Impact of Breast Cancer Screening Interval on Stage at Diagnosis and Overall Survival

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Annual mammographic screening appeared to be associated with a reduced risk of late-stage breast cancer and an overall survival benefit across clinical and demographic subgroups of patients older than age 40, according to an observational analysis reported by Zuley et al in the *Journal of Clinical Oncology*.

"Screening guidelines must balance the benefits of additional detection with the potential harms and costs associated with false positives," commented Senior Deputy Editor **Kathy D. Miller, MD, FASCO**, of The Indiana University Melvin and Bren Simon Comprehensive Cancer Center Women's Clinic in Indianapolis, in a statement. "This study complements results from modeling studies and supports annual screening for most women."

Study Details

Using a real-world institutional research breast data mart, the investigators identified 8,145 patients with breast cancer who were older than age 40 and underwent prediagnosis mammographic screening between 2004 and 2019. Of this population, 1,470 (18%) were aged 50 or younger at diagnosis, 4,312 (53%) were aged 60 or older, 7,287 (89%) were White, 6,224 (76%) were postmenopausal, and 2,305 (28%) had first-degree relatives with breast cancer. Early-stage (I–IIA; grade 2) and late-stage (IIB–V) disease was observed in 2,065 (25%) and 1,121 (14%) patients, respectively.

The investigators determined both the interval between the last two screening mammograms before diagnosis and the time until diagnosis (range = 24–28 days across all screening intervals). Screening intervals were classified into four categories:

- Baseline (n = 2,307; 28%): one screening episode before diagnosis
- Annual (n = 3,369; 41%): up to 15 months between the two most recent screenings
- Biennial (n = 1,340; 16%): more than 15 months to up to 27 months between the two most recent screenings
- Intermittent (n = 1,129; 14%): more than 27 months between the two most recent screenings.

The investigators primarily sought to determine the rate of late-stage cancer diagnosis. Subsequent overall survival was identified as the secondary endpoint of the study. The association of screening interval and late-stage cancer was analyzed using a multivariable logistic regression model adjusting for prediagnostic characteristics. A proportional hazards regression model was used for the survival analysis. The investigators analyzed the potential lead time using survival from a uniform fixed time point (December 31, 2009).

Impact of Breast Cancer Screening Interval

Late-stage cancer diagnosis rates were 9%, 14%, and 19% in the annual, biennial, and intermittent groups, respectively ($P < .001$), with this increasing trend by longer screening interval apparently persisting across age, race, and menopausal status.

Patients who underwent biennial (univariable hazard ratio [HR] = 1.42, 95% confidence interval [CI] = 1.11–1.82: multivariable HR [adjusted for age, race, menopausal status, and first-degree relatives with breast cancer] = 1.48) and intermittent (univariable HR = 2.69, 95% CI = 2.11–3.43; multivariable HR = 2.04) vs annual screening were found to have significantly worse overall survival ($P < .001$); this also seemed to hold true after adjusting for potential lead time, with hazard ratios of 1.39 (95% CI = 1.08–1.78, $P = .010$) and 2.01 (95% CI = 1.58–2.55, $P < .001$), respectively.

The investigators concluded: “Data from 16 years of screening mammography (which include full-field digital mammography, digital breast tomosynthesis plus full-field digital mammography, and digital breast tomosynthesis plus synthetic mammography) showed that annual screening is associated with a lower likelihood of having late-stage cancer, as well as higher overall survival, compared with biennial screening or intermittent screening. This benefit of annual screening persisted across all age, race, and menopause status categories. Our results show unequivocally the advantages of annual asymptomatic breast cancer screening starting at age 40.”

Margarita L. Zuley, MD, FACR, FSBI, of the University of Pittsburgh, is the corresponding author of the article in the *Journal of Clinical Oncology*.

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