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APPROACH OF FIVE-YEAR-AVERAGE HAZARD RATES FOR THE BREAST CANCER PATIENTS AND ANALYSES OF PROGNOSTIC FACTORS--AN APPLICATION OF COX REGRESSION MODEL

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Objective: To compare with five-year survival after surgery for the 116 breast cancer patients treated at the First Teaching Hospital (FTH) and the 866 breast cancer patients at Hôpital du Saint-Sacrement (HSS). Methods: Using Cox regression model, after eliminating the confounders, to develop the comparison of the five-year average hazard rates between two hospitals and among the levels of prognostic factors. Results: It has significant difference for the old patients (50 years old or more) between the two hospitals. Conclusion: Tumor size at pathology and involvement of lymph nodes were important prognostic factors.

Key words: Breast cancer, Prognosis, Five-year-average hazard rates

In document,[1] the Kaplan-Meier Product-Limit method[4] was used to compare survivals of the breast cancer patients initially treated at the First Teaching Hospital (FTH) of Norman Bethune University of Medical Sciences, Changchun, China, with those of patients seen at Hôpital du Saint-Sacrement (HSS) in Québec City, Canada. Following these comparisons, we used Cox proportional hazards regression models[2] to eliminate the confounders and develop the comparison of the five-year average hazard rates between two hospitals and among the prognostic factors.

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PATIENTS AND METHODS

As indicated in document,1 all data of this study were obtained from the medical records and follow-up for the 116 breast cancer patients treated at FTH and a special data bank for the 886 breast cancer patients who were treated at HSS. To assess whether the prognostic effect of variables was uniform across levels, we categorized each variable and created binary indicator variables as follow to estimate changes in hazard ratio across levels of each variable.

HSP	= 1;	if patient was treated at FTH
	= 0;	if patient was treated at HSS
AGE	= 1;	if age at diagnosis>50 years
	= 0;	otherwise
TS	= 1;	if tumor size at pathology>2 cm
	= 0;	otherwise
NOD	= 1;	if number of lymph nodes involved≥1
	= 0;	otherwise

Cox proportional hazards regression models were developed including above variable. This model provided adjusted hazard ratios (AHR) and 95%

confidence (95% CI) for each variable to evaluate the effects for each of the prognostic factors and to eliminate confunders. Wald Chi-Square statistic, $\chi^2_{df.w}$[6] was used for statistical testing.

All computations were carried out by use of SAS statistical software package.

RESULTS

Comparison of the Effect of Variables between Two Hospitals

Document[1] indicated that the crude five year survival after surgery for the breast cancer patients at the FTH (74.2%) was not significantly different from that at HSS (76.0%) (p=0.42). This paper calculated the five year average mortality rates (1/person year) stratified in different levels of the prognosis factor (Table 1), the Crude Hazard Ratio (CHR) and the 95% Confidence Interval of CHR between two hospitals (FTH/HSS) in each stratum of the factor (Table 2). These tables showed that the five year average mortality rate for the old women (aged 50 years or more at diagnosis) was substantially higher at FTH than at HSS (CHR=1.86; 95% CI:1.17-2.56), but not significantly different for the younger women (age at diagnosis less than 50 years) and for the other factors between the two hospitals.

Table 1. Five year average mortality rates stratified in different levels of the prognostic factors among breast patients treated at First Teaching Hospital (FTH), Changchun, China and Hôpital du Saint-Sacrement (HSS), Québec, Canada

Prognosis factor	Stratum level	FTH			HSS		
		Deaths	Person years	Crude mortality rate*	Deaths	Person years	Crude mortality rate*
Overall		24	398.7	6.0	129	2664.9	4.8
Age at diagnosis (years)	≤ 49	15	289.3	5.2	56	1012.3	5.5
	≥ 50	9	109.4	8.2	73	1652.6	4.4
Tumor size at pathology (cm)	≤ 2.0	6	151.4	4.0	39	1483.3	2.6
	> 2.0	13	190.5	6.8	77	1039.6	7.4
	n.a	5	56.9	8.8	13	142.0	9.2
Number of lymph node involvement	0	4	151.5	2.6	31	1424.5	2.2
	≥ 1.	20	240.7	8.3	76	970.4	7.8
	n. a	0	6.5	0	22	270.0	8.1

* Expressed per 100 person-years.

n.a: Information was unavailable

Table 2. Crude Hazard ratio (CHR) and 95% Confidence Intervals (95% CI) of CHR between two hospitals (FTH/HSS) in the different stratum-levels of prognosis factors

Prognosis factor	Stratum level	Crude Hazard Ratio (CHR)	
		CHR	95% CI
Over all		1.25	0.81 – 1.69
Age at diagnosis (years)	≤ 49	0.95	0.38 – 1.52
	≥ 50	1.86*	1.17 – 2.56
Number of lymph node involvement	0	1.18	0.14 – 2.22
	≥ 1	1.06	0.57 – 1.56
Tumor size at pathology (cm)	≤ 2.0	1.54	0.68 – 2.40
	> 2.0	0.92	0.33 – 1.51

* $P < 0.05$

Table 3. Adjusted Hazard Ratio(AHR) and 95% CI) of AHR stratified in the stratum-levels of the prognostic factors with combined data of the two hospitals

Prognosis factor	Stratum level	Adjusted Hazard Ratio*		*p*-value on Wald
		AHR	95% CI	Chi-Square test
Hospital	HSS	1		
	FTH	0.9	0.5 – 1.4	0.5024
Age at diagnosis	< 50	1		
(years)	≥ 50	0.8	0.6 – 1.1	0.2097
Lymph nodes	0	1		
involved	≥ 1	3.0	2.0 – 4.5	0.0001
Tumor size at	≤ 2.0	1		
pathology (cm)	> 2.0	2.2	1.5 – 3.2	0.0001

*Hazard ratio was obtained by Cox model with all variables in the table entered in the analysis simultaneously

Comparisons of the Effect of Variables across Stratum Levels

To evaluate the effects for each prognostic factor across stratum levels and to eliminate the bias produced by confounders, adjusted hazard ratios (AHR) and 95% confidence intervals (95% CI) were obtained by Cox proportional hazard regression model using the combined data of two hospitals (Table 3). After adjustment, we can see, the mortality of patients treated at FTH was similar to that at HSS (AHR=0.9, 95% CI: 0.5—1.4; χ^2_{1w} =0.49, p=0.5024), and there was no significant difference of mortality between old women (age≥50 years) and young women (age<50 years) (AHR=0.8, 95% CI: 0.6—1.1; χ^2_{1w} =1.62, p=0.2097). Tumor size and lymph node involvement are related to prognosis in the two hospitals. Patients with larger tumor size (>2.0 cm) have higher mortality rate compared to patients with smaller tumor size (≤2.0 cm) (AHR=2.2; 95% CI: 1.5—3.2; χ^2_{1w} =18.20; p=0.0001), and the mortality rate was higher among patients with lymph node involvement than among women without lymph node involvement (AHR=3.0; 95% CI: 2.0—4.5; χ^2_{1w}=29.58; p=0.0001).

DISCUSSION

Comparison between Two Hospitals

In old women group (age≥50 years), patients at FTH have higher mortality rate compared to patients at HSS. The major reason is that the proportion of patients with advanced breast cancer among women treated at FTH was obviously higher than that seen at HSS. In fact, the proportion of patients with lymph node involvement among women was 63.6% at FTH, but only 41.0% at HSS. The proportions of patients with larger tumor size (more than 2.0 cm) were 65.5% and 45.0% at FTH and HSS respectively. Among other stratum specific groups, however, there were no significant different average five year mortality rates in both hospitals.

Comparisons among Strata for the Prognosis Factors

This study showed that patients with larger tumor size (more than 2.0 cm) have about two times of average five year mortality rate compared to patients with smaller tumor size (no more than 2.0 cm) and the mortality rate among patients with lymph node involvement is three times that among women without lymph node involvement. These results implied that lymph nodes involved and tumor size at pathology are important prognostic factors for breast cancer patients. This conclusion is identified with the documents.[1,3,5]

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