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Onco TESE in Fertility Preservation

Key Points

- There is significant deleterious effect of chemoradiation on testicular function
- Effect on spermatogenesis (Germinal epithelium) is far more pronounced than effect on endocrine function.
- The extent of damage by chemotherapy is dependent on type of agents used, dose used and the stage of testicular maturity at which the therapy was given
- Increased survival following cytotoxic chemotherapy for testicular and lymphoproliferative disorders has raised interest in outcomes such as preservation of fertility in these patients.
- Advancements in techniques of sperm retrieval with micro TESE for Fertility Preservation allow higher retrieval and pregnancy outcomes, thus should be offered to all.

Gonadal dysfunction in men with malignancy occurs due to cancer itself (20-50%), or due to chemo/radiotherapy used to treat it. The degree of damage depends on the type of chemotherapy used, its dose, age of the patient, dose and the number radiation given and use of radiation shield to protect against scatter radiation. The **effects of chemotherapy** are **more pronounced** on the **germinal epithelium** of the testes than on the Leydig cells, resulting in a more profound effect on **spermatogenesis** than on testosterone production. The extent of germinal epithelial disruption is dependent on the level of sexual maturity of the testes and an **older post-puberta**l testis **is more likely to get damaged** than a younger prepubertal testis.

Sperm banking prior to initiation of therapy, either by collection of sample either by ejaculation, vibratory stimulation or electro-ejaculation, is essential to preserve fertility in these men. Surgical sperm retrieval may be necessary in azoospermic men.

Onco TESE (surgical sperm retrieval prior to / or after initiation of therapy) in men with malignancy may result in retrieval of sperms. Retrieval methods include Needle aspiration biopsy using a large bore butterfly needle (18G) / Testicular sperm extraction, single seminiferous tubule extraction and microdissection testicular sperm retrieval.

In a study by M Schrader et al, contralateral testicular biopsies were taken from 14 azoospermic patients with malignant testicular germ cell tumors and17 patients with malignant lymphomas underwent unilateral (n = 6) or bilateral (n = 11) testicular biopsy. In those with malignant testicular germ cell tumors, 6 had spermatozoa in their testicular biopsies, 5 had Sertoli cell-only syndrome and 3 had maturation arrest. Sperm recovery was successful in 8 of the 17 patients with malignant lymphoma, 4 had Sertoli cell-only syndrome, and 5 had maturation arrest.

Microdissection TESE has been used more recently for men with good chances of sperm retrieval. It is performed under general anesthesia and involves bi-valving the testes and examination under high power magnification. The larger opaque appearing tubules usually contain sperms. The procedure requires patience and coordination between the operating surgeon and embryologists.

Peter Schlegel et al reviewed their data from June 1995 to December 2009 where 1,072 testicular sperm extractions were performed by a single surgeon in 892 patients with nonobstructive azoospermia, including **73** patients with **persistent post-chemotherapy azoospermia**. All had at least two semen analyses confirming azoospermia before TESE. Complete medical evaluation, including a detailed medical history and physical examination were performed in all patients pre-operatively to detect any treatable conditions that may affect sperm production. Hormone abnormalities were treated medically before TESE. Genetic counselling was provided to all couples.

Operative Procedure - Onco micro TESE:

All TESE procedures were performed under general anesthesia or local anesthesia with sedation after a repeat semen analysis confirmed azoospermia on the day of planned sperm retrieval. After exposure of the testis, a transverse incision was made in the tunica albuginea enabling wide exposure and multiple biopsies were obtained. The testicular tissue was micro-dissected until sperm were found or the entire volume of each testis was examined. During microdissection, each seminiferous tubule was inspected for differences in tubule size and colour. Tubules that were more opaque and larger in diameter were collected.

The tubules were mechanically disrupted using fine scissors until they could be aspirated with and injected through a 24-gauge angiocatheter. An aliquot of this fluid was examined using phase contrast microscopy (at 200) by an embryologist. The procedure was continued until sperm were seen on wet mount or when all testicular tissue had been examined.

A total of 84 TESE procedures were performed in 73 patients with a history of prior chemotherapy. The mean age was 34.5 years with a mean FSH of 21.9 U/L. The average testicular volume was 9.1 mL. The mean time from chemotherapy to TESE was 19.0 years. Pre- or peri-TESE diagnostic testicular biopsy was available in 83.6% (61 of 73) of TESE patients. Of those patients, 90.2% (55 of 61) showed a Sertoli-cell only pattern and 9.8% (six of 61) showed hypo-spermatogenesis.

Sperm Retrieval and Reproductive Outcomes:

Sperm was successfully retrieved in 37% (27 of 73) of patients on initial TESE, with an overall sperm retrieval rate of 42.9% (36 of 84). The fertilization rate was 57.1% per injected oocyte (198 of 347). The clinical pregnancy rate was 50% (18 of 36) and the live birth rate was 42% (15 of 36) for the overall series. There were 15 deliveries with five twin births for a total of 20 healthy children born in the overall series. For first attempt TESE (per patient basis), the clinical pregnancy rate was 48.1% (13 of 27) and the live birth rate was 48.1% (13 of 27), resulting in delivery of 18 healthy children (five twin births and eight singleton births). The **highest retrieval rate** was seen in patients with **testicular cancer** (85%; six of seven) while the **lowest** was seen for patients with **sarcoma** (14%; one of seven).

References:

1. Schrader M, Muller M, Miller K et al. Urology 2003;61(2):421-5
2. Hsiao W, Stahl PJ, Schlegel PN et al. J Clin Oncol 2011;29:1607-1611.

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