Superficial Inguinal and Radical Ilioinguinal Lymph Node Dissection in Patients with Palpable Melanoma Metastases to the Groin

An Analysis of Survival and Local Recurrence

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The present study addresses the question whether an extended ilioinguinal dissection as compared to an only superficial inguinal dissection improves survival and/or local tumour control after the appearance of palpable melanoma metastases to the groin. We retrospectively analysed the data of 104 patients with 69 ilioinguinal and 35 superficial inguinal dissections (median follow up 127 months). Prognostic factors of survival and groin recurrence were assessed using Kaplan–Meier estimation and Cox proportional hazards model. By multifactorial analysis, metastatic involvement of two lymph nodes or less was associated with a significantly better survival rate than involvement of >2 or pelvic nodes ($p = 0.0002$). After radical ilioinguinal dissection, patients with extremity-located primaries had a better prognosis than patients with truncal primaries ($p = 0.03$). Tumour infiltration of the ilio-obturator compartment was found to be an independent factor of poor prognosis ($p = 0.0009$). The probability of recurrence in the dissected groin paralleled the number of positive nodes and significantly increased if intransits were observed ($p = 0.0002$). The extent of surgery, Breslow thickness, epidermal ulceration, sex, age and adjuvant chemotherapy neither significantly influenced survival nor local control rates. In summary, when metastatic inguinal nodes become palpable, the presence of pelvic metastases indicates systemic disease. After therapeutic groin dissection, local recurrence and survival depend rather on regional tumour burden than on the extent of surgery.

Presently, the standard procedure for lymph node metastases of cutaneous melanoma of the lower extremities and the lower part of the trunk is a complete node dissection of the affected groin. Since iliac and obturator nodes, the so called 'deep' or 'pelvic' nodes, have been found to be positive in approximately 30% of histological specimens (1–8), the therapeutic procedure for palpably enlarged metastases is an ilioinguinal dissection, i.e. the dissection of both superficial inguinofemoral nodes and iliac and obturator nodes as well. To date, a survival benefit after radical ilioinguinal dissection, as compared to superficial inguinal clearance only, has not been unequivocally demonstrated. Considering the poor prognosis of patients with iliac metastases and the increased lymph-oedema rate after iliac clearance, some surgeons advise to exclusively perform a superficial inguinal node dissection when inguinal nodes are palpably enlarged (6, 7). While in some retrospective studies no survival benefit of radical ilioinguinal dissection was observed (4, 6, 9, 10), others have reported an improved survival with little or no increase of morbidity (3, 8, 11, 12).

Furthermore, also concerning local tumour control, the impact of the extent of dissection (inguinal vs. ilioinguinal) is controversial. Local recurrences were observed in up to 57% after superficial groin dissection (3). Some authors emphasize the importance of ilioinguinal lymphadenectomy for an improved disease control of the lymphadenectomy region (3, 5) while others have questioned a benefit (4, 9). The value of these studies is limited by the fact that only percentages of recurrence were assessed and neither the Kaplan–Meier method nor log rank tests have been applied.

Moreover, most studies have compared heterogeneous populations including patients with positive elective dissections (2, 4, 6–9, 13, 14). This poses a bias to the results as patients with micrometastases (9) or skip metastases to the pelvic nodes (3, 8) often have turned out to be long-term survivors. Thus, surgeons dealing with the specific question

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how to handle an individual patient with palpable metastases of the groin cannot entirely base their decision on the 5-year survival rates reported in such studies. In the present retrospective study, we have exclusively analysed the group of melanoma patients with palpable groin nodes in order to assess the impact of the surgical approach (inguinal vs. ilioinguinal dissection) on local tumour control and on survival.

MATERIAL AND METHODS

We identified 104 consecutive patients with cutaneous melanoma who underwent therapeutic groin dissection at the Martin-Luther-University in Halle for palpable groin metastases without evidence of systemic disease. All of these patients were operated between September 1983 and August 1994. The median interval from the date of lymphadenectomy to reviewing the data was 127 months (range 42–177 months). For 30 patients who were still alive at the time of review the median follow up was 68 months (range 28–141 months). The follow up was closed in March 1998.

Local recurrence after lymphadenectomy was defined as any evidence of recurrent disease within the surgical bed of the nodal dissection including relapses after generalized metastases had become apparent. Intransit metastases were defined as any locoregional cutaneous melanoma relapse occurring at any stage of the disease, excluding relapses in the scar region of the previously performed lymph node dissection.

The general procedure was an ilioinguinal dissection. The inguinal part of this procedure consisted of *en bloc* removal of all lymph nodes within the femoral triangle, the lymph nodes above the inguinal ligament and the nodes anterior and medial to the common and superficial femoral vessels including Cloquet's node. The iliac part of the dissection included the lymphatics of the iliac, hypogastric and obturator vessels. If the deep (iliac and obturator) nodes appeared normal the upper border of the dissection constituted the bifurcation of the iliac vessels. In the case of iliac or obturator node enlargement the dissection was extended up to the aortic bifurcation.

An exclusively superficial (inguinal) dissection was performed in certain patients without clinical or radiological evidence of deep node involvement. This less aggressive operation was selectively applied to elderly patients with cardiopulmonary risk factors especially those with a single small groin metastasis, as they have a lower probability of pelvic metastases. Superficial dissection was also performed in some patients with very thick primary melanomas (> 10 mm) or those who presented with lymph node and locoregional cutaneous metastases as well.

The total number of inguinal node metastases, as proven by routine histology, was counted. It was also registered whether the deep nodes were involved.

For statistical analysis the prognostic variables were categorized as follows: age [≤ 54 years vs. > 54 years (median age)], sex, location of the primary tumour (extremity vs. trunk), Breslow thickness (≤ 1.5 mm vs. 1.5–4 mm vs. > 4 mm), ulceration, type of operation (superficial inguinal vs. radical ilioinguinal dissection). For the nodal tumour burden two categories were built. The whole group of 104 patients with inguinal or ilioinguinal dissections was stratified according to the presence of ≤ 2 superficial metastatic nodes only vs. > 2 superficial nodes or any pelvic metastases. The group of 69 patients with ilioinguinal dissections was stratified according to superficial node metastases vs. both superficial and pelvic metastases. Survival and recurrence probabilities were calculated using the method of Kaplan and Meier (15). Significance was assessed by the log rank test. The Cox proportional hazards model (16) was used to determine which set of independent variables had influenced survival.

RESULTS

Prognostic factors of survival for the whole study population

The 5- and 10-year survival rates after groin dissection were 30.4 and 18.4%, respectively. The median survival time after lymphadenectomy was 23 months. Patients with only 1–2 metastatic nodes had a median survival of 30 months and a 5-year survival of 41.4%. Patients with more than two involved nodes or iliac metastases had a median survival of 14 months and a 5-year survival of 13.9%. Using univariate analysis, the differences between these two groups were statistically significant [crude relative risk (RR) 2.4, 95% confidence interval (CI)—1.5–3.7, $p = 0.0006$). The following features did not significantly influence survival rates: Breslow thickness, epidermal ulceration, location of primary melanoma, age (≤ 54 years vs. > 54 years) and sex; neither had the adjuvant chemotherapy given to 63 patients enhanced survival probability. Finally, the extent of lymph node dissection (inguinal vs. ilioinguinal) did not have a significant effect on survival (Fig. 1). The clinical and histological data of these two treatment groups are shown in Table 1.

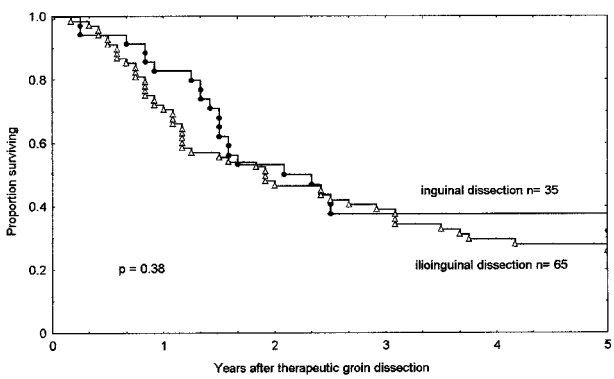

Fig. 1. Survival rates after therapeutic groin dissection by extent of operation (□ inguinal dissection, □ ilioinguinal dissection).

Table 1

Characteristics of 104 patients with groin dissection

Extent of operation	Ilioinguinal dissection	Superficial inguinal dissection
Number of dissections	69 (66.4%)	35 (33.6%)
Median age (years)	50	62
Gender		
Male	26 (37.7%)	11 (31.4%)
Female	43 (62.3%)	24 (68.6%)
Adjuvant therapy	51 (73.9%)	12 (34.3%)
Dacarbacine – monotherapy	7	2
Dacarbacine + interferon α	5	2
Polychemotherapy: (dacarbacine, 5-fluorouracil, vincristine, hydroxycarbamide)	39	8
No adjuvant therapy	18 (26.1%)	23 (56.7%)
Breslow (mm) (median)	3.2	3.7
≤1.5 mm	8 (11.6%)	3 (8.6%)
1.51–4.0 mm	33 (47.8%)	13 (37.1%)
>4.0 mm	20 (29.0%)	14 (40.0%)
Epidermal ulceration		
Ulceration present	34 (53.1%)	11 (36.7%)
Ulceration absent	30 (43.5%)	19 (54.3%)
Growth pattern		
SSM	24	8
NM	27	15
ALM	11	6
UCM	2	3
Location of primary lesion		
Trunk	8 (11.6%)	4 (11.4%)
Extremity	61 (88.4%)	31 (88.6%)
Nodal status		
Median number of histologically identified nodes	9	5
One metastatic node	25 (36.2%)	19 (54.3%)
Two metastatic nodes	12 (17.4%)	8 (22.9%)
More than two metastatic nodes	8 (11.6%)	8 (22.9%)
Iliac metastases	24* (34.8%)	—
Intransit disease	24 (34.8%)	13 (37.1%)

* 22 of 24 patients with deep lymph node metastases had >2 metastatic superficial nodes.

Focusing on the question whether the type of operation was an independent prognostic factor of survival, we applied multifactorial analysis. Again, the extent of node dissection had no influence on survival. Only the number of metastatic nodes (≤ 2 vs. >2 or iliac nodes) was a significant independent predictor of survival. Breslow thickness, epidermal ulceration, location of primary melanoma, age, sex and adjuvant chemotherapy were without significant effect on survival (Table 2).

Prognostic factors of survival for patients with radical ilioinguinal dissections

Of the 69 patients with ilioinguinal dissections, 24 (34.8%) had metastatic involvement of both superficial and pelvic nodes. The latter group had a median survival of 12 months, a 3-year survival rate of 25.0% and a 5-year survival rate of 6.2%. Two patients survived more than 60 months. The remaining 45 patients with superficial lymph node metastases and tumour-free deep nodes had a 5-year survival rate of 36.7% and a median survival of 30 months. These survival differences were significant (Fig. 2). Breslow thickness, epidermal ulceration, location of the primary, age, sex and adjuvant chemotherapy were without significant effect on survival in patients with ilioinguinal dissection.

In the subgroup with deep dissections, using multifactorial analysis, histologically proven metastases of deep nodes added a relative risk of 3.4 (95% CI—1.7–7.0, $p = 0.0009$). Patients with extremity-located primaries had a better prognosis than patients with trunk-located primaries (RR 2.9, 95% CI—1.1–7.5, $p = 0.03$). Breslow thickness, epidermal ulceration, age, sex and adjuvant chemotherapy were without significant effect on survival after ilioinguinal dissection.

Table 2

Risk factors of survival after therapeutic groin dissection by multifactorial analysis

Factor	Category	Adjusted RR	95% CI	p-value
Breslow thickness	1. </= 1.5 mm vs. 2. 1.51–4.0 mm vs. 3. >4.0 mm	1.47	0.95–1.93	0.08
Ulceration	Present or not	1.70	0.75–2.39	0.07
Site of primary tumour	Extremity vs. trunk	1.88	0.87–3.18	0.11
Number of metastatic nodes	1–2 vs. >2 or iliac metastases	2.97	1.69–5.23	0.0002
Age	</= 54 years vs. older	1.7	0.96–3.03	0.07
Sex	Female vs. male	1.09	0.62–1.91	0.76
Adjuvant chemotherapy	Not given vs. given	0.85	0.46–1.58	0.61
Extent of dissection	Inguinal vs. ilioinguinal	1.36	0.70–2.6	0.34

Likelihood ratio test for the model/p = 0.007.

Relapse in the previously dissected lymph node basin for the whole study population

After surgery of palpable lymph node metastases, melanoma recurrence in the dissected lymph node basin is a major concern. A total of 35 (33.6%) out of our 104 patients relapsed in the dissected lymph node basin. The median time interval between inguinal lymphadenectomy and groin recurrence was 9 months (range 1–34 months). The median survival after groin recurrence was 10 months.

Using univariate analysis, the type of operation (inguinal vs. ilioinguinal dissection) did not influence local control of the dissected lymph node basin (Fig. 3). The probability of groin relapse tended to depend on the number of metastatic nodes (results not shown) but this was not statistically significant. Breslow thickness, ulceration, location of the primary melanoma, age, sex and adjuvant chemotherapy had no effect on local control.

Also by multifactorial analysis, the number of metastatic nodes, although not significant, tended to be a predictor of recurrence probability. Again, none of the other above-mentioned factors reached significance (Table 3).

Interestingly, recurrence probability for the dissected nodal basin was significantly higher in those patients who developed intransit disease at any time point of their disease (Fig. 4). The majority of these patients (21 out of 35 with recurrence in the dissected nodal basin) suffered from intransit metastases, 12 presenting with intransits before the appearance of nodal recurrence. In contrast, only 16 out of 69 patients without recurrence in the dissected nodal basin developed intransit metastases in the course of their disease.

DISCUSSION

With respect to survival prognosis, there is still some controversy regarding the influence of ilioinguinal as compared to inguinal dissection in patients with cutaneous malignant melanoma. According to literature data, factors that undoubtedly determine survival rates after therapeutic groin dissection are the number of metastatic lymph nodes (1, 3, 4, 7, 9), tumour spread beyond the node capsule (4, 7, 17) and involvement of the iliac compartment (3, 9, 14).

In contrast to most of these previous reports (2, 4, 6–9, 13, 14), the present study was restricted to patients with clinically apparent inguinal nodes. By uni- and multifactorial analysis, we confirm that survival prognosis after

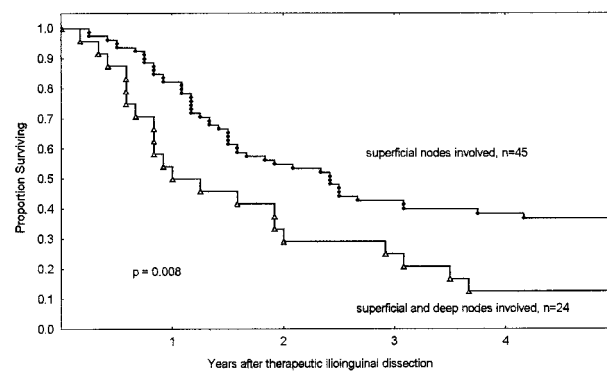

Fig. 2. Survival after radical ilioinguinal dissection by nodal tumour burden.

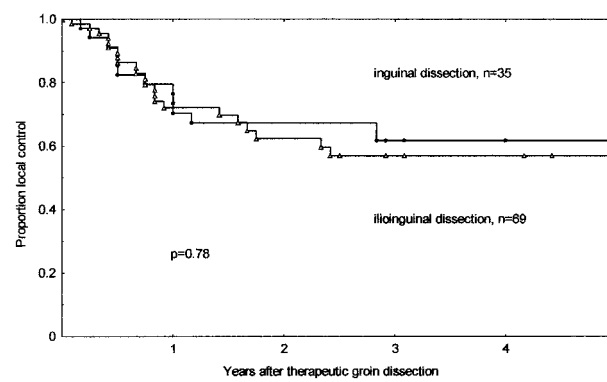

Fig. 3. Local control rate for the groin according to operative procedure (● inguinal dissection, △ ilioinguinal dissection).

Table 3

Risk factors of local recurrence after therapeutic groin dissection by multifactorial analysis

Factor	Category	Adjusted RR	95% CI	p-value
Breslow thickness	1. </= 1.5 mm vs. 2. 1.51–4.0 mm vs. 3. >4.0 mm	0.96	0.54–1.73	0.90
Ulceration	Present or not	1.43	0.65–3.14	0.37
Site of primary tumour	Extremity vs. trunk	0.48	0.11–2.41	0.33
Number of metastatic nodes	1–2 vs. >2 or iliac metastases	2.15	0.95–4.93	0.07
Age	</= 54 years vs. older	1.47	0.67–3.4	0.35
Sex	Female vs. male	1.19	0.65–3.7	0.70
Adjuvant chemotherapy	Not given vs. given	1.48	0.65–3.7	0.37
Extent of dissection	Inguinal vs. ilioinguinal	1.05	0.65–3.7	0.91

Likelihood ratio test for the model/p = 0.60.

therapeutic lymphadenectomy is governed by nodal tumour burden. The presence of only one to two positive inguinal nodes rather than more than two or pelvic nodes turned out to be the key-determinant of longer survival. In contrast, factors known to influence prognosis after primary melanoma (tumour thickness, ulceration and site of primary tumour, age and sex) had lost their prognostic significance after therapeutic groin dissection. Some of the authors have found that these features may sustained their prognostic significance after therapeutic lymph node dissection (8, 18–20). However, their study populations were heterogeneous as they had included patients with both micro- and macrometastases. Besides the present study there is only one more study which has focused on independent prognostic factors in patients with clinically detectable superficial nodes (3). In this study features of the primary tumour were also not significant confirming our data.

Several studies applying only univariate analysis have shown that the more extended ilioinguinal dissection was not of benefit for survival (4, 8–10). Our study confirms these results. Clearly, both our treatment groups were not homogenous. Patients with superficial inguinal dissections were older, had thicker primary melanomas and fewer chemotherapies (Table I). Although these factors were taken into account using multifactorial analysis, some restrictions have to be made, as the iliac tumour burden remains unknown in this group.

Other authors, however, having observed long-term survival rates of > 20% among patients with pelvic metastases (3, 8, 11, 12) concluded that the removal of deep lymph node metastases is worthwhile. Interestingly, all of these studies had included patients with micrometastases from elective dissections or patients with skip metastases (tumour-free superficial nodes), which turned out to have a beneficial effect on long-term survival (3, 8, 11). Moreover, some of these series had included patients with isolated limb perfusion or adjuvant irradiation of the dissected nodal basin (8, 11) which might have added to longer survival.

In the present study, which excluded patients with inguinal micrometastases or skip metastases, all of the 24 individuals with clinically enlarged inguinal metastases and additional pelvic node involvement developed visceral metastases in the course of their disease. Their 5-year survival rate was only 6.2% supporting the ominous outcome after pelvic metastases reported in most previous studies (Table 4). By multifactorial analysis, involvement of the pelvic nodes proved to be an independent factor of poor prognosis.

Generally, only those patients whose deep nodes are invaded by a tumour may benefit from the pelvic part of the dissection. According to the literature, the proportion of positive deep nodes after therapeutic ilioinguinal dissections is approximately 30% (1–8) pointing to the large proportion of 70% unnecessary deep dissections. Moreover, at best 20% of the patients with deep metastases are alive at 5 years. Consequently, the maximal benefit of performing an iliac dissection in terms of cure would be reduced to about 6% when related to the total population of patients with groin metastases. Obviously, the controversy about the extent of lymphadenectomy can only be

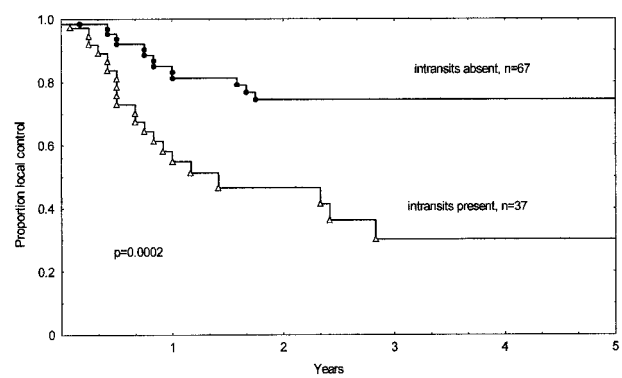

Fig. 4. Influence of intransit disease (at any time point of the disease) on local control in the lymph node basin.

Table 4

Long-term survivors among patients with positive iliac or obturator lymph nodes (literature data)

Reference	No. of patients with positive deep nodes	No. of patients alive at 5 years
Finck et al. (1)	23	4
McCarthy et al. (6)	4	0
Coit et al. (9)	34	1
Jonk et al. (11)	23	3
Karakousis et al. (13)	18	1
Fortner et al. (21)	46	4
Dasmahapatra & Karakousis (22)	10	4
Present study	24	2
Total	182	19 (10.4%)

resolved by a very large prospective trial, which clearly will not be available during the next years.

As a statistically significant survival benefit of ilioinguinal dissection could not be demonstrated in the present study, it becomes very important to consider the additional morbidity due to the pelvic part of this operation. The lymph-oedema rate after iliac clearance was described to be higher after ilioinguinal dissection (2, 3, 5, 10). Regrettably, also with regard to postoperative morbidity, a prospective study comparing inguinal and ilioinguinal dissection is lacking.

In addition, local disease control is of great importance as cutaneous ulceration, lymph oedema and pain considerably impair quality of life. Local recurrence after groin dissection has been reported to occur on average in 27% of the dissections performed (3, 4, 9, 13, 17, 23–25). However, local recurrence is not well defined and is often not recorded if it occurs after the appearance of visceral metastases. Some investigators found that the percentage of recurrences in the previously dissected nodal basin can be reduced by radical ilioinguinal clearance, suggesting that unresected pelvic metastases will become symptomatic when only a superficial inguinal dissection was performed (3, 5). No previous study dealing with prognostic factors of groin recurrence has used Kaplan–Meier-estimates or multifactorial analysis. Applying these from a statistical standpoint preferable methods (26), we were not able to demonstrate improved local control after radical ilioinguinal dissection.

Local recurrence was, however, influenced by regional tumour burden. The groin recurrence probability, although not significant, depended on the number of positive lymph nodes. Patients with iliac metastases, who should benefit most from an iliac dissection in terms of local tumour control, had the highest local failure rate of 59.1%.

Importantly, we found that local recurrence rates significantly increased if intransit metastases were observed. Thus, tumour cells, which are still *en route* to the lymph-node basin at the time of lymphadenectomy, might be a causal factor of recurrence in the dissected nodal basin. The results presented suggest that local control for the lymph node basin does not depend exclusively on the extent of dissection (27) and confirm our previous results. Rather, other factors such as the number of metastatic nodes, extranodal disease, tumour infiltration of the skin, intransit metastases and the quality of the surgical dissection contribute to groin relapse.

CONCLUSION

Besides the demand for adequate staging of patients who are candidates for adjuvant therapy trials, a 3-year survival probability of 25% for our patients with iliac metastases supports the current view of ilioinguinal dissection as the formal surgical procedure for palpable inguinal metastases. Pelvic metastases, which are clinically or radiologically evident, should be excised since therapeutic alternatives are lacking.

However, as no disadvantage could be demonstrated, a superficial inguinal dissection seems to be justified in selected patients with palpable superficial nodes who have no evidence of pelvic metastases. These are patients presenting with a higher general morbidity, pre-existing oedema of the leg or intransit metastases.

Regional tumour burden seems to predict not only survival but also local disease control. In the present study, recurrence in the dissected nodal basin correlated with both nodal tumour load and the appearance of intransit metastases. Since patients with more than two inguinal or pelvic metastases had a probability of recurrence in the nodal basin of $> 50\%$, adjuvant radiation therapy may be beneficial for this subgroup.

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