Recurrence and survival after neck dissections in cutaneous head and neck melanoma

Peter Stemann Andersen, Annette Hougaard Chakera, Andreas Key Milan Thamsborg, Stig-Frederik Trojahn Kølle, Grethe Schmidt, Helle Klyver & Krzysztof Tadeusz Drzewiecki

ABSTRACT

INTRODUCTION: An important prognostic factor in head and neck melanoma is the status of the regional lymph nodes since the presence of metastatic disease in the nodes greatly aggravates the prognosis. There is no consensus on the surgical treatment algorithm for this group. Our aim was to study if there is a difference in nodal recurrence and survival after radical, modified or selective neck dissection.

METHODS: A total of 57 patients treated for regional metastases of head and neck melanoma were analysed retrospectively with respect to type of neck dissection, use of sentinel node biopsy, nodal recurrence and survival.

RESULTS: After a median 127-month (range: 22–290) follow-up period, we showed that there was no significant difference in nodal recurrence between three different dissection groups (11% for radical node dissection, 24% for modified radical node dissection and 23% for selective node dissection, $p > 0.05$). No significant difference in five-year survival was observed between the dissection types (56% for radical node dissection, 61% for modified radical node dissection and 48% for selective node dissection, $p = 0.613$). Multivariate and univariate analysis revealed that patients with metastatic deposits in sentinel nodes had a better survival than patients with clinically palpable nodes (five-year survival rate: 70% versus 36%, $p = 0.008$).

CONCLUSION: The extent of neck dissection does not significantly influence the rate of recurrence or survival. This study indicates that there is a survival benefit for patients who undergo completion lymph node dissection following a positive sentinel node biopsy.

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One of the most important prognostic factors in melanoma is the status of the regional lymph nodes [1, 2]; presence of metastatic disease in the nodes greatly aggravates the prognosis [3]. A previous study from our institution describes an austere five-year survival rate of 27% in patients with head and neck melanoma who have regional lymph node metastasis [4].

The sentinel node biopsy (SNB) procedure has changed the standard surgical care of patients with melanoma [5]. Leong et al concluded that SNB is a reliable procedure for staging of head and neck melanoma [6]. There is consensus that a completion lymph node dissection (CLND) should be performed if the sentinel node (SN) contains metastatic deposits as it is regarded as the best option available to control regional metastatic disease [6-8]. There is still no consensus regarding the extent of the regional node dissection in these patients.

Radical neck dissection (RND), including removal of lymph nodes in levels I-V as well as the sternocleidomastoid muscle (SCM), the internal jugular vein (IJV) and the spinal accessory nerve (SAN), has historically been regarded as the gold standard [8-10]. However, this extensive procedure has a high morbidity. Some studies therefore advocate the use of a more selective approach where selected structures and even specific lymph node groups are preserved in order to diminish post-operative morbidity [11-14].

Recurrence rates following the different types of neck dissections are not well investigated. Reports published throughout the past three decades indicate that the overall regional nodal recurrence rate varies between 0% and 43% [9, 11-13, 15-22].

The purpose of the present retrospective study was to compare the three types of neck dissection in terms of the rate of regional nodal recurrence and disease-specific survival in 57 patients with cutaneous head and neck melanoma with clinically enlarged lymph nodes or micro-metastases to the lymph nodes.

METHODS

Reviewed for inclusion were the records of 60 consecutive patients with cutaneous melanoma on the head and neck and with regional lymph node metastases. All patients underwent neck dissection at the Department of Plastic Surgery, Rigshospitalet, between 1983 and 2009. The exclusion criteria were mucosal melanoma, ocular melanoma, other simultaneous cancer, unknown primary tumour or presence of distant metastases at the time of neck dissection. A total of 57 subjects were included in the study; 43 males (75%) and 14 females (25%); median age of 66 years (7-88 years) at the time of treatment of their primary tumour.

Clinical and epidemiological data were compiled from the Danish Melanoma Group Database, which prospectively collects various clinical and pathological data.

ORIGINAL ARTICLE

Department of Plastic Surgery, Breast Surgery and Burns Treatment, Rigshospitalet

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TABLE 1

Clinical and epidemiological characteristics (N = 57).

Gender, n (%)	
Male	43 (75)
Female	14 (25)
Age, median (range), yrs	66 (7-88)
Melanoma location, n (%)	
Scalp/hair-bearing area	11 (19)
Right ear	10 (18)
Left ear	3 (6)
Facial region, incl. frontal area	23 (40)
Posterior collum	3 (5)
Anterior collum	7 (12)
Excision margin, n (%)	
1 cm	8 (14)
2 cm	46 (81)
4 cm	1 (2)
5 cm	1 (2)
Unknown	1 (2)
Breslow thickness, n (%)	
≤ 1.00 mm	5 (9)
1.01-2.00 mm	10 (18)
2.01-4.00 mm	13 (23)
> 4.00 mm	14 (24)
Not measurable	15 (26)
Breslow thickness, median (range), mm	2.8 (0.5-18.1)

Follow-up data were collected retrospectively from the hospital records, including pathology reports.

No elective (prophylactic) lymph node dissections were performed at our institution. Prior to the use of SN biopsy, patients underwent therapeutic lymph node dissection (TLND). The extent of the lymph node dissection depended on the location of the primary melanoma and the extent of the disease. From 1998 and onwards, SNB has been the standard staging procedure at our institution. The procedure is performed in all patients with melanomas above 1 mm in thickness, or thinner melanomas with ulceration or Clark level IV-V. After the advent of the SNB technique, one of the more selective neck dissections has primarily been used.

TABLE 3

Estimated melanoma-specific overall survival and five-year survival from time of first neck dissection.

	Overall survival, months		5-year survival rate, %	χ^2-test	p-value
	mean	median			
RND	130	72	56		
MRND	45	–[a]	61		
SND	53	44	48		
Overall	112	56	49	0.980	0.613

MRND = modified radical node dissection; RND = radical node dissection; SND = selective node dissection.
a) Could not be calculated since half the MRND population has not deceased

A total of 70 lymph node dissections were performed in the 57 patients. Eleven patients underwent two dissections, and two underwent three dissections. All secondary dissections were performed due to recurrent nodal disease in a previously dissected regional lymph node basin in the neck ("neck failure").

Definitions

Synchronous metastases were defined as metastases to regional lymph nodes diagnosed simultaneously with or within six months of primary treatment of melanoma – conversely metachronous metastases were defined as metastases diagnosed more than six months after primary treatment of melanoma. Radical neck dissection was defined as a unilateral neck lymphadenectomy of levels I through V including the following non-lymphatic structures: the SCM, the SAN and the IJV.

Modified radical neck dissection was defined as unilateral lymphadenectomy of levels I-V and preservation of one or more of the non-lymphatic structures mentioned above. Selective node dissection was defined as unilateral lymphadenectomy with preservation of one or more lymph node levels relative to a modified radical neck dissection.

TABLE 2

Timing of neck dissection, nodes removed, and use of parotidectomy.

	RND (N = 9)	MRND (N = 17)	SND (N = 31)	Overall (N = 57)
Patients with synchronous nodal metastases, n (%)	2 (22)	12 (71)	20 (65)	34 (60)
Patients with metachronous nodal metastases, n (%)	7 (78)	5 (29)	11 (35)	23 (40)
Positive sentinel node biopsy, n (%)	0 (0)	12 (71)	11 (35)	23 (40)
Time from wide excision of primary tumour to first neck dissection, median (range), months	11 (4-50)	1 (0-63)	3 (0-54)	4 (0-63)
Nodes removed, median (range), with metastases, median (range), n[a]	11 (6-25) 3 (1-8)	23 (6-112) 1 (0-6)	9 (1-35) 1 (0-4)	3 (1-112) 1 (0-8)
Superficial parotidectomy, n (%)	9 (100)	17 (100)	26 (84)	55 (96)

MRND = modified radical node dissection; RND = radical node dissection; SND = selective node dissection.
a) In the therapeutical lymph node dissection specimen and the completion lymph node dissection specimen.

Statistics

Survival times were calculated from the time of first lymphadenectomy for regional lymph node metastases to death or last follow-up. Melanoma-specific overall survival and survival rates, including five-year survival rates, were estimated using the Kaplan-Meier method. When estimating the melanoma-specific survival, death due to other causes than melanoma was registered as censored observations. Survival curves were compared using the univariate log-rank comparison test. A proportional hazards regression analysis (Cox regression model) was performed in order to assess the influence of other prognostic factors on survival, well aware that the number of patients in the subgroups was small. The regression analysis was calculated from the time of the first neck dissection. Nodal recurrence data were compared in categories with Fisher's two-tailed exact test.

All statistical analyses were conducted with SPSS for Mackintosh software (Statistical Package for Social Science, IBM Inc. version 20). A p-value of 0.05 or less was considered statistically significant.

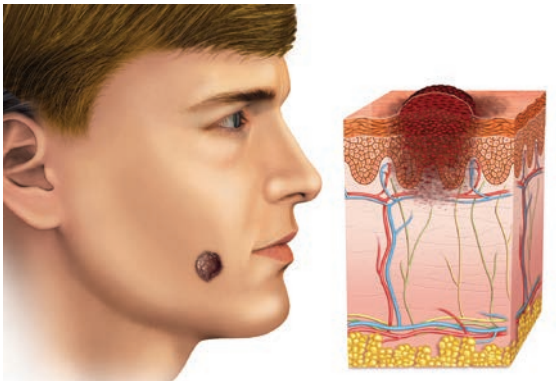
Trial registration: not relevant.

RESULTS

Lymphadenectomy

Clinical and epidemiological characteristics are visualised in **Table 1**. Among the 57 patients, 16% underwent RND, 30% modified radical node dissection (MRND) and 54% selective node dissection (SND) (**Table 2**). A total of 34 (60%) of the 57 patients underwent therapeutic lymph neck dissection due to palpable regional lymph nodes, 23 (40%) due to metastatic deposits in the SNs. In total, 26 patients underwent SNB. Three of these patients had no SN metastases, but later developed palpable metastases and therefore underwent a therapeutic neck dissection; the remaining 23 patients had a completion neck dissection due to a positive SN. Among the 23 patients in the SN-positive group, 12 underwent a completion MRND and 11 a completion SND (Table 2). Six of the 23 SN-positive patients (26%) had further metastatic non-sentinel lymph nodes in the neck specimens.

In all, 34 of the 57 patients (60%) had a neck dissection due to synchronous regional nodal metastases, 23 (40%) due to metachronous metastases; the median times from wide excision of primary melanoma to first neck dissection were 11 months (range: 4-50 months) in the RND group; one month (0-63 months) in the MRND group; and three months (range: 0-54 months) in the SND group (Table 2). The SN-positive group had a median of one (range: 1-6) metastatic node(s) removed totally, whereas the therapeutically treated group with palpable metastases had a median of one (range: 1-8) metastatic node(s) in the neck dissection specimen.



Cutaneous facial melanoma.

Recurrence

During the clinical follow-up time of median 39 months (7-117 months), 12 patients (21%) had regional nodal recurrence ("neck failure"); one in the RND group (11%), four in the MRND group (24%) and seven in the SND group (23%). Comparison of the three groups in regards to number of nodal recurrences revealed no statistically significant difference between the groups (two-tailed Fisher's exact test; $p > 0.05$). The median time from the first neck dissection to diagnosis of regional nodal recurrence was six months overall (1-67 months); six months (range: 0-6 months) in the RND group, 5.5 months (range: 3-31 months) in the MRND group, and eight months (range: 1-67 months) in the SND group.

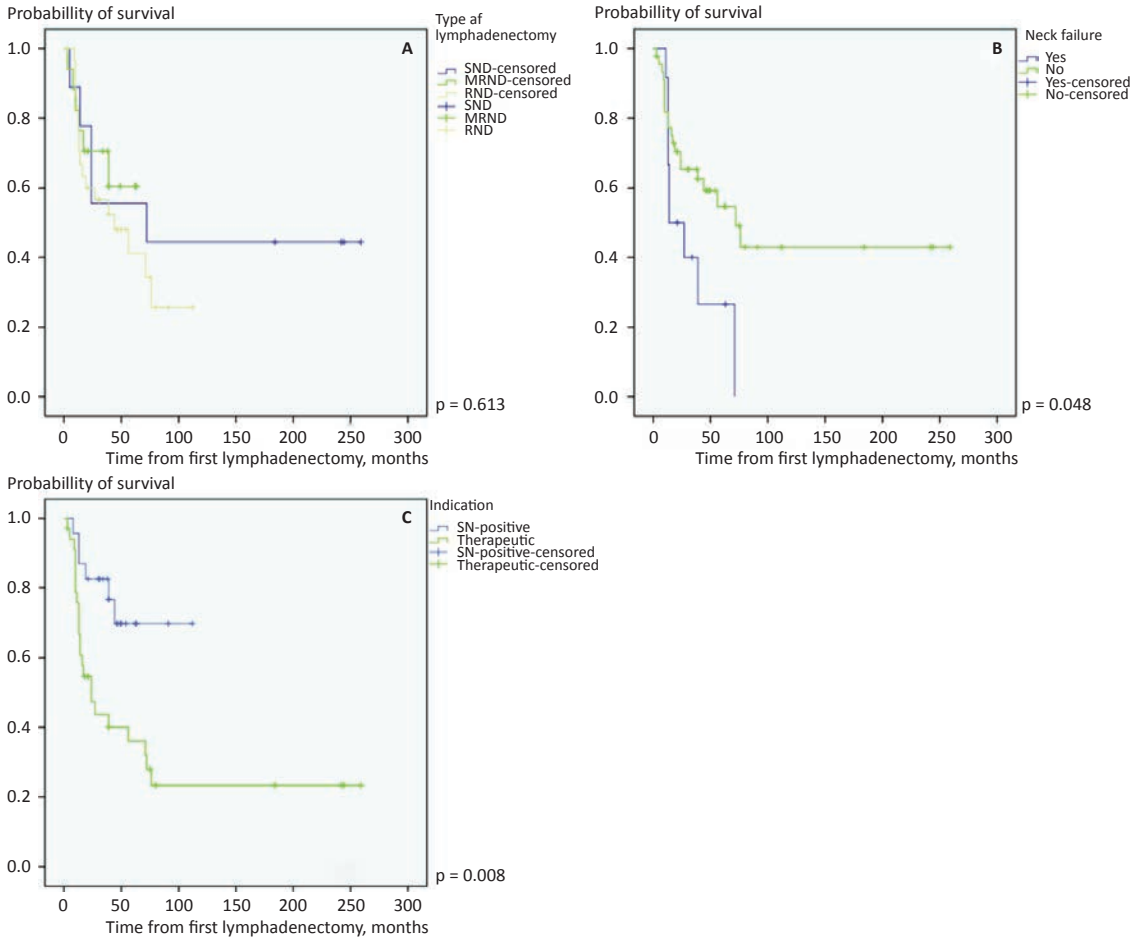
Survival

During the follow-up period from time of primary treatment to censoring or death a median 127 months (range: 22-290 months) later, 33 of 57 (58%) patients deceased; 26 due to metastasising melanoma, four due to non-melanoma reasons and three due to unknown reasons (these three were attributed as deaths due to melanoma). For the whole study group, melanoma-specific survival from the time of first neck dissection was a median 56 months (95% confidence interval (CI): 12.3-99.6) (**Table 3**). The melanoma-specific five-year survival from the time of first neck dissection overall was 49% – and it was 56%, 61% and 48% in the RND, MRND and SND groups, respectively (Table 3). No significant difference in survival between the three groups was seen (log-rank test, $p = 0.613$) (**Figure 1**A).

The melanoma-specific survival from first lymphadenectomy for the 12 patients (21%) who had neck failure was a median of 14 months (95% CI: 0.0-28.8) compared with 72 months (95% CI: 36.4-107.5) in the remaining 45 patients (79%) (Figure 1B). This difference was significant ($p = 0.048$).

When comparing the 23 patients (40%) having MRND or SND after positive SNB with the remaining 34 patients having neck dissection due to palpable lymph node meta-

FIGURE 1



Melanoma-specific survival from time of first neck dissection (N = 57). **A.** The different neck dissection groups (RND: n = 7, MRND: n = 17, SND: n = 31). **B.** The neck failure group and non-neck failure group (neck failure: n = 12, non-neck failure: n = 45). **C.** The SN-positive node group and the therapeutically treated group (SN-positive group: n = 23, therapeutically treated group; n = 34).

MRND = modified radical node dissection; RND = radical node dissection; SN = sentinel node; SND = selective node dissection.

stases (Figure 1C), there was a significant difference in estimated melanoma-specific survival calculated from the time of the first neck dissection; the five-year survival in the SN-positive group was 70% versus 36% in the group with palpable lymph nodes (log rank, p = 0.008).

According to the regression analysis, the SN-positive group had a significantly better outcome as regards to disease specific survival (a regression coefficient of –1.533, a p-value of 0.010 with a hazard ratio of 0.216 (95.0% CI: 0.067-0.690)). Sex, type of neck dissection, Breslow thickness (in categories), the presence of ulceration, and the presence of neck failure had no influence on survival (p ≥ 0.05).

DISCUSSION

From 1983 to 2009, 57 patients with cutaneous head and neck melanoma and regional lymph node metastases underwent radical node dissection, modified radical node dissection or selective node dissection of the neck.

Overall, 21% of the patients developed regional nodal recurrence (neck failure) following the first neck dissection. This number is within the range observed in other studies where loco-regional recurrences are reported to range between 0% and 43% [9, 11-13, 15-22]. Although the regional nodal recurrence rate for patients undergoing MRND and SND was more than double that of patients having RND, we did not detect any statistically significant difference; RND: 11% versus MRND: 24% versus SND: 23% (p > 0.05). The rates of neck failure in the three procedures are similar to those published by Martin et al [23] and White et al [11]. The time from the first neck dissection to diagnosis of nodal regional recurrence did not differ between the three groups (RND; a median six months, MRND; a median 5.5 months, SND a median eight months). As expected, we experienced that the neck failure group had a poorer prognosis than the non-neck failure group in univariate analysis (p = 0.048). This was not confirmed in the multivariate ana-

lysis. Although it was not statistically significant, the same trend was reported by O'Brien [9].

The melanoma-specific survival from the time of the first lymphadenectomy or CLND of a median of 56 months and the overall five-year survival of 49% were also comparable to those reported by other studies [11, 12, 15, 17]. No statistically significant difference in melanoma-specific survival was observed between the three neck dissection types (p = 0.613) – this was also the conclusion of several other studies [11, 12, 15, 17].

The use of SNB in the head and neck area is challenging due to the complicated and unpredictable lymph drainage patterns; a usually higher false negative rate compared with SNB performed for melanomas located elsewhere can be expected [24, 25]. However, in a larger study Erman et al [26] and Parret et al [25] concluded that SNB in the head and neck area is accurate, and its results are of prognostic importance. In the present study, 23 patients underwent neck dissection after positive SN. Multivariate analysis revealed that patients who had a neck dissection due to metastatic deposits in SN had a significantly better survival than the patients who had a neck dissection due to clinically palpable metastases when calculating from the time of the neck dissection (p = .010). A similar result was reported by Martin et al [23]. The five-year survival rate for the patients with subclinical SN metastases was 70% versus 36% for patients with clinically palpable lymph nodes. One could argue that the reason for the difference in outcome for these two groups might be a difference in disease volume. However, in this study, 26% had metastatic lymph nodes in the CLND specimens after SNB, meaning that many of the patients treated with SND/MRND also had high-volume disease. Despite this, they did not have more regional lymph node recurrences. Also, the median number of metastatic lymph nodes removed in the dissection specimens of the SN-positive group was equal to the median number of metastatic nodes removed in the dissection specimens of the therapeutically treated group (both had a median of 1, and ranges 1-6 and 1-8, respectively). Hence, the volume of disease was comparable in the two groups. A similar survival advantage of early CLND was published by de Rosa et al and Parrett et al [24, 25]. Furthermore, a resent large study by Morton et al concluded that biopsy-based management prolongs melanoma-specific survival for patients with nodal metastases from intermediate-thickness melanomas (1.20-3.50 mm). This is, however, not specified to specific regions [27].

The limitations of this study are the small population, heterogeneous groups (with or without SNB procedure) and the retrospective design. Accepting these weaknesses allowed us to compare different treatments over the years.

CONCLUSION

Taking the before-mentioned limitations into account, the results indicate that the extent of neck lymph node dissection does not significantly influence either the nodal recurrence rate or the survival of the patients with regional lymph node metastases of cutaneous melanoma in the head and neck area. In our materiel, patients with positive SN benefitted from early CLND as regards to recurrence and survival – however, larger prospective studies are required to confirm our results.

CORRESPONDENCE: *Peter Stemann Andersen,* Klinik for Plastikkirurgi, Brystkirurgi og Brandsårsbehandling, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark. E-mail: stemann@gmail.com

A full reference list can be obtained by contacting the corresponding author.

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