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Original article

Fertility preservation for men with testicular cancer: Is sperm cryopreservation cost effective in the era of assisted reproductive technology?

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Abstract

Introduction: Many patients do not cryopreserve sperm before undergoing cancer treatment because of high perceived costs of cryopreservation. We sought to investigate the cost-effectiveness of fertility preservation compared to posttherapeutic fertility treatment in testicular cancer patients.

Materials and methods: We performed a systematic search of the PubMed database for the following: risk of azoospermia 12 months after surveillance, chemotherapy, retroperitoneal lymph node dissection, and radiation therapy (RT); rates of natural conception, and rates of conception with the use of intrauterine insemination or assisted reproductive technology, with or without microsurgical testicular sperm extraction (microTESE). A decision tree was constructed using the TreePlan add-in for Microsoft Excel (TreePlan Software, San Francisco, California). Cost-effectiveness was calculated as the overall cost of a given management branch, divided by likelihood of pregnancy. Calculations accounted for variable number of years of cryopreservation, and variable costs of microTESE.

Results: 1,113 articles were identified; 44 were included in the final analysis. Overall probability of pregnancy was higher among couples who cryopreserved sperm, versus those who did not. In patients undergoing active surveillance or retroperitoneal lymph node dissection, cryopreservation was more cost-effective if storage time was short (<6 years) or microTESE cost was high (>7,000). Cryopreservation prior to chemotherapy was more cost-effective unless microTESE cost was low (<7,000). Cryopreservation prior to RT was more cost-effective in almost all scenarios.

Conclusions: Sperm cryopreservation prior to undergoing chemotherapy or RT remains the most cost-effective strategy for fertility preservation, across a range of possible costs associated with surgical sperm retrieval and in vitro fertilization/intracytoplasmic sperm injection.

Keywords: Testicular cancer; Fertility preservation; Oncofertility; Orchiectomy; Male infertility; Assisted reproductive technology

1. Introduction

Testicular Germ Cell Tumors (TGCT) are the most common solid organ tumors among U.S. men aged 15–35, with 8,850 new diagnoses expected in 2017 [1]. Early detection, combined with advances in surgical techniques and cytotoxic therapies, have resulted in excellent long-term

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survival rates among men with TGCT, nearing 100% in stage 1 disease, and >80% in metastatic cases [2]. Men diagnosed with testicular cancer generally have abnormal semen parameters at baseline [3]. Standard therapies for TGCT, which include radical orchiectomy plus, either surveillance, retroperitoneal lymph node dissection (RPLND), RT, or chemotherapy, additionally impair fertility potential [2,3].

Up to 77% of cancer survivors report an interest in paternity after completing cancer treatment [4]. Inability to achieve parenthood is associated with poor mental health outcomes, and has profound implications for the psychological and emotional well-being of young cancer survivors [5,6]. Therefore, addressing and optimizing fertility potential is an integral component of comprehensive cancer care for men with TGCT. There are 2 broad approaches for addressing fertility concerns in this patient population. The first option is to preserve fertility by sperm cryopreservation, or sperm banking, before initiating cancer therapy. The second option is to assess fertility potential after the completion of cancer therapy, and to facilitate fertility, when necessary, using assisted reproductive technologies (ART).

Although the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and American Society of Reproductive Medicine all recommend that physicians counsel their patients about sperm cryopreservation before initiating cytotoxic therapy [7–9], fertility preservation care for adolescents and young adults is not uniform among practitioners [10]. Patient and provider misconceptions about costs of sperm cryopreservation, recovery of spermatogenic function following cytotoxic therapies, and success rates of ART, may also discourage more widespread use of fertility preservation.

The goal of this study was to create a cost-effectiveness model to determine the most cost-effective option for promoting fertility among men with TGCT. We anticipate the results of this study will help guide clinicians in their conversations with patients, and be a useful guide to insurance providers and policy makers who are considering providing insurance coverage for fertility preservation.

2. Materials and methods

2.1. Literature review

In accordance with PRISMA guidelines, we conducted a systematic search of the National Library of Medicine Pubmed database from January 1967 to April 2016. Search sequences included: "(testicular cancer OR testis cancer OR seminoma OR nonseminoma) AND Orchiectomy AND surveillance AND (fertility OR azoospermia OR spermatogenesis)," "(testicular cancer OR testis cancer OR seminoma) AND radiotherapy AND (fertility OR azoospermia OR spermatogenesis)," "(testicular cancer OR testis cancer OR seminoma OR nonseminoma) AND (RPLND OR retroperitoneal lymph node dissection) AND (fertility OR azoospermia OR spermatogenesis)," "(testicular cancer OR testis cancer OR seminoma OR nonseminoma) AND (chemotherapy OR BEP) AND (fertility OR azoospermia OR spermatogenesis)." A series of exclusion criteria were then applied (Fig. 1). Articles were excluded if they were not written in the English language, or not available as full text articles. Studies that did not mention testicular cancer, fertility, or semen quality in the abstract were also excluded. Additionally, studies were excluded if the results did not separate and stratify testicular cancer from other included cancers. The final studies meeting the inclusion and exclusion criteria are summarized in Appendix 1 [11–51]. Data extracted from these publications included rates of azoospermia, achieved pregnancy rates, study sample size, and treatment modality. These data were used to create the decision tree model described later.

2.2. Decision tree

A decision tree was constructed using the TreePlan add-in for Microsoft Excel for Mac (TreePlan Software, San Francisco, CA), to compare feasibility and cost-effectiveness of fertility preservation versus fertility treatment options for men with TGCTs. The decision tree model is based on a postpubertal patient (Fig. 2). Clinically, sperm

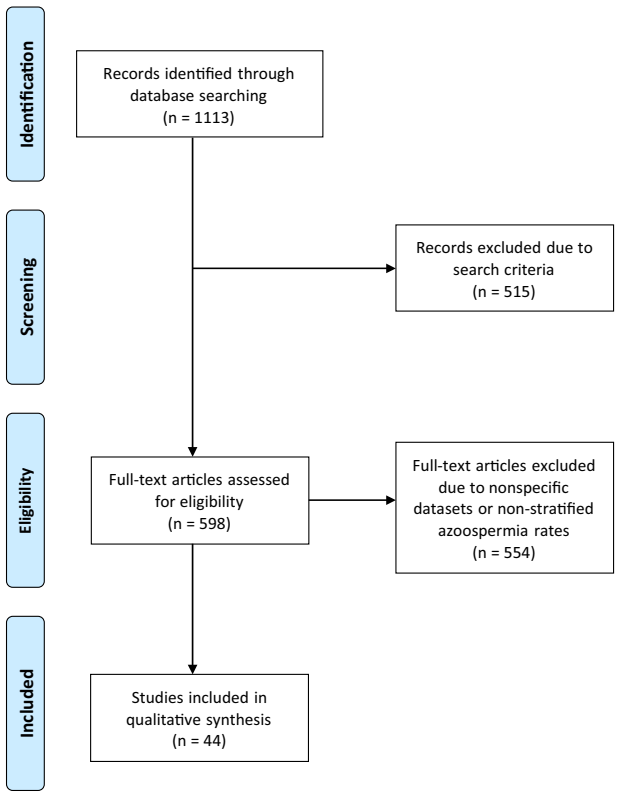

Fig. 1. Systematic review of literature and exclusion of inapplicable studies according to PRISMA guidelines.