The Role of Regular Mammograms in Finding Interval Breast Cancer

BY AMY GALLAGHER

Strategies beyond current mammographic screening practices are needed to reduce incidence, improve detection, and reduce deaths from interval breast cancers, according to a conclusive statement from a research study led by author Saroj Niraula, MD, MSc, a medical oncologist at CancerCare Manitoba and Assistant Professor at the University of Manitoba, Winnipeg, Canada.

“While screenings are based on noble principles, they do have harms,” said Niraula. “By and large, mammogram screenings are for healthy people.”

Accumulating 6 years of research data, the comparative study analyzed breast cancer tumor characteristics diagnosed within 2 years of normal screening mammogram, referred to as “interval” with respect to interval breast cancer (IBC), with screen-detected breast cancers (SBC) to identify the tumor differences and similarities in characteristics, incidences, and outcomes of breast cancer-specific mortality of IBC with SBC. IBC is the cancer detected after a normal screening mammogram and prior to the next scheduled mammogram.

“By its very definition, IBC defies assumptions necessary for screening mammography to be maximally effective,” he said. “A regular mammogram screening does not improve the outcome of an IBC because it does not capture it.”

Challenging the Effectiveness of Screenings

The researcher’s results shed light on the heterogeneity of breast cancer that poses three assumptions to prove the effectiveness of mammographic screening: 1) breast cancer likely grows in anatomic linearity starting in the breast, then metastasizes to distant organs mostly via regional lymph nodes; 2) breast cancers are mostly mammogram-sensitive; and 3) frequency of screening is coherent with natural history of breast cancer so that most cancers, particularly the more lethal and/or treatable ones, are detected early by screening.

“These conditions must be fulfilled for a mammogram screening to be effective,” said Niraula. “Because IBC is not detected by regular screenings, the question then becomes: Is the balance of benefit and the risk of only detecting SBC favorable enough?”

Evidence collected from the study suggests that breast cancer represents a heterogeneous group of highly indolent to fatally aggressive conditions, which presents as a major impediment in the effectiveness of mammographic screening.

Study Design, Setting & Participants

In this registry-based cohort study, Niraula and his team collected data about relevant tumor- and patient-related variables on women diagnosed with breast cancer between January 2004 and June 2010 who participated in the population-based screening program in Manitoba, Canada, and those diagnosed with breast cancer outside the screening program in the province.

“We performed multinomial logistic regression analysis to assess tumor and patient characteristics associated with a diagnosis of IBC compared with SBC, while competing risk analysis was performed to examine risk of death by cancer detection method,” Niraula explained.

The cohort of 69,025 women showed that IBCs accounted for one-fourth of breast cancers in routinely screened women, were 6 times more likely to be grade 3, and had 3.5 times increased hazards of breast cancer death compared with screen-detected cancers.

Main Outcomes & Measures

Niraula stated that, of the 1,687 women diagnosed with breast cancer, 705 were detected during the regular screening, with 206 diagnosed in-between screenings, thus the IBC when the cancer develops between the two mammogram screenings.

“This means that one-third of the patient cohort was IBC; 1 in 3 undiagnosed patients that are categorically more aggressive is unacceptable,” he said. “These are the patients who are dying.”

The IBC patient is 4 times more likely to die; the outcome for the IBC patient is looking terrible, added Niraula.

The results in differences in tumor characteristics and breast cancer–specific mortality showed that, after a median follow-up of 7 years, 170 women had died from breast cancer and 55 women died of other causes. Of the breast cancer deaths, 20 had SBC, 29 had IBC, 27 were noncompliant, and 94 were non-screening program detected.

Survival analysis demonstrated that, for a sojourn time of 2 years, the unadjusted risk of death from breast cancer was significantly higher for IBC compared with SBC (HR 3.55; 95% CI, 2.01-6.28). Compared with SBC, IBC was more likely to be of high grade and estrogen receptor-negative (odds ratios, 6.33 [95% CI, 3.73-10.75; P < 0.001] and 2.88 [95% CI, 2.01-4.13; P < 0.001], respectively). Breast cancer-specific mortality was higher for IBC during a median follow-up of 7 years compared with SBC.

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The greater reduction in hospital visits for cancer patients may be related to resource and supply chain constraints imposed by the influx of COVID-19 cases, as well as patient reluctance to use outpatient cancer services in the face of potential COVID-19 transmission. In April 2020, for example, billing frequencies for E/M services declined by 61 percent in independent practice settings compared to 71 percent in institutional settings.

Increased regulatory flexibilities have led to a significant rise in the use of telehealth services, but access remains an obstacle for many cancer patients, especially when the services needed cannot be feasibly rendered at a distance.

Providers in independent practice settings have had significantly greater adoption of telehealth in response to COVID-19 than have those in institutional settings. From March to July of 2020, usage claims for cancer-related telehealth ranged from 95 percent to 97 percent for independent community oncology practitioners, compared to 6 percent or lower for institutional settings during that time period. The study suggests that limited use of telehealth in hospital settings could be attributed to more limited hospital resources due to the additional strain of COVID-19 cases.

On Sept. 24, 2020, the COA Board of Directors issued a position statement supporting the use of telehealth as a valuable supplement to in-person visits during the pandemic and continued appropriate usage when the pandemic has subsided.

In the position statement, Patt stated, “Telehealth isn’t a replacement for in-person visits, but it has allowed us to keep seeing new and existing patients at a time when coming into the office could be life-threatening to them. Cancer doesn’t stop for COVID,” which is why it has been absolutely critical for us to continue seeing patients and getting them the care they need.”

Mark Thompson, MD, COA’s Medical Director of Public Policy, praised the federal government’s expansion of telehealth during the pandemic. “Prior to the COVID-19 pandemic, telehealth regulations were extremely cumbersome and limiting at the state and federal levels, with poor reimbursement,” he said. “The rapid response of federal policymakers to loosen telehealth restrictions and raise reimbursement rates were a true lifesaver for patients and practices.”

Reductions in cancer screenings have long-term implications for the number of biopsies in subsequent months, as these patients could now have delayed diagnoses until their next scheduled cancer screening or until their disease becomes symptomatic.

Reductions in infusion services in July 2020 and later months may be attributable to delayed and postponed cancer screenings. In April 2020 billing for chemotherapy services was down by 28 percent for independent community practices and 21 percent for institutional practices.

There were decreases in cancer-related surgeries in April 2020 and July 2020 compared to those months in 2019. Decreased cancer surgeries include mastectomies, colectomies, and prostatectomies. These decreases reflect the impact of COVID-19 on cancer treatment pathways; the decreases during the pandemic reflect treatment guidelines allowing surgeries to be delayed. Decreases in later months may also reflect the downstream impact of delayed or missed cancer screenings.

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Cancer Screening During COVID-19

Randall A. Oyer, MD, President of the American Association of Community Cancer Centers (ACCC) and Medical Director of the Oncology Program at Penn Medicine Lancaster General Health, expressed the ACCC’s concerns regarding cancer screening during the pandemic: “After so many years of steady decrease in both mortality and late-stage diagnosis rates, the health care community understood the catastrophic impact that COVID-19 might have on screenings and diagnoses. The rise in advanced metastatic rates and change in death rates we see…is a dire warning to all sectors of health care to do whatever it takes to encourage screenings and reassure patients.”

The ACCC recommends the following to improve cancer screening:

- Use of mobile medical clinics to deliver cancer screenings;
- Development and dissemination of safety protocols directly to patients—and through social media—to show how hospitals and clinics are keeping patients safe;
- Outreach and education to local media and community organizations about new measures to ensure safe screenings and the importance of not putting off regular appointments, and to ask for their help to disseminate this information and encourage patients to resume screenings; and
- Proactive outreach to patients to remind them of their need for screenings, and to engage in personal conversations to allay their fears, rather than waiting for patients to schedule or reschedule their appointments.

Oyer said the ACCC is using online resources to address the financial impact of COVID-19, which can affect patients’ decisions to delay cancer screenings or treatments.

Conclusions & Relevance

In this cohort study, IBCs were highly prevalent in women participating in population screening, represented a worse biology, and had a hazard for breast cancer death more than 3 times that for SBC.

“Improvement of breast cancer deaths and overall population mortality requires strategies above and beyond conventional screening mammography,” said Niraula.

Such strategies could be personalized screening strategies individualizing the screening test based on baseline risks; exploring other methods (e.g., tomosynthesis, magnetic resonance imaging after carefully defining target population, and demonstrating in clinical trials that these approaches improve outcomes at acceptable level of harms); use of artificial intelligence platforms to empower radiology professionals (our group is involved in one); a different frequency of screening, with attention to potential for and consequences of over diagnosis; and being open for reevaluation of population-based screening mammography concept based on risk-benefit ratio in the contemporary context.

In an action step to improve screening strategies, Niraula plans to expand the population of this study, looking at trends nationally, or perhaps a comparative analysis internationally with other countries.

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