

The relation between tumor marker Ca 15-3 and metastases in interpectoral lymph nodes in breast cancer patients

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ABSTRACT

Objective: We aimed at analyzing the metastatic involvement in interpectoral (Rotter's) lymph nodes (RLN) in relation to tumor marker CA 15-3.

Methods: The study included 177 female patients undergoing surgery for primary breast cancer at the University Hospital for Tumors, Zagreb, Croatia from November 2001 to March 2004. In addition to the standard surgical procedure, interpectoral RLNs were removed in all of the patients. Levels of the serum tumor marker CA 15-3 was determined prior to surgery.

Results: Rotter's lymph nodes were identified in 66.2% of the patients, with metastatic involvement revealed in 18.6% of the RLNs. Metastatic involvement of RLNs in patients with negative axillary lymph nodes was 2.8% and positive in 34.6%. Elevated serum levels of tumor marker CA 15-3 had 22 (12.4%) patients. Of 33 Rotter's

node-positive patients, 27.3% had elevated serum levels of tumor marker CA 15-3 and in Rotter's node-negative patients only 9% had elevated serum levels of tumor marker CA 15-3, with the level statistically significantly higher in Rotter's positive patients compared to those with negative (or absent) RLNs ($\chi^2=8.22$, $p=0.004$).

Conclusions: Tumor marker CA 15-3 is more frequently elevated in patients with positive RLNs. Elevated values of tumor marker CA 15-3 could be warning for possible positive interpectoral nodes. The removal of the RLNs may be beneficial for patients with (massive) axillary nodal involvement. For axillary node negative patients, sentinel node biopsy could avoid the unnecessary removal of the RLNs.

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The study is aimed at exploring the level of interpectoral (Rotter's) lymph node involvement in breast cancer patients and their relation to levels of the serum tumor marker CA 15-3. Tumor marker CA 15-3 values are obligative in preoperative evaluation of the patients with breast cancer. Increased preoperative values are potential sign of metastatic disease or advanced local finding of the breast cancer. Finally, the obtained results may come in handy as guidelines

on routine removal of RLNs in breast cancer patients with positive axillary lymph nodes. A special attention is paid to the analysis of overall, surgically confirmed presence and metastatic involvement of RLNs and their involvement in relation to preoperative levels of the serum tumor marker CA 15-3.

Methods. The study includes 177 female patients undergoing surgery for primary breast cancer and

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without distant metastasis at the Department of Surgery, University Hospital for Tumors, Zagreb, Croatia from November 2001 to March 2004. All the patients were operated on by the same surgical team. Standard preoperative evaluations included x-ray test of the lungs, spine and pelvis, abdominal and breast ultrasonography, mammography, complete laboratory tests and tumor marker CA 15-3.¹⁻³ All patients were with absence of distant disease and underwent surgical tumor biopsy, and surgery for biopsy confirmed breast cancer (either segmentectomy or mastectomy), as well as dissection of axillary nodes at all 3 levels and Rotter's lymph node extirpation.⁴⁻⁶ Exclusion criteria included: patients operated and had primary surgery for primary breast cancer; operated by the same surgical team and operated without any distant metastasis. Rotter's lymph nodes were extirpated through the same incision as axillary lymph nodes without resection of major or minor pectoral muscle.⁷ Pathohistologic evaluation of breast carcinoma performed with intraoperative frozen section biopsy was definitely confirmed on permanent tissue sections embedded in paraffin and stained with hemalum-eosin.

The statistical methods used were classical χ^2 test with the obtained values expressed in percentage as mentioned in the text.

Results. The study results showed that 177 breast cancer patients were in the age bracket between 28 and 86 years of age (median 57.8 years). Regarding localization, in 51.7% patients the tumor was present in the right breast and in 48.3% it was located in the left breast; 53.8% patients underwent mastectomy, and in 46.2% segmentectomy was performed. All of the 177 patients underwent radical dissection of axillary lymph nodes and removal of interpectoral fat tissue with possible presence of RLNs. The preoperative assessment of the serum tumor marker was carried out in all 172 patients. The levels were found to be elevated in 22 (12.4%) patients. The tumor's largest diameters (tumor size) measured by pathologist were classified into 3 groups according to the TNM classification. T1 tumors, <2 cm in their largest diameter, were found in 61.6% patients; T2 tumors, 2-5 cm in their largest diameter were found in 32.6%, and T3 tumors, >5 cm in their largest diameter, were found in 5.8% patients.⁸ Pathohistologic evaluation showed invasive ductal carcinoma in 157 (88.7%), mucinous carcinoma of the breast in 7 (3.9%), lobular carcinoma in 11 (6.2%) and papillary and medullary carcinoma of the breast in one (0.6%) patient each. Of 157 invasive ductal carcinomas, 23 (14.6%) were grade I, 88 (56%) grade II, and 46 (29.3%) grade

Table 1- Metastatic involvement of interpectoral (Rotter's lymph nodes (RLN) related to tumor marker Ca 15-3.*

Metastatic involvement of RLN	No. of tumor marker Ca 15-3 (%)				
	Normal values		Elevated values		Total
Negative	131	(91)	13	(9)	144 (81.4)
Positive	24	(72.7)	9	(27.3)	33 (18.6)
Total	155	(87.6)	22	(12.4)	177 (100)

III. Pathohistologic examination of axillary lymph nodes showed negative axillary nodes in 50.5%, while 49.5% patients were axillary lymph node positive. Interpectoral fat tissue of 33.8% patients did not contain any lymph nodes, while at least one lymph node was found in 66.2% patients. Tumor cell-positive Rotter's lymph nodes were found in 18.6%, and 81.4% patients had either not present or tumor-negative interpectoral nodes. Of patients with pathohistologically confirmed positive axillary lymph nodes, interpectoral (Rotter's) nodes were positive in 34.6%, and the remaining 65.4% were negative. Of 33 Rotter's node-positive patients, 24 (72.7%) had tumor marker CA 15-3 levels within normal range, and in 9 (27.3%) patients the levels were elevated. Tumor marker CA 15-3 levels was statistically significantly higher in Rotter's node-positive patients ($\chi^2=8.22$; $p=0.004$) compared to patients with negative Rotter's lymph nodes (Table 1).

Discussion. Preoperative diagnosis of RLNs in routine clinical practice is rather unsafe. According to some authors, RLNs can be detected by ultrasound in 10-35% cases.⁹⁻¹¹ Results obtained by a majority of authors show metastatic involvement in RLNs in approximately 10% of patients.¹²⁻¹⁴ Our results show that Rotter's node metastases are not so rare. This problem of breast cancer treatment has been tackled by some authors.^{15,16} Komenaka et al¹⁷ showed that interpectoral lymph nodes could be a possible site for tumor recurrence. Taking into consideration, removal of RLNs may play a particular role in the treatment of breast cancer.¹⁸ Tumor marker CA 15-3, if elevated, could alarm the surgeon and make him at least explore interpectoral space to search for possible positive RLNs, so they would not be left behind the surgery. With good communication between diagnostic and experienced and profiled surgical-pathologic

teams, the identification and removal of RLNs with metastatic involvement should not be a technical problem, especially with the early postoperative rehabilitation program, it does not make any difference to the patient.¹⁹ For many women undergoing surgery for breast cancer without RLNs removal, the nodes are responsible for further spreading of the disease, suggesting potential therapeutic benefits of this type of surgical management of breast cancer. The removal of the RLNs may be beneficial for patients with axillary nodal involvement. For axillary node negative patients, sentinel node biopsy could avoid the unnecessary removal of the RLNs.²⁰⁻²⁶

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