was assessed by ADP (ADP by PEA POD, COSMED, Italy). ADP assesses FM, fat mass percentage (FM%), fat-free mass (FFM), and fat-free mass percentage (FFM%) by direct measurements of body mass and body volume, based on the whole-body densitometric principle (26). Body mass was measured on the integrated scale of the PEA POD and body volume was measured inside the closed test chamber by applying pertinent gas laws that relate pressure changes to volumes of air. The PEA POD was calibrated every day, according to the protocol recommended by the supplier. At the age of 6 months, body composition was assessed in triplicate in 278 infants. Once by PEA POD and twice by DXA (Lunar Prodigy, GE Healthcare, UK): once with a vacuum cushion (465 75100, Schmidt, Germany) to prevent movement and once without. During all DXA scans, infants were wearing only a disposable diaper and were swaddled in a cotton blanket.

From 6 months onward, DXA with vacuum cushion to prevent movement was used in all infants at every visit. All DXA scans were performed with the same machine with daily quality controls. We used enCORE software version 14.1 and for analysis the enhanced analysis algorithm (27). FM% was calculated as total FM (gram) divided by total weight (gram) × 100 [FM/weight × 100]. As dependent on the position of the infant, a variable part of the vacuum cushion is considered as FFM by DXA. FFM was calculated by subtracting total FM (gram) from total weight (gram). Fat mass index (FMI) was determined by dividing FM (kg) by height squared (m^2) and fat-free mass index (FFMI) by dividing FFM (kg) by height squared (m^2).

Statistical analysis

Clinical characteristics are expressed as median and interquartile range [IQR]. Differences in clinical characteristics were determined by independent Student's t-test or Mann–Whitney U test for non-parametric parameters. Correlations were determined by Pearson's correlation coefficient, or Spearman for non-parametric parameters. Related Samples Wilcoxon signed-rank test was used to compare median FM% by ADP and DXA. Bland–Altman analysis was used for the level of agreement between PEA POD and DXA measurements. SPSS statistical package version 24 (SPSS Inc. Chicago, Illinois) was used. P values <0.05 were considered statistically significant. For the creation of sex-specific curves for FM%, FM, FMI, FFM, and FFMI, generalized additive models for location, scale, and shape (28) were used. To fit the parameters of kurtosis, a four parameter (μ, σ, ν, and τ) Box–Cox power exponential distribution was applied to construct the final curves (29). The distribution expresses the mean (μ), variance (σ), skewness (ν), and kurtosis (τ) that change as a function of age.

RESULTS

Clinical characteristics of the subjects are presented in Table 1. Fifty-four percent of the infants was male and 69.2% had Caucasian ethnicity. Median [IQR] birthweight was 3.37 [3.06–3.71] kg at a gestational age of 39.9 [38.9–40.7] weeks in the total group, and 3.46 [3.13–3.77] kg at 39.7 [38.9–40.6] weeks in boys and 3.29 [2.97–3.65] kg at 39.9 [39.0–40.7] weeks in girls.

ADP versus DXA with and without cushion at age 6 months in 278 infants

Mean FM% was 24.1 by ADP and 25.0 by DXA with cushion, with a mean difference of 0.9% between both measurements (p=0.004; Fig. 1). Bland–Altman analysis did not show a significant correlation (p=0.321) for the difference in FM% with the mean in FM% (Fig. 2), indicating that there is no proportional bias. Mean FM% was 24.1 by ADP and 36.6 by DXA without cushion, showing a much higher mean difference of 12.5% between both measurements (p<0.001). Bland–Altman analysis showed a significant correlation (p<0.001) for the difference in FM% with the mean in FM% (Fig. 2), indicating proportional bias.

DXA with versus without cushion at 6, 9, 12, 18, and 24 months

At age 6 months, measurements of FM% by DXA with and without cushion in 278 infants were significantly different (p<0.001), with a much higher mean FM% of +11.6% measured by DXA without cushion compared to DXA with cushion. Bland–Altman analysis showed a significant correlation (p=0.01) for the difference in FM% with the mean in FM%, indicating proportional bias. After the age 6 months, it proved extremely difficult to perform reliable DXA measurements in duplicate (with and without cushion) as it was almost impossible to

acquire reliable results of DXA without cushion due to movement artifacts. Movement artifact were present in ~70% of DXA without cushion compared to ~15% of DXA with cushion at age 9, 12, 18, and 24 months. Mean FM% measured by DXA without a cushion was, in infants with successful scans, 13.3% higher compared to DXA with cushion at age 9 months (n=8), 10.8% at age 12 months (n=5), 14.1% at 18 months (n=3), and 13.9% at age 24 months (n=4). It was not possible to perform Bland–Altman analyses due to the small group of infants with duplicate measurements after the age of 6 months.

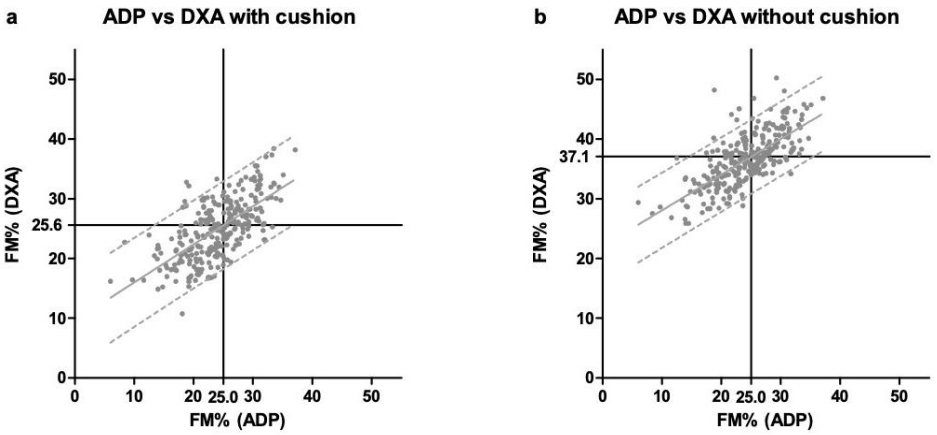

Figure 1. FM% by ADP versus DXA at 6 months of age.
Mean and 95% prediction interval for FM% a) ADP versus DXA with cushion *R=0.659, p<0.001* and b) ADP versus DXA without cushion *R=0.711, p<0.001*.

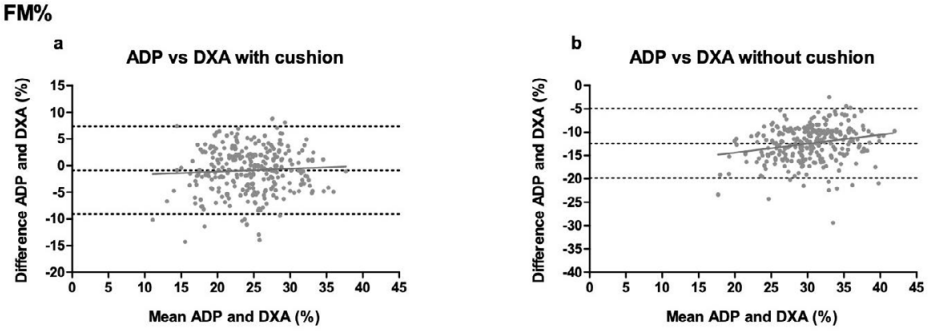

Figure 2. Bland-Altman analyses between ADP and DXA at 6 months of age, n=278.
The middle dashed line represents the mean difference between ADP and DXA. The upper and lower dashed lines represent ± 2 SD and the solid line represents the regression line. FM% by a) ADP versus DXA with cushion with *R=0.061, p=0.321*, and b) ADP versus DXA without cushion with *R=0.227, p<0.001*.

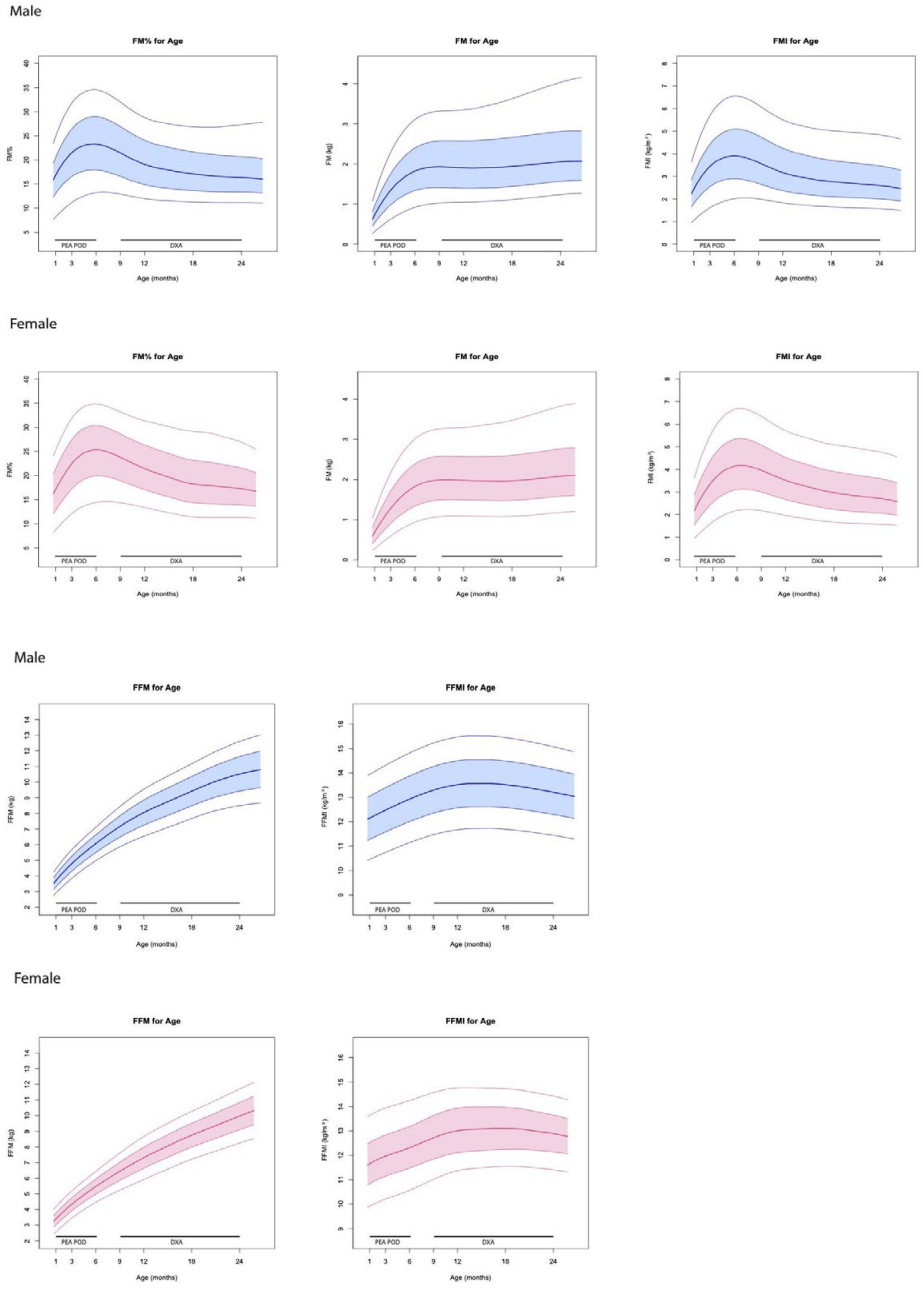

Figure 3. Longitudinal values of FM% (fat mass percentage), FM (fat mass), FMI (fat mass index), FFM (fat-free mass) and FFMI (fat-free mass index) for male and female.

Table 2. Longitudinal values of FM%, FM, FMI, FFM and FFMI.

	Male					Female				
	-2 SD	**-1 SD**	**0 SD**	**+1 SD**	**+2 SD**	**-2 SD**	**-1 SD**	**0 SD**	**+1 SD**	**+2 SD**
FM%										
1 month	8.1	13.0	16.8	20.4	24.8	8.7	12.8	17.1	21.3	25.2
3 months	11.2	16.5	21.5	26.4	31.7	12.1	17.2	22.5	27.4	31.8
6 months	13.2	17.9	23.3	29.0	34.5	14.4	19.9	25.4	30.4	34.9
9 months	12.9	16.6	21.5	26.9	32.0	14.4	18.9	23.8	28.7	33.2
12 months	12.0	14.9	19.1	24.1	28.8	13.4	17.1	21.5	26.3	31.4
18 months	11.3	13.6	17.1	21.7	26.9	11.4	14.4	18.2	23.2	29.2
24 months	11.1	13.3	16.3	20.7	27.3	11.3	13.9	17.3	21.6	26.9
FM (kg)										
1 month	0.32	0.53	0.73	0.95	1.25	0.28	0.47	0.69	0.94	1.20
3 months	0.63	0.98	1.35	1.76	2.30	0.59	0.91	1.28	1.71	2.18
6 months	0.92	1.34	1.82	2.40	3.10	0.94	1.34	1.83	2.39	3.01
9 months	1.03	1.41	1.93	2.57	3.31	1.08	1.49	1.99	2.58	3.26
12 months	1.04	1.39	1.90	2.57	3.34	1.09	1.49	1.98	2.57	3.30
18 months	1.11	1.44	1.94	2.66	3.63	1.08	1.48	1.97	2.60	3.47
24 months	1.24	1.56	2.05	2.81	4.03	1.18	1.58	2.08	2.77	3.83
FMI (kg/m^2)										
1 month	1.06	1.79	2.43	3.10	3.96	1.05	1.68	2.38	3.13	3.94
3 months	1.61	2.55	3.45	4.43	5.69	1.68	2.54	3.50	4.56	5.71
6 months	2.01	2.90	3.91	5.10	6.56	2.19	3.11	4.17	5.36	6.69
9 months	2.01	2.69	3.62	4.80	6.16	2.18	3.00	3.97	5.08	6.35
12 months	1.84	2.37	3.17	4.25	5.51	1.97	2.67	3.52	4.54	5.72
18 months	1.65	2.11	2.77	3.72	5.03	1.66	2.23	2.97	3.91	5.09
24 months	1.57	2.00	2.60	3.47	4.84	1.57	2.05	2.70	3.58	4.76
FFM (kg)										
1 month	2.91	3.30	3.70	4.10	4.45	2.57	3.01	3.39	3.77	4.17
3 months	3.86	4.31	4.80	5.27	5.69	3.45	3.92	4.34	4.76	5.19
6 months	4.98	5.50	6.07	6.63	7.12	4.47	4.99	5.47	5.95	6.44
9 months	5.86	6.48	7.17	7.84	8.43	5.23	5.86	6.44	7.02	7.62
12 months	6.54	7.25	8.06	8.86	9.55	5.92	6.63	7.31	7.98	8.67
18 months	7.68	8.48	9.42	10.36	11.18	7.21	7.99	8.75	9.51	10.27
24 months	8.50	9.43	10.52	11.64	12.61	8.25	9.10	9.97	10.84	11.70
FFMI (kg/m^2)										
1 month	10.46	11.28	12.15	13.05	13.94	9.91	10.83	11.65	12.52	13.63
3 months	10.75	11.59	12.48	13.40	14.31	10.21	11.14	11.97	12.83	13.94
6 months	11.15	12.01	12.93	13.88	14.82	10.57	11.48	12.31	13.18	14.24
9 months	11.47	12.35	13.29	14.26	15.22	11.02	11.84	12.72	13.62	14.57
12 months	11.67	12.57	13.52	14.50	15.47	11.37	12.10	13.00	13.93	14.76
18 months	11.69	12.58	13.52	14.49	15.45	11.55	12.24	13.09	13.96	14.72
24 months	11.44	12.30	13.21	14.14	15.07	11.41	12.14	12.89	13.65	14.42

Data expressed as median, ± 1 and ± 2 SD scores for male and female for FM% (fat mass percentage), FM (fat mass), FMI (fat mass index), FFM (fat-free mass) and FFMI (fat-free mass index), obtained by ADP (1, 3 and 6 months) and DXA with vacuum cushion (9, 12, 18 and 24 months). Comparison of triplicate measurements (ADP and DXA with versus without vacuum cushion) at age 6 months is described in the results section.

Longitudinal body composition measurements

Since FM% measured by DXA with cushion was comparable to FM% by ADP, all infants were measured by DXA with cushion from age 6 to 24 months. Table 2 presents the longitudinal values for FM and FFM as median ±1 and ±2 SD scores for boys and girls from age 1 to 24 months. Figure 3 shows the sex-specific longitudinal values for FM%, FM, FMI, FFM, and FFMI. Girls had a higher median FM% at age 6, 9, 12, and 18 months (p-values <0.001, <0.001, <0.001 and 0.009, respectively) and lower median FFM (p<0.001, all time points) than boys. In the total group, FM% was highest at age 6 months, with highest increment between 1 and 3 months of age. After 6 months, FM% decreased gradually until 24 months (Table 2, Fig. 3). We found a significant increase in FM% between 1 and 3 months (p<0.001), and 3 and 6 months (p<0.001), which were similar in boys and girls. Between 6 and 24 months, there was a significant decrease in FM% (p<0.001) in boys and girls alike.

DISCUSSION

To our knowledge, this is the first study to describe the use of a vacuum cushion in infants to prevent movement during DXA scan, showing reliable results for FM% comparable to FM% measured by ADP. This allowed us to construct longitudinal charts on body composition in infants from 1 until 24 months of age, which addresses an important topic and gap in research due to limited measurement options. We found a significant increase in FM% in the first 6 months after birth, followed by a gradual decline until 24 months, in both sexes.

Longitudinal data on body composition in infants are essential for clinical and research use, but very difficult to construct as ADP is available from birth until the upper limit of 8 kg (PEA POD) and from ~2–3 years of age onward (BOD POD, pediatric option) (17, 30). DXA reference data are only available from 4 years onward [21]. DXA scans can be performed in infants and have good reproducibility for total FM (intraclass correlation coefficient (ICC) 0.94 (0.89–0.97)) between DXA measurements in infants with successful scans (18), but reliable results are extremely difficult to obtain in infancy with a very high proportion of unusable scans due to movement artifacts (19, 24).

Since ADP and DXA measure body composition with a different technique, it is important to investigate whether body composition results of these two techniques are comparable at the transition point of 6 months. Previously, this comparison between ADP and DXA was determined in small groups and results were contradictory (23, 25). Fields et al. (23) showed that body composition measurements by DXA and ADP were highly correlated in 84 infants at age 6 months, but DXA measurements showed significantly higher FM%, which we also found when FM% was measured by DXA without cushion. However, the opposite was found

in a South African study in 92 infants at 2 weeks of age, with DXA measurements having lower FM% compared to ADP (25). Both studies measured FM% by DXA without vacuum cushion.

From age 6 months to 2 years, most children do not want to be held in place and it is impossible to swaddle them only in a cotton blanket and then obtain a reliable DXA scan without movement artifacts. The use of a vacuum cushion prevents infants from movement. Our study shows that at the age of 6 months, FM% measured by DXA with a vacuum cushion provides comparable FM% results as FM% measured by ADP, in contrast to DXA without cushion. Unfortunately, we were only able to determine the difference in FM measured by DXA with versus without vacuum cushion at ages after 6 months in a small group of infants, because of a high percentage (70%) of unsuccessful DXA scans without cushion due to movements artifacts, which is a limitation of the study. However, this indicates the difficulties in obtaining reliable DXA scans without cushion, as was previously described in other studies, where only 9 out of 578 newborns had reliable duplicate measurements without cushion (24) and also high percentages of unsuccessful scans without cushion were reported (19, 24).

With increasing strength when infants become older, it is even more difficult at later ages. We found that measurements with cushion are more successful (85%) than those without (30%) and were able to determine the correction factors between DXA measurements with and without cushion at age 9, 12, 18, and 24 months with the same DXA machine, software, and cushion, which need to be interpreted with caution. It is important to investigate if this factor remains stable in a larger group and is similar if other DXA machines, software, and cushions are used.

Strengths of this study are the large number of boys and girls with detailed body composition measurements and duplicate measurements at the transition point at 6 months in 278 infants, given the lack of a true gold standard suitable for longitudinal studies in young infants. Furthermore, a consistent approach was used by measuring body composition with the same DXA machine, software, and cushion in all infants.

We did not start the study directly after birth, but at age 1 month, because the neonates had to visit the hospital for the body composition measurements. This was too much of a burden for the infants and mothers in the first days after birth.

Our longitudinal data show a significant increase in FM% during the first 6 months and a gradual decrease in FM% from the age of 6 to 24 months. Similar to our findings, some studies reported a longitudinal increase in FM% during the first 6 months of life (31-34). The

decline in FM% after 6 months of age might, at least partially, be explained by the increase in physical activity from ~6 months onward when infants start to roll over, crawl, and walk. We also found that girls had higher FM and lower FFM than boys, as found previously at birth and until 6 months (35-37).

In conclusion, the use of a vacuum cushion to prevent movements during DXA scan in infants, provides reliable measurements of body composition and results are comparable to ADP measurements. This allows longitudinal measurements of body composition in infants until 2 years of age, which addresses a gap in research. We found that FM% increases during the first 6 months and gradually declines until 24 months.

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