Results, morbidity, and quality of life of melanoma patients undergoing sentinel lymph node staging
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Morbidity after inguinal sentinel lymph node biopsy and completion lymph node dissection in patients with cutaneous melanoma

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Robert J. van Ginkel
Harald J. Hoekstra

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Background: Aim of the study was to assess the short-term and long-term morbidity after inguinal sentinel lymph node biopsy (SLNB) with or without completion groin dissection (GD) in patients with cutaneous melanoma.

Methods: Between 1995 and 2003, 127 inguinal SLNBs were performed for cutaneous melanoma. Sixty-six patients, median age 50 (18-77) years, met the inclusion criteria and were studied. Short-term complications were analysed retrospectively, while long-term complications were evaluated using volume measurement and range of motion measurement of the lower extremities.

Results: Fifty-two patients underwent SLNB alone (SLNB group) and 14 patients underwent completion groin dissection after tumour-positive SLNB (SLNB/GD group). Morbidity after SLNB alone: wound infections (n=1), seroma (n=1), postoperative bleeding (n=1), erysipelas (n=1), and slight lymphedema 6% (n=3). Morbidity after SLNB/GD: wound infections (n=4), seroma (n=1), wound necrosis (n=1), postoperative bleeding (n=1), and slight lymphedema 64% (n=9). There were differences between the two groups in the total number of short-term complications (p<0.001), volume difference (p<0.001), flexion (p=0.009), and abduction (p=0.011) limitation of the hip joint.

Conclusion: Inguinal SLNB is accompanied with a low complication rate. However, SLNB followed by groin dissection is associated with an increased risk of wound infection and slight lymphedema.
INTRODUCTION

Since Morton et al. described the concept of sentinel lymph node biopsy (SLNB) for melanoma, it has been used to achieve more accurate staging in patients with clinical stage I and II melanoma and has now become the standard of care in staging.1 It has indeed proved possible to stage melanoma patients more accurately using SLNB.2-8 When metastases are found in the sentinel lymph node, completion lymph node dissection is indicated. Whether or not this lymph node dissection will ultimately be of influence in improving patient survival is currently studied.9 In the future, the results of this multicenter selective lymphadenectomy trial (MSLT-I) will definitively settle the issue.

The SLNB technique seems to be a minimally invasive surgical procedure; we recently reported low complication rates in axillary SLNB.10 In order to gain insight into the short-term and long-term morbidity of inguinal SLNB with or without completion inguinal lymph node dissection, we reviewed inguinal SLNB in patients with cutaneous melanoma.

PATIENTS AND METHODS

Patient population

Patients who had undergone an inguinal SLNB staging procedure for cutaneous melanoma (> 1.0 mm) at the University Medical Center Groningen in the period 1995-2003 were included. In cases with a positive SLNB, completion superficial and deep lymph node dissections were performed. Since 2002, patients with an immuno-histochemically positive SLN have been undergoing superficial groin lymphadenectomy alone, unless other lymph node metastases were diagnosed in the resected specimen, as this forms an indication for deep lymph node dissection (iliac and obturator lymph nodes).

Patients were excluded on the basis of the following characteristics: bilateral SLNB, undergoing follow-up elsewhere, pre-existing functional limitations and/or previous operations on the extremity concerned, pre-existing volume difference between the two extremities, severe comorbidity such as dementia, disseminated disease or patients receiving palliative care. Patients were also excluded if they were receiving treatment for local or loco-regional recurrence at the time of the study.

In the period 1995-2003, 277 patients underwent SLNB for cutaneous melanoma. In 127 of these patients, inguinal SLNB had been performed. On the basis of the above-described criteria, 29 patients had to be excluded from the study, 25 patients had died (21 patients died of disease related death). The remaining 73 patients were eligible for the retrospective study and informed consent was ultimately obtained from 66. The clinical and pathological data of these 66 melanoma patients are summarized in Table 1.

In this study, we evaluated morbidity after inguinal SLNB alone (SLNB) and after inguinal SLNB with completion inguinal lymphadenectomy, groin dissection (SLNB/GD). Short-
term morbidity was measured as the number of postoperative complications. Long-term morbidity was analysed in the form of lymphedema and range of motion restrictions of the affected extremities.

**SLNB technique**

The SLNB procedure, re-excision of the scar and possible completion lymph node dissection were conducted on an in-patient basis. The procedure was performed by a combination of lymphoscintigraphy, patent blue dye and a gamma ray detection. The technique has been described extensively in a previous study.\(^2\) SLNB was followed by re-excision of the scar of the primary melanoma with a margin of 1 or 2 cm, depending on the thickness of the melanoma \((\leq 2 \text{ mm}, 1 \text{ cm}; > 2 \text{ mm}, 2 \text{ cm margin})\). The excised lymph nodes were sent for routine histological examination with haematoxylin-eosin staining (HE staining) and when HE staining was negative, specific immuno-histochemical staining (IHC) was conducted for the protein S100 and melanoma-associated antigen HMB45. If histological examination showed that the sentinel node contained metastatic melanoma, the patient was considered for completion groin dissection.

**Groin dissection**

In the case of a tumour-positive SLNB in the groin, superficial and deep lymphadenectomy were performed, in which the femoro-inguinal lymph nodes and the lymph nodes along the iliac artery and vein were excised, together with the obturator lymph nodes. After superficial lymphadenectomy, the sartorius muscle was freed from its attachment to the anterior superior iliac spine, moved in a

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**TABLE I** Clinical and pathological characteristics (n=66)

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>15 (23)</td>
</tr>
<tr>
<td>Women</td>
<td>51 (77)</td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>50</td>
</tr>
<tr>
<td>Range</td>
<td>18-77</td>
</tr>
<tr>
<td><strong>Localization of the primary melanoma</strong></td>
<td></td>
</tr>
<tr>
<td>Upper leg</td>
<td>26 (39)</td>
</tr>
<tr>
<td>Lower leg</td>
<td>25 (38)</td>
</tr>
<tr>
<td>Feet</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Trunk</td>
<td>7 (11)</td>
</tr>
<tr>
<td><strong>Breslow thickness (mm)</strong></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>1.85</td>
</tr>
<tr>
<td>Range</td>
<td>1.0-11.0</td>
</tr>
<tr>
<td>1.0-2.0</td>
<td>41 (62)</td>
</tr>
<tr>
<td>2.01-4.0</td>
<td>19 (29)</td>
</tr>
<tr>
<td>&gt;4.0</td>
<td>6 (9)</td>
</tr>
<tr>
<td><strong>Clark level</strong></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>17 (26)</td>
</tr>
<tr>
<td>IV</td>
<td>47 (71)</td>
</tr>
<tr>
<td>V</td>
<td>2 (3)</td>
</tr>
<tr>
<td><strong>Ulceration</strong></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>22 (33)</td>
</tr>
<tr>
<td>Absent</td>
<td>43 (65)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (2)</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td></td>
</tr>
<tr>
<td>Superficial spreading</td>
<td>39 (59)</td>
</tr>
<tr>
<td>Nodular</td>
<td>21 (32)</td>
</tr>
<tr>
<td>Acrolentiginous</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (6)</td>
</tr>
<tr>
<td><strong>Localization SLNB</strong>*</td>
<td></td>
</tr>
<tr>
<td>Right groin</td>
<td>40 (61)</td>
</tr>
<tr>
<td>Left groin</td>
<td>26 (39)</td>
</tr>
<tr>
<td><strong>Tumour status SLNB</strong></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>14 (21)</td>
</tr>
<tr>
<td>Negative</td>
<td>52 (79)</td>
</tr>
</tbody>
</table>

*NS p = 0.085
medial direction and fixed to the ligament of Poupart. This technique has been described extensively in the past by Baas et al.\textsuperscript{11} Since 2002, patients with HE stain negative and IHC stain positive have been undergoing superficial lymphadenectomy alone; there is only an indication for iliac lymphadenectomy if other positive lymph nodes are found in the excised tissue.

All the patients who underwent lymphadenectomy had 10 days bed-rest with the leg elevated. The vacuum drains are left in situ at least 1 week. All the patients and were prescribed tailor-made support-stockings for a period of 6 months. The patients were also offered an extensive physiotherapy exercise programme. During immobilisation, the patients received low-weight heparin and no perioperative antibiotic prophylaxis.

Complications and lymphedema

In all patients, a note was made of postoperative complications that occurred within 30 days. Between January and July 2003, the patients were invited for volume measurements and a function evaluation of both legs (hips and knees). The volume of the legs was determined with the aid of an adapted version of the water-displacement technique described by Kissin et al.\textsuperscript{12} Each leg was slowly immersed up to the inguinal groove in a large, transparent water-filled cylinder. Then the leg was removed from the cylinder and the volume of displacement was refilled exactly and recorded as the volume of the leg. Both the affected and the unaffected legs were measured. Lymphedema was defined as the presence of 6.5\% or more difference in volume to the advantage of the affected leg. The cut-off point of 6.5\% was chosen on the basis of earlier literature data. Edema was then classified according to Baas et al.\textsuperscript{11} into four categories: normal (volume difference 0-6.5\%: no edema), slight edema (volume difference 6.5-20\%), moderate edema (20-40\%), and severe edema (>40\%).

Functional evaluation

The functional evaluation comprised flexion, extension, exorotation, endorotation and abduction of the hip joint and flexion and extension of the knee joint. Range of motion was measured in degrees with an extended goniometer while the patient was in the supine position. Both the affected and unaffected legs were evaluated. Clinically relevant functional limitation was defined as a difference in range of motion of 20 degrees or more compared to the contralateral joint.\textsuperscript{13}

Statistical analysis

Statistical differences were analysed with the t-test and the Chi-square test. Differences with a p value of < 0.05 were considered to be significant. All the analyses were performed with the SPSS software version 11.0 (SPSS Inc., Chicago, Illinois, USA).
RESULTS

SLNB was conducted in 15 men and 51 women. Median age at the time of diagnosis was 50 (18-77) years. There was a difference in average age between the two groups: 46 years for SLNB alone versus 57 years for SLNB/GD (p=0.009). Median follow-up at the time of the study was 51 (4-94) months; duration of follow-up did not differ between the two groups. There were no differences between the two groups for presence or absence of ulceration and Breslow thickness. Although SLNB can be performed on a day treatment basis, all the patients in this study had been hospitalized. Median duration of hospitalisation in patients with inguinal SLNB, combined with or without local re-excision and possible split skin grafting, was 5 (2-14) days versus 15 (9-22) days in the patients with SLNB/GD. Primary closure of the melanoma excision wound was possible in 48 patients, while the remaining 18 patients required a free split skin graft. Most of these patients had melanomas on their lower legs (11) or feet (6).

The median number of excised SLNBs was two (1-6). In 14 out of the 66 patients (21%), melanoma metastases were detected in the sentinel lymph node, which formed an indication for completion lymphadenectomy. Eleven patients underwent superficial and deep groin dissection (inguinal lymphadenectomy and para-iliac lymphadenectomy); one patient had one additional positive lymph node and one patient had two additional positive lymph nodes in the resection tissue. Three patients underwent superficial lymphadenectomy alone. The pathology reports described a median of nine (6-17) lymph nodes after completion lymphadenectomy. The median interval between SLNB and lymphadenectomy was 32 (14-56) days. The remaining 52 patients underwent SLNB alone.

Complications

None of the patients had died as a result of the surgical intervention. Three patients had developed complications after inguinal SLNB: one wound infection (treated with antibiotics), one postoperative haemorrhage (treated conservatively) and one seroma (treated with aspiration).

After SLNB/GD, four patients had developed wound infection that was treated with antibiotics. In two patients, additional surgical intervention was necessary in the form of incision and drainage.

One patient had developed seroma that was treated with aspiration. Wound necrosis occurred in one patient with an uncomplicated secondarily healing. In one patient with postoperative haemorrhage surgical reintervention was necessary.

After SLNB alone, three complications (6%) occurred versus seven complications after SLNB/GD (50%, p<0.001). The complications are summarized in Table 2. In the long-term, two patients developed erysipelas: one after SLNB alone and one after SLNB/GD.
In the total group who underwent inguinal SLNB, no volume difference was found between the patients with a primary melanoma on the trunk and those with a primary melanoma on the leg (p=0.4). Volume difference was found between primary closure of the excision wound and closure with a free split skin graft (p=0.044). In 11 patients (21%) with SLNB alone and in seven patients (50%) with SLNB/GD, the wound was closed with a free split skin graft (p=0.031). Only one patient in the SLNB alone group with a free split skin graft developed lymphedema (1/11 versus 2/41; p=0.6). Six patients in the SLNB/GD group with free split skin grafts developed lymphedema (6/7 versus 3/7; p=0.09).

There were no differences regarding body mass index between the SLNB group and the SLNB/GD group. There was no positive correlation between the number of excised SLNs and volume difference in the SLNB alone group.

Slight lymphedema was found in three patients with SLNB alone and in nine patients with SLNB/GD. In the SLNB/GD group, there was a trend of increased incidence of lymphedema in the patients with postoperative wound infection. (p=0.078).

There were no cases of moderate or severe lymphedema in either of the groups. A significant volume difference was found between the two groups (p<0.001). Figure 1 shows the volumetric data on the group with SLNB alone and the group with SLNB/GD.

**Functional outcome**

The average difference in degrees was significantly higher in the SLNB/GD group for flexion of the hip (p=0.009) and abduction of the hip (p=0.011). No functional limitations were observed in the SLNB alone group, whereas two patients had functional limitations in the SLNB/GD group: one had 25 degrees of hip extension limitation and the other patient had 30 degrees of knee flexion limitation.
Recently published studies also showed morbidity after SLNB in patients with melanoma.\textsuperscript{10,14} Wasserberg et al. found an overall wound complication rate of 13.6\% which was significantly associated with groin SLNB. When metastatic disease was found in the sentinel lymph node(s), this formed an indication for groin dissection, an operation that is often associated with complications. The high morbidity after groin dissection was also confirmed in this study, while the wound infection rate of 29\% was comparable with previous studies of Tonouchi et al.\textsuperscript{15} (24\%) and Beitsch and Balch\textsuperscript{16} (29\%). However, there was a considerable difference in wound infections compared to an earlier study at our centre by Baas et al.\textsuperscript{11}: 29\% versus 9\%. The groin dissection procedures were conducted in the same surgical-technical manner as in the past and there was no difference in complications between the various surgeons (p=0.109). Therefore, the high infection rate can only be explained by the combination of three surgical interventions within a few weeks: local excision of melanoma, SLNB and groin dissection.

Although the patients in the SLNB group were significantly younger, there was a much higher risk (<0.001) of volume difference in the SLNB/GD group than in the SLNB alone group. It was not so much the difference in age, but the completion groin dissection that explained the volume difference.

We found also a volume difference between primary closure of the excision wound and closure with a free split skin graft. However, in 11 patients (21\%) with SLNB alone and in seven patients (50\%) with SLNB/GD, the wound was closed with a free split skin graft.
Therefore, it is more likely that the volume difference was caused by the groin
dissection.

Until now, only two prospective studies have been published on complications after SLNB in melanoma patients. Wrightson et al. found complication rates of 8.1% after inguinal SLNB and 51.2% after SLNB/GD.\textsuperscript{17} Morton et al. reported complication rates of 10.1% after SLNB alone and 37.2% after SLNB followed by completion lymph node dissection in the multicenter selective lymphadenectomy trial (MSLT-I).\textsuperscript{18} These findings are comparable with the present study. Wrightson et al. also reported rates of lymphedema (SLNB alone: 1.5% and SLNB/GD: 31.5%).\textsuperscript{17} However, in contrast with the present study, lymphedema was not measured objectively in the study by Wrightson et al. and the patients were not classified according to severity. This means that the reliability of their rates can be questioned. In the present study, the incidence of lymphedema after SLNB/GD was 64%. This is a far higher percentage of lymphedema than after groin dissection alone. However, in these reports by other authors, the degree of lymphedema was only defined by Baas et al.\textsuperscript{11} In our own series, the percentage of patients with lymphedema was high, but the degree of edema could be classified as slight. The combination of three successive surgical interventions and wound infections contributed to the increased risk of the development of slight lymphedema.

After SLNB/GD, functional differences were found: limitations in abduction and flexion of the hip, as a result of the operation with transpositioning of the sartorius muscle. The presence of lymphedema hardly played any role in these functional limitations.

In summary, the short-term and long-term complications after inguinal SLNB were minimal. The combination of SLNB/GD involved an increased risk of short-term and long-term morbidity, such as wound infections and slight lymphedema of the affected extremity. This increased risk of wound infections and lymphedema was probably caused by damage to the lymph vessels during two or three successive surgical interventions in the groin region. In future, prophylactic antibiotic treatment might be indicated when groin dissection is performed after positive SLNB, to prevent wound infections.
REFERENCES


4. Statius Muller MG, van Leeuwen PA, de Lange-De Klerk ES et al. The sentinel lymph node status is an important factor for predicting clinical outcome in patients with Stage I or II cutaneous melanoma. Cancer 2001; 91: 2401-8.


