ELECTIVE SINGLE EMBRYO TRANSFER

Elective Set, Eset, E-Set, Elective Single Blastocyst Transfer, Esbt

The procedure of transfer one single good quality embryo in cleavage stage or in stage of blastocyst that was selected as the most appropriate.

About Elective single embryo transfer

The technique of selecting only one embryo to transfer to the woman is called elective-Single Embryo Transfer (e-SET) or, when embryos are at the blastocyst stage, it can also be called elective single blastocyst transfer (eSBT). It significantly lowers the risk of multiple pregnancies, compared with e.g. double embryo transfer (DET) or double blastocyst transfer (2BT), with a twinning rate of approximately 3.5% in SET compared with approximately 38% in DET, or 2% in eSBT compared with approximately 25% in 2BT. At the same time, pregnancy rates is not significantly less with eSBT than with 2BT. That is, the cumulative live birth rate associated with single fresh embryo transfer followed by a single frozen and thawed embryo transfer is comparable with that after one cycle of double fresh embryo transfer.

Given that the transfer of multiple embryos increases the risk of a multiple gestation, many have suggested a move towards elective single embryo transfer (eSET), although this recommendation has been focused mainly on women less than age 36. In a fresh IVF cycle, single-embryo transfer (SET) is associated with a lower rate of multiple pregnancies than other principles of embryo transfer. For this reason, SET became more popular in the past decade and had a good perinatal outcome in the US, in the Nordic countries, and even in Asia in recent years. Several randomized controlled trials in Europe have demonstrated that eSET significantly diminishes twin gestations and yields comparable live birth rates in good prognosis patients (Graph 1).
A handful of European studies have also addressed the role of eSET in the advanced maternal age population. One study found that eSET could be safely applied to patients aged 36–39, while dramatically decreasing the multiple gestation rate (MGR) and achieving similar pregnancy rates (PRs). Another study found that eSET could be offered to women younger than 38 in the first three IVF treatment cycles without compromising PR, although the mean patient age in this study was 32.5 years.

While these studies analyzing eSET have focused primarily on day 3 embryo transfer, blastocyst transfer (BT) has also emerged as a potential approach to reducing MGR as generally fewer embryos are transferred. Several studies have shown superior outcomes with BT compared to cleavage stage embryo transfer (see Tab. 1). The superior implantation rate seen with BT has mainly been attributed to better embryo selection.

Selection of the best embryo for transfer is crucial for the eSET. During the past 15 years, various approaches were suggested, including morphological classification, proteomic and metabolomic investigations and time lapse follow-up. The increasing incidence of aneuploidy with advanced maternal age requires a reliable diagnostic method for chromosome aneuploidies, and recent reports indicate that none of the non-invasive approaches are reliable enough for this purpose. Therefore, embryo biopsy, preferably at the blastocyst stage and accompanied by comprehensive chromosome screening may be advised in some patients with higher risk of aneuploidy.

**Success or failure factors**

Women who are indicated as proper candidate (age under 36, first assisted reproductive cycle, previous successful pregnancy by assisted reproduction, sufficiency of high-quality embryos and enough embryos for cryopreservation) have high potential of successful transfer (about 48%). If it is not fulfilled one of the recommendations above, potential decreases. There is also risk of failure. It can be selected under-quality embryo with potential abnormalities.

On the other hand, eSET is the only option how to minimalize multiple pregnancies.

**Complications**

Although the optimal outcome of assisted reproductive technology (ART) is a healthy singleton pregnancy, the rate of twin gestation from ART in women
over the age of 35 is persistently high. By eSET there is still some risk of twin pregnancy, about 2-3%. Twin gestations carry increased risk of adverse outcomes, such as prematurity, low birth weight, infant mortality, and maternal mortality. Twin gestations also compound the health threats to women of advanced maternal age, who are already at increased risk of developing complications such as gestational diabetes and preeclampsia. For example, women over the age of 35 with preeclampsia have three times the risk of pregnancy-related mortality than their younger counterparts. These adverse outcomes have had a considerable impact on public health and many have called for policy change to decrease the prevalence of multiple gestation.

**Prognosis**

Elective single blastocyst transfer appears to significantly lower the risk of multiple gestation without compromising PR. However, more studies, ideally prospective and randomized, are needed to further investigate the role of eSBT in older women with blastocysts available for cryopreservation, as women of advanced maternal age are at particularly high risk of complications associated with multiple gestations. Preliminary results suggest that good prognosis patients undergoing BT, including those of advanced maternal age, who wish to avoid a multiple gestation should transfer a single blastocyst, reassured that PRs do not seem to be significantly compromised.

**Find more about related issues**

**Diagnoses**

**Bicornuate uterus**
Inborn morphological deviation of the uterus - one of the Müllerian duct anomalies where the uterine cavity is divided in the upper part.
Learn more at: [www.fertilitypedia.org/therapy/diag/bicornuate-uterus](http://www.fertilitypedia.org/therapy/diag/bicornuate-uterus)

**Unicornuate uterus**
Congenital uterine anomaly (one of the Müllerian duct anomalies) usually associated with communicating or non-communicating rudimentary horn.
Learn more at: [www.fertilitypedia.org/therapy/diag/unicornuate-uterus](http://www.fertilitypedia.org/therapy/diag/unicornuate-uterus)
**Uterine malformations**
A type of female genital malformation resulting from an abnormal development of the Müllerian duct(s) during embryogenesis.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterine-malformations](http://www.fertilitypedia.org/therapy/diag/uterine-malformations)

**Uterus duplex**
Congenital uterine malformation where both Müllerian ducts develop but fail to fuse, thus the woman has a "double uterus".
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-duplex](http://www.fertilitypedia.org/therapy/diag/uterus-duplex)

**Uterus septus**
A form of a congenital malformation where the uterine cavity is partitioned by a longitudinal septum. It is one of Müllerian duct anomalies.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-septus](http://www.fertilitypedia.org/therapy/diag/uterus-septus)

**Uterus subseptus**
A form of a congenital malformation where the uterus is partially divided by a longitudinal septum. It is one of Müllerian duct anomalies.
Learn more at: [www.fertilitypedia.org/therapy/diag/uterus-subseptus](http://www.fertilitypedia.org/therapy/diag/uterus-subseptus)

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**Graph 1: Graphical representation of the results obtained after the introduction of the eSET policy**
*Impact of the eSET policy in cumulative DR and multiple pregnancy rate over the 4 years. While no differences are observed in cumulative DR, the MPR is significantly reduced after the intervention as assessed by logistic regression analysis.*

**Tab**
*Pregnancy outcomes in 108 women who chose eSBT were compared to 415 women who chose eDBT. The mean age of patients undergoing eDBT (35.0 years) was significantly higher than the mean age of patients undergoing eSBT (33.9 years).*

<table>
<thead>
<tr>
<th></th>
<th>eSBT ($n = 108$)</th>
<th>eDBT ($n = 415$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean [SD]</td>
<td>33.9 [3.2]</td>
<td>35.0 [3.6]</td>
<td>0.0006&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prior live birth (%)</td>
<td>28/108 (25.9)</td>
<td>76/339 (18.3)</td>
<td>0.08&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Oocytes, mean [SD]</td>
<td>17.0 [6.5]</td>
<td>17.2 [6.5]</td>
<td>0.58&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Embryos, mean [SD]</td>
<td>12.4 [5.8]</td>
<td>12.2 [4.9]</td>
<td>0.84&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Blastocysts, mean&lt;sup&gt;d&lt;/sup&gt; [SD]</td>
<td>6.5 [3.8]</td>
<td>6.2 [3.0]</td>
<td>0.77&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>PGD (%)</td>
<td>9/108 (8.3)</td>
<td>25/413 (6.0)</td>
<td>0.28&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clinical PR (%)</td>
<td>62/108 (57.4)</td>
<td>207/415 (49.9)</td>
<td>0.16&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Live birth/ongoing PR (%)</td>
<td>52/108 (48.1)</td>
<td>173/415 (41.7)</td>
<td>0.22&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>MGR (%)</td>
<td>1/62 (1.6)</td>
<td>67/207 (32.4)</td>
<td>0.00&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cesarean rate (%)</td>
<td>12/38 (31.6)</td>
<td>61/161 (37.9)</td>
<td>0.47&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Birthweight, mean (g)</td>
<td>3226.2</td>
<td>2832.2</td>
<td>0.001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> $P < 0.01$: t-test.
<sup>b</sup> $P < 0.00005$: chi-square test.
<sup>c</sup> $P < 0.005$: t-test.
<sup>d</sup>Blastocysts: mean includes blastocysts cryopreserved and transferred.
“Reduction of multiple pregnancies in the advanced maternal age population after implementation of an elective single embryo transfer policy coupled with enhanced embryo selection: pre- and post-intervention study” —by Ubaldi at al. licensed under CC BY-NC 4.0

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