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Factors predictive of pelvic lymph node involvement and outcomes in melanoma patients with metastatic sentinel lymph node of the groin: A multicentre study

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Abstract

Introduction: The optimal extent of the groin lymph node (LN) dissection for melanoma patients with positive sentinel LN biopsy is still debated and no agreement exist on dissection of pelvic LN. This study aimed at investigating predictors of pelvic LN metastasis and prognostic significance of having metastasis in the pelvic LNs.
Methods: Clinicopathologic data of 740 patients with positive groin sentinel LN who underwent ilioinguinal completion LN dissection at four Italian centre were analysed. Multivariable logistic and Cox regression analysis was used to identify independent predictors of pelvic LN metastasis and to adjust prognostic significance of pelvic LN metastasis.
Results: More than a quarter (26%) of patients had positive non-SLNs after inguinal and pelvic lymphadenectomy, which were located in their pelvis in the 12% of cases. Older patients [(OR) 1.69; 95% confidence interval (CI) 1.02–2.78] having thick primary (OR 1.6; 95% CI, 1.01–2.53) and $\geq$ 2 positive SLNs (OR 2.5; 95% CI, 1.4–4.47) were more likely to harbour pelvic LN metastasis. Interestingly, 4% of all patients (34% of patients with positive pelvic LNs) had pelvic LN metastasis with negative inguinal LNs. Pelvic LN metastasis was independently associated with higher risk of recurrence and lower survival. 5-year disease free and overall survival was 30% and 50%, respectively, for patients with pelvic LN metastasis.
Conclusions: Pelvic LNs are frequently positive after ilioinguinal lymphadenectomy and it should be considered for all patients, especially those who are older, have thick primary and $\geq$ 2 positive SLN. Patients with pelvic LN metastasis have worse prognosis.

Keywords: Melanoma; Sentinel lymph node; Node metastasis; Deep disease

Introduction

Lymphatic mapping and sentinel lymph node biopsy (SLNB) for patients with skin melanoma have become widely accepted procedures for staging regional lymph (LN) node field.[1–3] Although SLNB does not improve survival when compared with nodal observation in clinically lymph node negative melanoma patients, completion lymph node dissection (CLND) in sentinel lymph node (SLN) positive patient showed a 20% 10-year survival benefit compared to lymphadenectomy for clinically positive LN metastasis.[4,5]

The evidence supporting SLNB and CLND survival benefit was observed in non-randomized patients of the Multicentre Selective Lymphadenectomy Trial (MSLT) and given the lack of evidence from randomized studies

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it is not totally surprising that controversies still exist on performing a lymphadenectomy in SLN-positive patients.[4–8] Several population-based studies in Europe the US showed that roughly 40–50% of SLNB-positive patients have not been submitted to CLND.[9,10] Furthermore, the optimal technique of lymphadenectomy is still to be established and the optimal extension of surgery within each nodal field (neck, axilla and groin) to be determined, particularly when LN metastasis involved the groin.[11–13]

Groin lymphadenectomy is at greater risk of postoperative morbidity when compared with neck and axillary dissection.[14,15] Wound infection and dehiscence, seroma and lymphedema are the most frequently occurring postoperative adverse events and can happen in up to 80% of the patients with detrimental effects on long-term quality of life. Although it is commonly believed that pelvic dissection can increase morbidity of inguinal lymphadenectomy, there is no agreement about lesser morbidity when only the inguinal LNs are dissected.

Surgeons agree to remove the inguinal LNs during groin lymphadenectomy, but have different opinions on whether or not also pelvic LNs should be dissected particularly when patients have positive SLNB.[16] Some considered adequate the simply removal of the inguinal LNs, given the doubtful survival benefit and the risk of increasing morbidity.[17] Other surgeons performed routinely an inguinal and pelvic dissection, accounting for the risk of pelvic disease, which is roughly 10–15% in case of positive SLNB and the relatively small benefit of currently available adjuvant treatments.[11,18,19] Finally, some surgeons perform pelvic dissection when the number of positive inguinal LN is three or more, there are suspicious pelvic LNs at computed tomography (CT) scan, the Cloquet's LN is involved or there are second-tier LNs seen at lymphoscintigram.[20–23]

Clearly these heterogeneity mirrors the lack of randomized trials investigating the survival benefit and the morbidity associated with pelvic dissection and the lack of effective selection criteria since most of the selection criteria for pelvic lymphadenectomy have been established in the pre-SLNB era and have low accuracy.[24–27]

Establishing predictive factors of pelvic LNs metastasis and understanding the prognostic significance of having melanoma cells located in these LNs can offer more information for counselling patients on the extent of their surgery.

We designed a retrospective multi-centre study within four melanoma centres, where inguinal and pelvic dissection are routinely performed in for a positive groin SLNB, to investigate predictors of pelvic LN metastasis and the prognostic significance of having metastasis in the pelvic LNs.

Methods

Patients

The study was approved by the Research Committee of the Italian Melanoma Intergroup.

Patients who underwent a inguinal and pelvic lymphadenectomy for positive groin SLNB between January 1996 and December 2013 at four Italian Institutions were included in this study.

Patients were excluded when 1) they underwent pelvic dissection in delayed fashion following inguinal dissection; 2) received adjuvant radiotherapy or systemic treatment; and 3) had clinical evidence of involvement of the pelvic LNs or distant metastasis were found at the time of preoperative staging. All patients were staged with ultrasound scan and computed tomography (CT) to detect metastatic involvement of pelvic lymph nodes and distant metastasis. Higher risk patients in the most recent period also underwent a PET-CT scan.

The following data were extracted from the prospectively collected data-base of the participating institutions: patients age and sex, primary tumour site, thickness, level of invasion and ulceration, number of excised and positive SLN, inguinal LNs and pelvic.

Lymphatic mapping and SNB

Lymphatic mapping and SLNB were performed according to an established protocol.[28]

Briefly, SLNB was performed in patients with melanoma thicker than 1 mm. In case of thin melanoma, SLNB have been performed in case of ulceration and Clark's level IV–V. Tumours mitotic rate >1 has been introduced as selection criteria since the publication of the seventh edition of the AJCC TNM staging system. The SLN was identified by preoperative cutaneous lymphoscintigraphy using technetium 99 labeled colloidal albumin (Nanocoll, Sorin Biomedica, Saluggia, Italy) injected around the bioptic scar and planar gamma camera, intradermal injections of patent blue dye (Laboratoire Guerbet, Anenay- Sons Bois, France) and a γ probe (C-trak, care Wise Medical Products, California, Usa) at the time of surgery.

Groin lymphadenectomy

An S-shaped or a straight skin incision was carried from the apex of Scarpa's triangle to about 5 cm superomedial to the superior anterior iliac spine. In the inguinal LNs, the dissection was carried through adipose tissue to the femoral vascular sheath. The femoral vessels were exposed, the saphenous vein divided at the femoral entrance and at the apex of Scarpa's triangle and the LNs excised. The retroperitoneal space was entered through dividing the lower abdominal muscles, leaving the inguinal ligament intact to dissect the pelvic LNs. External iliac vessels were exposed by blunt dissection and retraction of the peritoneum. Dissection of the iliac lymphatic tissue was extended up to the common iliac bifurcation. The obturator LNs were accessed through mobilizing the external iliac vein. Obturator LNs were freed from obturator nerve and vessels and excised. LN specimens were marked according to their