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Total versus superficial parotidectomy for stage III melanoma

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Abstract

Background: The primary purpose of this study was to describe the parotid recurrence rates after superficial and total parotidectomy.

Methods: A retrospective cohort study was performed on patients with cutaneous melanoma metastatic to the parotid gland who underwent parotidectomy from 1998 through 2014. Primary outcome was parotid bed recurrence. Secondary outcomes were facial nerve function postoperatively and at last follow-up.

Results: One hundred twenty-nine patients were included in the study. Thirty-four patients (26%) underwent a total parotidectomy and 95 patients underwent superficial parotidectomy. Twelve patients (13%) developed parotid bed recurrence after superficial parotidectomy alone versus zero after total parotidectomy ($P = .035$). Facial nerve function, clinically detected disease, stage, and adjuvant treatment were not statistically different between the groups ($P = .32$, .32, .13, and 0.99, respectively).

Conclusion: Parotid bed melanoma recurrence was more common after superficial parotidectomy compared to total parotidectomy, and recurrence resulted in significant facial nerve functional deficit. Our results support total parotidectomy when metastatic melanoma involves the parotid nodal basin.

KEYWORDS
facial nerve function, malignant melanoma, regional recurrence, superficial parotidectomy, total parotidectomy

1 | INTRODUCTION

Over 144 860 new cases of melanoma, over 76 000 of which are invasive, will be diagnosed in the United States in 2016.[1] Living with melanoma is common with over 1.2 million melanoma survivors estimated in the United States alone. It is the third most prevalent cancer in men and the fifth most prevalent cancer in women in the United States.[2] Hence, quality of life after treatment is a valid consideration.

Although metastasis to the parotid gland is less common than to the cervical lymphatics, parotid lymphatic management is crucial as progression of parotid disease places facial nerve function at risk. The lymphatic system develops before the formation of the parotid capsule; therefore, lymph nodes are incorporated into the parotid parenchyma and without regard to facial nerve anatomy, as the facial nerve does not represent a fascial boundary to the lymphatic system.[3,4]

Cadaveric studies have demonstrated that lymph nodes are consistently present both superficial and deep to the facial nerve within the parotid gland.[5–7] When a total parotidectomy has been performed for metastatic melanoma and other parotid malignancy, metastatic disease has been found in lymph nodes deep to the facial nerve.[4,8,9] For metastatic melanoma, a 7% parotid bed recurrence rate after superficial parotidectomy is quoted in the literature,[10] compared with a 0% parotid bed recurrence rate after total parotidectomy.[8]

Despite the evidence that melanoma does metastasize to the deep lobe of the parotid gland and that parotid bed recurrence may be reduced with total parotidectomy, superficial parotidectomy alone is the recommended treatment in the current National Comprehensive

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Cancer Network guidelines.[11] Although studies have reported recurrence rates after superficial or total parotidectomy, no study has directly compared recurrence rates after these 2 surgeries.

Our primary purpose for this study was to describe parotid bed recurrence rates after superficial and total parotidectomy for stage III metastatic melanoma. The secondary purpose was to describe facial nerve function immediately postoperatively and at last follow-up.

2 | MATERIALS AND METHODS

Approval for this study was granted by the University of Michigan Medical School Institutional Review Board for Human Subject Research (HUM00048768). Our melanoma database was queried for patients diagnosed with primary cutaneous melanoma of the head and neck or melanoma metastatic to the parotid gland with unknown primary who underwent initial parotidectomy, either superficial or total, from 1998 through 2014. Patients were included in the study if they had biopsy-confirmed metastatic melanoma to their parotid gland either on fine-needle aspiration (performed when a palpable mass was detected on physical examination) or sentinel lymph node biopsy (occult nodal disease). Primary excision, sentinel lymph node biopsy, and/or other prior excision of the primary site may have been done at another institution and was not an exclusion criterion, however, all parotidectomies were performed at the University of Michigan by surgeons who were members of the University of Michigan Multidisciplinary Melanoma Tumor Board and regularly treated cutaneous malignancy, and/or otolaryngologists with head and neck surgery fellowship training.

Total parotidectomy was defined as removal of parotid tissue deep to the facial nerve in addition to removing gland superficial to the facial nerve. Typically, superficial parotidectomy, tracing each branch of the facial nerve, was performed first. Once superficial parotidectomy was complete, parotid tissue deep to the facial nerve was removed by carefully dissecting glandular tissue free of the overlying facial nerve. The procedure was altered as needed if there was clinically detected disease in both the superficial and deep lobe, preventing superficial and deep parotid tissue from being removed separately while removing the tumor en bloc.

The decision to perform total parotidectomy was surgeon dependent. One of our surgeons, Dr McLean, underwent a practice shift and began performing total parotidectomy on all patients with melanoma metastatic to the parotid gland in 2013. The remainder of the surgeons performed total parotidectomy when there was concern for metastatic disease deep to the facial nerve. For these surgeons, the decision to perform total parotidectomy was made preoperatively or intraoperatively depending on if there was preoperative imaging or intraoperative findings suggestive of possible disease deep to the facial nerve.

Demographics and clinical course/outcome measures were confirmed via the electronic medical records by manual abstraction. Interventions compared were superficial and total parotidectomy, which was determined by review of the surgeon's operative report. Primary outcome was parotid bed recurrence, confirmed by biopsy in all cases except 1 case that was confirmed with imaging. Variables were clinically detected versus occult nodal disease, stage, adjuvant treatment, and length of follow-up. All patients were pathologically staged using the American Joint Committee on Cancer seventh edition staging criteria.[12] Chemotherapy, immunotherapy, and radiation were all considered adjuvant treatment. Adjuvant treatment had to occur after surgery and before any recurrence to be included in this study.

Secondary outcomes were facial nerve function postoperatively and at last follow-up. Facial nerve function was classified as House-Brackmann 1-3 or 4-6.[13] Inpatient and outpatient postoperative notes were reviewed to identify postoperative facial nerve function and postoperative complications. Temporary facial asymmetry with full recovery of function was categorized based on worst deficit. If the facial nerve examination was not documented postoperatively, then the patient was excluded from analyses of facial nerve function. Only complications because of parotidectomy or general anesthesia were included. Complications because of neck dissection, such as cranial nerve XI injury, were not included when calculating the complication rates. Complications occurring during admission and after discharge within the first 3 months postoperatively were included.

Statistical analyses were performed using Microsoft Excel (Microsoft, Redmond, WA) and SPSS version 23 (IBM, Armonk, NY). The Fisher exact tests (for categorical variables) and Mann-Whitney *U* tests (for continuous variables) were used to assess statistically significant differences between patients undergoing superficial and total parotidectomy. Log-rank survival analysis was performed for parotid recurrence. A *P* value of .05 was considered statistically significant.

3 | RESULTS

One hundred twenty-nine patients underwent parotidectomy for metastatic melanoma. Thirty-four patients (26%) underwent total and 95 patients (74%) underwent superficial parotidectomy. Median follow-up was 22 months. See Table 1 for additional demographic data. Twelve patients (13%) developed parotid bed recurrence after superficial parotidectomy versus zero after total parotidectomy (Fisher exact test $P = .035$; Table 1). Survival analysis, censoring patients lost to follow-up, showed no statistically significant difference between interventions ($P = .10$; Figure 1).

Of the patients who had recurrences in the parotid bed, 3 (25%) had clinically detected (palpable) disease before superficial parotidectomy. Thirty-three percent of the patients had stage IIIa disease, 17% had stage IIIb, and 50% had stage IIIc. Twenty-five percent of the patients had adjuvant treatment before parotid bed recurrence, including radiation (n = 1), interferon (n = 1), and combination immune and chemotherapy (n = 1). Primary tumor characteristics, nodal disease burden, and adjuvant treatment were compared between patients whose cancer did and did not recur after superficial parotidectomy (Table 2). There were no significant differences in primary tumor characteristics or adjuvant treatment. The only significant difference was in the rate of N3 nodal disease ($P = .03$; Table 2).

TABLE 1 Comparison of variables by intervention (superficial versus total parotidectomy)

	Superficial parotidectomy n = 95[74] no. of patients (%)	Total Parotidectomy n = 34[26] no. of patients (%)	*P* value
Age at diagnosis	60 y	58 y	.68
Male	68 (72)	25 (74)	0.99
Length of follow-up	24 mo	16 mo	**.05**
Stage 3a	31 (33)	8 (24)	
Stage 3b	35 (36)	9 (26)	
Stage 3c	29 (31)	17 (50)	.13
Clinically detected disease	40 (42)	18 (53)	.32
Adjuvant treatment (all)	35 (36)	12 (35)	0.99
Radiotherapy	10 (11)	8 (24)	.08
Chemotherapy	0 (0)	1 (3)	.26
Immune therapy	23 (24)	2 (6)	**.02**
Combined	2 (2)	1 (3)	0.99
Facial nerve HB 1-3	68 (97)	30 (91)	
Facial nerve HB 4-6	2 (3)	3 (9)	.32
Complications	10 (11)	3 (9)	0.99
Parotid recurrence	12 (13) [3.4; 6.0-19.3]	0	**.04**

Abbreviation: HB, House-Brackmann Grading System.
Values shown as number of patients (%) except for age and length of follow-up, which are median values. For parotid recurrence, SE with 95% confidence interval (CI) is shown as [SE; 95% CI range]. Twenty-five patients who underwent superficial parotidectomy did not have facial nerve function documented. One patient who underwent total parotidectomy presented before surgery with facial paralysis. These 26 patients were excluded from facial nerve statistical analyses.
Figures in boldface indicate statistical significance.

Facial nerve function, complication rate, clinically detected versus occult nodal disease, stage, and adjuvant treatment, if administered, were not statistically different between groups (Table 1). When the type of adjuvant treatment was examined, significantly more patients who underwent superficial parotidectomy underwent adjuvant immune therapy with interferon (Table 1). The rate of radiotherapy, chemotherapy, and combined modality therapy was not significantly different between the groups (Table 1). Interferon was the only immune therapy that the patients in this study received.

The average length of follow-up in the superficial parotidectomy group was shorter than the total parotidectomy group (24 months vs 16 months; $P = .05$; Table 1), which is at least partially because there were more total parotidectomies performed in 2013 and 2014.

Twenty-five patients who underwent superficial parotidectomy had no postoperative facial nerve function documented and were, therefore, excluded from facial nerve function analyses. On the House-Brackmann Grading System, 2 patients had a grade of 4 or greater in the early postoperative period after superficial parotidectomy. Neither was due to an intraoperatively documented tumor on or surrounding the facial nerve. One patient regained complete eye closure over the first 6 months of follow-up. The other had no documented improvement in facial nerve function throughout their follow-up. Four patients were House-Brackmann grade 4 or greater in the early postoperative period after total parotidectomy. All 4 cases were due to tumor encasement of the facial nerve with intraoperative removal of the upper division (n = 2) or main trunk (n = 2). One of these patients was excluded

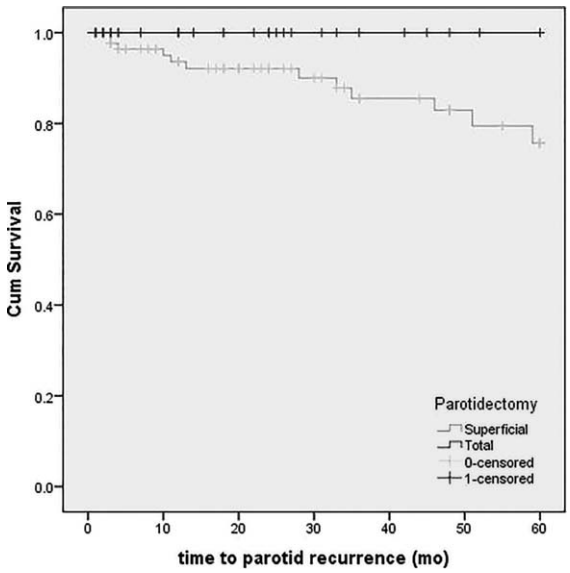

FIGURE 1 Parotid bed recurrence-free survival; $P = .10$

TABLE 2 Comparison of variables in patients who did and did not recur after superficial parotidectomy

	Parotid recurrence n = 12[13] no. of patients (%)	No parotid recurrence n = 84[87] no. of patients (%)	*P* value
Primary location			
Scalp/forehead	6 (50)	27 (34)	.34
Temple/periorbital	1 (8)	16 (20)	.45
Cheek	4 (33)	16 (20)	.45
Ear	0 (0)	17 (22)	.11
Nose/lip	1 (8)	0 (0)	.13
Neck	0 (0)	3 (4)	0.99
Melanoma subtype			
Nodular	3 (30)	22 (31)	0.99
Desmoplastic	1 (10)	4 (6)	.49
T classification			
T1	5 (41)	13 (17)	.12
T2	2 (17)	18 (25)	.72
T3	3 (25)	27 (37)	.53
T4	2 (17)	15 (21)	0.99
Ulceration present	2 (17)	27 (42)	.12
N classification			
N1	4 (33)	42 (50)	.36
N2	2 (17)	25 (30)	.5
N3	6 (50)	17 (20)	**.03**
Clinically detected disease	4 (33)	36 (43)	.76
Satellitosis	3 (50)	7 (41)	0.99
Adjuvant treatment			
Any	3 (25)	32 (38)	.53
Radiation	1 (8)	9 (11)	0.99
Interferon	1 (8)	22 (26)	.28

The primary tumor location was unknown in 5 patients who did not recur in the parotid bed after superficial parotidectomy. A melanoma subtype was not characterized for 14 patients, 12 of which did not recur. The depth of invasion was not documented for 11 primary tumors that did not recur. The presence or absence of ulceration was not documented in an additional 8 patients who did not recur. All percentages and *P* values were calculated using only cases in which this information was provided. Satellitosis is defined by American Joint Committee on Cancer (AJCC) staging guidelines and, thus, the denominator for percentages was total N3 disease. Values shown as number of patients (%).
Figures in boldface indicate statistical significance.

from facial nerve function analyses because they presented preoperatively, before the initial parotidectomy, with facial paralysis. See Table 1 for complete postoperative facial nerve function results. Of the 12 patients who had parotid bed recurrence, 10 had facial nerve function documented after recurrence, 5 of whom developed complete facial nerve paralysis because of recurrent melanoma.

Complications in the total parotidectomy group were: delayed wound healing (n = 1); rhabdomyolysis without sequelae (n = 1); and fall with radius fracture (n = 1). Complications in the superficial parotidectomy group were: seroma or hematoma (n = 3); delayed wound healing (n = 2); urinary tract infection (n = 2); pneumonia (n = 1); rhabdomyolysis requiring temporary hemodialysis (n = 1); and pulmonary edema (n = 1; Table 1).

4 | DISCUSSION

Our results show a reduced parotid bed recurrence rate after total parotidectomy compared to superficial parotidectomy for metastatic melanoma to the parotid gland. Additionally, no increased morbidity was associated with total parotidectomy compared to superficial parotidectomy in our cohort. These findings are consistent with the single prior report of total parotidectomy for metastatic melanoma, which also showed no recurrences in the parotid bed.[8] Reduced parotid bed recurrence is particularly important in the head and neck as optimal control of regional disease and patient quality of life are likely linked and clinically significant.

High-level evidence is lacking to precisely quantify the impact of parotid recurrence on quality of life. However, facial nerve function is important to patient quality of life and House-Brackmann scores have been inversely related to health-related quality of life.[14] It can be inferred that parotid bed recurrence with an associated 42% risk of facial paralysis in our cohort negatively impacted patient quality of life.

Primary tumor characteristics predictive of parotid bed recurrence after superficial parotidectomy would assist in selecting patients for total parotidectomy. Unfortunately, we were unable to identify any such characteristics in our cohort. Nodal disease burden was greater in patients who recurred in their parotid bed after superficial parotidectomy; however, this information is usually not known until after

parotidectomy is complete, so it is of limited use in selecting who should undergo total parotidectomy. This is an area in which additional research could provide more guidance on selecting patients for total parotidectomy.

It is important to carefully consider the potential for additional morbidity associated with total versus superficial parotidectomy. Given the more extensive facial nerve dissection required for total parotidectomy, postoperative facial nerve function is an important endpoint for consideration. Our results showed no increased facial asymmetry after total parotidectomy compared to superficial parotidectomy. We speculate that total parotidectomy did not result in greater facial nerve injury than superficial parotidectomy because the majority of risk to the facial nerve was during main trunk identification and initial dissection to delineate each branch. Deep lobe parotid excision usually occurred after all branches of the facial nerve were already clearly delineated and required only minimal freeing of the parotid gland from the underside of the facial nerve. Therefore, there was not significant additional manipulation of the nerve and any additional manipulation occurred with all nerve branches fully visualized. Similarly, other complication rates were equivalent between the 2 interventions. These findings are consistent with the single previous report of total parotidectomy for melanoma.[8]

Increased time required for surgery with subsequent longer anesthetic is another potential source of morbidity. In our cohort, no increased complication rate was identified because of longer surgical time. Still, total parotidectomy does take more time, which may be an important consideration especially in patients with high comorbidities. Finally, increased parotid gland removal results in increased soft tissue deficit. This is important to discuss preoperatively and may impact patient decision making and expectations. Our clinical impression is that although a noticeable increase in soft tissue deficit occurs after total parotidectomy, the degree is relatively small and cosmetically acceptable by the overwhelming majority of patients.

Our study has limitations, which are important to define for optimal design of future analyses. Given the retrospective nature of this dataset, a definitive causal relationship between total parotidectomy and reduced parotid bed recurrence (loss of regional control) cannot be established. It is possible other patient or disease characteristics account for the difference in recurrence rates observed. However, stage and clinically detected versus occult nodal disease were not statistically different between interventions.

The rate of adjuvant treatment was the same after superficial and total parotidectomy. However, there were differences in the type of adjuvant treatment received. Specifically, interferon was more often given after superficial parotidectomy and radiation after total parotidectomy (Table 1). This may be due to the higher percentage of patients with stage 3C melanoma in the cohort who underwent total parotidectomy. The authors do not think that the difference in parotid bed recurrence rates is due to this variation in adjuvant treatment because comparison of patients who did and did not recur after superficial parotidectomy showed no difference in adjuvant treatment rate or type.

Median length of follow-up was shorter in patients who underwent total parotidectomy (16 months), so it is possible that with longer follow-up more recurrences would be detected in this group. However, within the superficial parotidectomy group, 50% of the parotid bed recurrences occurred within the first 16 months. Thus, if the interventions had equivalent parotid bed recurrence rates one would expect to see some recurrences after total parotidectomy during the follow-up time of this analysis, of which we had zero. We intend to continue to study our cohort prospectively to allow for further determination of any recurrences and subsequent morbidity.

The retrospective design also affects uniformity of data. Specifically, facial nerve function reporting was variable in presence and quality. However, all patients who underwent total parotidectomy had postoperative facial nerve function documented. Although it is possible that patients without documented facial nerve function may have had paresis not included in the analysis, this would serve to increase facial nerve paresis rates after superficial parotidectomy, not total parotidectomy.

Finally, our data do not address larger questions such as: Does total parotidectomy improve disease-free survival or overall survival? Our suspicion is that it does not, but we believe reduction in parotid bed recurrence, and, therefore, facial nerve paralysis is compelling enough to consider total parotidectomy over superficial parotidectomy for metastatic melanoma in the parotid gland.

5 | CONCLUSION

Parotid bed melanoma recurrence was more common after superficial parotidectomy compared to total parotidectomy and recurrence resulted in significant facial nerve functional deficit. Postoperative complications and facial nerve function were comparable after superficial and total parotidectomy. Our results support total parotidectomy when metastatic melanoma involves the parotid nodal basin. Our data also provide a framework for optimal study design in the future to better answer important clinical questions pertaining to surgical treatment of parotid metastatic melanoma.

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