Mammography Screening in Women 40 to 49 Years: More Data to Fuel Debate

Miller AB, To T, Baines CJ, Wall C. The Canadian National Breast Screening Study-1: breast cancer mortality after 11 to 16 years of follow-up: a randomized screening trial of mammography in women age 40 to 49 years. Ann Intern Med 2002;137(5 Pt 1):305–12.

Study Overview

Objective. To determine if annual mammograms, regular breast examinations, and breast self-examination reduced mortality from breast cancer in women aged 40 to 49 years.

Design. Randomized controlled trial.

Setting and participants. 50,430 women aged 40 to 49 years were recruited between January 1980 to March 1985 from 15 Canadian centers. Exclusion criteria included pregnancy, previous diagnosis with breast cancer, and mammography within the preceding 12 months. All participants received an initial breast examination and instruction in breast self-examination. Subsequently, the patients were randomized either to annual mammography, regular breast physical examination, and instruction in self-examination (n = 25,214) or to usual care within the context of the Canadian health care system (n = 25,216).

Main outcome measures. Verified breast cancer incidence, breast cancer mortality, and total cohort mortality.

Main results. 105 breast cancer deaths occurred in the mammography group versus 108 deaths in the usual care group, yielding a cumulative rate ratio of 1.06 (95% confidence interval [CI], 0.80–1.40) after 11 to 16 years of follow-up. 592 cases of invasive cancer and 71 cases of in situ cancer occurred in the mammography group compared with 552 invasive cancers and 29 in situ cancers in the usual care group.

Conclusion. Annual mammography and regular breast examination in women aged 40 to 49 years did not reduce mortality from breast cancer in this cohort. Based on the statistical power of the study, a greater than 20% reduction in mortality is unlikely.

Commentary

Despite advances in breast cancer awareness and screening rates, breast cancer continues to be the second leading cause of death in women. Nearly half of these deaths occur in the absence of known major risk factors [1]. However, mammography for women between the ages of 40 and 49 years continues to be controversial. Five of 7 randomized trials show a small breast cancer mortality benefit with a summary relative risk of 0.85 (95% CI, 0.73–0.99), yet others, including this Canadian study, show no benefit. This study was the one of the few designed to specifically address screening benefits in the 40- to 49-year-old age group. The question is important not only because of cost, but also because of the patient morbidity and discomfort from follow-up diagnostic biopsies.

Are there flaws in this trial that would allow us to discount its contrarian conclusion? Few are apparent. The randomization was unbiased, the intervention was well-standardized, and the follow-up rates are exceptional, with more than 99% of participants completing follow-up in both the intervention and control cohorts. There was evidence of some contamination with 26% of control group participants undergoing mammograms outside the study, but this is unlikely to explain fully the null result. It also is possible to criticize the use of prescreened volunteers who may have differed from the general population. If they were indeed lower risk, then the results may be biased towards the null. As expected, periodic mammograms did detect a greater number of in situ (largely nonpalpable) cancers, but it is reasonable to argue that many of these may be indolent and would have remained clinically undetectable.

The addition of this well-designed randomized trial to the previous literature on breast cancer screening increases the uncertainty about the benefits of mammography screening in the 40- to 49-year-old age group. A systematic review of recent randomized trials of breast cancer screening [1], which did not include this study, concluded that mammography benefits still outweigh the risks with a summary relative risk of 0.84 (95% CI, 0.71–0.91). The cost is high, however, with an estimated 1792 mammograms needed to prevent 1 breast cancer death. All of the organizations that publish guidelines on breast cancer screening continue to recommend mammography. Despite this study's conclusions, more data on mortality and morbidity will be needed before the current recommendations could be changed.

Applications for Clinical Practice

Screening of women aged 40 to 49 years remains controversial but continues to be the current standard of care in the United States and should be continued until more high-quality evidence is gathered.

–Review by Josh F. Peterson, MD, MPH

References

1. Humphrey LL, Helfand M, Benjamin KS, et al. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137 (5 Pt 1):347–60.