

REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

More research, more responsibility: the expansion of duty to warn in cancer patients considering fertility preservation

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Due to advances in assisted reproductive technology (ART) men and women diagnosed with cancer have an increasing number of options to resolve fertility complications prior to, during, or after treatment. While non-biological parenting options (eg, adoption) can be pursued, there is increasing evidence that cancer survivors prefer to have biological children.¹⁻³ Cancer patients who receive gonadotoxic therapies and/or radiation are most likely to benefit from fertility preservation options when used prior to the initiation of therapy.⁴ For males, established options are sperm banking, testicular sperm extraction, and radiation shielding, while experimental options include testicular tissue freezing, hormonal manipulation, and testicular tissue grafting.⁵⁻¹⁰ For females, established options include embryo cryopreservation⁴ and ovarian transposition, and experimental options include oocyte cryopreservation, ovarian tissue cryopreservation, and ovarian suppression via gonadotropin-releasing hormone agonist hormone.¹¹⁻¹³ In October 2013, the American Society for Reproductive Medicine (ASRM) recommended

Reproductive technology is advancing at a steadfast pace. Researchers are successfully refining options for fertility preservation, to the benefit of the cancer community. Research has consistently shown cancer patients and survivors desire to have risks to fertility and preservation options disclosed, and major campaigns have been undertaken to refer these patients to fertility specialists. However, the decision to pursue fertility preservation is not an isolated judgment. A variety of future decisions may arise for the individual or couple, choices that may not have been relayed during the initial decision-making process. Future decisions include the length of time to continue to store frozen gametes, donating banked gametes to infertile couples, and whether embryos created with one partner would be accepted by a new partner. It is important to continue the advancement of fertility preservation not only in the scientific milieu, but also in addressing a patient's preparedness for long-term decision making.

Key words: decision making, fertility, health care, oncology, professional responsibilities, reproductive health

oocyte cryopreservation be removed from the list of experimental options due to the improved success rates.¹⁴ Overall, options of fertility preservation are based upon a number of factors including diagnosis, age, pubertal status, disease site, treatment, and pre-treatment fertility status.

Communication needs in cancer patients considering fertility preservation and the forgotten questions

A major step towards integration of fertility preservation options into clinical care was the American Society of Clinical Oncology (ASCO) 2006 guidelines, which detailed the duty of oncologists to discuss risks to fertility due to cancer or treatment, and outlined established vs experimental options for fertility preservation.¹⁵ This, in turn, led to research examining patient, provider, and systems-level factors that may impact adoption of these guidelines.¹⁶⁻²⁰ However, this work has led to a need for additional consideration of the extent to which health care providers may also need to inform patients considering fertility preservation about future choices, based on their current decisions. We discuss the future de-

isions relevant to fertility preservation with cancer patients and the responsibility of the health care professional to warn patients about the continuum of decision making.

Although dependent on the type of procedure, as shown in the Figure, most fertility preservation options have the potential to lead to a multitude of considerations and decisions. For instance, male cancer patients who sperm bank must decide the length of time they will be willing or able to pay for storage. They may need to consider whether this decision would change if they were able to father children without the use of ART or decided not to have children. Female cancer patients who undergo egg cryopreservation and have a surplus may be asked to donate their unused eggs to research or to infertile couples. Women who undergo embryo cryopreservation with their current partner, then in the future have a different partner, may be confronted with a dilemma if the current partner refuses use of the embryos, even if this is the woman's only chance for a biological child.²¹ A model of the potential future decisions the individual and/or couple may be faced with can be

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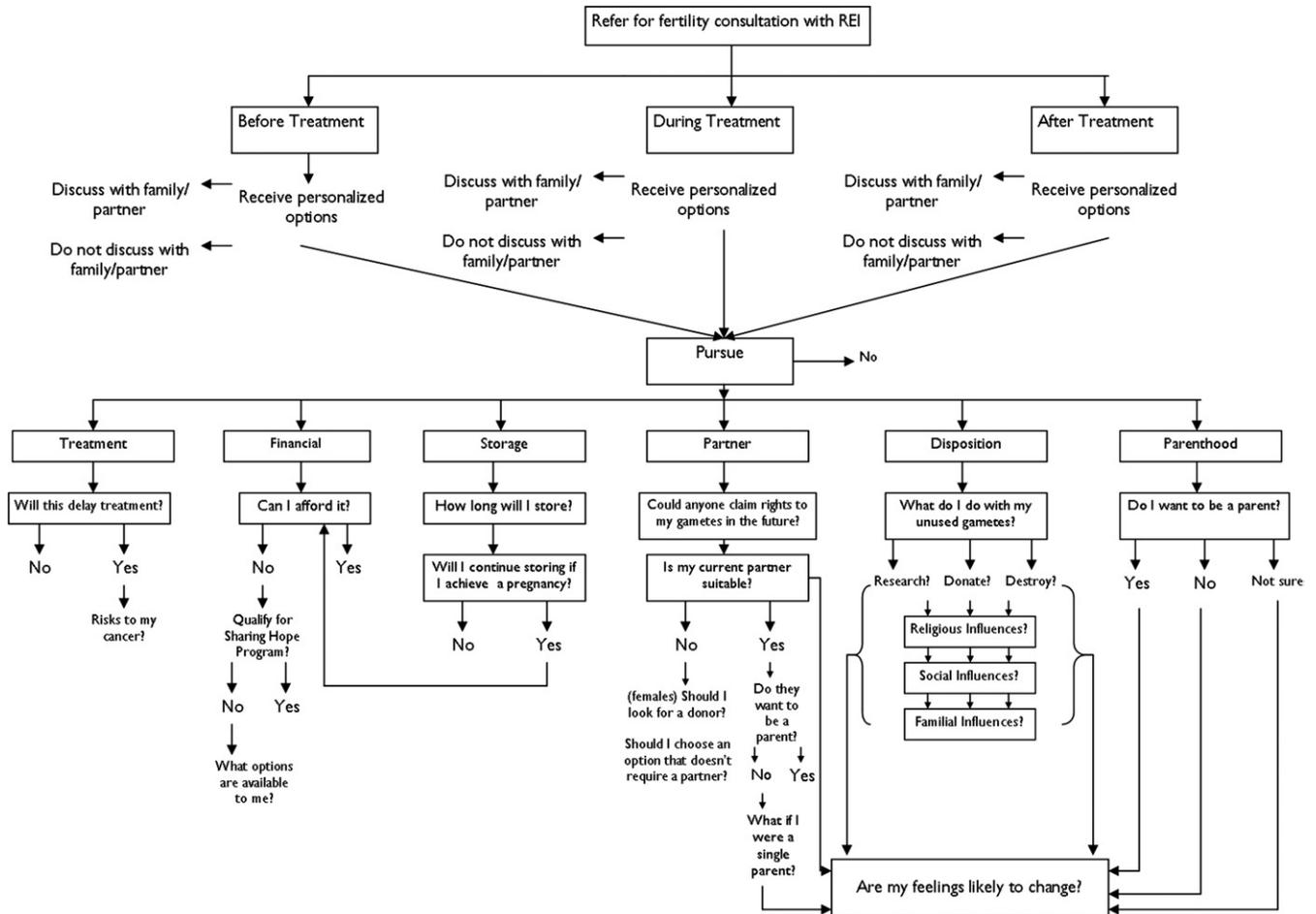
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FIGURE

Potential future decisions regarding fertility preservation



Quinn. Duty to warn in fertility preservation. *Am J Obstet Gynecol* 2013.

found in the Figure. The emotional turmoil of receiving a cancer diagnosis, the urgency to start treatment, and the need to consider fertility preservation prior to initiation of treatment creates chaos that is not always conducive to decision making.

Are patients prepared to make a decision about fertility preservation?

To understand the weight of these future decisions, it is important to examine a cancer patient's value of fertility and the hope placed on the fertility preservation procedure.

A 2005 study investigated how patients perceived their frozen embryos, whether or not they already had children. This study suggested patients described their frozen embryos as virtual children, siblings of living children, in-

surance policies, and reminders of their infertility; 72% of patients with an average of 4 years of storage had not made a decision about what to do with the unused embryos.²² These findings are similar to those of Klock et al²³ in an earlier study that found almost all infertile couples surveyed who originally decided to donate their surplus embryos to either research or other infertile couples eventually changed their minds. Infertile couples contemplating how to dispose of unused embryos have criticized the lack of available options and information provided to make an informed decision.²³ Individuals both with and without a previous cancer diagnosis who have utilized ART have reported feeling that decisions about stored gametes require arduous thinking and often neces-

sitate consultations with religious leaders and extended family, and concerns about perceptions of friends and social networks, all of which can invoke a new grieving process.²⁴⁻²⁷

Protection of human subjects

The future decisions regarding stored gametes that may arise for cancer survivors should be covered in the consent under potential risks of psychological harm as indicated by the Belmont Report.²⁸ However, the process of informed consent for fertility preservation procedures among cancer patients has not been well studied. Reproductive health decisions in the general population have been shown to be intertwined with personal values and identity of the individual or couple, in which case counseling about future ethical decisions is

deemed a private matter and outside the scope of the consent.²⁹ Insufficiency of the consent document and consenting process is not new; however it is unique for cancer patients who undergo fertility preservation as opposed to general procedures and clinical trials. Patients consenting to a magnetic resonance imaging procedure do not have to make a decision 5 years later if their estranged partner would have rights to the test results. Patients who consent to clinical trials are often followed for 5, 10, or even 20 years after the actual administration of the study drug is complete, and are warned via the consent that toxicities may still arise for which the study sponsor will cover treatment. However, cancer patients who undergo fertility preservation may not be monitored by these same standards. As such, the physician is obligated to disclose "any information which is necessary to form the basis of an intelligent consent by the patient for the proposed treatment."³⁰ The consenting process is meant to ensure a patient understands the risks and benefits of a procedure or study, and that they have enough information to make an informed decision. It is dangerous to assume patients are fully aware of the need for future decisions about their stored gametes by reading the standard statement in a consent form stating there may be emotional difficulties as a result of undergoing a procedure. A new task for ethics committees is to determine when these future decisions stop being a private matter, and start being recognized as true dilemmas that survivors face as a result of the fertility preservation process.

The presence of cancer patients into the world of ART suggests the need for additional training and the development of educational modules and ethical guidelines in the profession. But what information is necessary for a patient to be adequately and legally informed? For standard treatments and clinical trials, the risks, alternatives, and side effects are specifically outlined in the consent, and a physician is considered negligent if these are not sufficiently addressed.³¹ Does this hold true if the reproductive endocrinologist (REI) does not discuss future

ethical considerations with the patient, such as disposition of unused embryos?

Whose job is it?

ASCO suggested oncologists had a duty to discuss fertility risks and provide referrals to an REI. REIs are obstetrician/gynecologist physicians with advanced training related to understanding and treating a broad spectrum of reproductive disorders across the life span.³² They are aware of the laboratory, clinical, and storage considerations that are specific to the types of ART selected by patients. Through their training, they also gain the necessary skills to guide patients toward selecting reproductive options that are the best given a wide range of physical, emotional, and social factors unique to each patient and/or their family.³² The Ethics Committee of the ASRM has also provided practice guidelines specific to fertility preservation for cancer patients, indicating their support of REI professionals in providing this care to cancer patients.⁴ Thus, the REI plays a critical role in helping patients consider the additional issues that may result based on the decision to use fertility preservation methods. However, it is not known what experience and training the typical REI has with cancer and treatment, how many have established relationships with oncologists or cancer settings, or what the content of the discussion about fertility and preservation is and how it may vary based on available technology, physician preferences, and the cultural/political climate of the community. Future research is needed to establish the actual knowledge base of REIs.

We have identified multiple areas of communication about ART that can be improved by eliminating role confusion among health care providers. Role confusion is a problem in fertility preservation with cancer patients and creates the potential for vital information to fall through the cracks in patient care. Lack of standard procedures and assumptions will perpetuate this. The oncologist may assume referring a patient to a fertility specialist fulfills his or her duty as detailed in ASCO guidelines. The fertility specialist may assume the patient has already discussed clinical contraindications between

cancer treatment and fertility preservation methods, emotional decision-making aspects of ART, and disposition decisions about stored gametes with a health care professional from the oncology setting. The multiple health care professionals in a cancer patient's care highlight the need for role clarity. As such, medical education residency and fellowship programs may consider incorporating oncology-based fertility preservation into training programs and national medical organizations should provide continuing education opportunities in this domain.

After a cancer diagnosis, patients and families are inundated with information that can range from considering mortality, to attempting to understand a new world of medical terminology, to what procedures will and won't be covered by insurance. Health care professionals including physicians, nurses, psychologists, and social workers, diversify their roles as information providers so that patients may rely on individualized expertise from their treatment team. Health services research has shown conflicts regarding which health care professional should have the role of discussing threats to fertility, with one physician type (eg, surgeons) being noted to assume this is the responsibility of the medical oncologist or support staff.³³ ASCO guidelines clearly suggest this is the role of the medical oncologists, but radiation oncologist also may believe this is their role.^{15,34} Cancer patients on the other hand have unique information needs that may be better addressed by fertility specialists at designated time points during their treatment and survivorship. In a 2005 study by Thewes et al,³⁵ the majority of cancer patients thought that receiving fertility information was necessary at the time of diagnosis, and that speaking directly with a fertility specialist was the preferred format of receiving information. An interesting result in this study is that although the preferred format to receive fertility information was from a fertility specialist, only 29% reported having had this consultation. Of this sample, 86% received their fertility information from their treating oncologist (some reported receiving information from both sources).

The low proportion of discussions with fertility specialists may be due to the lack of a referral system, or a lack of access to this type of specialist.

The initial encounter with the treating oncologist is the best time to introduce risks to fertility from cancer treatment. Patients must enter into a trusting relationship with their oncologist from the start, and are typically not likely to challenge the information provided or the decisions made for them at this time. This bond of trust is unique because the patient is often so vulnerable that he or she may not truly consider their personal desires but rather may be influenced by the physician's direction or attitude towards fertility preservation.³⁶ This also calls into question the ethical issue of a physician's duty to warn. Many professions maintain a legal obligation to warn persons or authorities if there is a known threat to safety. Genetic counselors, for example, have a duty to warn family members of a genetic disease that will inevitably lead to an array of future decisions for the family.³⁷ In this instance genetic counselors are poised to assist with these future decisions such as testing and resource linking. Likewise, oncologists are in the best position to warn about potential risks to fertility then provide a referral, and REIs are in the best position to discuss the upcoming decisions that are inherent to the use of ART.

The important message to convey to the medical community is that oncologists do not have to be experts in reproductive endocrinology; REIs will fill that role. Oncologists have the initial responsibility of referring the patient to an REI. After that, REIs will communicate with the treating physician, counsel the patient about what the available options are, and counsel as to what the patient or couple can expect if choosing to preserve fertility. The knowledge and experience gained from providing service to the general population of people experiencing infertility gives REIs the distinct expertise to discuss the psychosocial and decision-making aspects of ART with cancer patients. Decades of research have taken the issue of fertility preservation in cancer patients this far; new formative research efforts are now needed

to uncover patient and provider preferences in communicating what decisions may naturally follow after undergoing fertility preservation. Existing research is also highlighting a need for developing expertise among REI specialists specific to oncology, which could facilitate the unique needs of cancer patients. The foundation for fertility preservation discussions in oncology has been laid; it is now time to improve the quality of this communication and thus overall quality of life for patients and survivors. ■

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