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New CUA guideline: A valuable reference for counselling men with azoospermia

The new CUA guideline statement on male infertility is an important new scientific analysis that focuses on three critical areas in the management of men with azoospermia. The guideline is excellent; it is evidence-based using the GRADE evidence-to-decision evaluation process, and valuable as a reference for physicians counselling and caring for couples where men have non-obstructive azoospermia (NOA).

The guideline's first area of focus is perhaps the most controversial, related to whether men with NOA should be initially managed with micro testicular sperm aspiration (TESE) with sperm cryopreservation or a simultaneous attempt at sperm retrieval with in vitro fertilization (IVF). The authors acknowledge that the level of evidence is weak and that a higher success rate may occur with simultaneous sperm retrieval and IVF but suggest upfront cryopreservation of surgically retrieved sperm for most couples with NOA.

It is important to recognize the weakness of data in this area; most studies using cryopreserved sperm from men with NOA are not intent-to-treat studies; they include primarily men in whom retrieved sperm survive cryopreservation and are usable for intracytoplasmic sperm injection (ICSI), a finding that is often not reliable for men with NOA. More recent data suggests that nearly 9% of men with prior findings of azoospermia will have adequate sperm in the ejaculate at the time of combined planned TESE and ICSI, suggesting that 1) prospective study is needed; and 2) sperm retrieval may be done unnecessarily in a substantial proportion of men who have intentional cryopreservation without a repeat careful semen analysis on the day of planned retrieval. The guideline appropriately manages the discrepancy between results of these two approaches with a "suggestion"

rather than a "recommendation" for cryopreservation of sperm.

The second guideline statement refers to the application of varicocele repair for a man with NOA and clinical varicocele. Of note, the evidence to support varicocele repair in this clinical scenario is of limited quality, although many articles have published anecdotes regarding detection of sperm in the ejaculate after varicocele repair; however, the rate of return of sperm to the ejaculate without varicocele repair surgery is not documented in many of these studies (uncontrolled trials), and the presence of rare, non-motile sperm in the ejaculate may not be enough to avoid microTESE, even after varicocele surgery. Since sperm adequate to allow ICSI is only found for 9.6% of men after varicocele repair in the largest published study referenced, the guideline conclusion that observation of varicoceles is recommended for most couples with NOA and a varicocele considering surgical sperm retrieval and IVF-ICSI as compared to pre-treatment with varicocelectomy appears warranted. Again, this is a conditional recommendation, with very low certainty of evidence, given the few, small, controlled studies.

The final guideline statement reviewed the common use of adjuvant hormone therapies for males with hypergonadotropic-hypogonadism NOA for the purpose of improving IVF-ICSI live birth rates. Current data do not support empiric adjuvant hormones for men with normal testosterone in this setting. All these areas of investigation critically need randomized controlled trials to provide higher-quality data to drive treatment decisions.

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