Original article

Optimal extent of completion lymphadenectomy for patients with melanoma and a positive sentinel node in the groin

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Background: **The optimal extent of groin completion lymph node dissection (CLND) (inguinal or ilioinguinal dissection) in patients with melanoma is controversial. The aim of this study was to evaluate whether the extent of groin CLND after a positive sentinel node biopsy (SNB) is associated with improved outcome.**

Methods: **Data from all sentinel node-positive patients who underwent groin CLND at four tertiary melanoma referral centres were retrieved retrospectively. Baseline patient and tumour characteristics were collected for descriptive statistics, survival analyses and Cox proportional hazards regression analyses.**

Results: **In total, 255 patients were included, of whom 137 (53·7 per cent) underwent inguinal dissection and 118 (46·3 per cent) ilioinguinal dissection. The overall CLND positivity rate was 18·8 per cent; the inguinal positivity rate was 15·5 per cent and the pelvic positivity rate was 9·3 per cent. The pattern of recurrence, and 5-year melanoma-specific survival, disease-free survival and distant-metastasis free survival rates were similar for both dissection types, even for patients with a positive CLND result. Cox regression analysis showed that type of CLND was not associated with disease-free or melanoma-specific survival.**

Conclusion: **There was no significant difference in recurrence pattern and survival rates between patients undergoing inguinal or ilioinguinal dissection after a positive SNB, even after stratification for a positive CLND result. An inguinal dissection is a safe first approach as CLND in patients with a positive SNB.**

Paper accepted 30 May 2017

Published online 2 November 2017 in Wiley Online Library (www.bjs.co.uk). **DOI:** 10.1002/bjs.10644

Introduction

Although evidence for a therapeutic benefit is still lacking pending the final results of Multicentre Selective Lymphadenectomy Trial (MSLT) II, many current melanoma guidelines advise consideration of completion lymphadenectomy (CLND) in case of a positive sentinel node biopsy (SNB)[1–4]. This is in line with the opinion of 91·8 per cent of 193 melanoma surgeons worldwide, but in practice only half of patients with a positive sentinel node (SN) actually undergo CLND[5,6]. In the groin area, CLND can be classified as an inguinal dissection with removal of all femoral and inguinal lymph nodes, or an ilioinguinal dissection with additional removal of all iliac (up to the bifurcation of the common iliac artery) and obturator lymph nodes.

The optimal surgical extent of CLND in the groin is controversial. Some authors[7–9] advocate ilioinguinal dissection to optimize regional control and possibly increase survival. Others[10–16] disagree and advocate an inguinal dissection, especially in patients with low suspicion of pelvic nodal metastasis, because ilioinguinal dissection is believed to be associated with increased morbidity and does not seem to affect outcome.

Few studies have compared the therapeutic benefit of inguinal and ilioinguinal dissection solely in patients with melanoma and a positive SNB. The majority of studies comparing these two types of dissection have been limited to those with palpable disease[7,11,15], or did not differentiate between patients with a positive SNB or palpable disease[8,17]. It has been demonstrated, however, that

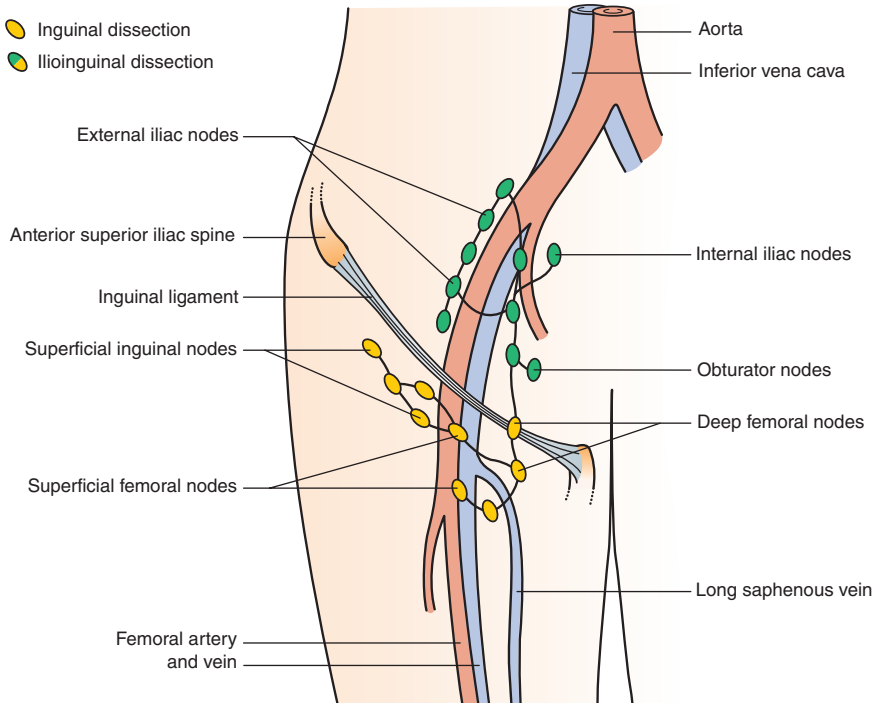


Fig. 1 Nodes removed in inguinal *versus* ilioinguinal completion lymph node dissection in the groin

patients with a positive SNB differ from those with palpable disease in tumour biology, rate of pelvic nodal involvement, recurrence pattern and survival rate[8,13,14,17–19].

The aim of the present study was to evaluate whether the extent of groin CLND in patients with a positive SNB was associated with better outcome. For this purpose, data from four tertiary large melanoma centres in the Netherlands were retrieved. Recurrence patterns, disease-free survival (DFS), distant metastasis-free survival (DMFS) and melanoma-specific survival (MSS) were compared after inguinal and ilioinguinal dissection.

Methods

Patients with a positive SNB and subsequent CLND in the groin were identified from retrospective SNB melanoma databases in four tertiary melanoma centres in the Netherlands, two of which routinely performed inguinal dissection and two ilioinguinal dissection. Patient characteristics (age, sex), tumour characteristics (histology, Breslow thickness), SN characteristics (tumour burden), CLND outcomes and follow-up data were extracted from the databases of the participating centres.

Sentinel node biopsy

SNB was performed for primary melanomas at least 1·00 mm thick, or shallower than 1·00 mm but with ulceration or other adverse tumour characteristics (Clark level IV–V or at least 1 mitosis/mm^2 depending on the AJCC staging edition at the time of diagnosis). The triple technique was used, as described previously[20–22].

Completion lymphadenectomy

In general, the Dutch Melanoma Guidelines[2] were adhered to by all participating centres for preoperative and postoperative management; preoperative or postoperative imaging was not indicated.

The local policy of centres 1 and 4 was inguinal dissection with removal of inguinal nodes only as standard treatment, whereas in centres 2 and 3 the routine practice was ilioinguinal dissection with additional removal of all iliac and obturator nodes (*Fig. 1*). Sometimes surgeons deviated from this routine practice, based on factors such as age, co-morbidities, drainage patterns during lymphoscintigraphy and number of positive SNs. Unfortunately, these reasons are heterogeneous and not amenable to

Table 1 Patient and tumour characteristics for all patients and those with a positive completion lymph node dissection result

	All patients			Positive CLND result		
	Inguinal dissection ($n = 137$)	Ilioinguinal dissection ($n = 118$)	P†	Inguinal dissection ($n = 15$)	Ilioinguinal dissection ($n = 33$)	P†
Baseline data						
Treatment centre			< 0·001			< 0·001§
1	67 (48·9)	5 (4·2)		8 (53)	2 (6)	
2	34 (24·8)	44 (37·3)		4 (27)	8 (24)	
3	17 (12·4)	63 (53·4)		1 (7)	22 (67)	
4	19 (13·9)	6 (5·1)		2 (13)	1 (3)	
Age (years)*	52 (39–62)	50 (38–63)	0·915‡	52 (40–56)	57 (44–65)	0·201‡
Sex (F : M)	78 : 59	52 : 66	0·040	11 : 4	8 : 25	0·001
Primary site			0·358			0·307
Leg	105 (76·6)	96 (81·4)		12 (80)	31 (94)	
Trunk	32 (23·4)	22 (18·6)		3 (20)	2 (6)	
Histological type			0·098			0·828§
SSM	69 (50·4)	62 (52·5)		10 (67)	16 (48)	
NM	36 (26·3)	35 (29·7)		4 (27)	10 (30)	
ALM	10 (7·3)	10 (8·5)		1 (7)	4 (12)	
Other	2 (1·5)	5 (4·2)		0 (0)	2 (6)	
Unknown	20 (14·6)	6 (5·1)		0 (0)	1 (3)	
Breslow thickness (mm)*	2·90 (1·74–4·50)	2·80 (1·80–4·70)	0·720‡	2·70 (2·00–5·50)	3·50 (2·40–5·20)	0·367‡
pT category (mm)			0·656§			0·465§
pT1 (< 1·00)	1 (0·7)	4 (3·4)		0 (0)	1 (3)	
pT2 (1·01–2·00)	38 (27·7)	31 (26·3)		4 (27)	3 (9)	
pT3 (2·01–4·00)	60 (43·8)	48 (40·7)		6 (40)	16 (48)	
pT4 (> 4·00)	37 (27·0)	34 (28·8)		5 (33)	13 (39)	
Unknown	1 (0·7)	1 (0·8)		0 (0)	0 (0)	
Ulceration			0·003			0·158§
No	60 (43·8)	64 (54·2)		6 (40)	15 (45)	
Yes	57 (41·6)	51 (43·2)		6 (40)	17 (52)	
Unknown	20 (14·6)	3 (2·5)		3 (20)	1 (3)	
SN analysis						
No. of SNs*	2 (1–2)	2 (1–3)	0·226‡	1 (1–2)	2 (1–3)	0·057‡
No. of non-SNs*	0 (0–0)	0 (0–0)	0·144‡	0 (0–0)	0 (0–0)	0·176‡
No. of positive SNs*	1 (1–1)	1 (1–2)	0·225‡	1 (1–1)	1 (1–2)	0·025‡
No. of positive non-SNs	0 (0)	0 (0)	1·000	0 (0)	0 (0)	1·000
SN tumour burden (mm)			0·003			0·164
< 0·1	16 (11·7)	4 (3·4)		0 (0)	0 (0)	
0·1–1·0	52 (38·0)	45 (38·1)		4 (27)	12 (36)	
>1·0	30 (21·9)	46 (39·0)		5 (33)	16 (48)	
Unknown	39 (28·5)	23 (19·5)		6 (40)	5 (15)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). CLND, completion lymph node dissection; SSM, superficial spreading melanoma; NM, nodular melanoma; ALM, acral lentiginous melanoma; SN, sentinel node. †χ^2 test, except ‡Mann–Whitney U test and §Fisher's exact test.

retrospective analysis. Ilioinguinal dissection was performed either via a single inguinal elliptical incision extending cranially, or via two separate transverse incisions, as described previously[15,23].

Pathology

SNs were processed according to the European Organisation for Research and Treatment of Cancer (EORTC) SN pathology protocol[24]. CLND specimens were processed in a standard fashion; all lymph nodes were bisected or trisected, and stained with haematoxylin and eosin. Pathology reports were considered adequate when the total number of removed and involved lymph nodes was mentioned. For ilioinguinal specimens, the number of both inguinal and pelvic nodes removed, and number of positive nodes were also recorded, if available.

Statistical analysis

Differences between the two treatment groups were calculated using χ^2 tests, Fisher's exact tests or non-parametric Mann–Whitney U tests, as appropriate. Where data were missing or unknown, an 'unknown' subcategory was

Table 2 Outcomes for all patients and those with a positive completion lymph node dissection result

	All patients			Positive CLND result		
	Inguinal dissection ($n = 137$)	Ilioinguinal dissection ($n = 118$)	P‡	Inguinal dissection ($n = 15$)	Ilioinguinal dissection ($n = 33$)	P‡
CLND result						
No. of LNs*	8 (5–11)	14 (10–20)	< 0·001§	7 (4–11)	15 (10–23)	< 0·001§
No. of positive LNs*	0 (0–0)	0 (0–1)	< 0·001§	1 (1–2)	2 (1–4)	0·125§
No. of LNs including SNBtot*	10 (7–13)	16 (12–22)	< 0·001§	9 (5–12)	18 (13–25)	< 0·001§
No. of positive LNs including SNBtot*	1 (1–2)	1 (1–3)	0·007§	2 (2–3)	3 (3–6)	0·009§
No. of inguinal LNs*	8 (5–10) ($n = 135$)	8 (5–11) ($n = 96$)	0·417§	7 (4–11)	9 (7–16) ($n = 29$)	0·062§
No. of positive inguinal LNs*	0 (0–0) ($n = 135$)	0 (0–0) ($n = 114$)	0·014§	1 (1–2)	1 (1–3) ($n = 29$)	0·842§
No. of pelvic LNs*	–	5 (3–9) ($n = 96$)	–	–	5 (2–9) ($n = 29$)	–
No. of positive pelvic LNs*	–	0 (0–0) ($n = 114$)	–	–	0 (0–1) ($n = 29$)	–
Positive LNs			0·018¶			0·018¶
Inguinal only	15 (100)	18 (55)		15 (100)	18 (55)	
Pelvic only	0 (0)	4 (12)		0 (0)	4 (12)	
Inguinal and pelvic	0 (0)	7 (21)		0 (0)	7 (21)	
Unknown	0 (0)	4 (12)		0 (0)	4 (12)	
Follow-up						
Adjuvant immunotherapy†			0·024			0·004¶
No	7 (5·1)	3 (2·5)		5 (33)	1 (3)	
Yes	16 (11·7)	4 (3·4)		1 (7)	1 (3)	
Unknown	114 (83·2)	111 (94·1)		9 (60)	31 (94)	
Adjuvant radiotherapy			< 0·001			0·001¶
No	36 (26·3)	98 (83·1)		4 (27)	23 (70)	
Yes	4 (2·9)	6 (5·1)		1 (7)	6 (18)	
Unknown	97 (70·8)	14 (11·9)		10 (67)	4 (12)	
Recurrence			0·786			0·287
No	72 (52·6)	60 (50·8)		2 (13)	9 (27)	
Yes	65 (47·4)	58 (49·2)		13 (87)	24 (73)	
Site of first recurrence			0·394			0·125¶
Locoregional	31 (48)	34 (59)		2 (15)	9 (38)	
Regional LNs	8 (12)	4 (7)		0 (0)	3 (13)	
Distant	26 (40)	20 (34)		11 (85)	12 (50)	
Any regional LN recurrence			0·132			1·000
No	120 (87·6)	110 (93·2)		13 (87)	28 (85)	
Yes	17 (12·4)	8 (6·8)		2 (13)	5 (15)	
Site of regional recurrence			0·181¶			0·095¶
Inguinal only	5 (29)	1 (13)		1 (50)	0 (0)	
Inguinal and pelvic	6 (35)	1 (13)		1 (50)	0 (0)	
Pelvic only	5 (29)	4 (50)		0 (0)	3 (60)	
Popliteal	1 (6)	0 (0)		0 (0)	0 (0)	
Unknown	0 (0)	2 (25)		0 (0)	2 (40)	

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †Interferon-α or dendritic cell therapy. CLND, completion lymph node dissection; LN, lymph node; SNBtot, number of sentinel nodes plus non-sentinel nodes during sentinel node biopsy. ‡χ^2 test, except §Mann–Whitney *U* test and ¶Fisher's exact test.

created and included in the analysis. MSS was calculated from the date of CLND until last follow-up or death from melanoma; deaths from other causes were censored. DFS was calculated from the date of CLND to the date of first recurrence or the date of last-follow-up or death. DMFS was calculated from the date of CLND to the date of first distant metastasis or date of last follow-up or death. The Kaplan–Meier method was used to estimate survival, and differences between groups were assessed by means of the log rank test. Multivariable Cox proportional hazards regression analyses were performed to identify prognostic co-variables. Two-sided $P < 0·050$ was considered statistically significant. SPSS® version 22.0 was used for all statistical analyses (IBM, Armonk, New York, USA).

Results

A total of 283 patients treated between 1994 and 2014 were identified from the SNB databases. Twenty-eight patients

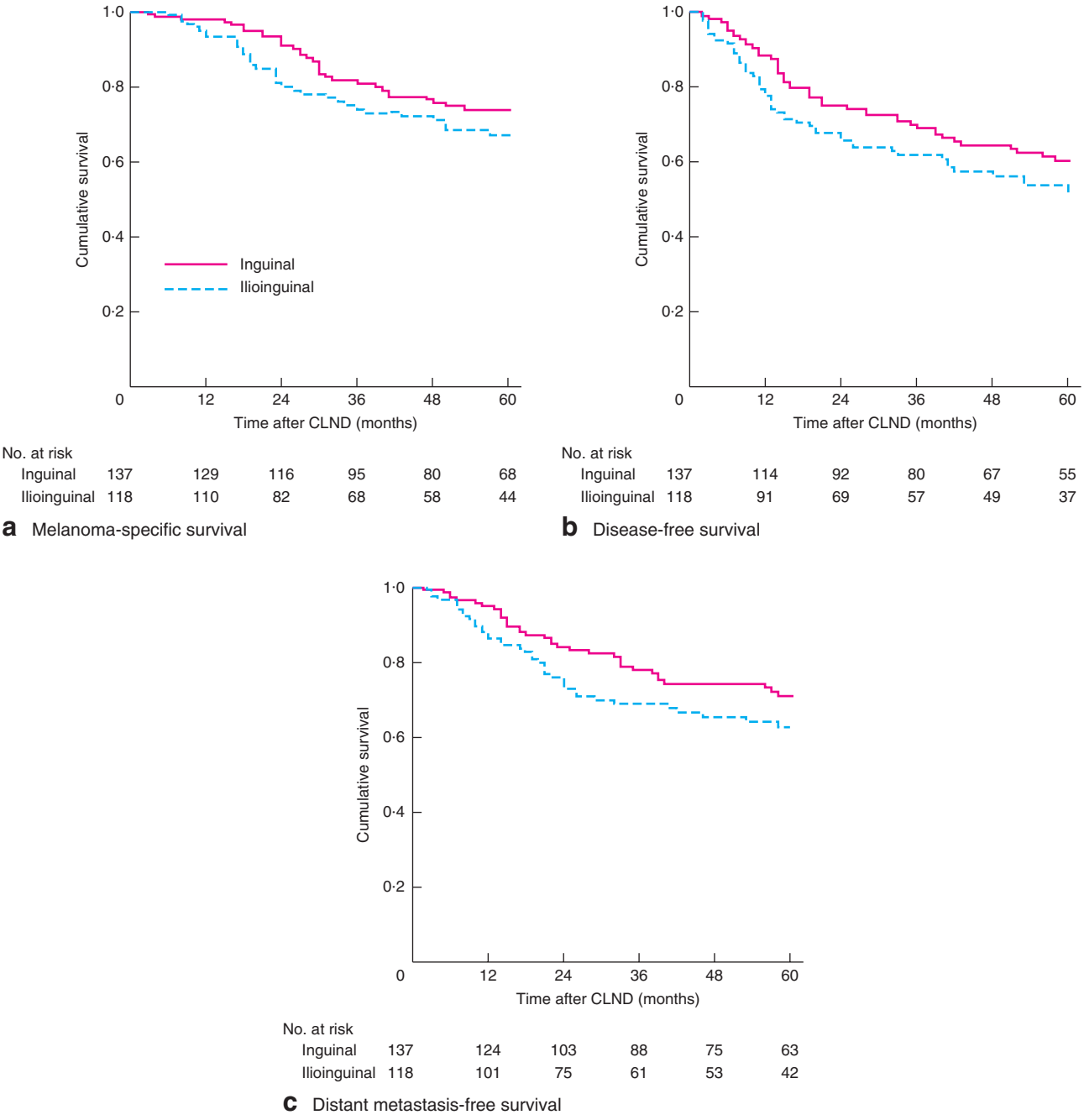


Fig. 2 Five-year **a** melanoma-specific survival, **b** disease-free survival and **c** distant metastasis-free survival after inguinal and ilioinguinal completion lymph node dissection (CLND). **a** $P = 0{\cdot}184$, **b** $P = 0{\cdot}169$, **c** $P = 0{\cdot}143$ (log rank test)

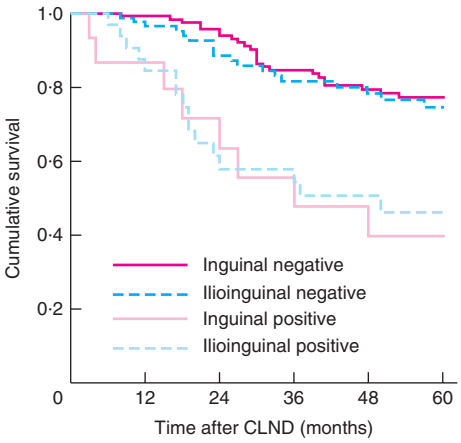
were excluded for the following reasons: palpable disease or distant metastases before surgery (9); missing data on CLND date and resected specimen (7); additional positive SNB outside the groin (9); no available follow-up (2); and altered choice of surgery owing to pregnancy (1). The remaining 255 patients were analysed. Median follow-up for all patients was 51 (i.q.r. 26–99) months. Baseline patient and tumour characteristics are shown in *Table 1*. An inguinal dissection was performed in 137 patients (53·7 per cent) and an ilioinguinal dissection in 118 (46·3 per cent).

The ilioinguinal group included more men ($P = 0{\cdot}040$) and had a significantly higher SN tumour burden ($P = 0{\cdot}003$).

Forty-eight patients (18·8 per cent) had additional lymph node metastases in the CLND specimen (positive CLND), 15 in the inguinal dissection group and 33 in the ilioinguinal dissection group. The overall inguinal positivity rate (with or without additional pelvic positivity) was 15·7 per cent (40 of 255), and the overall pelvic positivity rate (with or without additional inguinal positivity) was 9·3 per cent (11 of 118).

The median number of inguinal lymph nodes removed was similar for both dissection types ($P = 0{\cdot}417$), but the median number of positive inguinal lymph nodes was significantly greater for patients undergoing ilioinguinal dissection ($P = 0{\cdot}014$) (*Table 2*). In patients with a positive CLND, the median numbers of both removed and positive inguinal lymph nodes were similar for both dissection types ($P = 0{\cdot}062$ and $P = 0{\cdot}842$ respectively).

Twenty patients participated in an adjuvant immunotherapy trial, ten in an EORTC interferon-α trial[25] and ten in a dendritic cell therapy trial[26]. Another ten patients received adjuvant radiotherapy.



No. at risk

Inguinal negative	122	117	107	88	74	63
Ilioinguinal negative	85	82	65	52	47	36
Inguinal positive	15	12	9	7	6	5
Ilioinguinal positive	33	28	17	16	11	8

Fig. 3 Five-year melanoma-specific survival for patients with a positive or negative result of inguinal or ilioinguinal completion lymph node dissection (CLND). $P = 0{\cdot}767$, inguinal positive *versus* ilioinguinal positive (log rank test)

Recurrence

The overall recurrence rate was 47·4 per cent (65 of 137) after inguinal dissection and 49·2 per cent (58 of 118) after ilioinguinal dissection ($P = 0{\cdot}786$). For both dissection types, most patients presented with locoregional recurrence only (such as in-transit metastasis) or distant recurrence (distant subcutaneous, distant lymph nodes or distant visceral) at first presentation of relapse. First relapse in the regional lymph node basin (similar to the CLND basin) occurred less often, in 12 per cent (8 of 65) after inguinal dissection and 7 per cent (4 of 58) after ilioinguinal dissection ($P = 0{\cdot}394$). During follow-up, another nine patients in the inguinal dissection group and five in the ilioinguinal dissection group presented with a second relapse located in the regional lymph node basin. Thus, the overall regional lymph node recurrence rate was 12·4 per cent (17 of 137) after inguinal dissection and 6·8 per cent (8 of 118) after ilioinguinal dissection ($P = 0{\cdot}132$). The specified locations of regional lymph node recurrences are shown in *Table 2*.

The overall recurrence rate for patients with a positive CLND result was 87 per cent (13 of 15) after inguinal dissection and 73 per cent (24 of 33) after ilioinguinal dissection ($P = 0{\cdot}287$). The overall regional lymph node recurrence rate was 13 per cent (2 of 15) and 15 per cent (5 of 33) respectively ($P = 1{\cdot}000$) (*Table 2*).

Survival

Five-year estimated MSS, DFS and DMFS rates were 73·2, 59·2 and 70·4 per cent respectively after inguinal dissection, and 66·4, 53·1 and 62·5 per cent after ilioinguinal dissection ($P = 0{\cdot}184$, $P = 0{\cdot}169$ and $P = 0{\cdot}143$ respectively) (*Fig. 2*).

For patients with a positive CLND, the 5-year estimated MSS, DFS and DMFS rates were 40, 26 and 26 per cent respectively after inguinal dissection, compared with 46, 30 and 36 per cent after ilioinguinal dissection ($P = 0{\cdot}767$, $P = 0{\cdot}978$ and $P = 0{\cdot}651$ respectively). Results for MSS are illustrated in *Fig. 3*.

Univariable Cox proportional hazards regression analyses for DFS and MSS included all baseline and treatment characteristics. In multivariable analysis for DFS, advanced age, unknown histology, higher SN tumour burden and a positive CLND result were adverse prognostic factors (*Table 3*). In multivariable analysis for MSS, only advanced age and positive CLND were adverse prognostic factors (*Table 4*).

In univariable analysis of prognostic factors in the subgroup of 48 patients with a positive CLND, type of dissection was not a significant prognostic factor for DFS (hazard ratio (HR) (ilioinguinal *versus* inguinal dissection) 0·88, 95 per cent c.i. 0·44 to 1·76; $P = 0{\cdot}713$) or for MSS (HR 0·82, 0·38 to 1·79; $P = 0{\cdot}622$).

Table 3 Cox proportional hazards regression model for disease-free survival

		Univariable analysis		Multivariable analysis	
Variable	*n*	Hazard ratio	*P*	Hazard ratio	*P*
Age	255	1·02 (1·01, 1·04)	< 0·001	1·02 (1·01, 1·03)	0·002
Breslow thickness	253	1·10 (1·04, 1·15)	0·001	1·03 (0·96, 1·11)	0·377
Ulceration					
No	124	1·00 (reference)		1·00 (reference)	
Yes	108	1·70 (1·17, 2·48)	0·005	1·36 (0·90, 2·04)	0·143
Unknown	23	1·15 (0·60, 2·21)	0·671	0·61 (0·29, 1·28)	0·192
Histology					
SSM	131	1·00 (reference)		1·00 (reference)	
NM	71	1·66 (1·09, 2·52)	0·017	1·39 (0·89, 2·18)	0·148
ALM	20	2·04 (1·09, 3·83)	0·027	1·80 (0·91, 3·53)	0·090
Other	7	1·25 (0·39, 4·02)	0·704	0·65 (0·19, 2·22)	0·495
Unknown	26	1·91 (1·09, 3·36)	0·024	1·94 (1·01, 3·75)	0·048
SN tumour burden (mm)					
< 0·1	20	1·00 (reference)		1·00 (reference)	
0·1–1·0	97	6·12 (1·48, 25·30)	0·012	4·42 (1·05, 18·58)	0·042
> 1·0	76	10·33 (2·49, 42·86)	0·001	6·78 (1·60, 28·78)	0·009
Unknown	62	7·87 (1·90, 32·65)	0·004	6·12 (1·46, 25·73)	0·013
CLND type					
Inguinal	137	1·00 (reference)		1·00 (reference)	
Ilioinguinal	118	1·14 (0·80, 1·63)	0·464	0·80 (0·54, 1·19)	0·271
CLND result					
Negative	207	1·00 (reference)		1·00 (reference)	
Positive	48	2·83 (1·92, 4·17)	< 0·001	2·82 (1·84, 4·33)	< 0·001

Values in parentheses are 95 per cent confidence intervals. SSM, superficial spreading melanoma; NM, nodular melanoma; ALM, acral lentiginous melanoma; SN, sentinel node; CLND, completion lymph node dissection. The multivariable analysis was adjusted for age (continuous), Breslow thickness (continuous), ulceration, Rotterdam criteria, CLND type and CLND result. Not shown (not significant in univariable analysis): treatment centre, sex, location, total number of SNs, number of positive SNs and SN ratio. The categories adjuvant immunotherapy and radiotherapy were not included in the multivariable analysis; both were significant in univariable analysis, but this was no longer the case when the analysis was corrected for CLND result.

Table 4 Cox proportional hazards regression model for melanoma-specific survival

		Univariable analysis		Multivariable analysis	
Variable	*n*	Hazard ratio	*P*	Hazard ratio	*P*
Age	255	1·02 (1·00, 1·03)	0·015	1·02 (1·00, 1·03)	0·023
Breslow thickness	253	1·09 (1·02, 1·16)	0·012	1·03 (0·95, 1·12)	0·538
Ulceration					
No	124	1·00 (reference)		1·00 (reference)	
Yes	108	1·64 (1·05, 2·56)	0·031	1·38 (0·84, 2·26)	0·206
Unknown	23	1·18 (0·55, 2·54)	0·637	0·90 (0·41, 2·00)	0·795
SN tumour burden (mm)					
< 0·1	20	1·00 (reference)		1·00 (reference)	
0·1–1·0	97	1·99 (0·60, 6·67)	0·260	1·37 (0·40, 4·64)	0·618
> 1·0	76	4·93 (1·51, 16·16)	0·008	2·82 (0·83, 9·59)	0·097
Unknown	62	3·22 (0·98, 10·65)	0·055	2·51 (0·75, 8·48)	0·137
CLND type					
Inguinal	137	1·00 (reference)		1·00 (reference)	
Ilioinguinal	118	1·24 (0·81, 1·90)	0·319	0·91 (0·57, 1·46)	0·704
CLND result					
Negative	207	1·00 (reference)		1·00 (reference)	
Positive	48	3·12 (1·99, 4·90)	< 0·001	2·97 (1·82, 4·83)	< 0·001

Values in parentheses are 95 per cent confidence intervals. SN, sentinel node; CLND, completion lymph node dissection. The multivariable analysis was adjusted for age (continuous), Breslow thickness (continuous), ulceration, Rotterdam criteria, CLND type and CLND result. Not shown (not significant in univariable analysis): treatment centre, sex, location, histology, total number of SNs, number of positive SNs, SN ratio and adjuvant immunotherapy (interferon-α or dendritic cell therapy). The category adjuvant radiotherapy was not included in the multivariable analysis; it was significant in univariable analysis but this was no longer the case when the analysis was corrected for CLND result.

Discussion

The extent of groin CLND (inguinal or ilioinguinal dissection) did not affect recurrence patterns and survival rates in patients with melanoma and a positive SNB. Even when stratified for a positive CLND result, outcomes were not significantly different.

The overall CLND positivity rate was 18·8 per cent; the inguinal positivity rate was 15·7 per cent (including patients with additional positive pelvic nodes) and the pelvic positivity rate 9·3 per cent (including patients with additional positive inguinal nodes). Similar rates have been reported previously[27–29]. The inguinal positivity rate after ilioinguinal dissection was significantly higher than that after inguinal dissection, presumably as a result of unfavourable preoperative characteristics (such as higher SN tumour burden) as the median number of removed inguinal nodes was similar for both dissection types.

Both in the overall cohort and in the subgroup of patients with a positive CLND result there were no significant differences in recurrence patterns between dissection types, including regional lymph node recurrence. These results indicate that the extent of surgery was not associated with recurrence, even though the pelvic nodes remained *in situ* after inguinal dissection, with the theoretical possibility of microscopic disease being present already. It also seems that ilioinguinal dissection was not associated with superior regional disease control. A previous smaller study[19] of 94 patients reported a regional lymph node recurrence rate of 12 per cent after inguinal dissection compared with 17 per cent after ilioinguinal dissection ($P = 0{\cdot}66$).

Estimated 5-year MSS, DFS and DMFS rates did not differ significantly between patients undergoing inguinal or ilioinguinal dissection, both in the overall cohort and in the CLND-positive subgroup. Moreover, Cox regression showed that dissection type was not associated with DFS and MSS. These results indicate that a more radical dissection in the groin area in patients with a positive SNB is not associated with superior survival rates. Previous small studies reported an overall survival rate of 72 per cent after inguinal dissection compared with 69 per cent after ilioinguinal dissection ($P = 0{\cdot}38$), and 76 *versus* 80 per cent respectively ($P = 0{\cdot}80$)[29]. In another small study[30], there was no significant difference in estimated 5-year overall survival ($P = 0{\cdot}604$). Previously reported DFS rates were 54 per cent after inguinal dissection and 61 per cent after ilioinguinal dissection ($P = 0{\cdot}69$)[29]. Another study[19] reported no significant differences in pelvic node recurrence-free survival ($P = 0{\cdot}80$) and DFS ($P = 0{\cdot}44$) between the two dissection types.

The overall pelvic positivity rate was 9·3 per cent in this study. In contrast, pelvic positivity rates of approximately 30 per cent have been reported in patients with palpable disease[15,31]. However, even in these patients the extent of surgery does not seem to affect outcome[15]. Many patients, both those with a positive SNB and those with palpable disease, who undergo ilioinguinal dissection are therefore exposed to a potentially higher risk of morbidity but may not benefit from any therapeutic effect.

One limitation that must be considered when interpreting the present results is the retrospective study design, which is subject to numerous biases. Another is selection bias. The decision to deviate from routine practice differed by centre. Patients undergoing ilioinguinal dissection in centres where this was not standard practice presumably had an unfavourable preoperative prognosis. The potential therapeutic benefit of ilioinguinal dissection could therefore be partly counterbalanced by unfavourable prognostic factors. However, even in patients with a positive CLND result, recurrence patterns and estimated 5-year MSS, DFS and DMFS did not differ between the two dissection types. This indicates that the extent of CLND does not influence recurrence and survival positively or negatively. Other selection and treatment-based factors may also have played a considerable role, such as variation in local population, proportion of patients who underwent SNB, SN positivity rate per centre, the extent to which radical surgery was performed, the pathology protocol used, and the extent to which pathologists searched for nodes. Unfortunately, details of complications were not available for all patients in the present series, so this aspect could not be evaluated. The timing of CLND after diagnosis of melanoma was not assessed in this study, but it has been demonstrated recently that this does not seem to influence tumour load, DFS or MSS[32].

To date, the therapeutic value of CLND in patients with a positive SNB has not yet been proven in prospective randomized trials[33,34]. The DeCOG-SLT multicentre trial randomized patients with a positive SNB to undergo axillary or inguinal CLND, or observation. The trial showed no difference in DMFS, overall survival or DFS, not even a trend towards better survival for the CLND group. However, it was underpowered, and was criticized for having a majority of patients with a relatively low SN tumour load[34]. A more definitive answer to this controversial and long-standing question will be provided by MSLT-II, which has included a larger number of patients with long follow-up[4]. The EAGLE FM trial[35] is focusing on the question of whether to perform inguinal or ilioinguinal dissection in patients with groin metastases; patients with a positive SNB or palpable nodal metastases in the groin will be randomized to inguinal or ilioinguinal dissection. However, if MSLT-II does not show a survival benefit for

CLND, it will be less important to know whether to perform an inguinal or ilioinguinal dissection.

Despite these forthcoming developments, there remains a role for CLND in the near future. Currently all adjuvant therapy trials require complete pathological nodal staging of patients with stage III disease (by lymph node dissection) before inclusion. Eggermont and colleagues[36] reported that 10 mg/kg ipilimumab resulted in a significant increase of 11 per cent in recurrence-free and overall survival compared with placebo. The mortality risk was 28 per cent lower with ipilimumab than with placebo, and the risk of DMFS was 24 per cent higher. Although more research is necessary before ipilimumab can be implemented safely as standard adjuvant therapy, these results seem promising. Ongoing trials with other agents may also report a survival benefit in the next few years, all based on adjuvant therapy after lymph node dissection. Thus, CLND will remain a standard procedure for a while, either as a criterion for entry into trials or, for example, as a prerequisite for Food and Drug Administration/European Medicines Agency-approved adjuvant therapy.

The present study found no significant difference in recurrence pattern and survival rates between patients undergoing either inguinal or ilioinguinal dissection for a positive SNB, even in the subgroup with a positive CLND result. The risk of pelvic nodal involvement was low (9·3 per cent). Therefore, inguinal dissection seems a safe first approach to CLND in patients with a positive SNB.

Acknowledgements

D.V. and M.F.M. are joint first authors of this article.
Disclosure: The authors declare no conflict of interest.

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