Oncofertility: Issues and Updates

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Disclosures

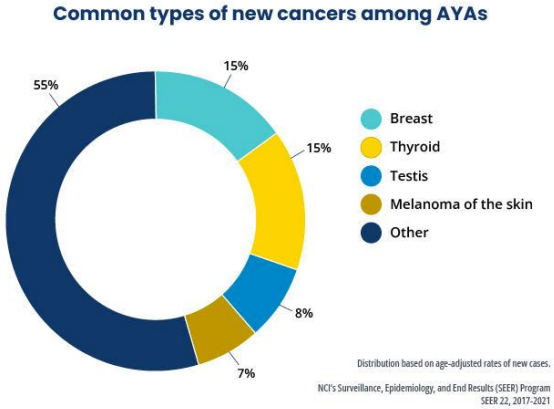
- Presenters have no financial disclosures

Objectives

1. Define oncofertility and the affected population
2. State of oncofertility nationally and within NM
3. Discussing oncofertility with patients
4. Gonadotoxic cancer treatments
5. Fertility preservation: common medications and procedures

Who are AYA Cancer Survivors

- Individuals age 15-39
- 84,100 AYAs will be diagnosed with cancer in the US in 2024 (NCI)
- Most common types of cancer
  - Breast
  - Thyroid
  - Testicular
  - Melanoma
  - Others include: brain/CNS tumors, cervical cancer, colorectal cancer, leukemia/lymphoma, sarcoma



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"Adolescents and Young Adults with Cancer." National Cancer Institute. https://www.cancer.gov/types/aya. Accessed June 6, 2024
Sehring J, et al. 2020. *Journal of Assisted Reproduction and Genetics. 2021. 38: 1745-1754.*

What is oncofertility?

- From 2008-2014, 85% of women with a cancer diagnosis under age 45, survived
  - Increased focus on quality of life after treatment
    - Includes preserving ability to have biological family
- Oncofertility = bridges oncology and reproductive endocrinology
  - Goals = discussion of 1) impacts of diagnosis and treatment on fertility, 2) patient desires regarding family planning, 3) fertility preservation

Discussing Oncofertility

- Timing
- Who is involved
- What should be discussed
  - Fertility desires
  - Risk of treatment
  - Options for fertility preservation

Barriers to Oncofertility Discussions

- Patient factors:
  - Advanced cancer; need for urgent treatment
  - Emotional burden of cancer diagnosis
  - Ethical or religious factors
  - Time and financial resources
- Provider factors:
  - Discomfort with topic
  - Lack of knowledge
- System factors:
  - Inadequate referral system
  - Lack of funding

Gonadotoxic Cancer Treatments

- Surgery
- Chemotherapy
- Radiation Therapy
- Endocrine Therapy
- Immunotherapy

Key points regarding premature ovarian failure

- Menstruation is not an accurate assessment of ovarian function
  - Women may continue to have menses, but still have a decreased ovarian reserve and thus, lower likelihood of pregnancy
- Hormone test to predict ovarian function:
  - AMH (Anti-Mullerian Hormone) may predict ovarian function post-treatment

Chemotherapy

- Gonadotoxicity most common with alkylating agents
  - Cause injury to quiescent and dividing ovarian cells
- Gonadotoxicity depends on:
  - type of medication
  - Dose
  - Cycles used
  - Patient's age

Severity of Toxicity	Chemotherapy Type
High Potential	Cyclophosphamide, Chorambucil, Melphalan
Moderate Potential	Platinum agents (Cisplatin, Carboplatin), Doxorubicin, Bevacizumab
Low Potential	Bleomycin, Actinomycin D, Vinca alkaloids (Vincristine, Vinblastine) Methotrexate, 5-fluorouracil, Doxil

Radiation therapy

- Dependent on dose, field, and fractionation scheme
- Radiotherapy depletes the primordial follicle pool in a dose-dependent manner
  - 6-Gy dose to gonads results in permanent ovarian failure
- RT may also damage uterine blood supply and tissue
  - May contribute to poor obstetrical outcomes: increased risk of pregnancy loss, preterm birth, and low birth weight
- Improved imaging and radiotherapy techniques have allowed greater gonadal shielding

Endocrine Therapy

- Endocrine therapies block hormone production
  - Fertility usually returns following cessation of HT
- Some patients are able to pause hormone therapy in order to achieve pregnancy
  - Pregnancy success rates equivalent to or higher than the general population

Fertility Preservation Options

- Male:
  - Sperm banking
  - Testicular tissue preservation (experimental)
- Female:
  - Embryo cryopreservation
  - Oocyte cryopreservation
  - Ovarian tissue preservation (experimental)
  - Shielding from RT and ovarian transposition
  - Ovarian function suppression with GnRH agonists

Sperm Banking and Other Methods for Males

- Sperm cryopreservation and banking
  - Safe, non-invasive, effective
  - Not timed with hormonal cycle
  - Widely available
- Hormonal gonadoprotection in men is not successful in preserving fertility
- Testicular tissue cryopreservation remains experimental
  - only option for prepubertal males

Embryo Preservation

PROS

- Established method
- Greatest success for live births
- Allows preimplantation diagnosis of cancer genetic syndromes

CONS

- Not available to prepubertal girls
- Requires sperm source, usually long term partner
- Requires controlled ovarian stimulation (10-14d)
  - May postpone beginning cancer treatment

Oocyte Preservation

PROS

- Established method for postpubertal females
- Does not require sperm source
- Provides reproductive autonomy for females without a partner
- Diminishes ethical issues regarding embryo freezing or donor sperm

CONS

- Not available for prepubertal girls
- Requires controlled ovarian stimulation (10-14d)
  - May postpone cancer treatment start
  - Timing no longer depends on menstrual cycle → less delay
- Hormone stimulation may pose a theoretical risk to those with hormone-sensitive malignancies
  - Aromatase-inhibitor based stim protocols well-established
  - Studies show NO increased cancer recurrence risk due to ovarian stimulation and subsequent pregnancy

Ovarian tissue preservation

PROS

- Available for prepubertal females
- Does not require hormonal stimulation
  - No delay of cancer management
- Encouraging fertility outcomes
  - Live birth rates of 37%
  - Endocrine function of 64%

CONS

- Experimental in US
- Requires surgical removal of ovarian tissue
  - Later reimplantation of tissue preserves hormonal and reproductive functions
- Potential risk of transferring malignant cells into the body at time of autotransplant (highest risk in leukemia)

Limiting Impact of Cancer Treatment on Fertility

- Shielding
  - Dependent on radiation field
- GnRH Agonists
  - Induces ovarian suppression without interfering with cancer therapy
  - Efficacy remains controversial
- Ovarian Transposition (Oophoropexy)
  - Increased odds of preserving normal ovarian function (65-94%)
  - Not beneficial to women receiving concurrent gonadotoxic chemotherapy
  - Ovaries not always protected due to radiation scatter
- Fertility sparing surgery

Posttreatment Options

- Donor oocytes, spermatocytes, or embryos
- Gestational carrier
- Adoption

REFERENCES

"Adolescents and Young Adults with Cancer." National Cancer Institute. https://www.cancer.gov/types/aya. Accessed June 6, 2024

Moussaoui D, Surbone A, Adam C, Diesch-Furlanetto T, Girardin C, Bénard J, Vidal I, Bernard F, Busiah K, Bouthors T, Primi MP, Ansari M, Vulliemoz N, Gumy-Pause F. Testicular tissue cryopreservation for fertility preservation in prepubertal and adolescent boys: A 6 year experience from a Swiss multi-center network. Front Pediatr. 2022 Sep 6;10:909000. doi: 10.3389/fped.2022.909000. Erratum in: Front Pediatr. 2023 Mar 20;11:1177389. doi: 10.3389/fped.2023.1177389. PMID: 36147816; PMCID: PMC9485727.

Sehring J, Hussain A, Grimm L, Rosen E, Esguerra J, Matevossian K, Louden E, Beltsos A, Jeelani R. A call to action: unified clinical practice guidelines for oncofertility care. J Assist Reprod Genet. 2021 Jul;38(7):1745-1754. doi: 10.1007/s10815-021-02142-z. Epub 2021 Mar 11. PMID: 33709343; PMCID: PMC8324617.

Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, Wallace WH, Wang ET, Loren AW. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol. 2018 Jul 1;36(19):1994-2001. doi: 10.1200/JCO.2018.78.1914. Epub 2018 Apr 5. PMID: 29620997.

Hussein RS, Kahn Z, Zhao Y. Fertility Preservation in Women: Indications and Options for Therapy. May Clinic Proc. 95(4): 770-783. doi: 10.1016/j.maocp.2019.10.009

Partridge AH, Niman SM, Ruggeri M, Peccatori FA, Azim HA Jr, Colleoni M, Saura C, Shimizu C, Sætersdal AB, Kroep JR, Mailliez A, Warner E, Borges VF, Amant F, Gombos A, Kataoka A, Rousset-Jablonski C, Borstnar S, Takei J, Lee JE, Walshe JM, Ruíz-Borrego M, Moore HCF, Saunders C, Bjelic-Radisic V, Susnjar S, Cardoso F, Smith KL, Ferreiro T, Ribi K, Ruddy K, Kammler R, El-Abed S, Viale G, Piccart M, Korde LA, Goldhirsch A, Gelber RD, Pagani O; International Breast Cancer Study Group; POSITIVE Trial Collaborators. Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer. N Engl J Med. 2023 May 4;388(18):1645-1656. doi: 10.1056/NEJMoa2212856. PMID: 37133584; PMCID: PMC10358451.

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