

Repetitive oocyte donation: a committee opinion

Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology

Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology, Birmingham, Alabama

Donors should be advised of the number of cycles/donations that a given oocyte donor may undergo. Although existing data cannot permit conclusive recommendations, concern for the issues of safety and well-being of oocyte donors warrants consideration. This document replaces the document of the same name, previously published in 2014. (*Fertil Steril*® 2020;113:1150–3. ©2020 by American Society for Reproductive Medicine.)

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Donor cycles are relatively common in assisted reproductive technology (ART), and the number of donor cycles using fresh and frozen oocytes was more than 7,800 cycles in 2016 in the United States (1). Women may choose to donate oocytes more than one time, giving rise to concerns about the optimal number of times that each woman should donate, both to protect the health of the donor and to avoid issues of consanguinity. This discussion will address the issue of whether limits should be advised on the number of cycles/donations that a given oocyte donor may undergo. Although existing data cannot permit conclusive recommendations, concern for the safety and the well-being of oocyte donors warrants consideration.

The practice of oocyte donation has potential risks for the donor, including the risks associated with ovarian stimulation, the oocyte retrieval procedure, and anesthesia, among others. Although the recipient derives a clear and tangible benefit from oocyte donation, the donor derives benefit only

through a sense of altruism and/or financial compensation for her services. Therefore, the question arises of whether the number of times that a given oocyte donor might donate her gametes should be limited. Despite the absence of definitive, long-term follow-up data, there has nonetheless been motivation on the part of ART practitioners to develop a consensus for a prudent approach. Unusual circumstances should be considered on an individual basis before surpassing the maximum number of donations proposed by these suggested limits.

RISKS OF INADVERTENT CONSANGUINITY

Inadvertent consanguinity resulting from oocyte donation could occur if a given donor has donated to two or more unrelated families and the offspring are unaware of their specific genetic heritage. Previous documents on donor insemination published by the American Society for Reproductive Medicine (ASRM) and others have advised informing offspring that they

are the product of donated gametes and maintaining a limit of no more than 25 pregnancies per sperm donor in a catchment area of 800,000 residences to minimize the risk of consanguinity (2–4). Subsequent studies have commented that additional factors, including the lifting of donor anonymity, genetic carrier screening, and social changes in mobility and attitude, could further reduce the risk of inadvertent consanguinity (5–7). Given that oocyte donation is a complex process and may result in cryopreserved oocytes, embryos, and an unpredictable number of pregnancies over a long period of time and a wide geographical region, it is reasonable to also limit the number of oocyte donations rather than the number of resulting pregnancies. The suggestions outlined here may require modification if the population using donor gametes represents an isolated subgroup or the specimens are distributed over a particularly small geographic area.

HEALTH RISKS TO THE OOCYTE DONOR Ovarian Stimulation

Ovarian stimulation entails both known and potential risks. The risk of severe ovarian hyperstimulation

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Correspondence: Practice Committee, American Society for Reproductive Medicine, 1209 Montgomery Highway, Birmingham, Alabama 35216 (E-mail: asrm@asrm.org).

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syndrome (OHSS) is reported to be approximately 1% to 2% per retrieval cycle. The incidence and severity of OHSS may in fact be lower in oocyte donors (8), in part owing to the absence of conception after stimulation. The use of a gonadotropin-releasing hormone (GnRH) agonist to induce final oocyte maturation compared with the traditional use of human chorionic gonadotropin (hCG) has been shown to dramatically reduce the risk of developing OHSS in oocyte donors in both large retrospective and smaller prospective studies (9–12).

Acute Procedural Risks

There are real, albeit small (<0.5%), risks of acute complications, including pelvic infection, intraperitoneal hemorrhage, or ovarian torsion (9, 13, 14). The risks associated with the low levels of anesthesia generally employed for oocyte retrieval in a young, healthy population should be very small. However, idiosyncratic reactions to anesthetic agents and other anesthetic complications (e.g., aspiration) may occur.

Cancer

The preponderance of data does not demonstrate an association between the use of ovarian-stimulation agents and cancer, including invasive ovarian and breast cancers (15–17). Moreover, the current understanding of the pathogenesis of ovarian cancer is rapidly evolving, calling into question traditional theories of the relationship between nulliparity and ovarian cancer (18).

Future Ovarian Reserve of the Donor

It is not presently known whether repetitive follicular aspirations affect the donor's future ovarian reserve. However, the physiologic mechanism of oocyte recruitment in ovarian stimulation is a reduction in follicles destined for atresia. Preliminary data indicate that repetitive and multiple cycles of oocyte donation do not decrease the donor's ovarian reserve, as assessed by serum antimüllerian hormone levels (19).

Psychological Risks

Oocyte donation may entail potential psychological risks (ambivalence, regret, etc.) that might occur around the time of the procedure or years later.

Loss of Intended Anonymity

Direct-to-consumer DNA testing, genealogy databases, and social media offer the opportunity to identify genetic connections to relatives with whom a consumer may or may not have a personal relationship. Despite the intention of anonymity, egg donors should be counseled that their anonymity could be compromised if their DNA or that of a close relative is added to a database. Although donors have control over their own participation in direct-to-consumer DNA testing, relatives of donors and donor-conceived offspring who choose to participate may find themselves linked. This may permit the recipient or donor-conceived offspring to deduce the identity of the donor, leading to unanticipated contact

with children conceived from their gametes in the future. These issues should be addressed during appropriate pretreatment screening and counseling (20).

RISK ASSESSMENT: MAXIMUM NUMBER OF CYCLES PER OOCYTE DONOR

Previous expert opinion has suggested a limit of six cycles per donor (21–24), a recommendation that this document continues to support. The basis for this recommendation is rooted in a concern over the potential cumulative risk accrued after a donor undergoes six ovarian-stimulation and egg-retrieval procedures. In a single ovarian-stimulation cycle, the donor's risk of severe OHSS is reported to be approximately 1% to 2% per retrieval cycle, and the risk of acute complications, including pelvic infection, intraperitoneal hemorrhage, or ovarian torsion, is estimated at <0.5%. Cumulatively, after six donation cycles, these risks to an individual donor aggregate to an overall risk of 8% to 13% of a serious adverse event, recognizing that this will vary among individuals. Further, it is reasonable to assume that some egg donors will require fertility services themselves, including in vitro fertilization, at a rate proportional to the general population stratified by age. Therefore, it may be prudent to limit the number of stimulated cycles for an individual donor to no more than six.

SUMMARY

- Oocyte donors are exposed to the risks attendant to ovarian stimulation, oocyte retrieval, and anesthesia.
- Severe OHSS is estimated to occur in 1% to 2% of donation cycles, but the risk may be further reduced by the use of GnRH agonists for triggering final oocyte maturation.
- The risk of serious acute complications associated with these procedures is small (<0.5%).
- The preponderance of data does not demonstrate a significant risk of future cancers in women undergoing stimulation and egg retrieval.
- The data are limited, but available evidence does not suggest that oocyte donation is associated with changes in the donor's ovarian reserve.

CONCLUSION

Currently, there are no clearly documented long-term risks associated with oocyte donation, and as such, no definitive data upon which to base absolute recommendations. Furthermore, there is a paucity of long-term follow-up data for repeat oocyte donors. However, because of the possible cumulative risks to and future needs of an individual donor, as outlined in the preceding discussion, it may be reasonable and prudent to limit the number of stimulated cycles for a given oocyte donor to no more than six. These recommendations will inevitably be modified as new data become available.

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service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Practice Committees and the Board of Directors of ASRM and SART have approved this report.

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Alan Penzias, M.D.; Ricardo Azziz, M.D., M.P.H., M.B.A.; Kristin Bendikson, M.D.; Samantha Butts, M.D., M.S.C.E.; Tommaso Falcone, M.D.; Susan Gitlin, Ph.D.; Clarisa Gracia, M.D., M.S.C.E.; Karl Hansen, M.D., Ph.D.; Micah Hill, D.O.; William Hurd, M.D., M.P.H.; Sangita Jindal, Ph.D.; Suleena Kalra, M.D., M.S.C.E.; Jennifer Mersereau, M.D.; Randall Odem, M.D.; Robert Rebar, M.D.; Richard Reindollar, M.D.; Catherine Racowsky, Ph.D.; Mitchell Rosen, M.D.; Jay Sandlow, M.D.; Peter Schlegel, M.D.; Anne Steiner, M.D., M.P.H.; Dale Stovall, M.D.; and Cigdem Tanrikut, M.D.

REFERENCES

1. Society for Assisted Reproductive Technology. Clinic Summary Report 2015. Available at: https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?reportingYear=2016.
2. De Boer A, Oosterwijk JC, Rigters-Aris CA. Determination of a maximum number of artificial inseminations by donor children per sperm donor. *Fertil Steril* 1995;63:419–21.
3. Curie-Cohen M. The frequency of consanguineous matings due to multiple use of donors in artificial insemination. *Am J Hum Genet* 1980;32:589–600.
4. Practice Committee of the American Society for Reproductive Medicine. Guidelines for therapeutic donor insemination. *Fertil Steril* 1998;70:1–4.
5. Ethics Committee of the American Society for Reproductive Medicine. Informing offspring of their conception by gamete or embryo donation: an Ethics Committee opinion. *Fertil Steril* 2018;109:601–5.
6. Janssens PM. No reason for a reduction in the number of offspring per sperm donor because of possible transmission of autosomal dominant diseases. *Hum Reprod* 2003;18:669–71.
7. Sawyer N, McDonald J. A review of mathematical models used to determine sperm donor limits for infertility treatment. *Fertil Steril* 2008;90:265–71.
8. Sauer MV, Paulson RJ, Lobo RA. Rare occurrence of ovarian hyperstimulation syndrome in oocyte donors. *Int J Gynaecol Obstet* 1996;52:259–62.
9. Bodri D, Guillen JJ, Polo A, Trullenque M, Esteve C, Coll O. Complications related to ovarian stimulation and oocyte retrieval in 2052 oocyte donor cycles. *Reprod Biomed Online* 2008;17:237–43.
10. Galindo A, Bodri D, Guillen JJ, Colodron M, Vernaev V, Coll O. Ovulation triggering with GnRH agonist vs. hCG in the same egg donor population undergoing donor oocyte cycles with GnRH antagonist: a prospective randomized cross-over trial. *J Assist Reprod Genet* 2009;26:251–6.
11. Melo M, Busso CE, Bellver J, Alama P, Garrido N, Meseguer M, et al. GnRH agonist versus recombinant HCG in an oocyte donation programme: a randomized, prospective, controlled, assessor-blind study. *Reprod Biomed Online* 2009;19:486–92.
12. Practice Committee of the American Society for Reproductive Medicine. Prevention and treatment of moderate and severe ovarian hyperstimulation syndrome: a guideline. *Fertil Steril* 2016;106:1634–47.
13. Bennett SJ, Waterstone JJ, Cheng WC, Parsons J. Complications of transvaginal ultrasound-directed follicle aspirations: a review of 2670 consecutive procedures. *J Assist Reprod Genet* 1993;10:72–7.
14. Ludwig AK, Glawatz M, Griesinger G, Diedrich K, Ludwig M. Perioperative and post-operative complications of transvaginal ultrasound-guided oocyte retrieval: prospective study of >1000 oocyte retrievals. *Hum Reprod* 2006;21:3235–40.
15. Venn A, Watson L, Lumley J, Giles G, King C, Healy D. Breast and ovarian cancer incidence after infertility and in vitro fertilization. *Lancet* 1995;346:995–1000.
16. Brinton LA, Sahasrabudhe VV, Scoccia B. Fertility drugs and the risk of breast and gynecologic cancers. *Semin Reprod Med* 2012;30:131–45.
17. Practice Committee of the American Society for Reproductive Medicine. Fertility drugs and cancer: a guideline. *Fertil Steril* 2016;106:1617–26.
18. Vaughan S, Coward JI, Bast RC Jr, Berchuck A, Berek JS, Brenton JD, et al. Rethinking ovarian cancer: recommendations for improving outcomes. *Nat Rev Cancer* 2011;11:719–25.
19. Bukulmez O, Li Q, Carr BR, Leader B, Doody KM, Doody KJ. Repetitive oocyte donation does not decrease serum anti-müllerian hormone levels. *Fertil Steril* 2010;94:905–12.
20. Harper JC, Kennett D, Reisel D. The end of donor anonymity: how genetic testing is likely to drive anonymous gamete donation out of business. *Hum Reprod* 2016;31:1135–40.
21. Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology. Repetitive oocyte donation: a committee opinion. *Fertil Steril* 2014;102:964–6.
22. Practice Committee of American Society for Reproductive Medicine. Repetitive oocyte donation. *Fertil Steril* 2008;90(Suppl):S194–5.
23. Practice Committee of the American Society for Reproductive Medicine. Repetitive oocyte donation. *Fertil Steril* 2006;86(Suppl):S216–7.
24. Practice Committee of the American Society for Reproductive Medicine. Repetitive oocyte donation. *Fertil Steril* 2004;82(Suppl):S158–9.

Donación repetitiva de ovocitos: una opinión del comité

Las donantes deben de ser informadas sobre el número de ciclos / donaciones a las que una donante de ovocitos puede someterse. Aunque los datos existentes no permiten realizar recomendaciones concluyentes, la preocupación por los temas de seguridad y bienestar de las donantes de ovocitos merecen tenerlo en consideración. Este documento reemplaza al documento del mismo nombre, publicado anteriormente en 2014