ABSTRACT

Background: Preterm infants have a higher fat mass (FM) percentage and a lower fat-free mass (FFM) than do term infants at the time of hospital discharge.

Objective: We determined perinatal and nutritional factors that affect the body composition of preterm infants at discharge.

Design: A total of 141 preterm infants born at <35 wk of gestation and admitted to Nantes University Hospital Neonatology Unit over a period of 2 y were enrolled. Nutritional intake and growth were monitored during hospitalization. Body composition was assessed by using air-displacement plethysmography at discharge. FFM was compared with reference data in term infants according to sex and gestational age.

Results: Linear regression produced an excellent model to predict absolute FFM from perinatal characteristics and nutrition ($R^2 = 0.82$) but not the FM percentage ($R^2 = 0.24$). Gestational and postnatal ages played an equal role in absolute FFM accretion, as did the initial growth (between birth and day 5) and growth between day 5 and discharge. Antenatal corticosteroid treatment slightly reduced initial growth (between birth and day 5) and growth between day 5 and discharge. Antenatal corticosteroid treatment slightly reduced initial growth (between birth and day 5) and growth between day 5 and discharge. Antenatal corticosteroid treatment slightly reduced initial growth (between birth and day 5) and growth between day 5 and discharge.

Conclusion: The initial growth and quality of nutrition were significantly associated with absolute FFM accretion during a hospital stay in preterm infants. This trial was registered at clinicaltrials.gov as NCT01450436.

INTRODUCTION

Weight gain is often the sole variable used to assess early growth (4). However, literature evidence has suggested that the composition of weight gain may be a key determinant of later metabolic outcome (5). Therefore, there is keen interest among neonatologists in the accurate determination of body FM and FFM to optimize the nutritional management of preterm infants. Over the past decade, air-displacement plethysmography has emerged as a noninvasive technique that is based on the measurement of body volume by using gas laws (6), and several studies have confirmed the reliability and accuracy of air-displacement plethysmography in animals (7), infants, and neonates (8).

Therefore, the main objective of the current study was to determine factors (both intrinsic and nutritional) that influence the FM percentage and FFM deficit measured at the time of hospital discharge in preterm infants born at <35 wk of gestation.

SUBJECTS AND METHODS

Patients

Enrolled subjects were preterm infants admitted to the Neonatal Intensive Care Unit at Nantes University Hospital over a period of 2 y when the equipment for air-displacement plethysmography (Peapod) and clinical research staff were available. Inclusion criteria were as follows: gestational age <35 wk, length of hospitalization >2 wk, and body-composition

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4 Abbreviations used: FFM, fat-free mass; FM, fat mass; HC, head circumference.
measurement performed between 36 and 38 wk postmenstrual age. Exclusion criteria were as follows: the presence of severe malformation, the use of supplemental oxygen or intravenous infusion at the time of hospital discharge, a transfer to another hospital before discharge, or the parent’s refusal to participate. This trial was registered at clinicaltrials.gov as NCT01450436.

Ethics

The study was approved by the Nantes Ethics Committee. Verbal consent was obtained from parents, and a statement of nonopposition was recorded in the infant’s clinical chart as required by French law for this kind of observational study.

Design

In this prospective, observational study, subject characteristics were recorded at birth [ie, birth weight, length, head circumference (HC), gestational age, and sex]. Gestational age was calculated on the basis of the date of last menstrual period and first-trimester ultrasound. Postmenstrual age was calculated as the sum of gestational age and postnatal age. Therapeutic regimens received (such as ventilatory support and parenteral and enteral nutrition), and events that occurred during the hospital stay (eg, infections) were also recorded along with growth measurements.

Body weight, length, and HC were measured according to standard procedures. Body weight was measured twice on an electronic scale accurate to the nearest 0.1g, and the mean value was used. Body length was measured on an infant-length board to the nearest 1 mm. HC was measured in the largest frontooccipital plane to the nearest 1 mm with a nonstretch measuring tape. Because newborn infants normally experience an initial weight loss during the first few days of life as a result of physiologic water loss and the contraction of extracellular volume, postnatal weight gain was assessed between birth and day 5 and between day 5 and discharge (9). Growth z scores were calculated according to sex with Olsen’s intrauterine curves (10). The change in weight z score was calculated by subtracting the weight z score at birth from the weight z score at the time of body-composition assessment. Body composition was assessed during the last week before discharge by using air-displacement plethysmography (PEA POD Infant Body Composition System; COSMED). Air-displacement plethysmography is a densitometric technique. Body mass was assessed on the high-precision electronic scale accurate to the nearest 0.1g, and the mean value was used. Body length was measured on an infant-length board to the nearest 1 mm with a nonstretch measuring tape. HC was measured in the largest frontooccipital plane to the nearest 1 mm with a nonstretch measuring tape. Because newborn infants normally experience an initial weight loss during the first few days of life as a result of physiologic water loss and the contraction of extracellular volume, postnatal weight gain was assessed between birth and day 5 and between day 5 and discharge (9). Growth z scores were calculated according to sex with Olsen’s intrauterine curves (10). The change in weight z score was calculated by subtracting the weight z score at birth from the weight z score at the time of body-composition assessment. Body composition was assessed during the last week before discharge by using air-displacement plethysmography (PEA POD Infant Body Composition System; COSMED). Air-displacement plethysmography is a densitometric technique. Body mass was assessed on the high-precision electronic scale. Body volume was determined measured in the test chamber of the PEA POD device by applying gas laws that relate pressure changes to volumes of air in the enclosed chamber. Measurements were performed in duplicate by the same operator. The PEA POD device has been validated for the measurement of body composition of neonates and young children in the unit (7).

Concerning FFM, we used reference data obtained by Hawkes (11) on term infants according to sex and range of gestational age (36–37, 38–39, and 40–41 wk). This reference population was made of 743 healthy term infants born in Ireland between March 2008 and October 2010. Body composition was assessed within the first 4 d of life by using air-displacement plethysmography. An FFM deficit was defined as a measured FFM >2 SD below the mean FFM in reference data of Hawkes (11).

Daily energy (kcal · kg body weight\(^{-1} \cdot \text{d}^{-1}\)), fat, carbohydrate, and protein intakes (g · kg body weight\(^{-1} \cdot \text{d}^{-1}\)) provided by parenteral and enteral nutrition during the hospital stay were obtained from medical records at postnatal days 5, 10, and 21 and discharge. In previous unpublished work (12), we observed a tight correlation between nutritional intakes assessed at days 5, 10, and 21 and intakes assessed day by day over the entire period between birth and 21 d of life. Energy and protein contents in preterm formula were 720 kcal/L and 20 g/L, respectively, and assumed to be 650 kcal/L and 13 g/L, respectively, in breast milk. Because human milk composition is highly variable, macronutrient intakes were calculated from mean macronutrient concentrations determined by the human milk analyzer (Miris) in 206 samples obtained in our milk bank (CY Boquien and C Boscher, personal communication, 2014). Calculated intake takes into account nutrients added by fortification. Sixty percent of infants were receiving their own mother’s milk.

Statistics

The analysis was performed in 2 steps. In the first step, we considered the FM percentage as a primary endpoint. Infants were classified into 3 tertiles of FM percentage because, to our knowledge, no reference values have been published. A comparison of perinatal characteristics, nutritional and ventilatory support, and growth between the 3 tertiles was performed by using the chi-square test or ANOVA. Risk factors of being in the upper tertile of the FM percentage were analyzed by logistic regression. Moreover, we performed a linear regression model with the FM percentage as a linear function of sex, gestational age, postnatal age, birth weight z score, antenatal corticosteroid treatment, change in weight z score between birth and day 5 and between day 5 and discharge, length of parenteral nutrition, and length of respiratory assistance. In the second step, we considered absolute FFM as the endpoint. First, we performed a linear regression model with absolute FFM as a linear function of the same factors. These factors were included in the linear regression because they were associated with FFM at discharge in the univariate analysis. Because gestational age and postnatal age are 2 very dependent variables, we performed 4 other models with the omission of specific variables [without gestational age, without postnatal age, without postnatal or gestational ages, and with postmenstrual age (sum of gestational and postnatal age)]. Second, we determined factors associated with a deficit of absolute FFM according to the reference of Hawkes (11) by performing univariate and multivariate analyses with logistic regression.

Descriptive data were expressed as the mean (±SD) or number (percentage) of observations. Statistical significance was set at \(\alpha = 0.05\). All statistical analyses were performed with SPSS software (version 19; SPSS Inc).

RESULTS

One hundred forty-one preterm newborns (71 boys) were enrolled in the study. Gestational age ranged between 25 and 34 wk, and birth weight ranged between 700 and 2660 g. Characteristics of the population are described in Table 1.
At birth

FM percentage at discharge 3.7–27.3

Data at hospital discharge

As concerns nutritional intake (*see* supplemental Table 1 under “Supplemental data” in the online issue), at day 5, mean energy intake was 92 ± 18 kcal·kg⁻¹·d⁻¹, protein intake was 2.4 ± 0.8 g·kg⁻¹·d⁻¹, fat intake was 3.9 ± 1.4 g·kg⁻¹·d⁻¹, and carbohydrate intake was 11.3 ± 3.3 g·kg⁻¹·d⁻¹. The protein:energy ratio was 2.6 ± 0.5 g·protein/100 kcal. At day 10, mean energy, protein, fat, and carbohydrate intakes were 112 ± 13 kcal·kg⁻¹·d⁻¹ and 2.8 ± 0.7, 5.1 ± 1, and 12.7 ± 2.6 g·kg⁻¹·d⁻¹, respectively. The protein:energy ratio was 2.5 ± 0.5 g·protein/100 kcal. At day 21, mean energy, protein, fat, and carbohydrate intakes were 118 ± 16 kcal·kg⁻¹·d⁻¹ and 3 ± 0.5, 5.5 ± 1, and 13.3 ± 2.2 g·kg⁻¹·d⁻¹, respectively. The protein:energy ratio was 2.5 ± 0.4 g·protein/100 kcal. The mean length of parenteral nutrition was 7.5 ± 13 d. At birth (Table 1), the mean weight z score was −0.32 ± 0.98, mean length z score was −0.48 ± 1.1, and mean HC z score was −0.25 ± 1.1. Postnatal growth was defined by the difference of z scores between birth and the day when body composition was measured. The change in weight z score between birth and discharge was −0.81 ± 0.7, the change in length z score was −0.87 ± 1.1, and the change in HC z score was −0.22 ± 1.

**FM percentage**

Within the population enrolled, there was a >7-fold range in the FM percentage at discharge (from 3.7% to 27.3%) despite similar body weights in the 3 FM tertile groups at discharge (Table 1). In the univariate analysis (Table 1), low gestational age and high postnatal age (ie, the length of hospital stay) were positively associated with being in the upper FM tertile at discharge. Maternal BMI (data not shown) was not associated with risk of being in the upper FM tertile at discharge. Antenatal corticosteroid treatment was significantly associated with risk of being in the upper FM tertile at discharge. The birth weight z score was significantly associated with the upper FM tertile (ie, the higher the birth weight z score, the higher the FM percentage at discharge). A greater loss in weight z score between birth and discharge, particularly a greater decline in the weight z score between birth and day 5, was associated with risk of being in the upper FM tertile. The weight z score change between day 5 and discharge was not different in the 3 tertiles of FM percentage. A higher length z score loss during the hospital stay was associated with risk of being in the upper FM tertile. There was no difference of the HC z score change between the 3 tertiles. In the multivariate analysis, each increase by 1 birth weight z score increased risk of being in the upper FM tertile by a factor of 2.9 (Table 2); thus, an infant who was born with a low birth weight had decreased risk of being in the upper FM tertile at discharge. Antenatal corticosteroid treatment more than tripled the risk of being in the upper FM tertile. After adjustment for gestational age, the duration of parenteral nutrition was not associated with risk of being in the upper FM tertile. No difference was observed between enteral and parenteral intakes for risk of being in the upper FM tertile (data not shown). The increase in weight z score between day 5 and discharge was significantly associated with risk of being in the upper FM tertile after adjustment. In contrast, the loss of weight z score between day 5 and discharge was not associated with risk of being in the upper
FM tertile at discharge. After adjustment for the birth weight, z score and postnatal growth, gestational age was no longer associated with risk of being in the upper FM tertile.

A poor correlation ($R^2 = 0.24$) was obtained when a linear regression model was applied with the FM percentage as a linear function of sex, gestational age, postnatal age, birth weight $z$ score, antenatal corticosteroid treatment, change in weight $z$ score between birth and day 5 and between day 5 and discharge, length of parenteral nutrition, and length of respiratory assistance (Figure 1A).

### Absolute FFM

When linear regression was used with absolute FFM as a linear function of the same factors as previously described, a strong correlation was shown ($R^2 = 0.82$) (Figure 1B). Factors tightly linked with absolute FFM (Table 3) were birth weight $z$ score and the change in weight $z$ score between birth and discharge, particularly between birth and day 5. Each loss of 1 weight $z$ score between birth and day 5 decreased absolute FFM at discharge by 349 g. Gestational and postnatal ages were significantly associated with absolute FFM. Each week of gestational and postnatal ages increased FFM by 143 and 137 g, respectively. Antenatal and postnatal growth equally affected FFM. Girls had a significantly lower FFM than boys at discharge.

The relevant equation, represented in Figure 1B, was

$$\text{FFM}(g) = 349 \times \text{birth weight} \times \text{weight} + 305$$

$$\times (\text{change in weight} \times \text{weight} \times \text{weight} \times \text{weight} \times \text{weight})$$

$$+ 287 \times (\text{change in weight} \times \text{weight} \times \text{weight} \times \text{weight} \times \text{weight})$$

$$+ 143 \times (\text{gestational age} \times \text{postnatal age} \times \text{wk} - 44)$$

$$\times (\text{number of antenatal corticosteroid course}^*)$$

$$- 8 \times (\text{length of ventilatory assistance})$$

$$- 105 \times \text{sex}^{**} \quad (1)$$

[Note: *One course of antenatal corticosteroid treatment is made of 2 injections (this variable ranged from 0.5 to 2); **sex = 0 for boys, and sex = 1 for girls.]

In the multivariate analysis (Table 4), factors associated with risk of absolute FFM deficit according to reference values of Hawkes (11) were lower gestational age, lower birth weight $z$ score, and male sex. Nutritional intake at day 5 was not associated with risk of FFM deficit. In contrast, an increased protein: energy ratio at days 10 and 21 significantly reduced risk of FFM deficit. Finally, a higher protein:energy ratio was a major determinant of improved FFM at the time of hospital discharge. The relation between clinical variables and FM was not as striking.

### DISCUSSION

In our population of preterm infants, clinical variables were highly correlated with FFM at discharge; the main determinants were antenatal growth (judged from the birth weight $z$ score), gestational age and postnatal age (both of which played an equal role), and initial growth rate (between birth and day 5) and growth between day 5 and discharge, both of which equally affected FFM. Finally, a higher protein:energy ratio was a major determinant of improved FFM at the time of hospital discharge. The relation between clinical variables and FM was not as striking.

The FM percentage at discharge was poorly influenced by nutritional intake in the current cohort study. There was an association of being in the upper FM tertile with both antenatal and postnatal growth patterns. As concerns antenatal status, this result was consistent with the lower FM observed by Roggero et al (13).
in preterm infants born small for gestational age. The increase in weight 
\( z \) score between day 5 and discharge was associated with 
risk of being in the upper FM tercile at discharge, which sug-
ggested that the protein:energy ratio might have been insufficient 
in the nutritional regimen administered to this cohort. Several 
previous studies have also shown that very premature infants are 
relatively fatter at discharge than are term infants (3, 14, 15). 
Whether this early postnatal FM deposition should also be 
considered adequate for premature infants is not known. Indeed, 
FM should not be viewed solely as an energy store but as an 
organ per se with important metabolic and endocrine functions.

Both preterm and term infants normally lose weight over the 
first week of life. In our study, the maximum weight loss had been 
reached, on average, by 5 d of life. Because this initial weight loss 
was attributable to obligatory water loss, the weight \( z \) score 
measured at day 5 may have been a more-appropriate bench-
mark to assess fetal and postnatal growth (9). Such data suggest 
that a rapid, early growth rate, both in utero and during the first 
few weeks of neonatal life, is a key determinant of early FM 
accretion. Nevertheless, the linear regression model was a rela-
vatively poor predictor of FM, and such factors did not completely 
explain the FM percentage. In term infants, the FM percentage 
increases physiologically with postnatal age (16). We speculate 
that, in more-preterm infants, the steep, physiologic rise in 
FM accretion may begin soon after birth rather than at a term 
equivalent age. Moreover, we do not know the impact of the 
wide range of FM observed in preterm infants at the time of 
discharge on long term metabolic and neurologic outcomes. The 
relation between the FM percentage at the time of discharge and 
long-term neurodevelopmental outcome is complex. Multiple 
and conflicting factors influence both variables. Although in-
trauterine growth restriction is associated with low FM and 
higher risk of impaired neurodevelopment in childhood (17), 
preterm birth increases the body FM percentage and decreases 
the developmental quotient at 5 y of age (18), whereas breast-
feeding tends to decrease FM accretion and improve the de-
velopmental quotient at 2 y of age (19, 20). Therefore, the FM 
percentage does not appear to be the best benchmark to assess 
the quality of growth in preterm infants.

In severely ill adults, absolute FFM has a better prognostic 
value than does FM (21). In our study, absolute FFM was tightly 
correlated with classic clinical variables \( R^2 = 0.82 \), which, in 
turn, were correlated with growth and are known to be associ-
ated with the long-term outcome (22). Therefore, we speculate 
that FFM may be a better prognostic marker for metabolic and 
neurologic outcomes of preterm infants than is FM. Antenatal 
and postnatal weeks affected absolute FFM to the same extent.

| TABLE 3 | Linear regression model with predicted absolute FFM as a function of birth weight \( z \) score, change in weight \( z \) score between birth and day 5 and between day 5 and discharge, gestational age, postnatal age, sex, antenatal corticosteroid treatment, and duration of parenteral nutrition and ventilatory support \(^1\) |
|-------------------------------|---------------------------------|-------------------------------|---------|
| Birth weight \( z \) score | 349 (315, 383) | 0.001 |
| Change in weight \( z \) score between birth and day 5 (\( /1 z \) score) | 305 (243, 367) | 0.001 |
| Change in weight \( z \) score between day 5 and discharge (\( /1 z \) score) | 287 (231, 343) | 0.001 |
| Gestational age (wk of gestation) | 143 (109, 177) | 0.001 |
| Postnatal age (wk of postnatal life) | 137 (105, 169) | 0.001 |
| Sex | | |
| M | 0 (reference) | — |
| F | —105 (−145, −65) | 0.001 |
| Antenatal corticosteroid treatment (\( /1 \) one full course) | −44 (−74, −14) | 0.006 |
| Length of parenteral nutrition (\( /wk\) | −8 (−28, −12) | 0.419 |
| Ventilatory assistance (\( /wk\) | −7 (−21, 7) | 0.334 |

\(^1\) \( R^2 \) of the model = 0.82. FFM, fat-free mass.

| TABLE 4 | Multivariate analysis for risk of FFM deficit at term equivalent age according to reference of Hawkes (11) by logistic regression \(^1\) |
|---------------------------------|-----------------|------|--------|
| Model 1 | | | |
| Gestational age (wk) | 0.64 (0.46, 0.90) | 0.011 |
| Birth weight \( z \) score | 0.14 (0.07, 0.29) | 0.001 |
| M | 4.1 (1.6, 10) | 0.003 |
| Antenatal corticosteroid treatment | 3.5 (0.83, 15) | 0.087 |
| Protein intake at day 5 (g \( \cdot \) kg\(^{-1} \) \cdot d\(^{-1} \)) | 0.48 (0.16, 1.4) | 0.187 |
| Protein:energy ratio at day 5 (g\( /100 \) kcal) | 1.8 (0.40, 8.0) | 0.447 |
| Length of parenteral nutrition (wk) | 1.1 (0.71, 1.7) | 0.668 |
| Model 2 | | | |
| Gestational age (wk) | 0.68 (0.48, 0.97) | 0.034 |
| Birth weight \( z \) score | 0.14 (0.06, 0.29) | 0.001 |
| M | 4.4 (1.7, 12) | 0.003 |
| Antenatal corticosteroid treatment | 2.5 (0.60, 11) | 0.207 |
| Protein intake at day 10 (g \( \cdot \) kg\(^{-1} \) \cdot d\(^{-1} \)) | 6.7 (1.3, 33) | 0.020 |
| Protein:energy ratio at day 10 (g\( /100 \) kcal) | 0.04 (0.01, 0.42) | 0.008 |
| Length of parenteral nutrition (wk) | 1.2 (0.73, 2.1) | 0.410 |
| Model 3 | | | |
| Gestational age (wk) | 0.61 (0.42, 0.89) | 0.011 |
| Birth weight \( z \) score | 0.15 (0.07, 0.33) | 0.001 |
| M | 6.9 (2.2, 22) | 0.001 |
| Antenatal corticosteroid treatment | 3.4 (0.75, 15) | 0.113 |
| Protein intake at day 21 (g \( \cdot \) kg\(^{-1} \) \cdot d\(^{-1} \)) | 1.4 (0.39, 5.4) | 0.582 |
| Protein:energy ratio at day 21 (g\( /100 \) kcal) | 0.11 (0.01, 0.95) | 0.045 |
| Length of parenteral nutrition (wk) | 1.07 (0.69, 1.7) | 0.774 |

\(^1\) Three models were performed because protein intake at days 5, 10, and 21 were linked together and could not be included in the same model. FFM, fat-free mass.
Therefore, we felt it was legitimate to compare absolute FFM of term and preterm infants at the term equivalent age by using reference values of Hawkes (11). Gestational age was associated with absolute FFM at discharge. In parallel, in the first few days of life, the FFM of preterm infants increases when gestational age increases (23). A low gestational age was positively associated with risk of an FFM deficit according to the reference of Hawkes (11), as was consistent with reports by Roggero et al (14). This lesser accretion of FFM illustrates the magnitude of postnatal growth restriction in premature infants. It suggests that postnatal nutritional intake is either insufficient or inadequate to promote adequate growth in such infants. In this study, a higher protein:energy ratio at days 10 and 21 was associated with lower risk of having an FFM deficit at discharge. This result was concordant with several earlier studies that suggested that a higher protein:energy ratio may improve FFM accretion and decrease FM deposition (24).

Sex also influences body composition, and boys are usually heavier with lower FM than that of girls. Nevertheless, this study showed that boys have higher risk of an absolute FFM deficit at discharge as judged by comparison with reference values of Hawkes (11). Consistent with our previous study (25), preterm infants had a lesser accretion in FFM, particularly in preterm boys.

Antenatal corticosteroid treatment had a dramatic impact on risk of being in the upper FM tertile and risk of lower FFM. We are not aware of any published data on the effect of glucocorticoids on adipose tissue development in preterm infants. However, corticosteroids have long been known to impair protein gain and produce growth failure. For instance, fetuses exposed to multiple courses of antenatal corticosteroid treatment are smaller at birth (26), and postnatal glucocorticoid treatment increases the protein breakdown in preterm infants (27). Thus, the greater FM deposition associated with antenatal corticosteroid treatment may be secondary to impaired FFM accretion in neonatal period. Long-term metabolic risks of antenatal corticosteroid treatment remain unclear. Although Dalziel et al (28) documented insulin resistance in young adults who had received antenatal corticosteroid treatment, Finken et al (29) did not report any adverse metabolic effect, and the long-term effect of antenatal glucocorticoids on abdominal fat in adulthood may depend on glucocorticoid receptor gene polymorphism (30).

What is the optimal body composition in preterm infants at a term equivalent age? The ultimate aim of neonatologists has long been to enhance early growth in an effort to mimic the growth pattern of a normal fetus at the same gestational age in terms of weight gain. However, during postnatal life, a sharp rise in the FM percentage is physiologic in term infants (16), and probably is in preterm infants as well. In contrast, a deficit in absolute FFM should be prevented at all costs. We speculate that extrauterine growth failure during a hospital stay should be redefined as an acquired deficit in FFM. Whether an FFM deficit correlates with impaired neurologic and metabolic outcomes must be validated by prospective observational studies with long-term follow-ups and the assessment of neurodevelopment and metabolic health.

The main limitation of the current study stemmed from its observational nature. In the current study, nutritional intakes are only fair estimates because 1) it is difficult to measure actual milk intake because of gastric residuals, forgotten feedings, and the lack of suitable methods for the evaluation of the exact amount of milk suckled from the breast, and 2) the human milk macronutrient content was not measured in individual milk samples. Taking into account the macronutrient composition of each individual, human milk may provide additional information. Moreover, nutritional intakes were assessed on the basis of intakes recorded only at days 5, 10, and 21 rather than on every single day, and we put enteral and parenteral intakes together. Controlled trials with widely different intakes would be needed to determine, for instance, the effect of enhancing protein intakes on body FM and FFM at the time of discharge. The second limitation of this study was the choice of the reference population because of the lack of body-composition data obtained in a large cohort of term infants in our region. Nevertheless, the reference population of Irish newborn infants should have been an acceptable surrogate because it was comparable with our small regional population of term infants published in 2011 (25). Moreover, the reference population was mostly of European white descent and with a socioeconomic status comparable to that in Western France.

In conclusion, in this observational study, absolute FFM in preterm infants at discharge correlates better with classic clinical variables reflecting perinatal growth and the severity of illness than does the FM percentage. We speculate that FFM may be more suitable than body weight or the FM percentage to assess the quality of growth in preterm infants. Antenatal growth and gestational and postnatal ages were the main determinants of FFM. Antenatal corticosteroid treatment and male sex were associated with higher risk of a FFM deficit at discharge, whereas a high protein:energy ratio at days 10 and 21 decreased risk of an FFM deficit at the time of discharge. Interventional studies would be needed to confirm such an effect. The model developed for predicting absolute FFM in the current study needs to be confirmed in a larger population of preterm infants. Whether FFM accretion during a hospital stay correlates with subsequent neurodevelopmental and metabolic outcomes at 2 and 5 y of age warrants additional long-term follow-up studies.

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The authors’ responsibilities were as follows—AF-C, DD, and J-CR: conceptualized and designed the study; LS, AF-C, CF, and J-CR: conducted the research; LS, J-CR, TS, and CF: analyzed data; LS, DD, and J-CR: wrote the manuscript; J-CR: had the primary responsibility for the final content of the manuscript; and all authors: read and approved the final manuscript. None of the authors had a conflict of interest.

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