COMMENTARY

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Lymphatic/vascular invasion has a negative impact on overall survival and disease-free survival in patients with breast cancer and positive axillary lymph nodes

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Breast cancer (BC) prognostic factors assessed in surgical specimens are of paramount importance in the clinical practice and are commonly used to designate adjuvant treatments. Lymphovascular invasion (LVI) may be present in 15.7%[1] to 55%[2] of invasive BC cases and, in recent studies, has been identified as an independent prognostic factor.[3,4] Conversely, some studies have demonstrated conflicting results concerning to patients with positive or negative axillae.[2,3,5,6] In this context, the aim of this study was to evaluate whether LVI in surgical specimens is associated with differences in DSF and OS in women with operable BC according to axillary involvement.

This is a nonconcurrent cohort study in women diagnosed with BC treated at the Cancer III Hospital/ Brazilian National Cancer Institute from January 1, 2008, to December 31, 2009. The study was approved by the institution's Research Ethics Committee (protocol 128/11).

Women ≥ 18 years who underwent surgical treatment by mastectomy or segmental breast resection and sentinel lymph node biopsy and/or lymphadenectomy were included in this study. OS was calculated from the date of surgery to death from any causes and DFS from the date of surgery to loco-regional recurrence or distant metastasis. Analysis was performed using Kaplan-Meier and Cox regression model.

A total of 1556 women were included. Patient characteristics are presented in Table 1. The mean follow-up time was 87 months (3-122 months). LVI was associated with a shorter DFS and OS time only between those with positive axillae (Table 2) and with the risk of recurrence and death (Table 3).

In two subanalysis, including patients with triple-negative tumors (n = 173) and those who underwent neo-adjuvant chemotherapy (n = 332), patients with LVI presented shorter DFS (P = .004 and P < .001, respectively) and overall survival (P = .001 and P < .001, respectively) (data not shown).

The findings observed in the present study are in agreement with authors that shown that LVI has a negative impact on OS and DFS

TABLE 1 Sociodemographic and clinical characteristics (n = 1556)

Characteristics	N (%[a])
Age at diagnosis, mean (±SD)	56.5 (±13.1)
Nonspecial type invasive carcinoma	1281 (82.3)
Advanced clinical stage (IIB, III)	727 (46.8)
Histologic grade 2 and 3	1028 (86.2)
Estrogen receptor positive	1210 (78.6)
Progesterone receptor positive	1056 (67.9)
HER-2 positive	296 (20.6)
Lymphovascular invasion	629 (40.4)
Mastectomy	1199 (77.1)
Axillary approach	1552 (99.7)
Positive lymph node status	771 (49.6)
Chemotherapy[b]	1041 (66.9)
Trastuzumab[b]	214 (13.8)
Hormone therapy[b]	1128 (72.5)
Radiotherapy[b]	746 (47.9)

Note: Missing data: clinical stage = 02 (0.1%); histologic grade = 363 (23.3%); estrogen receptor = 17 (1.1%); progesterone receptor = 18 (1.2%); HER-2 = 117 (7.5%); lymph node status not applicable = 04 (0.3%).

[a]Percentages are calculated based on valid data.

[b]Neo-adjuvant and/or adjuvant.

TABLE 2 Survival according to lymphovascular invasion, stratified by axillary status (n = 1556)

	Mean survival time					
	All patients		Negative axillae		Positive axillae	
	Months (95% CI)	*P* value	Months (95% CI)	*P* value	Months (95% CI)	*P* value
Disease-free survival						
With LVI	84.9 (81.4-88.5)	<.001	102.7 (98.2-107.2)	.235	77.3 (72.9-81.7)	<.001
Without LVI	104.6 (102.4-106.8)		109.6 (107.3-111.9)		92.7 (88.2-97.1)	
Overall survival						
With LVI	95.03 (92.0-98.0)	<.001	111.6 (108.0-115.1)	.945	89.0 (85.3-92.7)	<.001
Without LVI	107.2 (105.3-109.1)		110.9 (108.9-113.0)		100.1 (96.2-104.0)	

Abbreviations: CI, confidence interval; LVI, lymphovascular invasion.

TABLE 3 Risk of recurrence and death according to lymphovascular invasion, stratified by axillary status (n = 1556)

	Risk of recurrence and death					
	All patients		Negative axillae		Positive axillae	
	aHR[a] (95% CI)	*P* value	aHR[a] (95% CI)	*P* value	aHR[a] (95% CI)	*P* value
Disease-free survival						
With LVI	1.98 (1.61-1.43)	<.001	1.29 (0.82-2.02)	.270	1.62 (1.25-2.09)	<.001
Without LVI	Ref.		Ref.		Ref.	
Overall survival						
With LVI	1.70 (1.37-2.11)	<.001	0.96 (0.58-1.58)	.876	1.51 (1.16-1.97)	.002
Without LVI	Ref.		Ref.		Ref.	

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; LVI, lymphovascular invasion; Ref., reference.
[a]Adjusted for age at diagnosis and clinical stage.

in patients with BC and positive axillary lymph nodes[2,3] and has no impact on the prognosis of women with BC and negative axillae.[7,8] Other authors also observed that LVI is an independent predictor of local recurrence, distant metastases, and OS in patients undergoing neo-adjuvant chemotherapy.[9,10]

In conclusion LVI displays a negative impact on OS and DFS in patients with BC and positive axillae, in contrast with what was noted for patients with negative axillae.

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