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Nearly all Surveyed Reproductive Urologists Feel a Prospective Varicocelelectomy Trial is Important and Worthwhile

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Controversy exists whether varicocelectomy improves pregnancy rates in couples with male infertility. Unfortunately, the majority of data come from retrospective, poorly controlled studies (1), resulting in inadequate evidence regarding the efficacy of this procedure in improving semen quality (2–3). In addition, results from randomized controlled trials (RCTs) are conflicting and methodologically of poor quality because of heterogeneous inclusion criteria, limited enrollment, and high drop-out rates.

The Reproductive Medicine Network (RMN) is a multicenter clinical trial network funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) to design and conduct clinical trials focused on improving reproductive outcomes in subfertile populations. Under the RMN, a varicocele trial, “*A Prospective, Randomized Study of Microsurgical Varicocelectomy versus No Surgery in the Treatment of Male Partners with a Palpable Varicocele and an Abnormal Semen Analysis*,” was developed and prioritized to begin. Poor recruitment, however, led to closure by the Data Safety Monitoring Board. Critical review of the investigators’ collective experience from all 5 participating sites identified potential reasons for limited recruitment, including lack of interest by urologists (4). We therefore undertook a survey of USA members of the Society of Male Reproductive Urologist (SMRU) and Society of Reproductive Surgeons (SRS) to determine if they considered an NIH-funded varicocelectomy trial for the treatment of male infertility to be important and beneficial. The survey also explored other potential recruitment barriers including: (1) previous treatment of couples prior to referral, (2) lack of full initial evaluation of the male partner beyond a semen analysis, (3) preference of infertile couples for aggressive treatment with IUI/IVF, and (4) lack of interest in a placebo arm.

The survey (see supplemental materials) was a brief Survey Monkey questionnaire assessing the level of interest in prospectively studying outcomes of varicocelectomy surgery in infertile men. After Institutional Review Board (IRB) review, the American Society of Reproductive Medicine (ASRM) and SMRU boards approved an email survey of USA SMRU and SRS urology members. The survey was sent to 100 USA SMRU/SRS members who had email addresses on file with the ASRM. The 100 members represented 70 SMRU-only members, 29 members of both SMRU and SRS, and 1 SRS-only member. Of these, 25 members responded. A second email was sent to non-responders from the same 100-member cohort, resulting in 8 additional responses. Lastly, 17 additional responses were obtained by providing the same survey in paper form, to USA members attending the 2012 SMRU annual meeting. Of the 50 responses, two were excluded for premature survey termination. Ultimately, 48 responses were used to tabulate results, yielding a 48% response rate (see supplemental materials).

Of the 48 respondents, 46 (96%) indicated that a prospective varicocelectomy trial for the treatment of male infertility is important and should be performed. All respondents were familiar with the AUA/ASRM varicocelectomy guidelines. A total of 83% perform a microscopic inguinal varicocelectomy most of the time, with no one operating on subclinical varicoceles. When given a scenario of a patient with “normal” semen analysis (concentration > 20 M/mL and motility > 50%), 56% would still offer a varicocelectomy. Regarding “lessons learned” (perceived recruitment barriers), more than two-thirds of the respondents felt that two main recruitment impediments needed to be addressed to improve future trial

success: a lack of work up (beyond a semen analysis) and a couple's avoidance of a placebo arm.

A lack of consensus in the field regarding the efficacy of varicocelectomy repair in infertile men would benefit from reliable evidence to determine best practice (2–3). We continue to believe that a randomized, clinical trial is necessary to more definitively address this issue.

The goal of this study was to survey USA reproductive urologists to learn if there is support for a varicocelectomy RCT. Broad support for a trial should minimize the potential for physician recruitment bias. For example, it is possible that urologists could unwittingly communicate to potential patients that a varicocelectomy was their best option, believing that a randomized trial was neither necessary nor important. On the contrary, this survey shows that urology-based physician bias for a varicocelectomy trial was minimal. Not only did 96% of respondents feel that this study was valuable, but 85% were also willing to recruit patients from their own practice for such a trial. Thus, motivation for such a critical clinical trial exists, leaving trial design as the next step to be carefully considered.

A secondary goal of the survey was to consider ways to improve recruitment for future trials. Respondents focused on two areas: (1) 67% felt a more detailed evaluation of the male was in order, while (2) 73% felt that a couple's innate desire to avoid the placebo arm needed to be addressed. The male evaluation could include expanding the semen analysis to assess DNA damage and sperm function. The second area relates to the lack of incentive for men to participate in a study with a placebo arm, especially for those already failing prior treatment attempts. To overcome the "placebo barrier," a future study should offer ovarian stimulation and IUI cycles to both the treatment and placebo arms, in addition to offering men in the non-varicocelectomy (placebo) group crossover to the varicocelectomy arm after a pre-determined period of unsuccessful procreative cycles.

This survey was limited by its small sample size, with 100 surveys only forwarded to members of two ASRM subspecialty societies within the USA. Furthermore, colleagues within the field who provide male fertility (varicocele) referrals were not included in this survey. It is not possible to know whether the 52 non-responders were more likely to think the study was important or unimportant.

Nonetheless, this survey demonstrated overwhelming (96%) support of USA male fertility surgeons for a prospective varicocelectomy trial, with most respondents willing to recruit from their own practices. In addition to carefully considered male- and female-factor inclusion criteria, future trials should attempt to optimize recruitment by offering both stimulated IUI cycles and, a placebo-arm cross-over to varicocelectomy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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