The Role of the Urologist in a Reproductive Endocrinology and Infertility Practice

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KEYWORDS

• Urologists • Male infertility • Reproductive medicine • Men's health
• Medical practice management • Interdisciplinary communication

KEY POINTS

- A fertility practice with a reproductive urologist helps improve adherence to male infertility guidelines and allows for better care of general male health.
- When reproductive endocrinologists and urologists work in the same practice, there is added potential for collaboration and education, which can help improve clinical care and research endeavors.
- A joint practice improves convenience and access to care by allowing couples to be evaluated concurrently and offering enhanced flexibility with scheduling surgical sperm retrievals.
- Expanding a fertility practice to include men's health can help grow a business by bringing in new revenue and increasing the patient base.

INTRODUCTION

Approximately 15% of couples struggle with infertility and roughly 7 million couples seek infertility care annually in the United States.[1,2] Male factor infertility affects about 50% of infertile couples; in one-third of cases, the male partner is solely responsible.[3] Infertile couples present to a variety of different practitioners, with gynecologists or reproductive endocrinologists (RE) often performing the initial evaluation because women more commonly initiate medical assessment for fertility concerns.

The American Society for Reproductive Medicine and the American Urologic Association have published guidelines to assist health care providers with the evaluation and management of male infertility.[3,4] These guidelines state that for all infertile couples, the male partner should have an initial screening that includes, at a minimum, a reproductive history and two semen analyses (SAs). The male partner should be referred to a male reproductive specialist for a full evaluation if the initial screening demonstrates any abnormality or if the couple has unexplained infertility.

In many instances, these guidelines are not followed. National data from the United States show that among couples who seek infertility counseling, 18% to 27% of the male partners are

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not evaluated.[5] According to the National Survey of Family Growth, between 2006 and 2010, only 27% of subfertile men ages 25 to 44 had received any infertility-related advice.[6] It is clear from these data that in many infertile couples, only the female partner is evaluated. Accordingly, many potentially treatable and/or reversible male factor fertility issues are left undiagnosed, which can lead to a loss of time and resources for the couple. In addition, a thorough male infertility evaluation can often reveal other underlying medical issues, such as scrotal pathologies, endocrinopathies, or genetic disorders that affect the overall health of the patient.

Most fertility centers are made up of REs and other health care practitioners whose sole focus is to assess and treat female patients. This requires them to refer couples with male factor infertility to an outside urologist for evaluation of the male partner, not all of whom are fellowship-trained in reproductive urology. To date, few fertility centers offer in-house reproductive urology services, a construct that optimizes care for the male partners and allows better coordination of care for the couple, especially if both partners require an intervention via in vitro fertilization (IVF). This article provides a brief overview of the male fertility evaluation and emphasizes the benefits of having a reproductive urologist embedded within a fertility practice.

THE MALE INFERTILITY EVALUATION

Initial Male Evaluation

The goal of the evaluation of the infertile male is to identify correctable conditions to maximize the success of conception, identify couples who may need fertility treatments or assisted reproductive technologies (ART), detect genetic causes of male infertility, and diagnose underlying medical conditions that may present as infertility. Couples should be evaluated if they have failed to conceive within 1 year of regular unprotected intercourse (or 6 months if the female partner is older than 35 year old). The physician performing the initial assessment, often a gynecologist or RE, should obtain a thorough reproductive history and two SAs.[4] The reproductive history should include the following: (1) duration of infertility and prior fertility, (2) coital frequency and timing, (3) sexual history, (4) childhood illnesses and developmental history, (5) systemic medical illnesses and prior surgeries, and (6) gonadal toxin exposure. If the initial evaluation reveals any abnormalities, the patient should be referred to a male reproductive specialist for a comprehensive evaluation.

Comprehensive Male Evaluation

A full reproductive urologic evaluation should include a thorough medical, surgical, and reproductive history; a physical examination; and at least two SAs if not done previously. The physical examination should include assessment of secondary sex characteristics and evaluation of the penis, urethral meatus, testes, epididymides, and spermatic cord to document presence/absence of the vasa deferentia or varicoceles. With regards to the SAs, reference values are based on World Health Organization 2010[7] (**Table 1**), although it is important to keep in mind that these thresholds are not the minimum values needed for conception. Based on the results of the full evaluation, other diagnostic tests or procedures may be indicated.

THE ROLE OF A UROLOGIST WITHIN A FERTILITY PRACTICE

A reproductive urologist within a fertility practice performs the comprehensive male evaluation while determining which additional testing may be necessary. Further testing may include serum endocrine evaluation (up to 45% of infertile men present with hormonal abnormalities) and imaging studies, such as scrotal or transrectal ultrasonography.[8,9] The urologist also determines whether genetic testing is warranted and provides counseling based on those results. The comprehensive evaluation may reveal other medical or urologic problems that need to be treated, such as erectile dysfunction (ED) or prostatic enlargement. Finally, the urologist determines if surgical interventions, such as varicocelectomy, testicular sperm

Table 1
World Health Organization 2010 semen analysis reference values

Semen Parameter	Lower Reference Limit
Volume (mL)	1.5
Sperm count (10^6/mL)	15
Total sperm count (10^6)	39
Total motility (%)	40
Progressive motility (%)	32
Normal morphology (%)	4
Leukocyte count (10^6/mL)	<1.0
Vitality (%)	58
pH	≥7.2

Data from World Health Organization. WHO laboratory manual for the examination and processing of human semen. 5th ed. Geneva: WHO Press; 2010.

extraction, or vasectomy reversal, are necessary. In essence, the reproductive urologist creates a one-stop shop for male infertility and general men's health needs.

Adherence to Guidelines

In couples with infertility, a comprehensive male evaluation by a urologist is often not performed. One factor that explains this disparity is that the female partner tends to initiate the fertility evaluations, because studies have consistently shown that women use more health care services than men.[10,11] Another contributing factor is that, if there are sperm in the ejaculate, couples may be directed straight to IVF rather being referred to a urologist for the male evaluation. This practice pattern is likely influenced, in part, by broadening insurance coverage given that ART use has increased in states with infertility insurance mandates.[12–14]

Despite clear referral recommendations from the American Urologic Association and American Society for Reproductive Medicine, there are barriers toward implementation of these guidelines, such as a shortage of urologists with male infertility training and a lack of awareness of the guidelines. A review of 428 infertility clinics in the United States found that 22% of treatment centers did not mention male factor infertility on their Web sites and 14% did not mention any role for the male evaluation.[15] Only 23% of the Web sites mentioned referral to a urologist. Incorporating a reproductive urologist within a fertility practice allows for these guidelines to be followed routinely. If all of the REs in a particular practice can refer male patients to a urologist embedded within the practice, guideline-adherence could easily achieve 100%.

Collaboration Between Reproductive Endocrinologists and Reproductive Urologists

When REs and urologists work in the same practice, improved collaboration and education between these complementary specialties results. A survey of 336 REs performed by the Society for Reproductive Endocrinology and Infertility found that 43.5% of REs believed that their fellowship had a deficiency in male infertility training.[16] Similarly, andrology fellowships provide minimal exposure to female reproductive medicine. Some REs have argued that reproductive endocrinology and infertility (REI) fellowships should expand to include training in male physiology and infertility so that the routine male evaluation could become incorporated into their practice.[17] The opposing argument to this proposal is that even fewer appropriate male evaluations would be performed if REs deem it unnecessary to refer male partners to urologists for evaluation.[18] Furthermore, urologists are best suited and specifically trained to offer treatment of diagnoses that may arise during the course of the male infertility evaluation, including varicocele repair, orchiectomy (including testis-sparing) in the setting of incidentally discovered testicular masses, and sperm extraction. Ultimately, instead of training reproductive specialists to treat men and women, having REs and urologists work together in the same practice may provide the best outcome. Not only can this result in an improvement in care for the infertile couple, it can also enhance education and research collaboration.

Reproductive urologists in fertility centers also collaborate with their colleagues in the embryology and andrology laboratories within the practice. It is beneficial to have a close relationship with the embryology team, who can more readily team up with the urologist in the operating room during surgical sperm retrievals, and thereby improve the success of these procedures. Overall, a comprehensive center, whether colocated or virtual, affords a unique advantage for the entire fertility team to engage with and educate one other.

Sperm Retrieval

Infertile couples with azoospermia often need a female fertility specialist for ART and a male fertility specialist to perform sperm retrieval. If fresh sperm is desired for an ART cycle, the sperm retrieval procedure needs to be coordinated with the female partner's oocyte retrieval. An integrated reproductive urologist in a fertility practice can offer enhanced flexibility and ease of procedure scheduling for surgical sperm retrievals. Nassiri and colleagues[19] evaluated practice patterns for postvasectomy surgical sperm retrieval at 203 private practice fertility clinics in the United States and found that none of them had an on-site urologist. Only 40% of clinics reported performing sperm retrieval procedures in vasectomized men, with 9.4% of clinics using an on-staff RE to perform the procedures and 30.5% using a urologist who either came on-site for the sperm retrieval or performed it off-site.[19] It is evident that most private ART clinics in the United States do not have a relationship with a urologist who can perform one of the most common procedures in male infertility.

Access to Care

There are many significant barriers in access to infertility services in the United States, such as

sociocultural, geographic, infrastructure, and economic barriers.[20] Mehta and colleagues[21] studied the limitations of access to care for male factor infertility and found clear geographic barriers. At the time of that study's publication in 2016, 13 states had no male fertility specialists and many ART centers did not have a reproductive urologist within a 60-minute driving distance.[21] When a reproductive urologist works at an REI practice, the problem of accessibility to a urologist is removed from the equation. Other barriers may still exist for patients, but a joint practice allows both partners to be evaluated concurrently and efficiently. This level of convenience can help improve patient satisfaction with their fertility care.

Sexual Medicine

One of the main benefits of having a urologist in a fertility clinic is that subfertile or infertile men often need to be treated for sexual dysfunction in addition to infertility. Studies have found that compared with men in fertile couples, men in infertile couples have a higher prevalence of ED and premature ejaculation.[22–24] Just being diagnosed with infertility can have a negative impact on the psychological well-being of the patient, as evidenced by higher rates of anxiety and depression.[23] An infertility diagnosis has been shown to cause an increase in stress, resulting in reduced pleasure of sexual activity and decreased sexual desire.[25,26] Treatment with phosphodiesterase-5 inhibitors, such as sildenafil, is helpful for treating ED caused by the psychological stress of infertility treatment.[27] Phosphodiesterase-5 inhibitors have been found to be fertility-safe medications that could even modestly improve semen parameters.[27,28]

Infertility and sexual dysfunction are commonly linked with hypogonadism, a problem that also should be managed by a reproductive urologist. One study showed that infertile men, especially those with nonobstructive azoospermia, had a higher risk of hypogonadism compared with fertile control subjects.[29] Treatment of the infertile male should focus on much more than just infertility given that sexual dysfunction and androgen-deficiency are often concomitant problems that persist long after helping the patient have children. A urologist that is part of the fertility care-team can easily maintain a long-term relationship with the couple and continue to manage urologic issues beyond infertility.

General Male Health

Male infertility and ED are both considered proxies for general male health. Accordingly, the role of the urologist within a fertility practice is to also assess the overall health of the patient. There is a growing body of evidence that has demonstrated an increased risk of all cancers and testicular cancer, in particular, among infertile men.[30–34] In addition to cancer, male infertility may also serve as a biomarker for other health problems, such as cardiovascular, metabolic, and autoimmune disease.[30,35–37] Other medical problems and lifestyle behaviors that have been linked to infertility include smoking, obesity, and sleep disturbance.[30,38,39] Eisenberg and colleagues[40] found that men with impaired semen parameters have an increased mortality rate in the years following an infertility evaluation.

It is important for the reproductive urologist to manage the preconception paternal health of patients not only because it will benefit the patient himself, but also for the offspring, because there is significant evidence that a man's weight and toxic chemical exposures can impact the epigenetic profile of his progeny for generations.[38] It is also critical for the urologist to identify risks of transmitting disease to offspring by offering screening and performing genetic counseling, when indicated. For instance, patients with nonobstructive azoospermia or severe oligozoospermia may have a Y chromosome microdeletion of the AZFc region, a genetic mutation that will be transmitted to all sons. REs also routinely offer carrier screening for their female patients and male partners undergoing ART to determine the risk of transmitting autosomal-recessive or X-linked genetic disorders to their offspring. When urologists and REs work directly together, genetic screening and counseling can become a more collaborative endeavor.

Business Growth

When a fertility practice employs reproductive urologists, there are many opportunities for business growth. First, expanding to male infertility and men's health creates an entirely new source of revenue for the practice. Urology is a more surgical field than REI. Accordingly, if a fertility center has its own ambulatory surgical center, an employed urologist can increase its use. Second, reproductive urologists use the andrology and embryology laboratories for serum endocrine evaluations, SA evaluations, sperm retrievals, and sperm cryopreservation, which makes the laboratories more profitable. Lastly, REs and urologists within the same group serve as a referral source for each other, which helps grow the patient base. Although the female partner of a couple more frequently initiates the fertility evaluation, reproductive urologists

sometimes see male patients first, after an initial evaluation and referral by a general urologist or primary care physician (PCP). The female partner is then referred to an RE in the practice.

FUTURE DIRECTIONS

An additional benefit of having a joint RE-urology practice is the advantage of sharing the same electronic health record (EHR). Our EHR links the female patient to the male partner so that both charts are easily accessible and communication is streamlined. A future direction for fertility practices that would help improve care would be the addition of guideline-based algorithms to the EHR. For instance, for all female patients that are evaluated for infertility, there should be a male reproductive history section and order set for two SAs. When the results of this initial evaluation return, any abnormalities should flag an automatic referral to the practice's urologist within the EHR. The algorithm should automatically cue the provider to order genetic testing in oligozoospermic men, which can streamline the preliminary work-up.

There is evidence that embedding a multidisciplinary clinical care algorithm into the EHR can improve adherence to recommendations. For instance, when the 2012 US Preventive Services Task Force recommended against prostate-specific antigen screening for prostate cancer, studies showed a significant decrease in prostate-specific antigen testing, prostate biopsy, and prostate cancer incidence in the following years because of a decrease in referrals from PCPs to urologists.[41] In response to these screening recommendations, the Duke Cancer Institute created an algorithm and added it to the EHR that PCPs used, which led to an increased rate of screening among all age and race categories in their community.[42]

Many ART clinics may not be able to hire a reproductive urologist because of a lack of resources, patient volume, and access to fellowship-trained urologists. However, they can improve male infertility care by embedding guidelines and algorithms directly into the EHR, similar to the Duke Cancer Institute. Even if they are not working under the same roof at the same practice or institution, it is important for REs and reproductive urologists to maintain a close relationship so they can stay up-to-date on the ever-changing practice patterns of their counterparts.

SUMMARY

Although male factor infertility affects about 50% of infertile couples, the male partner often is not referred to a reproductive urologist for a thorough male evaluation because of poor access to male infertility specialists, practice patterns that favor going straight to IVF, and a lack of awareness of or adherence to guidelines. Fertility practices that incorporate a reproductive urologist within the practice can improve male reproductive potential, offspring health, and the general health of the male partner. Other advantages of this practice model include clinical and research advancements because of the ease of collaboration; better coordination of surgical procedures, such as sperm retrievals; and improvements in patient access and patient satisfaction. By obviating the need to refer patients to another clinic or unaffiliated practice, these constructs are able to establish a physician-patient relationship that can lay the foundation for lifelong general male health. As the fields of female and male reproduction continue to grow, more ART clinics may offer integrated reproductive urology services, allowing for optimized care of the infertile couple.

DISCLOSURE

P.J. Cheng: None. C. Tanrikut: Medical Director, Andrology Laboratory, New England Cryogenic Center, Advisory Board, Ferring Pharmaceuticals.

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