Increasing our understanding of dying of breast cancer: Comorbidities and care

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Background: Screening and treatment for breast cancer have improved. However, attention to palliative support and non-cancer co-morbidities has been limited. This study identified types of care for and co-morbidities of persons dying of breast cancer compared to persons dying from all cancers and from non-cancer causes.

Methods: Linked administrative data from population-based registries were used to examine 121,458 deaths in Nova Scotia from 1995 to 2009.

Results: Breast cancer decedents' mean age was similar to that of all cancer decedents (72.0 versus 72.1 years), but their age spread was greater (20–59 years: 23.1% versus 16.7%; 90+ years: 11.2% versus 6.5%). Among women dying of breast cancer, 15.6% were enrolled in the diabetes registry and 15.1% in the cardiovascular registry, indicating that they had these non-cancer conditions prior to their death. Compared to all cancer decedents, breast cancer decedents were twice as likely to have dementia as a cause of death, and were less likely to die in hospital but more likely to die in a nursing home. Breast cancer decedents had place of death rates more similar to non-cancer than cancer decedents.

Conclusions: Rates of dementia and diabetes among the breast cancer decedents were particularly note-worthy in this novel study given that these comorbidities have not received much attention in the breast cancer research literature. Further collaboration with non-cancer disease programs is advised. The extent of adequate comprehensive palliative support for the 20% of the breast cancer decedents who are nursing home residents requires investigation.

Keywords: Breast cancer, Survivor: Palliative, Mortality, Nursing home, Dementia, Diabetes, Cardiovascular disease

Introduction

In Canada, as in many other countries, persons diagnosed with breast cancer are younger[1] and have a better survival rate[1] than all persons diagnosed with any type of cancer. Screening and treatment have improved[1] and so persons diagnosed with breast cancer are living longer.[1] Therefore, the age profile of persons who die of breast cancer is considerably older than the age profile for those who are newly diagnosed with breast cancer – less than one-third (30%) of persons with breast cancer are 70 years or more at the time of their diagnosis, yet more than half (52%) are 70 years or more at death.[1]

Although age standardized breast cancer mortality rates are decreasing,[1] our aging population means that the overall number of persons being diagnosed and subsequently dying of breast cancer is not decreasing.[2] After lung cancer, breast cancer remains the second most common cancer cause of death for women.[1]

Studies on the supportive care needs of those with breast cancer typically focus on the time during either primary (active) cancer treatment[3–5] or on the initial years of follow-up care post-treatment.[6–7] However, breast cancer can recur 5, 10, or more years after the initial diagnosis.[1] Therefore, supportive care is also needed at recurrence and end of life. Supportive care includes the provision of symptom management and aims to improve the quality of life for persons living with life-limiting disease.[8]

As people age, there is a higher risk of being diagnosed with an increasing number of chronic diseases. In the United States, among women more than 65 years of age who were living with breast cancer, 32.2% had one or more chronic disease comorbidities.[9] Comorbidities also increased the risk of death in the first year after a breast cancer diagnosis.[10] This was

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particularly true for those with distant and unknown stage at diagnosis.[10] The comorbidity with the greatest impact was dementia; other diseases that increased the risk of death after a breast cancer diagnosis were mild liver disease, moderate to severe renal disease, and diabetes with end-organ damage.[10] Another study found that persons diagnosed with breast cancer had higher rates of dementia, diabetes, diseases of pulmonary circulation, and cardiovascular diseases.[11]

In addition, cardiotoxic and antiangiogenic effects of commonly used systemic and radiation therapies can lead to new cardiovascular disease as well as exacerbate pre-existing cardiovascular disease.[12] Recent survival and quality of life gains from screening and treatment may be compromised if we do not adequately address the non-cancer diseases being experienced by persons with breast cancer.[12]

There has been a lack of attention to the needs and experiences of people dying of breast cancer in contrast to the strong focus on early diagnosis, treatment, and survivorship. Therefore, the purposes of this study were to identity the co-morbidities and types of care experienced by persons *dying* of breast cancer, and to determine the extent to which the situation for persons dying of breast cancer was the same or different from that of all cancer decedents and non-cancer decedents.

Methods

Research ethics board approval was received from Capital Health in Halifax, Nova Scotia, Canada. Research grant funders had no influence on decisions on data collection, analysis and interpretation, and were not involved in manuscript approval.

Study subjects, design, and data

The study population was all 121,458 Nova Scotia residents who died in the province from 1995 to 2009. These decedents were identified in the Nova Scotia Vital Statistics (VS) database. Their VS data were linked to data from the population-based cancer, diabetes, and cardiovascular disease registries, as well as palliative program (PP) data from three health districts. Together, the three PPs care for approximately 65% of the people in Nova Scotia and have been described elsewhere.[13] The three PPs were operational throughout the study period, but electronically available data were unavailable for some years. PP rates were calculated using the data available. PP enrollment data for the Capital Health (CH) and Cape Breton PPs are for 1996–2009. CH late PP enrollment data is for 2005–2009. Colchester East Hants PP data are for 2002–2009.

Outcomes investigated were: PP enrollment, time from PP enrollment to death, and place of death (hospital, nursing home, own home). All causes of death were used to classify decedents into four population-based cause of death groups: those who died of breast cancer, any cancer, non-cancer, and the total of all deaths. The cancer and non-cancer groups are mutually exclusive; decedents are classified as non-cancer only if cancer is not listed as any of the causes of death. Breast cancer and cancer decedents are not mutually exclusive; breast cancer decedents are included in the cancer population.

Causes of death were coded using the International Classification of Diseases (ICD) 9th edition for 1995–1999 and 10th edition for 2000 onward. Up to 13 causes of death on the death certificates were examined. The provincial diabetes and cardiovascular registries began in the mid-1990s. Since it takes years for an incidence disease registry to include the majority of prevalent cases, only their most current data (2009) are reported. In contrast, the cancer registry was established in the mid-1960s.

Data analysis

Descriptive statistics on decedent characteristics, location and types of care, and comorbidities are reported by the four population-based cause of death groups. Statistical significance was measured across groups as the difference from the breast cancer population using t-tests for means and z-tests for proportions. Analyses were completed using SAS 9.2.

Results

Among all decedents, 2.8% had breast cancer and 32.2% had a cancer as a cause of death. The average (mean) age at death for those dying of breast cancer (72.0 years) was similar to that for all cancers (72.1 years), and significantly younger than for non-cancer decedents (75.7 years) (Table 1). However, the age distribution for breast cancer decedents was greater than for all cancer decedents (20–59 years: 23.1% versus 16.7%; 90+ years: 11.2% versus 6.5%). Diabetes program registration was similar at about 16% for all groups. Cardiovascular registration was lower for breast cancer (15.1%) than for all cancer (21.1%) and significantly lower than for non-cancer decedents (36.2%).

The average number of causes of death was 2.7 for persons dying of breast cancer, which was intermediate between and significantly different from 2.5 for cancer and 3.0 for non-cancer decedents (Table 2). Breast and all cancer decedents had similar rates of diabetes and cardiovascular comorbid causes of death. Renal and chronic obstructive pulmonary disease rates were significantly lower for breast cancer decedents than for all cancer decedents. In contrast, breast cancer decedents had a significantly higher rate of dementia (6.9%) than all cancer decedents (3.4%).

Table 1 Characteristics of the decedent groups, 1995–2009

Characteristic	Breast cancer (*n*=3398)	Cancer (*n*=39,091)	Non-cancer (*n*=82,367)	Total (*n*=121,458)
Age (mean, in years)	72.0	72.1	75.7*[a]	74.5*
	[71.5–72.5][b]	[72.0–72.2]	[75.6–75.8]	[74.4–74.6]
Age distribution				
20–59 years	23.1%	16.7%*	12.8%*	14.0%*
	[21.6–24.5]	[16.3–17.1]	[12.5–13.0]	[13.8–14.2]
60–89 years	65.7%	76.5%*	67.0%*	70.1%*
	[64.1–67.3]	[76.1–77.0]	[66.7–67.3]	[69.8–70.3]
90+ years	11.2%	6.5%*	18.3%*	14.5%*
	[10.2–12.3]	[6.3–6.8]	[18.1–18.6]	[14.3–14.7]
Sex (%female)	98.8%	46.4%*	51.0%*	49.5%*
	[98.5–99.2]	[45.9–46.9]	[50.6–51.3]	[49.2–49.8]
Disease registry enrollment in 2009				
Diabetes	15.6%	16.1%	16.3%	16.3%
	[10.7–20.4]	[14.7–17.5]	[15.3–17.3]	[15.3–17.1]
Cardiovascular	15.1%	21.1%	36.2%*	31.3%*
	[10.3–19.9]	[19.6–22.6]	[35.0–37.5]	[30.3–32.3]

[a]*Statistically different from breast cancer at *P* < 0.05.
[b][95% confidence intervals].

The PP enrollment rate and late enrollment rates were similar for breast and all cancer decedents (Table 3). Corresponding rates for non-cancer decedents were less favorable. However, analysis by year (data not shown) reveal that the non-cancer PP enrollment rates increased rapidly from 1.8% in 1996 to 15.2% by 2009. For breast and all cancer decedents, the PP enrollment rate increased from about 50% in 1996 to 73% in 2009.

A significantly higher proportion of breast cancer decedents (20.1%) were nursing home residents than all cancer decedents (11.7%) (Table 3). Since women are more likely than men to be nursing home residents,[14] this rate was also calculated for all women with cancer (14%). Significantly, fewer breast cancer decedents die in hospital (60.7%), and more in nursing homes (17.0%), than for all cancer decedents (70.0% and 8.9%, respectively). Corresponding rates for non-cancer decedents were 58.3% and 21.2%, respectively. Hospital and nursing home place of death rates for breast cancer decedents were more similar to those for non-cancer than for all cancer decedents.

Discussion

Persons dying of breast cancer had higher rates of dementia and being a nursing home resident compared to all cancer decedents. However, few evidence-based guidelines are available for elderly persons with frailty and/or multiple diseases.[15] The study findings demonstrate the need for concerted attention to developing guidelines and 'best practices' for elderly populations. The substantial proportion of persons dying of breast and all cancers who were in the cardiovascular and diabetes registries should also be considered. The epidemiological data reported herein reveal the need to address the gap in our knowledge of holistic multi-disease care, especially for elderly persons dying of breast cancer. Appropriate, comprehensive guidelines and palliative support are needed for all persons dying of breast cancer.

The similar and substantial rate of diabetes registry enrollment across all decedents means that all groups may need to consider diabetes care, including the moderation of glycemic control as death approaches.[16] Intensive blood glucose lowering can increase the

Table 2 Average number and percentage of selected causes of death by decedent group, 1995–2009

Causes of death	Breast cancer	Cancer	Non-cancer	Total
Average number	2.66	2.46*[a]	3.03*	2.85*
	[2.61–2.72][b]	[2.45–2.48]	[3.02–3.04]	[2.84–2.86]
Cardiovascular	12.0%	11.9%	41.9%*	32.2%*
	[10.9–13.1]	[11.6–12.2]	[41.6–42.2]	[32.0–32.5]
Diabetes	6.6%	6.0%	12.7%*	10.6%*
	[5.8–7.5]	[5.8–6.3]	[12.5–13.0]	[10.4–10.8]
Renal disease	3.5%	4.6%*	10.7%*	8.7%*
	[2.9–4.1]	[4.4–4.8]	[10.5–10.9]	[8.5–8.9]
COPD[c]	3.7%	7.9%*	13.2%*	11.5%*
	[3.0–4.3]	[7.6–8.2]	[13.0–13.5]	[11.3–11.7]
Dementia	6.9%	3.4%*	13.5%*	10.2%*
	[6.0–7.7]	[3.2–3.5]	[13.3–13.7]	[10.1–10.4]

[a]*Statistically different from breast cancer at *P* < 0.05.
[b][95% confidence intervals].
[c]COPD: chronic obstructive pulmonary disease.

Table 3   Types of care by decedent group

Types of care	Breast cancer	Cancer	Non-cancer	Total
Enrolled in palliative program (PP)[a]	65.8%	66.1%	9.2%*[b]	28.8%*
	[63.7–98.0][c]	[65.5–66.8]	[8.9–9.5]	[28.4–29.2]
Late PP enrollment				
<8 days	14.2%	14.4%	39.8%*	20.4%*
	[11.7–16.7]	[13.7–15.1]	[38.0–41.6]	[19.7–21.2]
8–14 days	21.4%	22.9%	49.9%*	29.3%*
	[18.5–24.3]	[22.1–23.8]	[48.1–51.8]	[28.5–30.2]
Nursing home resident	20.1%	11.7%*	28.4%*	23.0%*
	[18.7–21.4]	[11.3–12.0]	[28.1–28.8]	[22.8–23.3]
Place of death				
Hospital	60.7%	70.0%*	58.3%*	62.1%
	[59.0–62.3]	[69.5–70.4]	[58.0–58.7]	[61.8–62.4]
Nursing home	17.0%	8.9%*	21.2%*	17.3%
	[15.7–18.2]	[8.6–9.2]	[21.0–21.5]	[17.1–17.5]
Own home	22.4%	21.1%	20.4%*	20.6%*
	[21.0–23.8]	[20.7–21.5]	[20.1–20.7]	[20.4–20.9]

[a]Three District Health Authorities have Palliative Program (PP) data. Enrollment data for Capital Health (CH) and Cape Breton is for 1996–2009, and for Colchester East Hants is 2002–2009. CH late enrollment data is for 2005–2009.
[b]*Statistically different from breast cancer at *P* < 0.05.
[c][95% confidence intervals].

risk of hypoglycemia.[15] Older adults are at higher risk of developing hypoglycemia and are less capable of responding well to hypoglycemic episodes that occur, especially among persons with dementia.[15] Adverse effects include falls, fracture, hospitalization, confusion, and coma.[15] As the population of persons with advanced breast cancer ages, comprehensive palliative care for them must entail developing and adhering to elder-friendly guidelines for various co-morbidities.

Diabetes can lead to and therefore be associated with an increased risk of death from cardiovascular and renal disease.[16] In Nova Scotia, the diabetes and cardiovascular registries under-report persons diagnosed in nursing homes and those who do not enroll in preventive education.[16] Therefore, the rates of living with diabetes and cardiovascular disease as death approaches may be greater than those reported herein. For patient-centered care, accurate comprehensive data on all diagnoses need to be integrated. This cutting-edge study of one geographic area demonstrates how data can be aggregated to plan for comorbidity care for persons with advanced cancer, while also providing a baseline for comparison as further studies are carried out in other geographic areas.

The higher rate of dementia for persons dying of breast cancer was unexpected. However, it is consistent with the higher rate of breast cancer decedents dying in nursing homes, and a higher percentage dying at ages 90 years and over, when compared to all cancer decedents. The majority of nursing home residents have dementia and are women.[14] The majority of persons dying of breast cancer are women. In Nova Scotia, PP enrollment is lower for nursing home residents.[17] Together, these findings highlight the need to further

investigate the adequacy of palliative support[8] for the 20.1% of persons dying of breast cancer who are nursing home residents. As a case in point, while adequate pain management is critical in palliative care, pain is known to be underestimated and left untreated for many persons with dementia.[18] Far too often, pain-related behaviors are mistakenly interpreted as behavioral manifestations of dementia, leading to overtreatment with psychotropic drugs instead of appropriate pain management.[18] The typical 0–10 pain scale assessment cannot be accurately used for persons with dementia and so other forms of assessment such as the Abbey pain scale are advised.[18] Polypharmacy also needs to be addressed as the number of diseases, side effects and range of symptoms increases.[19]

This is the first known population-based comparative descriptive report of the comorbid causes of death, non-cancer disease registration, PP enrollment, and location of death for persons dying of breast cancer. As such, it helps to address a gap in our understanding of the wide age distribution, care, and non-cancer diseases of people dying of breast cancer. Rates of dementia and diabetes comorbidities among the breast cancer decedents were particularly noteworthy in this novel study given the lack of attention they have received to date attention in the breast cancer research literature. While the administrative data available to report herein were limited, the findings provide solid evidence of the need for further investigation.

Given our aging population and the number of women dying of breast cancer, we need a greater understanding of the full disease trajectory over time of persons with advanced breast cancer at diagnosis and after recurrence. While Reed and Corner[20] have

described three typical longitudinal trajectories of decline for persons with metastatic breast cancer, none have taken comorbidities into account. Our study demonstrates the need to build the effects of comorbidities into the functional decline trajectories for persons now living many years with advanced breast cancer.

Among persons with advanced breast cancer, we need to know if their supportive and palliative care needs are being adequately addressed for both their cancer and non-cancer diseases. This would require quality of care indicators derived from administrative data on health service use and also routinely collected patient-reported data on goals of care, needs, symptoms, and outcomes to understand the patient experience. Starfield[21] contends that we also must move away from disease-oriented care to person-based care, re-examine the role of specialists, and assess what adverse events and hospitalizations are preventable for persons with multiple health conditions. Parekh *et al.*[22] have provided a framework for how we can improve health outcomes and quality of life for persons with multiple conditions. Our paper supplies epidemiological data to support moving in these directions to provide integrated care for the substantial number of persons dying of breast cancer who are typically older and living in nursing homes with co-morbidities.

Conclusions

Few researchers have examined the specific circumstances of persons dying of breast cancer. We found that persons dying of breast cancer differ from those dying of all cancers and non-cancer diseases. Understanding these differences is imperative to improving the organization, management, and delivery of care for persons at the end of life. This is particularly true for persons diagnosed with breast cancer since they are living longer than in the past and thereby have a greater opportunity to develop non-cancer comorbid diseases that require appropriate and timely management. Collaboration across disease programs and with PPs to enable comprehensive advance care planning is advised for breast cancer survivors whose cancer or non-cancer disease becomes life-threatening, especially those in nursing homes.

Disclaimer statement

Contributors G.M.J. was responsible for the development of the manuscript, provided overall direction, and is corresponding author. R.U. assisted in the development of this paper, the literature review, and understanding of and critical reflection on the application of the findings to supportive care. L.L. was the data analyst including the presentation of

methods and results. M.M. advised on disease and registry implications, interpretation of findings, discussion and conclusions. All authors reviewed the manuscript and provided feedback during its development.

Conflict of interest The authors have no conflicts of interest to declare.

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