

Body composition in late preterm infants according to percentile at birth

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BACKGROUND: The data on body composition of late preterm infants, evaluated according to percentile at birth, are scarce. The study aimed to investigate body composition of late preterm infants, according to percentile at birth, and to compare their body composition with that of term newborns.

METHODS: A total of 122 (99 appropriate and 23 small for gestational age (SGA)) late preterm infants underwent growth and body composition assessment using an air displacement plethysmography system on the fifth day of life and at term. The reference group was composed of 42 healthy, term, breast-fed infants.

RESULTS: At birth, appropriate and SGA late preterm infants had lower fat mass and fat-free mass indexes than term newborns. The fat mass and fat-free mass content increased significantly throughout the study, irrespective of percentile at birth. At term, fat mass index, but not fat-free mass index, was higher in both appropriate and SGA late preterm infants than in term newborns.

CONCLUSION: Late preterm infants, irrespective of their percentile at birth, show postnatal growth characterized by predominant fat mass accretion. The potential long-term health clinical implications of these findings need to be further elucidated.

Late preterm birth, defined as a birth that occurs between 34 0/7 and 36 6/7 weeks of gestation, has markedly increased during the past two decades, accounting for 70% of all preterm births (1). Late preterm infants have been recognized as a high-risk group due to an increased mortality and morbidity compared with full-term newborn infants (2). In addition, although late preterm birth has been associated with a rapid postnatal catch-up growth within the first months of life (3,4), growth faltering up to 5 y of age has also been reported (5). With regard to body composition, late preterm infants at term-corrected age show a higher fat mass but a lower fat-free mass than full-term infants (3,4).

Early life has been recognized as a critical time window for metabolic programming. Hence, concern has arisen regarding

the potential implications of these findings on the long-term health outcomes of late preterm infants. Indeed, both early growth pattern and body composition development appear to contribute to the programming process for disease risk in later life (6).

While postnatal growth and body composition changes in very preterm infants have been widely investigated, considering percentile at birth (7,8), there is a paucity of data on body composition of late preterm infants, evaluated according to percentile at birth. The aim of our study was to investigate body composition changes from birth to term-corrected age in a cohort of late preterm infants, categorized according to percentile at birth, and to compare their body composition with that of full-term newborns.

RESULTS

Growth and body composition at term-corrected age data were available for 122 late preterm infants whose basic characteristics at birth are shown in **Table 1**. As expected, appropriate for gestational age (AGA) late preterm infants were heavier and longer and had a larger head circumference *z* score than the small for gestational age (SGA) late preterm infants. SGA late preterm infants showed a longer gestational age than AGA late preterm infants. Percentage of males was higher in the AGA group whereas no difference in the percentage of twins was detected. Mean birth weight and gestational age of full term infants were 3.228 ± 417 g and 38.9 ± 1.29 wks, respectively. Of the 42 full-term newborns, 18 (43%) were males. **Table 2** shows mode of feeding and mean protein and energy intake by the late preterm infants according to percentile at birth. No difference among SGA and AGA late preterm infants in the mean protein and energy intake on the fifth day of life and at term-corrected age was found. The full-term newborns were exclusively breast fed.

Anthropometric and body composition parameters in late preterm infants on the fifth day of life and at term-corrected age and in full-term infants on the third day of life are shown in **Table 3**.

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Received 5 July 2015; accepted 12 October 2015; advance online publication 3 February 2016. doi:10.1038/pr.2015.273

Table 1. Basic subject characteristics of the enrolled late preterm infants

	Enrolled late preterm infants (n = 122)	AGA late preterm infants (n = 99)	SGA late preterm infants (n = 23)
Birth weight (g)	2423 ± 333	2468 ± 331**	2111 ± 102
Birth weight z score	-0.26 ± 0.74	-0.11 ± 0.68**	-1.29 ± 0.26
Birth length (cm)	44.5 ± 1.9	45.5 ± 1.9*	44.1 ± 1.6
Birth length z score	-0.36 ± 0.79	-0.21 ± 0.73**	-1.23 ± 0.69
Birth head circumference (cm)	31.9 ± 1.2	31.9 ± 1.1	31.6 ± 1.1
Birth head circumference z score	-0.08 ± 0.77	-0.02 ± 0.76**	-0.55 ± 0.70
Gestational age (weeks)	35.4 ± 0.77	35.3 ± 0.8*	35.7 ± 0.6
Males, n(%)	64 (52)	47 (73) [§]	17 (27)
Twins, n(%)	72 (59)	55 (56)	17 (74)

Data are expressed as mean ± SD or n (%).

AGA, appropriate for gestational age; SGA, small for gestational age.

**P < 0.001 AGA late preterm infants vs. SGA late preterm infants. *P = 0.016 AGA late preterm infants vs. SGA late preterm infants. [§]P = 0.022 AGA late preterm infants vs. SGA late preterm infants.

Table 2. Mode of feeding and mean protein and energy intakes in late preterm infants according to percentile at birth

	Enrolled late preterm infants (n = 122)		AGA late preterm infants (n = 99)		SGA late preterm infants (n = 23)	
	Fifth day of life	Term-corrected age	Fifth day of life	Term-corrected age	Fifth day of life	Term-corrected age
Exclusively breastfeeding, n (%)	28 (23)	40 (33)	25 (25)	33 (33)	3 (15)	7 (29)
Any breastfeeding, n (%)	62 (51)	55 (45)	51 (52)	53 (54)	11 (46)	2 (7)
Exclusively formula feeding, n (%)	32 (26)	27 (22)	23 (23)	13 (13)	9 (39)	14 (64)
Post discharge formula, n (%)	31 (33)	20 (24)	22 (30)	15 (23)	9 (45)	5 (30)
Term formula, n (%)	63 (67)	62 (76)	52 (70)	51 (77)	11 (55)	11 (70)
Volume (ml/kg)	114.2 ± 18	200 ± 30	114.1 ± 18	199 ± 30	114.5 ± 20	207 ± 25
Energy (kcal/kg/d)	81 ± 14	140 ± 21	80 ± 14	138 ± 22	82 ± 13	144.5 ± 16
Protein (g/kg/d)	1.9 ± 0.45	3.1 ± 0.7	1.8 ± 0.5	3 ± 0.7	2.0 ± 0.4	3.2 ± 0.7

Data are expressed as mean ± SD or n (%).

AGA, appropriate for gestational age; SGA, small for gestational age.

At the time of first assessment, late preterm infants were lighter and shorter than full-term infants. However, when considering z score values for growth parameters, no difference between late preterm infants and full-term infants was found except for head circumference that was found to be larger in full-term infants. Regarding body composition, the percentages of fat mass and fat mass (g) and fat-free mass (g) content of late preterm infants on the fifth day of life were lower than those of full-term newborns on the third day of life. Fat mass and fat-free mass indexes were also lower in late preterm infants than in full-term newborns at birth. At term-corrected age, late preterm infants were heavier than full-term newborns on the third day of life, whereas no difference in length was found among the groups. When considering z score values for growth parameters, only length z scores were higher in full-term infants than in late preterm infants. Regarding body composition, fat mass content and fat mass index were significantly higher in late preterm infants than in full-term infants, whereas fat-free mass and fat-free mass index were similar.

Table 4 presents the anthropometric and body composition parameters on the fifth day of life in late preterm infants according to being born either AGA or SGA and in full-term newborns on the third day of life. When considering late preterm infants according to percentile at birth, both AGA and SGA late preterm infants on the fifth day of life were lighter and shorter than full-term infants on the third day of life. However, when considering z score values for growth parameters, only SGA late preterm infants showed lower z scores for weight and length than full-term infants. Regarding body composition, percentage of fat mass, fat mass (g) and fat-free mass (g) content and fat mass and fat-free mass indexes were significantly lower in both AGA and SGA late preterm infants on the fifth day of life than in full-term newborns at birth. In addition, SGA late preterm infants had a lower fat-free mass but a similar fat-free mass index compared to AGA late preterm infants. At term-corrected age, AGA late preterm infants were heavier than full-term newborns, whereas SGA late preterm infants showed a similar weight. No difference in length values was found among groups, although z score length values were

Table 3. Anthropometric and body composition parameters in late preterm infants on the fifth day of life and at term corrected age and in full term infants on the third day of life

	Late preterm infants on the fifth day of life (n = 122)	Late preterm infants at term-corrected age (n = 122)	Full-term newborns at birth (n = 42)
Weight (g)	2263 ± 312**	3415.3 ± 482**	3.062 ± 391
Weight z score	-0.62 ± 0.7	-0.22 ± 1.0	-0.47 ± 0.8
Length (cm)	45.2 ± 1.9**	49.5 ± 2.2	49.2 ± 1.9
Length z score	-0.3 ± 0.8	-0.47 ± 0.8*	-0.09 ± 1.0
Head circumference (cm)	32.0 ± 1.16**	35.2 ± 1.7 [§]	34.2 ± 1.2
Head circumference z score	-0.23 ± 0.7*	0.14 ± 0.9	0.1 ± 0.9
Fat mass (%)	4.7 ± 2.7**	14.2 ± 4.5**	8.86 ± 2.9
Fat mass (g)	112 ± 77.7**	495.1 ± 206.2**	274.6 ± 107
Fat mass index kg/m ²	0.54 ± 0.35**	2.0 ± 0.82**	1.1 ± 0.4
Fat free mass (g)	2153 ± 268.9**	2899.4 ± 371.6	2787.5 ± 340
Fat free mass index kg/m ²	10.5 ± 0.9**	11.8 ± 1.8	11.4 ± 1.1

Data are expressed as mean vs. SD.

**P < 0.0001 late preterm infants vs. full-term newborns. *P = 0.02 late preterm infants vs. full-term newborns. [§]P = 0.001 late preterm infants vs. full-term newborns

Table 4: Anthropometric and body composition parameters on the fifth day of life in late preterm infants according to percentile at birth and in full-term newborns on the third day of life

	AGA late preterm infants (n = 99)	SGA late preterm infants (n = 23)	Full-term newborns (n = 42)
Weight (g)	2308.2 ± 313**	1978 ± 86* [†]	3.062 ± 391
Weight z score	-0.47 ± 0.6	-1.6 ± 0.2* [†]	-0.47 ± 0.8
Length (cm)	45.5 ± 1.9**	44.1 ± 1.8* [†]	49.2 ± 1.9
Length z score	-0.18 ± 0.7	-1.28 ± 0.6* [†]	-0.09 ± 1.0
Head circumference (cm)	31.9 ± 1.1**	31.8 ± 1.2 [†]	34.2 ± 1.2
Head circumference z score	-0.2 ± 0.7	-0.6 ± 0.16 [§]	0.1 ± 0.9
Fat mass (%)	4.8 ± 2.5**	4.1 ± 2.1 [†]	8.86 ± 2.9
Fat mass (g)	116.7 ± 73.5**	81.0 ± 42 [†]	274.6 ± 107
Fat mass index	0.55 ± 0.32**	0.42 ± 0.21 [†]	1.1 ± 0.4
Fat free mass (g)	2193 ± 269**	1897 ± 79* [†]	2787.5 ± 340
Fat free mass index	10.58 ± 0.95**	9.98 ± 0.6 [†]	11.4 ± 1.1

Data are expressed as mean ± SD or n (%).

AGA, appropriate for gestational age; SGA, small for gestational age.

**P < 0.0001 AGA late preterm infants vs. full-term newborns. *P < 0.001 SGA late preterm infants vs. AGA late preterm infants. [†]P < 0.0001 SGA late preterm infants vs. full-term newborns. [§]P = 0.012 SGA late preterm infants vs. full-term newborns

lower in SGA late preterm infants than in AGA late preterm infants. Regarding body composition, percentage of fat mass, fat mass content and fat mass index were higher in both AGA and SGA late preterm infants than in full-term newborns. On the contrary, even though fat free mass content was higher in AGA late preterm infants than in SGA ones, fat-free mass index was similar among the groups (Table 5).

From birth to the corrected age, fat mass and fat-free mass content increased significantly both in AGA and SGA late preterm infants (P < 0.0001).

DISCUSSION

The present study demonstrates that both AGA and SGA late preterm infants, despite having lower weight, shorter length and lower fat mass and fat-free mass content at birth, showed

rapid postnatal growth and, as a result, at the term-corrected age, AGA late preterm infants were heavier than full-term newborns and had similar length, whereas SGA late preterm infants achieved similar anthropometric parameters, with the exception of length z scores that were found to be lower.

Regarding body composition, at birth, both AGA and SGA late preterm infants showed lower fat mass and fat-free mass content than the full-term newborns, even considering their length. This finding is actually not surprising because it is widely acknowledged that premature birth interrupts the physiologic development of body composition (10). Indeed, one would have expected a lower fat mass content in late preterm infants born SGA than in late preterm infants born AGA because SGA infants and infants born with low birth weight have been recognized to be characterized by a lack of fat mass

Table 5. Anthropometric and body composition parameters at term corrected age in late preterm infants according to percentile at birth and in full-term newborns on the third day of life

	AGA late preterm infants (n = 99)	SGA late preterm infants (n = 23)	Full-term newborns (n = 42)
Weight (g)	3491 ± 467**	3089 ± 413	3.062 ± 391
Weight z score	-0.04 ± 0.9 [§]	-0.96 ± 0.9*	-0.47 ± 0.8
Length (cm)	49.8 ± 2.2	48.6 ± 1.6	49.2 ± 1.9
Length z score	-0.34 ± 0.8	-1.0 ± 0.8*	-0.09 ± 1.04
Head circumference (cm)	35.2 ± 2.1 [§]	35 ± 0.9	34.2 ± 1.2
Head circumference z score	0.16 ± 0.9	0.04 ± 0.6	0.1 ± 0.9
Fat mass (%)	14.6 ± 4.6 [§]	12.7 ± 3.9 [†]	8.86 ± 2.9
Fat mass (g)	516 ± 210 [§]	404 ± 160 [†]	274.6 ± 107
Fat mass index	2.07 ± 0.85 [§]	1.6 ± 0.6 [†]	1.1 ± 0.4
Fat free mass (g)	2939 ± 365	2728 ± 354*	2787.5 ± 340
Fat free mass index	11.8 ± 1.9	11.5 ± 1.3	11.4 ± 1.1

AGA, appropriate for gestational age; SGA, small for gestational age.

** $P < 0.0001$ AGA late preterm infants vs. SGA late term infants and full-term newborns. * $P < 0.05$ AGA late preterm infants vs. SGA late term infants. [§] $P < 0.05$ AGA late preterm infants vs. full-term newborns. [†] $P < 0.05$ SGA late preterm infants vs. AGA late preterm infants and full-term newborns. [‡] $P < 0.05$ SGA late preterm infants vs. full-term newborns.

deposition (11). However, this finding could be partially explained by most SGA late preterm infants being actually constitutionally small rather than having intrauterine growth retardation.

Fat mass content was significantly increased from birth to term-corrected age, irrespective of the percentile at birth, so that both AGA and SGA late preterm infants showed a comparable fat mass accretion, achieving a fat mass content at the term-corrected age, after taking length into account, even higher than full-term infants. By contrast, fat-free mass content, also after considering length, was similar not only between AGA late preterm infants and full-term newborns but also between SGA late preterm infants and full-term newborns. These results, taken together, indicate that the postnatal weight gain shown by late preterm infants, irrespective of being born either SGA or AGA, was actually mainly represented by a preferential deposition of fat mass that led to increased total adiposity at the term-corrected age. In addition, AGA and SGA late preterm infants showed comparable fat mass accretion between birth and term-corrected age. The latter finding is somewhat surprising because a higher delta fat mass in SGA late preterm infants could have been expected, higher than that in the AGA late preterm infants because SGA very preterm infants have demonstrated rapid postnatal catch-up with respect to fat (12). However, it can be speculated that because protein intake has been reported to be associated with a significantly different weight gain composition (13,14), the lack of higher fat mass accretion in SGA late preterm infants could be because they actually received similar protein and energy intake compared to AGA late preterm infants.

Based on the present results, late preterm infants gain more fat mass than what they would have gained if they had remained *in utero*, a finding that is in agreement with previous studies. De Marini *et al.* (9). investigated body composition changes from birth to the term-corrected age using air displacement plethysmography in a cohort of 13 late preterm

infants. The authors found that weight, length, and percentage of fat mass were significantly decreased in late preterm infants at birth compared with those in full-term newborns. However, at the term-corrected age, late preterm infants were heavier and showed a higher percentage of fat mass than full-term newborns. Olhager *et al.* (4). have investigated body composition changes from birth to the term-corrected age in a cohort of 29 late preterm infants using air displacement plethysmography. The authors reported a significant increase in weight and fat mass and free mass content throughout the study ($P < 0.0001$). In addition, they found a significantly increased percentage of fat mass in late preterm infants at the term-corrected age compared with full-term infants (12.3 ± 4.9 vs. 8.1 ± 4.3 , $P < 0.0001$). However, contrary to our findings, they reported a significantly lower fat-free mass content ($2,631 \pm 309$ g vs. $2,794 \pm 329$ g, $P < 0.0001$).

The present findings confirm previous results from our research group. We have studied the body composition of 49 late preterm infants, born AGA, and reported a delta fat mass gain from birth to the term-corrected age of 18.2%, with a significantly higher percentage of fat mass at the term-corrected age in late preterm infants than in full-term infants at birth (3). To our knowledge, this is the first study that investigated the body composition in a cohort of late preterm infants, who were born SGA. By contrast, body composition changes in SGA very preterm infants have been investigated by several authors. Increased adiposity at the term-corrected age in 110 very preterm infants, born SGA, compared with full-term, SGA newborns has been reported (7). The restoration of fat mass stores appears to occur within the first 3–6 mo of life (8,15).

Based on the available evidence, the potential clinical implication of rapid postnatal catch-up growth associated with a predominant fat mass rather than fat-free mass accretion has not been clearly elucidated. Aly *et al.* (16). investigated insulin sensitivity in 41 AGA and 40 SGA late preterm infants at birth and in the second week of life and reported no evidence of

insulin resistance. By contrast, Wang *et al.* (17) found a plasma insulin level at birth 1.45-fold (95%CI, 1.25–1.65) higher in late preterm than in full-term infants.

While this study is of clinical interest, it presents some limitations. First, although we have conducted a longitudinal study on a large sample size of infants, the duration of follow-up has been relatively short. Furthermore, no metabolic parameter has been investigated alongside the postnatal catch-up fat.

This explorative, longitudinal study provides evidence that late preterm infants, irrespective of the percentile at birth, have a rapid postnatal catch-up growth, which occurs within the first weeks after birth and is characterized by predominant fat mass accretion. Whether this growth and body composition pattern may be of concern due to a potential negative effect on long-term health of these infants needs to be further elucidated.

METHODS

The study was approved by the Departmental Ethics Committee, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy, and informed written consent was obtained from the parents.

Patients

Of all the consecutive newborns admitted to the authors' institution from November 2014 to March 2015, 122 late preterm infants were included in the study. The reference group was constituted by 42 full-term, healthy, AGA according to the World Health Organization Charts (18), breast-fed newborns. Inclusion criteria were the following: gestational age from 34 0/7 to 36 6/7 wks and Caucasian parentage. Exclusion criteria were presence of congenital diseases, chromosomal abnormalities, severe cardiac, brain, renal, endocrinologic, gastrointestinal or infectious diseases, prepregnancy maternal BMI > 30 and need for parenteral nutrition or intravenous infusions.

Design

We conducted an observational, longitudinal study. Infants were enrolled at birth. At enrolment, basic subject characteristics such as birth weight, length, head circumference, gestational age, gender, and being a twin were recorded prospectively. Gestational age was based on the last menstrual period and first trimester ultrasonogram. Corrected age was calculated using the chronologic age and adjusting for gestational age—that is, for the number of additional weeks from term (40 wks).

The infants with a birth weight in the <10th or ≥10th percentile for gestational age, based on Fenton's growth chart (19), were, respectively, classified as having a weight that was SGA or AGA.

Nutritional Practices

Regarding late preterm infants, breastfeeding was encouraged in all mother-infant pairs. According to our internal nutritional procedure, human milk was not fortified. In case of unavailable or insufficient human milk, formula feeding was started. Infants born at 34 weeks gestational age and SGA infants born at 35–36 weeks gestational age, were fed a post-discharge formula (range of protein content: 2–2.4 g/100 ml; range of energy content: 73–82 kcal/100 ml) up to the maximum corrected age of 40 wks. AGA late preterm infants, born at 35–36 weeks of gestational age, were fed a regular-term formula (range of protein content: 1.3–1.7 g/100 ml; range of energy content: 66–68 kcal/100 ml). Infants were fed on demand. Infants' daily protein and energy intake during hospital stay were calculated from the infants' computerized medical chart. After discharge, parents were instructed to record the daily quantity of milk consumed by the infants in a diary. The average daily energy and protein intake were then calculated.

When infants were directly breast fed, mothers were asked to weigh their baby once a week before and after each feeding, so that the mean volumes assumed by the baby and, hence, the mean protein and

energy daily intake, could be calculated. Based on personal, unpublished data, we assumed the following human milk mean protein and energy content: 1.7 g/100 ml and 50 kcal/100 ml in the first week after delivery and 1.4 g/100 ml and 69 kcal/100 ml at the term-corrected age.

Full-term newborns were exclusively breastfed.

Growth and Body Composition Assessment

Regarding late preterm infants, anthropometric measurements and body composition were assessed on the fifth day of life and at term. Full-term newborns were measured on the third day of life (20). Body weight, length, and head circumference were measured according to standard procedures (21). Weight of each baby was measured on an electronic scale accurate to ±0.1 g (PEA POD Infant Body Composition System; Cosmed, Concord, CA). Body length was measured to the nearest 1 mm on a Harpenden neonatometer (Holtain, Crymch, UK). Head circumference was measured to the nearest 1 mm using non-stretch measuring tape. All measurements were performed by trained nurses. The full-term and late preterm infants' growth (weight, length, and head circumference) *z* scores were then calculated using, respectively, the software Anthro, version 3.2.2, January 2011 (World Health Organization, Geneva, Switzerland) and the online *z* score calculator provided by the University of Calgary, Calgary, Alberta, Canada (22).

Body composition was assessed using an air displacement plethysmography system (PEA POD Infant Body Composition System). A detailed description of the PEA POD's physical design, operating principles, validation, and measurement procedures is provided elsewhere (23,24). Briefly, the PEA POD assesses fat mass and fat-free mass by direct measurements of body mass and volume and application of a classic densitometric model in which percentage of body fat is calculated using body density and predetermined fat and fat-free mass density values. Body fat was defined as body weight minus fat-free mass. A constant fat mass density value of 0.9007 g/ml was used. Fat-free mass density values were calculated as the sum of the contributions of the various components in the fat-free mass compartment. Age- and sex-specific fat free-mass density values extrapolated from data reported in previous multicompartiment model studies were used.

The fat mass and fat-free mass were then normalized for length to yield fat mass and fat-free mass indexes, as suggested by VanItallie *et al.* (25).

Statistical Analysis

The data are expressed as the mean (SD) or *n* (%). Comparison among groups was performed using a χ^2 test for discrete variables. Comparison of intra and inter groups was performed by analysis of variance, using Bonferroni correction for the adjustment of the significance of multiple comparisons. Statistical significance was set at a level of 0.05. All statistical analyses were performed using SPSS software (SPSS, version 20; SPSS, Chicago, IL).

STATEMENT OF FINANCIAL SUPPORT

No financial assistance was received to support this study.

Disclosure: The authors have no conflicts of interest to declare.

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