Comparing the relationship between ultrasound-estimated fetal weight and birthweight in cohort of small for gestational age fetuses

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Conflicts of interest: None to declare

Funding: No funding

Key words: Fetal growth restriction, in utero compromise, fetal growth, fetal size, SGA

Abbreviations:

SGA- Small for gestational age

EFW- Estimated fetal weight

BWt- Birthweight

USS- ultrasound scan

SGA10- <10th percentile for birthweight

SGA 5- <5th percentile for birthweight

EFW10- estimated fetal weight <10th percentile for birthweight

Key message: Currently the antenatal recognition of SGA infants is poor. Estimated fetal weight over-estimates birthweight in our cohort.

Abstract

Introduction

Small for gestational age (SGA) confers a higher perinatal risk of adverse outcomes. Birthweight cannot be accurately measured until delivery, therefore accurate estimated fetal weight (EFW) based on ultrasonography is important in identifying this high-risk population.

We aimed to establish the sensitivity of detecting SGA infants antenatally in a unit with a selective third trimester ultrasound policy and investigate the association between EFW and birthweight in these babies.

Material and methods

A retrospective cohort study was conducted on non-anomalous singleton pregnancies delivered after 36 weeks gestation where SGA (<10th percentile) was diagnosed at delivery. The EFW at the time of the third trimester ultrasound scan was recorded using standard Hadlock formulae.

Results

In 2017 there were 8392 non-anomalous singleton pregnancies live born after 36 weeks, excluding late bookers. 797 were live born SGA <10th percentile for birthweight and 464 <5th percentile, who met our inclusion criteria. The antenatal detection rate of SGA was 19.6% for babies with birthweight <10th percentile and 24.1% <5th percentile. There was a significant correlation between the EFW and birthweight of fetuses undergoing ultrasound assessment within two weeks of delivery (P<0.001, r=0.73 (Pearson correlation). For these cases, EFW was greater than the birthweight in 65% of cases. After adjusting all EFWs using the discrepancy between EFW and actual birthweight for those babies born within 48 hours of the scan, the mean difference between the birthweight and adjusted EFW seven days prior to delivery was 111g (95% CI; 87g-136g) and at 14 days was 200g (95% CI; 153-248g). Despite adjusting the EFW, 61/213 cases (28.6%) apparently lost weight between the ultrasound scan and delivery.

Conclusions

Small for gestational age infants with a birth weight <10th percentile are poorly identified antenatally with little improvement for those <5th percentile. In SGA babies, ultrasound EFW overestimated birthweight. Discrepancies between birthweight and EFW are not explicable only by the limitations of third trimester sonography a reduction in fetal weight close to delivery in a proportion of liveborn SGA babies is plausible.

1. Introduction

Small for gestational age (SGA), (defined as birthweight (BWt) <10th percentile) babies are at increased risk of perinatal mortality and morbidity [1-4]. Birthweight cannot be measured until delivery, therefore an accurate estimated fetal weight (EFW) based on ultrasonography is important in identifying this high-risk population. The debate surrounding routine third trimester ultrasound scans (USS) in low risk pregnancies is ongoing as conflicting data exists as to whether such a policy improves outcomes [5-7]. Although USS itself is safe, the outcomes for pregnancies inaccurately thought to be SGA include iatrogenic prematurity, induction of labour and Caesarean section [6]. In accordance with Royal College of Obstetricians and Gynaecologists (RCOG) recommendations [8], the UK has a selective policy for third trimester fetal growth USS, where there is suspicion of SGA based on symphysio-fundal height measurements, in addition to other clinical indications. Fetuses ≤ 10th percentile EFW on USS are presumed to be SGA and these women should then be offered serial growth scans and umbilical artery Doppler.

Failure to identify a SGA fetus antenatally increases the risk of adverse outcomes including a 1.6-4.3 fold increased risk of fetal or perinatal death compared to diagnosed fetuses [1, 2, 4].

The sensitivity of detection of SGA babies (BWt <10th percentile) is reported to be between 20-33% [1, 9], with a slightly higher detection for severe SGA (<2.3rd percentile)[10]. Studies have used selected cohorts and limited data exists on the predictive value of growth scans in a non-research setting. Ultrasound estimation of EFW has inherent inaccuracies arising from the formulae used to calculate EFW and the inter-observer variability of ultrasound biometry. The formulae proposed by *Hadlock et al.* are most widely used and considered to be consistent across a normal population [11-13], but may overestimate fetal weight in SGA fetuses [12, 14, 15].

We aim to establish the sensitivity of detecting SGA fetuses antenatally in a mixed population in the UK using a selective ultrasound policy. We hypothesise that selective triage of women receiving third trimester scans identifies the majority of SGA fetuses. Secondly, we aim to determine whether EFW is an accurate predictor of BWt

specifically in an SGA cohort, and investigate relationship between EFW and BW when an USS is performed within 2 weeks of delivery.

2. Material and methods

A database study was conducted between January and December 2017 in the two maternity units of one UK inner city hospital Trust. Inclusion criteria included infants born SGA (<10th percentile for birthweight based on WHO criteria) who delivered after 36 weeks gestation [16]. Exclusion criteria were multiple pregnancies, in-utero transfers, known fetal anomalies and women who booked their pregnancies late and so did not undergo first trimester dating USS and stillbirths. Patient demographics, pregnancy information and USS data were collected from hospital databases. USS were performed by qualified ultrasonographers and obstetricians. All sonographers are qualified to a minimum of the PgC in Obstetric Ultrasound or equivalent. They undertake routine NHS practice and are involved in regular departmental audits. The EFW at time of the USS was recorded using Hadlock's formula, which incorporates four parameters; abdominal circumference, biparietal diameter, femur length and head circumference; where all four parameters were not available the Hadlock three parameter formula was used [13]. The standard for SGA was an actual BWt of less than the 10th percentile for sex and gestational age (SGA10), calculated using WHO reference values [16]. Pregnancy outcomes were obtained from computerised hospital records (Cerner, Kansas City, USA and Astraia, GMBH Munich, Germany).

Data were analysed to identify the sensitivity of detecting SGA babies antenatally using a selective third trimester ultrasound policy. We identified babies delivered SGA10 who were identified as having EFW10 (EFW <10th percentile for BWt) antenatally and SGA5 (<5th percentile for BWt) recorded as EFW10 antenatally. The groups are not mutually exclusive, the <10th percentile group includes the <5th percentile babies. We refer to SGA infants <10th percentile for BWt as SGA10, SGA infants <5th percentile for BWt as SGA5 and fetuses with EFW <10th percentile antenatally as EFW10.

A further analysis was completed including only those fetuses scanned within 2 weeks of delivery.

Statistical analyses

All statistical analysis was carried out using GraphPad Prism (v.6.04, GraphPad Prism Software Inc., California, USA). A normal distribution of the data was assessed by D'Agostino and Pearson normality test. Data with a normal distribution was analysed by Pearson correlation and data without a normal distribution by Spearman rank correlation, unless otherwise stated. $P<0.05$ was considered statistically significant.

Ethical approval

This study used pseudo-anonymised retrospectively ascertained data, and was registered with the Trust audit department under the title "Antenatal detection of the small for gestational age fetus". The study did not meet the HRA criteria for requiring submission for research ethics review (http://www.hra-decisiontools.org.uk/ethics/).

3. Results

Of the 8392 infants born meeting inclusion criteria during this period, 9.5% (n=797) were SGA10 infants [Figure 1]. 5.5% (n=464) of babies were born SGA5 [Figure 2]. Maternal characteristics are shown in Table 1. Women who had a SGA5 baby were significantly younger and had a lower BMI compared to the general population. Women who delivered an SGA5 and SGA10 baby were over three times more likely to be smokers compared to the general population.

On the third trimester scan, of SGA10 newborns 27.3% were EFW10 at any gestation, however only 19.6% were EFW10 on their final scan [Figure 1]. There was no difference in the diagnostic rate in each quarter of the year (analysed by Chi-square). Of the 72.6% of SGA10 fetuses not diagnosed during pregnancy, 51.0% of these had had an USS assessment for fetal growth during pregnancy, however, only 14.9% of these had had a USS within two weeks of delivery.

Of babies born SGA5 32.5% were EFW10 from USS during the third trimester, however only 24.1% were EFW10 on their final USS [Figure 2]. 313 fetuses (67.5%) were not diagnosed, of these 47.3% had had a third trimester USS during pregnancy, with 10.2% of these having an USS within two weeks of delivery.

Further analysis was completed to see if USS carried out closer to the delivery date provided a more accurate estimate of BWt. In babies delivered SGA10 who underwent an USS within two weeks of delivery (n=214), the mean time between final scan and delivery was 7 days. Within this cohort there was a strong positive correlation between the EFW and BWt [Figure 3] ($P<0.001$, r= 0.73) (Pearson rank correlation). The EFW was greater than the BWt in 65% of cases and linear regression resulted in a relationship of BWt=(EFW-310.1)/0.915.

A weak correlation was demonstrated between the change in weight between delivery and final scan (BWt-EFW) and the number of days to delivery ($P=0.0004$, r=0.24, Spearman rank correlation) [Figure 4]. An expected trend line was calculated based on the expected average daily weight gain for an SGA10 cohort [16].

EFW versus BWt was plotted for fetuses scanned within 48 hours of delivery (n=26), with the aim of accounting for discrepancies in EFW due to fetal growth. There was a

strong correlation between EFW and BWt (P<0.001, r=0.88, Pearsons correlation; linear regression: BWt=(EFW+130.6)/1.14).

In a second plot (Figure 5) of BWt-EFW against time to delivery, we compensated for the overestimation of EFW in the data set for deliveries within 14 days of USS (n=213) using the formula: *Adjusted EFW=(EFW+130.6)/1.14*.There was a correlation between change in weight and days to delivery (P<0.0001, r=0.29, Pearsons correlation).

4. Discussion

Selective triage of women to receive third trimester scans resulted in 35% of women who delivered a SGA10 baby not being identified as requiring a third trimester USS. We demonstrate that in a mixed population despite two thirds of women undergoing third trimester fetal growth assessment by USS, the detection rate of small for gestational age infants, based on population centiles, was poor. These rates are similar to those previously reported [1, 9]. For those women undergoing USS, less than one third of SGA10 babies were identified on their final USS and the detection rate of the SGA5 was very similar to the detection rate of SGA10 infants. We were unable to determine which factors influenced the low detection rate in this study. Possible reasons include over estimation of fetal weight using the Hadlock formula in an SGA cohort and technical difficulties in performing the measurements required for fetal growth assessment late in the third trimester [12].

In this study we used standard WHO reference values for BWt.[16]; these are based on multinational data therefore likely to be applicable to our mixed ethnic population and are standard birth percentile charts used for a UK population and are used for routine clinical care in all UK centres. Other ranges include those reported by the Intergrowth-21st Project [17], which report data on patients selected based on carefully specified characteristics and customised growth charts, these charts have not been shown to be superior to standardised growth charts [18].

Although we demonstrate a strong correlation between the unadjusted EFW and the BWt, the EFW at scan was greater than the final BWt for over half cases, despite the fetus remaining in-utero for up to a further two weeks. On average EFW over-estimates BWt by 92g (95% CI; 61g to 123g) based on linear regression modelling, despite the fetus remaining in utero for up to a further two weeks.

Furthermore, when infants were delivered within two days of their final USS, despite delivery being imminent, again on average the EFW overestimated the BWt by 250g (95%CI; 159g to 351g). This suggests that an USS EFW in SGA is a very poor predictor of BWt.

Despite controlling for the systematic over-estimation of EFW in our data, 61 (29.1%) infants still had a lower BWt than the adjusted EFW based on USS. Based on the distribution of EFW in relation to BWt prior to delivery, it is plausible that some SGA fetuses lose weight prior to delivery. Although some of the variance between EFW and BWt can undoubtedly be put down to inaccuracy of USS, if we assume that USS biometry leads to over measurement as often as it leads to under measurement, this cannot explain on its own the distribution of the differences between BWt and EFW shown in figure 5. A decline in growth velocity in fetal growth restriction and a loss of fetal weight following fetal demise are well reported phenomena [20-22] but no previous study has suggested compromised live infants may lose weight in utero. If the metabolic requirements of the fetus were to exceed the available placental supply of oxygen and nutrients, just as a new born baby may lose weight after delivery, the same process might apply prior to delivery. This theory has to our knowledge not been applied in the case of live fetuses before, however it has profound implications for our understanding of the pathophysiology and how we might apply clinical surveillance techniques. We report the relationship between EFW and BWt in a single scan, this allows for cross sectional interpretation of the differences between EFW and BWt and allows us to adjust for the discrepancy in weights at birth as a result of interval fetal growth. Whilst longitudinal ultrasound measurements might be desirable to follow the relationship between EFW and time in an individual fetus, the margin of ultrasound biometry error precludes ultrasound to be repeated more than once every 10-14 days.

A strength of this study is the large sample size of SGA infants from a non-selected population receiving standard antenatal care. This gives us insight into the detection rate of SGA in clinical practice. A weakness of the study is its retrospective design, hence we can gain little information on identifying specific changes that could improve clinical practice.

5. Conclusion

In this large population based study investigating antenatal diagnosis of small for gestational infants in the UK, we report a poor detection rate of SGA. Selective triage failed to identify over two thirds of women who delivered an SGA10 baby. USS estimate of fetal weight near delivery is a poor predictor of BWt. A possible explanation may be overestimation of EFW in a SGA population but we cannot exclude a reduction

228 in fetal weight in these small fetuses that are compromised in-utero. Based on these
229 data clinicians should interpret the results of fetal growth assessments with caution and
230 should not exclude the diagnosis of SGA solely on the basis of fetal USS.

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232 **Acknowledgements**

233 The authors wish to express their gratitude to Wayne Henry for his assistance with
234 extracting the data from hospital databases.

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Table 1. Demographic characteristics of all women who delivered in 2017 with singleton live born pregnancies, excluding late bookers. Data are shown as the mean (standard deviation) or number (%). BMI=body mass index. Statistical analysis completed for continuous data compared using unpaired t-test, and for categorical data using a Chi-Square test.

Characteristics	**Population (n=8392)**	**<10th percentile (n=797)**	**Significance of < 10th percentile vs. population**	**<5th percentile (n=464)**	**Significance of < 5th percentile vs. population**
Maternal age (years)	32.2 (5.4)	31.9 (5.5)	*P*=0.076	31.6 (5.5)	*P*<0.01
Maternal BMI (kg/m^2)	25.1 (5.1)	24.3 (5.2)	*P*<0.0001	24.3 (5.4)	*P*<0.0015
Parity Nulliparous	 4709 (56.1%)	 447 (56.1%)	*P*=0.988	 287 (61.9%)	*P*<0.01
Ethnicity Caucasian African/Caribbean Asian Other Unknown	 2744 (32.7%) 793 (9.4%) 1096 (13.1%) 1393 (16.6%) 2366 (28.2%)	 227 (28.3%) 168 (21%) 255 (31.9%) 146 (18.2%) 5 (0.6%)	*P*<0.0001	 122 (26.1%) 95 (20.3%) 159 (34.1%) 87 (18.6%) 4 (0.9%)	*P*<0.0001
Current smoker	211 (2.5%)	61 (8.0%)	*P*<0.00001	41 (8.8%)	*P*<0.00001

Table 2. Pregnancy Outcomes for pregnancies included in the study. Data presented as the mean (standard deviation) or number (percentage).

Characteristics	<10th percentile (n=797)	<5th percentile (n=464)
Pre-existing maternal health conditions:		
Hypertension	5 (0.6%)	4 (0.9%)
Diabetes	5 (0.6%)	4 (0.9%)
Renal disease	4 (0.5%)	2 (0.4%)
In-pregnancy complications:		
Gestational diabetes	88 (11.0%)	43 (9.3%)
Pregnancy induced hypertension/pre-eclampsia	46 (5.8%)	28 (6.0%)
Gestational age at delivery (days)	272 (8.3)	273 (9.0)
Birthweight (g)	2628.1 (236.3)	2551.5 (253.6)
Infant sex		
Male	368 (46.2%)	249 (53.7%)
Female	429 (53.8%	215 (46.3%)
Method of delivery:		
Elective caesarean section	92 (11.5%)	46 (9.9%)
Spontaneous vaginal delivery	439 (55.1%)	245 (52.8%)
Instrumental delivery	129 (16.2%)	89 (19.2%)
Emergency caesarean section	137 (17.2%)	84 (18.1%)

Figure 1. Antenatal diagnosis of live born small for gestational age fetuses. Data presented as the number (percentage). SGA10=small for gestational age infant <10th percentile

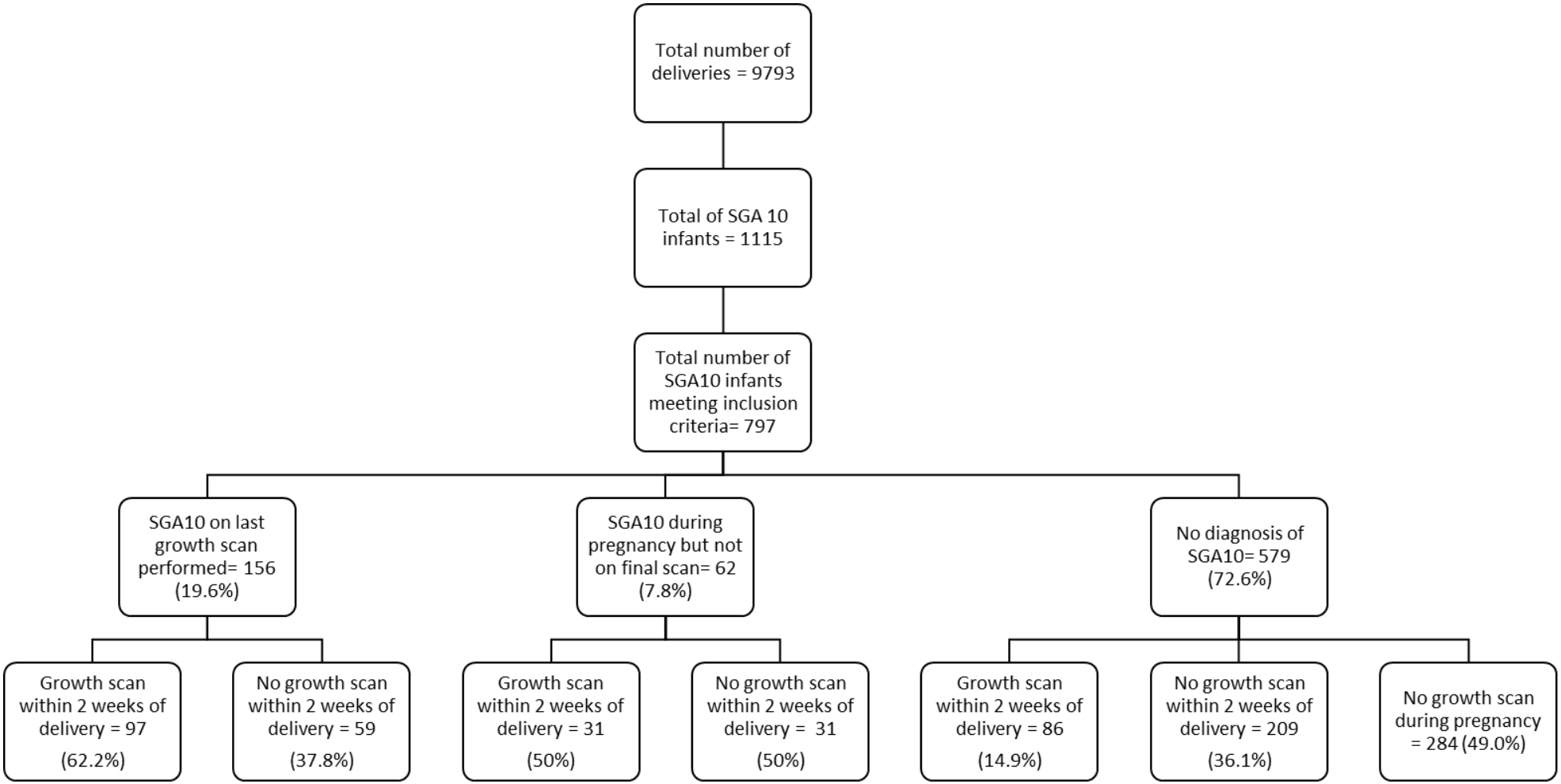

Figure 2. Antenatal diagnosis of live born <5th percentile fetuses. Data presented as number (percentage). SGA10=small for gestational age <10th percentile, SGA5=small for gestational age <5th percentile.

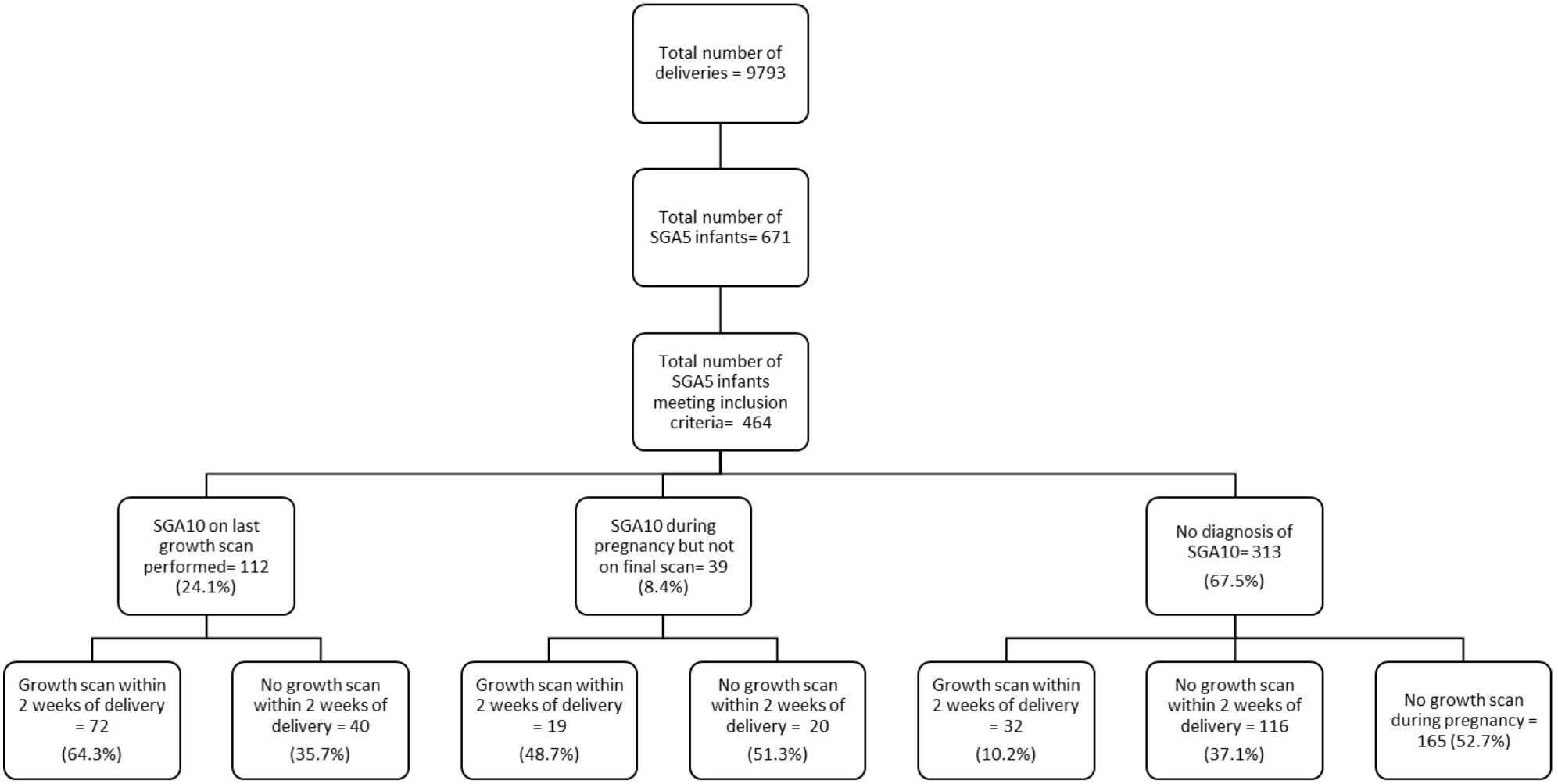

Figure 3. Relationship between estimated fetal weight and birthweight in infants undergoing ultrasound within 2 weeks of delivery. n=213, data analysed by Pearsons correlation, *P*<0.001, r=073. Linear regression y=(x-310.1)/0.915.

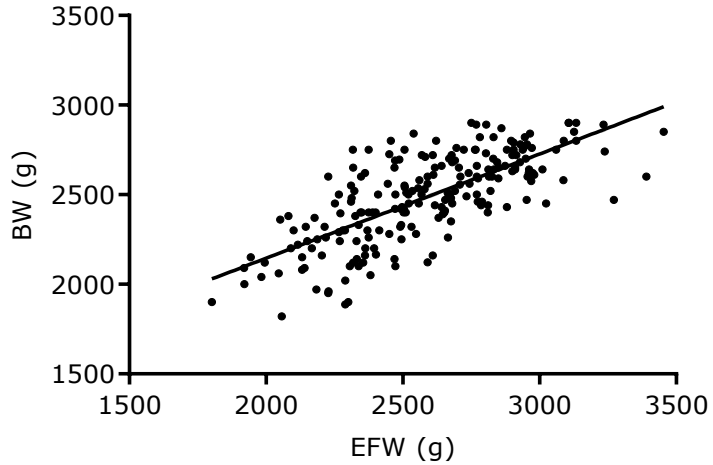

Figure 4. The difference birthweight and estimated fetal weight versus the time to delivery. n=213, data analysed by Spearman rank correlation, r=0.24, *P*=0.0004. Black line shows the linear regression of the data set, red line shows the expected trend based on the expected average daily weight gain within for the fetuses within our cohort.

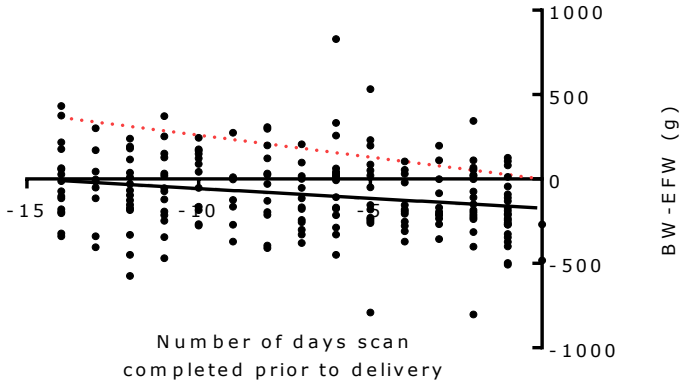

Figure 5. The difference between the birthweight and the adjusted estimated fetal weight versus the time to delivery. n=213, data analysed by Spearman rank correlation, r=0.29, *P*<0.0001. Linear regression: y=12.73x+22.29