Early postoperative complications and local relapses after nipple sparing mastectomy and immediate breast reconstruction using silicone implants

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SUMMARY
Purpose: Purpose of this study was to evaluate early complications and risk factors associated with nipple sparing mastectomy and immediate breast reconstruction. Methods: This retrospective study was made using data from 246 breast cancer patients treated at the Oncology Institute of Vojvodina in the period from January 2010 to December 2015. In all patients nipple sparing mastectomy was performed along with primary breast reconstruction. Results: The mean indication for nipple sparing mastectomy was multicentricity of the tumor (114 patients; 46.3%). The majority of surgically treated patients were in stage II of the disease. The total percentage of local relapses after the nipple sparing mastectomy was 1.6% (4 patients). Total percentage of early complications was 15% (37 patients). Median follow-up after nipple sparing mastectomy was 260 weeks (ranging from 417 to 104 weeks). Conclusion: Primary reconstruction of the breasts using heterologous implants is standard surgical procedure for breast cancer that does not lead to increased number of complications, nor to increased percentage of the local recurrence.

KEY WORDS: Nipples; Local relapses; Breast cancer; Postoperative Complications; Mastectomy

INTRODUCTION
Although efficient local control is the most important objective of breast cancer surgery, the long-term aesthetic outcome is also important. Better knowledge of the pathogenesis of breast cancer together with rising interest in improved cosmetic results has led to the consideration of nipple sparing mastectomy (NSM) in breast cancer treatment (1-8). Many predictive factors have to be considered in order to decide whether or not the nipple areola complex (NAC) can be preserved during mastectomy. These factors include the tumor-nipple distance, the size of the tumor and lymphovascular invasion. However, the most important and determining factor is the presence of tumor cells in retro areolar tissue (9-13). The main concerns for the preservation of the nipple areola complex (NAC) are: increased risk of new or recurring cancer in the retained NAC area, missing occult cancer in the nipple and/or areola area and partial as well as complete necrosis of the NAC after surgery. The aim of our study was to determine the rate of early complications and local recurrence in patients undergoing NSM.

MATERIAL AND METHODS
This retrospective study was undertaken using data from 246 breast cancer patients who were treated at the Oncology Institute of Vojvodina from January 2010 to December 2015. NSMs were performed in all patients with the simultaneous heterologous breast reconstruction using silicone breast implants. Histopathological confirmation of the diagnosis was established preoperatively using core biopsy or intraoperative fast frozen analysis of the primary tumor. In 18 patients (6.82%) to whom presence of cancer in subareolar cone tissue was confirmed using intraoperative fast frozen analysis, skin sparing mastectomy was performed with NAC incision and immediate reconstruction. But, those patients were not included the study.

All patients underwent preoperative clinical examination as well as imaging diagnostics - ultrasonography, mammography and magnetic resonance imaging (MRI) mammography. MRI mammography was performed when other methods could not exclude multicentricity of the tumor. Fifty-one patient (20.73%) with locally advanced disease received neoadjuvant chemotherapy. Radiotherapy was not applied in the neoadjuvant form. Thirty patients (12.2%) with previously performed conservative surgery received adjuvant radiotherapy treatment after the first operation. Histopathological examination of fast frozen section of sub-areolar cone tissue was a compulsory part of the NSM procedure. Mastectomy was performed in majority of cases (218 patients; 88.62%) through the curvilinear incision in the upper lateral quadrant, enabling simultaneous access to the armpit. The semicircle incision on the areola edge was used in 28 patients (11.38%) when axillary lymph nodes dissection was not indicated or in patients with previously performed dissections without metastases in the sentinel nodes (SN), and those with in situ carcinoma of the breast (DCIS). For tumors smaller than 3 cm, and in some cases of high grade DCIS, SN biopsy was performed as standard procedure with intraoperative ex tempore analysis of sentinel lymph nodes. All patients had primary breast reconstruction performed using heterologous contoured profile prosthesis (Mentor Contour Profile®, fixed volume implants; Minneapolis, USA). The volumes of the implants (in mL) were 10% - 20% higher compared to excised mammary gland tissue (in grams). The implants where placed into the muscle pocket created from musculus peectoralis major and musculus serratus anterior. Preparation of the space below both muscles was done simultaneously with cutting parts of muscle attachments. After selection of implants and their placement, the muscles were sutured with resorbive stitches and two drains were placed as a part of standard procedure.
All patients received preoperative prophylactic single-dose of broad-spectrum antibiotic (1.5 g of Cefuroxime) one hour before the operation, and the same dose following day. Postoperative radiotherapy was administered to 165 patients (67.1%) and adjuvant chemotherapy, either Cyclophosphamide, doxorubicin, and 5-fluorouracil (CAF) or Docetaxel/Paclitaxel (DC) to 157 patients (53.7%).

Patients were clinically evaluated by surgeon and medical oncologist every three months during the first year, and then every six months during the second year after the surgery. The appointments for further controls were made once a year. Median follow-up of patients after the NSM was 260 weeks (ranging from 104 to 417 weeks).

Statistical analysis
Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS, IBM; Version16). Fischer’s exact test and 2 test were used to compare the data between the groups. Values were considered as statistically significant when p<0.05.

RESULTS
Median patient age was 49 years old (ranging from 26 to 70 years). Majority of the patients were between 45 and 54 years old (107 patients). The main indication for NSM was multicentricity of primary tumor (114 patients; 46.3%). The other indications were the large size of primary tumor (67 patients; 27.2%), extensive DCIS and DCIS with micro invasion (35 patients; 14.23%) and local recurrence after conservative breast surgery (30 patients; 12.2%).

The most common histological type of tumor was ductal carcinoma (137 patients; 55.7%) followed by lobular carcinoma (68 patients; 27.6%). All other histological breast cancers types were present in smaller extent. The prevalence of the disease stages in our study was given in Figure 1.

The total percentage of local relapses after the NSM was 1.6% (4 patients). In two patients local recurrence appeared in the same quadrant (the upper lateral quadrant). In one patient with the primary tumor localized in the central quadrant the recurrence was in parasternal region. In one patient with primary tumor localized in the lower medial quadrant of the breast local relapse was found in the lower lateral quadrant. Skin (lenticular) metastases have occurred in three patients (1.2%), diffuse carcinomatous lymphangiosis in one patient (0.4%) and distant metastases in 11 patients (4.5%).

The total percentage of early postoperative complications was 15% (37 patients). The most common early complication was skin and/or NAC necrosis, which occurred in 17 patients (6.9%) and demanded surgical revision (Table 1).

In one patient with isolated NAC necrosis spontaneous healing occurred after 45 days. Extensive skin flap necrosis required prosthesis explanta-

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number</th>
<th>Percent (%)</th>
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<tbody>
<tr>
<td>Epidermolysis</td>
<td>3</td>
<td>1.20</td>
</tr>
<tr>
<td>Minor infection</td>
<td>4</td>
<td>1.60</td>
</tr>
<tr>
<td>Major infection</td>
<td>5</td>
<td>2.10</td>
</tr>
<tr>
<td>NAC necrosis</td>
<td>2</td>
<td>0.80</td>
</tr>
<tr>
<td>Skin and NAC necrosis</td>
<td>3</td>
<td>1.20</td>
</tr>
<tr>
<td>Major skin necrosis</td>
<td>4</td>
<td>1.60</td>
</tr>
<tr>
<td>Minor skin necrosis</td>
<td>8</td>
<td>3.30</td>
</tr>
<tr>
<td>Prolonged seroma formation</td>
<td>6</td>
<td>2.40</td>
</tr>
<tr>
<td>Hematoma</td>
<td>2</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>37</td>
<td>15.00</td>
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Table 1. Early complications
non-smokers and also between patients who received neoadjuvant polychemotherapy or radiotherapy and those who did not receive any therapy (Table 2).

**DISCUSSION**

In the present study, local recurrence appeared in very low percentage (1.6% of the total number of patients), compared to the results found in literature. Rusby and colleagues published their work in 2010 with less than 5% of local recurrence after the NSM (8). In general, our results show a great similarity with the results published in literature (6, 8, 14-16) where indications for NSM were that tumors were larger than 4.5 cm in size and at least 2.5 cm distant from the edge of the areola. In recent results published by Harness and associates who performed 43 NSMs from November 2004 to September 2009 after average follow-up of 18.5 months the percentage of local recurrences was 2.3% (1 patient) (12). However, the incidences of local relapse in the previous studies have varied from 4% to 20%, depending on the use of post mastectomy radiotherapy (14-18).

Our incidence rate of early postoperative complications is in a compliance with available data in literature (20 - 22). A slightly larger percentage of skin flap and NAC necrosis in the present study is most likely result of breast reconstruction with fixed volume implants and the fact that operations were performed by general surgeons with different times of experience in oncoplastic breast surgery. Also, previous studies have observed incidence rates of 8% for complete necrosis and 16% for partial necrosis of the nipples in association with breast reconstruction using fixed volume implants (20). In the present study, the choice of the incision did not have influence on the rate of complications (23). Smoking was associated with an increased risk of complications. Therefore, we do not recommend smoking in the preoperative and early postoperative period. However, neoadjuvant chemotherapy increased the number of serious early postoperative complications (23-25). The more advanced disease stage in these patients indicates aggressive adjuvant therapy, i.e. chemotherapy or postoperative irradiation. NSM is a complicated surgical procedure compared with standard mastectomy and is associated with a higher risk of complications. The significant risk of postoperative complications in patients with advanced stages of the disease may not only completely compromise the primary reconstruction, but also lead to unwanted delays in chemotherapy or radiotherapy.

**CONCLUSION**

NSM with immediate breast reconstruction is a feasible surgical procedure in carefully selected breast cancer patients who require mastectomy. The procedure is associated with a low risk of local recurrences and also with a relatively low risk of early postoperative complications. However, neoadjuvant polychemotherapy was associated with an increased risk of complications and the procedure seems questionable in patients with locally advanced breast cancer requiring neoadjuvant polychemotherapy. The risk of postoperative complications may lead to delay in further local and systemic adjuvant treatments in these patients.

**Declaration of Interests**

Authors declare no conflicts of interest

**REFERENCES**