Screening for a New Primary Cancer in Patients with Existing Metastatic Cancer.

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Abstract

Background
Cancer screening aims to detect malignancies early in their natural history when interventions might improve future outcomes. Such benefits are unclear when screening occurs for patients with an existing high risk of mortality. We studied the extent of routine cancer screening for a new primary cancer in patients with existing metastatic cancer.

Methods
We used administrative databases from Ontario, Canada to identify a cohort of adult residents of eligible screening age (age 50 or older) diagnosed with stage IV (metastatic) colorectal (CRC), lung, breast, or prostate cancer between 2007-2012. We calculated the cumulative incidence of cancer screening over time for CRC and breast cancer.

Results
Among the 20,992 patients with metastatic lung, breast, and prostate cancer, CRC testing within 1 year of cancer diagnosis occurred in 2.9%, 6.3%, and 13.3%, respectively. Within 3 years of diagnosis, rates reached 4.1%, 12.3%, and 27.5%, respectively (8.5% of all patients). Incidence of CRC testing was higher in patients diagnosed in more recent eras compared to those in earlier eras (p=0.0143). Among the 10,034 women with metastatic lung and CRC, breast cancer screening within 1 year following cancer diagnosis occurred in 8.7% and 8.0% of women, respectively. Within 3 years of diagnosis, screening rates reached 10.2% and 13.1%, respectively.

Interpretation
Our findings indicate excessive rates of cancer screening in metastatic patients who are unlikely to benefit. Further studies are warranted to identify predictors for screening, resource implications, potential and real harms borne by patients, and the impact of a recent Choosing Wisely statement recommending against the practice.

Interpretation

As the prevalence of cancer increases and the cost of care rises in parallel, it becomes increasingly important that resources for cancer care are judiciously applied. Screening for breast and colon cancer is now common due to demonstrated mortality benefits in healthy individuals when early-stage malignancy can be detected.[1-6] However, in patients with metastatic cancer, this long-term benefit is unlikely to be realized and is associated with potential harm and unnecessary resource consumption. Furthermore, excessive screening could impose further medical complications and discomfort (i.e. related to screening procedures themselves or subsequent investigations), added costs, and psychological burden on patients at their most vulnerable. These risks associated with testing are unlikely to be offset by any improvement in life expectancy or quality of life.

The *Choosing Wisely Canada* (CWC) campaign aims to initiate conversations about unnecessary treatments and procedures and guide high-quality care.[7] In particular, the CWC campaign in cancer seeks to reduce unnecessary interventions that are not supported by evidence or could contribute inordinately to the rising cost of cancer care (http://www.choosingwiselycanada.org/recommendations/oncology/). In 2013, a task force including representatives from the Canadian Association of Radiation Oncology, Canadian Association of Medical Oncology, and Canadian Society for Surgical Oncology was convened to develop cancer-specific CWC statements. The initial CWC Oncology list included the following statement: “Don’t perform routine cancer screening, or surveillance for a new primary cancer, in the majority of patients with metastatic disease”. However, it is unclear whether this practice occurs in Canada, in particular within a setting in which population-based screening programs for breast and colorectal cancer are prevalent and promoted. We sought to document the performance of routine cancer screening for a new primary cancer in patients with existing metastatic cancer and understand the trend over time of this practice.

Methods

This retrospective cohort study used population-based administrative health care databases from Ontario, Canada that are held at the Institute for Clinical Evaluative Sciences (ICES). The following datasets were linked using unique encoded identifiers and analyzed at ICES: the Ontario Cancer Registry (OCR), the Registered Persons database (RPDB), the Ontario Health Insurance Plan (OHIP), the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), the Ontario Breast Screening Program (OBSP), and the Ontario Crohn's and Colitis database. This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada.

The cohort included all adult residents of Ontario of eligible screening age who were diagnosed with incident colorectal (CRC), lung, breast, or prostate cancer between January 1, 2007 and December 31, 2012 (with follow-up up to December 31, 2013). Only individuals who had stage IV (metastatic or non-curable) cancer at diagnosis were included. We further restricted the cohort to individuals aged 50 years and older at diagnosis, based on the recommended age of breast and CRC screening in Canada.[8,9] We excluded individuals who had a prior history of any of the four cancers of interest, those who were diagnosed with multiple cancers on the same date, and individuals for whom stage information was not available at the time of diagnosis.

Outcomes of interest were the uptake of breast cancer screening using mammography and uptake of colorectal tests as a marker of CRC screening. CRC tests included use of fecal occult blood testing, flexible sigmoidoscopy or colonoscopy among those. In Ontario, a population-based province-wide screening program for colorectal cancer screening (ColonCancerCheck) recommends screening individuals aged 50 to 74 with fecal occult blood testing every 2 years (or flexible sigmoidoscopy every 10 years). For those with an increased risk of colorectal cancer (i.e. family history in one or more first-degree relative), colonoscopy at 50 years of age, or 10 years earlier than when their relative was diagnosed is recommended (https://www.cancercare.on.ca/pcs/screening/coloscreening/cccworks/).[9] Breast cancer screening was defined by mammography through the Ontario Breast Screening Program (OBSP) or an OHIP record of bilateral mammography. The OBSP (https://www.cancercare.on.ca/pcs/screening/breastscreening/OBSP/) is a province-wide breast screening program that provides high-quality screening investigations for women of average-risk who are ages 50 to 74 (and women of increased risk who are ages 30 to 69).[8] We documented CRC screening in patients diagnosed with lung, breast, and prostate cancer and excluded patients with a history of CRC, including those for whom it was their incident cancer diagnosis, and those with a previous history of inflammatory bowel disease. For the breast screening analysis, we documented screening in women with lung cancer and CRC, excluding male patients and females with breast cancer as their incident cancer diagnosis. We estimated screening rates stratified by the following age categories: 50 – 74 years, and ≥75 years. Given the high mortality rate of this population, the incidence of screening was calculated using the cumulative incidence function which takes into account the competing risk of death or the occurrence of the cancer for which the patient was being screened (prior to being screened).

We estimated the cumulative incidence of cancer screening at 1 year and 3 years after diagnosis; only the first screening tests after the cancer diagnosis were counted. We further investigated whether the year of diagnosis (from 2007 to 2012) impacted the probability of subsequent screening (to assess whether the probability of screening changed over time). A Fine-Gray subdistribution hazards model was used to study the impact of year of diagnosis on the incidence of cancer screening.[10] Given that the indication for colonoscopy is not available in the health administrative data, we performed a sensitivity analysis using a sub-cohort of patients with breast, lung, and prostate cancer who were deemed screen-eligible for CRC screening, in that they had not undergone FOBT testing in the prior 2 years, sigomoidoscopy in the prior 5 years, and colonoscopy in the 10 years prior to their cancer diagnosis.

Results

For CRC screening, 20,992 patients with an incident diagnosis of metastatic lung, breast, and prostate cancer were analyzed (Table 2A). Uptake of CRC tests within 1 year of an advanced cancer diagnosis occurred in 2.9%, 6.3%, and 13.3% for patients with lung cancer, breast cancer, and prostate cancer, respectively (4.9% across the three diagnoses combined). The probability of being screened was higher in the subgroup of patients age 50-74 (compared to patients older than 75). Fecal occult blood testing and colonoscopy were used at similar frequencies (Table 2A). Within 3 years of diagnosis, rates reached 4.1% for patients with lung cancer, 12.3% for patients with breast cancer, and 27.5% for patients with prostate cancer (8.5% across all patients combined; Figure 1). In sensitivity analysis, the sub-cohort of patients who were deemed CRC screen-eligible (n=12,056), the 1-year screening rate across all cancers was 3.7% and the 3-year screening was 6.0%.

For breast cancer screening, 10,034 women with metastatic lung cancer and CRC were identified (Table 2B). Breast cancer screening within 1 year following an advanced cancer diagnosis occurred in 8.7% and 8.0% of women with lung cancer and CRC, respectively (8.5% across all patients combined). Screening again occurred with a higher probability in patients age 50-74. Within 3 years of diagnosis, screening rates reached 10.2% and 13.1%, respectively (11.0% of all patients; Figure 2).

Screening rates were further analyzed by calendar year (Table 3). CRC screening increased from a cumulative incidence of 4.11% (95% confidence interval (CI) 3.45% - 4.84%) in 2007 to 5.04% (95% CI 4.12 % - 6.09%) in 2012. Based on the Fine-Gray regression model that studied the impact of year of diagnosis on incidence of screening, the incidence of CRC screening increased over the study time period (HR 1.05; 95% confidence limits 1.01-1.09; p=0.0143). In contrast, the incidence of breast cancer screening remained stable over the period (HR 0.97; 95% confidence limits 0.93-1.01; p=0.162).

Interpretation

Our findings suggest that a substantial proportion of patients with metastatic cancer with a known poor prognosis underwent screening tests for new primary cancers. Screening in this population is not only an inappropriate use of scarce health care resources, but could detract from the quality of care required of patients near the end of life. From a patient perspective, such screening exposes individuals to potential harms in addition to the extra testing, time, stress and financial burden but without a likelihood of benefit as a result.

Despite these concerns, in our cohort nearly 1 in 20 patients with advanced cancer had tests for colorectal cancer and nearly 1 in 11 women with advanced lung or CRC were being screened for breast cancer, all within a year of their diagnosis of metastatic disease. Not surprisingly, screening rates for both CRC and breast cancer were higher in individuals age 50 – 74, which includes the recommended ages in Ontario for screening in an average risk population. There is a potential that this excessive screening reflects and parallels the successful promotion of breast and CRC screening activities among Ontario physicians,[8,9] albeit without the careful individualized considerations that should encompass all patient care. Screening programs such as the OBSP clearly provide benefit at a population level, but physicians should be actively involved in assessing individual patients and engaging them in a discussion regarding their specific risks and benefits related to screening evaluations. In particular, in the context of metastatic cancer, engaging patients in a conversation around underlying prognosis and potential screening outcomes can be challenging; however, physicians should be guided by the overarching principles of patient-centered care in their endeavor to better understand patient preferences.[11]

We noted some variability in the screening rates according to the underlying metastatic diagnosis. Screening rates for both CRC and breast cancer were lowest in patients diagnosed with advanced lung cancer, potentially reflecting the anticipated short survival associated with this malignancy (4.5% survival at 5 years for patients with metastatic disease).[12] In contrast, very high rates of CRC testing were seen in men with prostate cancer, reaching 13% at 1-year and 27% at 3-years. Again, this may relate to a perception that metastatic prostate cancer may not be imminently fatal (29.8% survival at 5 years for patients with metastatic disease).[13] An alternative explanation may be that a proportion of the colonoscopies done in this prostate population were in fact completed for rectal bleeding (i.e. related to radiation therapy) and not screening. However, it is notable that fecal occult blood testing was the most common screening modality for CRC, and even this sole modality of screening was excessively applied in the study cohort. This may have led to increased subsequent investigations as well as unmeasured patient fear and anxiety due to abnormal test results.

Our work builds upon a previous study of screening in elderly Medicare enrollees with advanced cancer reported within the Surveillance, Epidemiology, and End Results (SEER) tumor registries in the United States.[14] In this earlier study, 8.9% of women received at least one screening mammogram following diagnosis of an advanced malignancy and 1.7% of all patients with advanced cancers received lower GI endoscopy. Accounting for differences between our studies related to cohort selection and the window for event ascertainment, the rates of breast cancer screening appear commensurate whereas the rates of lower GI endoscopy appear higher in our study.

Some of these differences may relate to the younger population included in our study, a group in which more aggressive care might be offered. Moreover, we note that the SEER study focused on an earlier time frame (1998-2005) than ours (2007-2012); we did find in our time trend analysis a continued increase in the use of colonoscopy but a relatively stable use of screening mammograms, which could explain the differential findings. Our current study was unable to determine the underlying factors that might drive the increase in CRC screening over time; these factors warrant further investigation.

Our study does have limitations. We did not include a control population of patients without advanced malignancy for comparative baseline screening rates in the population as our premise was that any screening that occurred among patients with metastatic cancer is likely inappropriate. As noted above, colonoscopy indication was not available for most of the colonoscopies performed in our cohort; therefore, we cannot rule out that a proportion were done to investigate symptoms such as bleeding and were as such not for screening purposes. Thus, the practice of screening if based solely on our estimates of colonoscopies would potentially be overestimated. However, the rate of fecal occult blood testing remained high in all groups, indicating that even with this modality alone, CRC screening was excessive. Similarly, our data also does not allow us to determine the reason for bilateral mammograms identified by OHIP (for example, some may have been performed for symptomatic masses detected on physical examination). Finally, our databases are specific to the Ontario population; we are unable to determine whether the practice of screening within a metastatic population is broadly generalizable across the Canadian population.

In sum, our findings suggest inappropriate use of screening in patients with metastatic cancers. Further investigation should be targeted to identify reasons for this practice, as well as costs to the health system (resource utilization), financial costs borne by patients (lost productivity and additional indirect costs), and non-financial implications for patients and caregivers (including harms resulting from screening and impact on quality of life and anxiety). Our study suggests that education of physicians and the general population is needed regarding the lack of utility of cancer screening for patients with non-curable cancer as well as further study into impact on patients; the Choosing Wisely campaign represents an important starting point to highlight such interventions that are unlikely to offer benefit.

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Table 1.

Database	**Description**
Ontario Cancer Registry (OCR)	Population-based registry with approximately 95% of all provincial cancer diagnoses captured.[15]
Ontario Health Insurance Plan (OHIP)	Contains all billing claims for physician services and certain other health professionals.[16]
Canadian Institute for Health Information Discharge Abstract Database	Contains demographic, administrative and clinical data related to hospital admissions (including provision of ICU care).
Registered Person's Database (RPDB)	Contains basic demographics and date of death for all Ontario residents eligible for OHIP coverage.
Ontario Breast Screening Program	The Ontario Breast Screening Program (OBSP) is a province-wide, organized breast screening program that provides high-quality breast cancer screening to women who are average-risk and high-risk for breast cancer.[8]
Ontario Crohn's and Colitis database	A population-based surveillance cohort of patients with inflammatory bowel disease.[17]

Table 2: Screening rates in patients with stage 4 colorectal, lung, breast or prostate cancer

Table 2A: Uptake of Colorectal Cancer Tests (%)				
	Lung Cancer N= 15,948	**Breast Cancer** N = 1,678	**Prostate Cancer** N = 3,366	**All Patients** N = 20,992
CRC screening rate (%) within 1 year after diagnosis				
Overall	2.9	6.3	13.3	4.9
By age				
Age 50 – 74 years	3.3	7.9	16.0	5.5
Age ≥ 75 years	2.1	3.1	9.8	3.7
By screening modality				
FOBT	1.5	3.2	7.3	2.6
Flexible sigmoidoscopy	0.2	<0.4	0.5	0.2
Colonoscopy	1.3	2.7-3.1*	5.5	2.1
CRC screening rate (%) within 3 years after diagnosis				
Overall	4.1	12.3	27.5	8.5

Table 2B: Breast Cancer Screening (%)				
	Lung Cancer N= 7,323	**Colorectal** N = 2,711		**All Patients** N = 10,034
Breast cancer screening rate (%) within 1 year after diagnosis				
Overall	8.7	8.0		8.5
By age				
Age 50 – 74 years	10.9	12.4		11.3
Age ≥ 75 years	4.4	3.0		3.9
Screening through OBSP				
OBSP	2.0	3.3		2.3
Non-OBSP mammogram	6.7	4.6		6.2
Breast cancer screening rate (%) within 3 years after diagnosis				
Overall	10.2	13.1		11.0

FOBT - Fecal Occult Blood Test; OBSP - Ontario Breast Screening Program
*data suppressed due to ICES small cells policy

Table 3. Screening by Calendar Year (2007-2012).

Breast Cancer Screening			
Year of Diagnosis	1-year CIF (%)	Lower 95% CI (%)	Upper 95% CI (%)
2007	8.52	7.20	9.97
2008	9.80	8.45	11.27
2009	8.25	7.04	9.57
2010	8.05	6.91	9.29
2011	8.36	7.21	9.62
2012	7.63	6.02	9.48

Uptake of CRC Tests			
Year of Diagnosis	1-year CIF (%)	Lower 95% CI (%)	Upper 95% CI (%)
2007	4.11	3.45	4.84
2008	5.13	4.43	5.89
2009	4.32	3.71	4.99
2010	4.72	4.11	5.38
2011	5.75	5.08	6.47
2012	5.04	4.12	6.09

Figure 1. Testing for colorectal cancer in patients with stage 4 lung, breast or prostate cancer

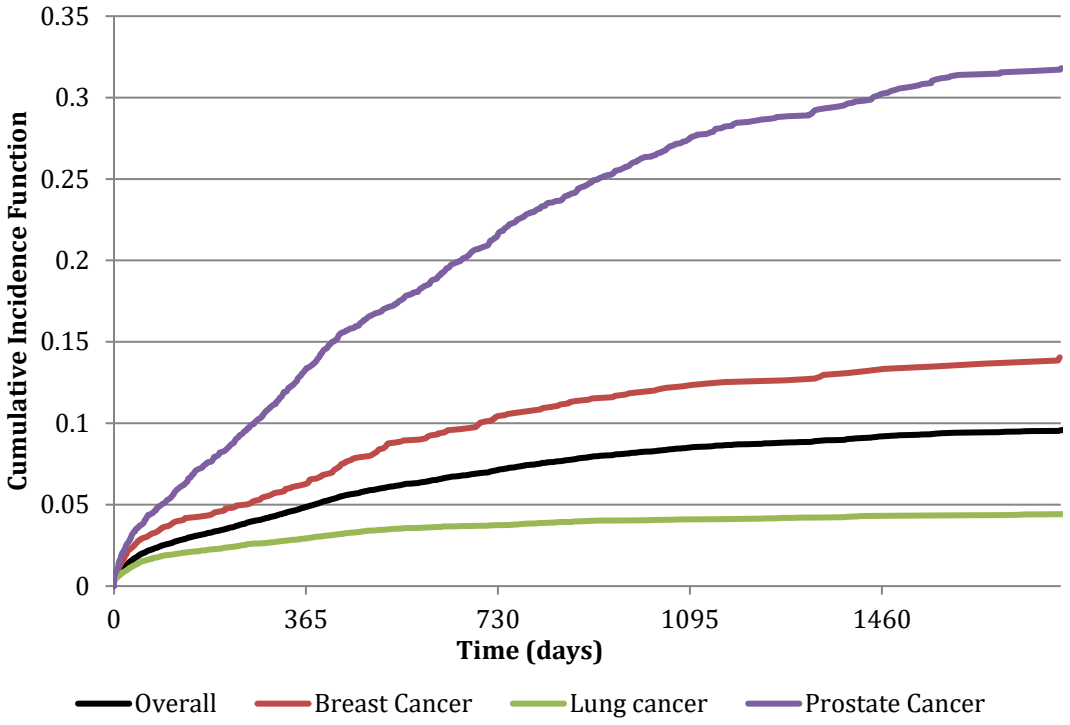

Figure 2. Breast cancer screening in patients with stage 4 lung or colorectal cancer.