Surgical risk factors of breast reconstruction and their clinical implications

Woerdeman, L.A.E.

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Routine histological examination of 728 mastectomy scars:
Did it benefit our patients?

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Introduction

Routine histological examination of clinically unsuspected mastectomy scars that are excised during secondary corrective surgery is considered good practice\(^1\) as these scars may contain metastases caused by spilling of the tumor during the initially curative mastectomy.\(^2\) The same may hold true for scars after prophylactically performed mastectomies because de novo invasive or non-invasive tumors may have developed in any normal glandular tissue that was left or spilled during initial surgery.\(^5\) Still, the microscopic detection of a metastasis in clinically unsuspected mastectomy scars is rare and,\(^1\) in the current era of cost-controlled and evidence-based medicine, optimal use of histological services is required. Therefore, the occurrence rate of metastases in such scars needs to be established to assess the possible benefit of their routine histological examination.

To date, only Soldin et al.\(^7\) tried to establish this rate but they admitted that the number of scars they included in their study (n = 48) was too small to yield any statistical significance to their study. Furthermore, over half of the patients in their limited series had their scar excised more than 3 years after the excision of the primary cancer,\(^7\) while up to 90 percent of local recurrences occur within these 3 years.\(^8\) Hence, we assessed the results of routine histological examination of 728 clinically unsuspected scars, 503 (or 70\%) of which were excised within the first 3 postmastectomy years.
Materials and Methods

Scars
All clinically unsuspected scars excised during secondary breast reconstruction or scar correction after mastectomy or breast conservation therapy (BCT) and submitted by the plastic surgeons of the Netherlands Cancer Institute for histological examination from January of 1994 through May of 2004 were traced. This was done by cross-linkage of a database containing all plastic surgical data on breast surgery, and a database containing the pathology reports that featured the keywords scar, thorax, breast, or mamma. The databases where linked using Microsoft Access (MS-Office 2000 Professional, Microsoft Corporation, Redmond, Washington). This way, 728 scars could be included in this retrospective analysis.

Histological examination
The 728 clinically unsuspected scars had been examined for metastases following initial curative therapy, or for de novo invasive or non-invasive tumors subsequent to prophylactic treatment. Each specimen had been macroscopically examined for evidence of tumor and multiple representative slides had been made and stained by hematoxylin and eosin for microscopic examination. Occurrence of tumor or normal glandular spilling had been noted in the pathology reports.

Recorded and analyzed data
The date, indication (curative or prophylactic), and side (left or right) of initial mastectomy or BCT were entered in a computer database created in Microsoft Excel and Microsoft Access (MS-Office 2000 Professional, Microsoft Corporation, Redmond, Washington), along with the age of the patient at the time of initial surgery and the data on any adjuvant therapy. The dates of subsequent secondary surgery were entered to calculate the time interval since initial breast surgery. Furthermore, it was recorded whether or not recurrence or metastasis of the tumor outside the scar had occurred prior to secondary surgery. The histological findings of all 728 scars, the period of follow-up after secondary surgery and, finally, any local recurrence or distant metastasis during that period were also recorded.
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Results

Data on initial breast surgery

The 728 scars were obtained from 546 breasts of 1 man and 423 women who had undergone unilateral or bilateral, prophylactic or curative mastectomy, or BCT (Table 1). The mean age of these patients at the time of initial breast surgery had been 43.6 years (range, 23.6 - 74.1 years). Of the 307 who underwent curative mastectomy patients, 174 had received adjuvant radiotherapy, chemotherapy, or hormonal therapy. Additionally, 52 patients underwent post-operative radiotherapy as part of BCT. In 285 of the 395 breasts of 361 patients

<table>
<thead>
<tr>
<th>Table 1: Indications for the 546 mastectomies or breast conservation therapies among our 424 patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Curative mastectomy *</td>
</tr>
<tr>
<td>Curative BCT</td>
</tr>
<tr>
<td>Curative lumpectomy</td>
</tr>
<tr>
<td>Prophylactic mastectomy #</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Note that curative mastectomy was combined with contralateral breast conservation therapy in 5 patients so the total number of curatively treated patients appears to amount to 366 rather than 361. Because, furthermore, unilateral curative mastectomy or BCT was combined with contralateral prophylactic mastectomy in 45 other patients, the sum of curatively and prophylactically treated patients amounts to 474 rather than 424.

* Curative mastectomies included radical, modified radical, and skin sparing mastectomies

# Prophylactic mastectomies included modified radical and skin sparing mastectomies

<table>
<thead>
<tr>
<th>Table 2: Pathology reports on the 546 mastectomies or breast conservation therapies among our 424 patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Invasive cancer</td>
</tr>
<tr>
<td>DCIS / LCIS</td>
</tr>
<tr>
<td>No malignancy</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Note that curative mastectomy was combined with contralateral breast conservation therapy in 5 patients so the total number of curatively treated patients appears to amount to 366 rather than 361. Because, furthermore, unilateral curative mastectomy or BCT was combined with contralateral prophylactic mastectomy in 45 other patients, the sum of curatively and prophylactically treated patients amounts to 474 rather than 424.

DCIS / LCIS: ductal carcinoma in situ / lobular carcinoma in situ
who initially underwent curative breast surgery, invasive breast cancer had been present, whereas non-invasive ductal or lobular tumors (DCIS or LCIS) had been found in the 110 remaining specimen of these curatively treated breasts (Table 2). The pathology reports on all 395 specimen mentioned adequate tumor-free margins.

Mean follow-up of the 361 curatively treated patients to date was 7.3 years (range, 8 months – 32 years). Twenty-three of these patients had a local recurrence and 41 patients had distant metastases during this follow-up period. Nine of the 23 local recurrences occurred before secondary breast surgery and scar examination had been performed but none occurred within the mastectomy scar.

In none of the 151 specimens of the 108 patients who initially underwent prophylactic mastectomy, invasive or non-invasive tumors had been found. Mean follow-up after initial surgery of these patients to date was 4.6 years (range, 11.3 months – 25.7 years). None of these patients developed a de novo breast tumor during follow-up.

Data on secondary breast surgery

Subsequent to their initial treatment, 214 of the 424 patients had their breast scar excised and histologically examined only once, whereas the remaining 210 patients had multiple scars excised and examined or had their scars excised on multiple occasions (Table 3). As held true for initial breast surgery, the scars were equally divided between the left and right breast. Of all 728 scars, 542 were excised following curative breast surgery whereas the remaining 186 were

Table 3: Number of scars examined per patient.

<table>
<thead>
<tr>
<th>No. of Scars per patient</th>
<th>No. of Patients</th>
<th>Total No. of Scars</th>
<th>Right-sided</th>
<th>Left-sided</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>214</td>
<td>214</td>
<td>106</td>
<td>108</td>
</tr>
<tr>
<td>2</td>
<td>148</td>
<td>296</td>
<td>150</td>
<td>146</td>
</tr>
<tr>
<td>3</td>
<td>39</td>
<td>117</td>
<td>61</td>
<td>56</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>68</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>25</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>424</td>
<td>728</td>
<td>367</td>
<td>361</td>
</tr>
</tbody>
</table>

Note that 214 of the 424 patients had their breast scar excised and histologically examined only once, whereas the remaining 210 patients had multiple scars excised and examined or had their scars excised on multiple occasions.
Table 4: Time interval between mastectomy and resection and examination of mastectomy scar per scar (and per patient).

<table>
<thead>
<tr>
<th>Time interval</th>
<th>No. of scars examined after curative mastectomy</th>
<th>No. of scars examined after prophylactic surgery</th>
<th>Total no. of examined scars</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 year</td>
<td>128 (108)</td>
<td>121 (78)</td>
<td>249 (186)</td>
</tr>
<tr>
<td>≤ 2 years</td>
<td>254 (192)</td>
<td>166 (95)</td>
<td>420 (287)</td>
</tr>
<tr>
<td>≤ 3 years</td>
<td>333 (240)</td>
<td>170 (97)</td>
<td>503 (337)</td>
</tr>
<tr>
<td>≤ 4 years</td>
<td>387 (266)</td>
<td>175 (100)</td>
<td>562 (366)</td>
</tr>
<tr>
<td>≤ 5 years</td>
<td>422 (282)</td>
<td>181 (104)</td>
<td>603 (386)</td>
</tr>
<tr>
<td>≤ 31.4 years</td>
<td>542 (361)</td>
<td>186 (108)</td>
<td>728 (424)</td>
</tr>
</tbody>
</table>

Mean 46.0 (46.0) months | 17.0 (17.0) months | 39.0 (39.0) months
Minimum 1.1 (1.1) months | 1.5 (1.5) months | 1.1 (1.1) months
Maximum 31.4 (31.4) years | 18.8 (18.8) years | 31.4 (31.4) years

Note that the total number of patients amounts to 469 rather than 424 because 45 patients underwent unilateral curative treatment combined with contralateral prophylactic treatment.

excised subsequent to prophylactic mastectomy (Tables 1 and 2). The mean time interval between initial breast surgery and resection and histological examination of the scars was 38.5 months (range, 34 days – 31.4 years) (Table 4).

No evidence of metastatic or de novo tumor was found in any of the 728 scars but residual glandular tissue was found in 11 scars. Because no scar metastases or de novo tumors were observed during the entire post-mastectomy follow-up of 6.9 years, we conclude that the risk of tumor in clinically unsuspected scars in our series is less than 1 in 728. Because no scar tumors were found, moreover, we were unable to objectify any possible relation between the indication of initial surgery, the type of initial tumor and treatment, possible local recurrence or distant metastasis, and occurrence of microscopic scar metastasis.

Discussion

Time interval, frequency and site of local recurrence following initially curative surgery

Local recurrence following mastectomy or BCT for malignant breast disease occurs in 5 to 19 percent of the patients.¹¹⁻¹⁶ Local recurrence is related to tumor stage and time lapse since treatment of the primary tumor.¹⁶⁻¹⁷ There are no
significant differences in local recurrence and overall survival rates between modified radical mastectomy and BCT, or between modified radical mastectomy and skin sparing mastectomy. However, there is a significant difference between mastectomy and BCT in the disease free time interval as 80 to 90 percent of local recurrences occurs within three years after modified radical mastectomy, whereas only 30 to 40 percent occurs within 5 years after BCT. In general, local recurrence may cause distant metastasis but may, equally, indicate such metastasis. Distant metastases often appear simultaneously with, or shortly after, the local recurrence and, because they feature a poor prognosis, early detection of the recurrence may benefit the patient.

Recurrences of breast tumors are rarely located in the mastectomy or BCT scar, with occurrence rates estimated to be 0.3 percent of mastectomies or 3.7 percent of local recurrences following mastectomy, and 0.5 to 2 percent of lumpectomies or 4.8 percent of local recurrences after lumpectomies. Such scar metastases are reportedly often clinically obvious, one of possibly few exceptions being the case recorded recently by Zambacos et al. Their patient had been maximally treated for a locally advanced cancer the year before secondary breast reconstruction. Even though preoperative consultation had not revealed any signs of local recurrence, routine histological examination of the mastectomy scar revealed the presence of carcinoma. None of the 23 local recurrences observed in our series to date involved the mastectomy scar. Likewise, no malignancy was found in any of the scars that were examined within 3 years after surgery in 240 of the 361 curatively treated patients (67%), while up to 90 percent of local recurrences might have been expected to occur within that period of time. Still, we do not know how many patients possibly were not referred by the surgical oncologist for secondary breast reconstruction or scar correction as a consequence of scar metastasis and this may present a potential limitation of our retrospective analysis. Moreover, the Netherlands Cancer Institute is a center of tertiary referral and it is not clear how many patients had their mastectomy or BCT scar secondarily excised and examined elsewhere after having had primary treatment in our institute.

Time interval, frequency and site of de novo tumors following initially prophylactic surgery

Following bilateral prophylactic mastectomy, Hartmann et al. and Rebbeck et al. found de novo invasive or non-invasive breast tumors to occur of 1.1 to 1.9 percent of women with a moderate to high risk of such cancers. Most of these
de novo tumors only occur after a median of 6 years (range, 2-25 years) and, more often than not, feature a favorable prognosis.\textsuperscript{5,6} So far, none of the breast cancers observed after prophylactic mastectomy was reported to occur in the mastectomy scar.\textsuperscript{5}

In our study, we did not observe de novo tumor growth in any of our 108 prophylactically operated patients (186 breasts). Still, the time interval between prophylactic mastectomy and scar examination was less than 3 years in 97 of the 108 patients (Table 4) and de novo breast tumors usually present six years after prophylactic mastectomy.\textsuperscript{5,6} Therefore, we can not rule out any cases to still present among our patients.

The benefits of routine histological examination of unsuspected mastectomy scars

In all, early detection of local recurrence after curative breast surgery is of great importance and the question is if routine histological examination of secondarily excised unsuspected mastectomy scars enhances such early detection. To date, only very few local recurrences have reportedly been found in macroscopically unsuspected scars,\textsuperscript{1,4} but it seems accurate to recommend to routinely perform histological examination as such examination may most accurately detect early local recurrence within an unsuspected scar. Still, only a very small, so-called representative part of the scar is being examined in such cases and early malignancy in any other part of the specimen may easily be overlooked. Moreover, additional native breast skin that is often removed during autologous secondary breast reconstruction is usually not examined routinely. As we did not observe any macroscopic or microscopic scar malignancy during long-term follow-up and regardless of primary tumor stage and time lapse since primary diagnosis, we conclude that the routine submission of these scars for histological examination did not benefit the early detection of such malignancy in our patients over the last 10 years. Given the extremely low yield of such submission and the poor natural prognosis of local recurrences per se, the medico-legal consequences of refraining to routinely submit unsuspected scars are presumably non-existing in the Netherlands. The pathologist may very well be the only one to benefit from such examination even though, in the Netherlands, only 50 Euro (or US$ 65) may be charged per scar.

A more secure and less elaborate method of early detection of superficial local recurrences in the mastectomy scar was mentioned in 1995, when Ciatto observed that palpation currently is accepted to be highly sensitive for such
The occurrence of tiny painless nodules is the most common form of presentation of local recurrence and, accordingly, Ciatto advised regular palpation as the screening test of choice for local recurrences and recommended the addition of ultrasonography and aspiration cytology to improve the diagnostic accuracy, only in questionable cases.\textsuperscript{25}

Conclusion

Based on their limited study, Soldin et al.\textsuperscript{7} surmised that histological examination of breast scar at the time of secondary reconstruction provides no oncological benefit for patients in whom comprehensive clinical examination or radiological imaging after BCT had not already detected local recurrence. Because we found no evidence of tumor in any of the 728 scars we, more convincingly, support and extend their conclusion in that routine submitting of clinically unsuspected scars excised at the time of breast reconstruction or scar correction after prophylactic or curative breast surgery did not benefit our patients.

Acknowledgment

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Chapter 8

References

Routine histological examination of mastectomy scars

Leonie A.E. Woerdeman