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Social determinants of health affecting treatment of pediatric brain tumors

Jillian M. Berkman, MD[1,5], **Jonathan Dallas, BS**[1,2], **Jaims Lim, MD**[1,6], **Ritwik Bhatia, MD**[1,2], **Amber Gaulden, BS**[1], **Stephen R. Gannon, BS**[1,3], **Chevis N. Shannon, DrPH**[1,3], **Adam J. Esbenshade, MD, MSCI**[4], **John C. Wellons III, MD, MSPH**[1,3]

[1]Surgical Outcomes Center for Kids, Monroe Carell Jr. Children's Hospital at Vanderbilt

[2]Vanderbilt University School of Medicine

[3]Department of Neurological Surgery, Vanderbilt University Medical Center

[4]Department of Pediatrics, Division of Hematology-Oncology, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, Tennessee

[5]Department of Internal Medicine, Brigham and Women's Hospital, Boston, Massachusetts

[6]Department of Neurosurgery, School of Medicine and Biomedical Sciences, University of Buffalo, State University of New York at Buffalo, New York

Abstract

OBJECTIVE—Little is understood about the role that health disparities play in the treatment and management of brain tumors in children. The purpose of this study was to determine if health disparities impact the timing of initial and follow-up care of patients, as well as overall survival.

METHODS—The authors conducted a retrospective study of pediatric patients (< 18 years of age) previously diagnosed with, and initially treated for, a primary CNS tumor between 2005 and 2012 at Monroe Carell Jr. Children's Hospital at Vanderbilt. Primary outcomes included time from symptom presentation to initial neurosurgery consultation and percentage of missed follow-up visits for ancillary or core services (defined as no-show visits). Core services were defined as healthcare interactions directly involved with CNS tumor management, whereas ancillary services were appointments that might be related to overall care of the patient but not directly focused on treatment of the tumor. Statistical analysis included Pearson's chi-square test, nonparametric

Correspondence: Jillian Berkman: Brigham and Women's Hospital, Boston, MA. jberkman1@partners.org.

Author Contributions

Conception and design: Berkman, Gannon, Shannon, Esbenshade, Wellons. Acquisition of data: Berkman, Dallas, Lim, Bhatia, Gaulden, Gannon. Analysis and interpretation of data: Berkman, Dallas, Lim, Gannon, Shannon. Drafting the article: Berkman, Dallas, Lim. Critically revising the article: Berkman, Dallas, Lim, Shannon. Reviewed submitted version of manuscript: Berkman, Dallas, Lim, Shannon. Approved the final version of the manuscript on behalf of all authors: Berkman. Statistical analysis: Shannon. Administrative/technical/material support: Gannon, Shannon. Study supervision: Gannon, Shannon, Wellons.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Supplemental Information

Previous Presentations

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univariable tests, and multivariable linear regression. Statistical significance was set a priori at $p < 0.05$.

RESULTS—The analysis included 198 patients. The median time from symptom onset to initial presentation was 30.0 days. A mean of 7.45% of all core visits were missed. When comparing African American and Caucasian patients, there was no significant difference in age at diagnosis, timing of initial symptoms, or tumor grade. African American patients missed significantly more core visits than Caucasian patients ($p = 0.007$); this became even more significant when controlling for other factors in the multivariable analysis ($p < 0.001$). African American patients were more likely to have public insurance, while Caucasian patients were more likely to have private insurance ($p = 0.025$). When evaluating survival, no health disparities were identified.

CONCLUSIONS—No significant health disparities were identified when evaluating the timing of presentation and survival. A racial disparity was noted when evaluating missed follow-up visits. Future work should focus on identifying reasons for differences and whether social determinants of health affect other aspects of treatment.

Keywords

brain tumor; health disparity; pediatric; race; oncology

Brain tumors are the second most common malignancy of childhood and have the highest mortality rate of all childhood cancers.[2,7] Survival of children after diagnosis is largely dependent on age at diagnosis, histological type of tumor, location of the tumor in the brain, and treatment pattern.[4] However, other variables have been shown to affect health outcomes, including social determinants of health. The first publications to observe that black Americans have higher rates of death as a result of certain cancers compared with white Americans were published in the early 1970s.[5,8] More recently, in 2003, the Institute of Medicine published a comprehensive review of racial and ethnic disparities in adult healthcare and indicated that income, education, and health insurance coverage influenced access to appropriate care, impacting early detection, treatment, and palliative care.[9] Furthermore, Hispanic and black patients have higher mortality rates, even when controlling for surgical management, among adult patients with solid tumors of the CNS.[6] Insurance status has also been linked to health outcomes in this population.[6]

Notably, these disparities are much less defined in the pediatric population, and, historically, studies have been contradictory. If the medical community can identify health disparities across the pediatric population with brain tumors, we can better target groups with interventions in hopes of creating a more equitable healthcare environment and improving outcomes. Additionally, other tactics may be used to address implicit bias if race or ethnicity were the only drivers of disparity.

Most reports of health disparities in the pediatric population focus on other countries (with nationalized healthcare) or study hematological malignancies.[3] One study looked at socioeconomic disparities in childhood cancer survival in Switzerland and linked low socioeconomic status with decreased survival.[1] A British study reported that survival of children with primary malignant brain tumors was associated with age, morphology, WHO

grades, tumor sites, and periods of diagnosis but not socioeconomic status (SES).[13] In a US study in 2016, Austin et al. examined health disparities in disease stage at presentation and survival within a cohort of children with CNS solid tumors in Texas.[2] In their cohort, Hispanic patients were more likely to present with advanced-stage disease, and both Hispanic and non-Hispanic black patients had a decreased overall survival compared to white patients. They also found that among individuals with malignant tumors, non-Hispanic black patients had worse survival than non-Hispanic white patients.[2] While this study showed that disparity does exist in the pediatric brain tumor population, the authors were unable to ask granular questions about what other social determinants of health contributed to these disparities.

We investigated whether the same health disparities that exist in the adult population are present in the pediatric CNS tumor population at Monroe Carell Jr. Children's Hospital at Vanderbilt (MCJCHV) University in Nashville, Tennessee. This is a study of a single tertiary care center, and, by looking more in depth at one center, we were able to examine more detailed aspects of a patient's care, such as the timing of presenting symptom until initial consultation and percentage of missed follow-up visits. Additionally, Vanderbilt has a wide catchment area within the Southeast that differs from the Texas regional study. We designed this study under the presumption that it is critical for pediatric brain tumor patients to obtain treatment in a timely fashion and to have follow-up visits after diagnosis. As such, the primary aim of this study was to determine whether social determinants of health among CNS tumor patients would have an impact on 1) time to presentation, 2) follow-up care and missed visits, and 3) overall patient survival.

Methods

We retrospectively identified 202 patients (age range 0–17 years) who underwent treatment for a primary brain tumor at the MCJCHV. Of these, race (either Caucasian or African American) could be determined for 198 patients. Patients were included if they were diagnosed with a CNS tumor between January 1, 2005, and March 1, 2012. The study was approved by the institutional review board of Vanderbilt University.

To better understand factors impacting a patient's ability to receive care, we focused on the "accessibility" of healthcare resources. We defined "accessibility" as whether the family had adequate resources (e.g., insurance status, median household income, distance traveled for care) which allowed them to utilize available resources. All demographic patient information was abstracted from electronic medical records. Information regarding the patient's symptoms and time of onset were recorded as documented in the medical record via patient report.

Outcome Measures

Multiple outcome measures were included in this study, including follow-up information that was extracted from the patient's electronic medical record. First, we collected the total number and percentage of missed follow-up appointments (if applicable, these were stratified by whether they occurred before or after disease recurrence). This only included no-show visits in which the patient/family did not cancel beforehand. Follow-up

appointments were stratified into core and ancillary visits. Core visits were defined as any healthcare-related visits that related to management of the CNS tumor. For example, this includes neurosurgery, hematology/oncology, and radiation oncology visits. Ancillary visits were defined as other healthcare appointments that do not directly address CNS tumor treatment but are related to effects of the CNS tumor. Examples of these appointments include: endocrine, ophthalmology, audiology, nutrition, infectious diseases, and neurology appointments. Additionally, we noted the number of days that had passed between initial symptom onset and the patient's first neurosurgical consult/appointment. This was collected via the patient's (or family's) report in the neurosurgical consultation note when possible. Admission and discharge dates were recorded when available for all inpatient hospitalizations.

Explanatory Variables: Social Determinants

We collected sex, age, race, ethnicity, number of household members (both adults and children), insurance status, tumor grade, distance from hospital, and median household income to determine whether any of these social determinants of health adversely affected patient care, either through delay of presentation or an increase in missed follow-up visits. A list of all collected variables is provided in Table 1.

To calculate the distance between a patient's primary residence and the hospital, their recorded zip code was used. In order to determine median household income, the patient's county was determined using the United States Zip Codes database. Using the county of their primary residence, median household income was determined via information from the 2012 US Census (specifically noting families with at least one child younger than 18 years).[14]

Statistical Analysis

Univariable analysis was initially performed to evaluate trends in the data. Because of the nonnormal distribution of continuous variables, nonparametric tests were used for analysis (consisting of Wilcoxon rank-sum test, Kruskal-Wallis test, and Spearman's correlation when appropriate). Categorical variables were assessed using Pearson's chi-square tests. To further assess the relationship between race and percentage of missed visits, subsequent multivariable linear regression was used. Variables predictive of missed core visits at a relaxed p value in univariable analysis ($p < 0.10$) were included in the multivariable linear regression. Overall statistical significance was set a priori at $p < 0.05$.

Results

Overall, 198 pediatric brain tumor patients were included in the analysis. There were no patients of a race other than Caucasian or African American. A demographic summary of these 198 patients, including a breakdown by race, is shown in Table 2. There was no significant difference in tumor grade between Caucasian and African American patients. Statistical significance was seen when stratifying insurance status by race. Caucasian patients were more likely to have private insurance than African American patients, and African American patients were more likely to have public insurance than Caucasian

patients. African American patients were significantly more likely to live closer to MCJCHV than Caucasian patients (28.5 miles vs 41.0 miles, p = 0.037).

Outcome variables for treated patients (percentage of missed visits and the time from symptom onset to presentation) were then evaluated. African American patients missed a higher percentage of core visits (11.76% vs 3.12%, p = 0.007). Overall, patients missed a median of 3.25% of core visits (Table 3). There was a significant correlation between insurance status and missed core visits (p = 0.021). There were no significant associations with ethnicity, sex, median income, or distance with percentage of missed core or ancillary visits.

To further assess the relationship between race and missed core visits, a multivariable linear regression model was used. The model included variables that were univariably predictive of race at a relaxed p value; these included 1) race, 2) insurance status, and 3) tumor grade. The results of this model are shown in Table 4. As shown, even when controlling for tumor grade and insurance status, African American race was still a significant predictor of missed core visit percentage (+6.90%, p < 0.001). Self-pay/lack of insurance was also independently associated with an increase in missed visits (+8.46%, p = 0.005).

A number of variables were investigated to see whether they had an impact on patient survival (measured at both 2 years and 5 years). As expected, both the type and grade of the tumor were noted to have a significant effect on patient survival (p < 0.001). The number of days to presentation following symptom development also had a significant effect, wherein patients who presented sooner were more likely to have died sooner (Table 5). Note that this does not control for tumor type or grade.

It took a median of 30 days for patients to present to Vanderbilt. There was a significant association between age and number of days with known symptoms before presentation (p < 0.001). There was no association with time from first symptom to presentation and race, sex, insurance status, distance to Vanderbilt, or median family income. The median time to presentation for Hispanic patients was significantly less than the time for non-Hispanic patients to present (Table 6, p = 0.031). There was a significant relationship between tumor grade and time to presentation (p = 0.040). Specifically, patients with a grade III tumor presented at a median of 14 days, whereas patients with a grade II tumor presented at a median of 126 days (Table 6). Additionally, patients who presented sooner were less likely to have survived at both 2 years (p = 0.037) and 5 years (p = 0.081), although this was only significant at the 2-year mark.

Discussion

In 2003, the Institute of Medicine published their report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care,* which included a call to the healthcare community to work to reduce the many disparities that exist.[11] In 2013, the US Department of Health and Human Services released its 10th annual report on health disparities and laid out three specific goals: achieve health equity; ensure access to quality, cultural-competent care for vulnerable populations; and improve data collection and measurement.[15] Given the

importance that social determinants play in overall health and treatment, this study sought to investigate a number of previously unidentified and addressable factors that could be used to improve overall patient care in these domains.

Insurance Status

Insurance status has previously been shown to be an important social determinant of health and has an impact on survival differences among patients.[6] Curry et al. examined insurance status as a predictor of in-hospital mortality in adults with CNS tumors and found that patients receiving Medicaid as compared to Medicare had a significantly increased mortality rate and those with private insurance had a decreased mortality rate.[6] However, unlike the adult population, almost all children should be covered by state insurance if not under private insurance. In this cohort, there was a significant difference in insurance status: African American patients were more likely to have public insurance and Caucasian patients were more likely to have private insurance ($p = 0.009$ and $p = 0.004$). Insurance status was also a predictor of a higher percentage of missed visits until first recurrence ($p = 0.021$). Of note, insurance status was not associated with survival.

Race

Most of the previous US studies in this area have used large database-driven studies instead of a single hospital cohort and provided conflicting conclusions regarding the role of race and survival. One study used SEER data from 1973 to 1996 and did not find any disparity in overall survival when comparing Hispanics, Asians, African Americans, and non-Hispanics.[4] However, Austin et al. used data from the Texas Cancer Registry (1995–2009) to show that 1) Hispanic patients were more likely to present with advanced-stage disease, and 2) Hispanic and African American patients had a decreased overall survival compared with Caucasian patients, with malignant tumor status being the best predictor of overall survival.[3]

We found that race was not associated with tumor grade at presentation or overall survival at 2 or 5 years. However, we did find a disparity in treatment adherence: African American patients were more likely to miss treatment visits even though they were also more likely to live closer to the treatment center than Caucasian patients ($p = 0.007$ and $p = 0.037$). Although matters do not indicate that disparities in treatment adherence manifest in overall survival rates, they could point to other differences, such as in the overall cost of treatment, complication rates, and so on. Additional studies would be needed to investigate further the causes and effects of this discrepancy.

SES

We did not find a relationship between SES and the percentage of missed visits or overall survival at our institution. Austin et al. did find an association among SES, advanced-stage CNS solid tumors, and survival outcomes at 1 and 5 years, with SES determined using the Agency for Healthcare and Quality formula and 2007–2011 US Census block group data.[2] In this study, SES is based off of zip code and is not patient specific. In the geographic area surrounding MCJCHV, there is a high level of income variability within individual zip codes. As stated above, there was a difference in insurance status based off of race, and

insurance status can be a proxy for SES. However, a prospective study would be needed to gather accurate and specific socioeconomic information about each patient.

Time to Presentation

The median time from symptom onset to presentation in our cohort was 30 days. There were no differences in median number of days that a symptom was present and time to presentation when looking at African American patients versus Caucasian patients; however, there was a significant difference in time to presentation for Hispanic versus non-Hispanic patients. These findings are similar to those of prior studies; for example, Austin et al. found that Hispanic patients were more likely to present with advanced disease,[2] and Stocco et al. found that for 75 patients in Italy, the median time to presentation was 4 weeks.[12]

Our data also show that the patients who presented sooner were less likely to have survived both at 2 years ($p = 0.037$) and at 5 years ($p = 0.081$), although this was only significant at the 2-year mark. Of note, this is univariable analysis and did not control for tumor type or grade, instead looking at presentation times across all CNS tumors. Separately, we did find a significant relationship between tumor grade and time to presentation. Specifically, our data suggest that grade II and grade III tumors have the greatest difference in presentation times. Tumor grade also had a significant effect on overall 2- and 5-year mortality rates. As such, this relationship could be explained by more dangerous tumors growing faster or to a larger size, thereby causing symptoms sooner.

Travel Distance for Treatment

Prior studies of this, such as that using the SEER database, have used the closest potential treatment center and not the center that patients necessarily used.[2] This was investigated based on the previously shown relationship between geographic access to care and outcomes.[10] When comparing travel distance by race in this study, there was a significant difference in median number of miles that Caucasian and African American patients traveled to reach MCJCHV, with African American patients living closer than Caucasian patients ($p = 0.037$). That said, we did not find a significant difference in whether distance affected percentage of missed visits overall or percentage of missed visits until first recurrence ($p = 0.447$ and $p = 0.502$). Similarly, travel distance was not found to affect overall survival.

Limitations

The fact that this is a single-center study introduces regional bias into the data. As such, it may not be generalizable to other patient populations or geographic areas. Cultural practices and views of medicine differ regionally and have the potential to influence factors such as time to presentation. Additionally, it has the inherent limitations associated with any retrospective analysis; for example, this research relied on electronic medical record documentation and thus required physicians to accurately and thoroughly document visits. Finally, there are some variables that could be improved. For example, symptom descriptions are a result of subjective patient/family reporting, and zip code–based income estimation may not reflect the accurate income/net worth of an individual resident.

Conclusions

This was a retrospective, single-center study that sought to investigate health disparities in the treatment of pediatric CNS tumors. While there were no identified disparities that resulted in higher mortality rates, both African American race and public insurance were univariably associated with an increased rate of missed follow-up appointments. Interestingly, there was an increase in mean missed core visits versus ancillary visits, which may reflect the burden of increased core visits once a patient has been diagnosed. While it is still unclear what exact social drivers contribute to this trend, the previously unreported healthcare disparities highlighted by this study can be used as the basis for a prospective, multicenter investigation that seeks to better achieve healthcare equity among CNS tumor patients.

ABBREVIATIONS

MCJCHV	Monroe Carell Jr. Children's Hospital at Vanderbilt
SES	socioeconomic status

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TABLE 1.

List of categorical and continuous variables included in this study

Descriptive Variables
Age at diagnosis (yrs)
Race
Caucasian
African American
Biological sex
Male
Female
Ethnicity
Non-Hispanic
Hispanic
Insurance
Private
Public
Self-pay
Other (i.e., military)
Zip code (numerical)
Median household income (of patient's zip code) (USD)
Mean distance to hospital (of patient's zip code) (miles)
Tumor grade
I
II
III
IV
Unknown
Tumor group
Ependymoma
Germ cell
Glioma (high grade)
Glioma (low grade)
Medulloblastoma/PNET/ATRT
Other (high grade)
Other (low grade)
Outcomes
Time from symptom onset to neurosurgical consultation (days)
Percentage of missed core visits (appointments related to treatment of tumor)
Percentage of missed ancillary visits (appointments not related to treatment of tumor)
Survival (2 yrs)

Descriptive Variables
Yes
No
Survival (5 yrs)
Yes
No

ATRT = atypical teratoid rhabdoid tumor; PNET = primitive neuroectodermal tumor.

TABLE 2.

Demographic information stratified by patient race

Variable	No. of Patients (%) or Median (IQR)			p Value
	Overall Cohort (n = 198)	African American (n = 33)	Caucasian (n = 165)	
Biological sex				
Male	117 (59)	18 (55)	99 (60)	0.561
Female	81 (41)	15 (45)	66 (40)	
Ethnicity				
Hispanic	10 (6)	1 (3)	9 (6)	0.488
Non-Hispanic	171 (94)	32 (97)	139 (94)	
Insurance				
Private	101 (51)	10 (30)	91 (55)	
Public	71 (36)	19 (58)	52 (32)	**0.025**
Self-pay	14 (7)	3 (9)	11 (7)	
Other (military)	12 (6)	1 (3)	11 (7)	
Insurance				
Private vs other	101 (51) vs 97 (49)	10 (30) vs 23 (70)	91 (55) vs 74 (45)	**0.009**
Public vs other	71 (36) vs 127 (64)	19 (58) vs 14 (42)	52 (32) vs 113 (68)	**0.004**
Median household income (USD)	47,506 (45,654, 58,273)	50,287 (47,506, 56,945)	47,506 (45,643, 58,550)	**0.031**
Mean distance (miles)	40.5 (22.8, 73.8)	28.5 (11.4, 61.0)	41.0 (24.3, 74.1)	**0.037**
Tumor grade category				
High	68 (37)	11 (37)	57 (37)	0.991
Low	117 (63)	19 (63)	98 (63)	
Tumor grade				
I	73 (37)	11 (34)	62 (38)	
II	19 (10)	2 (6)	17 (10)	
III	18 (9)	4 (12))	14 (9)	0.930
IV	36 (18)	7 (22)	29 (18)	
Unknown	52 (26)	9 (27)	43 (26)	

Boldface type indicates statistical significance.

TABLE 3.

Outcome information stratified by patient race

Variable	Overall Cohort (n = 198)	African American (n = 33)	Caucasian (n = 165)	p Value
Age at diagnosis (yrs)	7.67 (2.97, 13.62)	9.39 (5.80, 11.75)	7.33 (2.89, 14.08)	0.646
Time from symptom onset to neurosurgical consult (days)	30.0 (13.8, 99.2)	25.5 (14.0, 72.2)	30.0 (14.0, 106)	0.827
Percentage of missed core visits	3.25 (0, 9.16)	11.76 (1.69, 21.43)	3.12 (0, 7.64)	**0.007**

Boldface type indicates statistical significance. Values are presented as the median (25%, 75%).

TABLE 4.

Multivariable linear regression assessing predictors of missed visits

Variable	Change in Missed Visit	p Value
Race		
Caucasian	Ref	—
African American	+6.90%	**<0.001**
Insurance		
Private	Ref	—
Public	+2.13%	0.191
Other (e.g., military)	+3.63%	0.232
Self-pay	+8.46%	**0.005**
Tumor grade		
Low	Ref	—
High	+1.77%	0.251

Boldface type indicates statistical significance.

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TABLE 5.

Demographic and outcome variable effects on 2- and 5-year survival

Variable	Overall 2-Yr Survival		p Value	Overall 5-Yr Survival		p Value
	Yes	No		Yes	No	
Tumor group						
Ependymoma	13 (8)	2 (12)		11 (8)	2 (10)	
Germ cell	4 (2)	0 (0)		2 (1)	0 (0)	
Glioma (high grade)	3 (2)	3 (19)		1 (1)	4 (20)	
Glioma (low grade)	85 (49)	1 (6)	**0.001**	74 (51)	1 (5)	**<0.001**
Medulloblastoma/PNET/ATRT	34 (20)	9 (56)		28 (19)	12 (60)	
Other (high grade)	3 (2)	1 (6)		2 (1)	1 (5)	
Other (low grade)	28 (16)	0 (0)		24 (17)	0 (0)	
Tumor grade						
High	51 (31)	14 (88)	**<0.001**	41 (30)	18 (90)	**<0.001**
Low	115 (69)	2 (12)		96 (70)	2 (10)	
Ethnicity						
Hispanic	10 (6)	0 (0)	0.377	8 (6)	0 (0)	0.324
Non-Hispanic	153 (94)	12 (100)		131 (94)	16 (100)	
Race						
Caucasian	144 (83)	13 (93)	0.327	119 (82)	17 (94)	0.169
African American	30 (17)	1 (7)		27 (18)	1 (6)	
Biological sex						
Female	73 (41)	6 (38)	0.757	60 (41)	8 (40)	0.944
Male	103 (59)	10 (62)		87 (59)	12 (60)	
Days primary symptom present (median [25%, 75%])	30.0 (14.0, 106.0)	14.0 (7.0, 30.0)	**0.037**	30.0 (14.0, 106.0)	21.0 (7.0, 44.5)	0.081
Percentage of missed core visits (median [25%, 75%])	3.27 (0, 8.42)	2.40 (0, 3.93)	0.211	3.23 (0, 7.93)	2.78 (0.89, 5.92)	0.376

Boldface type indicates statistical significance. Values are presented as the number (%) of patients unless otherwise indicated.

TABLE 6.

Time to presentation after symptom onset

Variable	No. of Pts	Symptom Onset to Neurosurgical Consult (days)	p Value
Ethnicity			
Hispanic	10	14 (10, 14)	**0.031**
Non-Hispanic	172	30 (14, 99.25)	
Tumor grade			
I	75	21 (8.5, 76)	**0.040**
II	18	126 (47.75, 205.75)	
III	18	14 (7, 46)	
IV	36	29 (20.25, 61)	
Unknown	51	42.5 (15.5, 296.75)	
Tumor grade category			
Low	120	30 (14, 183)	0.097
High	69	30 (14, 61)	

Pts = patients.

Boldface type indicates statistical significance. Values are presented as number of patients or median (25%, 75%).