## Performance of Intergrowth 21<sup>st</sup> Growth Charts in the Diagnosis of Small and Large for Gestational Age in Term and Preterm Newborns



# O Desempenho das Curvas do *Intergrowth 21<sup>st</sup>* no Diagnóstico de Leve e Grande para a Idade Gestacional em Recém-nascido de Termo e Pré-termo

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#### ABSTRACT

**Introduction:** Birth weight is a major contributor to neonatal morbidity and mortality and is associated with chronic diseases in adulthood. This study aimed to evaluate the use of Intergrowth 21<sup>st</sup> instead of the Fenton & Kim 2013 growth charts in the diagnosis of small and large for gestational age in a group of Portuguese newborns.

**Material and Methods:** We conducted an analytical and retrospective study to evaluate birth weight of term and preterm newborns using both growth charts. Groups studied: 'Term-weeks' and 'Term-days' (term newborns with gestational age in weeks and days, respectively), 'Preterm-weeks' and 'Preterm-days' (preterm newborns with gestational age in weeks and days, respectively).

**Results:** A total of 14 056 newborns were included, 6% preterm. Using the Intergrowth  $21^{st}$  growth charts, the groups 'Term-weeks' (n = 12 081), 'Term-days' (n = 1118), 'Preterm-weeks' (n = 617) and 'Preterm-days' (n = 240), classified as small for gestational age according to the Fenton & Kim 2013 growth charts were adequate for gestational age in 52.8%, 57.8%, 37.7% and 9.3% respectively; and 9.2%, 9.2%, 5.9% and 0.6% of adequate for gestational age newborns were large for gestational age, respectively. In the 'Preterm-days' group, 7.9% of adequate for gestational age newborns were small for gestational age and 22.2% of large for gestational age newborns were adequate for gestational age newborns were adequate for gestational age newborns were small for gestational age and 22.2% of large for gestational age newborns were adequate for gestational age, all with gestational age below 231 days.

**Discussion:** The use of the Intergrowth 21<sup>st</sup> growth charts in this sample resulted in a lower number of newborns being classified as small for gestational age, except in very preterm newborns.

**Conclusion:** Considering the results obtained, we suggest that Portuguese maternity hospitals use the Intergrowth 21<sup>st</sup> instead of the Fenton & Kim 2013 growth charts. However, more studies are needed to confirm these results.

Keywords: Anthropometry; Birth Weight; Gestational Age; Growth Charts; Infant, Newborn; Infant, Premature; Portugal

## RESUMO

**Introdução:** O peso ao nascer é importante na morbimortalidade neonatal e está relacionado com o desenvolvimento de doenças crónicas na idade adulta. Este estudo pretende avaliar a utilização das curvas de crescimento *Intergrowth 21st* em alternativa às de Fenton e Kim 2013 no diagnóstico de leve e grande para a idade gestacional num grupo de recém-nascidos Portugueses.

Material e Métodos: Estudo analítico e retrospetivo avaliando o peso ao nascer de recém-nascidos de termo e pré-termo segundo ambas as curvas de crescimento. Grupos estudados: 'Termo-semanas' e 'Termo-dias' (recém-nascidos de termo com idade gestacional em semanas e dias, respetivamente), 'Pré-termo-semanas' e 'Pré-termo-dias' (recém-nascidos pré-termo com idade gestacional em semanas e dias, respetivamente).

**Resultados:** Foram incluídos 14 056 recém-nascidos, 6% pré-termo. Usando as curvas de crescimento *Intergrowth 21st*, os grupos 'Termo-semanas' (n = 12 081), 'Termo-dias' (n = 1118), 'Pré-termo-semanas' (n = 617) e 'Pré-termo-dias' (n = 240) classificados como leves para a idade gestacional segundo Fenton e Kim 2013 foram classificados como adequados para a idade gestacional em 52,8%, 57,8%, 37,7% e 9,3% respetivamente; e 9,2%, 9,2%, 5,9% e 0,6% dos adequados para a idade gestacional foram classificados como grandes para a idade gestacional, respetivamente. No grupo 'Pré-termo-dias', 7,9% dos adequados para a idade gestacional seriam leves para a idade gestacional e 22,2% dos grandes para a idade gestacional seriam adequados para a idade gestacional, todos com idade gestacional abaixo de 231 dias.

**Discussão:** O uso do *Intergrowth 21st* nesta amostra resultou num menor número de recém-nascidos classificados como leves para a idade gestacional, exceto nos recém-nascidos muito prematuros.

**Conclusão:** Tendo em conta os resultados obtidos, sugerimos que as maternidades portuguesas considerem a utilização das curvas de crescimento *Intergrowth 21<sup>st</sup>* em detrimento das de Fenton e Kim 2013. Contudo, mais estudos são necessários para confirmar estes resultados.

Palavras-chave: Antropometria; Gráficos de Crescimento; Idade Gestacional; Peso ao Nascer; Portugal; Recém-Nascido; Recém--Nascido Prematuro

## INTRODUCTION

Birth weight is an important factor in neonatal morbidity and mortality, and is also associated with the development of chronic diseases in adulthood.<sup>1</sup> According to the American Academy of Pediatrics, small for gestational age newborns are those with a birth weight below the 10<sup>th</sup> percentile for gestational age; adequate for

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gestational age newborns are those with a birth weight between the 10<sup>th</sup> and the 90<sup>th</sup> percentile and large for gestational age newborns are those with a birth weight above the 90<sup>th</sup> percentile.<sup>2</sup> Other cut-offs were suggested as the third and fifth percentile for the definition of small for gestational age and the 95<sup>th</sup> and 97<sup>th</sup> percentile for the definition of large for gestational age.<sup>3</sup>

A newborn is small for gestational age due to constitutional reasons or because of fetal growth restriction (associated, for example, with maternal conditions or socioeconomic factors). These newborns have a higher risk of neonatal complications, such as neonatal asphyxia, meconium aspiration syndrome, hypoglycemia, polycythemia, bronchopulmonary dysplasia, and neurodevelopmental disorders.<sup>4–7</sup> Large for gestational age newborns present a greater predisposition for obstetric complications, traumatic delivery, hypoglycemia, hyperbilirubinemia, polycythemia, neonatal asphyxia, longer hospital stay and neonatal death.<sup>8,9</sup> In the long term, both situations are associated with metabolic syndrome, arterial hypertension, dyslipidemia, coronary disease and type 2 diabetes mellitus.<sup>10–13</sup>

Percentiles or z-score charts are applied to interpret birth weight. Growth expressed in percentiles or z-scores can be reference charts, describing how individuals grew at a given time and place; or standard charts, which reflect how individuals should grow when nutritional, environmental, and health restrictions are minimal.<sup>14,15</sup>

The Fenton & Kim growth charts are widely used and were last updated in 2013.14,16 These charts are commonly used in Portuguese maternity hospitals to evaluate birth weight in term and preterm newborns. They are almost standard charts that provide data between 24 and 50 weeks of gestational age for both genders. These charts result from a meta-analysis which included six studies from different countries conducted between 1991 and 2007 (Germany, Australia, Canada, Scotland, United States of America and Italy) with a total of 3 986 456 newborns with weight, head circumference and length of up to 40 weeks of gestational age. It also included the WHO Multicentre Growth Reference Study (2006) with 882 term newborns. Thus, these growth charts include birth weight data between 24 and 40 weeks of gestational age that result from a meta-analysis of six studies and birth weight data of term newborns from the WHO study.<sup>16</sup> In order to harmonize the transition between the anthropometry measurements of the meta-analysis group of newborns and the group of newborns from the WHO study, statistical softeners were used between 36 and 50 weeks of gestational age.16,17

However, the Fenton & Kim 2013 growth charts<sup>16</sup> have some limitations.<sup>14,17</sup> These charts do not take into account the physiological weight loss in the two weeks after birth in more immature preterm newborns, which influences their growth evaluation.<sup>14,16,17</sup> On the other hand, between 36 and 50 weeks of gestational age, statistical smoothing was used to standardize data, which means that after 36 weeks of gestational age their use is not precise.<sup>16,17</sup>

The Intergrowth 21<sup>st</sup> (International Fetal and Newborn

Growth Consortium for the 21st Century) project aimed to complement the WHO Multicentre Growth Reference Study (2006), developing international standards for fetuses, newborn infants and the postnatal growth period of preterm newborns.<sup>17–19</sup> This project was conducted between 2009 and 2014 in eight countries (Brazil, China, India, Italy, Kenya, Oman. United Kingdom and United States of America) with growth, health, nutrition and neurodevelopment from 14 weeks of gestational age to two years of age being studied.18 The inclusion criteria were well defined. It included low-risk and well-nourished pregnant women, with good pregnancy surveillance, whose fetuses showed adequate growth.<sup>18,19</sup> The NCSS (Newborn Cross-sectional Study) aimed to obtain standard curves of weight, length and head circumference at birth for gestational age. It included 20 486 newborns that fulfilled the inclusion criteria, with charts between 33 and 43 weeks of gestational age being obtained.<sup>19</sup> Subsequently, 408 newborns younger than 33 weeks, some with risk factors for fetal growth restriction (initially excluded), were added to the study in order to obtain data below 33 weeks of gestational age.<sup>20,21</sup>

Nevertheless, the project did not consider some factors that could also influence birth weight, such as maternal and paternal birth weight and maternal weight gain during pregnancy. Therefore, local validation studies were suggested.<sup>22,23</sup>

This study aimed to evaluate the use of the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> instead of the Fenton & Kim 2013 growth charts<sup>16</sup> in the diagnosis of small and large for gestational age in term and preterm newborns born to normal weight women with low-risk pregnancies in a Portuguese maternity hospital.

## MATERIAL AND METHODS

## Type of study

A retrospective study was conducted in Santa Maria Hospital, Lisbon, Portugal, with data regarding birth notification between 2006 to 2015 and data from the Portuguese Very Low Birth Weight database between 2010 to 2015. All data used was from Santa Maria Hospital. Repeated data from the two sources were removed, and therefore data from the Portuguese Very Low Birth Weight database prevailed.

Given this was a retrospective study and that the analysis of data was anonymous, Ethical Committee approval was not considered required. Nevertheless all the procedures were done according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

#### Participants

Inclusion criteria were as follows: maternal age between 18 and 35 years, adequate pregnancy surveillance and absence of chronic maternal disease. Exclusion criteria were as follows: maternal obesity [body mass index (BMI)  $\geq$  30 kg/m<sup>2</sup>], any use of tobacco, alcohol or drugs during pregnancy, multiple pregnancy, high risk pregnancy, assisted reproductive treatments, fetal growth restriction (estimated fetal weight <  $10^{th}$  percentile), fetal malformations, stillbirths and deaths.

## Variables

The following variables were analyzed: gestational age in weeks, gestational age in days (data not interchangeable), birth weight in grams, percentile of birth weight according to the Fenton & Kim 2013 growth chart,<sup>16</sup> percentile of birth weight according to Intergrowth 21<sup>st</sup> growth chart<sup>19,20</sup> and percentile of birth weight according to Intergrowth 21<sup>st</sup> growth chart<sup>19,20</sup> after categorization according to the Fenton & Kim 2013 growth chart.<sup>16</sup> Growth charts where used according to gender.

## Definitions

Both growth charts were applied to each newborn and the following categorization was used: small for gestational age (SGA) — birth weight below the  $10^{th}$  percentile;<sup>2</sup> adequate for gestational age (AGA) — birth weight between the  $10^{th}$  and  $90^{th}$  percentile;<sup>2</sup> large for gestational age (LGA) — birth weight above the  $90^{th}$  percentile.<sup>2</sup>

Term newborns were defined as those who were born with gestational age of 37 weeks or more (259 days or more); and preterm newborns as those who were born with gestational age less than 37 weeks (258 days or less).

Four groups were considered: 'Term-weeks' group term newborns with gestational age in weeks; 'Term-days' group — term newborns with gestational age in days; 'Preterm-weeks' group — preterm newborns with gestational age in weeks; 'Preterm-days' group — preterm newborns with gestational age in days.

## Statistical analyses

Data was analyzed with Microsoft Excel 2010<sup>®</sup> and IBM<sup>®</sup> SPSS<sup>®</sup> Statistics v.22.0<sup>®</sup>. For nominal or ordinal variables, descriptive statistics and exploratory data analysis

were applied, using absolute and relative frequencies, simple or conditional. Scale variables were characterized with minimum and maximum values and median. The median was chosen as a measure of central tendency, being more adequate than the mean for clinical context. Statistical inference was also used: inference about proportion was performed by 95% confidence intervals [95% CI (p)], based on the Wilson score method.

## RESULTS

## Sample description

The sample was composed of 14 056 newborns, of which 857 (6%) were preterm. In the group of term newborns (n = 13 199) the median gestational age was 39 weeks (minimum 37 weeks, maximum 42 weeks), and the median birth weight was 3250 g (minimum 1240 g, maximum 5150 g). In the group of preterm newborns, the median gestational age was 35 weeks (minimum 24 weeks, maximum 36 weeks), and the median birth weight was 2315 g (minimum 430 g, maximum 3905 g).

## 'Term-weeks' Group (Tables 1, 2 and 3)

This group consisted of 12 081 newborns. The median gestational age was 39 weeks (minimum 37 weeks, maximum 42 weeks), and the median birth weight was 3255 g (minimum 1830 g, maximum 5150 g). According to the Fenton & Kim 2013 growth charts,<sup>16</sup> 1679 (13.9%), 10 155 (84.1%) and 247 (2.0%) newborns were classified as SGA, AGA and LGA, respectively, and according to the Intergrowth 21<sup>st</sup> growth charts,<sup>19,20</sup> 792 (6.6%), 10 110 (83.7%) and 1179 (9.8%) newborns were classified as SGA, AGA and LGA, respectively. When applying the Intergrowth 21<sup>st</sup> growth charts,<sup>16</sup> 792 (47.2%), 9223 (90.8%) and 247 (100%) were classified as SGA, AGA and LGA in both charts, respectively. However, 887 (52.8%) of those classified as SGA in the Fenton & Kim 2013 growth charts<sup>16</sup> were

Table 1 – Sample description: categorization in each group as SGA, AGA and LGA according to the Fenton & Kim 2013 growth chart and the Intergrowth 21st growth chart

		Fenton & Kim 2013 % (n)	Intergrowth 21 <sup>st</sup> % (n)
'Term-weeks' Group	SGA	13.9 (1679)	6.6 (792)
	AGA	84.1 (10 155)	83.7 (10 110)
	LGA	2.0 (247)	9.8 (1179)
'Term-days' Group	SGA	13.1 (147)	5.5 (62)
	AGA	85.2 (952)	84.9 (949)
	LGA	1.7 (19)	9.6 (107)
'Preterm-weeks' Group	SGA	8.6 (53)	5.3 (33)
	AGA	85.4 (527)	83.6 (516)
	LGA	6.0 (37)	11.0 (68)
'Preterm-days' Group	SGA	22.5 (54)	26.3 (63)
	AGA	73.8 (177)	70.4 (169)
	LGA	3.8 (9)	3.3 (8)

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age

#### Table 2 – Group proportion analyses

		Proportion	(95% CI ( <i>p</i> ))
'Term-weeks' Group	SGA (F&K2013) to AGA (IG21)	52.8%	(50.4% – 55.2%)
	AGA (F&K2013) to LGA (IG21)	9.2%	(8.6% – 9.8%)
'Term-days' Group	SGA (F&Kim2013) to AGA (IG21)	57.8%	(49.7% – 65.5%)
	AGA (F&Kim2013) to LGA (IG21)	9.2%	(7.6% – 11.3%)
'Preterm-weeks' Group	SGA (F&Kim2013) to AGA (IG21)	37.7%	(25.9% – 51.2%)
	AGA (F&Kim2013) to LGA (IG21)	5.9%	(4.2% – 8.2%)
'Preterm-days' Group	SGA (F&Kim2013) to AGA (IG21)	9.3%	(4.0% – 19.9%)
	AGA (F&Kim2013) to LGA (IG21)	0.6%	(0.1% – 3.1%)
	AGA (F&Kim2013) to SGA (IG21)	7.9%	(4.8% – 12.8%)
	LGA (F&Kim2013) to AGA (IG21)	22.2%	(6.3% – 54.7%)

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age; F&K2013: Fenton & Kim 2013; IG21: Intergrowth 21st

Table 3 – 'Term-weeks' group categorization as SGA, AGA and LGA according to the Intergrowth 21st growth chart and the Fenton & Kim 2013 growth chart in each category

'Term-weeks' Group		Fenton & Kim 2013			
(n = 12 081)		SGA, % (n)	AGA, % (n)	LGA, % (n)	
Intergrowth 21 <sup>st</sup>	SGA	47.2 (792)	0.0 (0)	0.0 (0)	
	AGA	<b>52.8</b> (887)	90.8 (9223)	0.0 (0)	
	LGA	0.0 (0)	<b>9.2</b> (932)	100.0 (247)	
Total, % (n)		100.0 (1679)	100.0 (10 155)	100.0 (247)	

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age

classified as AGA in the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> [95% CI (*p*): 50.4% – 55.2%] and 932 (9.2%) of those classified as AGA in the Fenton & Kim 2013 growth charts<sup>16</sup> have been classified as LGA in the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> [95% CI (*p*): 8.6% – 9.8%].

#### 'Term-days' Group (Tables 1, 2 and 4)

This group included 1118 newborns. The median gestational age was 278 days (minimum 259 days, maximum 292 days), and the median birth weight was 3240 g (minimum 1240 g, maximum 4395 g). The classification of SGA, AGA and LGA according to the Fenton & Kim 2013 growth charts<sup>16</sup> and the Intergrowth 21st growth charts<sup>19,20</sup> was similar to the previous group, as shown in Table 1. Likewise, when the Intergrowth 21st growth charts<sup>19,20</sup> were applied after categorization with the Fenton & Kim 2013 growth charts,16 62 (42.2%), 864 (90.8%) and 19 (100%) were classified as SGA, AGA and LGA in both charts, respectively. However, 85 (57.8%) newborns classified as SGA in the Fenton & Kim 2013 growth charts<sup>16</sup> were classified as AGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 49.7% - 65.5%] and 88 (9.2%) newborns classified as AGA in the Fenton & Kim 2013 growth charts<sup>16</sup> have been classified as LGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (*p*): 7.6% - 11.3%].

## 'Preterm-weeks' Group (Tables 1, 2 and 5)

A total of 617 newborns were studied in this group. The median gestational age was 35 weeks (minimum 25 weeks, maximum 36 weeks), and the median birth weight was 2490 g (minimum 705 g, maximum 3905 g). According to the

Fenton & Kim 2013 growth charts,<sup>16</sup> 53 (8.6%), 527 (85.4%) and 37 (6.0%) newborns were classified as SGA, AGA and LGA, respectively, and according to the Intergrowth 21st growth charts,<sup>19,20</sup> 33 (5.3%), 516 (83.6%) and 68 (11.0%) newborns were classified as SGA, AGA and LGA, respectively. When the Intergrowth 21st growth charts<sup>19,20</sup> were applied after categorization with the Fenton & Kim 2013 growth charts,16 33 (62.3%), 496 (94.1%) and 37 (100%) were classified as SGA, AGA and LGA in both charts, respectively. However, 20 (37.7%) newborns classified as SGA in the Fenton & Kim 2013 growth charts<sup>16</sup> were classified as AGA in Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 25.9% - 51.2%] and 31 (5.9%) newborns classified as AGA in the Fenton & Kim 2013 growth charts<sup>16</sup> have been classified as LGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 4.2% – 8.2%].

#### 'Preterm-days' Group (Tables 1, 2 and 6)

In this group, 240 newborns were included. The median gestational age was 213 days (minimum 168 days, maximum 258 days), and the median birth weight was 1295 g (minimum 430 g, maximum 3825 g). According to the Fenton & Kim 2013 growth charts,<sup>16</sup> 54 (22.5%), 177 (73.8%) and 9 (3.8%) newborns were classified as SGA, AGA and LGA, respectively, and according to the Intergrowth 21<sup>st</sup> growth charts,<sup>19,20</sup> 63 (26.3%), 169 (70.4%) and 8 (3.3%) newborns were classified as SGA, AGA and LGA, respectively. When the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> were applied after categorization with the Fenton & Kim 2013 growth charts<sup>16</sup>, 49 (90.7%), 162 (91.5%) and 7 (77.8%) were classified as SGA, AGA and LGA in both charts, respectively. However, 5

Table 4 – 'Term-days' group categorization as SGA, AGA and LGA according to the Intergrowth 21<sup>st</sup> growth chart an the Fenton & Kim 2013 growth chart in each category

'Term-days' Group		Fenton & Kim 2013			
(n = 1118)		SGA, % (n)	AGA, % (n)	LGA, % (n)	
Intergrowth 21 <sup>st</sup>	SGA	42.2 (62)	0.0 (0)	0.0 (0)	
	AGA	<b>57.8</b> (85)	90.8 (864)	0.0 (0)	
	LGA	0.0 (0)	<b>9.2</b> (88)	100.0 (19)	
Total, % (n)		100.0 (147)	100.0 (952)	100.0 (19)	

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age

Table 5 – 'Preterm-weeks' group categorization as SGA, AGA and LGA according to the Intergrowth 21st growth chart and the Fenton & Kim 2013 growth chart in each category

'Preterm-weeks' Group		Fenton & Kim 2013			
(n = 617)		SGA, % (n)	AGA, % (n)	LGA, % (n)	
Intergrowth 21 <sup>st</sup>	SGA	62.3 (33)	0.0 (0)	0.0 (0)	
	AGA	<b>37.7</b> (20)	94.1 (496)	0.0 (0)	
	LGA	0.0 (0)	<b>5.9</b> (31)	100.0 (37)	
Total, % (n)		100.0 (53)	100.0 (527)	100.0 (37)	

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age

Table 6 – 'Preterm-days' group categorization as SGA, AGA and LGA according to the Intergrowth 21<sup>st</sup> growth chart and the Fenton & Kim 2013 growth chart in each category

'Preterm-days' Group		Fenton & Kim 2013			
(n = 240)		SGA, % (n)	AGA, % (n)	LGA, % (n)	
Intergrowth 21st	SGA	90.7 (49)	<u>7.9</u> (14)	0.0 (0)	
	AGA	<b>9.3</b> (5)	91.5 (162)	<u>22.2</u> (2)	
	LGA	0.0 (0)	<b>0.6</b> (1)	77.8 (7)	
Total, % (n)		100.0 (54)	100.0 (177)	100.0 (9)	

SGA: small for gestational age; AGA: adequate for gestational age; LGA: large for gestational age

(9.3%) newborns classified as SGA in the Fenton & Kim 2013 growth charts<sup>16</sup> were classified as AGA in the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> [95% CI (p): 4.0% – 19.9%] and 1 (0.6%) newborn classified as AGA in the Fenton & Kim 2013 growth charts<sup>16</sup> was classified as LGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 0.1% – 3.1%]. Nevertheless, below 231 days of gestational age (33 weeks, n = 183), there were 14 (7.9%) newborns classified as AGA in the Fenton & Kim 2013 growth charts<sup>16</sup> which were classified as SGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 4.8% - 12.8%] and 2 (22.2%) newborns classified as LGA in the Fenton & Kim 2013 growth charts<sup>16</sup> were classified as AGA in the Intergrowth 21st growth charts<sup>19,20</sup> [95% CI (p): 6.3% – 54.7%). This group under 231 days of gestational age had a median gestational age of 207 days (minimum 179 days, maximum 230 days) and a median birth weight of 964 grams (minimum 570 g, maximum 1880 g).

#### DISCUSSION

Although widely used in Portugal, the Fenton & Kim 2013 growth charts<sup>16</sup> have some limitations.<sup>14,16,17</sup> Therefore, the existence of more reliable growth charts is important. Intergrowth 21<sup>st</sup> is a prospective, multiethnic, multicentre and population-based project which showed that birth anthropometry was identical in low-risk women. Thus,

growth charts developed in this project were intended to be used both within populations and to compare different nationalities.<sup>15,18,19</sup>

Our study included a sample of Portuguese term and preterm newborns. It showed that fewer term newborns classified as small for gestational age were observed when the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> were applied in birth weight: 13.9% with the Fenton & Kim 2013 growth charts<sup>16</sup> vs 6.6% with the Intergrowth 21st growth charts<sup>19,20</sup> in the 'Term-weeks' group and 13.1% with the Fenton & Kim 2013 growth charts<sup>16</sup> vs 5.5% with the Intergrowth 21st growth charts<sup>19,20</sup> in the 'Term-days' group. Furthermore, more than 50% of newborns of 'Term-weeks' group [sample proportion 52.8%, 95% CI (p): 50.4% - 55.2%] and more than 50% of newborns of 'Term-days' group [sample proportion 57.8%, 95% CI (p): 49.7% - 65.5%] classified as small for gestational age according to the Fenton & Kim 2013 growth charts<sup>16</sup> would be classified as adequate for gestational age in the new Intergrowth 21st growth charts.<sup>19,20</sup> There were similar findings in other studies. In a New Zealand study, it was found that the Intergrowth 21st growth charts<sup>19,20</sup> identified fewer small for gestational age newborns than the locally used charts (4.5% vs 11.6%). However, the authors established that infants not identified by the Intergrowth 21st growth charts19,20 as small for gestational age had an

increased risk of adverse neonatal outcomes.<sup>23</sup> Another study that included 1.25 million term pregnancies yielded identical results, with 10.5% of newborns being classified as small for gestational age according to a standard growth chart, while with the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> only 4.4% were identified. However, in the same study it was found that the differences appeared to be related to physiological differences between different populations (such as maternal height).<sup>24</sup>

Results were different in preterm newborns ('Pretermweeks' and 'Preterm-days' groups). In the 'Preterm-weeks' group there was also a reduction in the amount of small for gestational age newborns when the Intergrowth 21st growth charts<sup>19,20</sup> were applied: 8.6% with the Fenton & Kim 2013 growth charts<sup>16</sup> vs 5.3% with the Intergrowth 21<sup>st</sup> growth charts.<sup>19,20</sup> Moreover, an important percentage of preterm newborns [sample proportion 37.7%, 95% CI (p): 25.9% -51.2%] classified as small for gestational age according to the Fenton & Kim 2013 growth charts<sup>16</sup> would be classified as adequate for gestational age with the new Intergrowth 21<sup>st</sup> growth charts.<sup>19,20</sup> However, in the 'Preterm-days' group the amount of small for gestational age newborns is higher when the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> were used, unlike what happened in previous groups: 22.5% with the Fenton & Kim 2013 growth charts<sup>16</sup> vs 26.3% with the Intergrowth 21st growth charts.<sup>19,20</sup> In this group, it was also found that a small number of newborns classified as adeguate and large for gestational age according to the Fenton & Kim 2013 growth charts<sup>16</sup> would be classified as small and adequate for gestational age, respectively, according to the Intergrowth 21<sup>st</sup> growth charts.<sup>19,20</sup> This may be related with gestational age itself, as these newborns all have a gestational age below 33 weeks. Furthermore, the 'Pretermdays' group had a median gestational age lower than the 'Preterm-weeks' group (30 weeks + 3 days vs 35 weeks). A study comparing the use of the Fenton & Kim 2013 growth charts<sup>16</sup> with the Intergrowth 21<sup>st</sup> growth charts<sup>19,20</sup> in preterm newborns also found similar results: a higher amount of small for gestational age newborns using the latest charts (15% vs 12%).17 Thus, it may be suggested that in very preterm infants, the Intergrowth 21st growth charts<sup>19,20</sup> may increase the number of those classified as small for gestational age in comparison with the Fenton & Kim 2013 growth charts.<sup>16</sup>

Our study showed that it would be beneficial for Portuguese newborns to use the Intergrowth 21<sup>st</sup> growth charts.<sup>19,20</sup> The consequences of being small for gestational age are well known. The increased risk of hypoglycemia, polycythemia and hypothermia, for instance, leads to specific interventions and investigations in order to prevent these situations. Other frequent situation in these newborns is dietary supplementation, with increased risk of obesity and metabolic syndrome in future.<sup>12,13,24</sup>

By replacing the Fenton & Kim growth charts<sup>16</sup> with the Intergrowth 21<sup>st</sup> growth charts,<sup>19,20</sup> there would be fewer newborns classified as small for gestational age, with fewer unnecessary or potentially harmful interventions (glucose monitoring or dietary supplementation, for example). It would be important to carry out a prospective study to confirm these findings.

This study has some limitations. Although a large sample was analyzed (more than 14 000 newborns), this is a retrospective study, using previously existing data, not collected for the purpose of the study. Furthermore, data was from a specific hospital in Lisbon. So, this sample is not representative of the Portuguese population. Furthermore, the inclusion and exclusion criteria were different from those used in the Intergrowth 21<sup>st</sup> project<sup>18,19</sup>: data such as maternal height, maternal body mass index, socioeconomic situation, previous gynecological history, number of previous abortions and obstetric history were not considered. Therefore, we propose a multicentre national prospective study using the same criteria as the Intergrowth 21<sup>st</sup> project,<sup>18,19</sup> in order to make a more reliable comparison of charts, including the evaluation of length and head circumference.

#### CONCLUSION

The use of the Intergrowth 21st growth charts<sup>19,20</sup> in this study, instead of the Fenton & Kim 2013 growth charts,16 resulted in a lower number of newborns being classified as small for gestational age. However, in very premature newborns the opposite was found, with more newborns classified as small for gestational age with the Intergrowth 21st growth charts<sup>19,20</sup> than with the Fenton & Kim 2013 growth charts.<sup>16</sup> The use of more suitable growth charts in birth weight evaluation would lead to more appropriate attitudes towards each newborn, which could influence their neonatal approach and eventual risk of chronic disease as adults. Considering the methodology of the Intergrowth 21st project and the results obtained in this study, we suggest that Portuguese maternity hospitals use the Intergrowth 21st instead of the Fenton & Kim 2013 growth charts. However, more studies are needed to complement these results.

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## **PROTECTION OF HUMANS AND ANIMALS**

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

## DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

## **CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

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