

First-trimester inter- and intrafetal size discrepancies in bichorionic twins conceived by in vitro fertilization: can it predict pregnancy outcome?

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Objective: To evaluate the association between first-trimester inter- and intrafetal size discrepancies and pregnancy outcome, among bichorionic-biamniotic twins conceived by IVF.

Design: A retrospective study design was used.

Setting: Tertiary university-affiliated medical center.

Patient(s): All women with a viable first-trimester bichorionic-biamniotic twin gestation, who conceived after IVF in 2007–2015.

Intervention(s): None.

Main Outcome Measure(s): The association between fetal size differences and pregnancy outcome was analyzed. Intrafetal size discordance was defined as a difference between the actual gestational age calculated by ovum pickup (OPU) date and the evaluated gestational age by crown–rump length (CRL), for each twin. Intertwin size discrepancy was defined as a difference in CRL between the twins. The primary outcome was the number of live-born fetuses; the secondary outcome measures were gestational age at birth, birth weight percentile, and birth weight discordancy.

Result(s): A total of 277 women met the study criteria and were divided into three groups by outcome: 218 (78.7%) live-born twins, 41 (14.8%) live-born singleton, and 19 (6.5%) non-live-born pregnancy. Among the smaller than expected twin, the association of CRL-OPU differences with the primary outcome was significant for twin live-born delivery (–1.43 day), singleton live-born delivery (–4.12 days), and non-live-born pregnancy (–6.72 days). For the relatively larger twin, the association was significant for non-live-born pregnancy (–4.33 days) compared with any live-born delivery, either singleton (–0.95 days) or twin (–0.21 days).

Conclusion(s): Among IVF conceived twin gestations, a CRL-OPU gap was associated with an increased risk of a negative pregnancy outcome. (Fertil Steril® 2017; ■: ■–■. ©2017 by American Society for Reproductive Medicine.)

Key Words: Adverse pregnancy outcome, crown–rump length, in vitro fertilization, twin pregnancy

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Accurate estimation of gestational age (GA) is essential for appropriate antenatal care. Traditionally, GA is calculated according to the first day of the last menstrual period (LMP), which is an innately

imprecise method (1). Alternatively, GA can be determined during the first trimester by sonographic measurement of the crown–rump length (CRL) (2). In pregnancies conceived by IVF the timing of ovum pickup (OPU) and ET

are known, and they serve as the most accurate method to establish GA. Other than its significance in verifying or establishing GA, CRL, particularly when smaller than expected compared with LMP, is associated with adverse pregnancy outcomes, including pregnancy loss, small for gestational age (SGA), and preterm delivery (3–21). However, some of these reports that addressed early growth discrepancies in singleton pregnancies were methodologically limited because LMP is inherently

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inaccurate in spontaneous conceptions (3–7). To overcome this drawback, others compared CRL dating in IVF gestations, to establish accurate dating according to ET, and then evaluated pregnancy outcome according to discrepancies from actual CRL (8, 9). This approach may also be biased, because some of the suggested adverse outcomes may be confounded by the use of assisted reproductive technologies (10). This has been demonstrated specifically for twin gestations conceived by assisted reproduction, showing an increased rate of perinatal complications compared with spontaneous twin pregnancies (22, 23). An approach to evaluating first-trimester fetal growth that overcomes the above-mentioned flaws is to determine intertwin CRL disparity. Such studies report conflicting associations to a variety of adverse outcomes and include heterogeneous populations of both spontaneous and assisted conceptions as well as bichorionic and monochorionic gestations (11–21). Because the aforementioned studies are limited by confounders, the aim of the present study was to examine an association of first-trimester intrafetal and intertwin size discrepancies to pregnancy outcome among a strictly defined population of bichorionic-biamniotic (BC-BA) twins conceived by IVF. Intrafetal and intertwin size discrepancies were evaluated as either the gap between actual GA, as calculated by OPU, and the evaluated GA determined by CRL measurements for each twin (intrafetal size discrepancy); or by CRL discrepancies between the twins (intertwin discrepancy). These measurements ensure the most precise GA estimation, both absolutely (according to OPU) and relatively (between twins), without an effect of chorionicity and mode of conception.

MATERIALS AND METHODS

A retrospective study design was used. The cohort included all women with a viable first-trimester BC-BA twin gestation who conceived after IVF at a single tertiary, university-affiliated medical center, from 2007 to 2015. The study was approved by the local institutional review board of the Rabin Medical Center.

Study Population

Eligibility criteria included conception after IVF, in which a viable BC-BA twin gestation was sonographically detected during the first trimester, between 6+0 and 14+0 gestational weeks, as determined by OPU dating. Women with a monochorionic twin gestation were excluded, as well as women for whom data on pregnancy outcome were unavailable.

Data Collection

Data were extracted from maternal and neonatal medical records, as well as from the hospital's computerized antenatal sonographic database, fertility clinic treatment protocols, and delivery ward neonatal birth records. Collected data for each participant included maternal age, LMP, ET and OPU dates, CRL measurements, and pregnancy outcomes: delivery, abortion or termination, number of fetuses at birth, fetal gender, GA at delivery, and birth weight.

Data Analysis

We analyzed the association between first-trimester fetal size discrepancies and adverse pregnancy outcomes. Intrafetal and intertwin size discrepancies were evaluated as either the gap between actual GA, as calculated by OPU, and the evaluated GA determined by CRL measurements for each twin (intrafetal size discrepancy); or by CRL discrepancies between the twins (intertwin discrepancy).

Definitions

Actual GA was calculated by subtracting 14 days from the date of OPU. Estimated GA was evaluated according to CRL measurements for each twin. Crown-rump length measurements were obtained by experienced physicians and technicians, according to previously established guidelines (24), using transvaginal ultrasound. Bichorionic-biamniotic gestations were determined according to the presence of an extension of placental tissue at the base of the intertwin membrane, visualized by ultrasonography as the λ sign; or according to the presence of two separate gestational sacs, depending on GA at the ultrasound examination (25).

For each of the fetuses, Δ GA was defined as the gap, expressed in days, between the estimated GA according to CRL and the actual GA according to OPU (i.e., CRL-OPU). Consequently, a positive Δ GA indicated that the twin was absolutely larger than the actual GA; and a negative Δ GA indicated that the fetus was smaller than expected. Accordingly, for each twin gestation, the relatively larger twin was termed "Max" and the relatively smaller twin was termed "Min," regardless of their absolute sizes compared with the expected GA according to OPU. Additionally, another parameter, Δ Gap, was defined as the Δ GA difference between the twins.

Pregnancy outcome, in relation to the number of live-born fetuses, was subdivided into three categories: live-born twin delivery, live-born singleton delivery (due to abortion, termination, or intrauterine fetal death [IUFD] of one of the twins), and non-live-born pregnancy (due to abortion, termination, or IUFD of both twins). Abortion was considered as any spontaneous pregnancy loss prior to 20 weeks gestation. Intrauterine fetal death was defined if pregnancy loss occurred spontaneously after 20 weeks' gestation. Termination of pregnancy was performed electively after 20 weeks' gestation, according to maternal request and pending legal approval, because of severe chromosomal or anatomic malformations. Birth weight percentiles were defined for a given GA, per fetal gender, according to national accepted growth curves for multiple gestations (26).

Outcome Measures

The primary outcome measure was the number of live-born infants. Secondary outcome measures were GA at birth, birth weight percentile, and intertwin birth weight discordancy.

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