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Guidelines for the Number of Embryos to Transfer Following In Vitro Fertilization

This guideline was reviewed by the Reproductive Endocrinology and Infertility Committee and the Maternal-Fetal Medicine Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada and the Board of the Canadian Fertility and Andrology Society.

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Abstract

Objective: To review the effect of the number of embryos transferred on the outcome of in vitro fertilization (IVF), to provide guidelines on the number of embryos to transfer in IVF-embryo transfer (ET) in order to optimize healthy live births and minimize multiple pregnancies.

Options: Rates of live birth, clinical pregnancy, and multiple pregnancy or birth by number of embryos transferred are compared.

Outcomes: Clinical pregnancy, multiple pregnancy, and live birth rates.

Evidence: The Cochrane Library and MEDLINE were searched for English language articles from 1990 to April 2006. Search terms included embryo transfer (ET), assisted reproduction, in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), multiple pregnancy, and multiple gestation. Additional references were identified through hand searches of bibliographies of identified articles.

Values: Available evidence was reviewed by the Reproductive Endocrinology and Infertility Committee and the Maternal-Fetal Medicine Committee of the Society of Obstetricians and Gynaecologists of Canada and the Board of the Canadian Fertility and Andrology Society, and was qualified using the Evaluation of Evidence Guidelines developed by the Canadian Task Force on the Periodic Health Exam.

Benefits, Harms, and Costs: This guideline is intended to minimize the occurrence of multifetal gestation, particularly high-order multiples (HOM), while maintaining acceptable overall pregnancy and live birth rates following IVF-ET.

Recommendations

The recommendations made in this guideline were derived mainly from studies of cleavage stage embryos—those cultured for two or three days.

1. Individual IVF-ET programs should evaluate their own data to identify patient-specific, embryo-specific, and cycle-specific determinants of implantation and live birth in order to develop embryo transfer policies that minimize the occurrence of multifetal gestation while maintaining acceptable overall pregnancy and live birth rates. (III-B)

2. In general, consideration should be given to the transfer of fewer blastocyst stage embryos than cleavage stage embryos, particularly in women with excellent prognoses and high-quality blastocysts. (I-A)

Summary Statement

The following recommendations are generally intended for cleavage stage embryos transferred on day two or three. Because

Table 1. Criteria for quality of evidence assessment and classification of recommendations

Level of evidence*	Classification of recommendations†
I: Evidence obtained from at least one properly designed randomized controlled trial.	A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
II-1: Evidence from well-designed controlled trials without randomization.	B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group.	C. There is poor evidence regarding the inclusion or exclusion of the condition in a periodic health examination.
II-3: Evidence from comparisons between times or places with or without the intervention. Dramatic results from uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.	D. There is fair evidence to support the recommendation that the condition not be considered in a periodic health examination.
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.	E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

∗The quality of evidence reported in these guidelines has been adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on the Periodic Health Exam.[55]
†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on the Periodic Health Exam.[55]

blastocyst stage embryos have higher implantation rates than cleavage stage embryos, fewer blastocyst stage embryos may need to be transferred. (II)

Recommendations (continued)

3. In women under the age of 35 years, no more than two embryos should be transferred in a fresh IVF-ET cycle. (II-2A)
4. In women under the age of 35 years with excellent prognoses, the transfer of a single embryo should be considered. Women with excellent prognoses include those undergoing their first or second IVF-ET cycle or one immediately following a successful IVF-ET cycle, with at least two high-quality embryos available for transfer. (I-A)
5. In women aged 35 to 37 years, no more than three embryos should be transferred in a fresh IVF-ET cycle. In those with high-quality embryos and favourable prognoses, consideration should be given to the transfer of one or two embryos in the first or second cycle. (II-2A)
6. In women aged 38 to 39 years, no more than three embryos should be transferred in a fresh IVF-ET cycle. (III-B) In those with high-quality embryos and favourable prognoses, consideration should be given to the transfer of two embryos in the first or second cycle. (III-B)
7. In women over the age of 39 years, no more than four embryos should be transferred in a fresh IVF-ET cycle. (III-B) In those older women with high-quality embryos in excess of the number to be transferred, consideration should be given to the transfer of three embryos in the first IVF-ET cycle. (III-B)
8. In exceptional cases when women with poor prognoses have had multiple failed fresh IVF-ET cycles, consideration may be given to the transfer of more embryos than recommended above in subsequent fresh IVF-ET cycles. (III-C)
9. In donor–recipient cycles, the age of the oocyte/embryo donor should be used when determining the number of embryos to transfer. (II-2B)
10. In women with obstetrical or medical contraindication to multifetal gestation, fewer embryos should be transferred to minimize the chance of multifetal gestation. In such cases, pre-treatment consultation with a maternal-fetal medicine specialist should be pursued. (III-C) Whenever reasonable, consideration should be given to the transfer of a single embryo. (II-3B)
11. Couples should be adequately counselled regarding the obstetrical, perinatal, and neonatal risks of multifetal gestation to facilitate informed decision making regarding the number of embryos to transfer. (II-3B) Emphasis on healthy singleton live birth as the measure of success in IVF-ET may be beneficial in promoting a reduction in the number of embryos transferred. (III-C)
12. A strategy for public funding of IVF-ET must be developed for the effective implementation of guidelines limiting the number of embryos transferred. In the context of this strategy, total health care costs would be lower as a result of reductions in the incidence of multifetal pregnancies and births. (III-C)
13. Efforts should be made to limit iatrogenic multiple pregnancies resulting from non–IVF-ET ovarian stimulation through the development of suitable guidelines for cycle cancellation and the removal of financial barriers to IVF-ET. (III-B)

Validation: This guideline was reviewed by the Reproductive Endocrinology and Infertility Committee and the Maternal-Fetal Medicine Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada and the Board of the Canadian Fertility and Andrology Society.

Sponsor: Society of Obstetricians and Gynaecologists of Canada.

The quality of evidence reported in this document has been described using the Evaluation of Evidence criteria outlined in the Report of the Canadian Task Force on the Periodic Health Exam (Table 1).

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INTRODUCTION

In Canada, 1645 deliveries resulted from embryo transfer following in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) in 2001.[1] Of these, 31.5% were multiple births. Data from the Canadian Fertility and Andrology Society (CFAS) show that the incidence of multiple deliveries after IVF-embryo transfer (ET) had