

Review: Screening mammography reduces risk for breast cancer mortality but increases other risks in women 40 to 49 years of age

Armstrong K, Moye E, Williams S, Berlin JA, Reynolds EE. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. *Ann Intern Med.* 2007;146:516-26.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆☆ Oncology ★★★★★☆☆☆

QUESTION

In women 40 to 49 years of age, what are the risks and benefits of screening mammography?

METHODS

Data sources: MEDLINE (1966 to 2005), Pre-MEDLINE, Cochrane Central Register of Controlled Trials, and bibliographies of relevant studies (to May 2005).

Study selection and assessment: English-language randomized controlled trials (RCTs), meta-analyses, cohort studies, or observational studies that evaluated breast cancer mortality, false-positive mammograms, effects of screening mammography on treatment, or other risks in women ≥ 40 years of age. Case series and ecological studies were excluded (except for those evaluating ductal carcinoma in situ [DCIS]). 117 studies met the selection criteria; most were cohort studies. Quality assessment of individual studies was based on criteria from the Oxford Centre for Evidence-based Medicine.

Outcomes: Included breast cancer mortality, morbidity, radiation-induced cancer or death, overdiagnosis (DCIS), false-positive mammograms, and procedural pain.

MAIN RESULTS

Meta-analysis of RCTs showed that screening mammography reduced risk for breast cancer mortality in women 40 to 49 years of age, although the effect size was smaller than in women ≥ 50 years of age (Table). Screening

increased risk for mastectomy and radiation therapy but reduced risk for chemotherapy and hormone therapy compared with a control (Table). Radiation increased risk for breast cancer, but incidence of radiation death was low (Table). Screening increased the incidence of DCIS, but the proportion of women with DCIS who developed invasive breast cancer was variable (Table). Screening led to a high cumulative incidence of false-positive mammograms (Table). The prevalence of procedural pain was variable (Table).

CONCLUSION

Screening mammography reduces risk for breast cancer mortality, chemotherapy, and hormone therapy but increases risk for mastectomy, radiation therapy, radiation-induced breast cancer, diagnosis of ductal carcinoma in situ, and cumulative false-positive mammograms in women 40 to 49 years of age.

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Risks and benefits of screening mammography in women 40 to 49 years of age*

| Outcomes | Number of studies | Summary of findings |
|--------------------------------------|-------------------|---|
| Breast cancer mortality | 1† | 7% to 23% risk reduction but smaller effect size than in women ≥ 50 y (women 40 to 49 y vs women ≥ 50 y = RR 0.85, 95% CI 0.73 to 0.99 vs RR 0.78, CI 0.70 to 0.87) |
| Morbidity | 1 | 25% risk increase for mastectomy, 24% risk increase for radiation therapy; risk reduction for chemotherapy and hormone therapy compared with a control |
| Radiation-induced breast cancer | 20 | Increase in risk (14 studies, RR 1.3 to 11); no risk increase in 6 studies |
| Radiation death | 4 | 30 to 200 deaths per 100 000 women screened; increase in risk (2 studies, RR 3.15 and SMR 1.69); no risk increase in 2 studies |
| Diagnosis of DCIS | 4 | Increased incidence of DCIS with screening |
| Breast cancer from DCIS | 7 | 8.2% to 66% of women with DCIS developed invasive breast cancer at 5 to 22 y |
| Cumulative false-positive mammograms | 3 | 20% to 56% incidence after 10 mammograms |
| Procedural pain | 22 | 0.9% to 77% prevalence |

*RR = relative risk; SMR = standardized mortality ratio; DCIS = ductal carcinoma in situ. CI defined in Glossary.

†Meta-analysis of RCTs.

COMMENTARY

Most health insurers in the United States pay for screening mammography in women 40 to 49 years of age. Whether this is a wise public policy for this age group has been debated for ≥ 20 years. The comprehensive systematic review by Armstrong and colleagues focuses on non-breast cancer mortality outcomes in women serially screened for breast cancer with mammography.

First, mammography is effective for detecting cases of early-stage cancer and leads to some reduction in breast cancer deaths. Unfortunately, the relative risk reduction (RRR) (14% vs 25%) and absolute risk reduction (RRR \times incidence/y) in this age group are lower than in women > 50 years of age. Second, the review highlights that women with a first-degree relative with breast cancer have about a 75% increased risk for breast cancer during their 40s. However, the efficacy of mammography in high-risk women and in women without a family history did not differ. Third, the epidemic of DCIS is succinctly reviewed. In women 40 to 49 years of age, $> 25\%$ of cases of cancer are DCIS, of which $> 85\%$ are detected by mammography. Our knowledge of the natural history of DCIS is limited. Are women with DCIS overtreated, thus incurring substantial physical and psychological stress? (2) Other adverse effects of screening younger asymptomatic women include

potential false-positive results; low exposure to radiation; procedural pain; and increased risk for mastectomy, lumpectomy, or other treatment methods (because of detecting breast pathology).

The review by Armstrong and colleagues provides the components that women and their physicians must weigh before initial testing (3). The math is complex—closer to calculus than arithmetic. The authors reach a reasonable conclusion: “A woman 40 to 49 years of age who had a lower-than-average risk for breast cancer and higher-than-average concerns about false-positive results might reasonably delay screening. Measuring risks and benefits accurately enough to identify these women remains a challenge.”

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