

Review

Complications following completion lymphadenectomy  
versus therapeutic lymphadenectomy for melanoma – A  
systematic review of the literature



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**Abstract**

**Purpose:** Completion lymph node dissection (CLND) following a positive sentinel lymph node biopsy (SLNB) has been reported to be less morbid than lymphadenectomy for palpable disease (therapeutic lymph node dissection; TLND). The reporting of morbidity data can be heterogeneous, and hence no 'average' surgical complication rates of these procedures has been reported. This review aims to determine complications rates to inform patients undergoing surgery for metastatic melanoma.

**Methods:** A systematic review of English-language literature from 2000 to 2017, reporting morbidity information about CLND and TLND for melanoma, was performed. The methodological quality of the included studies was performed using the methodological index for non-randomised studies (MINORS) instrument and Detsky score. Pooled proportions of post-operative complications were constructed using a random effects statistical model.

**Results:** After application of inclusion and exclusion criteria, 18 articles progressed to the final analysis. In relation to TLND (1627 patients), the overall incidence of surgical complications was 39.3% (95% CI 32.6–46.2); including wound infection/breakdown 25.4% (95% CI: 20.9–30.3); lymphoedema 20.9% (95% CI: 13.8–29.1); and seroma 20.4% (95% CI: 15.9–25.2). For CLND (1929 patients), the overall incidence of surgical complications was 37.2% (95% CI 27.6–47.4); including wound infection/breakdown 21.6% (95% CI: 13.8–30.6); lymphoedema 18% (95% CI: 12.5–24.2); and seroma 17.9% (95% CI: 10.3–27). The complication rate was marginally lower for CLND but not to statistical significance.

**Discussion:** This study provides information about the incidence of complications after CLND and TLND. It can be used to counsel patients about the procedures and it sets a benchmark against which surgeons can audit their practice.

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**Keywords:** Complications; Lymph node dissection; Completion; Therapeutic; Lymphadenectomy; Melanoma

**Introduction**

Estimated to affect about 2.5 million people, melanoma is a significant disease in Europe.<sup>1</sup> Its incidence is rapidly increasing across the developed world; with a 119% increase since 1990 in the UK.<sup>2</sup> Survival rates have improved greatly since 1970, with a current 10-year disease-specific survival

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rate of 90%.<sup>3</sup> However, mortality from advanced disease remains significant: patients with regional lymph node involvement have a five-year survival rate between 40% and 78%.<sup>3</sup>

In our previous report,<sup>4</sup> we investigated the incidence of surgical complications associated with sentinel lymph node biopsy (SLNB) in over 9000 melanoma patients. Subsequent to a positive SLNB, current evidence suggests improved disease-specific and disease-free survival benefit with an immediate completion lymph node dissection (CLND) for intermediate thickness melanoma.<sup>5</sup> CLND is defined as lymphadenectomy of all remaining lymph nodes in the affected basin following a positive SLNB in the absence of clinically palpable disease.<sup>6</sup> Indeed, 92% of surgeons would recommend CLND to positive SLNB patients,<sup>7</sup> but according to analysis of the National Cancer Data Base from 2004 to 2005, only half of SLNB positive patients actually undergo CLND.<sup>8</sup> This lower than expected uptake may be due to concerns about the morbidity associated with CLND; however, this has yet to be thoroughly evaluated.

Therapeutic lymph node dissection (TLND) is an option for those who have clinically palpable lymph node involvement, either following SLNB or in the absence of SLNB.<sup>9</sup> It is currently unknown whether CLND results in fewer complications than TLND, as no pooled comparative analysis of the procedures has been conducted. We hypothesize that TLND is associated with increased surgical morbidity, as the patient cohort may have greater disease burden and the possible need for more extensive surgery compared to those undergoing CLND. At present, surgical morbidity associated with both of these procedures is high and variably reported in the literature, with overall complications ranging from 21.4%<sup>10</sup> to 50.9%<sup>11</sup> for TLND and from 11.5%<sup>12</sup> to 72.9%<sup>13</sup> for CLND.

The aim of this review is to compare the reported surgical complications of CLND and TLND. Post-operative complications will be divided into short-term, occurring within 30-days of the surgical procedure (wound infection, dehiscence, seroma, haematoma, nerve injury); and long-term, occurring after 30-days (lymphoedema). For melanoma of all thickness, no significant difference in disease-specific survival has been found between patients undergoing CLND or TLND.<sup>5</sup> As such, the morbidity of these procedures may aid the clinician, and the patient, in the decision about how best to manage the melanoma: either with SLNB and immediate CLND, or with clinical observation and TLND if subsequent palpable disease develops.

## Materials and methods

### Data sources

A systematic literature review of publications in English of the following electronic databases was performed: Cochrane Database of Systematic Reviews, MEDLINE and EMBASE. The following keywords were used: (lymph node dissection OR lymphadenectomy) AND melanoma

AND (complications OR morbidity OR adverse events). The publication date range for studies was from 01/01/2000 to 31/01/2017.

### Study selection

Two researchers (JH, JM) independently conducted the literature search. Study eligibility was defined using the population, intervention, comparator, outcome, and study design approach (PICOS),<sup>14</sup> which is summarised with the inclusion and exclusion criteria in Table 1. Articles were included if a subgroup of patients fulfilling the inclusion criteria could be extracted from the reported cohort (e.g. complications of CLND extracted from a mixed cohort of SLNB patients). If data was not extractable, or incomplete from a mixed cohort, it was excluded. In the initial literature search, titles and abstracts were excluded if they, or the article metadata indicated incorrect article type (e.g. literature review, case reports) or lack of surgical morbidity data (e.g. experimental study, chemotherapy trial). We included abstracts that contained numbers or percentage of reported complications, or abstracts that alluded to the reporting of morbidity data. In order to minimise inclusion of studies at high risk of selection bias, papers were excluded if the study cohort contained fewer than 50 patients.

According to the criteria of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA),<sup>14</sup> our study selection was performed through three levels of screening. Initially, title screening included studies with the following word combinations: 1) lymph node dissection, metastases or biopsy, and melanoma; 2) morbidity, adverse events or complications and melanoma; 3) lymphadenectomy and melanoma; 4) groin, inguinal, ilioinguinal, axilla, axillary or cervical dissection and melanoma. Studies were excluded if these phrases were omitted, or if the study title stated the number of participants were fewer than 50. In the second level of screening, abstracts were reviewed according to our inclusion and exclusion criteria (Table 1). The papers that proceeded to the third level of screening were read in their entirety and screened according to the same inclusion and exclusion criteria. Studies were only included if they succeeded all levels of screening. With the consensus of all authors that the included studies fulfilled the inclusion and exclusion criteria, the finalised list of articles were agreed upon.

### Assessment of methodological quality

The methodological quality of the included non-randomised studies was performed using the methodological index for non-randomised studies (MINORS) instrument.<sup>15</sup> Non-comparative and comparative studies were given a score out of 16 and 24 respectively. The included RCTs were assessed according to the Detsky score, the maximum result of which is 20.<sup>16</sup> Consistent with other research, the studies that were assigned a score of >75% were considered high quality.<sup>17,18</sup>

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