Effect of Community Population Size on Breast Cancer Screening, Stage Distribution, Treatment Use and Outcomes

Robert A. Olson, MD,[1-4] Alan Nichol, MD,[2,3] Nadine R. Caron, MD,[3-6] Ivo A. Olivotto, MD,[2,3] Caroline Speers, BA,[2] Stephen Chia, MD,[2,3] Ashley Davidson, MD,[3,7] Andy Coldman, PhD,[2,3] Chris Bajdik, PhD,[2,3] Scott Tyldesley, MD[2,3]

ABSTRACT

Objective: Residents of rural communities have decreased access to cancer screening and treatments compared to urban residents, though use of resources and patient outcomes have not been assessed with a comprehensive population-based analysis. The objectives of this study were to investigate whether breast cancer screening and treatments were utilized less frequently in rural BC and whether this translated into differences in outcomes.

Methods: All patients diagnosed with breast cancer in British Columbia (BC) during 2002 were identified from the Cancer Registry and linked to the Screening Mammography database. Patient demographics, pathology, stage, treatments, mammography use and death data were abstracted. Patients were categorized as residing in large, small and rural local health authorities (LHAs) using Canadian census information. Use of resources and outcomes were compared across these LHA size categories. We hypothesized that mastectomy rates (instead of breast-conserving surgery) would be higher in rural areas, since breast conservation is standardly accompanied by adjuvant radiotherapy, which has limited availability in rural BC. In contrast we hypothesized that cancer screening and systemic therapy use would be similar, as they are more widely dispersed across BC. Exploratory analyses were performed to assess whether disparities in screening and treatment utilization translated into differences in survival.

Results: 2,869 breast cancer patients were included in our study. Patients from rural communities presented with more advanced disease (p=0.01). On multivariable analysis, patients from rural, compared to urban, LHAs were less likely to be screening mammography attendees (OR=0.62; p<0.001). Women from rural communities were less likely to undergo breast-conserving surgery (multivariable OR=0.47; p<0.001). There was no significant difference in use of chemotherapy (p=0.54) or hormonal therapy (p=0.36). The 5-year breast cancer-specific survival for large, small and rural LHAs was 90%, 88% and 86%, respectively (p=0.08), while overall survival was 84%, 81% and 77%, respectively (p=0.01). On multivariable analysis with 7.4 years of median follow-up, neither breast cancer-specific survival (HR=1.16; 0.76-1.76; p=0.49) nor overall survival (HR=1.25; 0.92-1.70; p=0.16) was significantly worse for patients from rural compared to large LHAs.

Conclusion: There was a significant difference in screening mammography use, stage distribution and loco-regional treatments use by population size of LHA. After controlling for differences in patient and tumour factors by LHA, survival was not significantly different.

Key words: Breast cancer; mammography; breast conserving surgery; mastectomy; rural; hormonal therapy; chemotherapy

La traduction du résumé se trouve à la fin de l'article.

Can J Public Health 2012;103(1):46-52.

Historically, rural populations appear to have unique challenges accessing cancer services, though the impact on patient outcomes is not well understood. In British Columbia (BC)[1] and in Canada as a whole,[2] screening mammography utilization rates were historically lower in rural compared to urban communities, and a smaller percentage of rural women's malignancies were detected through mammograms.[3] Utilization of radiation therapy services has been documented as lower in rural versus urban populations in the United States,[4,5] Australia[6,7] and Canada.[8,9] Furthermore, increased distance to a radiation therapy centre has been negatively correlated with utilization of radiation treatment.[10-12]

In BC, the BC Cancer Agency (BCCA) has the mandate for cancer control for the population. Since its formation in 1974, the BCCA has worked to overcome challenges inherent in providing specialized prevention, screening and cancer care services in a timely and equitably accessible manner to BC's vast geography and diverse populations. Specific efforts have included the development of fixed and mobile components to the province-wide screening mammogram program, a General Practitioner in Oncology (GPO) program to train family physicians to administer chemotherapy in community hospitals, and expansion of radiation therapy access from two sites up to 1995 (Vancouver and Victoria) to six radiation therapy-capable centres by 2012 (Figure 1). However, many breast cancer care services in BC are regionalized to urban centres – most notably radiotherapy – and therefore are less geographically accessible for patients in rural locations. In fact, the main rationale for the current construction of the BCCA Centre for the North (Figure 1) is to improve access to radiotherapy services. The primary objective of this study was to determine whether mastectomy is used more frequently (over breast-conserving surgery) in rural BC, since radiotherapy is routinely offered in the setting of breast conservation, which is less available

Author Affiliations

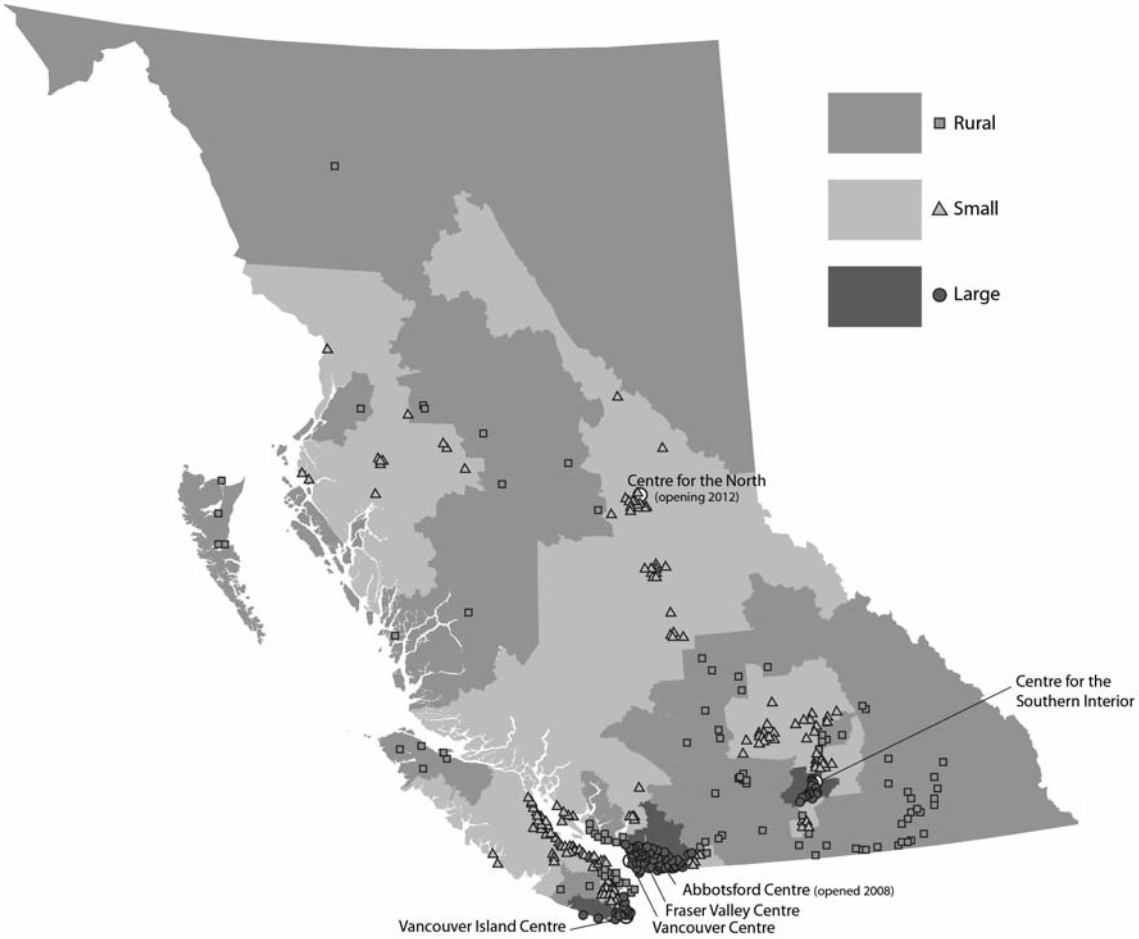
1. BC Cancer Agency, Centre for the North, Prince George, BC
2. BC Cancer Agency, Vancouver Centre, Vancouver, BC
3. University of British Columbia, Vancouver, BC
4. University of Northern British Columbia, Prince George, BC
5. University Hospital of Northern British Columbia, Prince George, BC
6. Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
7. BC Cancer Agency, Fraser Valley Centre, Surrey, BC

Correspondence: Dr. Robert A. Olson, 600 West 10th Ave, Vancouver, BC V5Z 4E6, Tel: 604-877-6000, Fax: 604-877-0505, E-mail: rolson2@bccancer.bc.ca

Acknowledgements: S. Tyldesley and C. Bajdik are recipients of Career Investigator Awards from the Michael Smith Foundation for Health Research. We thank the province's family physicians for their participation in the care of patients with breast cancer, and for the contributions they make to the patients' outcomes. We thank Jane Rowlands and Pablo Santibanez for their help with figures. This study was presented at the 2011 American Society of Clinical Oncology (ASCO) Annual Meeting, in Chicago, IL, June 3-7, 2011.

Conflict of Interest: None to declare.

Figure 1. Map of British Columbia divided by population size category of each local health authority, as defined by the BC Ministry of Health during the study period



Each patient is mapped to the coordinates of their postal code, and represented by squares, triangles and circles where their population size category is rural, small and large, respectively.

in rural BC. Secondary objectives were to investigate whether breast cancer screening and other treatments were utilized less frequently in rural BC and whether differences in screening and treatment utilization translated into differences in survival.

METHODS

Study subjects

The BCCA Cancer Registry (BCCR) was used to identify all patients diagnosed with breast cancer in BC in 2002, with universal coverage across the province. The BCCA had four regional cancer centres during the study era, which provided all radiotherapy (RT) and managed the budget for all anti-neoplastic systemic therapy administered in BC. Approximately 85% of all patients with breast cancer were referred to a BCCA facility in this era for consultation and/or treatment and were therefore captured within the Breast Cancer Outcomes Unit (BCOU) database which includes full TNM staging and adjuvant therapies delivered. The remaining patient data were abstracted through chart review. Mammography usage was collected from the Screening Mammography Program of BC database, which captures all patients who received mammograms in BC.

During the study period, the province of BC was divided into 90 administrative local health authorities (LHAs) by the BC Ministry of Health, and was categorized by the study investigators as large, small and rural, using Canadian census data based on patients' postal code (Figure 1).[13] A LHA was categorized as large if at least 95% of its residents lived in a community of over 100,000. Both small and rural LHA were populated by communities under 100,000. A LHA was categorized as small if less than 50% of its population resided in communities of under 10,000. A LHA was categorized as rural if greater than 50% of its population resided in communities of under 10,000. The mean female population of large, small and rural LHAs are 60,780, 20,998 and 4661, respectively. The rural LHAs all had female populations of less than 15,000, and the majority of the communities in these LHAs had populations of less than 10,000, most of these being remote from a Radiotherapy Centre (Figure 1). The large regions are all in the greater Vancouver, Kelowna and Victoria areas (Figure 1). The small LHAs were generally on the outskirts of the urban areas, or were smaller cities or towns (Figure 1). Using these definitions, based on Population BC statistics, 70% of women lived in urban LHAs, 22% lived in small LHAs and 8% lived in rural LHAs. The socioeconomic status (SES) of patients' community was obtained from the 2002 Canadian census data.[13] Driving times from each health authority to the closest cancer centre were estimated using the British Columbia Automobile Association website.[14] The distance from patients' postal code to the nearest cancer centre was estimated using "Manhattan Distance".[15]

Table 1. Patient and Tumour Characteristics by Population Size of Local Health Authority

Characteristics		Population Size of LHA*			p-value
		Large (N=1955)	Small (N=621)	Rural (N=293)	
Mean age (years)		60.8	61.5	63.7	0.003
Mean (maximum) distance† from CC‡ in km		11 (68)	87 (748)	104 (1113)	<0.0001
Cases within a 2-hour drive to CC (%)		100%	42%	47%	<0.0001
Community SES§	Q1	18%	21%	26%	<0.0001
	Q2	20%	16%	26%	
	Q3	18%	17%	14%	
	Q4	19%	18%	18%	
	Q5	23%	21%	10%	
Stage	DCIS	16%	11%	13%	0.01
	1	38%	36%	40%	
	2	34%	40%	30%	
	3	8%	8%	11%	
	4	4%	5%	6%	
Grade	1	27%	28%	23%	0.20
	2	36%	35%	36%	
	3	30%	30%	30%	
	Unknown	6%	7%	11%	
ER‖ positive		82%	78%	79%	0.15
LVI¶ positive		21%	30%	19%	<0.001
Node positive		33%	38%	36%	0.08

* Local health authority.
† Manhattan distance from patients' postal code at diagnosis to nearest cancer centre.
‡ Cancer centre.
§ Socio-economic status: community SES quintiles, Q1 lowest through Q5 highest.
‖ Estrogen receptor.
¶ Lymphatic or venous invasion.

Table 2. Univariate Comparison of Breast Cancer Screening and Treatment Utilization by Population Size of Local Health Authority

Screening/Treatment		Population Size of LHA*			p-value
		Large (N=1955)	Small (N=621)	Rural (N=293)	
Mammogram attendee	Overall	62%	62%	50%	<0.001
	<50	47%	38%	37%	0.10
	50-70	77%	77%	64%	0.002
	>70	53%	53%	39%	0.04
Local treatment	Biopsy only	3%	3%	5%	
	Lumpectomy no RT†	10%	9%	9%	
	Lumpectomy with RT	49%	45%	33%	<0.001
	CM‡ no RT	24%	28%	38%	
	CM with RT	13%	16%	15%	
Nodal RT	All cases	19%	21%	19%	0.36
	Node positive	58%	51%	39%	0.12
Chemo use	All cases	32%	41%	33%	0.001
	Node positive	67%	73%	64%	0.64
Hormone use	All cases	61%	59%	60%	0.84
	ER§ positive	83%	80%	85%	0.23

* Local health authority.
† Radiotherapy.
‡ Complete mastectomy.
§ Estrogen receptor.

Statistical analyses

We hypothesized that the percentage of women who receive mastectomy would be higher in rural compared to urban locations, as a result of decreased access to radiotherapy; based on a US study, we estimated the rates at 60% and 45%, respectively.[16] Given our sample size of 2,869, an estimated 10% rural population and an estimated 70% urban population, we calculated that we would have 99% power to detect a difference in mastectomy rates, with a type I error probability of 5%. Differences in continuous and categorical variables were assessed with t-tests and chi-square tests, respectively. Logistic regression modelling was used to assess use of resources, after adjusting for potentially confounding variables. Time-to-event distributions were computed by use of Kaplan-Meier estimates and compared using log-rank tests. Multivariable survival analyses were performed using Cox proportional hazards regression modelling to identify significant prognostic factors for overall (OS) and breast cancer-specific survival (BCSS). All tests were two-sided and significance was defined by $p<0.05$. All analyses were conducted using Statistical Package for Social Sciences, version 17.0 (SPSS, Chicago, IL).

RESULTS

Patient characteristics

There were 2,869 patients diagnosed with breast cancers in BC in 2002. Table 1 presents selected patient and pathology characteristics based on category of residence. There were significant differences in the age, distance from a cancer centre, community socio-economic status, stage and lymphovascular invasion (LVI) status (Table 1).

Breast cancer screening and treatment utilization by population size of LHA

Table 2 presents the proportions of patients in large, small and rural LHAs who used the organized breast cancer screening program at least once prior to diagnosis and the major breast cancer treatment interventions. After controlling for age at diagnosis, patients from rural LHAs were less likely to be mammography attendees, compared to patients from large LHAs (OR 0.62, 95% CI 0.48-0.79; $p<0.001$). In contrast, patients from small LHAs were similarly like-

Table 3. Multivariable Analysis Assessing Impact of Patient Characteristics on Decision to Pursue Breast Conservation Versus Complete Mastectomy, in Patients with Early Stage Breast Cancer

Characteristic		Odds Ratio of Receiving Breast Conservation	95% CI	p-value
Age (continuous increments)		1.00	0.99-1.01	0.72
LHA* size	Large (reference)	1.00	–	–
	Small	0.82	0.65-1.03	0.08
	Rural	0.47	0.33-0.65	<0.001
ER† positive (vs. negative)		1.25	0.94-1.67	0.13
Grade	1 (reference)	1.00	–	–
	2	0.72	0.57-0.91	0.01
	3	0.67	0.57-1.03	0.08
LVI‡ positive (vs. negative)		1.10	0.85-1.42	0.33
Stage	DCIS§ (reference)	1.00	–	–
	1	1.70	0.48-5.98	0.41
	2	0.80	0.23-2.80	0.72

* Local health authority.
† Estrogen receptor.
‡ Lymphatic or vascular invasion.
§ Ductal carcinoma in situ.

Figure 2A. Kaplan-Meier analysis of overall survival by population size of local health authority

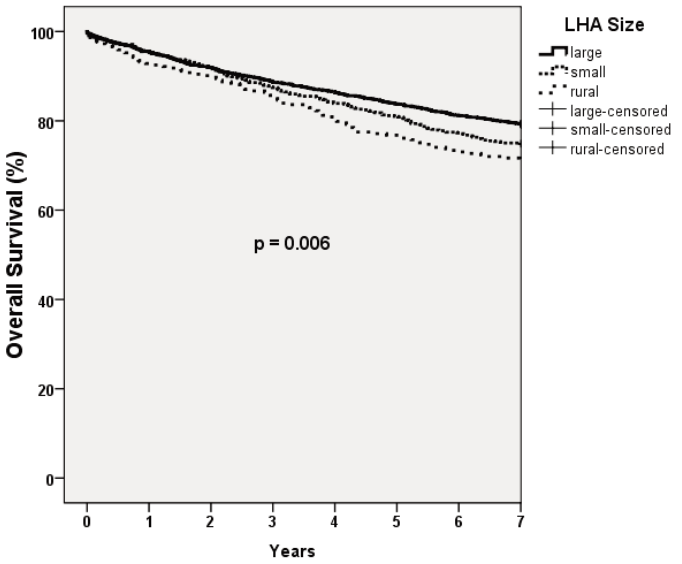
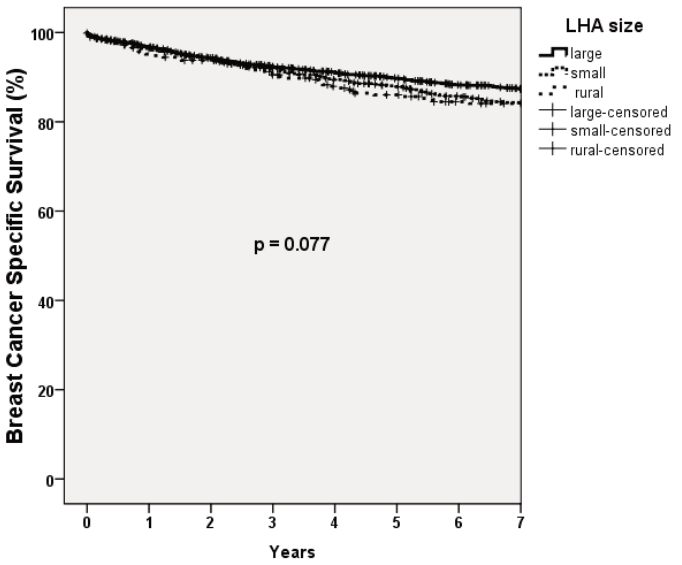


Figure 2B. Kaplan-Meier analysis of breast cancer-specific survival by population size of local health authority



ly as those from large LHAs to be mammography attendees (OR 1.00, 95% CI 0.83-1.20; p=0.96).

Rural patients with early stage breast cancer were less likely to receive breast-conserving surgery, even after controlling for potentially confounding factors (Table 3). After controlling for age, stage, grade, LVI status, ER status, margin status, systemic therapy use, and type of breast surgery used, there was no significant difference in breast/chest wall, or nodal radiotherapy utilization by population size of LHA. In a multivariable analysis restricted to patients who received lumpectomy, rural patients were similarly likely to receive adjuvant radiotherapy as patients from large LHAs (OR 1.23, 95% CI 0.69-1.83; p=0.65). After controlling for age, stage, grade, LVI status, ER status, margin status, and type of surgery, there were no significant differences in use of chemotherapy (p=0.54) or hormonal therapy (p=0.36) by population size of LHA.

Survival analysis by category of LHA population size

As shown in Figure 2, the overall survival (OS), but not the breast cancer-specific survival (BCSS), was significantly different among LHA sizes after a median follow-up of 7.4 years. The 5-year breast cancer-specific survival for large, small and rural LHAs was 90%, 88% and 86%, respectively (p=0.08). The 5-year overall survival for large, small and rural LHAs was 84%, 81% and 77%, respectively (p=0.01). Table 4 presents the multivariable analyses assessing the impact of patient, tumour and treatment characteristics on BCSS and OS. Neither subjects from small (HR 1.32, 95% CI 0.99-1.75; p=0.06) nor those from rural (HR 1.16, 95% CI 0.76-1.76; p=0.49) LHAs had significantly different BCSS compared to patients from large LHA. Likewise, neither subjects from small (HR 1.12, 95% CI 0.89-1.40; p=0.35) nor those from rural (HR 1.25, 95% CI 0.92-1.70; p=0.16) LHAs had significantly different OS compared to patients from large LHA. Exploratory analyses did not reveal any significant relationship between patient outcomes and drive time distance to nearest cancer centre.

DISCUSSION

This population-based study demonstrates that patients with breast cancer who lived in rural LHAs were less than half as likely to receive breast-conserving therapy (lumpectomy and radiotherapy) as patients from more populous LHAs, consistent with our primary hypothesis. In addition, they utilized screening mammography less, and presented with more advanced stage at diagnosis.

Table 4. Multivariable Analysis Assessing Impact of Patient, Tumour and Treatment Characteristics on Breast Cancer-specific and Overall Survival

Characteristic		Breast Cancer-specific Survival		Overall Survival	
		Hazard Ratio	95% CI	Hazard Ratio	95% CI
Age (continuous increments)		1.01	1.00-1.02	1.04	1.03-1.05
T stage	1 (reference)	1.00	–	1.00	–
	2	2.33	1.73-3.13	1.68	1.36-2.07
	3	3.18	1.99-5.08	2.37	1.62-3.47
	4	6.71	3.89-11.55	3.99	2.54-6.25
	In situ	0.01	0.001-0.06	0.13	0.07 -0.24
Number of nodes positive	0 (reference)	1.00	–	1.00	–
	1-3	1.89	1.35-2.65	1.35	1.05-1.73
	4+	3.01	2.16-4.45	2.28	1.73-3.01
Metastases (vs. none)		5.08	3.71-6.96	3.40	2.58-4.49
Grade	1 (reference)	1.00	–	1.00	–
	2	1.84	1.23-2.76	1.20	0.95-1.52
	3	3.27	2.14-4.98	1.50	1.01-2.22
ER* positive (vs. negative)		0.45	0.31-0.64	0.59	0.45-0.78
LVI† positive (vs. negative)		1.43	1.11-1.87	1.46	1.18-1.80
Lumpectomy (vs. mastectomy)		0.95	0.71-1.27	1.11	0.89-1.38
Margin positive (vs. negative)		1.44	0.96-2.15	1.39	1.01-1.91
Radiotherapy (vs. none)		0.71	0.54-0.94	0.60	0.48-0.75
Chemotherapy (vs. none)		0.63	0.47-0.84	0.77	0.61-0.98
Hormonal therapy (vs. none)		0.83	0.60-1.14	0.97	0.78-1.22
LHA‡ size	Large (reference)	1.00	–		
	Small	1.32	0.99-1.75	1.12	0.89-1.40
	Rural	1.16	0.76-1.76	1.25	0.92-1.70

* Estrogen receptor.
† Lymphatic or vascular invasion.
‡ Local health authority.

Although patients from rural LHAs had inferior survival, at 7.4 years of median follow-up it was not significantly different from that of patients from more populous regions of BC, after controlling for potential confounding variables. However, the relatively short follow-up period and small sample size limit this interpretation.

In contrast to our hypothesis, patients in rural BC used the screening mammography program less and presented with more advanced disease. It is possible that patients who lived in rural locations presented with more advanced stage breast cancer, in part due to the decreased utilization of screening mammography or a tendency to seek medical attention later than women from urban locations, though causality cannot be assessed in this retrospective study. Others have reported similar correlations.[17-19] A study from Ontario demonstrated that First Nations women were less likely to have screen-detected breast cancers and were more likely to present with higher stage disease.[20] Rural health districts in BC had higher proportions of First Nations women compared to other health districts in BC. The observation that lower rates of screening program attendance were associated with more advanced stage and rural residence might be useful in guiding the further development of the organized breast screening program. Surprisingly, we also found a significant difference in LVI by geography. It has long been known that LVI is particularly subjective.[21] Furthermore, pathology review increases the chance of LVI being detected, and since patients from peripheral hospitals in BC are more likely to have pathology reviews, we hypothesize that this may explain the increased detection of LVI in small LHAs.

Numerous randomized trials comparing breast-conserving therapy to mastectomy have demonstrated that these interventions achieve equivalent survival.[22-26] The current study demonstrated that patients with early stage breast cancer in rural BC were much more likely to receive mastectomy rather than breast-conserving therapy compared to their urban counterparts, a finding that has been observed in other jurisdictions.[4-7,12] We hypothesize that there are two main reasons for the decreased utilization of breast conservation in rural BC patients. First, women who live in rural communities may choose to have a mastectomy, either because of a desire to avoid radiation or a lower preference to conserve their breast. For example, cultural differences in First Nations communities – which are more abundant in rural BC – may influence their choice of local breast treatment. Other investigators have documented different preferences for type of breast surgery by racial or ethnic group.[27,28] Second, some rural women who might have chosen breast conservation may instead have a total mastectomy because of surgeon recommendation based on a perception of difficulty in accessing radiotherapy services. This is supported by research suggesting surgeon recommendation has a strong influence on patient's choice of breast surgery.[29-31] This study also found a significant relationship between tumour grade and type of surgery, which was somewhat unexpected (Table 3). We hypothesize that physicians' estimate of risk of recurrence, which is dependent on tumour grade, may influence their recommendation or patients' choice to pursue a mastectomy. Alternatively, grade may correlate with an unmeasured confounder that was not included in the multivariable analysis.

As hypothesized, systemic therapy use was independent of subject residence. This observation may be due to the widely dispersed Communities Oncology Network which administers chemotherapy in sites distant from urban cancer centres, or the long-standing use and wide distribution of Cancer Management Guidelines developed by the BCCA.[32] The difference in availability of systemic and radiotherapy services across BC may explain in part the disparate use of radiotherapy, though not systemic therapy, for women from rural BC.

The results of this study should be considered in the context of its strengths and limitations. British Columbia is uniquely situated to capture population-based treatment and outcome data because the BCCA is the sole provider of radiotherapy services, funding for both oral and intravenous anti-neoplastic agents, and screening mammography. Also, the BCCA maintains the BC Cancer Registry

and developed the Breast Cancer Outcomes Unit since 1994 to prospectively evaluate outcomes data for patients referred to a BCCA facility. The BCCA system therefore allows for accurate estimates of resource utilization and patient outcomes, relatively free from selection bias. However, this study was limited by its relatively small sample size, particularly among the rural population. In addition, HER-2 status testing was not routinely available during the study period and therefore could not be assessed. The relatively short follow-up period limits interpretation of the non-significant differences in survival by location of residence. Despite this, the sample size was sufficiently large to assess the primary objective and find highly significant differences in resource utilization by location of residence.

CONCLUSION

This population-based study of 2,869 patients with breast cancer identified disparities in use of breast cancer screening, stage distribution and breast-conserving therapy by the population size of the patients' local health authority at the time of diagnosis. Future research is needed to explore methods to improve access and use of breast cancer screening in rural communities. Research is also needed to explore the decision-making process for type of breast cancer surgery in First Nations, rural and remote communities. The challenges faced by patients from rural BC are likely generalizable to most rural communities in Canada, and it is proposed that nationwide efforts should be undertaken to reduce these disparities.

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Received: June 18, 2011
Accepted: August 2, 2011

RÉSUMÉ

Objectifs : Comparativement aux résidents des zones urbaines, les résidents des communautés rurales ont moins accès au dépistage et aux traitements du cancer, mais l'on n'a pas encore évalué l'utilisation des ressources par les patients, ni les résultats sanitaires de ces patients, à l'aide d'analyses populationnelles globales. Notre étude visait à déterminer si le dépistage et les traitements du cancer du sein étaient utilisés moins souvent dans les régions rurales de la Colombie-Britannique (C.-B.), et si cela se traduisait par des résultats différents.

Méthode : Nous avons répertorié toutes les personnes ayant reçu un diagnostic de cancer du sein en C.-B. en 2002 en consultant le Registre du cancer, et nous avons lié ces données à celles de la base de données des mammographies de dépistage. Nous en avons extrait les données démographiques, la pathologie, le stade, les traitements, le recours à la mammographie et les données de mortalité des patientes. À l'aide des

données du Recensement du Canada, nous avons classé les patientes selon leur lieu de résidence (leur autorité sanitaire locale [ASL] : petite, grande ou rurale), puis comparé l'utilisation des ressources et les résultats sanitaires pour chaque catégorie d'ASL. Nous avons supposé que les taux de mastectomie (par opposition à la chirurgie mammaire conservatrice) seraient supérieurs dans les régions rurales, la conservation du sein étant normalement accompagnée par la radiothérapie adjuvante, laquelle est peu disponible dans les zones rurales de la province. Par contre, nous avons supposé que les taux d'utilisation du dépistage du cancer et des traitements systémiques seraient semblables, car ces services sont disponibles dans toute la province. Nous avons effectué des analyses exploratoires pour déterminer si les disparités dans l'utilisation du dépistage et des traitements se traduisaient par des écarts dans la survie.

Résultats : Notre étude a porté sur 2 869 femmes atteintes de cancer du sein. Les patientes des communautés rurales se sont présentées avec des cancers à un stade plus avancé (p=0,01). Après analyse multivariée, les patientes provenant des ASL rurales, et non urbaines, étaient moins susceptibles d'avoir subi une mammographie de dépistage (RC=0,62; p<0,001). Les femmes des communautés rurales étaient moins susceptibles d'avoir subi une chirurgie mammaire conservatrice (RC multivarié=0,47; p<0,001). Il n'y avait aucun écart significatif dans l'utilisation de la chimiothérapie (p=0,54) ou de l'hormonothérapie (p=0,36). Les taux de survie propres au cancer du sein après cinq ans étaient de 90 % dans les grandes ASL, de 88 % dans les petites ASL et de 86 % dans les ASL rurales (p=0,08), tandis que les taux de survie globaux étaient de 84 %, 81 % et 77 %, respectivement (p=0,01). Après analyse multivariée avec une médiane de 7,4 années de suivi, ni la survie propre au cancer du sein (coefficient de danger [CD]=1,16; 0,76-1,76; p=0,49), ni la survie globale (CD=1,25; 0,92-1,70; p=0,16) n'étaient significativement inférieures chez les patientes des ASL rurales comparativement à celles des grandes ASL.

Conclusion : On observe des écarts significatifs dans le recours aux mammographies de dépistage, la distribution selon le stade de cancer et l'utilisation locale-régionale des traitements en fonction de la taille de la population de l'ASL. Compte tenu des écarts par ASL dans les facteurs liés aux patientes et aux tumeurs, la survie n'était pas significativement différente.

Mots clés : cancer du sein; mammographie; chirurgie mammaire conservatrice; mastectomie; rural; hormonothérapie; chimiothérapie