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COMMENTARY

Breast cancer screening in average-risk women: towards personalized screening

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ABSTRACT

Breast cancer screening is widely recognized for reducing breast cancer mortality. The objective in screening is to diagnose asymptomatic early stage disease, thereby improving treatment efficacy. Screening recommendations have been widely debated over the past years and controversies remain regarding the optimal screening frequency, age to start screening, and age to end screening. While there are no new trials, follow-up information of randomized controlled trials has become available. The American College of Physicians recently issued a new guidance statement on screening for breast cancer in average-risk women, with similar recommendations to the U.S. Preventive Services Task Force and to European guidelines. However, these guidelines differ from those ofother American specialty societies. The variations reflect differences in the organizations' values, the metrics used to evaluate screening results, and the differences in healthcare organization (individualized or state-organized healthcare). False-positive rates and overdiagnosis of biologically insignificant cancer are perceived as the most important potential harms associated with mammographic screening; however, there is limited evidence on their actual consequences. Most specialty societies agree that physicians should offer mammographic screening at age 40 years for average-risk women and discuss its benefits and potential harms to achieve a personalized screening strategy through a shared decision-making process.

INTRODUCTION

Breast cancer screening is widely recognized for reducing breast cancer mortality. The objective in screening is to diagnose asymptomatic early-stage disease, thereby improving treatment efficacy. Despite the consensus regarding the benefits of screening, controversy remains regarding the optimal screening frequency, age to start screening, and age to end screening.[1,2]

CURRENT GUIDELINES

Recently, the American College of Physicians (ACP) issued a new guidance statement on breast cancer screening in average-risk women.[3] In summary, ACP recommends biennial mammography for women aged 50–74 years, that clinicians discuss the potential benefits and harms of screening with women aged 40–49 years, and that screening is discontinued for women over 74 years or with a life expectancy less than 10 years.

These recommendations are similar to those of the U.S. Preventive Services Task Force (USPSTF), published in 2016.[4] However, other American specialty societies such as the American College of Radiology (ACR), American Cancer Society (ACS), and National Comprehensive Cancer Network (NCCN) agree that screening should be performed annually in average-risk women beginning at age 40 years.[1,5] These variations reflect the differences in values between the organizations and correspondingly the specific metrics and relative weight of the metrics used to evaluate mammographic screening results. The ACP and USPSTF evaluate the cost-effectiveness of screening based on the reduction of mortality as well as the perceived harms. Meanwhile, medical specialty societies that are directly involved in the management of breast cancer patients assess other benefits of screening besides reduced mortality, such as fewer aggressive treatments through early detection, reduction of morbidity associated with advanced stages

Table 1. Recommendations for breast cancer screening in average-risk women

	ACR	NCCN	ACS	ACP, USPSTF	EUSOBI	ESMO
Age to initiate (years)	40	40	45; offer at 40–44	50; individualize at 40–49	50; Consider also 40–49	50; Consider also 40–49
Screening interval	Annual	Annual	Annual for 40–54; biennial or annual >55	Biennial	Biennial for 50–69; Annual for 40–49	Annual or biennial for 50–69
Age to end	Not yet established; Continue if life expectancy >5–7 years	Not yet established; Continue if life expectancy ≥10 years	Continue if life expectancy ≥10 years	74	69; Consider also 70–74	69; Consider also 70–74

ACP, American College of Physicians; ACR, American College of Radiology; ACS, American Cancer Society; ESMO, European Society of Medical Oncology; EUSOBI, European Society of Breast Imaging; NCCN, National Comprehensive Cancer Network; USPSTF, U.S Preventive Services Task Force.

of the disease, and years of life lost to breast cancer. Annual screening appears to result in fewer deaths from breast cancer, especially in younger women, although it does lead to higher costs associated with additional recalls and invasive procedures.[5] However, where each organization determines where to draw the line between what is acceptable or not varies.

In Europe, each country has differently organized breast cancer screening programs. Most of the European programs suggest biennial screening from 50 to 70 years. These practices are in line with the recommendations of the European Society of Breast Imaging (EUSOBI). EUSOBI recommends biennial mammography screening for women aged 50–69 years and also suggests the extension of mammography screening for women aged 40–49 years and 70–75 years, annually and biennially, respectively.[6] Of note, the United Kingdom National Health Service offers screening every 3 years for women aged 50–70 years, although some subspecialty societies recommend more frequent screening, *i.e.* the Royal College of Radiologists suggests that a 2-year interval would be more appropriate.[7] The European Society for Medical Oncology (ESMO) recommends annual or biennial screening mammography in women aged 50–69 years and suggests that regular mammography may also be performed in women aged 40–49 years and 70–74 years, although noting that the evidence of benefit is less well established.[8] Table 1 summarizes the recommendations of the most important societies for breast cancer screening in average-risk women.

POTENTIAL HARMS OF SCREENING MAMMOGRAPHY

When discussing the criticisms of screening mammography, it is important to note the larger perspective and thus the main context for the criticisms: is the perspective a societal one with state-organized national screening programs where cost-effectiveness or economic aspects are likely to be emphasized; or is the perspective a patient-centered one with individualized healthcare where medical and psychological implications of screening are likely to be emphasized?

The most important potential harms associated with mammographic screening are false-positive diagnosis and overdiagnosis, leading to economic and medical implications.

False-positive recalls lead to increased costs of screening, thus reducing the benefit-to-cost ratio, because it leads to additional imaging and invasive procedures and can increase screening-associated morbidity. In general, recall rates tend to be higher in opportunistic screening than in organized screening programs where specified (low) recall rates are enforced. Screening with improved radiographic breast imaging methods such as digital breast tomosynthesis (DBT) can reduce false-positive recalls, especially in younger [9]women; however, DBT is not yet widely used for population-based screening and reduced costs due to reduced false-positive calls are counter-weighted by increased costs for equipment and radiologist reading of DBT studies. From a medical or individual perspective, the potential harms related to false-positive results might be overestimated; usually less than 5% of all false-positive recalls result in invasive procedures. A recent meta-analysis has shown that women value the possibility of an earlier diagnosis over the risks of a false-positive result, and they understand that false-positive diagnoses are an unavoidable part of radiologists' attempts to find breast cancer as early as possible.[10]

Overdiagnosis is defined as the detection of a biologically insignificant cancer that would not reduce an individual's well-being and life expectancy in the absence of screening. Estimates of its magnitude are unreliable.[7] Even now, with recent advances in molecular biology, it is not possible to identify tumours that do not progress to clinically significant disease. Overdiagnosis is related to age; in a woman in her 40s or 50s, overdiagnosis is rare; however, in a woman in her 80s, it becomes an issue.[11] Therefore, overdiagnosis should not be a factor to decide when to start screening or how often screening should be performed. Delaying the onset or increasing the screening interval will raise the rate of overdiagnosed cancers and retard the diagnosis of rapid-growing and more biologically aggressive cancers, leading to underdiagnosis. The devastating consequences of a late diagnosis should also be recognized, especially for young women, who are the most adversely affected by the years of life lost due to the disease. Although the adverse effects of overdiagnosis can be relieved by providing patient information and proper management, the lethal consequences of underdiagnosis cannot be mitigated.[12]

RISK ASSESSMENT AND RISK-ADAPTED SCREENING

The ACR has issued new guidelines recommending that breast cancer risk assessment should be performed in all women at the age of 30 years to guide counselling regarding surveillance, genetic testing, and risk reduction treatments.[13] For screening purposes, a woman is considered at average risk if she does not have a personal history of breast cancer, strong family history of breast cancer, high-risk predisposition syndromes or genetic mutations, and no history of thoracic radiation therapy before the age of 30 years.[14] Risk assessment can be performed with validated statistical tools, such as the Gail, Claus, Tyrer–Cuzick, BRCAPRO, and BOADICEA models; a woman with 15% or less lifetime risk of breast cancer is considered as average risk. Women with higher than average risk should undergo different screening strategies, *i.e.* supplemental imaging modalities such as MRI or ultrasound.[13,15]

Risk assessment models have been validated in specific populations based on different variables including classical risk factors such as age, first- and second-degree family history, and personal medical and reproductive history.[16] These models are usually not applicable to women with hereditary cancer syndromes; thus, using guidelines to determine if a patient is a candidate for genetic counselling and possibly genetic testing are essential components to a comprehensive breast cancer screening program.[16] Additionally, polygenic risk scores based on low penetrance single nucleotide polymorphisms (SNPs) will probably play an important role in breast cancer risk assessment in the future.[17] It is also important to note that mathematical risk assessment models vary in their ability to accurately incorporate risk associated with the presence of high-risk lesions in prior biopsies, such as atypical ductal hyperplasia and lobular neoplasia, and that most of these models do not include mammographic density assessment, which is an independent risk factor for breast cancer.[18] Recently, deep learning models using mammographic images demonstrated the potential to substantially improve risk discrimination compared with an established breast cancer risk model that includes breast density.[19] These findings reinforce the need to develop more individualized and accurate risk assessment tools that include classical risk factors, genetic assessment, and image features.

The American College of Obstetricians and Gynecologists (ACOG) guidelines, published in 2017, stated that average-risk women should be offered screening mammography at age 40 years and that the screening strategy should be made through a shared decision-making process between patient and physician.[20] In this context, it is important that the information provided to women about the benefits and potential harms of screening should be available in a transparent and objective way so they can make informed decisions. Because high breast density is a known risk factor for breast cancer and will reduce the diagnostic accuracy of mammography, density reporting laws in the United States support the awareness of this condition and supplemental screening for these women. The implementation of risk-adapted breast screening strategies incorporating breast density could further refine the risk assessment process in average-risk women. Based on risk stratification, women may be offered screening with an individually adjusted starting age and different imaging modalities. Because annual screening appears to provide additional benefit over biennial screening, particularly in younger women, the ACS recommends that women should be offered the opportunity to begin annual screening at age 40 years and that women aged 55 years and older should transition to biennial screening or could continue screening annually.

CONCLUSION

The differences between guidelines and recommendations are the relative value that different groups place on the perceived harms of screening. Despite the different recommendations, most agree that mammographic screening should be offered at age 40 years for average-risk women and that the benefits and potential harms should be discussed to achieve a personalized screening strategy through a shared decision-making process.

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COMPETING INTERESTS

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