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Recommendation of Charts and Reference Values for Assessing Growth of Preterm Infants: Update by the Portuguese Neonatal Society.

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Abstract

The growth charts and reference values for preterm infants are revisited and recommendations for their use updated by the Portuguese Neonatal Society.

To assess intrauterine growth: The cross-sectional sex specific Fenton 2013 charts, based on birth weight, length and head circumference, are the most appropriate. Neonates born with weight < 3rd percentile are classified as small-for-gestational age and those born >97th percentile are classified as large-for-gestational age. The Olsen 2015 body mass index curves can be used to assess proportionality at birth, although accuracy of some length measurements has been questioned.

During hospitalization: The online calculator www.growthcalculator.org, based on recent longitudinal curves, is recommended to assess weight gain; it provides an accurate graphic display of the current weight percentile, target weight and its deviation. Fenton 2013 charts may be an alternative to monitor linear and head growth while in the neonatal unit. In the neonatal period, velocity rates of 15–20 g/kg/d for weight, 0.9–1.1 cm/week for length, and 0.9–1.0 cm/week for head circumference, are adequate goals.

After discharge: The longitudinal Intergrowth-21st standards are adequate to monitor growth from 32 to 64 weeks' postmenstrual age, for infants born with more than 27 weeks gestation. After that postmenstrual age, the WHO Growth Standards 2006 for infants born at term can be used.

Key-words: anthropometry, growth charts, preterm infant, recommendation, reference values

Recomendação de Curvas e Valores de Referência para Avaliar o Crescimento de Crianças Nascidas Pré-Termo: Atualização pela Sociedade Portuguesa de Neonatologia.

Resumo

A Sociedade Portuguesa de Neonatologia revisita e atualiza as recomendações do uso de curvas e valores de referência para avaliação do crescimento de crianças nascidas pré-termo.

Avaliação do crescimento intrauterino: As curvas de Fenton 2013, específicas para o sexo, baseadas no peso, comprimento e perímetro cefálico ao nascer, são as mais adequadas; se o peso for < percentil 3, o recém-nascido é classificado leve para a idade gestacional e se > percentil 97, grande para a idade gestacional. As curvas do índice de massa corporal de Olsen 2015 podem ser usadas para avaliar a proporcionalidade no nascer, embora o rigor de algumas medições do comprimento tenha sido questionado.

Durante o internamento: Para avaliar a evolução ponderal, é recomendada a calculadora *on-line* www.growthcalculator.org, baseada em curvas longitudinais recentes; assinala graficamente, de forma precisa, o percentil do peso atual, assim como o peso alvo e o desvio. As curvas de Fenton 2013 podem ser uma alternativa para monitorar o crescimento linear e cefálico enquanto na unidade neonatal. Durante o período neonatal, são adequadas velocidades de 15 a 20 g/kg/d para o peso, 0,9-1,1 cm/semana para o comprimento e 0,9-1,0 cm/semana para o perímetro cefálico.

Após a alta: As curvas padrão Intergrowth-21 são apropriadas para monitorar o crescimento das 32 às 64 semanas de idade pós-menstrual, em crianças nascidas com mais

de 27 semanas de gestação. Após essa idade pós-menstrual, podem ser usadas as curvas padrão da OMS 2006 para crianças nascidas de termo.

Palavras-chave: antropometria, curvas de crescimento, pré-termo, recomendação, valores de referência

Introduction

The most commonly used anthropometric measurements to assess growth of infants born preterm are body weight, length and head circumference [1]. In this population, the appropriateness of reference values depends on the purpose and period of life [2-4]: 1) at birth, to diagnose intrauterine growth deviations; 2) during hospitalization, to monitor the effectiveness of prescribed nutritional support and the impact of morbidity; and 3) after discharge or during prolonged hospitalization, to monitor medium- or long-term growth.

Measurements can be compared with standard values (prescriptive) or reference values (descriptive). While the former are intended to represent optimal growth, reference values describe how infants actually grow [1,5]. The ideal tool would be standard curves, constructed from a representative long-term follow-up cohort, recruited at the prenatal period, including from the threshold of viability to term gestational ages, to be used throughout all periods of life. Unfortunately, such a tool has not yet been developed.

In 2013, the Portuguese Society of Neonatology critically reviewed the published growth curves for preterm infants and made recommendations for clinical practice [6]. These recommendations became outdated after the publication of the Intergrowth-21st standards [7] and more recently, the availability of an accurate online growth calculator to monitor weight gain during hospitalization [8,9].

Growth charts and reference values to assess growth of preterm infants, from birth to the post-neonatal period, are revisited and recommendations for their use are updated by the Portuguese Neonatal Society (Table 1). Levels of evidence (LE) and strengths of recommendation (SR) [10] are provided for each chart (Table 2).

1. To assess intrauterine growth

Curves constructed from anthropometric records at birth are appropriate to assess intrauterine growth; they should not be confused with curves based on fetal ultrasound measurements, which are appropriate to monitor fetal growth [11].

1.1. Weight, length, and, head circumference

Recommended: Fenton 2013 charts (LE 2, SR B)

The cross-sectional sex and gestational age specific Fenton 2013 charts [12] are the most appropriate to assess intrauterine growth, and include directly measured birth weight, length, and head circumference (Table). These charts are based on a meta-analysis of six large population-based surveys of size at birth, from 22 to 36 weeks gestation. They were harmonized with the longitudinal WHO Growth Standards for infants born at term [13], smoothing the data between the preterm and WHO estimates while maintaining integrity with the data from 22 to 36 weeks and at 50 weeks [12]; the portion of the curves between 37 and 50 weeks were validated by comparing them using weight gain patterns of contemporary preterm infants [14].

An application based on the Fenton 2013 charts [12] is available at PediTools.org (https://peditools.org/fenton2013/index.php) and allows the online calculation of the z-scores from measured weight, length, and head circumference and the quantification of extreme deviations.

Strengths:

- This meta-analysis included the largest homogeneous sample to date, including almost 4 million neonates with measured weight, 151,527 with measured length, and 173,612 with measured head circumference.
- The curves are stratified into percentiles 3 to 97, allowing a more precise classification.

- The charts are free access.

Limitations:

- Although the meta-analysis [12] was based on selected studies from developed countries, the curves are not a standard for intrauterine growth, since in some of the included studies twin pregnancies, morbidity during pregnancy, and poor surveillance and nutrition of pregnant women were not exclusion criteria [6].
- For elaboration of percentile curves [12], studies only considering ages in complete weeks have been included, except for the study by Voigt *et al.* [15] in which gestational age in weeks and days was used; in the remaining reference curve proposals, gestational ages between full weeks had been mathematically extrapolated.
- To determine the values of each reference percentile (3, 10, 50, 90, and 97) for weight, length, and head circumference, the meta-analysis [12] used percentiles calculated in each study that met the inclusion criteria for each age, instead of values of each individual, thus reducing the accuracy by accumulation of rounding and estimation errors [6].

<u>Classification of intrauterine growth</u>: to classify intrauterine growth, birth weight should be related with gestational age; accordingly, neonates are classified as large-, appropriate-, or small-for-gestational age [2]. There is no consensus regarding the cut-offs for this classification [16,17]. While some authors define the 10th and 90th percentiles as lower and higher thresholds, others consider as lower thresholds the 5th percentile, 3rd percentile, or -2 standard deviations to classify as small-for-gestational age, and the 95th percentile, 97th percentile or +2 standard deviations as higher thresholds to classify as large-for-gestational age [16,17]. The ability of a chart to estimate statistically defined thresholds is dependent on the sample size for each gestational age group of interest, and only samples greater than 120 individuals have enough statistical power to define the 3rd or the 5th percentiles [18-20]. Hence, using the Fenton 2013 curves [12], the 3rd and 97th percentiles may

be used as the statistical thresholds for small-for-gestational age and large-for–gestational age infants, respectively. While these are statistical definitions for deviations of size measurement, the definition of clinically significant thresholds requires prospective longitudinal studies rather than cross-sectional assessments [17,21]. Due to the skewed distribution of weight by gestational age, the use of reference curves based on percentiles is preferred to those based on average and standard deviations [22].

1.2. Body mass index

Recommended: Olsen BMI curves (LE 2, SR B)

The Olsen BMI curves are based on cross-sectional birth data [23]. These curves propose the use of body mass index (BMI) to assess proportionality at birth, distinguishing between asymmetrical and symmetrical types of intrauterine growth restriction [23]. Based on the same cross-sectional birth data, the BMI was found to be more appropriate to assess body proportionality than either weight-for length ratio or ponderal index [24].

Strength:

- The Olsen BMI curves [23] were based on cross-sectional birth data collected from a large sample of 391,681 infants from 248 US hospitals [25].

Limitation:

- The accuracy of the Olsen BMI curves has been questioned [26], as in the original multicenter study [25], tapes have been used for length measurements, a method recognized as of doubtful reliability [27,28].

2. To monitor growth during hospitalization

2.1. Weight

Recommended: the online calculator: www.growthcalculator.org (LE 2, SR B)

A recent large longitudinal study showed that, provided postnatal adaptation is uncomplicated, preterm infants transit to a weight gain trajectory of 0.8 SD below birth weight at the 21th postnatal day [8]. Therefore, it is neither expected nor desirable that preterm weight gain approximates intrauterine growth during the first postnatal month [8,29], contrarily to what has been suggested for more advanced postnatal ages [30]. This means that charts that do not consider this initial physiological weight loss, such as the Fenton 2013 charts [12], are not appropriate to monitor early postnatal growth in preterm infants [29].

Based on the aforementioned large longitudinal study [8,9], an online calculator (www.growthcalculator.org) was developed to accurately monitor the weight gain in the neonatal ward.

Strengths:

- This is a reliable, free-access online tool.
- It displays graphically in which percentile the current weight is plotted, as well as the target weight and the deviation of the current weight in grams.

Limitation:

- This tool does not provide a graphic trend or curve from weight records.

Weight gain velocity: a recent analysis of growth velocities concluded that body weight rates of 15–20 g/kg/d is an adequate goal for infants born at 23–36 weeks gestation [31].

2.2. Length and head circumference

Recommended: Fenton 2013 charts (LE 2, SR B)

Scientific pediatric societies recommend that optimum growth of preterm infants should be equivalent to intrauterine rates [32,33]. Birth size measurements can be used as a proxy of intrauterine growth [12]. Contrarily to body weight, characterized by an initial postnatal

physiological decrease, body length and head circumference continuously increase after birth. The sex and gestational age specific Fenton 2013 charts [12] can be an alternative to monitor postnatal linear growth and head growth from birth to 50 weeks postmenstrual age, despite being cross-sectional records of size at birth.

Strength:

- Fenton 2013 meta-analysis [12] included a large sample of neonates with measured length (151,527) and head circumference (173,612) at birth.

Limitation:

- Fenton 2013 curves [12] are based on cross-sectional measurements of size at birth. Ideally, postnatal growth would be more appropriately assessed using longitudinal measurements of infants with an uneventful clinical course. However, a representative sample with longitudinal measurements, including neonates from the threshold of viability to term gestational age at birth, is currently unavailable.

Length and head circumference velocities: a rate of approximately 0.9–1.1 cm/week for length and 0.9–1.0 cm/week for head circumference are adequate goals, particularly for 23–30 weeks postmenstrual ages [12,34,35].

3. To monitor growth after discharge

3.1. Weight, length, and head circumference

Recommended: Intergrowth-21st standards (LE 2, SR B)

The longitudinal Intergrowth-21st standards were designed for the follow up of infants born with more than 26 weeks and less than 37 weeks gestation [7]. For the development of these charts, a cohort of 4,607 healthy pregnant women from eight geographical areas of the world were enrolled, and fetal growth was monitored from 14 weeks gestational age

to birth [36]. These charts included 201 preterm infants who met the criteria to be considered healthy and stable and they were followed up to 64 weeks postmenstrual age [7].

After 64 weeks postmenstrual age, the preterm Intergrowth-21st standards overlap with the longitudinal WHO Growth Standards for infants born at term [13]. Therefore, after 64 weeks postmenstrual age the WHO Growth Standards should be used [7].

Strengths:

- To date, the Intergrowth-21st charts are the only standard charts (prescriptive) designed to monitor long-term growth of preterm infants.
- These standards are robust for neonates with gestational ages at birth between 33 and 36 completed weeks.
- An online calculator is available at: http://intergrowth21.ndog.ox.ac.uk/preterm/en/ManualEntry/Compute

Limitations:

- Among 201 healthy and stable preterm infants included in the Intergrowth-21st cohort, only 28 infants born at 33 weeks' gestation or earlier contributed data to these standards [7]. Consequently, Intergrowth-21st standards are reliable for monitoring postnatal growth only from 32 weeks' postmenstrual age in infants born with more than 27 weeks gestation [7].

Conclusions

The ideal charts to assess growth of preterm infants, should be standard (prescriptive) curves, constructed from a large long-term follow-up cohort of infants, recruited at the prenatal period from uneventful pregnancies and including neonates from the threshold of viability to term gestational age at birth, without significant neonatal morbidities, thus

allowing their use through all life periods. Such a tool has not yet been developed. Until then, it is not accurate to attribute the maximum LE and SR to the existing charts.

From the currently available charts, the Portuguese Neonatal Society recommends the use of:

- The Fenton 2013 charts to assess intrauterine growth, based on direct measured birth weight, length and head circumference. These cross-sectional charts are an alternative to monitor postnatal linear and head growth in the neonatal ward, since longitudinal charts accurate enough to classify the length and the head circumference of preterm infants unavailable yet.
- The online calculator www.growthcalculator.org to monitor weight gain while staying in the neonatal unit. During this period, velocities of 15–20 g/kg/d for weight, 0.9–1.1 cm/week for length, and 0.9–1.0 cm/week for head circumference, are adequate goals.
- The Intergrowth-21st standards to monitor growth after discharge, from 32 to 64 weeks' postmenstrual age, for infants born with more than 27 weeks gestation. After that postmenstrual age, the WHO Growth Standards 2006 for infants born at term can be used.
- Olsen 2015 BMI curves to assess proportionality at birth, although accuracy of some length measurements used in calculations has been questioned.

Acknowledgement

This recommendation has been approved by the Direction of the Portuguese Neonatal Society on the 19th November 2019.

Conflicts of Interest

There are no conflicts of interest to declare.

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Table 1. Comparison between previous *versus* current recommendations of growth charts for preterm infants, from the Portuguese Neonatal Society.

Purpose	Recommendations 2013 [27]	Recommendations 2019
- To assess intrauterine growth	- Fenton 2013 charts [12]	- Fenton 2013 charts [12]
- To monitor weight gain during hospitalization	- Ehrenkranz 1999 charts [37]	- Online calculator www.growthcalculator.org
- To monitor growth after discharge	- Fenton 2013 charts [12] up to 50 weeks postmenstrual age	- Intergrowth-21st standards [7] up to 64 weeks postmenstrual age

Table 2. Growth charts recommended for preterm infants.

Chart	Indication	LE*	SR*
Fenton 2013 charts [12]	- To assess intrauterine growth based on weight, length, and head circumference at birth	2	B
	- To monitor linear and head growth during hospitalization	2	B
The online growth calculator www.growthcalculator.org	To monitor weight gain during hospitalization	2	B
Intergrowth-21st standards [7]	To monitor growth after discharge from 32 weeks' postmenstrual age, for infants born with more than 27 weeks gestation	2	B
BMI Olsen charts [23]	- To assess proportionality at birth	2	B

LE - level of evidence; SR – strength of recommendation; * Adapted from Ebell *et al*[10].