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ARTICLE

IVF outcomes in average- and poor-prognosis infertile women according to the number of embryos transferred

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Abstract Outcome measures of IVF success, which account for effectiveness of IVF and perinatal outcome risks, have recently been described. The association between number of embryos transferred in average and poor-prognosis IVF patients, and the chances of having good or poor IVF and perinatal outcomes, was investigated. Good IVF and perinatal outcome was defined as the birth of a live, term, normal-weight infant (≥2500 g). Poor IVF and perinatal outcome was defined as no live birth or birth of a very low weight neonate (<1500 g) or severe prematurity (birth at <32 weeks gestation). Each neonate was analysed as a separate outcome. A total of 713 IVF cycles in 504 average and poor-prognosis patients from January 2010 to December 2013 were identified. The odds of having good IVF and perinatal outcomes increased by 28% for each additional embryo transferred. The odds of poor IVF and perinatal outcome decreased by 32% with an additional embryo transferred. The likelihood of live birth with good perinatal outcome in average- and poor-prognosis patients after IVF increases with additional embryos being transferred. These data add to recently reported evidence in favour of multiple embryo transfer in older women and those with average or poor IVF prognosis.

KEYWORDS: IVF, perinatal outcomes, poor prognosis patients, poor responders

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Introduction

Decreasing the use of multiple embryo transfer (MET) after IVF is a major objective of the American Society for Reproductive Medicine (Practice Committee of Society for Assisted Reproductive Technology and Practice Committee of American Society for Reproductive Medicine, 2012). This initiative corresponds to years of indiscriminate use of MET to achieve higher pregnancy rates, which also led to higher order pregnancies and their associated perinatal complications, such as prematurity and low birth weight (ACOG, 2014). Indeed, MET unquestionably increases IVF pregnancy rates per cycle; therefore, there is an impulse from practitioners, as well as patients, to increase the number of embryos being transferred (Pandian et al., 2013). To decrease the high incidence of multiple pregnancy rates, the use of single embryo transfer (SET) has significantly increased. Outcome data from the Society for Assisted Reproductive Technologies (SART) demonstrate a 65% increase in the use of elective SET in fresh IVF cycles, from 8.8% to 14.5% from 2012 to 2013 (SART, 2013), consistent with efforts to limit the number of embryos transferred (Practice Committee of Society for Assisted Reproductive Technology and Practice Committee of American Society for Reproductive Medicine, 2012). The increase in use of SET has been successful in decreasing the number of twin pregnancies by 16.8% (SART, 2013).

Improving embryo selection and increasing live birth rates has been a decade-old goal in IVF, and several methods, including extended embryo culture (EEC) to blastocyst stage and preimplantation genetic screening (PGS), have been proposed to achieve both and facilitate the transfer of a single embryo (Gardner et al., 1998). Although EEC has been a basic premise of SET; however, both EEC and PGS, have so far been shown to be effective only in good-prognosis patients (Blake et al., 2007). Paradoxically, EEC and PGS are, however, widely used in poor-prognosis patients. Indeed, European data suggest that EEC and PGS are preferentially used in older women (De Rycke et al., 2015). Not surprisingly then, European assisted reproduction technique practitioners recently recommended elective single embryo transfer (eSET) for women above the age of 40 years (Niinimaki et al., 2013).

A recent study from The Center for Disease Control and Prevention (CDC), therefore, was highly relevant in reporting that young good-prognosis patients demonstrate best IVF and perinatal outcomes with eSET; yet, older patients with average or poor IVF prognosis demonstrated better chances of singleton full term live birth after MET (Kissin et al., 2014).

In poor-prognosis patients especially, the overall efficacy of SET remains unclear. In most IVF centres, such patients typically account for a relative small percentage of total IVF cycles, and are often denied access to reproductive care (Gleicher et al., 2007). Our centre is uniquely positioned to address this knowledge gap because such patients represent a majority of our population. Therefore, the objective of the present study was to assess IVF and perinatal outcomes in such patients depending on number of embryos being transferred (Gleicher et al., 2015).

Following the precedent of the CDC study, we selected an outcome measure of IVF success that simultaneously accounts for effectiveness of IVF (live-birth rates) and perinatal outcome risks (prematurity and low birth weight) (Kissin et al., 2014).

Materials and methods

Institutional Review Board approval

Our centre maintains patient medical information in an anonymized electronic research database. Our centre's Institutional Review Board approved use of this database, on 21 April 2015 (reference number ER03302015-01), for research on an expedited basis contingent upon receipt of informed consent from patients in advance, thus assuring confidentiality of the medical record and anonymity of the patient. These conditions were met for this study.

Study population and definitions

The electronic research database was searched for fresh non-donor IVF cycles with embryo transfer between January 2010 and December 2013. Only patients with either average or poor prognosis were included in this study, following the same criteria used to designate prognosis in IVF in the recent CDC study (Kissin et al., 2014). Favourable prognosis patients, defined as those undergoing first IVF cycles with excess embryos available for cryopreservation or women who had a previous successful IVF cycle, were excluded, as well as patients that underwent eSET. Previous failed IVF cycles (no previous live births) and no extra embryos for cryopreservation were defined as poor prognosis. Average prognosis was defined as patients undergoing first IVF cycles with no extra embryos for cryopreservation or those who had previous failed IVF cycles but had extra embryo(s) cryopreserved. Patients who underwent multiple IVF cycles could change prognosis categories based on above definitions in each cycle.

Ovarian stimulation

We previously reported our standard ovarian stimulation protocol for average and poor-prognosis patients (Gleicher et al., 2013). In short, patients are pre-supplemented with dehydroepiandrosterone and CoQ10 until normal levels of testosterone and sex hormone binding globulin are documented. They then undergo ovarian stimulation with daily FSH 300–450 IU concurrent with 150 IU of human menopausal gonadotropin, primarily in microdose agonist cycles. Once the lead follicle reaches 19–22 mm, 10,000 IU of HCG are administered and ultrasound-guided oocyte retrieval is carried out 34 h later. Average- and poor-prognosis patients undergo embryo transfer at the cleavage stage under ultrasound guidance. Embryo culture to blastocyst stage, PGS, or both, is only carried out in favourable prognosis patients in our practice, as both of these practices do not seem to be supported by current evidence in average- and poor-prognosis patient populations (Gleicher et al., 2015). Therefore, patients undergoing blastocyst stage transfer, PGS, or both, were not included in this study.

Outcome measures

A similar definition of good IVF and perinatal outcome was used, as recently published by the CDC (Kissin et al., 2014).