Treatment of primary nonmetastatic melanoma at high-volume academic facilities is associated with improved long-term patient survival

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Background: Previous studies of cancer care have demonstrated improved long-term patient outcomes for those treated at high-volume centers. The influence of treatment center characteristics on outcomes for primary nonmetastatic melanoma is not currently established.

Objective: We aimed to investigate the association of cancer treatment center case volume and academic affiliation with long-term patient survival for cases of primary nonmetastatic melanoma.

Methods: Cases of melanoma diagnosed in US adults from 2004 to 2014 and included in the National Cancer Database were identified. Hospitals were grouped by yearly case-volume quartile: bottom quartile, 2 middle quartiles, and top quartile.

Results: Facility case volume was significantly associated with long-term patient survival ($P < .0001$). The 5-year survival rates were 76.8%, 81.9%, and 86.4% for patients treated at institutions in the bottom, middle, and top quartiles of case volume, respectively. On multivariate analysis, treatment at centers in both middle quartiles (hazard ratio, 0.834; 95% confidence interval, 0.778-0.895) and in the top quartile (hazard ratio, 0.691; 95% confidence interval, 0.644-0.741) of case volume was associated with improved survival relative to that of patients treated at hospitals in the bottom quartile of case volume. Academic affiliation was associated with improved outcomes for top-quartile- but not middle-quartile-volume facilities.

Limitations: Disease-specific survival was not available.

Conclusions: Treatment at a high-volume facility is associated with improved long-term patient survival for melanoma. High-volume academic centers have improved patient outcomes compared with other high-volume centers. (J Am Acad Dermatol 2019;80:979-89.)

Key words: case volume; melanoma; NCDB; outcomes; survival.

Melanoma is rapidly growing in incidence, with an estimated 91,270 new cases and 9320 melanoma-related deaths expected to occur in the United States in 2018.[1] Although multiple treatment guidelines exist, adherence is incomplete and there is widespread heterogeneity in care.[2-4] Previous work studying other diseases has demonstrated that facility characteristics influence both the degree of guideline adherence and the outcomes of patients treated at these facilities.[5-7] However, there is a relative lack of data on the influence of treatment facility characteristics on melanoma outcomes in the United States.

Among health care system factors influencing patient survival, one of the most relevant is the case volume of the treatment facility. A landmark

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study of outcomes following major cancer resections and cardiovascular procedures revealed that hospital volume significantly influenced 30-day mortality rate, with an up to 5% reduction in mortality in patients treated at high-volume facilities.[8] Hospital volume has also been shown to significantly affect long-term survival in multiple malignancies.[9-12] Additionally, in the case of lung and breast cancers, patients treated at academic institutions have improved short- and long-term survival.[13-15]

In comparison with other malignancies, little is known about the influence of hospital characteristics on melanoma treatment and outcomes. In a study of US practice patterns, Bilimoria et al found that patients with melanoma treated at National Cancer Institute–designated centers were more likely to receive guideline-adherent nodal evaluation.[16] Similarly, a study of specialized regional care centers in Alberta, Canada, found that these centers were more likely than others to adhere to provincial guidelines concerning sentinel lymph node biopsy.[17] Studies of outcomes have been limited in scope but have shown lower inpatient mortality for patients with melanoma who were receiving high-dose interleukin 2 (IL-2) at hospitals with a higher volume of treatment with high-dose IL-2 and improved long-term survival for patients with metastatic melanoma treated at hospitals with higher annual metastatic melanoma treatment volumes.[18,19] Nevertheless, the impact of facility characteristics such as volume and academic affiliation on the long-term survival of patients with primary nonmetastatic melanoma is not yet established. The objective of the current study was to explore the relationship between facility characteristics and the long-term outcomes of patients with primary nonmetastatic melanoma.

CAPSULE SUMMARY

- Volume-outcome relationships in cancer care have motivated calls for regionalization of care. We have demonstrated that high-volume academic facilities achieve improved outcomes for patients with melanoma.
- Increased utilization of those aspects of these centers that increase patient survival, whether by regionalization of care or dissemination of these practices, may improve patient outcomes.

METHODS

Data source

The data originated from the National Cancer Database (NCDB) from 2004 to 2018, with diagnosis dates of 2004 to 2014. The NCDB is a nationwide clinical surveillance resource data set that includes approximately 70% of all newly diagnosed malignancies in the United States from more than 1500 cancer programs, as previously described.[20] The NCDB has been used in a number of studies of system-related influences on cancer outcomes.[21-24] This study was determined to be exempt from institutional review by the Yale Human Investigation Committee.

Study population

The study selection criteria are outlined in Fig 1. We initially excluded patients if they were younger than 18 years at the time of diagnosis, did not receive definitive surgical excision, had any other malignancies, had distant metastases, or had missing or incomplete follow-up data. For multivariate analysis and propensity score–matched analyses, we excluded patients if information on the following items was lacking for them: Breslow depth, nodal status, radiation administration status, chemotherapy administration status, immunotherapy administration status, or lymph node dissection status.

Statistical analysis

Patients were categorized as having government insurance if their primary insurance carrier was Medicare, Medicaid, or another government-administered insurance carrier. Patients were categorized as having received chemotherapy if they had received any chemotherapeutic agent. We considered patients to have received radiotherapy if they had received external beam radiation. Patients were categorized as having received immunotherapy if they had received any immunotherapeutic agent. Facilities were divided into bottom (first)-quartile, middle (second and third)-quartile, and top (fourth)-quartile groupings. The dividing points between these groups were as follows: a first-quartile value of 7 and a third-quartile value of 33 cases/y. The primary outcome was overall survival.

Kaplan-Meier analyses stratified by facility yearly case volume were performed. We then conducted a multivariate survival analysis by using a Cox proportional hazards model. The variables outlined in Table I were tested for appropriateness for inclusion in this model by using Akaike information criterion minimization to decrease the likelihood of overfitting data.[25] The 3-, 5-, and 10-year survival rates were analyzed for patients with sufficient follow-up, whereas cases with insufficient follow-up for the respective time points

Abbreviations used:

BQV: bottom-quartile-volume
CI: confidence interval
HR: hazard ratio
IL-2: interleukin 2
MQV: middle-quartile-volume
NCDB: National Cancer Database
SE: standard error
TQV: top-quartile-volume

were excluded from the calculation of these metrics. Propensity score matching was conducted for cohorts of patients from bottom- and middle-quartile facilities as well as for patients from middle- and top-quartile facilities. Propensity score matching was also conducted for patients treated at middle-quartile facilities between those treated at academic versus at nonacademic facilities as well as for patients treated at top-quartile facilities between those treated at academic versus at nonacademic facilities. This methodology controls for potential differences in outcomes due to systemic differences between the 2 groups.[26-32] Scores were calculated by using a logit model with the factors outlined in Table I, except for facility volume. Groups were generated by using a 1:1 nearest neighbor match without replacement. Between-group differences were tested by using the 2-tailed Student *t* test for continuous variables and the chi-square test for categoric variables. *P* values less than .05 were considered statistically significant. Data analysis was performed by using Stata software (version 13, StataCorp LP, College Station, TX).

RESULTS

The characteristics of the study population are outlined in Table I. The majority of patients (95.7%) were identified as white, with a comorbidity score of 0 (89.4%) and private insurance (58.3%). Facilities in the top quartile of yearly case volumes treated the majority of patients (72.8%), and academic facilities treated 40.4% of patients. Among cases with known staging, most (60.7%) were 1 mm or less in depth and without nodal metastases (96.2%). Among patients with known adjuvant therapy, 1.3% received radiotherapy, 1.0% received chemotherapy, and 3.7% received systemic immunotherapy. In all, 75% of patients were treated at facilities that treated 33 or fewer patients with melanoma per year, with 25% treated at facilities that treated fewer than 7 patients per year and 50%

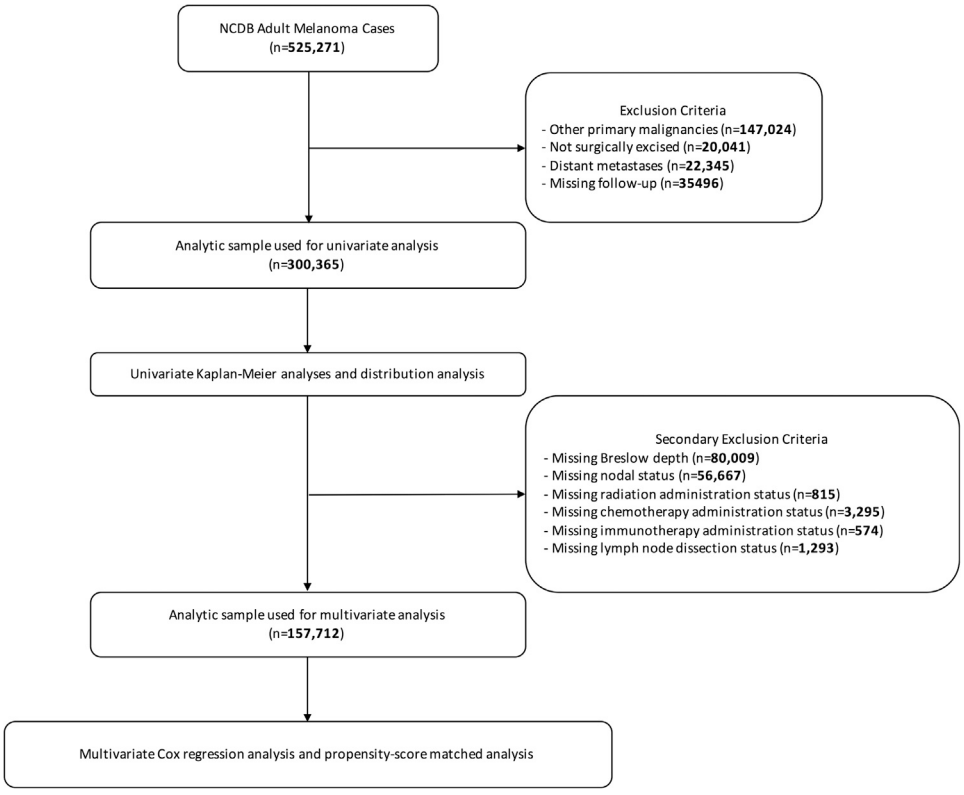

Fig 1. Consolidated Standards of Reporting Trials diagram for patient selection. *NCDB,* National Cancer Database.

Table I. Characteristics of the analytic sample and multivariate analysis of factors associated with survival

Variable	n (%)		Hazard ratio (*P* value)	95% CI
	Overall (N = 300,365)	Cases with nonmissing data (n = 157,712)		
Age, median, y (SD)	59 (16.4)	59 (16.6)	1.055 (<.001)	1.054-1.057
Sex				
Female	137,467 (45.8)	72,056 (45.7)	1 [reference]	—
Male	162.898 (54.2)	85,656 (54.3)	1.371 (<.001)	1.334-1.408
Race				
White	287,325 (95.7)	151,666 (96.2)	1 [reference]	—
Black	1663 (0.6)	760 (0.5)	1.395 (<.001)	1.215-1.602
Hispanic	3925 (1.3)	2002 (1.3)	1.042 (.470)	0.932-1.164
Asian/Pacific Islander	836 (0.3)	452 (0.3)	0.929 (.508)	0.748-1.155
Other/Unknown	6616 (2.2)	2832 (1.8)	1.006 (.906)	0.907-1.116
Charlson/Deyo score				
0	268,506 (89.4)	138,800 (88.0)	1 [reference]	—
1	26,696 (8.9)	15,806 (10.0)	1.293 (<.001)	1.249-1.339
2	4019 (1.3)	2412 (1.5)	1.993 (<.001)	1.865-2.131
≥3	1144 (0.4)	694 (0.4)	2.889 (<.001)	2.590-3.222
Insurance				
Private	175,146 (58.3)	93,438 (59.2)	1 [reference]	—
Government	111,132 (37.0)	57,786 (36.6)	1.312 (<.001)	1.266-1.360
None	7217 (2.4)	4067 (2.6)	1.927 (<.001)	1.777-2.089
Unknown	6870 (2.3)	2421 (1.5)	1.459 (<.001)	1.316-1.617
Facility type				
Academic	121,463 (40.4)	64,997 (41.2)	1 [reference]	—
Other	178,902 (59.6)	92,715 (58.8)	1.046 (.002)	1.016-1.617
Facility volume quartile				
Bottom (first)	8220 (2.7)	3788 (2.4)	1 [reference]	—
Middle (second and third)	73,606 (24.5)	35,545 (22.5)	0.834 (<.001)	0.778-0.895
Top (fourth)	218,539 (72.8)	118,379 (75.1)	0.691 (<.001)	0.644-0.741
Breslow depth				
≤1.0 mm	131,930 (43.9)	95,769 (60.7)	1 [reference]	—
1.01-2.00 mm	43,752 (14.6)	30,947 (19.6)	1.466 (<.001)	1.413-1.521
2.01-4.00 mm	26,078 (8.7)	18,138 (11.5)	2.447 (<.001)	2.361-2.537
>4.00 mm	18,596 (6.2)	12,858 (8.2)	3.741 (<.001)	3.605-3.881
Missing	80,009 (26.6)	—		
No. of positive nodes				
0	218,460 (72.7)	151,678 (96.2)	1 [reference]	—
1	4524 (1.5)	3797 (2.4)	1.851 (<.001)	1.748-1.960
2-3	1769 (0.6)	1461 (0.9)	1.993 (<.001)	1.842-2.156
≥4	960 (0.3)	776 (0.5)	3.295 (<.001)	2.998-3.621
Missing	74,652 (24.8)	—		
Local lymph node dissection				
Not performed	262,771 (87.5)	136,641 (86.6)	1 [reference]	—
Performed	34,139 (11.4)	21,071 (13.4)	1.329 (<.001)	1.282-1.378
Missing	3455 (1.2)	—		
Radiotherapy				
Not administered	294,615 (98.1)	155,679 (98.7)	1 [reference]	—
Administered	3591 (1.2)	2033 (1.3)	1.313 (<.001)	1.227-1.404
Missing	2159 (0.7)	—		
Chemotherapy				
Not administered	289,564 (96.4)	156,219 (99.0)	1 [reference]	—
Administered	2873 (1.0)	1493 (1.0)	1.676 (<.001)	1.541-1.822
Missing	7928 (2.6)	—		
Systemic immunotherapy				
Not administered	287,352 (95.7)	151,945 (96.3)	1 [reference]	—
Administered	9922 (3.3)	5767 (3.7)	1.405 (<.001)	1.331-1.484
Missing	3091 (1.0)	—		

All initial variables remained in the multivariate survival model after utilization of Akaike information criterion minimization.

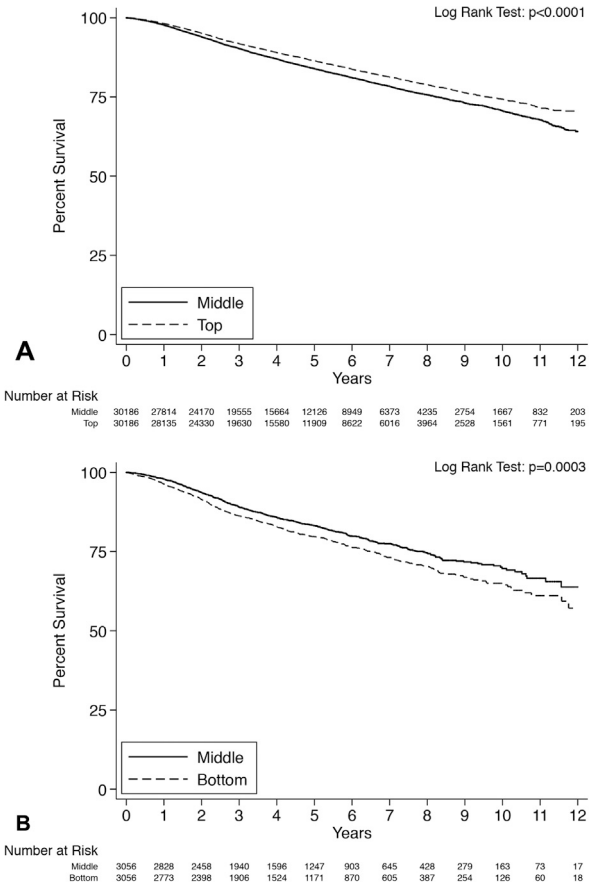

Fig 2. Long-term survival for propensity score–matched cohorts of patients treated at top (fourth)-quartile-volume facilities versus for those treated at middle (second and third)-quartile-volume facilities **(A)** and bottom (first)-quartile-volume facilities versus for those treated at middle (second and third)-quartile-volume facilities **(B)**.

treated at facilities with yearly case volumes between 7 and 33, inclusive. Among 1330 facilities included in the analysis, 191 (14.4%) had an academic affiliation. Among academic centers, 59.7% were within the top quartile of case volume, whereas 19.5% of other centers were within the top quartile of case volume. The mean follow-up time was 5.05 years, with a maximum follow-up time of 13.09 years.

Kaplan-Meier univariate analysis revealed significantly improved survival for patients treated at middle-quartile-volume (MQV) facilities versus at bottom-quartile-volume (BQV) facilities, as well as for patients treated at top-quartile-volume (TQV) facilities versus at MQV facilities ($P < .0001$). The 3-, 5-, and 10-year survival rates were 84.1% (standard error [SE], 0.4), 76.8% (SE, 0.5), and 62.6% (SE, 0.8) respectively, for patients treated at BQV facilities; 88.4% (SE, 0.1), 81.9% (SE, 0.2), and 68.6% (SE, 0.3), respectively, for patients treated at MQV facilities; and 91.7% (SE, 0.1), 86.4% (SE, 0.1), and 75.1% (SE, 0.2), respectively, for patients treated at TQV facilities.

Improved survival for patients treated at higher volume facilities was also found on multivariate analyses. Cox multivariate analysis revealed that treatment at both MQV (hazard ratio [HR], 0.834; 95% confidence interval [CI], 0.778-0.895) and TQV (HR, 0.691; 95% CI, 0.644-0.741) facilities was associated with improved survival compared with treatment at BQV facilities (Table I). We also found that treatment at nonacademic facilities was associated with poorer survival (HR, 1.046; 95% CI, 1.016-1.617). Patients undergoing lymph node dissections were also noted to have a poorer prognosis (HR, 1.329; 95% CI, 1.282-1.378).

Propensity score–matched analysis demonstrated similar results. In matched cohorts of patients treated at TQV facilities versus at MQV facilities, we demonstrated that patients treated at TQV facilities exhibited improved survival ($P < .0001$). Within these matched cohorts, the 3-, 5-, and 10-year survival rates were 90.2% (SE, 0.2), 83.9% (SE, 0.2), and 70.6% (SE, 0.5), respectively, for patients treated at MQV facilities and 91.8% (SE, 0.2), 86.4% (SE, 0.2), and 74.3% (SE, 0.5), respectively, for patients treated at TQV facilities (Fig 2, *A*). Similarly, matched cohorts of patients treated at BQV facilities versus at MQV facilities revealed that patients treated at BQV facilities exhibited poorer survival ($P = .0003$). Within these matched cohorts, the 3-, 5-, and 10-year survival rates were 89.4% (SE, 0.6), 82.4% (SE, 0.8), and 69.3% (SE, 1.5), respectively, for patients treated at MQV facilities and 86.2% (SE, 0.7), 79.6% (SE, 0.8), and 64.4% (SE, 1.6), respectively, for patients treated at BQV facilities (Fig 2, *B*).

Characteristics of patients treated at BQV, MQV, and TQV facilities are presented in Table II. The proportion of black patients treated at TQV facilities (0.4%) was smaller than that treated at BQV facilities (1.2%). Similarly, the proportion of Hispanic patients treated at TQV facilities (1.2%) was smaller than that treated at BQV facilities (2.6%). Additionally, more patients treated at TQV facilities had private insurance (61.1%) than did patients treated at MQV (54.1%) and BQV (50.9%) facilities. Conversely, uninsured patients made up a greater proportion of patients treated at BQV facilities (4.5%) than at MQV (3.5%) and TQV (2.2%) facilities. Among patients treated at TQV facilities, 51.8% were treated at academic centers, compared with 9.9% and 4.5% treated at MQV and BQV facilities, respectively.

When propensity score–matched cohorts of patients treated at MQV academic versus at

Table II. Characteristics of top (fourth)-quartile-volume versus middle (second- and third)- and bottom (first)-quartile-volume facilities

	Before propensity score matching			After propensity score matching for bottom quartile		After propensity score matching for top quartile	
Variable	Bottom (first) quartile, n (%)	Middle (second and third) quartiles, n (%)	Top (fourth) quartile, n (%)	Bottom (first) quartile, n (%)	Middle (second and third) quartiles, n (%)	Top (fourth) quartile, n (%)	Middle (second and third) quartiles, n (%)
Age, median, y (SD)	$P = .442$		$P < .001$	$P = .982$		$P = .960$	
	60 (16.8)	60 (16.4)	58 (16.6)	60 (16.4)	60 (16.4)	60 (16.3)	60 (16.3)
Sex	$P = .386$		$P = .014$	$P = .959$		$P = 1.000$	
Female	1737 (45.9)	16,037 (45.1)	54,282 (45.8)	1405 (46.0)	1403 (45.9)	13,615 (45.1)	13,615 (45.1)
Male	2051 (54.1)	19,508 (54.9)	64,097 (54.2)	1651 (54.0)	1653 (54.1)	16,571 (54.9)	16,571 (54.9)
Race	$P < .001$		$P < .001$	$P = 1.000$		$P = .994$	
White	3567 (94.2)	34,203 (96.2)	113,896 (96.2)	3017 (98.7)	3017 (98.7)	29,727 (98.5)	29,728 (98.5)
Black	45 (1.2)	179 (0.5)	536 (0.4)	2 (0.1)	2 (0.1)	28 (0.1)	31 (0.1)
Hispanic	100 (2.6)	546 (1.5)	1356 (1.2)	17 (0.6)	17 (0.6)	152 (0.5)	149 (0.5)
Asian/Pacific Islander	14 (0.4)	85 (0.2)	353 (0.3)	1 (0.0)	1 (0.0)	13 (0.0)	12 (0.0)
Other/Unknown	62 (1.6)	532 (1.5)	2238 (1.9)	19 (0.6)	19 (0.6)	266 (0.9)	266 (0.9)
Charlson/Deyo score	$P = .578$		$P < .001$	$P = 1.000$		$P = 1.000$	
0	3205 (84.6)	30,243 (85.1)	105,352 (89.0)	2670 (87.4)	2670 (87.4)	26,665 (88.3)	26,665 (88.3)
1	473 (12.5)	4387 (12.3)	10,946 (9.2)	340 (11.1)	340 (11.1)	3138 (10.4)	3139 (10.4)
2	88 (2.3)	709 (2.0)	1615 (1.4)	39 (1.3)	39 (1.3)	323 (1.1)	323 (1.1)
≥3	22 (0.6)	206 (0.6)	466 (0.4)	7 (0.2)	7 (0.2)	60 (0.2)	59 (0.2)
Insurance	$P < .001$		$P < .001$	$P = 1.000$		$P = .999$	
Private	1927 (50.9)	19,221 (54.1)	72,290 (61.1)	1631 (53.4)	1631 (53.4)	17,284 (57.3)	17,277 (57.2)
Government	1641 (43.3)	14,543 (40.9)	41,602 (35.1)	1310 (42.9)	1311 (42.9)	12,050 (39.9)	12,054 (39.9)
None	172 (4.5)	1236 (3.5)	2659 (2.2)	94 (3.1)	93 (3.0)	567 (1.9)	567 (1.9)
Unknown	48 (1.3)	545 (1.5)	1828 (1.5)	21 (0.7)	21 (0.7)	285 (0.9)	288 (1.0)
Facility type	$P < .001$		$P < .001$	$P = 1.000$		$P = 1.000$	
Academic	172 (4.5)	3508 (9.9)	61,317 (51.8)	79 (2.6)	79 (2.6)	2952 (9.8)	2952 (9.8)
Other	3616 (95.5)	32,037 (90.1)	57,062 (48.2)	2977 (97.4)	2977 (97.4)	27,234 (90.2)	27,234 (90.2)
Breslow depth	$P < .001$		$P < .001$	$P = 1.000$		$P = 1.000$	
≤1.0 mm	2255 (59.5)	21,536 (60.6)	71,978 (60.8)	2008 (65.7)	2008 (65.7)	19,919 (66.0)	19,916 (66.0)
1.01-2.00 mm	646 (17.0)	6800 (19.1)	23,501 (19.8)	514 (16.8)	514 (16.8)	5703 (18.9)	5707 (18.9)
2.01-4.00 mm	461 (12.2)	4051 (11.4)	13,626 (11.5)	319 (10.4)	318 (10.4)	2844 (9.4)	2844 (9.4)
>4.00 mm	426 (11.2)	3158 (8.9)	9274 (7.8)	215 (7.0)	216 (7.1)	1720 (5.7)	1719 (4.7)
No. of positive nodes	$P < .001$		$P < .001$	$P = 1.000$		$P = .965$	
0	3539 (93.4)	33,987 (95.6)	114,152 (96.4)	3021 (98.8)	3021 (98.8)	29,959 (99.2)	29,964 (99.3)
1	163 (4.3)	1037 (2.9)	2597 (2.2)	29 (1.0)	29 (1.0)	190 (0.6)	187 (0.6)
2-3	48 (1.3)	336 (1.0)	1077 (0.9)	3 (0.1)	3 (0.1)	28 (1.0)	28 (0.1)
≥4	38 (1.0)	185 (0.5)	553 (0.5)	3 (0.1)	3 (0.1)	9 (0.0)	7 (0.0)
Local lymph node dissection	$P = .008$		$P < .001$	$P = .961$		$P = .988$	
Not performed	3282 (86.6)	31,318 (88.1)	102,041 (86.2)	2831 (92.6)	2830 (92.6)	27,876 (92.4)	27,877 (92.4)
Performed	506 (13.4)	4227 (11.9)	16,338 (13.8)	225 (7.4)	226 (7.4)	2310 (7.6)	2309 (7.6)

Radiotherapy	$P = .003$		$P < .001$	$P = 1.000$			$P = .712$	
Not administered	3706 (97.8)	35,000 (98.5)	116,973 (98.8)	3048 (99.7)	3048 (99.7)		30,125 (99.8)	30,129 (99.8)
Administered	82 (2.2)	545 (1.5)	1406 (1.2)	8 (0.3)	8 (0.3)		61 (0.2)	57 (0.2)
Chemotherapy	$P = .001$		$P < .001$	$P = 1.000$			$P = .701$	
Not administered	3717 (98.1)	35,100 (98.8)	117,402 (99.2)	3051 (99.8)	3051 (99.8)		30,154 (99.9)	30,157 (99.9)
Administered	71 (1.9)	445 (1.2)	977 (0.8)	5 (0.2)	5 (0.2)		32 (0.1)	29 (0.1)
Systemic immunotherapy	$P = .002$		$P = .135$	$P = .904$			$P = .793$	
Not administered	3617 (95.5)	34,299 (96.5)	114,029 (96.3)	3022 (98.9)	3021 (98.8)		29,822 (99.8)	29,829 (98.8)
Administered	171 (4.5)	1246 (3.5)	4350 (3.7)	34 (1.1)	35 (1.2)		364 (1.2)	357 (1.2)

P values were generated from the Student 2-tailed test comparing group to the middle-quartiles group for the age variable and from the chi-square test comparing group to the middle-quartile group for all other variables.

nonacademic facilities were generated, no significant difference in survival was noted ($P = .9963$). However, propensity score–matched cohorts of patients treated at TQV academic versus at nonacademic facilities demonstrated improved survival for patients treated at academic facilities ($P < .0001$). The 3-, 5-, and 10-year survival rates for patients within these matched cohorts were 88.1% (SE, 0.3), 80.9% (SE, 0.4), and 67.1% (SE, 0.7), respectively, for patients treated at nonacademic facilities and 90.0% (SE, 0.2), 83.8% (SE, 0.3), and 71.6% (SE, 0.7), respectively, for patients treated at academic facilities. All results were unchanged when analyses were repeated with exclusion of patients who received immunotherapy and exclusion of patients with acral lentiginous tumors.

DISCUSSION

In the present study, we found that the case volume of treatment centers is significantly associated with long-term survival for patients with primary nonmetastatic melanoma. This is consistent with the findings that have been reported for both metastatic melanoma[18] and other malignancies.[10,11,18,33-37] A number of theories have been proposed to explain this observed pattern of improved outcomes for patients treated at higher-volume facilities.

A growing body of evidence from studies of cancer treatment practices suggests that high-volume centers are more likely to follow evidence-based treatment guidelines.[5,6,38-40] Data from Sweden suggest that one cause of this effect may be an increased likelihood of discussion of patients at multidisciplinary tumor conferences at high-volume hospitals, which is an independent predictor of the delivery of guideline-adherent care.[40,41] Indeed, discussion of patients at multidisciplinary panels often leads to changes in treatment recommendations.[42-44] Adherence to treatment guidelines is particularly important given the evidence that it leads both to improved patient survival and to decreased expenditures.[45-50]

Studies of surgical outcomes have proposed that surgeon volume, which is perhaps a proxy for technical skill, may be the driver of the volume-outcome relationship at the hospital level.[51-53] However, studies following providers who practice in more than 1 institution have shown that the same provider achieves improved outcomes when practicing in a higher-volume center, suggesting that hospital-level factors play an important role in patient outcomes independent of providers.[54,55]

We have also demonstrated that treatment at an academic center is an independent predictor of

improved patient survival. Interestingly, when we assessed this relationship within volume quartiles, we found that academic institutions did not show improved outcomes within MQV institutions but within TQV institutions, treatment at an academic center was associated with significantly improved survival. Previous analyses have suggested improved patient survival and guideline adherence at academic institutions but did not differentiate these centers by volume.[13-15,56] Notably, although academic centers did have higher yearly case volumes, 40.3% were within the bottom 3 quartiles of case volume.

Furthermore, although the association of facility case volume with survival remained significant after controlling for the demographic and clinical characteristics of the patients they treated, there were noteworthy differences between the patient populations treated at these centers. First, there was a significant difference between racial demographics, with black patients comprising triple and Hispanic patients comprising more than double the proportion of patients treated at BQV facilities than at TQV facilities. Additionally, there were significantly higher proportions of uninsured patients and lower proportions of patients with private insurance who were treated at MQV and BQV facilities versus at TQV facilities. Indeed, disparities in melanoma survival by patient race and insurance status are well documented.[57-61] Although multiple reasons for these disparities likely exist, one component may be a lack of access to higher-quality care centers. In fact, work in the cardiac surgery literature has shown that racial minorities and those with government insurance or no insurance are less likely to gain access to high-quality providers and care centers.[62-65] Notably, patients treated at BQV facilities were also slightly more likely to have positive lymph nodes and large (>4 mm) tumors. Accordingly, BQV facilities were more likely to administer nodal dissections and to utilize adjuvant therapies. However, the variance in outcomes between BQV, MQV, and TQV facilities persisted after propensity score matching had eliminated differences in disease status and treatment regimen, making it unlikely that these differences were the primary reason for the poorer survival found for patients treated at lower-volume facilities.

With high-volume facilities currently treating slightly more than 70% of cases, further shifting of patient care toward these centers may improve overall survival of melanoma patients. Most of the current push for such regionalization of cancer care has focused on decreasing perioperative mortality in high-risk cancer surgery, and where it has occurred, this regionalization has indeed resulted in improved patient survival and decreased cost of care.[66-71] In certain health care systems, including in some Canadian provinces, such centralized care for complex procedures is a matter of policy.[72-74] Regionalization presents its own challenges, including its potential to overwhelm the resources of high-volume centers, the lack of sufficient case density to support a high-volume center in certain geographic areas,[75] and its potential to lead to underuse of health care in rural areas. Nevertheless, if these problems are addressed, regionalization of melanoma care to high-volume regional cancer centers may provide an avenue to improve long-term outcomes. Alternatively, the fuller identification of those elements of the larger academic treatment centers that are most responsible for the observed survival advantage at these centers may suggest beneficial alterations in the practice and procedures of smaller local facilities that could improve their patient outcomes.

We also noted that patients receiving lymph node dissections exhibited poorer overall survival than those who did not. It is not clear from our data whether this is due to treatment effect or, in our opinion more likely, to a selection bias of patients with adverse features such as ulceration or perineural invasion for lymph node dissections.

There were several limitations to this study. First, although we were able to control for the use of chemotherapy and immunotherapy, we did not have any details regarding specific drugs, dosages, or regimens followed, which limited our ability to differentiate between classes of medications. Especially given the strides made in melanoma immunotherapy between development of interferon therapy and newer checkpoint inhibitors,[76,77] differential use of these drugs may influence outcomes. To address this limitation, we repeated our analysis for patients who did not receive immunotherapy and found that our results were unchanged. Furthermore, we were unable to control our analysis for additional factors that may have provided further controls, such as patient skin type and extent of sun damage, owing to their absence from the data set. Finally, we had no data on local control or disease-specific survival and could not determine whether the survival benefit noted in our analysis extended to disease-free survival.

Nonetheless, this is, to our knowledge, the first study to demonstrate a volume-outcome relationship for the treatment of primary nonmetastatic melanoma. We have also shown that within high-volume facilities, academic facilities achieve improved outcomes. Our results, which have been drawn from nationwide data, suggest that increased utilization of those aspects of high-volume academic centers that

most influence patient survival, whether by further regionalization of care to these centers or by identification and more widespread implementation of these outcome-improving practices, may provide an opportunity for improving the long-term outcomes of patients with melanoma.

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