Outcomes of Fresh and Cryopreserved Oocyte Donation

Use of oocytes donated for in vitro fertilization (IVF) has increased in recent years. Donated fresh oocytes traditionally have been used immediately, creating embryos for transfer into the uterus, with extra embryos being cryopreserved for later use. In January 2013, the American Society for Reproductive Medicine declared the technique of oocyte cryopreservation (egg freezing) no longer experimental, although it called for “more widespread clinic-specific data on the safety and efficacy of oocyte cryopreservation ... before universal donor oocyte banking can be recommended.”

Based on data that IVF outcomes with cryopreserved and fresh donor oocytes are comparable, some IVF centers established frozen donor egg banks. However, data reflecting IVF outcomes in routine clinical practice with cryopreserved donor oocytes have not been published.

Methods | We used data from the 2013 annual report of US IVF center outcomes published by the Society for Assisted Reproductive Technology to compare live birth and cycle cancellation rates using either fresh or cryopreserved donor oocytes. This aggregate data set is based on center-specific voluntarily reported outcomes from 380 of 467 (81.4%) US-based fertility centers, which in 2013 collectively performed 91.7% of all IVF cycles. Once verified, data are transmitted to the US Centers for Disease Control and Prevention in accordance with legal requirements.

Annual validation via select onsite visits, including chart review, suggests low-discrepancy rates (<5%) for reported data, which are publicly available online. Because individual patients cannot be identified, the study received expedited institutional review board approval and a waiver of the need for informed consent. Cycles involving cryopreserved embryos were excluded.

Canceled cycles and live births per recipient IVF cycle start and per embryo transfer procedure were compared using the 2-tailed Fisher exact test and the Wilson test for binomial proportions. The number of embryos transferred was compared using a 2-sided Wald test and a P value for Poisson distribution. A 2-sided P value of <.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc).

Results | Of 11,148 oocyte donation cycles, 2,227 (20.0%) involved use of cryopreserved donor oocytes (Table). Initiated cycles were canceled in 11.7% of fresh oocyte cycles vs 8.5% of cryopreserved oocyte cycles (difference, 3.2% [95% CI, 1.9%-4.6%]; P < .001). Per started recipient cycle, the live birth rates were 49.6% with fresh vs 43.2% with cryopreserved oocytes (difference, 6.4% [95% CI, 4.1%-8.7%]; P < .001). Per embryo transfer, the live birth rates were 56.1% with fresh vs 47.1% with cryopreserved oocytes (difference, 9.0% [95% CI, 6.6%-11.4%]; P < .001). Patients using fresh oocytes had a mean of 1.7 embryos transferred vs 1.6 embryos for patients using cryopreserved oocytes (difference, 0.1 [95% CI, 0-0.2]; P = .001).

Discussion | In 2013, 20.0% of all studied donor egg recipient cycles used cryopreserved oocytes. In vitro fertilization using cryopreserved donor oocytes was associated with lower cancellation rates, but also lower live birth rates than donor cycles using fresh oocytes.

Availability of cryopreserved oocytes simplifies IVF logistics because coordination with the donor’s cycle is no longer necessary. Banked oocytes also may reduce costs per IVF cycle because oocytes from one donor can be shared by several recipients. However, the added convenience and lower cycle costs must be balanced against the lower live birth rates with use of cryopreserved oocytes.

The reasons for lower live birth rates with use of cryopreserved oocytes remain to be established. One possible explanation is less opportunity for proper embryo selection due to smaller starting numbers of oocytes, leading to fewer embryos available for transfer. Alternatively, oocyte quality may be negatively affected by cryopreservation and thawing. These findings need to be viewed with caution because they are based on anonymized aggregate outcomes, which...

<table>
<thead>
<tr>
<th></th>
<th>Fresh Donor Oocytes</th>
<th>Cryopreserved Donor Oocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Per*</td>
</tr>
<tr>
<td>Live birth per recipient start</td>
<td>4425</td>
<td>8921</td>
</tr>
<tr>
<td>Live birth per embryo transfer</td>
<td>4418</td>
<td>7875</td>
</tr>
<tr>
<td>Canceled cycles</td>
<td>1046</td>
<td>8921</td>
</tr>
<tr>
<td>Mean No. of embryos transferred</td>
<td>1.7</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

* Per started recipient cycle, the live birth rates were 49.6% with fresh vs 43.2% with cryopreserved oocytes (difference, 6.4% [95% CI, 4.1%-8.7%]; P < .001).

** Indicates the 95% CI for the mean.
Letters

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Author Contributions: Dr Kushnir had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis. Study concept and design: Kushnir, Barad. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Kushnir. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Kushnir, Darmon. Administrative, technical, or material support: Barad, Gleicher.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Kushnir reported serving as a consultant to the US Centers for Disease Control and Prevention. Dr Barad reported being a shareholder in Fertility Nutraceuticals LLC and owner of the Center for Human Reproduction (CHR). The CHR routinely reports in vitro fertilization outcome data annually to the CDC and the Society for Assisted Reproductive Technology.

In BRIGHT, patients in the heparin-only group received a bolus dose of 100 U/kg. Asian patients are more susceptible to heparin, and their optimal dose is about 10 U/kg lower than for non-Asian patients.4 Furthermore, no convincing data exist for East Asian patients to support the clinical benefit of a glycoprotein Ilb/Ilia inhibitor due to an increased risk of major bleeding. For the heparin plus tirofiban group in BRIGHT, a standard dose of tirofiban (10 μg/kg) was given instead of the guideline-recommended high dose (25 μg/kg), but this regimen also increased the bleeding risk.

The risk of stent thrombosis did not increase with bivalirudin vs heparin infusion in BRIGHT, which used a high-dose infusion after percutaneous coronary intervention (PCI) for a median of 3 hours. The European Ambulance Acute Coronary Syndrome Angiography (EUROMAX) study also used a bivalirudin infusion after PCI for a median of 4.5 hours, and half of the patients were also treated with potent P2Y12 inhibitors.3

The 30-day risk of stent thrombosis appeared lower in BRIGHT than in EUROMAX (0.6% vs 1.6%). Pharmacokinetic and pharmacodynamic profiles of bivalirudin are similar between Chinese and white patients, but differences in hypercoagulable states between the races may explain this disparity.3

Taken together, East Asian patients have shown a unique response to antithrombotic agents and have a potentially different risk-benefit profile than Western populations. Simple application of Western guidelines, mostly based on clinical data derived from Western populations, may not be appropriate for East Asian patients. Therefore, BRIGHT is an important step toward the concept of race-tailored antithrombotic therapy.

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COMMENT & RESPONSE

Varying Responses to Antithrombotic Treatment by Race/Ethnicity

To the Editor An increasing body of data has shown that East Asian patients have a lower risk of thrombosis and an increased risk of bleeding during antithrombotic treatment for acute coronary syndrome than do white patients.1 The Bivalirudin in Acute Myocardial Infarction vs Heparin and GPI Plus Heparin Trial (BRIGHT) was conducted in China.2 Most of the patients received a loading dose of clopidogrel of 300 mg to 600 mg.

Because East Asian patients have a higher prevalence of the cytochrome P450 2C9 loss-of-function allele than white patients (approximately 65% vs approximately 25%),3 the antiplatelet effect achieved with clopidogrel loading is more limited among East Asian patients. However, the risk of reinfarction or stent thrombosis in BRIGHT was similar or lower than in other studies of Western populations.3,4

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