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THE MARGIN STATUS IN BREAST CONSERVATIVE SURGERY

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Abstract: *The objectives of this population-based study were to determine the specific surgical factors associated with the obtaining of a negative surgical margin after BCS in patients with early stage breast cancer. This study shows the importance of surgical diagnosis and technique in managing early-stage breast cancer with BCS. Low positive margin rates can be achieved.*

Key words: *retrospective analysis, excision margin status, breast conservative surgery.*

1. Introduction

The main objective of BCS is to remove completely the mammary malign tumor simultaneously with the adequate preserving of the breast tissue in order to obtain an acceptable cosmetic result. As numerous studies demonstrate, the presence of a microscopically clear surgical margin is considered the most valuable indicator that ensures completeness of surgical excision after partial mastectomy or lumpectomy [4, 7]. Meanwhile, a positive surgical margin is a major predictor of local recurrence, independent of tumor factors and other adjuvant therapies.

Published rates of positive margins after partial mastectomy vary widely, ranging from 4% to 31%., and might be attributed to inconsistent definitions of a positive margin, variations in the use of intraoperative pathological assessment of margins, variations in the handling of surgical specimens and pathological sampling of margins, whether surgery was diagnostic or therapeutic in intent, and variations in the actual number of surgical resections that were performed to generate the published positive margin rates [8].

In multivariate analyses, tumor size is most frequently identified as a predictor of positive margins while, in our opinion, the factors under surgical control associated with positive margins are not as well known [16]. Routine dissection of cavity margins at the time of partial mastectomy has been shown to decrease the rate of positive margins.

The objectives of this population-based study were to determine the specific surgical factors associated with the obtaining of a negative surgical margin after BCS in patients with early stage breast cancer.

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2. Methods

This population-based study was a retrospective analysis of 490 patients diagnosed with early-stage breast cancer (clinical stage I and II) who underwent BCS for invasive breast carcinoma from January 2000 to December 2008.

The study protocol followed the ethic Romanian legislation concerning population studies. Exclusion criteria included patients who underwent initial mastectomy, ductal carcinoma *in situ* only, recurrent disease, or T3/T4 disease. Relevant data were abstracted from clinical, pathological and operatory reports. A positive margin was defined as microscopically confirmed disease (invasive or in situ) at the inked margin. Tumors were classified as nonpalpable if a needle-localization procedure was required for excision. Preoperative diagnosis was considered confirmed if malignant cells were identified by either fine needle aspiration or core biopsy.

Tissue was considered a cavity margin if labeled specimens distinct from the main surgical specimen was identified in the pathology report. Pathology reports were also used to document specimen orientation labeling. The volume of lumpectomy specimens was defined as the product of the 3-dimensional lengths of the surgical specimen as documented in the pathology report. Statistic analysis was used to evaluate the effect of potential technical and tumor-related factors on margin status.

3. Results

Over the 9 years study period, 490 cases were available for review.

Patient and tumor characteristics are shown in tables 1 and 2.

Table 1

Patients demographic characteristics compared with margin status

VARIABLE	POSITIVE MARGIN	NEGATIVE MARGIN	P value
Age			.483
>51	30%	70%	
<50	28%	72%	
Obesity			.251
Yes	31%	69%	
No	27%	73%	

Disease characteristics compared with status margin Table 2

VARIABLE	POSITIVE MARGIN	NEGATIVE MARGIN	P value
Type of lesion			.087
Palpable	33%	67%	
nonpalpable	26%	74%	
Histologic type			.003
Ductal	25%	75%	
Lobular	32%	68%	
Tumor grade			.040
I	21%	79%	
II	29%	71%	
III	36%	64%	
Tumor grade			.040
I	21%	79%	
II	29%	71%	
III	36%	64%	
Tumor size			.026
T1a/b	25%	75%	
T2	30%	70%	
T3	35%	65%	
Nodal status			016
No	26%	74%	
N1	32%	68%	
Multifocal disease			.000
Present	35%	65%	
Absent	22%	78%	
Estrogen receptor status			000
Present	25%	75%	
Absent	32%	68%	
Extensive intraductal component			.026
Positive	33%	67%	
Negative	27%	73%	
Lymphovascular invasion			.017
Present	34%	66%	
Absent	27%	73%	

Patients distribution according the margin status dimensions is presented in table 3.

Patients histological characteristics compared with margin status Table 3

Type	Number	Percentage
Free unspecified margins	49	8.1%
Free margins 1-5 mm	107	17.7%
Free margins over 5 mm	334	55.5%
Microscopic affected margins	49	8.1%
Macroscopic affected margins	4	0.7%
Undertermined margin status	60	10%

Free margin status microscopically evaluated larger than 5mm were obtain in more than half of patients.

Positive margin data are shown in Table 4.

Rate of positive margins Table 4

SURGICAL MARGIN STATUS	PERCENTAGE
Cases with confirmed preoperative diagnosis	
Positive margins	27%
Negative margins	73%
Final margin status	
Positive margins	29%
Negative margins	71%

The rate of positive margins was 29% for the entire sample and 27% when there was a confirmed preoperative diagnosis.

Discussions

The goal of breast-conserving surgery is to remove completely the cancer while preserving adequate breast tissue in order to obtain a cosmetically acceptable result. This entails appropriate patient selection and the attainment of clear surgical margins.

Ideally, a clear surgical margin should be achieved after a single, definitive surgical procedure [16]. Combined with postoperative irradiation, most women will have a satisfactory cosmetic outcome and low risk of recurrence.

Margin status definition as "free" is variable, some authors considering that a 1 cm safety margin as inadequate [14, 15]. According NSABC criterion there are considered as "positive margins" the situations where might be microscopically identified tumor tissue at the level of the excision margins [11, 12].

Data published in the literature indicate variable rates of positive margins after mastectomy part between 4 and 31% [9]. These variations are attributed to the inconsistent definitions of positive margins, to the changes in the use of intraoperatory pathologic margins evaluation, variations in surgical specimen handling and manipulation of pathological specimens taken from the edges or to different variants of the currently used of surgical techniques.

Simultaneously, numerous studies have consistently shown that a positive surgical margin is an independent predictor of local recurrence and can lead to further surgery with associated morbidity [5, 6]. In this study, overall positive margin rates were similar to published results [2]. Meanwhile, we consider that the biological and patient factors that are related to positive margins cannot be altered by the surgeon. This study confirms that certain tumor characteristics influence margin status. The tumor size, grade, and histology (lobular versus ductal) are all associated with positive margins and should be considered when planning the extent of resection.

O study realized by Joint Center for Radiation Therapy (JCRT) on 1970 patients with mammary cancer type I and II presented the following classification of the margin status [7]:

- Negative margins >1 mm (no invasive carcinoma or *in situ carcinoma* in less than 1mm for the sample margin);
- Negative margins <1 mm: presence of an invasive carcinoma or *in situ carcinoma* in less than 1mm for the sample margin;
- Positive margin: confirmed presence of the carcinoma in the sample margin;
- Positive margins „focal" or „minimally": present on 1-3 microscopic fields;
- Positive margins „extensive" present on more than 4 microscopic fields.

The main factors considered as predictive identified at the margins are: preoperatory diagnosis, the cavitary margins, the presence of palpable lesions, a large volume of the excised tumor, the tumors dimensions, the absence of the multifocal lesions, the presence of a ductal histology, the absence of lymphovascular invasion.

In fig.1 and 2 are presented histological comparative images in positive and negative margins.

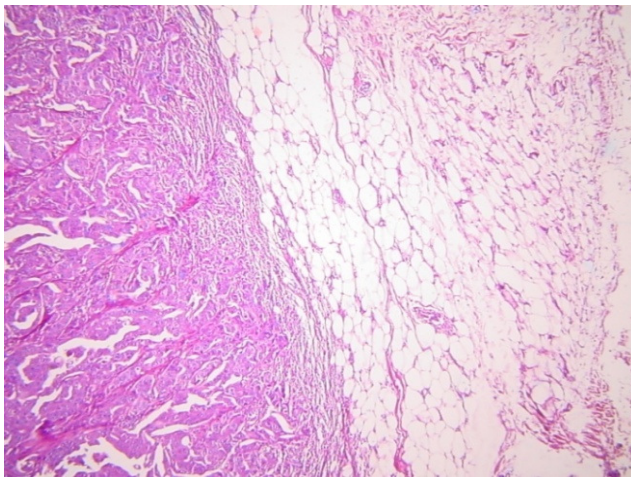

Fig. 1. *Free margin status*

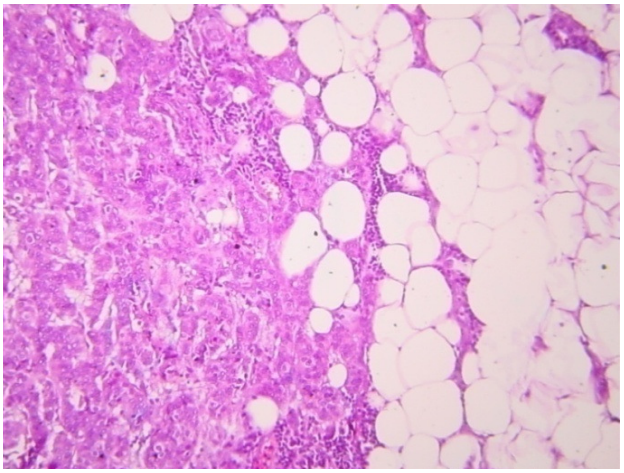

Fig. 2. *Negative margin status*
(personal collection)

The excision margins are influenced by histologic factors that should be carefully considered when choosing the surgical treatment, namely the extension of resection. In general terms, the cancer is characterized by the presence of extensive protrusional spiculi and the extensive sectioning of breast tissue around the tumor [1]. The presence of cancer cells at the periphery of breast cancer decreases progressively with distance from the tumor margins (59% and 17% from 1cm to 3cm). Therefore it becomes intuitive that a larger excision in health breast tissue can get clear margins, followed by a better local control and a lower local recurrence rate.

Veronesi comparative analysis

of quadrantectomy *versus* lumpectomiei demonstrated a significant decrease in local recurrence with an increasing amount of mammary excised tissue [15].

Meanwhile, there are a number of factors that may affect the determination of margin status that are not under the surgeon operatory influence, such as the cancer progression model, the effects of specimen handling, or the variations in specimen processing.

Invadated margins involve reexcision. If positive margins are diagnosed histologically after reexcision, mastectomy is required. The presence of ductal carcinoma, of multicentricity, multifocality, are indication of radical surgery [11].

In our opinion, the ideal free margins should be obtained after the first surgery. Combined with radioterapy, the results are mainly favorable, with good esthetic prognosis and a low risk of reccurency. Correct evaluation of the tumor dimensions, lobular histology, multifocality, are factors that increase the risk of positive margins, and are ussually unknown preoperatory, situation that reflects the inherent technique difficulties of any resection, especially in nonpalpable mmamary tumors and the differences between the biological behavior of the breast tumors. An appropriate preoperatory diagnosis is essential in planning optimal the operatory design and assures the correct and safe margin excision.

Conclusion

Numerous factors can influence the determination of margin status that are generally beyond the control of the surgeon. The irregular growth pattern of cancers, effects of specimen handling and processing, and variations in pathological sampling and reporting all influence margin status.

Despite these caveats, margin status is still the most important indicator of complete excision. This study shows the importance of surgical diagnosis and technique in managing early-stage breast cancer with BCS. Low positive margin rates can be achieved.

The goal of surgical therapy is to identify patients who are suitable for BCS. BCT is optimal in patients with multicentric tumors preoperatory histological identified.

Proper preoperative assessment and diagnosis, surgical planning, adequacy of resection, and pathological assessment are essential.

Combined with adjuvant therapies, acceptable outcomes and optimal cosmetics can be achieved.

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