ORIGINAL RESEARCH

Accretion Rates of Fat and Fat-free Mass in Infants at 30–45 weeks' Postmenstrual Age

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Abstract

Background: Body composition assessment using noninvasive air displacement plethysmography (ADP) can help determine the quality of postnatal growth in infants. The accretion rates of fat mass (FM) and fat-free mass (FFM), both are known to change in various clinicopathological situations in a discordant fashion, can also help evaluate the short-term impacts of nutritional interventions on body composition.

Objectives: To determine the FM and FFM accretion rates from 30 to 45 weeks' postmenstrual age (PMA) and whether these rates are different between male and female infants.

Methods: We used previously published normative data with median FM and FFM values for infants at 30–45 weeks' PMA (Norris et al., 2019). Weekly gains in FM and FFM in g/week and g/kg/week were calculated using early one-point and average two-point methods.

Results: FM and FFM accretion rates calculated by the early one-point method were higher than the average two-point method. Male and female infants had similar FM and FFM accretion rates. Constant accretion rates of FM and FFM were not aligned with individual weekly accretion rates, which showed a twofold–fourfold change. A composite index (FFM/FM accretion rate ratio), which we named the "body composition accretion ratio" (BCAR), was more sensitive than the individual weekly accretion rates and showed a ninefold change during the study period.

Conclusions: Weekly FM and FFM accretion rates can help assess quality of postnatal growth in young infants, but BCAR can be a more useful, sensitive index for early identification of body composition changes and may possibly guide nutritional interventions.

Keywords: Body composition, Postnatal growth, Preterm infants.

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Introduction

The quality and quantity of early postnatal growth can impact the survival, neurodevelopment, and later metabolic function in preterm infants.[1–3] Body composition studies in preterm infants have observed that early body composition, especially with a gain in fat-free mass (FFM), is associated with better long-term neurodevelopmental outcomes.[4–6] Current nutritional practices in neonatal intensive care units (NICUs) that attempt to grow preterm infants along the *in utero* growth curves using weight-based calorie intake goals are often associated with deficit in fat-free mass (FFM) and increased fat mass (FM) at term-corrected age compared to term-born peers.[7–11] Such disproportionate growth in FM and FFM has raised concerns about weight-based nutritional interventions. With the availability of safe, reliable, noninvasive infant body composition assessment using air displacement plethysmography (ADP, trade name "PEA POD"—an infant version of the ADP device), body composition assessment is increasingly clinically used to determine the quality of postnatal growth in preterm infants.[12,13] Also, normative, sex-specific reference charts for body composition for the first 6 months of life to monitor growth are now available (Norris body composition charts).[14]

To calculate the short-term growth in infants being treated in the NICUs, growth velocity calculated over a defined time period (e.g., weekly) is often used and a weight gain of 15–20 g/kg/day is often considered acceptable.[15–17] This growth velocity rate is usually expected to be similar in both male and female infants, and a sex-specific growth velocity rate for weight is not usually used.[16] However, unlike weight gain, there is no readily available data for the FM and FFM accretion rate over a defined time period. These data are important for clinicians to assess the short-term impact on the body composition of various nutritional interventions aimed to optimize the postnatal growth of preterm infants. Also, previous data suggest that male infants have higher FFM, lower FM, and lower body fat% compared to female infants.[14] This difference in body composition between male and female infants may be best evaluated with sex-specific FM and FFM accretion rates. The objective of this study was to determine the

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expected sex-specific weekly FM and FFM accretion rates for infants across the postmenstrual ages (PMAs) 30–45 weeks calculated based on the Norris body composition charts, and we hypothesized that these accretion rates would be different between male and female infants.

Methods

This study is a secondary analysis of the previously published Norris body composition charts that were created using pooled data from four studies comprising both term and preterm infants (n ~ 1,450 which included 222 preterm infants) from three high-income countries (Ireland, Italy, and the United States).[14] Institutional review board approval was not needed for this secondary analysis of data that are available in the public domain. The infants included in these studies were born singleton, medically stable, and without significant perinatal morbidity. Using the combined data, sex-specific centiles for FM (kg), FFM (kg), and body fat percentage were estimated using the lambda-mu-sigma (LMS) method. For each sex and measure (e.g., FM), these charts also include postconceptional charts, ranging from 30.3 to 67.3 weeks' PMA, which enable serial postnatal monitoring of body composition in preterm infants.

To determine weight growth velocity, the three common calculation methods used are early one-point method, average two-point method, and exponential two-point method.[16,17] The exponential model was not suitable in this study because of the assumption that growth occurred at a constant fraction of the previous weight over time; existing data show that FM accumulation usually increases rapidly toward term gestation. As defined earlier, the early one-point method was calculated as [(W2 – W1)/(W1 ÷ 1000]/number of days. The average two-point method was computed as (W2 – W1)/[(W1 + W2) ÷2 ÷ 1000]/number of days.[17] First, we calculated the FM and FFM absolute values (g) corresponding to the median (50th percentile) for 30–45 weeks' PMA according to the Norris body composition charts for male and female infants. Then, the weekly gain in FM and FFM in g/week and g/kg/week (by early one-point method and average two-point method) was calculated. For example, for FM, we used the following formulas for early one-point method [FM week 2–FM week 1/weight at week 1] × 1,000 and average two-point method [FM week 2–FM week 1/(weight week 1 + weight week 2)/2] × 1000.

Statistics

Student t-test was used for parametric continuous variables (FM and FFM gain and weekly accretion rates) to identify the unadjusted differences between male and female infants. All quantitative data were expressed as the mean ± standard deviation (SD). A $p \leq 0.05$ was considered statistically significant. The statistical software IBM SPSS Statistics version 24 (SPSS, Chicago, Illinois) was used for the statistical analysis of the data.

Results

The reference median rates of FM and FFM accretion across 30–45 weeks' PMA for male and female infants are shown in Tables 1 and 2. Both FM gain and FFM gain (g/week) increase with advancing PMA in both male and female infants (Tables 1 and 2, Figs 1A and D). FM and FFM median weekly accretion rates (g/kg/week) by early one-point method were higher than those by the average two-point method in both male and female infants throughout the gestational age ranges studied (Tables 1 and 2, Figs 1B to F). The FM accretion rates increased gradually with advancing PMA, while FFM accretion rates decreased with advancing PMA, suggesting a relatively higher FM accretion toward later gestational weeks in both male and female infants.

The cumulative average FM and FFM gain and accretion rates in males and female infants are given in Table 3. The cumulative average FM accretion rate (g/kg/week) across the whole 30–45 weeks' PMA for males and females was 16.1 and 15.8 by early one-point and 10.4 and 10.3 each by average two-point method, respectively. Similarly, the cumulative average FFM accretion rate (g/kg/week) across the whole 30–45 weeks' PMA for males and

Table 1: Reference weekly fat mass (FM) and fat-free mass (FFM) median accretion rate (50th percentile) in male infants from 30 to 45 weeks' postmenstrual age (PMA) according to the calculation method based on the Norris body composition chart

			Males			
PMA, weeks	*FM (g) gain/week*	*FM (g) gain/kg/ week—early one-point method*	*FM (g) gain/kg/week—average two-point method*	*FFM (g) gain/ week*	*FFM (g) gain/kg/ week—early one-point method*	*FFM (g) gain/kg/ week—average two-point method*
30–31	7.5	5.0	3.3	76.3	51.1	33.4
31–32	14.8	9.4	6.1	143.2	90.8	58.6
32–33	17.2	9.9	6.4	154.6	89.1	57.5
33–34	19.9	10.4	6.7	165.5	86.8	56.0
34–35	22.5	10.8	7.0	173.0	82.7	53.5
35–36	25.4	11.1	7.2	176.4	77.1	49.9
36–37	28.1	11.3	7.3	175.9	70.6	45.8
37–38	32.0	11.9	7.7	170.7	63.4	41.2
38–39	37.8	13.1	8.5	164.3	56.7	37.0
39–40	46.9	15.1	9.9	158.7	51.2	33.4
40–41	60.1	18.2	11.9	156.0	47.2	30.8
41–42	64.2	18.2	11.9	160.3	45.5	29.7
42–43	116.2	31.0	20.2	164.4	43.9	28.6
43–44	113.9	28.3	18.4	166.0	41.2	26.9
44–45	119.8	27.8	18.2	164.0	38.1	24.8
45–46	116.2	25.3	16.6	159.0	34.6	22.6

Table 2: Reference weekly fat mass (FM) and fat-free mass (FFM) median accretion rate (50th percentile) in female infants from 30 to 45 weeks' postmenstrual age (PMA) according to the calculation method based on the Norris body composition chart

Females						
PMA, weeks	*FM (g) gain/week*	*FM (g) gain/kg/week—early one-point method*	*FM (g) gain/kg/week—average two-point method*	*FFM (g) gain/week*	*FFM (g) gain/kg/week—early one-point method*	*FFM (g) gain/kg/week—average two-point method*
30–31	8.2	6.0	6.0	72.5	52.8	34.5
31–32	17.1	11.7	11.7	142.5	98.0	63.0
32–33	19.7	12.2	12.2	156.0	96.6	62.2
33–34	22.2	12.4	12.4	167.0	93.3	60.1
34–35	24.8	12.5	12.5	175.5	88.7	57.2
35–36	27.5	12.6	12.6	179.0	82.1	53.1
36–37	30.2	12.7	12.7	177.0	74.2	48.1
37–38	33.5	12.9	12.9	170.0	65.6	42.6
38–39	38.3	13.7	13.7	160.0	57.2	37.3
39–40	45.0	15.0	15.0	146.9	49.0	32.0
40–41	54.4	17.1	17.1	137.1	43.0	28.1
41–42	67.6	20.0	20.0	132.5	39.2	25.6
42–43	80.4	22.5	22.5	132.5	37.0	24.2
43–44	91.3	24.1	24.1	133.8	35.3	23.1
44–45	98.1	24.4	24.4	134.0	33.4	21.8
45–46	99.9	23.5	23.5	132.2	31.1	20.4

females was 60.6 and 61.0 by early one-point and 39.4 and 39.6 by average two-point method, respectively (Table 3). The similar trend in FM and FFM accretion rates in male and female infants is shown in Figure 2.

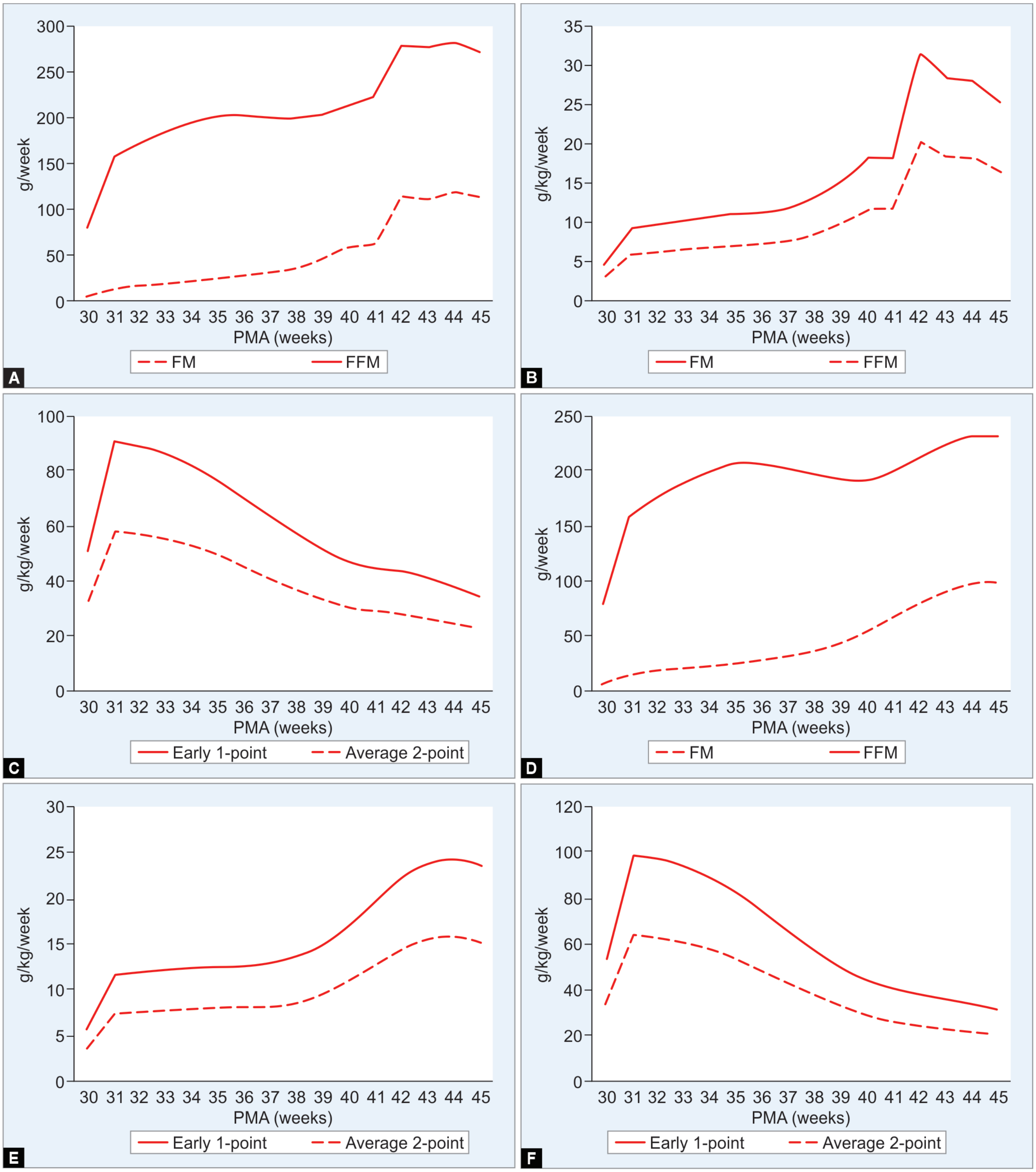
Since there were no significant differences in FM and FFM accretion rates between male and female infants, an average of these was taken to calculate the constant FM accretion rate for the 30–45 weeks' PMA by early one-point (16.0) and average two-point (10.4) and constant FFM accretion rate by early one-point (61.0) and average two-point (39.5), respectively. The constant FM and FFM rates were then superimposed over the weekly reference FM and FFM accretion rates to see the overlap (Fig. 3). The concordance for reference and constant accretion rates for both FM and FFM were limited to a short range of PMA weeks (Fig. 3). For FM, the constant average two-point rate (10.4) was more aligned with the reference before 37-week PMA, and the constant early one-point rate (16.0) after 37 weeks' PMA. On the contrary, for FFM, the constant early one-point rate (61.4) was more aligned with the reference before 37 weeks' PMA, and the constant average two-point rate (39.4) after 37 weeks' PMA.

We did not find the constant accretion rates to simulate the reference accretion rates. Hence, we also computed individual weekly normative FM and FFM accretion rates by averaging the median accretion rates of male and female infants for 30–45 weeks' PMA (Table 4). We also calculated a composite index comprised of the ratio of weekly median FFM/FM accretion rates, which we named as the "body composition accretion ratios" (BCAR) based on early-1 point and average two-point methods (Table 4). Irrespective of the calculation method used, BCAR were similar across the studied PMA. The BCAR ratios trended downwards with advancing gestation suggesting a relatively higher proportional FM accretion, compared to FFM (Fig. 4). Compared to the individual weekly accretion rates which showed a 2–4-fold change during the study period, the BCAR showed a 9-fold change, suggesting that it is a more sensitive metric for weekly body composition changes.

Discussion

There is increasing emphasis on improving the quality of postnatal growth in preterm infants as cumulative data suggest that the trajectory of postnatal growth in terms of FM and FFM accretion rate and proportion can influence short-term and long-term clinical outcomes.[5,6,13,18–20] Noninvasive body composition assessment using ADP is a validated technique in infants, and many NICUs are using this tool for quality improvement initiatives as well as an objective way of assessing the impact of nutritional interventions in routine NICU clinical practice.[12] Our data reported here on the expected weekly changes in FM and FFM accretion rates and BCAR across the gestational age range of 30–45 weeks' PMA can be a clinically meaningful, readily available practical guide to monitor and compare the quality of postnatal growth and nutrition in NICU infants.

Body composition data during the early postnatal weeks in preterm infants suggest that absolute body weight, FM, and FFM increase with advancing gestation.[14] However, our data show that FM and FFM accretion rates follow a contrasting trend. FM accretion rates increases, while FFM accretion rate decreases with advancing postnatal age because of the relatively higher FM deposition resulting in a higher percentage of body fat. The progressively higher fat deposition with advancing gestation in the first 3–4 months of life is secondary to the physiological adaptation process to extrauterine life from the age-related changes in total body water and its compartments—as the total body water decreases with gradual contraction of extracellular

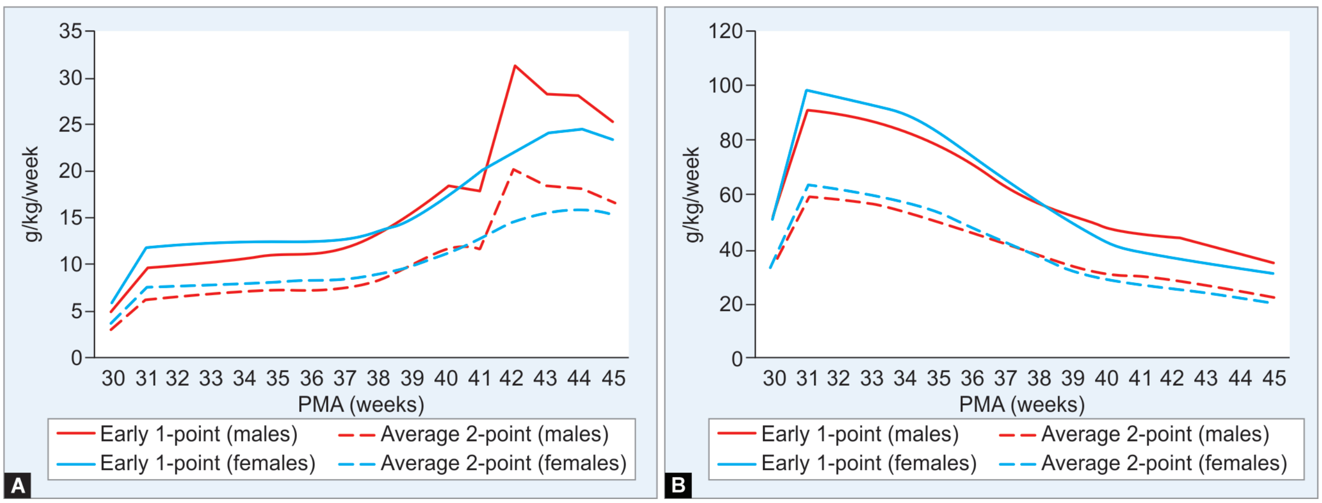


Figs 1A to F: Postnatal fat accretion during 30-45 weeks' postmenstrual age, compared by gender. (Panels A, D), Total FM and FFM gain/week (data from males in A, females in D); (Panels B, E), FM median accretion rate per unit weight (g/kg/week; data from males in B, females in E); and (Panels C, F), FFM median accretion rate per unit weight (g/kg/week; data from males in C, females in F). The figures show the temporal evolution of these indices in the Norris body composition charts. FM, fat mass; FFM, fat-free mass; PMA, postmenstrual age

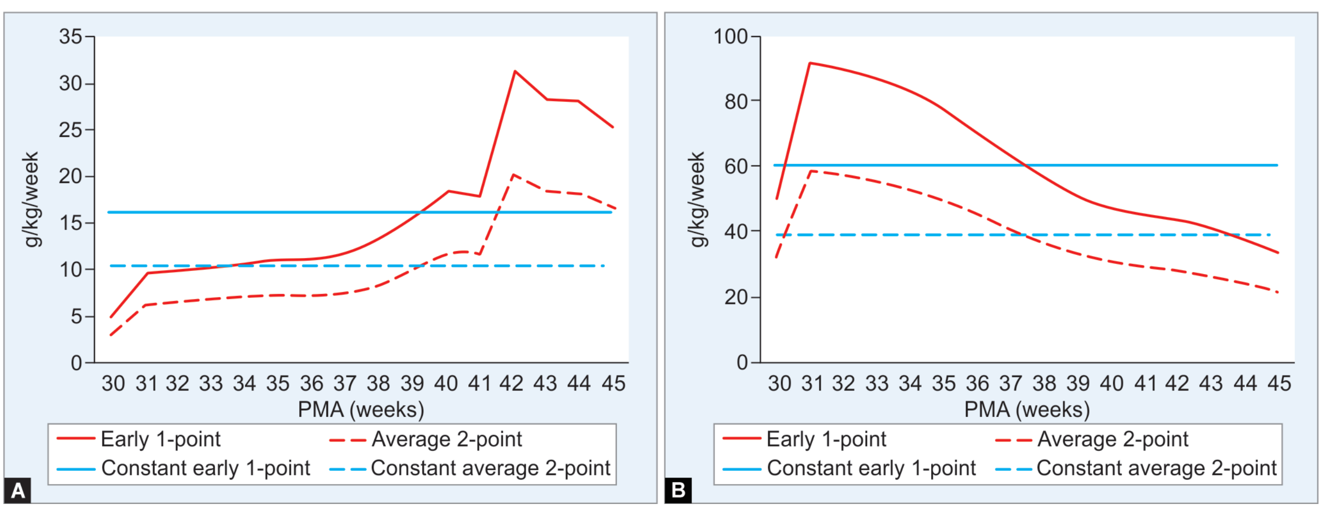
fluid, the body fat proportionately increases.[21] Recent data suggest that energy intake, appetite, and energy expenditure in young infants are strongly associated with metabolically active, energy-using tissues in FFM, but not FM.[22] However, the status quo, as it pertains to nutritional practices in the NICU, is guided by weight gain trends and not based on the quality of growth (i.e., changes in body composition). Our attempts to meet the *one-size-fits-all* conventional weight-based feeding volume targets (150–160 mL/kg/day) do not account for the possible variations in underlying body composition. It is possible that feeding and milk intake volume

Table 3: The cumulative average weight, fat mass (FM), and fat-free mass (FFM) gain and weekly accretion rates in males and female infants across 30–45 weeks' postmenstrual age (PMA) according to the calculation method based on the Norris body composition chart

Characteristics	*Males*	*Females*	*p value*
Weight (g)	3070.7 ± 1036.5	2904.4 ± 960.8	0.64
FM (g)	360.7 ± 262.5	379.3 ± 234.9	0.83
FFM (g)	2710.0 ± 786.2	2525.0 ± 735.9	0.50
FM gain (g)/week	52.7 ± 41.0	47.4 ± 30.7	0.68
FM (g) gain/kg/week—early one-point method	16.1 ± 7.9	15.8 ± 5.5	0.93
FM (g) gain/kg/week—average two-point method	10.4 ± 5.2	10.3 ± 3.6	0.93
FFM gain (g)/week	158.0 ± 23.4	146.8 ± 26.5	0.21
FFM (g) gain/kg/week—early one-point method	60.6 ± 19.5	61.0 ± 24.5	0.96
FFM (g) gain/kg/week—average two-point method	39.4 ± 12.5	39.6 ± 15.6	0.97



Figs 2A and B: Weekly FM (A) and FFM (B) Median accretion rate (g/kg/week) across the 30–45 weeks' PMA calculated based on early one-point and average two-point method compared between male and female infants. FM, fat mass; FFM, fat-free mass; PMA, postmenstrual age



Figs 3A and B: Weekly FM (A) and FFM (B) Median accretion rate (g/kg/week) across the 30–45 weeks' PMA calculated based on early one-point and average two-point method compared to the constant rate. FM, fat mass; FFM, fat-free mass; PMA, postmenstrual age

Table 4: Normative weekly FM and FFM median accretion rate (50th percentile) and FFM/FM weekly accretion rate ratio (BCAR) in infants from 30 to 45 weeks' PMA according to the calculation method based on the Norris body composition chart

PMA, weeks	*FM (g) gain/kg/week—early one-point method*	*FM (g) gain/kg/week—average two-point method*	*FFM (g) gain/kg/week—early one-point method*	*FFM (g) gain/kg/week—average two-point method*	*FFM/FM accretion rate ratio—early one-point method (BCAR)*	*FFM/FM accretion rate ratio—average two-point method (BCAR)*
30–31	5.5	3.6	51.9	34.0	9.4	9.4
31–32	10.6	6.8	94.4	60.8	8.9	8.9
32–33	11.0	7.1	92.9	59.8	8.4	8.4
33–34	11.4	7.4	90.0	58.1	7.9	7.9
34–35	11.6	7.5	85.7	55.3	7.4	7.4
35–36	11.9	7.7	79.6	51.5	6.7	6.7
36–37	12.0	7.8	72.4	47.0	6.0	6.0
37–38	12.4	8.1	64.5	41.9	5.2	5.2
38–39	13.4	8.7	57.0	37.1	4.3	4.3
39–40	15.1	9.8	50.1	32.7	3.3	3.3
40–41	17.6	11.5	45.1	29.5	2.6	2.6
41–42	19.1	12.5	42.4	27.7	2.2	2.2
42–43	26.7	17.4	40.5	26.4	1.5	1.5
43–44	26.2	17.1	38.3	25.0	1.5	1.5
44–45	26.1	17.1	35.7	23.3	1.4	1.4
45–46	24.4	16.0	32.9	21.5	1.3	1.3

FM, fat mass; FFM, fat-free mass; BCAR, body composition accretion ratio; PMA, postmenstrual age

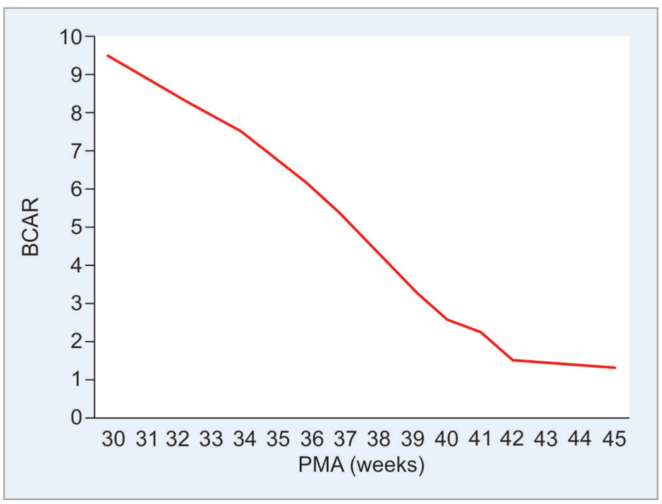


Fig. 4: Weekly FFM/FM accretion rate ratio (body composition accretion ratio, BCAR) across the 30–45 weeks' PMA

in convalescent NICU infants may be determined by FFM volume and proportion. Further studies are needed to test the hypothesis that whether optimizing milk intake volume and nutrition based on serial body composition will improve the growth and clinical outcomes in NICU infants.

Because of FM and FFM accretion rates are similar in both male and female infants across the gestational weeks studied, it is reasonable to use a common FM and FFM accretion rates for both sexes that is calculated by averaging the median accretion rates for male and female infants for each individual week (Table 4). The sex difference in body composition is appreciated even in early life with probable contribution from sex steroids (testosterone and estrogen).[23] Longitudinal body composition studies from birth to 5 months have shown that male infants accumulate 17 g/week additional FFM, compared to female infants.[23] For practical purposes, a common FM and FFM accretion rates for male and females during the 30–45 weeks' PMA is reasonable, but it is possible that the difference in accretion rates may become significant with further period of growth, such that sex-specific accretion rates may become necessary.

Compared to the constant weight velocity of 15–20 g/kg/day, the constant FM and FFM accretion rates were covering only a limited PMA ranges, suggesting that FM growth and FFM growth are not constant during this period of growth. Therefore, for more accurate results, it is better to use the individual weekly FM and FFM accretion rates as given in Table 4. We believe that the early one-point accretion rate can be used to predict the expected gain in FM and FFM (g) over the next week when at least one ADP measurement is available, while the average two-point method can be used to compare the FM and FFM accretion rate (g/kg/week) when ADP data are available at two time points. Similar to the growth velocity calculation for weight, we apply caution while using early one-point method to summarize the FM and FFM accretion rate of more than one week duration because of the use of smaller denominator (using early body weight), thereby producing a larger estimate than average two-point method.[16] When trying to calculate the FM and FFM accretion rate over a longer period (e.g., 2–4 weeks apart), we suggest using the constant average two-point method accretion rate by averaging the weekly accretion rate of each individual week included in the defined time period.

Most conventional indices in FM and FFM showed twofold–fourfold changes over the 30–45 weeks' PMA study period. Because the accretion rates of FM and FFM changed in different trajectories during the studied period of postmenstrual age, we sought to determine whether a composite index of the ratio of FFM/FM accretion rates could be useful. We named this index the body composition accretion ratio (BCAR; Table 4). Interestingly, this index showed a ninefold change during the study period, indicating that the BCAR could be a much more sensitive measure of the accretion of lean body mass than the direct measurements of FFM and FM. Clearly, these observations suggest a need for further investigation in this area. Because the accretion of FFM is related to better clinical outcomes, a higher BCAR may be preferable and could be a useful measure of the accretion efficiency of nutrition being currently provided.

We acknowledge that our study has both strengths and limitations. The ADP technique is sensitive enough to detect a 30–45 g change in FFM in measurements taken one week apart and was therefore appropriate for these studies.[20] One limitation of this, and all studies focused on the utility of nutritional interventions, is in the limitations of the normative reference charts. The Norris reference charts included only 222 preterm infants, which is a considerably smaller cohort than the ones used to construct the anthropometric reference growth charts commonly used by clinicians.[14,24,25] This may limit the applicability at the extremes of growth, below the 10th percentile and greater than the 90th percentile. Additionally, the limited cohort of preterm infants in the Norris reference who were recruited in the US cohort included may not represent a more global population. There may be other population-based factors that alter the growth potential including genetic and ethnic differences. Similar to the Fenton growth charts, the Norris growth charts are a reference intrauterine growth chart instead of a "prescriptive" postnatal curve. Still, despite all shortcomings, these findings suggest that the ADP technique may be a useful bedside tool for clinicians to interpret body composition trajectory in NICU infants and merit further evaluation of these findings in a larger, multicentric cohort.[26]

Abbreviations

ADP: Air displacement plethysmography
FM: Fat mass
FFM: Fat-free mass
NICU: Neonatal intensive care unit
PMA: Postmenstrual age

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