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Reducing Margins of Wide Local Excision in Head and Neck Melanoma for Function and Cosmesis: 5-Year Local Recurrence-Free Survival

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Background: The proximity of head and neck (H&N) melanomas to critical anatomical structures requires that surgeons achieve a balance between adequate margins of excision and the functional and cosmetic needs of patients. This study sought to determine the risk associated with reducing margins of wide local excision (WLE) in H&N melanoma and to identify risk factors of recurrence.
Methods: Seventy-nine cases of primary, invasive H&N melanoma were treated by WLE and followed prospectively for local recurrence. Forty-two WLEs were performed according to current practice guidelines (1cm for lesions <1.0 mm thick, 1–2 cm for lesions 1.01–2.0 mm thick, and 2 cm for lesions >2.0 mm thick). Reduced margins (0.5 cm for lesions ≤ 1.0 mm thick, 0.5–1.0 cm for lesions 1.01–2.0 mm thick, and 1.0 cm for lesion >2.0 mm thick) were utilized in 37 cases to preserve critical anatomical structures such as the eyelid, nose, mouth and auricle.
Results: Overall local recurrence rate was 8.9% over a mean follow-up period of 71.3 months and a minimum of 60 months. Reducing margins of WLE did not increase local recurrence rates as demonstrated by local recurrence-free survival (90.4% vs. 91.9%, $P = 0.806$).
Conclusion: Margins of WLE may be safely reduced in melanomas in close proximity to structures of the H&N without affecting local recurrence rates.
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KEY WORDS: melanoma; head and neck; wide local excision

INTRODUCTION

Approximately 15–20% of primary cutaneous melanomas occur in the head and neck region [1]. Although wide local excision is the standard treatment for primary melanomas [2], the extent of surgical margin in head and neck melanomas remains controversial due to several factors. First, melanomas of the head and neck exhibit a higher rate of recurrence and worse prognosis than lesions in other body locations [3]. Second, these melanomas are in close proximity to critical anatomical and functional structures of the face including the eyelids, nose, mouth, and auricle, where wide margins of excision are often not feasible. Therefore, head and neck melanomas require that surgeons achieve a balance between adequate margins of excision and the functional and aesthetic needs of patients.

The current National Comprehensive Cancer Network (NCCN) Clinical Practice Guideline recommendations for wide local excision margins are based upon currently available prospective data for malignant lesions less than 4.0 mm in Breslow thickness [4–9] (category 1) and expert consensus for in-situ lesions and malignancies thicker than 4.0 mm (category 2). Current wide local excision margin recommendations are 0.5 cm for in situ lesions, 1 cm for lesions ≤ 1.0 mm thick, 1–2 cm for lesions 1.01–2.0 mm thick, and 2 cm for lesions ≥ 2.01 mm thick. These recommendations are the same for head and neck melanomas and those located in other locations [2].

The practicality of large wide local excision margins varies with the site of the lesion. In head and neck melanomas, especially for lesions located in critical areas such as the eyelid and nose, wide margins are not always technically feasible or may lead to considerable functional deformities. In addition, large defects often require soft tissue reconstruction with flaps because they cannot be closed primarily [10–12]. For this reason, surgeons often rely on their own judgment when determining surgical margins in head and neck melanomas located on or near critical structures.

The NCCN Clinical Practice Guidelines state that surgical margins may be modified to accommodate individual anatomical or functional considerations [2]. However, the amount of margin reduction and evidence supporting the safety of this measure remains unknown. This study sought to assess whether reducing wide local excision margins to 0.5 cm for lesion ≤ 1.0 mm thick, 0.5–1.0 cm for lesions 1.01–2.0 mm thick, and 1.0 cm for lesion >2.0 mm thick was associated with an increase in local recurrence rates in a cohort of patients with head and neck melanomas. Second, we attempted to identify risk factors for recurrence in these patients.

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PATIENTS AND METHODS

The institutional review board approved this study. The design of this study was a retrospective review of a prospectively maintained institutional database. Between 2001 and 2008, 79 primary, invasive cutaneous melanomas of the head and neck were treated with wide local excision by a single surgeon (JDW). Lesions were classified into several categories based upon location, Breslow classification, histological type, presence of ulceration or regression prior to surgery, and American Joint Committee on Cancer (AJCC) defined stage.

Patients were non-randomly assigned to one of two cohorts based on margin of wide local excision. Wide local excisions were performed according to current NCCN Clinical Practice Guidelines (1 cm for lesions <1.0 mm thick, 1–2 cm for lesions 1.01–2.0 mm thick, and 2 cm for lesions >2.01 mm thick) when melanomas were located in areas where complete margins of excision were attainable without significantly affecting critical facial structures. Reduced margins (0.5 cm for lesion ≤1.0 mm thick, 0.5–1 cm for lesions 1.01–2.0 mm thick, and 1.0 cm for lesion >2.0 mm thick) were utilized in cases were melanomas were located on or near critical anatomical structures of the face (eyelid, nose, mouth, and auricle) and it was believed that utilizing recommended margins would lead to a functional or cosmetic deformity. The plastic surgeon's ability to decrease the complexity of the reconstruction played a major role in determining margins for patients, and factors that determined this included defects that did not cross a difficult to reconstruct anatomical border and the ability to use a more simplified reconstructive technique. Margins were measured using a ruler from the scar or from the margin of any residual pigmented lesion. Wood's lamp was not used to find the edge of the pigment. Upon excision, the entire raw surface of the excised specimen was marked with methylene blue ink. Sentinel lymph node biopsy and/or lymph node dissection were performed in selected patients abiding to recommendations outlined in the current NCCN Clinical Practice Guidelines. All specimens were histologically evaluated by a dermatopathologist. If tumor was present anywhere along the inked margin of the wide excision specimen, it was categorized as persistent disease. In-transit metastases (>2 cm from the initial primary) were classified as a stage IIIC (regional/nodal) recurrence. Persistent melanomas were re-excised abiding to NCCN guidelines with margins for wide-local excision determined by the thickness of the primary lesion. In patients with melanoma-in-situ, our practice is to re-excise either with 0.5 cm margin or by Mohs, and we observed patients with atypical melanocytic hyperplasia.

Patients were followed prospectively for evidence of recurrence for a minimum of 60 months by either a surgical oncologist or dermatologist in accordance with NCCN follow up guidelines [2]. Local recurrence was defined by biopsy confirmed melanoma at the site of previous melanoma excision. The time to recurrence was defined as the duration from surgery to biopsy of first recurrence. Local recurrence rates between the two cohorts were compared using Kaplan–Meier estimates and the log-rank test. Smaller subgroup analyses were compared directly at 60 months post-operatively by Fisher's exact analysis. Statistical analyses were performed using SPSS Statistical Analysis Software (SPSS, Version 17.0, Chicago, IL).

RESULTS

All 79 melanoma excisions were performed without major complication. Comparison of the two patient cohorts stratified by patient demographics and melanoma clinicopathologic factors are presented in Table I. With the exception of location and Breslow depth there no baseline differences between cohorts. Lesions within the reduced margins group tended to be located on or near the eyelid, nose, and ear, while lesions in recommended margins group tended to be located on the forehead, neck, or scalp. Lesions of the reduced margins group were likely to have a greater Breslow Depth. This correlated with larger margins of excision and greater need for reduction of margins if lesions were located in functionally sensitive areas of the face.

Breslow thickness was utilized to determine margins of excision in all cases. Forty-two (53.2%) wide local excisions were performed according to current NCCN Clinical Practice Guidelines. These patients had melanomas located in areas where complete margins of excision were attainable without significantly affecting critical facial structures. Reduced margins were utilized in 37 (46.8%) cases where melanomas were located on or near critical anatomical structures of the face. In addition to wide local excision, 46 patients underwent sentential lymph node biopsies and 7 of those underwent complete lymph node dissections for node positive disease. Fewer patients with reduced margins required skin grafts (3.4% vs. 17.5%, $P = 0.057$) or local flaps (27.6% vs. 50.0%, $P = 0.097$), but these differences trended towards significance. Additionally, the rates of primary closure were increased in those with reduced margins (65.6% vs. 32.5%, $P = 0.063$), and the average area was significantly smaller (4.1 cm^2 vs. 9.2cm^2,$P = 0.041$). No patients received postoperative external beam radiation.

Persistent disease (positive margins) was identified in seven patients. All persistent lesions were less than <1.0 mm in thickness and six of the seven where of the lentigo maligna subtype. Three of these patients were in the recommended margins cohort (1.0 cm margin), and four in the reduced margins cohort (0.5 cm margin) ($P = 0.713$). All patients underwent re-excision with 1.0 cm margins abiding to NCCN guidelines in the area of persistent disease with negative margins upon re-excision. There were no patients with in-situ lesions at the periphery of any of the excised lesions.

The mean follow up time was 71.3 months for all patients. Mean follow-up time for patients in the recommended margins group was 74.1 months, while mean follow up time for patients in the reduced margins group was 68.2 months. All patients completed at least 60 months of follow up. Of the 79 cases, seven patients (8.9%) experienced local recurrence of their melanoma. (Table II) Reducing margins of wide local excision did not affect local recurrence rates as demonstrated by recurrence free survival (90.4% vs. 91.9%, $P = 0.806$; Fig. 1). Four of the patients with local recurrence were in the recommended margins cohort, while the other three were in the reduced margins cohort. None of the recurrences were in patients who have re-excision for positive margins. Mean time to local recurrence was 13.5 months for the patients in the recommended margins cohort and 17.7 months for patient in the reduced margins cohort.

Subgroup analyses were performed with follow up censored at 60 months to allow direct comparisons of the groups. (Table II) For melanomas less than 1.0 mm thick, there was no difference in local recurrence between patients receiving 1.0 cm margins and 0.5 cm margins (4.0% vs. 0.0%, $P = 0.465$). For 1.01–2.0 mm thick lesions, there was no difference in local recurrence rates between patients receiving 10.0–2.0 cm and 0.5–1.0 cm margins (8.3% vs. 0.0%, $P = 0.375$). For melanomas 2.01–4.0 mm in thickness, there was no difference in local recurrence between patient receiving 2.0 cm margins and 1.0 cm margins (33.3% vs. 22.2%, $P = 0.700$). For lesions greater than 4.01 mm in thickness, there is also no difference in local recurrence between patients receiving 2.0 cm margins and 1.0 cm margins (0.0% vs. 16.7%, $P = 0.346$).

As a secondary outcome measure, four (5.0%) additional patients experienced regional lymph node and seven (8.9%) distant metastatic recurrence of their melanoma for an overall recurrence rate of 22.8% (18 of 79 patients). No patients who had local recurrence of melanoma demonstrated either regional or distant metastases. There was no difference in overall recurrence rates between patients receiving recommended margins of wide local excision and reduced margins overall (26.2% vs. 18.9%, $P = 0.610$) or for any Breslow Depth category. (Table II)

Due to small size of our study, we examined factors associated with overall recurrence using univariate analysis. (Table III) Factors associated with recurrence included higher AJCC stage ($P = 0.003$)

TABLE I. Patient Demographics and Clinicopathologic Factors

		Recommended Margins	Reduced Margins	Significance
Demographics	Number	42	37	
	Age	54.3 +/− 14.2	51.6 +/− 12.2	$P = 0.371$
	Male	23 (55%)	23 (62%)	$P = 0.648$
	Female	19 (45%)	14 (38%)	
Histological Type	Superficial Spreading	14 (33%)	16 (43%)	$P = 0.601$
	Nodular	14 (33%)	13 (35%)	
	Lentigo Maligna	12 (29%)	6 (16%)	
	Other	2 (2.6%)	2 (5.4%)	
Location	Eye	1 (2.4%)	6 (16%)	$P = 0.008$
	Nose	2 (4.8%)	7 (19%)	
	Ear	3 (7.1%)	8 (22%)	
	Cheek	16 (38%)	10 (27%)	
	Forehead	6 (14%)	2 (5.4%)	
	Neck	9 (21%)	2 (5.4%)	
	Scalp	5 (12%)	2 (5.4%)	
Breslow Depth	<1.0 mm	25 (60%)	13 (35%)	$P = 0.030$
	1.01–2 mm	12 (29%)	9 (27%)	
	2.01–4 mm	3 (7.1%)	9 (27%)	
	>4.0 mm	2 (4.8%)	6 (16%)	
Ulceration	Present	7 (17%)	5 (14%)	$P = 0.762$
	Absent	35 (83%)	32 (86%)	
Regression	Present	4 (9.5%)	5 (14%)	$P = 0.727$
	Absent	38 (90%)	32 (86%)	
AJCC Stage	Stage I	31 (74%)	20 (54%)	$P = 0.102$
	Stage II	7 (17%)	14 (38%)	
	Stage III	4 (9.5%)	3 (8.1%)	
	Stage IV	–	–	–

and thicker lesions ($P = 0.030$). The type of melanoma ($P = 0.353$), location ($P = 0.938$), presence of ulceration ($P = 1.000$) or regression ($P = 0.676$) were not associated with overall recurrence.

DISCUSSION

Surgical excision is the standard of care for localized melanoma of the head and neck. Although current NCCN guidelines state that margins of wide local excision may be modified to accommodate the anatomical and functional considerations of individual patients, the safety of this practice remains unknown. This study sought to determine whether reducing excision margins to 0.5 cm for lesion ≤1.0 mm thick, 0.5–1.0 cm for lesions 1.01–2.0 mm thick, and 1.0 cm for lesion >2.0 mm thick adversely affected local tumor recurrence. The results suggest that in this small population of patients from a single institution, local recurrence rates are comparable for reduced and recommended wide local excision margins.

Several large prospective randomized trials have been conducted in an effort to clearly define the most optimal surgical margins for melanoma. In a 90-month, prospective follow-up study by the World Health Organization, 612 patients with primary melanoma less than 2.0 mm thickness were randomized to wide local excision with 1.0 cm or 3.0 cm margins [5,6]. Local recurrence, disease-free and overall survival rates were similar in both groups. In a prospective, randomized trial in patients with primary melanoma greater than 2.0 mm in thickness comparing 1.0 cm and 3.0 cm margins, there was no difference in local recurrence or in melanoma-specific survival. There was, however, a slightly lower rate of overall recurrence with the 3.0 cm margin. The National Intergroup Trial randomized 468 patients with lesions 1.0–4.0 mm in thickness to wide local excision with 2.0 or 4.0 cm margins and followed them for a period of 10 years [7,8]. There were no differences in local recurrence, disease-free or overall survival. Other studies [4,13–15] also contributed to the current NCCN Clinical Practice Guidelines for surgical management of melanomas, however, no studies have considered head and neck melanoma alone or provided evidence for selectively reducing margins in these cases.

The results of this study suggest that margins may be reduced in selected patients without significantly affecting recurrence rates. The decision to reduce the surgical margin in the 37 patients presented in this series was guided clinically when it was determined that utilizing the

TABLE II. Local and Overall Recurrence Rates for All Patients at 60 Months

Breslow Depth	Clinical Margin	Number	Local Recurrence	Significance	Overall Recurrence	Significance
<1.0 mm	0.5 cm	13	0 (0.0%)	$P = 0.465$	1 (7.7%)	$P = 0.681$
	1.0 cm[a]	25	1 (4.0%)		3 (12.0%)	
1.01–2.0 mm	0.5–1.0 cm	9	0 (0.0%)	$P = 0.375$	1 (11.1%)	$P = 0.2956$
	1.0–2.0 cm[a]	12	1 (8.3%)		5 (41.7%)	
2.01–4.0 mm	1.0 cm	9	2 (22.2%)	$P = 0.700$	2 (22.2%)	$P = –0.480$
	2.0 cm[a]	3	1 (33.3%)		2 (66.7%)	
>4.01 mm	1.0 cm	6	1 (16.7%)	$P = 0.346$	3 (50.0%)	$P = 1.00$
	2.0 cm[b]	2	1 (0.0%)		1 (50.0%)	

[a]NCCN recommended wide local excision margins based upon categorical level 1 evidence.
[b]NCCN recommended wide local excision margins not based upon categorical level 1 evidence.

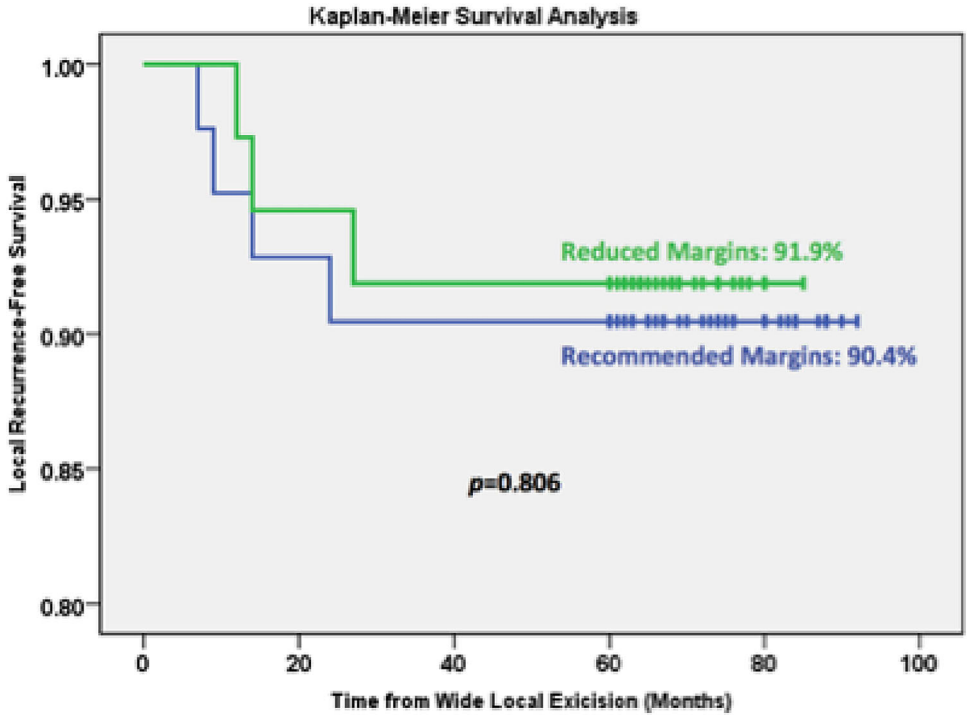

Fig. 1. Comparison of local recurrence free survival with recommended versus reduced margins.

standard margin of excision would cause significant deformity to critical structures of the face. This was determined by the proximity of the lesion to difficult to reconstruct structures, such as the eyelids, nose, mouth, and auricle as well as the planned margin of excision as determined by the Breslow Depth. Often, our team will consult a plastic and reconstructive surgeon when making this decision to reduce the margin of wide local excision, since they are involved with the reconstruction of these structures. With greater Breslow Depths, larger margins are recommended yet these margins lead to a greater functional deformity. As seen by Table I, it was more common for us to reduce these margins in lesions with greater Breslow Depth, because they more commonly led to greater deformity then thinner lesions. Given that the pathological characteristics of the reduced margins group were generally worse than the group with standard margins, the issue of competing mortality can be considered as a possible cause for a reduced local recurrence rate if patients died from distant metastases and were not alive to be at risk for

TABLE III. Clinicopathologic Factors of Head and Neck Melanoma Associated With Overall Recurrence by Univariate Analysis

		Number	Overall Recurrence	Significance
Histological Type	Superficial Spreading	30	9 (30.0%)	$P = 0.353$
	Nodular	27	5 (18.5%)	
	Lentigo Maligna	18	4 (22.2%)	
	Other	4	0 (0.0%)	
Location	Eye	7	2 (28.6%)	$P = 0.938$
	Nose	9	1 (11.1%)	
	Ear	11	2 (18.2%)	
	Cheek	26	5 (19.2%)	
	Forehead	8	2 (25%)	
	Neck	13	4 (30.8%)	
	Scalp	7	2 (28.6%)	
Breslow Depth	<1.0 mm	38	4 (10.5%)	$P = 0.030$
	1.01–2 mm	21	6 (28.6%)	
	2.01–4 mm	12	4 (33.3%)	
	>4.0 mm	8	4 (50%)	
Ulceration	Present	12	3 (25.0%)	$P = 1.000$
	Absent	67	15 (22.4%)	
Regression	Present	9	1 (11.1%)	$P = 0.676$
	Absent	70	17 (24.3%)	
AJCC Stage	Stage I	51	6 (11.8%)	$P = 0.003$
	Stage II	21	8 (38.1%)	
	Stage III	7	4 (57.1%)	
	Stage IV	0	–	

local recurrence. We observed no deaths in the reduced margins group and two deaths in the standard margins group at the end of the follow-up period; therefore, competing mortality likely did not play a role in the observed local recurrence rate in the reduced margins group. Overall, reduction of surgical margins is pursued in approximately 40% of invasive head and neck melanomas referred to our institution.

Histological examination of excised specimens may have played a crucial role in our ability to reduce margins of wide local excision. In this study, seven patients had persistent disease following wide local excision, with three in the recommended margins cohort and four in the reduced margins cohort. All these patients underwent re-excision according to NCCN guidelines, which may have reduced recurrence rates in our reduced margins cohort. Specific to the histological type, our study identified persistent disease in 6 of the 18 lentigo maligna subtype melanomas which were excised. This type of melanoma presents a unique problem because there is often extension of atypical junctional melanocytic hyperplasia that invades several centimeters beyond visible margins. Although recurrence rates were not increased in patients with lentigo maligna subtype on univariate analysis, this may suggest that margins should not be reduced in these patients.

Furthermore, few studies have evaluated the clinicopathological factors of head and neck melanoma associated with recurrence; one study examining 534 patients with Stage I disease demonstrated that tumor thickness, anatomical site, and ulceration are the major predictors of recurrence [14]. This study identified several additional risk factors that may be associated with recurrence that may influence a surgeon's decision to reduce surgical margins in individual patients. These included AJCC stage, Clark level and histological type had a significant impact on overall recurrence rate.

The demographic data of our study is comparable to other published reports [1], with the exception of type and location. Superficial spreading melanomas normally compromise 70% of head and neck melanomas, yet only compromised approximately one-third of our cases. Our study also noted an increased percentage of lentigo maligna melanomas (approximately 25%), while other series customarily report that they compromise 5% of cases. Combined reports from approximately 2,000 head and neck melanoma cases demonstrated that the face was the most common location of melanomas, which compromised approximately two-thirds of cases in this series. However, previous studies have reported a higher incidence of neck (30%) and scalp (27%) tumors than our series. It is now common practice at our institution to sub-categorize melanomas of the head and neck into those involving the face (eyelids, nose, mouth, ears), which often require reduced margins for cosmesis, from melanomas of the scalp, forehead, and neck, which are less disfiguring and can be treated with recommended margins of excision.

It should be noted that local recurrences rates reported in our results are higher than some previous studies, including those in the standard margins group [7,16]. The elevated local recurrence rates in comparison to the these trials may be attributed to several differences in our study. First, our study has a small sample size, which is inarguably a source of bias. Inherent to such bias, our study contained a large percentage of patients with lentigo maligna, who demonstrated more positive margins after initial excision compared to other subtypes of melanoma. Lastly, increased local recurrence rates can also be due to institutional differences in protocol. Our patients are highly reliable and are followed closely by a multidisciplinary team consisting of dermatologists, surgical oncologists, and medical oncologists, all of who have a relatively liberal approach to biopsing suspicious lesions. Therefore, we do not believe that the efficacy of current standard margins should be called into question given the results of our study, but that the results do show that reducing margins in this specific subset of patients did not increase recurrence rates above baseline.

This study is subjected to a number of limitations associated with a retrospective study design, including selection bias and unknown or undocumented variables that could potentially confound the results. In addition, this report is limited by the small cohort size and number of recurrences, thus the study is insufficiently powered to definitively support reduced margins. With the current sample size and 1.5% difference in recurrence rates that were observed between the two cohorts, and a sample size of 155 patients would be required to achieve a power of 0.80. However, our data does suggest that reduced margins do not result in an unexpectedly high local recurrence rate. Another important finding to note is that all patients who experienced local recurrence in this study were successfully treated by re-excision and that none demonstrated evidence of regional or distant metastasis, suggesting that reduction of margins may be attempted without increased risk for spread of disease beyond the initial site. A particular strength of the study is the 5-year follow up. Most recurrences occur within the first 5 years of diagnosis [2] suggesting that most recurrences should be accounted for in the analysis.

In conclusion, our results support the notion that reduced margins of excision may be acceptable in locations where critical facial structures are likely to be disfigured by currently recommended margins. While a prospective, randomized trial clearly delineating whether this remains valid in a larger number of patients would be difficult, further study of this issue using multi-institutional data is warranted.

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17. Please check Synopsis for Table of Contents.