

Lymph node retrieval rates in melanoma: a quality assessment parameter

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ABSTRACT

Introduction Regional lymph node dissection (RLND) for melanoma with nodal metastasis is a specialized procedure that is associated with improved disease-specific survival in selected patients. Furthermore, there is evidence that a higher lymph node retrieval rate (LNRR) is associated with improved local control. Currently, no consensus has been reached on the definition of an adequate LNRR. A minimum LNRR has been proposed as a quality assessment parameter that has to be validated.

Methods We conducted a retrospective cohort analysis at the Princess Margaret Cancer Centre (University Health Network, Toronto, ON). The LNRRs for all patients who underwent RLND for malignant cutaneous melanoma during 2000–2010 were recorded. Indications for RLND were a positive sentinel lymph node biopsy or clinical lymphadenopathy (palpable or radiologically detected).

Results Of the 207 identified RLNDs, 146 (70.5%) were subsequent to a positive sentinel lymph node biopsy, and 61 (29.5%) were performed for clinical lymphadenopathy. The median LNRR was 24 nodes (range: 9–47 nodes; 10th percentile: 14 nodes) for axillary RLND, 12 nodes (range: 5–30 nodes; 10th percentile: 8 nodes) for inguinal RLND, and 16 nodes (range: 10–21 nodes; 10th percentile: 11 nodes) for ilioinguinal RLND. The results were similar when comparing patients with positive sentinel lymph nodes and those with clinical lymphadenopathy, and the same surgical techniques were used in both groups.

Conclusions The LNRRs at our institution are similar to rates reported at other tertiary-care melanoma centres. A minimum acceptable LNRR can be considered a quality assessment parameter in the surgical management of melanoma with nodal metastasis.

Key Words Melanoma, lymph node retrieval rates, quality assessment

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BACKGROUND

The incidence of melanoma is increasing¹. Prognosis is poor in patients with advanced or recurrent disease². Regional lymph node dissection (RLND) is currently recommended for patients with isolated gross nodal disease (palpable or detected by medical imaging) and for patients with a positive sentinel lymph node biopsy (SLNB)^{3,4}. A higher lymph node retrieval rate (LNRR) has been shown to be an independent predictor of local disease control, and assessment of the burden of nodal disease is an important element of staging⁵. The LNRR has therefore been proposed as a quality indicator, whereby surgeons and pathologists should aim to retrieve and identify more than a predetermined

minimum number of lymph nodes if a resection is to be considered adequate⁶.

A similar metric has been used for other solid tumours. For example, in colon cancer, the minimum LNRR required for staging is 12, and that number has been used as a marker of a quality resection and pathology assessment⁷. However, in the setting of RLND for melanoma, no minimum required number of lymph nodes has yet been set—a deficiency that was previously noted by Spillane and colleagues^{6,8} from the Melanoma Institute of Australia. They reported the LNRR from cases in their prospective database and proposed that the minimum number of excised lymph nodes should be greater than the 10th percentile of the number of lymph nodes excised in their patient cohort.

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An editorial in *Annals of Surgical Oncology* encouraged other institutions to publish their LNRRs to validate the Australian data by assessing LNRRs in various populations and countries⁹. Subsequently, Rossi *et al.*¹⁰ published the LNRRs from 9 Italian centres, obtaining results similar to those in the Australian study. Our aim was to compare the LNRRs at our specialized Canadian cancer centre with previously published rates so as to provide external validity in establishing quality standards for RLND in metastatic melanoma. Additionally, we sought to determine whether the minimum LNRRs can be applied to all patients by examining whether the LNRRs were different for patients with clinical lymphadenopathy (CL—that is, palpable or radiographic nodal disease) and for patients undergoing completion lymph node dissection after a positive SLNB.

METHODS

Our retrospective cohort analysis, conducted at the Princess Margaret Cancer Centre (Toronto, ON) included all patients who underwent RLND for cutaneous malignant melanoma during 2000–2010. Patients were identified from prospective surgeon-maintained databases of all patients treated with surgery for melanoma at our institution. All procedures were undertaken by a group of fellowship-trained surgical oncologists who performed similar comprehensive axillary (levels 1–3) and complete inguinal and ilioinguinal node dissections⁴. Data were collected from clinical notes, operative notes, and pathology reports. The study protocol was approved by the institution's research ethics board.

The final study cohort consisted of 196 patients who had undergone a total of 207 RLNDs. In 9 patients, a synchronous bilateral RLND was performed; 2 patients underwent an initial RLND and then subsequently developed a regional recurrence at a different basin, undergoing a second RLND at that time. The primary outcome was the LNRRs for axillary, inguinal, and ilioinguinal RLNDs. We also compared LNRRs between patients with CL and patients with a positive SLNB. The patient groups were compared with respect to patient and tumour characteristics and also with respect to the burden of nodal disease measured by the number of positive nodes and the ratio of positive nodes to the total number of nodes examined (lymph node ratio). The total number of nodes retrieved included all nodes retrieved at the time of RLND and SLNB if applicable.

A univariable analysis was performed to compare patient characteristics in both the positive SLNB and CL cohorts. The chi-square test or Fisher exact test (in cases in which the expected count was less than 5) was used to compare categorical variables. A 2-sample t-test or Wilcoxon rank-sum test was used to examine continuous variables (normally and non-normally distributed respectively). Results were considered significant at the level of $p \leq 0.05$. All statistical analyses were performed using the SAS software application (version 9.3: SAS Institute, Cary, NC, U.S.A.).

RESULTS

Of the 207 RLNDs, 146 (70.5%) were subsequent to a positive SLNB, and 61 (29.5%) were performed in the setting of CL.

Mean age was 53.2 years in the SLNB group compared with 58.6 years in the CL group ($p = 0.017$). The most common location of the primary was the trunk in patients with a positive SLNB; the most common location in the CL group was the leg. Ulceration of the primary was present in 42.5% of patients in the SLNB group and in 66.7% of patients in the CL group ($p = 0.014$). No significant difference between groups was observed in sex distribution, tumour thickness, or histologic subtype (Table 1).

The median number of positive lymph nodes was higher in the CL group than in the SLNB group (2 vs. 1, $p = 0.015$). The median lymph node ratio was also higher in the CL group than in the SLNB group: 14% (range: 2%–100%) and 9% (range: 2%–92%) respectively ($p = 0.026$).

The median LNRR was 24 nodes (range: 9–47 nodes; 10th percentile: 14 nodes) for axillary RLND, 12 nodes (range: 5–30 nodes; 10th percentile: 8 nodes) for inguinal RLND, and 16 nodes (range: 10–21 nodes; 10th percentile: 11 nodes) for ilioinguinal RLND (Table 1). The LNRR for each procedure type was not significantly different for patients undergoing RLND for either positive SLNB or CL: The mean LNRR in axillary RLND was 25.3 ± 1.0 nodes for positive SLNB ($n = 85$) compared with 26.3 ± 1.6 nodes for CL ($n = 30$), $p = 0.59$; in inguinal LNRR, it was 12.4 ± 0.6 nodes for positive SLNB ($n = 55$) compared with 13.4 ± 0.9 nodes for CL ($n = 26$), $p = 0.32$; and in ilioinguinal LNRR, it was 17.3 ± 1.5 nodes for positive SLNB ($n = 6$) compared with 14.0 ± 1.7 nodes for CL ($n = 5$), $p = 0.17$.

DISCUSSION

Delivering quality health care is a priority. There is increasing awareness and adoption of the National Surgical Quality Improvement Program from the American College of Surgeons¹¹. Participating hospitals report risk-adjusted outcomes data for patients undergoing surgical procedures. Hospitals adopting the program have benefited with enhanced performance¹². There is interest in incorporating new outcomes variables that are oncology-specific, and LNRR might be a suitable candidate as a measure of surgical quality for melanoma surgery. Although the anatomic boundaries of each basin's RLND have been described, awareness of the anatomic landmarks might not be sufficient to ensure an adequate resection⁴. Furthermore, although the Multicenter Selective Lymphadenectomy Trial II is incomplete, some surgeons are offering ultrasonography surveillance of the nodal basin after positive sentinel lymph node biopsy¹³. As a result, surgeons are performing fewer RLNDs, which have become specialized procedures. However, RLND is still recommended for some patients (for example, in the presence of CL), and therefore an objective quality measure would be valuable in assessing the performance of this uncommon procedure.

By direct comparison to results from the Melanoma Institute of Australia^{6,8} and the Italian Melanoma Inter-group¹⁰ studies, the mean and 10th percentile axillary and inguinal LNRRs at our institution were at least as good as those achieved by the other two groups. Our LNRRs for ilioinguinal dissection were lower, but those procedures numbered too few in our cohort ($n = 11$) to permit any definite

conclusions to be drawn. Globally, it seems that our LNRRs are comparable to those at other large centres. Although our sample size might be too small to provide significant external validity, our results successfully demonstrate that a reproducible LNRR might be achievable and could be used as a quality indicator.

An important consideration in applying the LNRR as a quality indicator is that LNRR has not been correlated with outcomes in our patients. It is possible that, beyond a certain LNRR, removal of additional nodes might be of no oncologic benefit. Furthermore, removal of additional nodes puts patients at increased risk for lymphedema.

TABLE I Patient and tumour characteristics

Characteristic	Lymph node group			p Value (SLNB vs. CL)
	All dissections	Sentinel node positive (SLNB)	Clinical lymphadenopathy ^a (CL)	
Patients (n)	207	146	61	
Mean age (years)	54.8±14.6	53.2±14.1	58.6±15.2	0.017
Sex [n (%)]				
Men	127 (61.4)	90 (61.6)	37 (60.7)	0.89
Women	80 (38.6)	56 (38.4)	24 (39.3)	
Melanoma site [n (%)]				
Trunk	102 (49.3)	77 (52.7)	25 (41.0)	0.022
Leg	79 (38.2)	51 (34.9)	28 (45.9)	
Arm	23 (11.1)	18 (12.3)	5 (8.2)	
Occult	3 (1.4)	0 (0)	3 (4.9)	
Melanoma primary [n (%)]				
Thickness				
<1 mm	13 (7.0)	8 (5.6)	5 (11.6)	0.20
1.01–2 mm	65 (34.9)	55 (38.5)	10 (23.3)	
2.01–4 mm	53 (28.5)	39 (27.3)	14 (32.6)	
>4 mm	55 (29.6)	41 (28.7)	14 (32.6)	
Occult or unavailable	21	3	18	
Type [n (%)]				
Superficial spreading	71 (49.3)	64 (52.9)	7 (30.4)	0.14
Nodular	43 (29.9)	33 (27.3)	10 (43.5)	
Acral lentiginous	20 (13.9)	15 (12.4)	5 (21.7)	
Other	10 (6.9)	9 (7.4)	1 (4.4)	
Unavailable	63	25	38	
Ulceration [n (%)]				
Present	81 (47.6)	57 (42.5)	24 (66.7)	0.014
Absent	89 (52.4)	77 (57.5)	12 (33.3)	
Unavailable	37	12	25	
Surgical procedure [n (%)]				
Axillary RLND	115 (55.6)	85 (58.2)	30 (49.2)	0.32
Inguinal RLND	81 (39.1)	55 (37.7)	26 (42.6)	
Ilioinguinal RLND	11 (5.3)	6 (4.1)	5 (8.2)	
Positive lymph nodes (n)				
Median	1	1	2	0.015
Range	1–26	1–15	1–26	
Mean	2.7±3.3	2.1±2.1	4.1±4.8	
Lymph node ratio ^b (%)				
Median	9	9	14	0.026
Range	2–100	2–92	2–100	
Mean	15±16.2	12.1±12.1	22.4±21.8	

^a Palpable or detected on medical imaging.

^b Positive nodes / total nodes harvested.

RLND = regional lymph node dissection.

TABLE II Comparison of lymph node (LN) retrieval between centres

Region dissected	Nodes retrieved (n)		
	Princess Margaret Hospital, Toronto, ON	Italian Melanoma Intergroup ¹⁰	Melanoma Institute of Australia ^{6,8}
Axillary retrieval	115	1150	1023
LN retrieval rate			
Mean	25.5	22	21.2
Median	24	20	20
10th Percentile	14	12	10
Inguinal retrieval	81	209	105
LN retrieval rate			
Mean	12.7	12	12.1
Median	12	11	11
10th Percentile	8	6	8
Ilioinguinal retrieval	11	955	88
LN retrieval rate			
Mean	15.8	22	22
Median	16	21	21.5
10th Percentile	11	13	14

The usefulness of reviewing an institution's LNRR is that surgeons and pathologists who might benefit from additional education to improve their technique could be identified. The LNRR can also serve as an entry criterion for patients enrolling in randomized controlled trials for adjuvant therapy. Furthermore, as novel surgical approaches such as minimally invasive inguinal lymph node dissection are incorporated into surgical care, reviewing the LNRR of those procedures for comparison with our published LNRRs in a conventional open approach can be used to quickly validate the completeness of the new techniques¹⁴.

Research into quality improvement in surgery has focused on the effect of surgeon and hospital volume on outcomes^{15,16}. Spillane *et al.*^{6,8} demonstrated a higher LNRR for surgeons at the high-volume Sydney Melanoma Unit than for other Australian surgeons. Similarly, at our own institution, where our LNRR for ilioinguinal dissections compares poorly with those at reference centres, the difference might be a result of our lower volume for that specific procedure. Our results and those of the other published groups can be used as a benchmark that other surgeons and hospitals can use in a comparison of their LNRRs for RLNDs in melanoma. In cases in which fewer than the minimum expected number of nodes is retrieved, surgeons should critically assess their surgical technique and perhaps refrain from performing the procedure if volumes are low and consider referring patients to specialty centres.

A limitation of our conclusions is that the LNRR does not exclusively depend on surgical technique. Pathologists at different centres might process surgical specimens differently and with variable scrutiny. A study investigating the LNRR in colorectal cancer specimens revealed that repeat examination of the specimen by pathologists can reveal previously unseen nodes¹⁷. As a quality indicator

of surgical technique, LNRR might therefore have to be a combined quality indicator of the surgeon and the pathologist. All specimens included in our study were examined by experienced melanoma-specific pathologists.

At our institution, the surgical procedure is the same whether the indication is a positive SLNB or CL, and therefore, not surprisingly, the LNRR was not significantly different between those patient groups. The use of adjuvant systemic therapies has led some authors to advocate observation alone or limited axillary dissection for patients with positive sentinel lymph nodes^{13,18,19}. It might therefore be appropriate that, in future, different standards for LNRR be set based on the indication for the procedure.

We encourage the U.S. National Comprehensive Cancer Network to critically review our data and the previously published data with respect to LNRR in melanoma to establish guidelines that can aid surgeons and hospitals in assessing the quality of their surgical treatment of melanoma with lymph node metastases. A RLND is a specialized procedure, and surgeons need quantitative feedback on their performance.

CONCLUSIONS

There is a reproducible minimal number of lymph nodes retrieved that defines an adequate lymph node dissection for metastatic melanoma that can be applied to patients with a positive SLNB or CL.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none

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