Breast Cancer Screening

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Abstract

It is expected in 2016 246,660 women in the United States will be newly diagnosed with breast cancer and 40,450 women will die of the disease. The purpose of breast cancer screening is to identify preclinical disease in asymptomatic women as breast cancer survival is improved with early detection. Digital mammography remains the mainstay of breast cancer screening. Tomosynthesis (3-D mammogram) has improved sensitivity with fewer false-positive studies, especially in women with dense breasts. Concerns have been raised about harms of false positives (repeat imaging and/or biopsies for benign findings), overdiagnosis of clinically insignificant breast cancers, and overtreatment. Thus, breast cancer screening recommendations range from initiation of screening at 40 years and performed annually to initiation at 50 years and performed biannually.

All guidelines recommend cancer risk assessment with a physician and development of an individualized screening program.

Women with the strongest risk factor for breast cancer, including personal history of cancer or atypical breast biopsy or family history of breast cancer, should undergo annual screening mammography. Women known to carry a familial breast cancer gene or at a lifetime risk of breast cancer greater than 20% should undergo annual breast MRI in addition to annual mammogram. Screening should conclude when a woman's life expectancy is less than 5 years.

Keywords

Breast cancer risk factors • Familial breast cancer syndromes • Breast cancer risk assessment • Mammography • Breast MRI • Tomosynthesis • BIRADS score

Contents

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© Springer International Publishing AG 2017
D. Shoupe (ed.), *Handbook of Gynecology*,
DOI 10.1007/978-3-319-17798-4_74

1 Introduction

It is expected in 2016 246,660 women in the United States will be newly diagnosed with breast cancer and 40,450 women will die of the disease (American Cancer Society 2016). One in 12 women will develop breast cancer in their lifetime, a statistic that has not decreased in recent years. The purpose of breast cancer screening is to identify preclinical disease in asymptomatic women as breast cancer survival is improved with early detection (Nelson et al. 2009). Implementation of screening mammography (regular mammograms performed in asymptomatic women with normal breast exams) has been associated with improved survival from breast cancer of 23–40% (Lauby-Secretan et al. 2015). Breast cancer mortality has been dropping by 1.9% per year, likely due to a combination of improved early detection (screening) and improved treatment (Ryerson et al. 2016). However, concerns have been raised about harms of false positives (repeat imaging and or biopsies for benign findings), overdiagnosis of clinically insignificant breast cancers, and overtreatment. Thus, breast cancer screening recommendations are in flux, and the optimal age of initiation and screening interval is controversial for low-risk women. Major medical associations have released conflicting screening recommendations leading to confusion and frustration among physicians and patients. As research has demonstrated a better understanding of how breast cancer risk changes over a woman's lifetime, screening recommendations are moving to an individualized risk-based approach. This chapter will summarize the range of recommendations for breast cancer screening in low-risk women and briefly summarize the data behind them. Risk factors for breast cancer will be reviewed as well as screening recommendations for women at risk for breast cancer.

2 Who Is at Increased Risk for Breast Cancer?

Risk factors for breast cancer are listed in Table 1 with their relative risks. As demonstrated below factors associated with the highest risk of breast cancer are female gender, older age, history of previous breast cancer, family history of breast cancer in a first-degree relative, and history of atypical breast biopsy. Patients with both a family history of breast cancer in a first-degree relative and a personal history of an atypical breast biopsy are at highest risk, with relative risk approaching those of *BRCA* mutation carriers (Dupont and Page 1985).

A strong family history of breast or related cancers is a red flag for an inherited familial breast cancer syndrome. Each patient should be assessed for familial cancer syndromes by eliciting a three-generation family history that includes ethnicity, any cancers in the family, who was diagnosed with cancer and their relationship to the patient, how the cancer was diagnosed and treated, if the afflicted family member survived or died, and if any genetic testing was performed. If there is a pattern of cancers running through the family or a clustering of rare cancers occurring in related relatives, consideration should be given to a genetic counseling referral. Table 2 lists the American College of Obstetricians and Gynecologists recommendations for genetic testing and counseling. Table 3 includes characteristics of the most common familial breast cancer syndromes.

Personalized cancer risk assessment is an important tool to guide physicians and patients in quantifying breast cancer risk and designing an appropriate screening regimen. Counseling should focus on lifestyle changes targeting high-risk behaviors (see lifestyle factors above) and estimating risk from intrinsic risk factors like family history, past medical history, and atypical cells on biopsy. Clinicians should be aware of the various familial breast cancer syndromes and refer

Table 1 Risk factors for breast cancer

Risk factor	Type	Relative risk
Highest risk		
Female gender	Reproductive	**>4**
Increasing age	Reproductive	
Inherited gene mutation (i.e., *BRCA*)	Familial	
>2 young first-degree relatives with breast cancer	Familial	
Personal history of breast cancer	Personal medical history	
History of atypical breast biopsy	Personal medical history	
Moderate risk		
One first-degree relative with breast cancer	Familial	**2.1–4**
History of chest wall radiation <30	Personal medical history	
Slightly increased risk		
First term birth >30 years	Reproductive	**1.1–2**
Menarche <12 years	Reproductive	
Menopause >55	Reproductive	
Nulliparity	Reproductive	
No history of breast feeding	Reproductive	
Use of combination hormone replacement therapy	Personal medical history	
Postmenopausal weight gain	Lifestyle	
Alcohol consumption	Lifestyle	
Smoking	Lifestyle	
Physical inactivity	Lifestyle	

Table 2 ACOG recommendations for genetic counseling referral

Cancer diagnosed at young age (i.e., breast cancer younger than 50)
Several different cancer diagnoses in the same individual (i.e., breast and ovarian or colon and endometrial)
Close blood relatives with the same type of cancer (i.e., mother-daughter pairs)
Unusual cancer presentation (i.e., male relative with breast cancer)
Ashkenazi Jewish ancestry
Occurrence of adult cancer known to be associated with familial cancer syndromes:
Triple negative breast cancer (ER/PR/her 2 neu negative suggestive of BRCA 1 mutation)
Epithelial or serous ovarian cancer (suggestive of a BRCA mutation)
Colorectal or endometrial cancer with DNA mismatch repair deficiency (suggestive of Lynch syndrome)

Table 3 Familial breast cancer syndromes

Syndrome	Gene mutation	Lifetime breast cancer risk	Associated cancers
Hereditary breast and ovarian cancer syndrome	*BRCA 1* and *2*	80% (*BRCA 1*)	Ovarian
		60% (*BRCA 2*)	Prostate
			Pancreatic
			Melanoma
Li-Fraumeni	*p53*	90% (all cancer types)	Bone and soft tissue sarcoma
			Brain
			Adrenocorticoid
			Colon
			Leukemia
Cowden	*pTEN*	30–50%	Endometrial
			Nonmedullary thyroid
Hereditary diffuse gastric cancer	*CDH1*	40–50%	Lobular breast cancer
			Diffuse gastric cancer

patients with suspicious family history for genetic counseling and possible genetic testing. Table 3 describes the more common hereditary cancer syndromes and relative risks of breast cancer. For further discussion of ovarian cancer, please see chapter "▶ Diagnosis and Management of Epithelial Ovarian Cancer."

The US Preventive Services Task Force recommended in 2009 each patient consult their physician regarding their personal risk of breast cancer and designs an individualized screening program (Nelson et al. 2009). Several online calculators have been designed and made publicly available to assist in breast cancer risk assessment, including the Gail model, IBIS, and BRCAPro. They incorporate varying details of family history, population-based risk factors like menstrual history and age at first birth, as well as personal

history of breast atypia. For the highest risk patients, if lifetime breast cancer risk exceeds 20%, annual screening breast MRI is recommended (National Comprehensive Cancer Network 2016). Please see "Breast MRI" section for further explanation.

3 Breast Screening Techniques and Technologies

Breast screening modalities include breast exam, self-administered (self breast exam or SBE) or by a clinician (clinical breast exam or CBE), mammography which can include full field, digital, or tomosynthesis (three dimensional), breast ultrasound, or breast MRI. Table 4 lists the sensitivities and specificities of each. The remainder of the chapter will discuss the relative advantages and drawbacks to each.

3.1 Breast Exam

Breast exam is the most commonly utilized breast screening tool but is falling out of favor due to low sensitivity and specificity. Self breast exam has been demonstrated to increase patient anxiety without improving cancer detection and is no longer routinely recommended. Breast self-awareness can be taught at a routine health maintenance visit. It entails being aware of the normal texture of one's breast tissue, as well as knowledge of any benign masses or cysts that may be present, so a patient can seek medical attention if changes occur. Breast self-awareness should also involve education of menstrual patients regarding the expected fluctuations in breast tissue associated with phases of the menstrual cycle.

Table 4 Sensitivity of common breast cancer screening modalities

Modality	Sensitivity	Specificity
Self breast exam	2–4%	Finds more benign than malignant disease
Clinical breast exam	40–69%	88–99%
Mammography	77–95%	94–97%
Tomosynthesis	90%	79%
Breast MRI	71–100%	81–97%

3.2 Clinical Breast Exam

Clinical breast exam is perhaps the most commonly utilized breast cancer screening tool as it is commonly included in well woman annual health screening. However, because of its low sensitivity, annual CBE is no longer recommended outside high-risk patient populations.

3.3 Mammography

Screening mammography is the mainstay of breast cancer screening. The identification of breast cancer before it becomes clinically apparent leads to improved survival, as demonstrated in several randomized control trials in the United States and Europe starting in the 1970s. Screen-detected cancers were diagnosed at earlier stage and led to lower cancer-related mortality (Tabar et al. 1985, 2000; Andersson et al. 1988). This was confirmed in subsequent meta-analyses (Oeffinger et al. 2015). Recently, controversy has arisen over screening guidelines for average-risk women, specifically at what age to initiate regular screening and at what frequency (Nelson et al. 2009). Concerns were raised by the US Preventive Services Task Force in 2009 regarding potential harms of overscreening including false-positive studies requiring additional imaging and/or biopsy and overdiagnosis leading to over-treatment and additional costs. The American Cancer Society stratified their screening recommendations by age-adjusted risk. The American College of Radiology and American College of Obstetricians and Gynecologists have continued to recommend annual screening due to benefits of early detection. Table 5 summarizes recommendations from several major medical societies regarding screening mammogram for average-risk women. Women with a high risk factor like breast atypia should undergo screening mammogram annually. Women with a family history of

Table 5 Summary of breast cancer screening recommendations

Society	Age	Recommended screening for average-risk women
American Cancer Society	40–44	Optional annual screening mammogram
	45–55	Annual screening mammogram
	>55	Screening mammogram every 2 years; screen until life expectancy is <10 years
US Preventive Services Task Force	40–49	Screening optional at patient's discretion
	50–74	Screening mammogram every 2 years
	>75	No recommendations due to lack of evidence
American College of Obstetricians and Gynecologists	>40	Annual screening mammogram
American College of Radiology	>40	Annual screening mammogram
National Cancer Institute	>40	Annual screening mammogram
National Comprehensive Cancer Network	>40	Annual screening mammogram

breast cancer should undergo screening mammography annually starting 5–10 years younger than the youngest affected family member or at age 30. For the women with extensive family history, MRI should be considered in addition to annual mammography. (Please see "MRI" section.)

The variation among recommendations has caused confusion among patients and providers and concern regarding insurance coverage of breast cancer screening in women under 50. A careful reading of all published guidelines demonstrates an emphasis by each of personalized screening based on the patient's risk factors and concern regarding cancer detection. Guidelines agree that average-risk women should have the option to start mammographic screening at 40 should they desire screening for early cancer detection and understand the risks of false-positive studies.

3.4 Tomosynthesis

A major advance in mammographic screening has been three-dimensional digital breast tomosynthesis (DBT). Tomosynthesis takes a series of images that allows the mammographer to review images in thin reconstructed slices, allowing the viewer to scroll up and down or side to side through breast tissues. Radiation exposure is comparable to standard mammography (Gur et al. 2009). The technology is better able to discern overlapping normal tissues and underlying lesions (Lei et al. 2014). Tomosynthesis was found in a recent meta-analysis of breast imaging techniques to have a higher sensitivity and specificity (90% and 79%, respectively) than digital and plain field mammography. DBT was found to have reduced recall rate and improved detection of breast lesions, resulting in fewer false positives and false negatives. It has been found to be most effective with increased invasive cancer detection rate when used in conjunction with full-field digital mammography but requires two radiation exposures of the patient (Hodgson et al. 2016). Patients with dense breasts may particularly benefit from tomosynthesis as a screening technique. Dense breasts impede cancer detection on screening mammography as suspicious lesions can be obscured by overlapping dense tissues. By allowing mammographers to scroll through breast tissue in 1 mm slices, tomosynthesis has been shown to increase cancer detection and reduce false-positive studies in women with dense breasts (Houssami and Turner 2016).

3.5 Breast Ultrasound

Breast ultrasound has been investigated as a breast screening tool due to its ease of use, minimal patient discomfort, and lack of radiation exposure. It has been demonstrated to minimally improve cancer detection but at the cost of increased false-positive studies prompting further investigations

to identify benign disease (Berg et al. 2008). Thus, it remains a diagnostic tool, useful for clarifying physical exam, mammography, or MRI findings and assessing axillary lymph nodes.

3.6 Breast MRI

Breast MRI affords the greatest sensitivity for breast cancer detection. Utilizing intravenous contrast, breast MRI demonstrates blood flow through the breast in addition to detailed soft tissue imaging, highlighting cancers by both their appearance and their preferential perfusion. Limitations include risks of false positives, limited resources (breast MRI requires a dedicated breast coil and software), placement of intravenous access, and contrast administration. Contrast allergies are rare but can occur, and IV contrast is contraindicated in patients with underlying renal disease. Additionally claustrophobic patients may find MRI challenging.

Generally, when lifetime risk of breast cancer exceeds 20%, consideration should be given to add annual breast MRI to annual mammogram. For women with a family history of breast cancer, screening with annual mammography is recommended to begin 10 years younger than the youngest affected family member, although not before 30. Patients who carry a *BRCA* mutation screening with annual breast MRI are recommended to start at 25 years with the addition of annual breast mammogram at 30. Women who have a history of an atypical breast biopsy are recommended to undergo annual screening mammography starting at 40 or at the time of identification of the lesion.

4 Characterization of Image-Detected Breast Lesions

Lesions identified on mammography that raise the concern of breast cancer include calcifications, masses, architectural distortion, and asymmetry. To reduce confusion regarding mammographic findings, the American College of Radiology has devised a scoring system that reflects levels of concern for occult malignancy. Table 6 summarizes the BIRADS scoring system and the associated risk of cancer.

Table 6 Summary of BIRADS scoring system of radiographically detected breast lesions

BIRADS score	Description	Associated risk of breast cancer
0	Incomplete	Needs additional testing
1	Negative	No or minimal risk
2	Benign	No or minimal risk
3	Probably benign	0–2%
4	Suspicious	2–95%
4A	Low suspicion	2–10%
4B	Moderate suspicion	10–50%
4C	High suspicion	50–90%
5	Highly suspicious	95% or greater
6	Tissue-confirmed cancer	Biopsy-proven cancer

Modified from Sickles et al. (2013. http://www.acr.org/Quality-Safety/Resources/BIRADS/About-BIRADS/How-to-Cite-BIRADS)

Low-risk lesions (BIRADS 3) should be reevaluated with short-term repeat imaging, usually in 6 months. Lesions that confer a suspicion of cancer (BIRADS 4 or 5) warrant a biopsy. Image-guided needle biopsy is preferable over open surgical biopsy to allow for most complete evaluation while minimizing risk to the patient (Silverstein et al. 2005). Needle biopsy has not been shown to cause cancer metastasis and avoids the risks of surgery for patients with benign lesions. Discordant biopsies (benign results in a highly suspicious lesion) should be further evaluated by repeat needle biopsy or surgical excision to avoid missing an underlying breast cancer.

5 When to Conclude Breast Cancer Screening

Breast cancer risk continues to rise through the eighth decade of life and remain elevated until the end of life (American Cancer Society 2016). More than one-third of cases are diagnosed after age 65 years (cite 2007 lancet oncology). There are

Table 7 Summary of breast screening protocol

Population	Modality	Age at initiation	Frequency
All women	Clinical breast exam and breast cancer education	20 years	Annual
Average-risk women	Mammography	40–50 years	1–2 years
Increased-risk women	Mammography	40 years	Annual
Women with a family history of breast cancer	Mammography	10 years younger than the youngest affected family member or 25 years	Annual
Familial breast cancer syndrome or known gene mutation carriers	Mammography and breast MRI	25 years (MRI)	Annual
		30 years (mammography)	

no randomized control studies demonstrating a survival benefit from breast cancer screening over age 70 (Nelson et al. 2009). When to stop screening is confusing. The US Preventive Services Task Force declined to issue a recommendation regarding breast cancer screening due to lack of evidence. Because breast cancer risk remains elevated in later decades of life and women are living longer and with better health, most experts including the American Cancer Society recommend an individualized decision between the patient and physician regarding ongoing breast cancer screening.

> If the patient is in good health and has life expectancy of more than 5–10 years, then continuing screening mammography is reasonable.

6 Conclusion

Despite recent confusion regarding breast cancer screening, early detection of breast cancer remains an important method to reduce breast cancer mortality and improve survival. Individualized breast cancer risk assessment allows physicians to educate patients about modifiable risk factors and design a personalized screening regimen. Screening guidelines are conflicting for average-risk women only; all guidelines agree that at-risk women should undergo annual screening mammography. By encouraging a dialogue between patients and providers regarding breast cancer risk, benefits of early detection and intervention, and harms of false-positive studies, providers can increase breast cancer awareness. Table 7 summarizes a reasonable approach to breast cancer screening.

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