Minimally Invasive Inguinal Lymph Node Dissection (MILND) for Melanoma: Experience from Two Academic Centers

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ABSTRACT

Background and Aim. Regional lymph nodes are the most frequent site of spread of metastatic melanoma. Operative intervention remains the only potential for cure, but the reported morbidity rate associated with inguinal lymphadenectomy is approximately 50%. Minimally invasive lymph node dissection (MILND) is an alternative approach to traditional, open inguinal lymph node dissection (OILND). The aim of this study is to evaluate our early experience with MILND and compare this with our OILND experience.

Methods. We conducted a prospective study of 13 MILND cases performed for melanoma from 2010 to 2012 at two tertiary academic centers. We compared our outcomes with retrospective data collected on 28 OILND cases performed at the same institutions, by the same surgeons, between 2002 and 2011. Patient characteristics, operative outcomes, and 30-day morbidity were evaluated.

Results. Patient characteristics were similar in the two cohorts with no statistically significant differences in patient age, gender, body mass index, or smoking status. MILND required longer operative time (245 vs 138 min, \(p = 0.0003\)). The wound dehiscence rate (0 vs 14%, \(p = 0.07\)), hospital readmission rate (7 vs 21%, \(p = 0.25\)), and hospital length of stay (1 vs 2 days, \(p = 0.01\)) were all lower in the MILND group. The lymph node count was significantly higher (11 vs 8, \(p = 0.03\)) for MILND compared with OILND.

Conclusions. MILND for melanoma is a novel alternative to OILND, and our preliminary data suggest that MILND provides an equivalent lymphadenectomy while minimizing the severity of postoperative complications. Further research will need to be conducted to determine if the oncologic outcomes are similar.

Melanoma is the leading cause of skin cancer death, and 9,000 people are estimated to die from melanoma in the USA in 2012.1 Regional lymph nodes are a common site of metastasis, and lymphadenectomy is recommended for patients with regional nodal metastases.2 Unfortunately, the morbidity associated with traditional, open inguinal lymph node dissection (OILND) is quite high, with rates of approximately 50%.3-9 The most common complications reported in the literature include wound infection, wound dehiscence, seroma, chronic lymphedema, and venous thromboembolic events (VTE). Wound complications are common and can be severe, often requiring hospital admission and extensive wound care, which can lead to delay in adjuvant therapy (Fig. 1).

Minimally invasiveinguinal lymph node dissection (MILND) is a novel alternative to the conventional open approach. This technique has been described for penile and vulvar cancer.10-14 Currently, only one center in the USA has reported their experience of MILND.15,16 The aim of this study is to compare short-term outcomes between MILND and OILND among patients with metastatic melanoma from two institutions.

METHODS

We conducted a multicenter study to compare outcomes of MILND versus OILND from 2002 to 2012 at two tertiary academic centers. We prospectively collected data on all MILND cases performed from 2010 to 2012. A total of 15 MILND cases were performed during this time period. Two MILNDs performed for nonmelanoma malignancies were
excluded, leaving 13 cases which make up the study cohort. The MILND group was compared with retrospective data collected from OILND cases performed for melanoma at the same institutions from 2002 to 2011. All MILND and OILND cases were performed by the same two surgeons (T.M.T. and J.W.J.). All patients undergoing concomitant deep pelvic lymphadenectomy or isolated limb perfusion were excluded. Patients with positive sentinel lymph node biopsy or palpable lymphadenopathy were included in both cohorts. Institutional Review Board (IRB) approval was obtained at each center.

Surgical Technique

The femoral triangle was used to delineate our anatomic boundaries including the inguinal ligament superiorly, adductor longus muscle medially, sartorius muscle laterally, and femoral vessels deep. These anatomic landmarks were used for both the OILND and MILND procedures. A three-port technique was employed in which a 12-mm balloon port was placed 3 cm distal to the apex of the femoral triangle and two additional ports at the medial and lateral border of the femoral triangle. A subcutaneous dissection plane was first developed with either a balloon dissector or blunt finger dissection in combination with initial insufflation pressure of 25 mm Hg for the first 10 min. The operative space was then maintained with CO₂ insufflation pressure of 15 mm Hg. The anterior tissue flap was created using an ultrasonic dissector superficial to Scarpa’s fascia. The dissection was continued proximal to the inguinal ligament. The fascia overlying the adductor longus and sartorius was scored and included en bloc with the lymphadenectomy specimen. After defining all borders the saphenous vein was ligated distally. The lymph node packet was retracted cephalad to allow dissection along the adventitia of the femoral vessels. The saphenous vein was then divided with an endovascular stapler proximally at the saphenofemoral junction. The specimen was removed en bloc in a retrieval bag or utilizing a wound protector. A closed suction drain was placed through one of the trocar sites (Fig. 2). Coverage of the femoral vessels with a sartorius muscle flap and excision of the sentinel lymph node biopsy site was not performed in any of the MILND cases. All patients received perioperative antibiotics, and chemical VTE prophylaxis was administered at the discretion of the operating surgeon.

Outcomes

Operative time, estimated blood loss, number of lymph nodes retrieved, drain duration, and hospital length of stay

FIG. 1 Wound dehiscence seen after open lymphadenectomy

FIG. 2 Postoperative appearance after MILND
(LOS) were recorded. Adverse events as defined by the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4 were recorded. These events included 30-day wound infection, 30-day wound dehiscence, incidence of VTE and seroma. Per the Centers for Disease Control and Prevention definition of surgical wound infection, cellulitis by itself is not considered a wound infection and was not included in our definition when clinically diagnosed and treated with complete resolution by a single course of oral outpatient antibiotics. As a result, we included only CTCAE v4.0 grade III or higher wound infections. Any incision cephalad to the apex of the femoral triangle greater than 30 mm was considered a conversion.

Statistical Analysis

Descriptive statistics are reported as median and interquartile range or number and frequency. Continuous variables such as body mass index (BMI), total operative time, estimated blood loss (EBL), and hospital LOS were compared between the two cohorts using a Student’s t test. For the variable, number of lymph nodes, a significant outlier was detected using the maximum normed residual test (Grubb’s test). A nonparametric Wilcoxon test and exclusion of the outlier and Student’s t test obtained the same p value. A chi-square test was used for binomial variables. An odds ratio was used to estimate the effect size. All calculated p values were two-sided, and p values less than 0.05 were considered statistically significant. Analysis was performed using JMP version 10 software (Cary, NC).

RESULTS

A total of 28 OILND (T.M.T. 17, J.W.J. 11) and 13 MILND (T.M.T. 6, J.W.J. 7) cases performed from 2002 and 2012 were included in our analysis. One OILND and one MILND were performed for melanoma of the anus; the remainder were performed for cutaneous melanoma.

Age, sex, BMI, location of primary tumor, and smoking status of the patients did not differ between the treatment groups (Table 1). In the MILND cohort, one case was converted secondary to inability to complete the proximal dissection as a result of placement of the trocars too distally. Operative time was significantly longer [245 min, interquartile range (IQR) 205–366 min] for MILND as compared with OILND (138 min, IQR 102–179 min, p = 0.0003). A consistent reduction in operative time with successive cases was not yet evident with this early experience. Median blood loss was similar in the two cohorts (MILND 30 cc, IQR 12–150 cc vs OILND 25 cc, IQR 20–30 cc, p = 0.07), and no blood transfusions were administered. MILND was associated with a significant reduction in median LOS (1 day, IQR 1–1.5 days vs 2 days, IQR 1–2 days, p = 0.01) (Table 2).

Median follow-up for MILND cases (5 months) was substantially less than for OILND (13 months); therefore, the incidence of lymphedema and disease-free and overall survival could not be compared. As an indirect measure of oncologic adequacy, we evaluated the total number of lymph nodes pathologically examined. The total median number of lymph nodes pathologically identified in the lymphadenectomy specimen was significantly higher in MILND cases (11 nodes, IQR 9–15) than in OILND cases (8 nodes, IQR 6–12, p = 0.03). When the number of SLNs from the same basin were included in the total lymph node count, the total lymph node count remained higher (MILND n = 13, IQR 10–16 vs OILND n = 10, IQR 7–13, p = 0.04) (Table 2).

The incidence of infection was reduced fourfold in the MILND cohort (n = 1, 8 %) compared with the OILND cohort (n = 8, 29 %, p = 0.13). The infection that did occur in the MILND cohort was treated with outpatient oral antibiotics. In contrast, five of the eight (62 %) infections in the OILND cases required hospital readmission and intravenous antibiotics. The incidence of wound dehiscence was greater in the OILND group (n = 4, 14 %) compared with the MILND group (n = 0, 0 %); however, this difference did not reach statistical significance (p = 0.07). The incidence of hospital readmission was threefold greater in the OILND (n = 6, 21 %) cohort than in the MILND (n = 1, 7 %) cohort, but this difference was not statistically significant (p = 0.25). None of the MILND patients developed a VTE, while two patients in the OILND group developed a postoperative VTE (p = 0.32). Despite the less invasive technique, the drain duration (MILND 28 days, IQR 18–45 days vs OILND 24 days, IQR 19–34 days, p = 0.25) and postoperative seroma rates (MILND n = 5, 38 % vs OILND n = 6, 21 %, p = 0.26) did not differ between the MILND and OILND groups (Table 3).

DISCUSSION

Inguinal lymphadenectomy for metastatic melanoma has a high rate of morbidity despite numerous strategies and surgical techniques developed to reduce the incidence and severity of wound complications. Here we report the first multi-institutional series of MILND. The early results from this study are promising and indicate that MILND may be a safe, effective alternative to OILND for treatment of melanoma metastatic to theinguinal basin. In our initial experience with 13 patients, we have demonstrated a lower
The major advantage of MILND compared with OILND is the elimination of a large groin incision. By decreasing the length of incision in the groin, we may potentially reduce the impact that postoperative wound infections can have on a patient’s quality of life. Although the rates of wound infection were not statistically different between the two cohorts, the severity and clinical importance of these infections were substantially different between the MILND and OILND procedure. Only one patient required hospital readmission for a seroma, and no cases of wound dehiscence were reported in the MILND group. In the OILND group a 21 % readmission and a 14 % wound dehiscence rate were observed. Traditionally, wound infection and dehiscence have been a significant cause of morbidity, cost, and decreased quality of life following OILND. The rate of overall complications after traditional open lymphadenectomy is approximately 50 %.3–9 Data collected from prospective studies suggest that the rate may be even higher.7–9 Chang et al. reported a 77.4 % 30-day wound complication rate in 53 melanoma patients enrolled into two prospective clinical trials from 2005 to 2008. Wound infection was the most common complication (54.7 %), followed by wound dehiscence (53.8 %) and seroma (28.3 %). In this study, 56.6 % (n = 30) patients had deep iliac/obturator node dissection in addition to OILND; however, on multivariate analysis, pelvic dissection was not associated with an increased risk of complications [odds ratio (OR) = 0.5; 95 % confidence interval (CI) 0.1, 2.8].9 These findings are further supported by two other prospective studies reporting wound complication rates of 64 and 71 % in patients undergoing OILND for melanoma.7,8 The origin of MILND began in the setting of gynecologic and urologic cancers. Mathevet et al. in France first reported on their technique of gasless endoscopic inguinal lymph node dissection for patients with vulvar and

TABLE 1 Comparison of demographic and clinical characteristics between the OILND and MILND cohorts

<table>
<thead>
<tr>
<th></th>
<th>OILND (n = 28)</th>
<th>MILND (n = 13)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)a</td>
<td>53 (43–67)</td>
<td>53 (48–62)</td>
<td>0.74</td>
</tr>
<tr>
<td>Male</td>
<td>10 (36 %)</td>
<td>6 (46 %)</td>
<td>0.52</td>
</tr>
<tr>
<td>BMI (kg/m²)a</td>
<td>25 (22–31)</td>
<td>29 (25–35)</td>
<td>0.06</td>
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<tr>
<td>Current smoker</td>
<td>3 (11 %)</td>
<td>0</td>
<td>0.21</td>
</tr>
<tr>
<td>Breslow depth (cm)a</td>
<td>2.3 (1.58–4.05)</td>
<td>2.5 (1.45–2.95)</td>
<td>0.34</td>
</tr>
<tr>
<td>Ulceration</td>
<td>8 (29 %)</td>
<td>2 (15 %)</td>
<td>0.33</td>
</tr>
<tr>
<td>Macroscopic lymph node metastasis</td>
<td>10 (36 %)</td>
<td>2 (15 %)</td>
<td>0.18</td>
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</tbody>
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OILND open inguinal lymph node dissection, MILND minimally invasive lymph node dissection, BMI body mass index

a Values reported as median (interquartile range)

TABLE 2 Comparison of surgical endpoints and oncologic adequacy of OILND and MILND

<table>
<thead>
<tr>
<th></th>
<th>OILND (n = 28)</th>
<th>MILND (n = 13)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time (min)</td>
<td>138 (102–179)</td>
<td>245 (205–366)</td>
<td>0.0003*</td>
</tr>
<tr>
<td>Estimated blood loss (cc)</td>
<td>25 (20–30)</td>
<td>30 (12–150)</td>
<td>0.07</td>
</tr>
<tr>
<td>Number of LN in inguinal specimen</td>
<td>8 (6–12)</td>
<td>11 (9–15)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Total number of inguinal LN + SLN</td>
<td>10 (7–13)</td>
<td>13 (10–16)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Length of stay</td>
<td>2 (1–2) days</td>
<td>1 (1–1.5) days</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

All values reported as median (interquartile range)

OILND open inguinal lymph node dissection, MILND minimally invasive lymph node dissection, LN lymph node, SLN sentinel lymph node

*Statistically significant

incidence of surgical-site infection and wound dehiscence, though this did not reach statistical significance. The minimally invasive technique also resulted in a significant reduction in hospital LOS from 2 days after the open technique to 1 day. Given our short follow-up, we are unable to assess the oncologic adequacy of the operation; however, it appears promising as we have demonstrated a significantly higher lymph node yield at the time of surgery with the MILND approach. Although operative time was significantly longer in the MILND group, this observation likely reflects a technical learning curve and would be expected to improve with continued experience. A multi-institutional educational study analyzing the learning curve of the MILND procedure is currently underway (NCT01500304).
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vaginal carcinoma. Tobias-Machado et al. adapted these techniques to develop their technique called video endoscopic inguinal lymphadenectomy (VEIL), which they used for inguinal lymphadenectomy in patients with penile cancer. They demonstrated the feasibility of this technique in seven patients and have published additional data on outcomes in 20 VEIL procedures compared with ten traditional open procedures. In their series, ten patients had VEIL in one limb and the open procedure in the contralateral limb, and five patients had bilateral VEIL procedures. The authors found that the VEIL procedure resulted in a significant reduction in overall complication rate (VEIL 20 %, open 70 %, \( p = 0.01 \)) with equivalent average lymph node retrieval (VEIL 10.8, open 9.7, \( p = 0.40 \)). The wound complications experienced in the VEIL group included a small area of skin necrosis in one patient, lymphatic complications in two patients, and a local hematoma that resolved spontaneously in one patient. Sotelo et al. reported on their outcomes after 14 procedures performed in eight patients with penile cancer. They observed complications in only three patients, all of whom developed a lymphocele. The average lymph node count reported in that study was nine lymph nodes.

Use of MILND in the setting of melanoma is less well studied. Delman et al. published their technical feasibility study, reporting on their first five cases of patients with inguinal metastases from melanoma. In that series, two of the five patients developed cellulitis but there were no cases of wound dehiscence or lymphatic complications. They later noted that this postoperative erythema may not be cellulitis, but simply postoperative changes from the procedure and have become less inclined to treat with antibiotics for erythema alone. The mean operative time was 180 min (range 142–223 min), and the authors noted that they experienced a reduction in operative time with experience. Delman et al. published another series that included 45 procedures performed in patients with inguinal metastases from various malignancies (23 penile or scrotal cancer, 2 neuroendocrine carcinoma of the anus, 2 extramammary Paget disease, and 18 melanoma). The authors reported complications in eight patients (18 %) with six patients developing cellulitis, one seroma, and one focal skin necrosis. Only two patients required readmission for intravenous antibiotics, and no patients experienced wound dehiscence. The oncologic adequacy of this technique was also promising, with median lymph node retrieval of 11, which is similar to the lymph node count reported in our study.

These data, in combination with our results, demonstrate the feasibility of MILND for melanoma. We acknowledge the limitations of this study, most importantly, the small number of patients in both the OILND and MILND cohort. Therefore, these results should be interpreted with caution and the understanding that further research is needed to determine the oncologic adequacy and morbidity of MILND compared with OILND. Additional limitations include the retrospective nature of the OILND data collection, and the short-term follow-up available for the MILND cohort. Minor differences in surgical technique between the two academic centers may exist despite standardization of our methods.

Though our early results are promising, the long-term outcomes remain unknown. We are currently leading a phase I/II trial in which we are training 16 surgeons from 13 different institutions across the nation in MILND. Our goal is to determine the safety and feasibility of MILND in a multi-institutional, prospective fashion (NCT01500304). Continued surveillance with larger series and longer follow-up is required before the oncologic adequacy of MILND is known.

In conclusion, although the number of patients undergoing MILND in this study is only 13, the early outcomes reported in this series and by Delman et al. demonstrate that a minimally invasive approach to the inguinal basin may be a safe and effective alternative to OILND. If further reports support our findings, a prospective randomized controlled trial may ultimately be necessary to demonstrate the oncologic noninferiority of MILND compared with OILND.

REFERENCES


