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Is the placental disk really an ellipse?

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Abstract

The mean surface shape of placenta is round [1,2] and common abnormalities of shape are associated with vascular abnormalities and reduced placental functional efficiency. A long-standing approach is to describe shapes as elliptic, and to quantify them by “length” and “breadth”. We test this description in two cohorts: National Collaborative Perinatal Project and Pregnancy, Infection and Nutrition Study. We conclude that quantifying placental shape as elliptic is ambiguous and problematic. The “breadth” of the placenta should be interpreted as a combination of two different measurements: placental size and irregularity of the placental surface. It has no intrinsic functional significance.

INTRODUCTION

The mean placental surface shape is round [1]. Modeling of placental vascular growth [2] suggests that common shape abnormalities are associated with abnormal vascular development.

Traditionally, [3,4] placental shape is described as “oval” or “elliptic”, and non-roundness measured as “breadth” vs. “length”. However, placental shapes are often variable, and quantifying them can be challenging. A meaningful approximation of a shape by an ellipse can be ambiguous and mathematically problematic [5,6].

In light of recent proposals that placental minor axis “breadth” has unique value in determination of fetal growth [4], we compare analyses of placental shape in the multi-institutional National Collaborative Perinatal Project (NCP) and a more recent single-institution UNC Pregnancy, Infection and Nutrition Study (PIN).

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METHODS

NCPP

As described elsewhere, [7,8] from 1959 to 1965, placental gross morphology was examined in a sample of 24,061 subjects. Chorionic disk size was quantified by two “diameters”.

Thus, a visual fit by an ellipse would be made by the observer at the time of gross examination, and the major and minor axes of that ellipse were recorded as “larger diameter” and “smaller diameter”.

UNC PIN study

1,100 women in Phase 2 consented to a detailed placental examination [9,10]. Digital photographs of the fetal chorionic surface after trimming of membranes and umbilical cord were obtained prior to fixation. The site of umbilical cord insertion was marked and the disk perimeter traced. An algorithm for approximating placental surface shape with an ellipse [6] produced, for each placenta, the lengths L_{big} , L_{small} of the major and minor semi-axes (halves of the main axes) of the best-fit ellipse. We used two previously described [1] measures of differentiation of placental shapes, which we denoted Δ and σ , each measuring aspects of differences between the chorionic surface shape and a circle. Each ranges between 0–1, 0 corresponding to a perfectly round placenta.

Statistics

Linear regression was used in both cohorts to relate the major and minor axes to birthweight. In the PIN cohort, we also computed the dilatation of the ellipse (the ratio of major and minor axes L_{big}/L_{small}) and explored correlations of this value with placental shape descriptors. Pearson’s and Spearman’s correlations were used for normally and non-normally distributed variables, respectively. Fitting of probability distributions was performed using Mathwave EasyFit.

RESULTS

Site dependence of major/minor axes correlations with birthweight in the CPP

The major and minor axes generally had independent predictive values for birthweight. However, the magnitude of the points estimates of effects of the major and minor axes varied enormously among the 12 sites, from 1.74–33.6 and from 15.8–35.4 (centered major and minor axes respectively (Table a).

Distributions of variables in the PIN cohort

In PIN, birthweight and L_{small} are normally distributed. The distributions of L_{big} and the ratio of major and minor axes, L_{big}/L_{small} are lognormal – their logarithms are normally distributed (Figure). In regression analysis, the use of logarithms of these variables, rather than the variables themselves, is appropriate.

Statistical analysis of the UNC PIN cohort

The ratio L_{big}/L_{small} showed an excellent correlation with our placental shape descriptors Δ and σ ($\rho=0.844$, $p<0.001$ and $\rho=0.745$, $p<0.001$, respectively). Both L_{big} ($\rho=0.304$) and L_{small} ($r=0.384$) exhibit significant correlations with birthweight ($p<0.001$).

Taken alone, L_{small} has a significant association with birthweight ($R^2=0.146$). The regression based on the pair of variables (L_{big} , L_{big}/L_{small}) is slightly better at predicting birthweight ($R^2=0.147$). If L_{big} , and L_{big}/L_{small} are normalized by taking the appropriate logarithms (Figure), their association with birthweight strengthens ($R^2=0.158$).

In a regression with birthweight as the dependent variable, controlling for gestational age, L_{small} and the centered logarithm of L_{big} have a comparable total effect (Table b). When either of our shape descriptors are included in the regression, L_{small} loses all predictive value for birthweight (Table c).

CONCLUSIONS

Approximating placental shape by an ellipse is ambiguous and mathematically problematic [5]. The substantial site variability of the regression analysis results in the CPP highlights this difficulty. Different observers “saw” the chorionic surface as an ellipse differently. The measurement of the major axis, or the diameter of the placenta, can be done consistently. But measuring the minor axis of a non-elliptic object involves individual judgment which cannot be made “by eye” with consistency. In view of the planning of the National Children’s Study, this begs for implementation of digital image capture of placental chorionic surfaces and standardized processing.

As we demonstrated in the PIN cohort, finding a best-fit ellipse can be implemented numerically based on the digital photographs of the chorionic surface. A best-fit algorithm which calculates major and minor axes yields useful measurements, which correlate well with sophisticated measures of shape.

Describing placental shape as elliptic may lead to confusion. Consider the assertion of [4] that “breadth” (L_{small}) plays specific biological role in nutrient transfer since it alone, independently of the “length” (L_{big}), can be used to predict birthweight in a regression.

Both “length” and “breadth” are measures of placental size and hence correlate with the birthweight. However, “breadth” is clearly not a measure of a single placental aspect. Rather, it is a ratio of a measure of placental size (L_{big}) and dilatation (L_{big}/L_{small}) that proxies irregularity of placental shape. Irregularity of shape has been shown [1] to indicate deformation of vascular structure, and consequently, a reduction in placental metabolic efficiency, which leads to a smaller birthweight for a given placental weight.

The “breadth” combines a measure of placental size with a measure of irregularity – hence it is a better predictor of birthweight than the “length”. Combining the two measurements into one loses some information: L_{small} alone has a poorer predictive value for birthweight than a linear regression based on L_{big} and the dilatation (L_{big}/L_{small}) or on their logs. And in a regression, in which an accurate measure of the placental irregularity is included, the “rough” measurements of placental irregularity, “breadth” and dilatation lose their predictive value entirely.

Thus the findings of [4] can be explained without ascribing functional importance to the minor axis of best-fit ellipse, which is merely a mathematical abstraction.

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Figure 1.
Normalized statistical distributions of ellipse measurements.

Table 1

(a) CPP cohort by site, controlling for placental weight, length of cord, cord displacement, shape descriptor, and placental disk thickness.		
Site	Centered major axis (point estimates of effect)	Centered minor axis (point estimates of effect)
1	14.5 (p<0.001)	31.5 (p<0.001)
2	15.5 (p=0.008)	33.1 (p<0.001)
3	17.3 (p=0.005)	33.9 (p<0.001)
4	22.3 (p=0.001)	21.8 (p=0.011)
5	21.9 (p<0.001)	36.6 (p<0.001)
6	23.4 (p=0.001)	15.8 (p=0.028)
7	32.3 (p<0.001)	32.6 (p<0.001)
8	23.7 (p<0.001)	19.9 (p<0.001)
9	33.6 (p<0.001)	35.4 (p<0.001)
10	13.7 (p=0.001)	34.2 (p<0.001)
11	30.4 (p<0.001)	24.3 (p<0.001)
12	1.74 (p=0.900)	24.3 (p=0.102)

(b) UNC PIN cohort (point estimates of effect)	
$\ln (L_{big}-5.662)$ (p=0.001)	379
L_{small} (p=0.027)	70
$\ln (L_{big}/L_{small}-0.987)$ (p=0.100)	-72
Gestational days (p<0.001)	16.5

(c) UNC PIN cohort with a measurement of placental shape irregularity (σ) included. (point estimates of effect)	
$\ln (L_{big}-5.662)$ (p<0.001)	794
L_{small} (p=0.539)	-23
$\ln (L_{big}/L_{small}-0.987)$ (p=0.031)	-95
Gestational days (p<0.001)	16.4
σ (p<0.001)	-2105