DEBATE: The single embryo transfer myth

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Proponents of elective single embryo transfer (eSET) are trying to avoid twin pregnancies, which they believe carry greater risks and costs than singleton pregnancies. Transfer of only one embryo, of course, avoids almost all twin pregnancies. eSET in comparison to 2-embryo transfers (2ET), however, significantly reduces clinical pregnancy and live birth chances in IVF.

Proponents of eSET consider these decreases more than compensated by above noted lower outcome risks for singletons, especially since two consecutive eSETs (one fresh and one frozen) result in similar clinical pregnancy and live birth rates than a 2ET. We have argued that proponents of eSET are mistaken in claiming higher outcome risks and costs for twin over singleton pregnancies because their conclusions were incorrectly based on comparisons of outcomes between 2 twins and 1 singleton, while correct statistical comparisons have to be matched for outcomes (i.e. 2 children). If this is done and outcomes are compared between 2 twins and 2 consecutive singletons, twins do no longer demonstrate significantly increased clinical outcome risks and costs.

This means that eSET reduces pregnancy chances without compensatory gains and, therefore, should not be used, unless patients do not wish to conceive twins and/or have medical contraindications to twin deliveries. This argument applies even more to intermediate and especially poor prognosis patients because eSET is usually combined with extended embryo culture to blastocyst stage, which in poor prognosis patients, by itself, reduces pregnancy and live birth chances.

Finally, the Duch investigators Helmerhorst et al already in 2004 reported that treatment outcomes after IVF and after spontaneous conception could not be assumed to be the same for either singleton or twin births (BMJ 2004; 328:261). After reviewing the literature up to that point, they concluded that twins born after IVF demonstrated approximately 40% lower outcome risks than spontaneously conceived twins, while in singletons the opposite was true: IVF singletons demonstrated higher outcome risk that spontaneously conceived twins. Since by proponents of eSET alleged higher twin risks were based on spontaneously conceived twins, these data overestimated twin risks after IVF, therefore, by ca. 50%.

Since obstetrical practice patterns have changed over the last decade, our recently published study set out to determine whether Helmerhorst et al in 2004 were still valid [*Gleicher et al., Risks of spontaneously and IVF-conceived singleton and twin pregnancies differ, requiring reassessment of statistical premises favoring elective single embryo transfer (eSET) Reprod Biol Endocrinol 2016;14:25)]* and, indeed, reaffirmed the Dutch report by demonstrating that severe outcome risks are approximately 50% lower for IVF than spontaneous twins, while milder perinatal outcome risks are exaggerated by approximately 25% if data are taken from spontaneously conceived twins. IVF twins, thus, do not appear to generated increased outcome risks in comparison to IVF singletons, raising serious questions about the increasing utilization of eSET.

This conclusion is also supported by longitudinal live birth rate dat in regions of the world that integrated eSET into routine IVF practice more aggressively. These regions uniformly demonstrated

significant declines in live birth rates and often also compensatory increases in IVF cycle starts, thereby raising further questions about the alleged cost-effectiveness of eSET.

Translational relevance: Based on here presented data eSET appears neither medically nor economically indicated, unless patients oppose twin pregnancies for persona/social reasons or exhibit medical contraindications