ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Factors associated with the use of elective single-embryo transfer and pregnancy outcomes in the United States, 2004–2012

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Objective: To evaluate factors associated with elective single-embryo transfer (eSET) utilization and its effect on assisted reproductive technology outcomes in the United States.
Design: Historical cohort.
Setting: Not applicable.
Patient(s): Fresh IVF cycles of women aged 18–37 years using autologous oocytes with either one (SET) or two (double-embryo transfer [DET]) embryos transferred and reported to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System between 2004 and 2012. Cycles were categorized into four groups with ([+]) or without ([−]) supernumerary embryos cryopreserved. The SET group with embryos cryopreserved was designated as eSET.
Intervention(s): None.
Main Outcomes Measure(s): The likelihood of eSET utilization, live birth, and singleton non–low birth weight term live birth, modeled using logistic regression. Presented as adjusted odds ratios (aORs) and 95% confidence intervals (CIs).
Result(s): The study included 263,375 cycles (21,917 SET[−]cryopreservation, 20,996 SET[+]cryopreservation, 103,371 DET[−]cryopreservation, and 117,091 DET[+]cryopreservation). The utilization of eSET (SET[+]cryopreservation) increased from 1.8% in 2004 to 14.9% in 2012 (aOR 7.66, 95% CI 6.87–8.53) and was more likely with assisted reproductive technology insurance coverage (aOR 1.60, 95% CI 1.54–1.66), Asian race (aOR 1.26, 95% CI 1.20–1.33), uterine factor diagnosis (aOR 1.48, 95% CI 1.37–1.59), retrieval of $\geq$16 oocytes (aOR 2.85, 95% CI 2.55–3.19), and the transfer of day 5–6 embryos (aOR 4.23, 95% CI 4.06–4.40); eSET was less likely in women aged 35–37 years (aOR 0.76, 95% CI 0.73–0.80). Compared with DET cycles, the likelihood of the ideal outcome, term non–low birth weight singleton live birth, was increased 45%–52% with eSET.
Conclusion(s): Expanding insurance coverage for IVF would facilitate the broader use of eSET and may reduce the morbidity and healthcare costs associated with multiple pregnancies. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Assisted reproductive technology, elective single-embryo transfer, in vitro fertilization, multiple pregnancy

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Historically, the transfer of multiple embryos with IVF was performed to maximize pregnancy rates but frequently resulted in multiple gestations (twins, triplets, and higher-order multiples gestations) (1). Transferring more than one embryo has been shown to have a harmful effect on intrauterine growth and length of gestation, even when only one embryo implants (2). Complications of prematurity associated with multiple gestation have been the most persistent adverse outcome of assisted reproductive technology (ART) and confer significant neonatal morbidity and healthcare expenditures (3). Refinements of controlled ovarian hyperstimulation protocols, extended embryo culture, and embryo selection criteria have resulted in fewer embryos transferred per cycle and improved ART pregnancy rates (4, 5). As a result, the rate of triplets and higher-order multiple gestation has been significantly reduced, but the incidence of ART twins has remained as high as 25%–40% per ET (6–11). It is desirable to modify current ET practices to increase term singleton live birth rates (12, 13).

Elective single-embryo transfer (eSET) was first utilized in Europe to reduce the rate of multiple gestation pregnancy and increase the rate of singleton pregnancy (14). With national ART insurance coverage legislation, several European nations have successfully implemented mandatory eSET policies while maintaining acceptable pregnancy rates (14, 15). An increase in eSET use in the United States has been observed since the first ET guidelines to recommend this practice in 2004 (16, 17). However, the use of eSET has been inconsistent (18, 19). Because eSET practice continues to evolve in the United States, it is timely to investigate the factors associated with this practice and its associated pregnancy outcomes. The objective of this study was to evaluate factors associated with eSET utilization and pregnancy outcomes using the Society for Assisted Reproductive Technology (SART) Clinic Online Reporting System from 2004 through 2012. This study encompassed analyses of cycle outcomes in women aged <38 years because this favorable-prognosis age group is most consistently considered for eSET.

This study was designed by the Clinical Research/Reproductive Scientist Training program, in collaboration with SART (20). Its goal is to provide clinicians in academic or private practice with training and networking opportunities that enable them to better contribute to clinical research in reproductive medicine. The Clinical Research/Reproductive Scientist Training scholars chose to evaluate factors associated with the use of eSET because the topic is of immediate relevance for practicing clinicians and patients. We hope that this report will help to inform the ongoing discussion regarding optimal ART treatments.

MATERIALS AND METHODS

The data for this study were obtained from the SART Clinic Outcome Reporting System (SART CORS), which contains comprehensive data from more than 90% of all clinics performing ART in the United States. Data were collected and verified by SART and reported to the Centers for Disease Control and Prevention, in compliance with the Fertility Clinic Success Rate and Certification Act of 1992 (Public Law 102-493). The Society for Assisted Reproductive Technology maintains Health Insurance Portability and Accountability Act–compliant business associates agreements with reporting clinics. In 2004, after a contract change with the Centers for Disease Control and Prevention, SART gained access to the SART CORS data system for the purposes of conducting research. The national SART CORS database for 2004–2012 contains 1,250,545 cycles among 642,715 women, resulting in 196,912 live births. The database includes information on demographic factors (age, race/ethnicity); ART factors (infertility diagnoses, oocyte source and state, use of micromanipulation, number of embryos transferred); treatment outcomes (number of fetal heart beats on early ultrasound, early pregnancy loss); and pregnancy outcomes (live born, stillborn, length of gestation, plurality, and genders). The data in the SART CORS are validated annually (21), with some clinics having on-site visits for chart review based on an algorithm for clinic selection. During each visit, data reported by the clinic were compared with information recorded in patients' charts. In 2012, records for 2,045 cycles at 35 clinics were randomly selected for full validation, along with 238 egg/embryo banking cycles (21). The full validation included review of 1,318 cycles for which a pregnancy was reported. Among the nondonor cycles, 331 were multiple-fetus pregnancies. Ten of 11 data fields selected for validation were found to have discrepancy rates of $\leq$5%. The exception was the diagnosis field, which, depending on the diagnosis, had a discrepancy rate between 2.1% and 9.2%.

This study included cycles reported to the SART CORS from January 1, 2004 through December 31, 2012. Cycles were limited to women who were US residents, between the ages of 18 and 37 years at cycle start, who used their own fresh oocytes and their partner's semen. The study was limited to cycles initiated in women aged <38 years because these patients are most consistently considered eSET candidates. Cycles were additionally limited to those with either one (SET) or two embryos transferred (double-embryo transfer, DET) and were categorized into four groups if additional embryos were or were not cryopreserved (i.e., SET without cryopreservation, SET with cryopreservation, DET without cryopreservation, DET with cryopreservation) during the same cycle. Excluded were all cycles that used gestational carriers, were designated as research cycles, or that had preimplantation genetic diagnosis or screening analysis.

Independent variables included reporting year of the cycle (2004–2012); insurance coverage in the woman's state of residence (mandated coverage [inclusive of ART (IVF)] or some coverage [not inclusive of ART (IVF)]); region of country of the infertility clinic (Northeast [subregions: New England, Mid-Atlantic], Midwest [subregions: East-North-Central, West-North-Central], South [subregions: South Atlantic, East-South-Central, West-South-Central], and West [Mountain, Pacific]); woman's age (continuous, and as 18–29, 30–34, and 35–37 years at cycle start), race/ethnicity (white, Asian, black, Hispanic, other, and unknown), body mass index (14.0–18.4, 18.5–24.9, 25.0–29.9, 30.0–34.9, $\geq$40.0 kg/m^2, and not stated), smoking status (current, prior 3 months, and nonsmoker), gravidity (0, 1, $\geq$2), and