Six years' experience in ovum donation using vitrified oocytes: report of cumulative outcomes, impact of storage time, and development of a predictive model for oocyte survival rate

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Objective: To describe the clinical outcomes achieved after 6 years' experience in ovum donation conducted with vitrified oocytes; to attempt to find predictors of survival; and to provide information about the probability of having a baby according to the number of oocytes consumed.
Design: Retrospective, observational study.
Setting: Private university-affiliated in vitro fertilization center.
Patient(s): Recipients of vitrified oocytes (January 2007–March 2013), including all the warming procedures (n = 3,610) and all the donations made during the same period (n = 3,467).
Intervention(s): None.
Main Outcome Measure(s): Survival rate per warming procedure, cumulative delivery rates (CDR) per single donation cycle, oocyte-to-baby rate, and cumulative live birth rate (CLBR) per oocyte consumed.
Result(s): Oocyte survival rate was 90.4%. It was not possible to develop a predictive model for survival owing to the lack of prognostic value of the studied variables. Implantation, clinical, and ongoing pregnancy rates per donation cycle were 39.0% (95% confidence interval [CI], 37.8–40.5), 48.4% (95% CI, 46.7–50.1), and 39.9% (95% CI, 38.3–41.5), respectively. Statistical differences were found when comparing blastocysts versus day 3 ETs (42.5%; 95% CI, 40.4–45.2 vs. 37.5%; 95% CI, 35.3–39.7 ongoing pregnancy rate). The CDR/donation cycle, including cryotransfers, was 78.8% (95% CI, 73.5–84.1). The oocyte-to-baby rate was 6.5%. CLBR increased progressively according to the number of oocytes consumed.
Conclusion(s): We provide detailed information about the high efficiency of using vitrified/warmed oocytes. There is currently no way of estimating donors' oocytes survival when considering baseline characteristics, storage time, or controlled ovarian stimulation parameters. The probability of achieving a baby using vitrified oocytes increases progressively with the number of oocytes consumed. (Fertil Steril® 2015;104:1426–34. ©2015 by American Society for Reproductive Medicine.)
Key Words: Ovum donation, vitrification, survival rate, delivery rate, predictive value, live birth

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Vitrification is currently the gold standard for female gamete cryopreservation. Oocyte banks were established when high postwarming survival was ensured thanks to a technique capable of eliminating the harmful effects caused by ice crystals, which, from the cost/benefit point of

view, has made the use of such protocols in a number of classic indications and other recently introduced ones reasonable.

The contemporary oocyte vitrification application has also been reported in infertile patients, whose own oocytes have been used for IVF (1, 2), and also in fertility preservation cases for either cancer or other medical and nonmedical conditions (3). Currently, vitrified oocytes within ovum donation programs are used in several centers worldwide (4–9). A large prospective randomized study proved that the ongoing pregnancy rate (OPR), on the basis of an intention to treat analysis (ITT), was comparable between vitrified and fresh oocytes (10). A very high survival rate, which led to a high incidence of vitrification of surplus embryos, also offered the added advantage of possibly increasing the cumulative outcomes obtained from single donations (11).

Efficient oocyte cryobanking has eliminated the need for synchronization between donor and recipient. This strategy has proven efficient to overcome the drawback related to long waiting lists while helping with travel-related logistics and setting ET dates so that patients feel much less stressed and more confident and comfortable.

Although information in the literature on outcomes achieved with vitrified oocytes has increased in recent years, we are still far from eliminating fresh donations, and definitively switch to egg banking. This is perhaps because there are still some loose ends left to tie up, especially in relation to lack of experience, availability of a wide variety of protocols and vitrification devices, very little knowledge about the management and logistics of such banks, and lack of success predictors and information on the probability of achieving a baby according to number of oocytes.

After 6 years of wide oocyte vitrification applications in our clinical setting for either ovum donation or own oocytes, we observed that although efficiency after vitrification was very good, sporadic cases can emerge in which survival can be very low, or even zero. In such cases, it is likely that the donation is cancelled if some other suitable cryostored oocytes are not available at the time, with the resulting inconveniences for the recipient. We must not fail to add the negative consequences of cancellations for the IVF center, such as loss of time, labor, and material, which all result in a significant economic burden. These problems can worsen if vitrified oocytes come from a different IVF center, which is common practice in some countries running egg-banking donation programs.

One possible cause for the decline in survival has been attributed to storage time, especially in relation to the devices that use a minimum vitrification solution volume or where the eggs have been stored in vapor tanks (12). All the drawbacks presented by random lack of survival after vitrification can be overcome, or at least anticipated, if we have some keys to predict the survival of stored oocytes. In line with this, the development of a predictive survival model would be more than welcome. Our experience in cryobanking oocytes has made available a large database. This database could be most useful for not only describing the scope of the egg-banking strategy for clinical efficiency and yielding donations in a well-established and consistent program but also for analyzing all potentially influencing factors and for attempting to find oocyte survival predictors. Being able to calculate the number of oocytes that have been consumed by recipients to achieve a baby will be most interesting for patients and also for physicians so that they can provide counseling about patients' chances according to the number of oocytes consumed while on treatment(s). Alternatively, all this information could be generalizable, to some extent, to fertile and/or infertile patients who have vitrified oocytes for either fertility preservation purposes or for part of their IVF treatment.

In this observational study, we describe our experience and the outcomes we have achieved after 6 years of ovum donation conducted with vitrified oocytes. This experience involves analyzing the oocyte survival rate, the possible effects of storage time on survival, and other relevant factors, including donors' baseline and controlled ovarian stimulation (COS) parameters, in an attempt to find predictors of oocyte survival. The oocyte-to-baby rate and a model for calculating the cumulative live birth rate (CLBR) according to the number of oocytes used up have been developed. This study also provides a descriptive analysis of the clinical outcomes obtained to date in the largest ever available series, which, to some extent, can contribute to knowledge in this field.

MATERIALS AND METHODS

Study Population

During the period covering January 2007 to March 2013, 2,140 donors (n = 3,146 vitrification cycles and 3,610 warming procedures), involving 42,152 metaphase (MII) vitrified oocytes, were recruited (Supplemental Fig. 1). Institutional Review Board approval was obtained for this study. A vitrification cycle comprised each COS cycle, which ended in ovum pick-up (OPU), plus MII vitrification. A warming procedure was defined as the process during which a previously defined number of oocytes from a donor was warmed up for the purpose of carrying out a donation. The number of initially assigned oocytes depends on the number of MII oocytes retrieved, proven donor fertility, the recipient's previous reproductive history, and the programmed day of ET (day 3 or the blastocyst stage). This may result in a range of 8–15 oocytes for each patient. Occasionally, more than one warming procedure per vitrification cycle was performed if many oocytes from a vitrification cycle were available. A donation cycle was also defined as the process during which a group of oocytes from a single warming procedure was actually allocated to a recipient for the purpose of performing the corresponding planned IVF procedures according to patient requirements.

Protocol for Donors

All the donors in our program fulfilled our inclusion criteria: [1] women with good physical and mental health, under 35 years of age, with regular menstrual cycles of 21–35 days, and no family history of hereditary or chromosomal diseases; [2] normal karyotype; [3] body mass index (BMI) of 18–29 kg/m^2; [4] absence of polycystic ovaries, endometriosis, more than two previous miscarriages, or gynecological or medical disorders; and [5] a negative screening result for