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Impact of customized growth curves on screening for small for gestational age twins

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ABSTRACT

Objective: The choice of a growth curve determines the screening for small-for-gestational-age (SGA) fetuses and little data is available on SGA twins. Our aim was to evaluate small-for-gestational-age (SGA) detection rate in twin pregnancies and assess whether the use of a customized curve allowed better identification of SGA fetuses.
Study design: Retrospective study including all twins between 2010 and 2013. Two groups were formed: the SGA and the non-SGA group. Four curves were compared: Hadlock's curve, a customized curve, EPOPé M0 and EPOPé M1. We defined a composite neonatal complication criterion (transfer to intensive care unit, respiratory distress and death).
Result: 472 fetuses were included with a 34.3% prevalence of SGA. Hadlock's curve showed better sensitivity for the detection of SGA <10th percentile (67.3% vs. 63%, 59.9% and 57.4% respectively). Diagnostic Odd Ratio were comparable for the detection of SGA. For the composite variable, there was a significant difference between the 2 groups using a customized curve adjusted for fetal sex (EPOPé M1).
Conclusion: The EPOPé (M0 and M1) and customized curves do not improve screening for SGA infants below the 10th percentile. The reduced effectiveness of customized curves can be related to the greater impact of placentation or cord insertion on the potential for fetal growth.

Introduction

Multiple pregnancies are more and more frequent especially because of the use of Assisted Reproductive Techniques (ART). The multiple birth rate was 17 per 1000 in 2013 representing 13,687 twin births in France [1]. Twins are at risk of more frequent growth abnormalities [2], which are associated with an increased risk of neonatal morbidity and mortality. According to Monier et al., the detection rate of Intra Uterine Growth Retardation (IUGR) in singletons would be only 22% and this rate is poorly appreciated in twin pregnancy [3]. However, choosing a weight curve largely determines the screening for and diagnosis of small-for-gestational-age (SGA) fetuses. According to the latest recommendations, reference ultrasound, the use of growth curves adjusted for size, weight of the mother and fetal sex is recommended for singletons [4]. However, in ultrasound screening, the use of these customized curves has yet to be assessed [5]. These recommendations are for singleton pregnancies but do not specify the screening and monitoring of twin pregnancies.

Screening for SGA has a significant impact on neonatal morbidity and mortality. Indeed undiagnosed SGA are responsible for 23% of intrauterine fetal deaths among term singletons [6,7]. Obstetric teams must be able to track the SGA and IUGR to establish the date of delivery in order to optimize perinatal health and neurological development [8]. Thus ultrasound screening is a valuable tool for the detection of SGA and can lead to improved neonatal outcomes [7]. However, literature data is missing on SGA screening rates and the use of customized curves for screening in twin pregnancies.

Thus, the objective of our study was to evaluate the SGA screening rates in twin pregnancies and to evaluate whether the use of adjusted or customized curves curve could help to better identify SGA fetuses.

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Methods

This retrospective study included all twin live births between 1 January 2010 and 31 December 2013 at the Jeanne de Flandre tertiary care maternity in Lille (France). The study was approved by the ethics committee for research in obstetrics and gynecology (OBS CEROG 2014-04-02).

The exclusion criteria, because of the peculiarity of the disease, were as follows: twin-to-twin transfusion syndrome during pregnancy or TAPS (Twin Anemia Polycythemia Sequence), malformation syndrome or intrauterine death in one twin.

The collected data was maternal characteristics (age, body mass index in kg/m2, gestity), estimated fetal weight (EFW) for each twin in the latest ultrasound performed less than 30 days before birth, fetal gender and twins' respective weights at birth.

Gestational age at delivery (completed gestational weeks) was determined from the caudal cranial measurement performed on the smallest fetus during 1st trimester ultrasound. The fetal weight was calculated according to the formula of Hadlock: log10 (EFW) = 1.3596 – (0.00386 ACxFL) + (0.0064 HC) + (0.00061 BIPxAC) + 0.0424 AC + 0.0174 LF 10 (AC: abdominal circumference, LF: femoral length, HC: head circumference and BIP: biparietal diameter) [9]. SGA was defined by EFW less than the tenth percentile of the curve used [10].

Four growth curves were compared: the Hadlock's curve (used routinely in our center) [9], the customized curve (including maternal weight and height, parity and fetal sex) [11], the EPOPé unadjusted (M0) [12] and adjusted on the fetal sex (M1) curves [12].

The small weight for gestational age at birth was defined by a weight less than the 10th percentile according to the French curves by Leroy and Lefort – that are used by the neonatologists in our center [13].

Neonatal outcome was evaluated by an Apgar score <7 at 5 min, umbilical arterial pH below 7.10, respiratory distress, transfer to intensive care unit and neonatal death. We defined a composite variable of neonatal complications, as previously described by Gardosi et al. [14], comprising: respiratory distress, transfer to intensive care unit and neonatal death.

Statistics

The data was extracted from medical records and entered via the CLINSIGHT software (Version 6.2.300, 2011). Data are presented as frequency and percentage for qualitative variables and mean ± standard deviation (SD) (or median (interquartile range (IQR)) for non-Gaussian distribution) for quantitative variables. Normality of distribution was checked graphically and tested using the Shapiro-Wilk test.

Two main groups were created: Non-SGA group and SGA group (EFW < 10th percentile). Population characteristics were compared between the two groups using the Chi-square test (or Fisher's exact test when excepted cell frequency was <5) for qualitative variables and the Student *t*-test (or Mann-Whitney *U* test for non-Gaussian distribution) for quantitative variables. The percentage error, sensitivity, specificity, positive predictive value, negative predictive values, positive likelihood ratio, negative likelihood ratio and diagnostic odd-ratio of SGA diagnosis through the use of Hadlock, customized, M0 and M1 curves were calculated using the standardized neonatal curve by Leroy and Lefort as gold standard [13]. The study had two steps in evaluation, first using EFW < 10th percentile, then using EFW < 3rd percentile. Statistical testing was done at the two-tailed α level of 0.05. Statistical analyzes were performed using SAS software (SAS Institute Version 9.4).

Results

472 fetuses were included from 236 twin pregnancies. 162 fetuses (34.3%) had a SGA <10th percentile at birth and among these 44 (9.3%) were below the third percentile. Table 1 summarizes maternal characteristics. The data of the 2 groups

Table 1
Population characteristics (n = 236 twin pregnancies).

	Non-SGA (n = 113)	SGA T1 or T2 (n = 123)	*p*
Age (years)	31.9 +/− 5.5	29.9 +/− 5.6	0.0055
ART	41 (36.3)	40 (32.5)	0.54
Chorionicity	89 (79.5)	90 (73.2)	NA
Bichorial-Biamniotic	20 (17.8)	32 (26.0)	
Monochorial-Biamniotic	3 (2.7)	1 (0.8)	
Monochorial-Monochorial			
PIH	7 (6.2)	8 (6.6)	0.91
Diabetes	3 (4.5)	0	NA
Nulliparity	48 (42.5)	71 (57.7)	0.0193
Smoking	16 (14.2)	32 (26.0)	0.0238
Scarred uterus	9 (8.0)	15 (12.3)	0.27
BMI (kg/m^2)	23.3 (20.6–26.9)	22.7 (20.1–26.8)	0.61
Preeclampsia	5 (4.5)	11 (9.1)	0.17
Gestational diabetes mellitus	25 (27.8)	21 (22.8)	0.44
Preterm PRM	25 (22.9)	22 (17.9)	0.34
Cholestasis of pregnancy	6 (5.4)	8 (6.6)	0.70
Placenta previa	2 (1.8)	1 (0.8)	NA
TPL	49 (43.8)	60 (48.8)	0.44
Cesarean	28 (25.0)	53 (43.1)	0.0036
PPH	37 (32.7)	58 (47.5)	0.0209
Gestational age at birth	36 (33–37)	36 (33–37)	0.93
Birth weight T1 (g)	2500 (1810–2800)	2200 (1660–2530)	0.0058
Birth weight T2 (g)	2515 (1945–2865)	2070 (1510–2380)	<0.0001

Results are presented as n (%), mean+/− standard deviation or median (IQR).
SGA = Small for gestational age.
ART = Assisted Reproductive Techniques; BMI = Body Mass Index; BiBi = Bichorial Biamniotic; MonoBi = Monochorial Biamniotic; MonoMono = Monochorial Monoamniotic; PRM = premature rupture of membranes; PIH = pregnancy-induced hypertension; TPL = threatened preterm labour; PPH = postpartum haemorrhage; GA = gestational age. NA = Non applicable.