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Factors associated with imaging in patients with early breast cancer after initial treatment

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ABSTRACT

Background Overuse of surveillance imaging in patients after curative treatment for early breast cancer (EBC) was recently identified as one of the Choosing Wisely Canada initiatives to improve the quality of cancer care. We undertook a population-level examination of imaging practices in Ontario as they existed before the launch of that initiative.

Methods Patients diagnosed with EBC between 2006 and 2010 in Ontario were identified from the Ontario Cancer Registry. Records were linked deterministically to provincial health care databases to obtain comprehensive follow-up. We identified all advanced imaging exams [AIEs: computed tomography (CT), bone scan, positron-emission tomography] and basic imaging exams (BIEs: ultrasonography, chest radiography) occurring within the first 2 years after curative treatment. Poisson regression was used to assess associations between patient or provider characteristics and the rate of AIEs.

Results Of 30,006 women with EBC, 58.6% received at least 1 BIE, and 30.6% received at least 1 AIE in year 1 after treatment. In year 2, 52.7% received at least 1 BIE, and 25.7% received at least 1 AIE. The most common AIEs were chest CTs and bone scans. The rate of AIEs increased with older age, higher disease stage, comorbidity, chemotherapy exposure, and prior staging investigations ($p < 0.001$). Imaging was ordered mainly by medical oncologists (38%), followed by primary care physicians (23%), surgeons (13%), and emergency room physicians (7%).

Conclusions Despite recommendations against its use, imaging is common in EBC survivors. Understanding the factors associated with AIE use helps to identify areas for further research and is required to lower imaging rates and to improve survivorship care.

Key Words Early breast cancer, imaging overuse, curative treatment

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INTRODUCTION

Breast cancer is the most common cancer diagnosed in Canadian women, and the second most common cause of cancer death. Advances in detection and treatment have resulted in 5-year survival rates exceeding 80%[1], which translates to approximately 20,000 new breast cancer survivors annually in Canada. Optimal survivorship care for patients diagnosed with early breast cancer (EBC) includes management of the short- and long-term sequelae of cancer treatment, monitoring for recurrent or secondary cancers, and improving quality of life[2]. The care for EBC survivors is often shared between multiple providers, including primary care physicians, oncologists, and surgeons[3]. As breast cancer survivors become more prevalent, the care of these women has the potential to significantly affect health care resource utilization.

Current survivorship guidelines recommend that, outside of annual screening mammography, no imaging is indicated in asymptomatic survivors during follow-up[4,5]. Surveillance imaging in asymptomatic EBC patients who have completed curative treatment does not lead to clinically meaningful improvements in survival[6,7]. Unnecessary imaging has also been shown to increase patient anxiety, health care costs[8,9], and radiation exposure in a population already vulnerable to secondary malignancies[8,10,11]. Despite the evidence and the guidelines, surveillance imaging continues to occur in breast cancer survivors after curative treatment. The issue has prompted both the American Society for Clinical Oncology and Choosing

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Wisely Canada to cite reduction in the overuse of surveillance imaging in women who have completed curative treatment for EBC as one of their top recommendations[12,13].

Determining the reasons behind imaging overuse is complex. Prior studies have correlated factors such as younger age, more comorbidity, and higher disease stage with rates of imaging[14–16], but few studies have examined the post–curative treatment population, and actionable causative factors have yet to be identified. We conducted a population-level assessment of recent imaging practices in Ontario in women treated for EBC to identify potentially actionable areas for quality improvement.

METHODS

Study Cohort

Using unique encoded identifiers, multiple administrative health care databases were linked to create a comprehensive population-level data source for the study. All women diagnosed with early-stage (I–III) breast cancer between 1 January 2006 and 31 December 2010 in Ontario were identified from the Ontario Cancer Registry. Patients who were male, were less than 18 years of age, lacked a record of curative-intent surgery within 12 months of diagnosis, had stage IV disease, or had been diagnosed with ductal carcinoma *in situ* were excluded.

Imaging Definitions

Imaging occurring within years 1 and 2 after completion of treatment was identified using physician billings from the Ontario Health Insurance Plan database. To avoid capturing perioperative or staging investigations, the start point for follow-up care was defined as 30 days after completion of chemotherapy or 6 months after surgery if no chemotherapy was given.

Imaging was considered to be for surveillance if the exam had a likelihood of detecting distant metastases. Imaging was categorized as either an advanced imaging exam [AIE: computed tomography (CT), positron-emission tomography, bone scan] or a basic imaging exam (BIE: radiography, ultrasonography). Breast imaging (mammography or ultrasonography) and bone radiographs were not included in the analysis. The specialty of the ordering physician was determined using the Physician Database at the Institute for Clinical Evaluative Sciences.

Covariates

Cancer stage and patient age were obtained from the Ontario Cancer Registry. Comorbidity was assessed using the Charlson comorbidity index, modified for abstraction from administrative data[17]. Socioeconomic data were obtained using the Registered Persons Database.

Chemotherapy regimen details were obtained from the New Drug Funding Program database. Patients were categorized as having received neoadjuvant chemotherapy if they had at least 1 record of chemotherapy before curative surgery, and adjuvant chemotherapy if they had at least 1 record of chemotherapy within 4 months of surgery, but not before surgery. If no chemotherapy record was present, then the patient was categorized as "surgery, no chemotherapy."

Information about prior health care utilization and staging imaging was obtained using the Ontario Health Insurance Plan database. Health care utilization was determined by the frequency of primary care physician (PCP) and emergency department visits over a 1-year period starting 2 years before the date of the breast cancer diagnosis. A PCP visit was defined as any visit to a general practitioner. Any visit to a hospital emergency department, regardless of subsequent hospital admission, was also recorded. A history of staging imaging was noted if a patient had a record of CT thorax, abdomen, or pelvis, or bone scan within 3 months of diagnosis.

Geographic region was defined by the governing Local Health Integration Network corresponding to the patient's postal code. Within Ontario, 14 Local Health Integration Network bodies administer the delivery of health care within their defined regional area.

Validation Analysis

To validate the indications for AIEs, a targeted primary chart abstraction was conducted at 5 treating hospitals. The institutions were selected to represent a mix of academic hospitals, regional cancer centres, and community hospitals. A chart cohort was created by randomly selecting eligible patients from the larger administrative cohort at the identified institutions for patients diagnosed in 2010, the last year of the study. The sample size was selected to have 90% power to detect a 10% difference in concordance between administrative data and chart. The selected chart cohort underwent a primary chart abstraction in which all AIEs performed at the treating institution during the imaging window were identified. The reason for the imaging was adjudicated by the reviewer to be "surveillance," "symptoms," or "other" as indicated in the clinical notes.

All eligible AIEs that were identified within the chart cohort were compared with the number of imaging exams identified in the matched administrative cohort. Within the chart cohort, the proportions of exams having an indication of surveillance, symptoms, or other were identified. The proportion of patients within the chart cohort who had undergone at least 1 AIE was calculated. Because the chart cohort was restricted to imaging performed at the single institution only, advanced imaging was identified significantly more often in the administrative cohort than in the chart cohort. As a result, formal sensitivity and specificity calculations were not felt to be appropriate.

Statistical Analyses

All analyses were conducted at the Institute for Clinical Evaluative Sciences, a not-for-profit organization that conducts health research for the province of Ontario using administrative data covering all health care encounters for Ontario residents.

Descriptive statistics are used to examine the distribution of patient and provider characteristics within the entire cohort and for groups stratified by treatment type. The numbers of surveillance exams occurring in years 1 and 2 after diagnosis were assessed for each type of exam. The distribution of AIEs based on the ordering physician's specialty was also assessed. Patients frequently underwent more than 1 advanced imaging exam, and therefore a

multivariable Poisson regression model was used to determine associations between the patient and provider covariates and the rate of advanced imaging within the first 2 years of follow-up care. The natural logarithm of each patient's follow-up time was incorporated as an offset term. Covariate selection was based on *a priori* knowledge of factors that might drive imaging and on the strength of the association at univariate analysis. All database manipulation and statistical analyses were conducted using the SAS software application (version 9.3: SAS Institute, Cary, NC, U.S.A.).

RESULTS

Cohort Characteristics

Table I outlines the characteristics of the 30,006 identified EBC patients. Mean age was 60.5 years, and most patients had either stage I (44%) or II (41%) disease. Treatment was classified as adjuvant chemotherapy in 12,362 women (41.2%), surgery only in 16,065 women (53.5%), and neoadjuvant chemotherapy in 1579 women (5.3%).

Imaging Trends

Within years 1 and 2 respectively, 22,894 and 20,872 imaging exams were performed. In year 1, 58.6% of patients had at least 1 BIE, and 30.6% had at least 1 AIE. In year 2, the proportions were 52.2% and 25.7%. The median number of exams per patient in each year was 2 (interquartile range: 1–3). The most common AIE (Figure 1) was chest CT ($n = 5713$, year 1), followed by a bone scan ($n = 5323$, year 1). Most imaging was ordered by medical oncologists (38%), followed by primary care physicians (23%, Figure 2).

Factors Associated With Imaging

A multivariable Poisson regression was performed to identify factors associated with the rate of AIEs within the first 2 years of follow-up (Table II). Disease characteristics such as higher stage [II vs. I relative risk (RR): 1.22; 95% confidence interval (CI): 1.18 to 1.27; $p < 0.0001$; III vs. I RR: 1.73; 95% CI: 1.64 to 1.82; $p < 0.0001$] and chemotherapy exposure (yes vs. no RR: 1.07; 95% CI: 1.03 to 1.12; $p = 0.0009$; neoadjuvant vs. no RR: 1.38; 95% CI: 1.27 to 1.50; $p < 0.0001$) were associated with a significantly higher rate of AIEs, as were patient factors such as age and presence of comorbidities. Patients who underwent AIEs as part of their staging work-up at diagnosis had an increased rate of AIEs (RR: 1.18; 95% CI: 1.14 to 1.23; $p < 0.0001$), as did patients who had a history of high health care utilization as determined by history of either PCP or emergency department visits before their breast cancer diagnosis. No significant association between imaging and neighbourhood income quintile, rurality, or geographic location was observed.

Validation

In the 705-patient chart cohort, 229 AIEs were identified. The proportion of patients with at least 1 AIE was higher in the administrative cohort (38.9%, $n = 197$) than in the chart cohort (13.8%, $n = 97$). The indication for the AIEs was divided chiefly between symptoms ($n = 91$, 39.7%) and surveillance ($n = 112$, 48.9%); for a small proportion of the AIEs, the indication was unclear (11.4%).

DISCUSSION

In this population-based cohort study, a high rate of both BIEs and AIEs during the first 2 years of follow-up care was found in EBC patients treated in Ontario; those findings are consistent with reports from other jurisdictions[14,15]. The descriptions set out here of disease, patient, and provider characteristics associated with the use of AIEs provide valuable insight into trends in survivorship care within Ontario and could help to identify actionable areas for improvement.

The Choosing Wisely Canada campaign has highlighted the overuse of imaging investigations in EBC patients in two distinct clinical scenarios: peri-diagnosis staging investigations, and surveillance to detect disease recurrence in EBC patients after completion of curative treatment[12,13]. Simos *et al.*[16] recently reported overuse of peri-diagnosis staging imaging in EBC patients in Ontario despite recommendations against the practice. They found that 85% of EBC patients underwent at least 1 imaging for staging, of which 30% were AIEs. Similarly, we found that EBC patients continue to have a high rate of AIEs in the first 2 years after completing curative treatment. In contrast to the peri-diagnosis period, during which most imaging was ordered by surgeons, surveillance imaging during follow-up was ordered primarily by medical oncologists and PCPs, suggesting that overuse of imaging is not being driven simply by individual physician practice.

Overuse of surveillance imaging might in part be a downstream effect of the overuse of peri-diagnosis staging investigations, in which follow-up imaging is recommended once nonspecific abnormalities are found. We found that undergoing at least 1 AIE in the peri-diagnosis period was associated with a significant increase in the rate of AIEs during follow-up. Interventions that target the overuse of AIEs in the peri-diagnosis period have the potential to decrease imaging rates, both at time of diagnosis and in the years after curative treatment.

Patterns of survivorship care vary both provincially and regionally within Canada[3,18]. In Ontario, the bulk of the care receive by EBC patients is provided by PCPs and medical oncologists in a shared-care model[19,20]. The frequent lack of comfort and knowledge on the part of PCPs about survivorship care for EBC patients[21–23] might be driving some of the imaging overuse. A high rate of AIEs was identified in patients with a history of frequent health care utilization. Although imaging in that population might in part be driven by non-cancer-related symptoms and comorbidities, higher utilization might also reflect anxious patients who undergo unnecessary imaging for reassurance[14,24].

Current survivorship guidelines or campaigns such as Choosing Wisely Canada that have brought increased awareness to the potential for imaging overuse in breast cancer patients could in part address the overuse; however, they are unlikely to result in sustained change. A recent study by Rocque *et al.*[25], reporting on practices participating in the American Society for Clinical Oncology Quality Oncology Practice Initiative, which followed the launch of Choosing Wisely (2013–2015) in the United States, found that only 67.7%–74.2% of centres were compliant with surveillance imaging recommendations, whereby 25.8%–32.3% of patients underwent an AIE within year 1.

TABLE I Demographics and clinical characteristics of the study patients

Characteristic	Patient group							
	Overall		Adjuvant chemotherapy		Surgery, no chemotherapy		Neoadjuvant chemotherapy	
Patients (*n*)	30,006		12,362		16,065		1,579	
Age at diagnosis (years)								
Mean	60.46±13.39		53.65±10.55		66.54±12.46		51.93±11.91	
Median	60		53		67		51	
IQR	50–70		46–61		58–76		44–60	
Disease stage [*n* (%)]								
1	13,268	(44.2)	2,692	(21.8)	10,524	(65.5)	52	(3.3)
2	12,287	(40.9)	7,046	(57.0)	4,734	(29.5)	507	(32.1)
3	4,451	(14.8)	2,624	(21.2)	807	(5.0)	1,020	(64.6)
Score on the CCI [*n* (%)]								
0	27,808	(92.7)	11,863	(96.0)	14,411	(89.7)	1534	(97.2)
1	654	(2.2)	142	(1.1)	499	(3.1)	13	(0.8)
≥2	1,544	(5.1)	357	(2.9)	1,155	(7.2)	32	(2.0)
LHIN [*n* (%)]								
A	1763	(5.9)	699	(5.7)	980	(6.1)	84	(5.3)
B	2442	(8.1)	967	(7.8)	1321	(8.2)	154	(9.8)
C	1684	(5.6)	658	(5.3)	945	(5.9)	81	(5.1)
D	3936	(13.1)	1555	(12.6)	2173	(13.5)	208	(13.2)
E	948	(3.2)	423	(3.4)	457	(2.8)	68	(4.3)
F	1375	(4.6)	606	(4.9)	710	(4.4)	59	(3.7)
G	2617	(8.7)	1040	(8.4)	1393	(8.7)	184	(11.7)
H	3956	(13.2)	1751	(14.2)	2011	(12.5)	194	(12.3)
I	3793	(12.6)	1627	(13.2)	2009	(12.5)	157	(10.0)
J	1411	(4.7)	519	(4.2)	808	(5.0)	84	(5.3)
K	3134	(10.4)	1312	(10.6)	1614	(10.1)	208	(13.2)
L	1184	(3.9)	504	(4.1)	633	(3.9)	47	(3.0)
M	1139	(3.8)	427	(3.5)	686	(4.3)	26	(1.6)
N	609	(2.0)	271	(2.2)	315	(2.0)	23	(1.5)
Income [*n* (%)]								
Q1 (lowest)	5,245	(17.5)	1,997	(16.2)	2,949	(18.4)	299	(19.0)
Q2	5,756	(19.2)	2,214	(18.0)	3,248	(20.3)	294	(18.7)
Q3	5,813	(19.4)	2,467	(20.0)	3,040	(19.0)	306	(19.5)
Q4	6,338	(21.2)	2,745	(22.3)	3,254	(20.3)	339	(21.6)
Q5 (highest)	6,760	(22.6)	2,898	(23.5)	3,528	(22.0)	334	(21.2)
Regimen [*n* (%)]								
AC-P (dose dense)	—	—	2,233	(18.1)	—	—	227	(14.4)
AC-D	—	—	218	(1.8)	—	—	736	(46.6)
FEC	—	—	866	(7.0)	—	—	60	(3.8)
FEC-D	—	—	5,879	(47.6)	—	—	358	(22.7)
TC	—	—	1,296	(10.5)	—	—	27	(1.7)
Other[a]	—	—	1870	(15.1)	—	—	171	(10.8)

[a] Non-epirubicin, non-taxane regimens (that is, doxorubicin, cyclophosphamide).

IQR = interquartile range; CCI = Charlson comorbidity index; LHIN = local health integration network; AC-P = doxorubicin, cyclophosphamide, paclitaxel; AC-D = doxorubicin, cyclophosphamide, docetaxel; FEC = 5-fluorouracil, epirubicin, cyclophosphamide; FEC-D = 5-fluorouracil, epirubicin, cyclophosphamide, docetaxel; TC = docetaxel, cyclophosphamide.

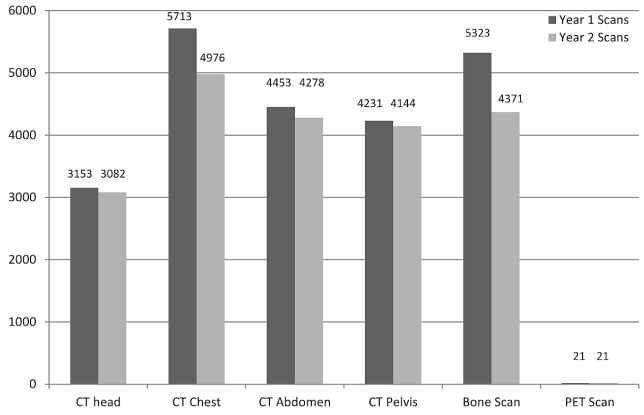

FIGURE 1 Surveillance imaging by type within years 1 and 2 after diagnosis in patients with early breast cancer. CT = computed tomography; PET = positron-emission tomography.

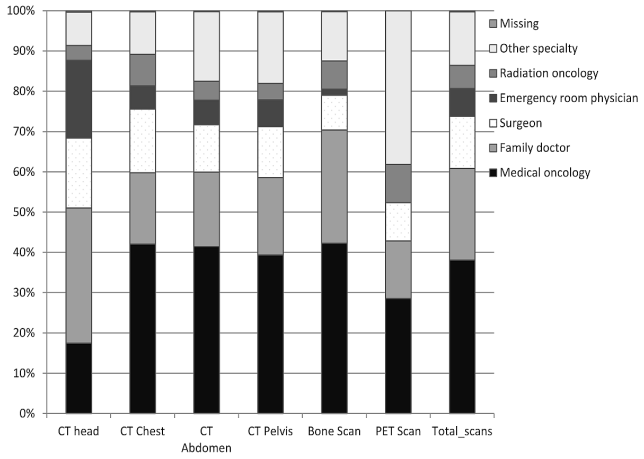

FIGURE 2 Distribution of advanced imaging by speciality of the ordering physician. CT = computed tomography; PET = positron-emission tomography.

Justifying that trend is likely complicated; however, some clinicians argue that the evidence related to breast cancer surveillance might be outdated and might therefore require newer studies[26–28]. Those debates could partly explain why AIE rates remain high. Likewise, the finding here that medical oncologists, a group in which knowledge of guidelines is high, were responsible for most of the imaging suggests that the current guideline might not be generally accepted and that an update of the clinical guideline evidence might be warranted.

Our study should be interpreted in the context of its limitations. A key drawback is the lack of information about the indications for imaging. In our validation study,45% of the imaging at the treating hospital was investigating symptoms. The use of imaging in that situation is very appropriate and is reflected in the higher rate of imaging observed in patients at highest risk of relapse (increased stage, chemotherapy exposure). The validation study that was done for the cancer clinics might overestimate the proportion of symptom-related imaging in the community (that is, exams ordered by PCPS). Even accounting for those situations, much of the imaging was performed either for

TABLE II Results of the multivariable Poisson regression model[a] for the rate of advanced imaging exams in patients with early breast cancer

Variable	RR	95% CI	*p* Value
Age at Dx (5-year increments)	0.99	0.98 to 0.99	0.0006
Score on the CCI			
0	Reference		
1	1.36	1.23 to 1.50	<0.0001
2+	1.32	1.24 to 1.41	<0.0001
Breast cancer stage			
1	Reference		
2	1.22	1.18 to 1.27	<0.0001
3	1.73	1.64 to 1.82	<0.0001
Treatment			
No CTx	Reference		
Adjuvant CTx	1.07	1.03 to 1.12	0.0009
Neoadjuvant CTx	1.38	1.27 to 1.50	<0.0001
Year of breast cancer follow-up			
1	Reference		
2	0.89	0.87 to 0.91	<0.0001
Advanced imaging at diagnosis			
No	Reference		
Yes	1.18	1.14 to 1.23	<0.0001
ED visits in the year before breast cancer Dx			
0	Reference		
1	1.17	1.13 to 1.22	<0.0001
2	1.41	1.32 to 1.49	<0.0001
3+	1.82	1.69 to 1.96	<0.0001
Outpatient PCP visits per year			
1	Reference		
2	1.16	1.10 to 1.22	<0.0001
3	1.30	1.24 to 1.37	<0.0001
4+	1.56	1.49 to 1.63	<0.0001
Neighbourhood income quintile			
1 (lowest)	Reference		
2	0.97	0.92 to 1.02	0.20
3	0.96	0.91 to 1.00	0.08
4	0.97	0.92 to 1.02	0.18
5 (highest)	0.96	0.90 to 0.99	0.02
Rural residence			
No	Reference		
Yes	0.96	0.91 to 1.01	0.10

[a] Also controlled for local health integration network (*p* value non-significant).

RR = rate ratio; CI = confidence interval; Dx = diagnosis; CCI = Charlson comorbidity index; CTx = chemotherapy; ED = emergency department; PCP = primary care provider.

surveillance or for no clear indication, signalling potential overuse. Second, the use of administrative data limits the amount of clinical information available for analysis, and unmeasured clinical factors could possibly be influencing the patterns of imaging. However, that limitation is common to all similar studies. The effect of radiation therapy on AIEs was not assessed in this present study; some patients could have had radiation therapy during the first 2 months of their year 1 assessment window. In that case, radiation could possibly have had a small effect on imaging patterns during that time; however, AIEs remained high in year 2, remote from radiation therapy, making it unlikely that radiation therapy is a primary driver.

CONCLUSIONS

The present study strengthens the evidence showing that rates of advanced imaging remain high despite clinical guidelines recommending against the practice, with more than half the exams having no clear indication. The findings here suggest that quality improvement interventions targeting overuse of staging investigations would have a downstream effect in lowering the number of AIEs in follow-up. Likewise, improved knowledge translation and care coordination with PCPs might reduce the overuse of AIEs in EBC patients.

Although potential actionable areas for improvement have been identified here, further work will be required to translate those findings into improvements. Providers, practices, or health systems will have to adapt these learnings to their local context, planning and implementing targeted quality improvement interventions focusing on the identified gaps, and following the effects over time. As the population ages and the number of cancer survivors grows, governing bodies should renew their focus on survivorship care to reduce the potential burden on the health care system—and more importantly, on the survivors themselves.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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