Pregnancy Screening in Patients With Cancer

Annika M. Gustafson, MHA, BSN, RN; Deborah J. Goldfrank, MD;
William A. Dunson, MD; Daniel L. Mulkerin, MD; Rebecca L. Caires, MBA;
and Keith D. Eaton, MD, PhD

Unknowingly treating a pregnant patient is a preventable harm. Screening appropriate patient populations for pregnancy is a preventive measure that can help avoid this “never” event. Yet, pregnancy screening is not consistently integrated into cancer care. The details of screening policies vary, with some organizations lacking a policy altogether. Pregnancy screening should be integrated into treatment pathways, clinical guidelines, and organizational policies, as well as into clinical workflows to avoid the unintentional treatment of a pregnant patient with cancer.

In the United States, half of all pregnancies are unintended, and more women of childbearing potential (WOCBPs) are choosing to delay pregnancy than in previous years.^{1,2} Due to the later age of onset of most cancers, pregnancy and cancer often are not concurrent (Table 1).³ The incidence of simultaneous cancer and pregnancy is 0.1% to 0.2%.⁴

WOCBPs are defined as women with the ability to conceive a fetus. This includes all female patients between the onset of menses and menopause (defined by the absence of menses for 12 consecutive months), excluding those who have had prior medical intervention leading to infertility, such as a hysterectomy. Because it is difficult to know with certainty whether a woman is capable of childbearing, a practical solution includes screening of all women aged 10 to 55 years, although this age range is disputable. An audit at an individual NCCN Member Institution showed that over the course of a year and more than 1,000 pregnancy tests, no unsuspected pregnancies were found in women between the ages of 51 and 55 years. A review of the literature revealed a pregnancy rate without artificial reproductive technology of <2% in women aged >50 years. Pregnancy in this age group is most often correlated with grand multiparity (≥5 previous pregnancies). Based on this data review, the institution's pregnancy testing policy was adjusted to include WOCBPs within the age range of 11 to 50 years, without incidence of unidentified pregnancies in women aged >50 years.

The emotional experience of receiving a cancer diagnosis can make it difficult for a patient to provide an accurate medical history, and symptoms of pregnancy may be attributed to cancer. Providers may also be distracted and overlook the reproductive portion of the review of systems. Although extensive literature has been published about cancer treatment during pregnancy, limited research is available about pregnancy testing before cancer treatment. Guidelines have inconsistent recommendations on pregnancy testing. Consequently, not all cancer care organizations have a pregnancy screening policy, and content varies significantly between policies that do exist. Prevention of adverse outcomes is the shared responsibility of patients, providers, and healthcare organizations.

Background

Cancer treatment modalities include chemotherapy, radiation, hormone therapy, and surgery, all of which can have adverse effects on a fetus. The consequences of unknowingly

Annika M. Gustafson, MHA, BSN, RN

Annika M. Gustafson, MHA, BSN, RN, is a clinical quality analyst at the Seattle Cancer Care Alliance. She received her undergraduate degree in nursing from Pacific Lutheran University and went on to complete her master's degree at the University of Washington. Ms. Gustafson's work focuses on shared deliberation and decision-making between patients and providers during care decisions to align patient preferences and the care provided.

Table 1. Common Cancers Diagnosed Among Pregnant Women

Type of Cancer	Incidence
Breast cancer	1:3,000–10,000
Lymphoma	1:1,000–6,000
Cervical cancer	1–2:2,000–10,000
Ovarian cancer	1:10,000
Thyroid cancer	0.2–1.4:10,000

Adapted from Salani R, Billingsley C, Crafton S. Cancer in pregnancy: an overview for obstetricians and gynecologists. *Am J Obstet Gynecol* 2014;211:9, with permission.

doi: 10.6004/jnccn.2017.7059

The ideas and viewpoints expressed in this commentary are those of the author and do not necessarily represent any policy, position, or program of NCCN.

Gustafson et al

Deborah J. Goldfrank, MD

Deborah J. Goldfrank, MD, is Head of General Gynecology at Memorial Sloan Kettering Cancer Center in New York City. She completed her Obstetrics/Gynecology residency at New York University Medical Center and Cancer Genetics fellowship at Memorial Sloan Kettering. Her practice focuses on managing gynecologic complications of cancer treatment as well as surveillance for women at increased, inherited risk for gynecologic cancers.

William A. Dunson, MD

William A. Dunson, MD, received his medical degree from the Bowman Gray School of Medicine at Wake Forest University in North Carolina. He completed residency at the University of Utah, where he was chief resident his final year. Dunson then worked at the University of Utah and at Madsen Health Center as a primary care physician. Currently, he practices at the Huntsman Cancer Hospital where he evaluates acutely ill cancer patients in the Acute Care Service.

exposing a fetus to cancer treatment can be devastating and depend on multiple variables, such as dosage, duration and timing of exposure, placental permeability, and gestational age.⁵ For example, pregnant patients with cancer who receive multidrug chemotherapy in their first trimester have an increased risk of spontaneous abortion, fetal demise, and fetal malformations.⁶ Radiation therapy can result in lowered IQ and fetal malformation, depending on gestational age of the fetus and exposure level.⁶ Hormonal treatments such as tamoxifen can result in a high frequency of congenital abnormalities, requiring the use of reliable birth control during treatment.⁷ Given the risk of harmful exposure to a fetus from cancer treatment, it is necessary to have preventive guidelines, policies, and practices in place.

Prevention

Guidelines and Policy

Guidelines and policies can be used to mitigate the risk of an adverse event. A guideline contains recommendations or suggestions, whereas a policy is a rule or mandate.

Pregnancy testing is needed in many different areas of healthcare. For surgery and anesthesia, the American Society of Anesthesiologists (ASA) recommends informing WOCBPs of the risks, benefits, and alternatives related to preoperative pregnancy testing if the result would alter the patient's management. This consent/assent process allows for patient autonomy.^{8,9} For radiation, the International Atomic Energy Agency's Radiation Protection of Patients recommends that WOCBPs are carefully interviewed for the likelihood that they may be pregnant before imaging or treatment.¹⁰ The American College of Radiology (ACR) recommends screening WOCBPs with questions to assess for pregnancy status.¹¹ Patient answers can be used to indicate the possibility that the patient may be pregnant, and if so, the ACR recommends obtaining consent for a pregnancy test. Patients who are to receive procedures that risk exposing a fetus to high doses of radiation should undergo a pregnancy test within 72 hours before the procedure. For adolescents, who may not be as forthcoming with their pregnancy status, the ACR suggests an alternative method: an institutional policy that requires all minors who have started menses to undergo pregnancy testing before any procedure that could "impart a level of uterine radiation above a specific dose to the uterus."¹¹

Due to the harm cancer treatment can have on a fetus and the high possibility of unplanned pregnancy in WOCBPs, regular pregnancy screening and testing is recommended.¹² ASCO/Oncology Nursing Society (ONS) Chemotherapy Administration Safety Standards¹³ inform overall treatment planning, and do not explicitly recommend pregnancy testing for WOCBPs before beginning cancer treatment such as chemotherapy and radiation. Instead, these organizations have general guidelines that recommend a complete medical history and essential workup of each patient to include pregnancy status when appropriate.

The NCCN Clinical Practice Guidelines in Oncology for Adolescent and Young Adult Oncology include recommendations for cancer treatment during pregnancy, pregnancy prevention, and fertility counseling, but do not include pregnancy testing before cancer treatment.¹⁴ NCCN also has disease-specific guidelines (available at NCCN.org), some of which recommend pregnancy testing, and others which address pregnancy during treatment, pregnancy status, and fertility counseling. Overall, there is much more guidance available for cancer treatment during pregnancy and fertility counseling than pregnancy testing before cancer treatment. The absence of a consistent recommendation for pregnancy testing in disease-specific guidelines presents the risk of pregnancy status not being assessed.

Because professional society guidelines currently lack consistency, it makes sense that there is also variation among institutional policies.¹⁵ Policies are created and implemented by individual organizations, yet Hu et al¹⁶ showed that pregnancy screening policy compliance was low, at approximately 20%. The NCCN Best Practices Committee conducted a survey regarding pregnancy screening in which 23 of the 27 NCCN Member Institutions responded (unpublished data, 2016). Detailed review of 6 NCCN Member Institution policies showed significant variation, including the role and responsibilities of healthcare

Pregnancy Screening in Patients With Cancer

providers involved in the pregnancy screening process. The survey showed that 67% of responding NCCN Member Institutions include information regarding pregnancy screening in patient education materials. Regarding policies and guidelines, 30% of responding institutions had no policy or guideline, 22% had a policy, and 48% had a guideline or recommendation (Figure 1). Of the centers that have a policy, 67% perform audits to ensure compliance (N=6; Figure 2).

Figure 1. Results from the 2016 Survey of NCCN Member Institutions' Pregnancy Screening Question, "Does your institution have a guideline (ie, recommendation) or policy (ie, requirement) on screening for pregnancy prior to chemotherapy, therapeutic radiation, or surgery?"

Figure 2. Results from the 2016 Survey of NCCN Member Institutions' Pregnancy Screening Question, "Does your institution perform audits to ensure compliance to its pregnancy screening policy?"

Pregnancy Screening and Testing

Pregnancy screening in WOCBPs can reduce the chances of a fetus being exposed to the harmful effects of cancer treatment. In healthcare, the spectrum of options for pregnancy screening is as follows:

- No policy or screening
- History alone
- History and selected testing
- Universal testing

None of these approaches is perfect. Screening questions in a medical history may alert a provider about a risk for pregnancy, but the questions have low sensitivity and specificity for detection. Blood serum human chorionic gonadotropin (hCG) testing is preferred, because it is the most sensitive pregnancy test available; it allows providers to determine pregnancy status earlier than urine testing. Blood draws are part of treating and monitoring cancer, making blood serum testing cost-effective and convenient in oncology. The optimal timing and frequency of pregnancy testing has not been defined by research studies. The most rigorous schedule is suggested by Patel et al,¹² who recommended that, "A pregnancy test should be administered to rule out pregnancy before each course of chemo- or radiotherapy, and thereafter at each subsequent visit before delivering additional therapy."

No testing strategy would entirely mitigate the risk of pregnancy concurrent with cancer treatment. Entry into oncologic care is arguably the most important time point for screening. The optimal testing frequency likely varies with patient population and risk.

Fertility and Contraception Counseling

Patient education helps to engage patients and inform them of their health conditions and treatment options.¹⁷ Fertility counseling educates patients about how cancer treatment can affect their reproductive health and presents options to assist in reproduction or address infertility after cancer treatment, if desired by the patient. Discussing the possibility that treatment may result in infertility can be misinterpreted by some patients to mean that treatment prevents pregnancy. Therefore, it is important to convey to patients that cancer treatment is not birth control.¹⁸ Given its relationship to reproductive health, fertility counseling should include educating WOCBPs and their partners about the importance of contraception, including the use of nonhormonal birth control, regardless of the patient's hormone receptor

Daniel L. Mulkerin, MD

Daniel L. Mulkerin, MD, completed training in Medical Oncology at the UW Hospital and Clinics, and is currently appointed as Associate Professor of Medicine, UW School of Medicine and Public Health. His clinical practice focuses on patients with gastrointestinal malignancies at the UW Carbone Cancer Center where he also serves as medical director. He is a member of the NCCN Best Practices Committee.

Rebecca L. Caires, MBA

Rebecca L. Caires, MBA, is currently Director of Operations for Oncology at Northwestern Medicine in Chicago Illinois. She has more than 30 years of executive leadership experience in both academic and community healthcare system positions focused in ambulatory operations, oncology administration and research. Additionally, Ms. Caires serves as an Executive Committee Member, Board Member and Best Practices Committee Member of the National Comprehensive Cancer Network (NCCN). She holds an MBA from Saint Leo University in Florida and a BA from National-Louis University in Illinois.

Gustafson et al

Keith D. Eaton, MD, PhD

Keith D. Eaton, MD, PhD, is a medical oncologist specializing in thoracic and head and neck cancers at the University of Washington/Seattle Cancer Care Alliance. He currently serves as the Medical Director of Quality, Safety and Value, Medical Director of Infusion and Pharmacy, and Clinical Director of the Thoracic, Head and Neck Oncology program. His research interests are in immunotherapy, molecular targeted therapies, and quality improvement.

status.¹⁹ Pregnancy testing before, during, and after cancer treatment should be discussed. A shared decision-making approach to pregnancy testing and cancer treatment is an effective way to involve patients while maintaining their autonomy.²⁰ Using patient education to engage patients can increase the likelihood that they will adhere to treatment.²¹ Education about reproductive and fetal harm from cancer treatment could boost patient adherence to effective contraception and pregnancy testing. These counseling activities should occur around the teachable moments at the start of treatment.

Clinical Practice

Screening WOCBPs and offering a pregnancy test is accepted practice before a surgical procedure,⁹ but in cancer treatment it is not as deeply ingrained as a standard part of workflow. Manley et al²² examined the safety standard of performing pregnancy testing before elective surgery, which then shared the decision to proceed between the providers and patients. Within this process, patients were informed of the rare occasion of a false-positive pregnancy test as well as the potential risks and fetal harms related to anesthesia. Patients were apprised of the importance of the first trimester of pregnancy and the different treatment options. Finally, the decision was made in alignment with the patients' values. Clinical trials also require pregnancy testing of all WOCBPs before treatment initiation. The same process should be applied in the cancer care setting.

System Structure

Oncology practice must be supported by clinical infrastructure that ensures that best practices are implemented by physicians. Current guidelines and standard system structures use patients' medical history, physical examination, and laboratory test results to detect their pregnancy status. Serum hCG testing is the preferred pregnancy test, because it can detect pregnancy within 7 to 9 days after conception and results can be obtained with few changes in workflow structure or staff.²² Organizational policies must direct healthcare providers on the use of serum hCG pregnancy testing in the appropriate patient population before cancer treatment. Policy compliance must be audited to track adherence.

Technology can be used in system structure to ensure that best practices for testing WOCBPs can be sustained. Electronic health records (EHRs) can prompt providers to order pregnancy testing when prescribing cancer treatment. Hayward et al²³ found that including a pregnancy test as part of chemotherapy medication order sets in the EHR was the most effective intervention in increasing pregnancy screening rates among adolescent female patients with cancer. Use of an EHR in this manner is effective and upholds the Centers for Medicare & Medicaid Services EHR Incentive Programs' meaningful use specifications.²⁴

Recommendations

- Clinical guidelines and pathways should explicitly emphasize the importance of pregnancy screening for all WOCBPs.
- Organizational policy should reflect national guideline standards and give direction for all healthcare providers involved.
- Pregnancy screening/testing should be bundled with cancer treatment orders in EHRs to prompt healthcare providers to screen the appropriate patient population.
- The importance of pregnancy prevention before, during, and after cancer treatment should be included in patient education and fertility counselling.
- Providers and systems should be audited for pregnancy screening policy adherence.

Conclusions

WOCBPs should be screened for pregnancy before and during cancer treatment. Due to poor adherence with this practice, system structure and technology must bolster preg-

Pregnancy Screening in Patients With Cancer

nancy screening to decrease the burden of responsibility on individual providers. More research is needed on optimal screening strategies during treatment. Guidelines and policies are necessary in directing cancer care standards and should reflect the specific need for pregnancy screening before cancer treatment. Providers and patients need to be educated and engaged to uphold policy.

References

1. Finer L, Zolna M. Shifts in intended and unintended pregnancies in the United States, 2001-2008. *Am J Pub Health* 2014;104(Suppl 1):S43-48.
2. National Center for Health Statistics. Delayed Childbearing: More Women Are Having Their First Child Later in Life. CDC Web site. Available at: <https://www.cdc.gov/nchs/products/databriefs/db21.htm>. Accessed March 2, 2017.
3. Salani R, Billingsley C, Crafton S. Cancer in pregnancy: an overview for obstetricians and gynecologists. *Am J Obstet Gynecol* 2014;211:7-14.
4. Esposito S, Tenconi R, Preti V, et al. Chemotherapy against cancer during pregnancy: a systematic review on neonatal outcomes. *Medicine (Baltimore)* 2016;95:e4899.
5. Koren G, Carey N, Gagnon R, et al. Cancer chemotherapy and pregnancy. *J Obstet Gynecol Canada* 2013;35:263-278.
6. Pereg D, Koren G, Lishner M. Cancer in pregnancy: gaps, challenges and solutions. *Cancer Treat Rev* 2008;34:302-312.
7. Braems G, Denys H, De Wever O, et al. Use of tamoxifen before and during pregnancy. *Oncologist* 2011;16:1547-1551.
8. Homi H, Ahmed Z. Preoperative Pregnancy Testing: to Test or Not to Test? (An Anesthesiologist's Dilemma). *SPA News* 2012;25. Available at: <http://www2.pedsanesthesia.org/newsletters/2012winter/pregnancy.html>. Accessed February 17, 2017.
9. American Society of Anesthesiologists. Pregnancy Testing Prior to Anesthesia and Surgery. Committee of Origin: Quality Management and Departmental Administration. Available at: <http://webcache.googleusercontent.com/search?q=cache:P1pmBkHWZrQJ:www.asahq.org/~media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/pregnancy-testing-prior-to-anesthesia-and-surgery.pdf+&cd=1&hl=en&ct=clnk&gl=us>. Accessed December 12, 2017.
10. International Atomic Energy Agency. Radiation Protection of Patients (RPOP). Available at: <https://www.iaea.org/resources/rpop>. Accessed December 12, 2017.
11. American College of Radiology. ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women With Ionizing Radiation. 2008 (Res. 26). Available at: http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/prevalence_survey/imaging_pregnant_arc.pdf. Accessed December 12, 2017.
12. Patel A, Sreedevi M, Sutaria R, et al. Reproductive health issues in women with cancer. *J Oncol Pract* 2008;4:101-105.
13. Neuss MN, Gilmore TR, Belderson KM, et al. 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, including standards for pediatric oncology. *Oncol Nurs Forum* 2017;44:31-43.
14. Coccia PF, Pappo AS, Beaupin L, et al. NCCN Clinical Practice Guidelines in Oncology: Adolescent and Young Adult Oncology. Version 2.2018. Accessed December 12, 2017. To view the most recent version of these guidelines, visit NCCN.org.
15. Rao P, Li Y, Getz K, et al. Low rates of pregnancy screening in adolescents before teratogenic exposures in a national sample of children's hospitals. *Cancer* 2016;122:3394-3400.
16. Hu L, Kichenadasse G, Martin H, et al. Pregnancy screening prior to chemotherapy administration. *Intern Med J* 2016;46:1222-1224.
17. Stacey D, Legare F, Col N, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2014;CD001431.
18. Patel A, Schwartz EB, for the Society of Family Planning. Cancer and contraception: release date May 2012. *SFP Guideline* #20121. *Contraception* 2012;86:191-198.
19. Hickey M, Peate M, Saunders CM, Friedlander M. Breast cancer in young women and its impact on reproductive function. *Hum Reprod Update* 2009;15:323-329.
20. Dehlendorf C, Grumbach K, Schmittiel J, Steinauer J. Shared decision making in contraceptive counseling. *Contraception* 2017;95:452-455.
21. Légaré F, Witteman H. Shared decision making: examining key elements and barriers to adoption into routine clinical practice. *Health Aff (Millwood)* 2013;32:279-284.
22. Manley S, de Kelaite G, Joseph N, et al. Preoperative pregnancy testing in ambulatory surgery: incidence and impact of positive results. *Anesthesiology* 1995;83:690-693.
23. Hayward K, Haaland WL, Hrachovec J, et al. Reliable pregnancy testing before intravenous cyclophosphamide: a quality improvement study. *Pediatrics* 2016;138:pil: e20160378.
24. Medicare & Medicaid EHR Incentive Program Registration & Attestation System. Available at: <https://ehrincentives.cms.gov/hitech/login.action>. Accessed February 08, 2017.