Clinical Predictors of Survival for Patients with Atypical Teratoid/Rhabdoid Tumors

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Research Article

Keywords: Pediatric tumor, National Cancer Database Study, Pediatric NCDB, Pediatric brain tumor

Posted Date: January 12th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1114936/v1

Version of Record: A version of this preprint was published at Child's Nervous System on April 1st, 2022.
See the published version at https://doi.org/10.1007/s00381-022-05511-w.

Abstract

Purpose: Atypical teratoid/rhabdoid tumors (AT/RT) are malignant central nervous system (CNS) neoplasms of the young. Our study analyzed a large AT/RT cohort from the National Cancer Database (NCDB) to elucidate predictors of short-term mortality and overall survival (OS).

Methods: Information was collected on patients with histologically-confirmed AT/RT using the NCDB (2004-2016). Kaplan-Meier analysis indicated OS. Prognostic factors for 30-day mortality, 90-day mortality, and OS were determined via multivariate Cox proportional-hazards (CPH) and logistic regression models.

Results: Our cohort of 189 patients had a median age of 1 year (IQR [1, 4]) and tumor size of 4.7±2.0 cm at diagnosis. Seventy-two percent were under 3 years old; 55.6% were male and 71.0% were Caucasian. Fifty (27.2%) patients received only surgery (S) (OS=5.91 months), 51 (27.7%) received surgery and chemotherapy (S+CT) (OS=11.2 months), and 9 (4.89%) received surgery and radiotherapy (S+RT) (OS=10.3 months). Forty-five (24.5%) received S+CT+RT combination therapy (OS=45.4 months), 13 (17.1%) received S+CT+BMT/SCT (bone marrow or stem cell transplant) (OS=55.5 months), and 16 (8.70%) received S+CT+RT+BMT/SCT (OS=68.4 months). Bivariate analysis of dichotomized age (HR=0.550, 95% CI[0.357, 0.847], p=0.0067) demonstrated significantly increased patient survival if diagnosed at or above 1 year old. On multivariate analysis, administration of S+CT+RT, S+CT+BMT/SCT, or S+CT+RT+BMT/SCT combination therapy predicted significantly ($p<0.05$) increased OS compared to surgery alone.

Conclusion: AT/RTs are CNS tumors where those diagnosed under 1 year old have a significantly worse prognosis. Our study demonstrates that while traditional CT, RT, and BMT/SCT combination regimens prolong life, overall survival in this population is still low.

Introduction

Atypical Teratoid/Rhabdoid Tumors (AT/RT) are rare, monogenic, grade IV cancers of the central nervous system as defined by the National Cancer Institute [29]. They are associated with biallelic mutations in the tumor suppressor gene SMARCB1 (INI-1). AT/RTs are overwhelmingly diagnosed in pediatric populations and represent 1-2% of all brain tumors in the population. Because AT/RTs are fast-growing, their presence is often accompanied by worsening symptoms including headaches, vomiting, and increasing head size in infants [21, 29]. The 5-year survival rate for patients diagnosed with AT/RT is 32.3%, and the majority undergo surgery prior to adjuvant chemotherapy, radiation, and other treatment regimens.

Due to the rare nature of AT/RTs, there have been relatively few large-scale studies characterizing their clinical outcomes and even fewer studies compiling multicenter information that can adequately represent the full spectrum of the disease. Recent studies have analyzed aggregate patient data from the oncological Surveillance, Epidemiology, and End Results registry, reporting the epidemiology, prognosis,

and survival of AT/RT patients [12, 19]. Our study seeks to complement these investigations by characterizing specific demographic and clinical prognostic factors for both OS and short-term mortality in all patients with AT/RTs within the National Cancer Database (NCDB), with the goal of optimizing future treatment strategies for AT/RT patients.

Methods

This study was based on patient data obtained from the National Cancer Database (NCDB), a clinical oncology surveillance method sponsored by the American College of Surgeons and American Cancer Society which represents over 70% of incidental cancer cases nationally [30]. Analyzed information was pulled from de-identified NCDB Participant User File (PUF) data, exempting it from Institutional Review Board approval.

Patient Cohort and Variables Analyzed

The NCDB was queried for histologically-confirmed cases of AT/RTs, corresponding with ICD-O-3 (International Classification of Diseases for Oncology, Third Edition) pathology code “9508” and further categorized via topography codes for site of origin (C700-C701, C709-C725, C728-C729). Mass location was classified as supratentorial (cerebrum [C710], frontal lobe, [C711], temporal lobe [C712], parietal lobe [C713], occipital lobe [C714], ventricle [C715]), infratentorial (cerebellum [C716], brain stem [C717]), overlapping (overlapping brain lesion [C718], spinal cord/brain overlap [C728]), and not otherwise specified (C719). Tumors were also characterized by lesion size (<3cm or ≥3cm), and extent of resection (biopsy, subtotal resection, gross total resection) as defined by Facility Oncology Registry Data Standards (FORD) [3]. Collected demographics included age, race, sex, year of diagnosis, insurance type, and comorbidities based on Charlson-Deyo score, which is a modified version of the Charlson Comorbidity Index that takes into account both the presence of pre-existing conditions and their severity [10]. Information on aggregate treatment and outcome data was also analyzed, including type of treatment regimen, readmission rates, and 30- and 90-day mortality. Treatment regimens consisted of surgery plus combinatory chemotherapy, radiation, and/or bone marrow/stem cell transplant.

Statistical Analyses

Statistical analyses were all conducted using SAS version 9.4 (SAS Institute). First, univariate survival analysis was performed using Kaplan-Meier curves to model OS. Second, bivariate Wald χ^2 and log-rank tests were used to assess the statistical impact of different factors on OS. Third, a multivariate analysis was carried out via Cox proportional hazards model to predict OS; covariates with a p-value of <0.2 in the bivariate analysis were included in the final multivariate model [16, 24]. Factors with p <0.2 on univariate analysis were also used in a logistic regression model to determine factors associated with 30- and 90-day survival [7, 22, 23]. Hazard ratios with a p-value <0.05 were considered significant.

Results

Patient Characteristics

Our study identified a total of 189 patients with histologically-confirmed AT/RT between 2004 and 2016. All patient demographics can be found in **Table 1**. With a median age at diagnosis of 1 year (interquartile range 0.00 – 4.00), the majority of the cohort was male (105, 55.6%), Caucasian (130, 71%), and lacked Charlson-Deyo comorbidities (157, 83.1%).

The tumor characterization and outcome data of our patient cohort is displayed in **Table 2**. The average tumor size was 4.75 ± 2.02 cm with 126 (80.8%) patients presenting with a brain mass ≥ 3cm at diagnosis. Sixty-one (34.1%) patients had supratentorial tumors, 51 (28.5%) had infratentorial tumors, 11 (6.15%) had overlapping brain lesions, and 56 (31.3%) had tumors in unspecified locations. Among those under the age of three with specified tumor locations, the largest proportion of patients had infratentorial lesions (35%) compared to those over the age of three, where the majority of patients whose tumor location was specified had supratentorial lesions (50%). Similarly, when dichotomized at the age of one, the largest grouping of younger patients had infratentorial lesions (38%) while in those over the age of one, the most common specified tumor location was supratentorial (40%). Regarding surgical treatment, 97 (53.6%) patients underwent gross total resections, 53 (29.3%) underwent subtotal resections, and 31 (17.1%) underwent biopsy only. Adjuvant treatment consisted of different combinations of chemotherapy, radiation, and bone marrow/stem cell transplant. Overall, 126 (68.1%) patients received chemotherapy, 70 (37.6%) received radiation, and 29 (15.3%) received a bone marrow/stem cell transplant. More specifically, 50 (27.2%) patients underwent surgery only, 51 (27.7%) received surgery with adjuvant chemotherapy, 9 (4.9%) received surgery with adjuvant radiation, 45 (24.5%) received surgery with both adjuvant chemotherapy and radiation. Furthermore, 13 (7.07%) received adjuvant chemotherapy and bone marrow/stem cell transplant while 16 (8.7%) patients received adjuvant chemotherapy, radiation, and a bone marrow/stem cell transplant. Of the 29 patients who received bone marrow/stem cell transplants, the majority (65.5%) were less than 3 years old. More specifically, 6 patients (20.7%) were under 1 year of age when they received a bone marrow/stem cell transplant, 8 patients (27.6%) were 1 year old, 5 patients (17.2%) were 2 years old, 1 patient (3.4%) was 3 years old, 5 patients (17.2%) were 4 years old, 1 patient (3.4%) was 6 years old, 2 patients (6.9%) were 8 years old, and 1 patient (3.4%) was 9 years old. Thirty-nine (20.6%) patients were readmitted within 30 days of surgery; 30- and 90-day survival was 93.5% and 84.4%, respectively.

Survival Analysis

The median OS for patients with AT/RT tumors was 17.8 months (Figure 1). Univariate Kaplan-Meier analysis demonstrated a significant increase in median survival with increasing age and the administration of chemotherapy, radiation, or bone marrow/stem cell transplant, regardless of regimen (Figure 2). Notably, no association was found between OS extent of resection, or the presence of comorbidities according to Charlson-Deyo classification.

Bivariate analysis of dichotomized age (HR=0.550, 95% CI[0.357, 0.847], p=0.0067) demonstrated significantly increased patient survival if diagnosed with an AT/RT at or above the age of one year, with

OS being 7.9 months if under the threshold age and 27.2 months if above the threshold age. Furthermore, those who received the adjuvant chemotherapy and radiation regimen (Hazard Ratio [HR]=0.353, 95% CI[0.201, 0.618], p=0.0003), chemotherapy and bone marrow/stem cell transplant regimen (HR=0.297, CI[0.115, 0.764], p=0.0118), and adjuvant chemotherapy, radiation, and bone marrow/stem cell transplant regimen (HR=0.228, CI[0.088, 0.586], p=0.0022) had significantly prolonged survival compared to patients who only received surgery. Results of all bivariate analyses can be found in **Table 3**.

Similarly, multivariate analysis demonstrated that OS was significantly increased by adjuvant chemotherapy and radiation regimen (HR=0.377, CI[0.21, 0.68], p=0.0012), chemotherapy and bone marrow/stem cell transplant regimen (HR=0.296, CI[0.11, 0.77], p=0.0109), and adjuvant chemotherapy, radiation, and bone marrow/stem cell transplant regimen (HR=0.272, CI[0.10, 0.74, p=0.0121) when compared to patients who only received surgery. Of note, age did not remain a significant prognostic factor after accounting for treatment regimen. Multivariate modelling of factors impacting OS results are summarized in **Table 4**.

Further analysis demonstrated that extent of resection, the presence of comorbidities, and treatment type were significantly associated with 30-day mortality, as seen in **Table 5**. Specifically, gross total resection (HR=13.8, CI[1.69, 112], p=0.0144) and adjuvant chemotherapy (HR=21.1, CI[1.95, 229], p=0.0121) corresponded with an increased 30-day mortality, whereas the presence of comorbidities (HR=0.117, CI[0.018, 0.742], p=0.0229) was associated with decreased 30-day mortality. On multivariate analysis of 90-day survival, only adjuvant chemotherapy (HR=5.16, CI[1.500, 17.8], p=0.0092) was significantly associated with increased survival.

Discussion

Prior Research

Numerous studies within the neurosurgical literature have previously investigated prognostic factors associated with survival among AT/RT patients. A 2005 study by Tekautz et al. analyzed a cohort of 37 AT/RT patients and found that patients diagnosed after 3 years of age had significantly longer event-free ($p<0.01$) and (OS; $p<0.001$) compared to those diagnosed before the age of 3 [25]. However, additional research by Fossey et al. and Lu et al. established that the clinical profile and prognosis of AT/RT in patients younger than 3 is highly variable depending on the exact age of diagnosis, with additional factors such as treatment modalities and socioeconomic conditions significantly influencing OS in certain patient subsets [6, 13].

Regarding treatment regimens, a 2017 paper by Fischer-Valuck et al. utilizing patient data from the NCDB found that AT/RT patients treated without trimodal combination therapy (surgery, chemotherapy, and radiation therapy) had significantly decreased OS compared to patients who were (HR=2.52, $p<0.01$), and they also noted that patients aged 0-2 years were significantly less likely to receive trimodal therapy ($p<0.001$) relative to older patients [5]. And furthermore, a recent study by the Japan Children's Cancer

group found that metastasis stage at diagnosis (HR=2.68, p=0.034) and gross tumor resection (HR=3.49, p=0.048) were both significantly associated with PFS, while radiotherapy field treatment (HR=8.45, p=0.045) and high-dose chemotherapy (HR=3.26, p=0.025) were both associated with OS. Notably, none of these factors remained significant in multivariate analysis of PFS or OS [28]. Using the SEER database, research by Lau et al. and Quinn et al. identified distant metastases (OR=4.6, p<0.01) and combination therapy (OR=0.4, p<0.01) as significant prognostic factors, and also demonstrated that infants (<1 year old; HR=0.34, p=0.02) and toddlers (1-2 years old; HR=0.31, p<0.001) benefitted significantly more from trimodal combination therapy relative to older children aged $\geq$ 3 years. A 2020 meta-analysis by Underiner et al. demonstrated that radiation therapy (HR=0.42, p<0.001), intrathecal chemotherapy (HR=0.56, p=0.012), and marrow-ablative chemotherapy with autologous hematopoietic cell rescue (HR=0.21, p<0.0001) were all significantly and independently associated with reduced risk of death.[27]

Regarding optimal treatment protocols, a 2020 study by Reddy et al. found that combination chemotherapy and radiotherapy significantly reduced the risk of event-free survival events (HR=0.43, p<0.001) in a cohort of 65 AT/RT patients., validating earlier work by Chi et al [1, 20]. Park et al. further substantiated these claims by demonstrating that high-dose chemotherapy (p<0.01) and adjuvant radiotherapy (p<0.01) were significantly and independently associated with progression-free survival (PFS) in AT/RT patients younger than 3 [18]. Finally, recent work by Theruvath et al. showed that B7-H3 chimeric antigen receptor (CAR) T-cells are effective against AT/RT tumors both in vitro and in mouse models, suggesting that immunotherapy may be a promising future AT/RT treatment modality [26].

Demographic Characteristics

Building upon this line of research, our study analyzed the age, gender, race, and presence of comorbidities of one of the largest all-age AT/RT patient cohorts based on data from the NCDB. Results indicated a higher incidence of AT/RT in males and Caucasians, though with no impact on OS, similar to prior studies [17, 28]. While this type of tumor mostly occurs in children under the age of three, our cohort of patients were diagnosed at a significantly higher mean age of 5.67 years [15, 26]. Considering a lower median age (1 year), the negatively-skewed age distribution of our patient subset may be attributed to the inclusion of all cases classified as AT/RTs in the NCDB, both pediatric and adult. Specifically, our cohort has a lower pediatric: adult ratio of 10.8:1 (n = 16 adults) whereas adult cases in the general population have been described as “exceedingly rare” with only 50 adult cases having been found to date [31].

Interestingly, data regarding the presence of comorbidities in AT/RT patients is largely limited to case reports [4, 14]. For example, Nemes et al. reported an increased incidence of both intra- and extra-central nervous system (CNS) rhabdoid tumors in children with Rhabdoid Tumor Predisposition Syndrome (RTPS), diagnosed via family history and SMARCA4/SMARCB1 gene variants [14]. Still, while those with RTPS may present with a higher incidence of schwannomas and renal tumors (other comorbidities), those with these conditions have not been show to have a higher chance of developing AT/RTs within the central nervous system, specifically. The majority of patients in our study lacked comorbidities based on Charlson-Deyo scoring; this may be due to the young age at which most patients are diagnosed, resulting in less time to develop conditions outside those congenitally acquired. While the presence of

comorbidities did not impact OS, it did significantly correlate with decreased 30-day survival on multivariate regression analysis. Based on our current knowledge, this is the first study to find a negative correlation between this prognostic factor and 30-day survival. Thus, aggressive adjuvant treatments for patients with comorbidities should be carefully weighed in the context of individual potential for recovery. Furthermore, if ultimately undergoing surgery, these patients should be subject to close monitoring during the post-operative process.

Tumor Characteristics

The majority of patients in the study presented with tumors greater than 3 cm in size at diagnosis. Common symptoms of brain masses at this size can be related to mass effect and hydrocephalus which can precipitate morning headaches, nausea/vomiting, and gait instability. Location-wise, prior literature suggests that primary AT/RTs are more likely to develop in the infratentorial region in younger patients, especially under the age of one [6, 28]. The results of our study aligns with this prior data when dichotomized at the aforementioned age. Furthermore, when categorized as below and above the age of 3 years, there is a similar characterization in tumor location. Notably, there was a non-negligible percentage (32%) of non-specified tumor locations in our cohort's aggregate information provided by the NCDB that needs to be considered when interpreting provided data.

Treatment Characteristics

All 189 patients in our study underwent surgery; the majority were further treated with varying combinations of chemotherapy, radiation, and/or bone marrow/stem cell transplant. Consistent with previously published literature the administration of adjuvant chemotherapy was associated with significantly increased (OS; $p < 0.01$) [30]. While adjuvant chemotherapy and radiation are mainstay modalities to address AT/RT tumors, hematological transplant concomitant with high-dose chemotherapy has been more recently explored as a supplementary treatment [8, 9, 20, 25]. High-dose chemotherapy with autologous stem cell rescue was initially adopted as a method to defer radiation therapies in younger patients; its administration has grown in frequency after being found to increase radiation-free survival, especially in patients above the age of five [21]. These results were further substantiated in a subsequent 2020 meta-analysis of treatment modalities by Underiner et al., who found that autologous stem cell transplantation was associated with a 79% reduction in mortality [27]. Our study similarly demonstrated an increased OS of 63.3 months in patients who received a bone marrow/stem cell transplant compared to those who did not receive a bone marrow/stem cell transplant. When examining specific treatment regimens, receiving adjuvant chemotherapy + radiation + bone marrow/stem cell transplant significantly conferred the greatest increase in OS on bivariate analysis, followed by adjuvant chemotherapy + bone marrow/stem cell transplant and then adjuvant chemotherapy + radiation, after controlling for age, the presence of comorbidities, and hospital readmission.

Interestingly, our study found no association between extent of resection and OS. This deviates from the results of prior studies that have established gross total resection as associated with increased OS [2, 11];

we suspect this difference is directly due to the data subset provided by the NCDB seeing as at least two other studies drawing from the same data pool have reached a similar conclusion regarding the statistical, but likely not clinical insignificance of gross total resection on overall survival [5, 13]. Interestingly, gross total resection was found to be associated with an increased 30-day survival.

Limitations

The utilization of aggregate data sourced from a larger national registry poses several barriers to case-based patient analysis and examination of clinical variables absent from the database. Missing patient characteristics in the NCDB may have impacted the types of variables that were found to determine study outcomes. Additionally, collected data between the years of 2004 and 2016 does not account for treatment protocols that have changed since that time. However, despite these limitations, the study covers a broad range of demographic and clinical characteristic in AT/RT patients. While most studies focus on pediatric patients under the age of three due to the higher disease incidence in that population, our study includes those above that age, resulting in an intrinsic database bias towards those living to an older age and likely with a better prognosis. Furthermore, due to our analysis' utility of and therefore inherent reliance on a database, the strength of our findings are heavily based on the accuracy of provided values. Given the extreme rarity of AT/RTs diagnosed in the adult population, it must be taken into account that not every "diagnosed AT/RT" in those over the age of five years in the study would still meet criteria for this tumor if re-evaluated based on the more recent differentiation between medulloblastomas and atypical teratoid/rhabdoid tumors. Finally, it is important to note that this was a retrospective cohort study, and further prospective studies are required to validate conclusions.

Conclusion

Our study of 189 patients with AT/RTs from the NCDB demonstrated that in addition to more traditional chemotherapy and radiation combination regimens, bone marrow/stem cell transplant is emerging as a supplementary treatment option whose impact on overall survival requires more data to establish causality. Those above the age of one year had a significantly better prognosis. And while gross total resection was found to decrease 30-day mortality, the presence of comorbidities increased the same metric. These findings indicate the need for future investigation regarding the optimal treatment course for patients diagnosed with this rare tumor type in order to increase long-term survival and better guide clinical decision-making.

Declarations

Statements and Declarations: The authors received no financial support for the research, authorship, and/or publication of this article. On behalf of all authors, the corresponding author states that there is no conflict of interest.

Authorship Statement: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Vismaya S. Bachu, Pavan Shah, and Adham M.

Khalafallah. The first draft of the manuscript was written by Vismaya S. Bachu and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Reporting Guidelines: We found no applicable reporting guidelines that would apply to this article. By following the EQUATOR reporting guidelines decision tree, (http://www.equatornetwork.org/wp-content/uploads/2013/11/20160226-RG-decision-tree-for-Wizard-CC-BY-26- February-2016.pdf), we found that none of the most popular checklists are appropriate for our study design.

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Tables

Table 1: Demographics of patients with atypical teratoid/rhabdoid tumors (NCDB database, 2004-2016)

Variable	Number of Patients, N = 189
Age at Diagnosis, years	
Median (IQR)	1 (0.00-4.00)
Gender, N (%)	
Male	105 (55.6)
Female	84 (44.4)
Hispanic, N (%)	
Yes	29 (15.7)
No	156 (84.3)
Race, N (%)	
White	130 (71.0)
Black	34 (18.6)
Asian	8 (4.37)
Other	11 (6.01)
Charlson-Deyo score, N (%)	
0	157 (83.1)
1	13 (6.88)
2	16 (8.47)
3	3 (1.59)
Insurance Type, N (%)	
Private	95 (50.8)
Government	89 (47.6)
Uninsured	3 (1.60)

Table 2: Tumor and treatment characterization of patients with atypical teratoid/rhabdoid tumors (NCDB database, 2004-2016)

Variable	Number of Patients, N = 189
Tumor Size, N (%)	
<3cm	30 (19.2)
3cm	126 (80.8)
Tumor Site, N (%)	
Supratentorial	61 (34.1)
Infratentorial	51 (28.5)
Overlapping lesion	11 (6.15)
Non-specified (in brain)	56 (31.3)
Extent of Resection	
Gross Total Resection	97 (53.6)
Subtotal Resection	53 (29.3)
Biopsy	31 (17.1)
Treatment Received, N (%)	
S	50 (27.2)
S+C	51 (27.7)
S+R	9 (4.9)
S+C+R	45 (24.5)
S+C+T	13 (7.07)
S+C+R+T	16 (8.7)
Hospital 30 Day Readmission, N (%)	
Not Readmitted	149 (78.8)
Readmitted	39 (20.6)
Unknown	1 (0.53)
Outcome, N (%)	
30 Day Survival	158 (93.5)
90 Day Survival	141 (84.4)

Table 3: Analysis of maximum likelihood estimates from univariate Cox proportional hazards regression modelling of all examined variables; **Age** , **C+R**, **C+T**, and **C+R+T** were found to predict significantly increased overall survival in AT/RT patients.

Analysis of Maximum Likelihood Estimates		
Variable (Reference)	**Hazard Ratio (95% CI)**	**p-value**
Age at diagnosis (<1)		
	0.550 (0.357-0.847)	**0.0067**
Gender (male)		
Female	0.859 (0.574-1.29)	0.4616
Hispanic (no)		
Yes	0.986 (0.568-1.71)	0.9610
Race (white)		
Black	0.887 (0.515-1.53)	0.6668
Asian	1.79 (0.651-4.94)	0.2584
Other	0.556 (0.203-1.52)	0.2534
Comorbidities – CDEYO score (0)		
1	0.921 (0.424-2.00)	0.8341
2	0.558 (0.243-1.28)	0.1692
3	1.64 (0.516-5.19)	0.4036
Year of Diagnosis (2004-2013)		
2013-2016	0.919 (0.612-1.38)	0.6830
Insurance Type (uninsured)		
Private	0.885 (0.215-3.64)	0.8653
Government	0.838 (0.203-3.46)	0.8063
Tumor Size (< 3cm)		
3cm	0.829 (0.483-1.421)	0.4947
Tumor Site (supratentorial)		
Infratentorial	0.865 (0.517-1.45)	0.5792
Overlapping lesion	0.691 (0.245-1.95)	0.4856
Non-specified (in brain)	1.007 (0.616-1.64)	0.9792
Extent of Resection (Biopsy)		
Gross Total Resection	0.928 (0.539-1.59)	0.7863

Subtotal Resection	0.807 (0.448-1.45)	0.4739
Treatment Received (S)		
S+C	0.686 (0.420-1.122)	0.1331
S+R	0.479 (0.169-1.36)	0.1653
S+C+R	0.353 (0.201-0.618)	**0.0003**
S+C+T	0.297 (0.115-0.764)	**0.0118**
S+C+R+T	0.228 (0.088-0.586)	**0.0022**
Hospital 30 Day Readmission (not readmitted)		
Readmitted	0.631 (0.378-1.06)	0.0795

Table 4: Analysis of maximum likelihood estimates from multivariate Cox proportional hazards regression modelling **overall survival**, including variables with **p < 0.2** in bivariate analysis; **C+R, C+T, and C+R+T** were found to be predictive of significantly higher overall survival in patients with AT/RT compared to surgery alone.

Analysis of Maximum Likelihood Estimates		
Variable (Reference)	**Hazard Ratio (95% CI)**	**p-value**
Age (<1)		
1	0.663 (0.407-1.08)	0.0985
CDEYO (0)		
1	1.186 (0.530-2.65)	0.6783
2	0.734 (0.306-1.76)	0.4886
3	0.823 (0.251-2.70)	0.7478
Readmitted (No)		
Yes	0.769 (0.434-1.36)	0.3686
Treatment (S)		
S+C	0.672 (0.401-1.13)	0.1314
S+C+R	0.408 (0.226-0.738)	**0.0030**
S+C+R+T	0.291 (0.107-0.789)	**0.0152**
S+C+T	0.310 (0.119-0.803)	**0.0159**
S+R	0.539 (0.187-1.55)	0.2522

Table 5: Multivariable logistic regression analysis of factors affecting **30-day survival**, including all variables with **p < 0.2** in bivariate analysis**; gross total resection** and receiving **surgery+chemotherapy** were associated with increased 30-day survival. The presence of **comorbidities** was associated with decreased 30-day survival. On bivariate analysis (not shown here), receiving **surgery+chemotherapy** was associated with significantly decreased 30-day mortality.

Variables (Reference)	Odds Ratio (95% CI)	p-value
Intercept	-	0.5266
Extent of Resection (Biopsy)		
Gross Total Resection	13.8 (1.69-112)	**0.0144**
Subtotal Resection	2.89 (0.443-18.8)	0.2678
Comorbidities (No)		
Yes	0.117 (0.018-0.742)	**0.0229**
Treatment (S)		
S+C	21.12 (1.95-229)	**0.0121**
S+C+R	>999 (<0.001->999)	0.9453
S+C+R+T	>999 (<0.001->999)	0.9691
S+C+T	>999 (<0.001->999)	0.9756
S+R	1.22 (0.111-13.3)	0.8732

Figures

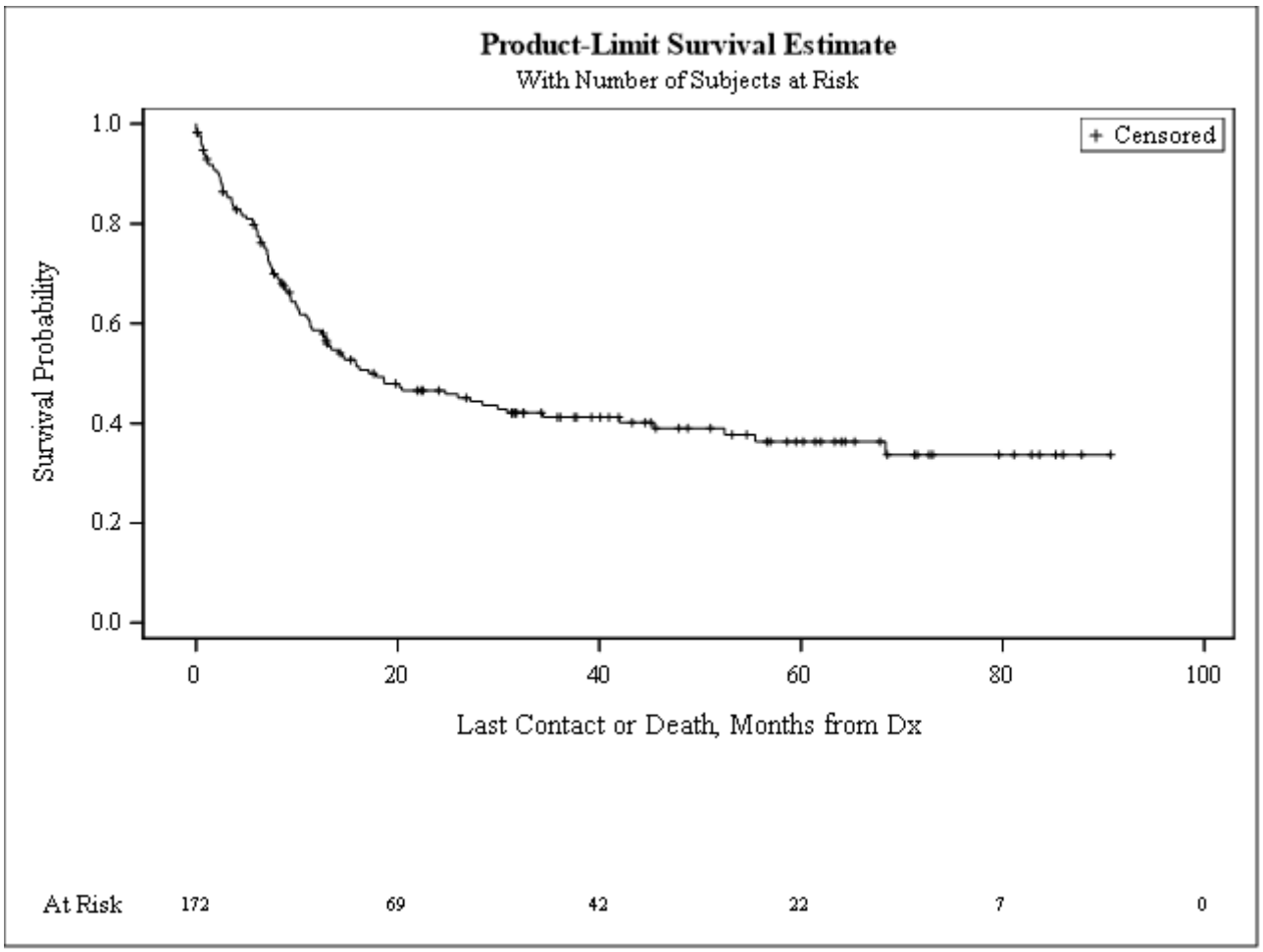

Figure 1

Kaplan-Meier survival curve depicting patients with histologically-confirmed atypical teratoid/rhabdoid tumors (AT/RT)

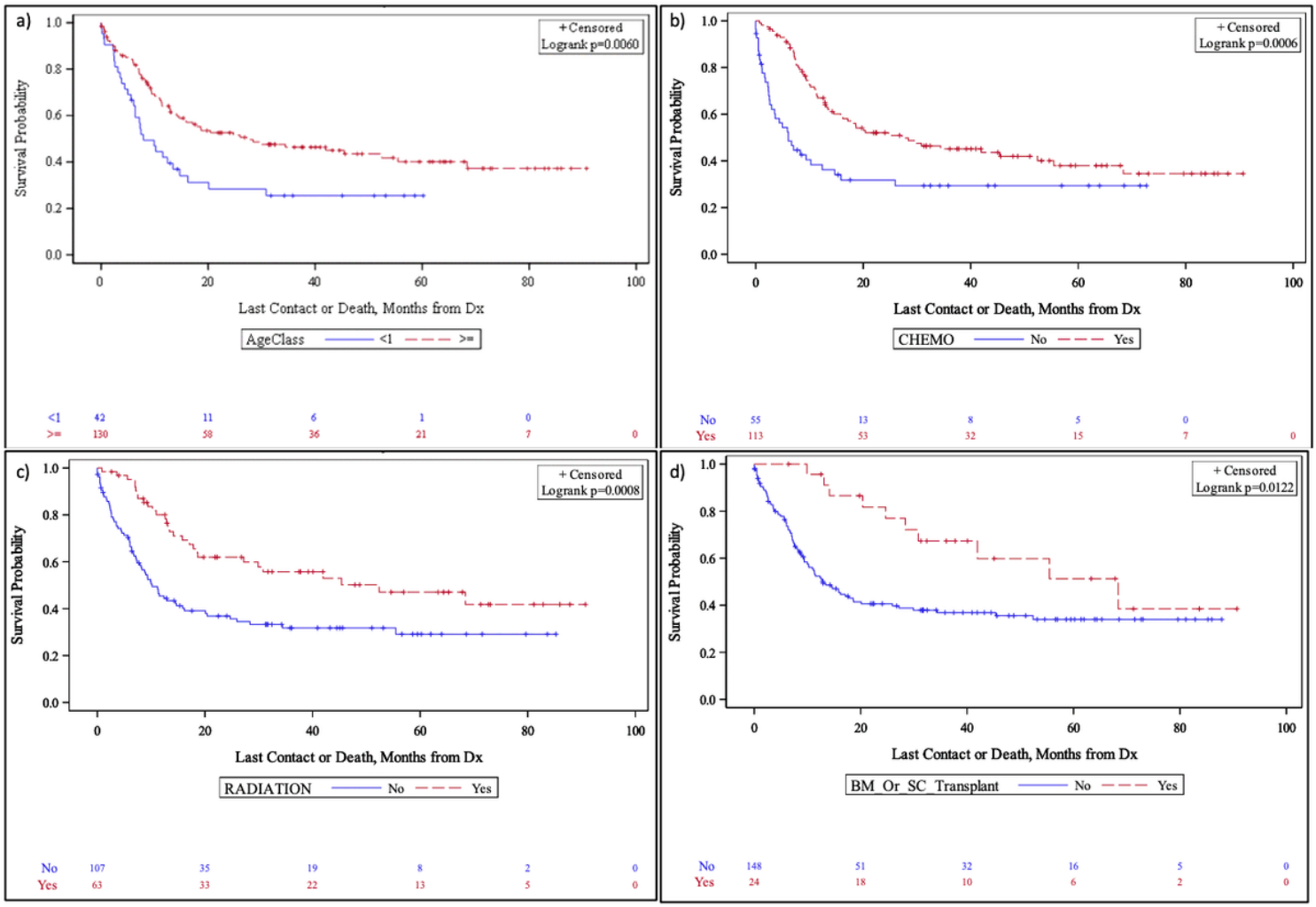

Figure 2

a-d: Figure 2a: Kaplan-Meier survival curve comparing overall survival in AT/RT patients by age dichotomized at one year; Figure 2b: Kaplan-Meier survival curve comparing overall survival in AT/RT patients receiving/not receiving chemotherapy; Figure 2c: Kaplan-Meier survival curve comparing overall survival in AT/RT receiving radiation treatment; Figure 2d: Kaplan-Meier survival curve comparing overall survival in AT/RT patients receiving/not receiving bone marrow or stem cell transplant.

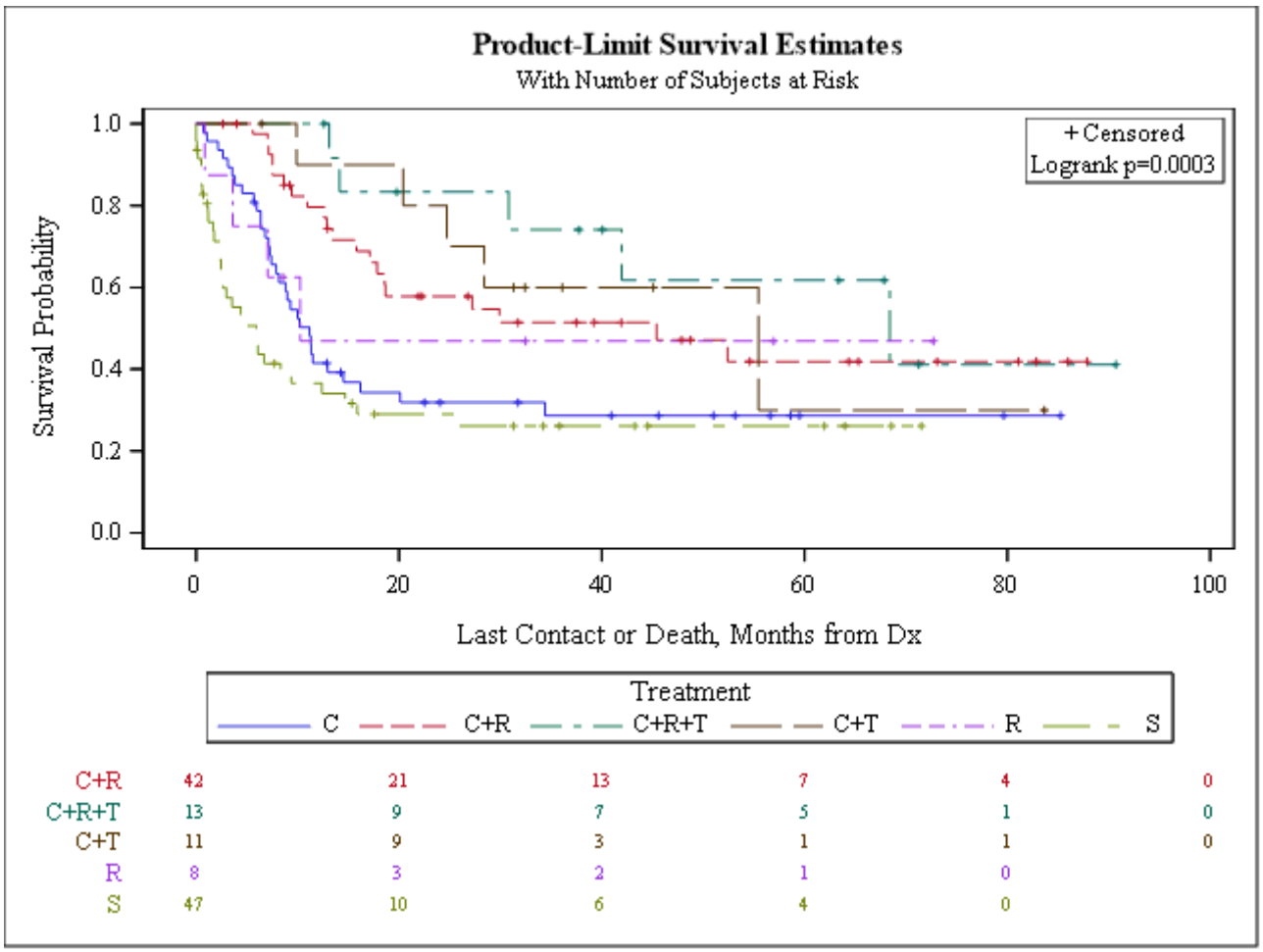

Figure 3

Kaplan-Meier survival curve comparing overall survival in AT/RT receiving different combinations of treatment regimens (S = surgery only, C = surgery + chemotherapy, R = surgery + radiation, C+R = surgery + chemotherapy + radiation, C+T = surgery + chemotherapy + bone marrow or stem cell transplant, C+R+T = surgery + chemotherapy+ radiation + bone marrow or stem cell transplant)

Median Overall Survival:

Ref = 5.91 (2.43-12.4)

C = 11.2 (7.89-16.2)

T = N/A

R = 10.3 (0.85 - *)

C+R = 45.4 (17.12 - *)

C+T = 55.5 (9.89 - *)

C+R+T = 68.4 (14.13 - *)