Journal of Clinical Neuroscience xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical study

Prognostic role of chemotherapy, radiotherapy dose, and extent of surgical resection in adult medulloblastoma

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ARTICLE INFO

Article history:
Received 16 January 2020
Accepted 2 April 2020
Available online xxxx

Keywords:
Medulloblastoma
Chemotherapy
Surgery
Resection
Radiation therapy

ABSTRACT

Purpose: Adult medulloblastoma is rare, and management is extrapolated from pediatric cases. This investigation evaluated the prognostic role of chemotherapy (and sequencing thereof), the degree of resection, and craniospinal irradiation (CSI) dose.
Methods: The National Cancer Database was queried for adult (age ≥18) medulloblastoma. Resection was coded as gross (GTR) or subtotal resection (STR) or biopsy only; concurrent chemoradiotherapy (CRT) was defined as receipt within 14 days of each other. Statistics included Kaplan-Meier overall survival (OS) analysis and Cox proportional hazards modeling.
Results: Of 1144 patients, 613 had coded surgical information; 242 (39%) did not undergo surgery, 277 (45%) underwent STR, and 94 (15%) had GTR. A total of 428 (37.4%) did not receive chemotherapy, 348 (30.4%) received sequential CRT, and 368 (32.2%) underwent concurrent CRT. Of the 711 patients with CSI dose information, 202 (28.4%) received 23–30 Gy CSI and 509 (71.6%) patients received 30–36 Gy. Median follow-up was 56.5 months. Extent of resection did not correlate with 10-year OS (74.2% biopsy only, 72.7% STR, 82.2% GTR, $p > 0.05$ all comparisons) or on Cox multivariate analysis. Chemotherapy was associated with higher OS (65.6% vs. 51.2%, $p = 0.035$) and a trend towards significance on multivariate assessment ($p = 0.082$). Sequencing of chemotherapy and CSI dose were not associated with OS ($p > 0.05$ for both).
Conclusions: Although causation cannot be implied, neither the extent of resection nor CSI dose associated with OS in adult medulloblastoma. Chemotherapy could have utility in higher-risk patients; concurrent administration may not be beneficial, especially given therapy-induced neuro-cognitive sequelae.

1. Introduction

Although medulloblastoma is one of the most common primary central nervous system tumors in children, it is relatively rare in adults [1]. As compared to pediatric cases, adult medulloblastoma (AM) is characterized by distinct phenotypes, molecular characteristics, patterns of spread, and prognosis [2–5].

Despite the distinctions between pediatric and AM, many aspects of AM management are extrapolated from the pediatric setting [3], such as the general paradigm of surgical resection followed by radiotherapy (RT) and chemotherapy. The National Comprehensive Cancer Network (NCCN) recommends adjuvant craniospinal RT (CSI) with or without chemotherapy for standard-risk patients, and CSI with concurrent and adjuvant chemotherapy for high-risk patients [6].

Given that AM is a rare neoplasm, it remains unknown whether the extent of resection is a prognostic factor. In pediatric medulloblastoma, emerging data suggest that the degree of resection does not predict for outcomes in most molecular subtypes [7], but this notion has not been well-studied in AM. Additionally, the role of chemotherapy in AM remains relatively understudied; small reports have produced conflicting results [8–10]. Given the questionable benefit, some prospective studies have attempted to deliver sequential RT and chemotherapy in efforts to avoid potentially additive toxicities from concurrent therapy [11–13]. The comparative efficacy of sequential versus concurrent chemoradiotherapy (CRT) is also not well-characterized. Lastly, the dose of CSI in adults is also unresolved, and largely remains extrapolated from pediatric patients as well. Although AM is a rare neoplasm, the goal of the present study was to better address these notions with high-volume data.

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https://doi.org/10.1016/j.jocn.2020.04.002
0967-5868/

2. Materials & methods

The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society, which consists of de-identified information regarding tumor characteristics, patient demographics, and survival for approximately 70% of the US population [14]. All pertinent cases are reported regularly from CoC-accredited centers and compiled into a unified dataset, which is then validated. The data used in the study were derived from a de-identified NCDB file (2004–2016). The American College of Surgeons and the CoC have not verified and are neither responsible for the analytic or statistical methodology employed nor the conclusions drawn from these data by the investigators. As all patient information in the NCDB database is de-identified, this study was exempt from institutional review board evaluation.

Inclusion criteria for this study were patients age ≥18 with newly-diagnosed, pathologically confirmed medulloblastoma. That particular age cutoff was chosen because the NCDB file for this study does not contain patients less than 18 years of age. The only exclusion criteria were lack of information on surgery, RT, and/or chemotherapy. Concurrent CRT was defined as starting both modalities within 14 days of each other as per other studies [15]; the remainder were categorized as sequential. In accordance with the variables in NCDB files, information collected on each patient broadly included demographic, clinical, and treatment data.

All statistical tests were two-sided, with a threshold of $p < 0.05$ for statistical significance, and were performed using STATA (version 14, College Station, TX). Survival analysis was performed per the Kaplan-Meier method, and group comparisons done with the log-rank test. Overall survival (OS) referred to the interval between the date of diagnosis and the date of death, or censored at last contact. Univariate analysis determined factors associated with OS; subsequently, Cox multivariate analysis was performed and included variables that were either significant or showed a strong trend to statistical significance on univariate analysis. The proportional hazards assumption was checked graphically using log-log plots.

3. Results

Supplemental Fig. 1 depicts a flow diagram of patient selection. Altogether, 1144 patients were included (Table 1). Of the 613 patients with available surgical information, 242 (39%) did not undergo surgery, 277 (45%) underwent subtotal resection (STR), and 94 (15%) had gross total resection (GTR). A total of 428 (37.4%) did not receive chemotherapy, 348 (30.4%) received sequential CRT, and 368 (32.2%) underwent concurrent CRT. Of the 711 patients with available RT dose information, 202 (28.4%) received reduced-dose (23–30 Gy) CSI and 509 (71.6%) patients were administered standard-dose CSI (30–36 Gy). Patient characteristics stratified by surgical extent, chemotherapy, and RT dose are displayed in Tables 2–4.

Fig. 1 illustrates OS based on the aforementioned comparisons; the median follow-up was 56.5 months. The extent of resection did not seem to correlate with OS, as the 10-year OS for patients having undergone biopsy only was 64.7% (95% confidence interval, 53.0–74.2%), as compared to 65.0% (55.9–72.7%) for STR and 70.9% (54.9–82.2%) for GTR (biopsy only vs. STR $p = 0.721$; vs. GTR $p = 0.909$). Next, chemotherapy was associated with higher OS (70.7% (65.6–75.1%) vs. 58.5% (51.2–65.2%), $p = 0.035$). Sequencing of chemotherapy with RT did not demonstrate significant differences (70.9% (62.6–77.6%) for concurrent vs. 70.5% (63.8–76.2%) for sequential, $p = 0.881$). Lastly, OS by RT dose was similar for patients receiving a dose of 23 Gy to <30 Gy (63.9%% [51.8–73.7%%]) vs. patients receiving 30 to 36 Gy (64.6%% [57.8–70.7%]), $p = 0.395$.

Table 1
Clinical characteristics for the overall population.

Characteristic	All patients (n = 1144)
Age	
18–20	156 (13.6%)
21–30	477 (41.7%)
31–40	284 (24.8%)
41–50	136 (11.9%)
50+	91 (8.0%)
Sex	
Male	690 (60.3%)
Female	454 (39.7%)
Race	
White	948 (82.9%)
African American	126 (11.0%)
Other/not recorded	70 (6.1%)
Charlson-Deyo comorbidity score	
0	1008 88.1%)
1	107 (9.4%)
2	21 (1.8%)
≥3	8 (0.7%)
Practice type	
Academic	138 (12.1%)
Non Academic	104 (9.1%)
Not recorded	902 (78.9%)
Insurance status	
Medicare	35 (3.1%)
Private	707 (61.8%)
Medicaid	235 (20.5%)
Not insured	117 (10.2%)
Other government/not recorded	50 (4.4%)
Extent of resection	
Biopsy only	242 (21.2%)
Sub total resection	277 (24.2%)
Gross total resection	94 (8.2%)
Surgery NOS	531 (46.4%)
Craniospinal radiation dose	
23 to <30 Gy	194 (17.0%)
30–36 Gy	517 (45.2%)
Other/not reported	433 (37.9%)
Chemotherapy	
Concurrent	368 (32.2%)
Yes, non-concurrent	348 (30.4%)
No	428 (37.4%)
Socioeconomic status	
<$63,000	774 (67.7%)
$63,000 +	363 (31.7%)
Not reported	7 (0.6%)
M stage	
M0	912 (79.7%)
M1-3	82 (7.2%)
Not reported	150 (13.1%)
Radiation therapy type	
Photon	1070 (93.5%)
Proton	74 (6.5%)

Table 5 shows the results of Cox proportional hazards regression for candidate prognostic factors in the overall population. On multivariate analysis, poorer OS was associated with advancing age ($p = 0.012$), greater comorbidities ($p = 0.039$), and non-uninsured/private insurance ($p < 0.05$ for both). Additionally, there were trends for higher OS with chemotherapy (but not sequencing thereof) ($p = 0.082$) and M0 disease ($p = 0.056$). Extent of resection was not significant on univariate analysis so as to be incorporated into the multivariate model, and CSI dose (standard vs. lower-dose) was also not significant ($p = 0.191$).

4. Discussion

Because AM is a rare malignancy, the vast majority of existing studies are generally of smaller sample sizes. This study of a large,

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Table 2
Clinical characteristics by extent of surgery.

Characteristic	Biopsy only (n = 242)	Subtotal resection (n = 277)	Gross total resection (n = 94)	p
Age				
18–20	26 (10.7%)	40 (14.4%)	14 (14.9%)	0.151
21–30	102 (42.2%)	121 (43.7%)	41 (43.6%)	
31–40	57 (23.6%)	67 (24.2%)	30 (31.9%)	
41–50	34 (14.1%)	25 (9.0%)	5 (5.3%)	
50+	23 (9.5%)	24 (8.7%)	4 (4.3%)	
Sex				
Male	157 (64.9%)	159 (57.4%)	63 (67.0%)	0.115
Female	85 (35.1%)	118 (42.6%)	31 (33.0%)	
Race				
White	196 (81.0%)	224 (80.9%)	79 (84.0%)	0.959
African American	31 (12.8%)	34 (12.3%)	10 (10.6%)	
Other/not recorded	15 (6.2%)	19 (6.9%)	5 (5.3%)	
Charlson-Deyo comorbidity score				
0	207 (85.5%)	247 (89.2%)	81 (86.2%)	0.085
1	22 (9.1%)	25 (9.0%)	13 (13.8%)	
2	9 (3.7%)	4 (1.4%)	0 (0.0%)	
≥3	4 (1.7%)	1 (0.5%)	0 (0.0%)	
Practice type				
Academic	39 (16.1%)	31 (11.2%)	3 (3.2%)	0.013
Non Academic	23 (9.5%)	25 (9.0%)	6 (6.4%)	
Not recorded	180 (74.4%)	221 (79.8%)	85 (90.4%)	
Insurance status				
Medicare	7 (2.9%)	12 (4.3%)	3 (3.2%)	0.799
Private	149 (61.6%)	163 (58.8%)	52 (55.3%)	
Medicaid	53 (21.9%)	68 (24.6%)	29 (30.9%)	
Not insured	22 (9.1%)	24 (8.7%)	8 (8.5%)	
Other government/not recorded	11 (4.6%)	10 (3.6%)	2 (2.1%)	
Craniospinal radiation dose				
23 to <30 Gy	38 (15.7%)	64 (23.1%)	16 (17.0%)	0.255
30 to 36 Gy	115 (47.5%)	115 (41.5%)	41 (43.6%)	
Other/not reported	89 (36.8%)	98 (35.4%)	37 (39.4%)	
Chemotherapy				
Concurrent	88 (36.4%)	94 (33.9%)	36 (38.3%)	0.862
Yes, non- concurrent	73 (30.2%)	89 (32.1%)	31 (33.0%)	
No	81 (33.5%)	94 (33.9%)	27 (28.7%)	
Socioeconomic status				
<$63,000	172 (71.1%)	173 (62.5%)	63 (67.0%)	0.268
$63,000 +	68 (28.1%)	102 (36.8%)	31 (33.0%)	
Not reported	2 (0.8%)	2(0.7%)	0 (0.0%)	
Distance from facility (miles)				
0–<20	125 (51.7%)	157 (56.7%)	65 (69.2%)	0.073
20–50	57 (23.6%)	68 (24.6%)	12 (12.8%)	
>50	58 (24.0%)	50 (18.1%)	17 (18.1%)	
Not reported	2 (0.8%)	2 (0.7%)	0 (0.0%)	
M stage				
M0	177 (73.1%)	211 (76.2%)	68 (72.3%)	0.045
M1-3	24 (9.9%)	10 (3.6%)	5 (5.3%)	
Not reported	41 (16.9%)	56 (20.2%)	21 (22.3%)	
Radiation therapy type				
Photon	217 (89.7%)	239 (86.3%)	86 (91.5%)	0.291
Proton	25 (10.3%)	38 (13.7%)	8 (8.5%)	

Table 3
Clinical characteristics by receipt of chemotherapy and sequencing thereof.

Characteristic	No chemotherapy (n = 428)	Concurrent chemo. (n = 368)	Sequential chemo. (n = 348)	p
Age				
18–20	36 (8.4%)	73 (19.8%)	47 (13.5%)	<0.001
21–30	160 (37.4%)	171 (46.5%)	146 (42.0%)	
31–40	116 (27.1%)	77 (20.9%)	91 (26.2%)	
41–50	63 (14.7%)	31 (8.4%)	42 (12.1%)	
50+	53 (12.4%)	16 (4.4%)	22 (6.3%)	
Sex				
Male	267 (62.4%)	209 (56.8%)	214 (61.5%)	0.238
Female	161 (37.6%)	159 (43.2%)	134 (38.5%)	
Race				
White	346 (80.8%)	318 (86.4%)	284 (81.6%)	0.094
African American	54 (12.6%)	36 (9.8%)	36 (10.3%)	
Other/not recorded	28 (6.5%)	14 (3.8%)	28 (8.1%)	

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Please cite this article as: W. Haque, V. Verma, E. Brian Butler et al., Prognostic role of chemotherapy, radiotherapy dose, and extent of surgical resection in adult medulloblastoma, Journal of Clinical Neuroscience, https://doi.org/10.1016/j.jocn.2020.04.002

Table 3 (*continued*)

Characteristic	No chemotherapy (n = 428)	Concurrent chemo. (n = 368)	Sequential chemo. (n = 348)	p
Charlson-Deyo comorbidity score				
0	376 (87.9%)	328 (89.1%)	304 (87.4%)	0.888
1	40 (9.4%)	30 (8.2%)	37 (10.6%)	
2	8 (1.9%)	8 (2.2%)	5 (1.4%)	
≥3	4 (0.9%)	2 (0.5%)	2 (0.6%)	
Practice type				
Academic	69 (16.1%)	25 (6.8%)	44 (12.6%)	<0.001
Non Academic	52 (12.2%)	26 (7.1%)	26 (7.5%)	
Not recorded	307 (71.7%)	317 (86.1%)	278 (79.9%)	
Insurance status				
Medicare	18 (4.2%)	6 (1.6%)	11 (3.2%)	0.685
Private	259 (60.5%)	231 (62.8%)	217 (62.4%)	
Medicaid	90 (21.0%)	72 (19.6%)	73 (21.0%)	
Not insured	42(9.8%)	42 (11.4%)	33 (9.5%)	
Other government/not recorded	19 (4.4%)	17 (4.6%)	14 (4.0%)	
Extent of resection				
Biopsy only	81 (18.9%)	88 (23.9%)	73 (21.0%)	0.035
Sub total resection	94 (22.0%)	94 (25.5%)	89 (25.6%)	
Gross total resection	27 (6.3%)	36 (9.8%)	31 (8.9%)	
Surgery NOS	226 (52.8%)	150 (40.8%)	155 (44.5%)	
Craniospinal radiation dose				
23 to <30 Gy	40 (9.4%)	95 (25.8%)	59 (17.0%)	<0.001
30 to 36 Gy	219 (51.2%)	141 (38.3%)	157 (45.1%)	
Other/not reported	169 (39.5%)	132 (35.9%)	132 (37.9%)	
Socioeconomic status				
<$63,000	294 (68.7%)	236 (64.1%)	244 (70.1%)	0.308
$63,000 +	133 (31.1%)	129 (35.1%)	101 (29.0%)	
Not reported	1 (0.2%)	3 (0.8%)	3 (0.9%)	
M stage				
M0	361 (84.4%)	292 (79.4%)	259 (74.4%)	0.003
M1-3	19 (4.4%)	34 (9.2%)	29 (8.3%)	
Not reported	48 (11.2%)	42 (11.4%)	60 (17.2%)	
Radiation therapy type				
Photon	412 (96.3%)	329 (92.1%)	319 (91.7%)	0.014
Proton	16 (3.7%)	29 (7.9%)	29 (8.3%)	

Table 4
Clinical characteristics by radiation dose.

Characteristic	23 to <30 Gy (n = 194)	30 to 36 Gy (n = 517)	p
Age			
18–20	54 (27.8%)	41 (7.9%)	<0.001
21–30	92 (47.4%)	203 (39.3%)	
31–40	31 (16.0%)	146 (28.2%)	
41–50	8 (4.1%)	79 (15.3%)	
50+	9 (4.6%)	48 (9.3%)	
Sex			
Male	108 (55.7%)	318 (61.5%)	0.157
Female	86 (44.3%)	199 (38.5%)	
Race			
White	163 (84.0%)	433 (83.8%)	0.947
African American	22 (11.3%)	57 (11.0%)	
Other/not recorded	9 (4.6%)	27 (5.2%)	
Charlson-Deyo comorbidity score			
0	174 (89.7%)	454 (87.8%)	0.243
1	19 (9.8%)	47 (9.1%)	
2	1 (0.5%)	11 (2.1%)	
≥3	0 (0.0%)	5 (1.0%)	
Practice type			
Academic	14 (7.2%)	77 (14.9%)	<0.001
Non Academic	6 (3.1%)	58 (11.2%)	
Not recorded	174 (89.7%)	382 (73.9%)	
Insurance status			
Medicare	2 (1.0%)	16 (3.1%)	0.277
Private	123 (63.4%)	328 (6.4%)	
Medicaid	46 (23.7%)	103 (19.9%)	
Not insured	18 (9.3%)	45 (8.7%)	
Other government/not recorded	5 (2.6%)	25 (4.8%)	
Extent of resection			
Biopsy only	38 (19.6%)	115 (22.2%)	0.027
Sub total resection	64 (33.0%)	115 (22.2%)	
Gross total resection	16 (8.3%)	41 (7.9%)	
Surgery NOS	76 (39.2%)	246 (47.6%)	
Chemotherapy			
Concurrent	95 (49.0%)	141 (27.3%)	<0.001
Yes, non-concurrent	59 (30.4%)	157 (30.4%)	
No	4 (20.6%)	219 (42.4%)	
Socioeconomic status			
<$63,000	135 (69.6%)	332 (64.2%)	0.102
$63,000 +	57 (29.4%)	184 (35.6%)	
Not reported	2 (1.0%)	1 (0.2%)	
M stage			
M0	161 (83.0%)	410 (79.3%)	0.002
M1-3	3 (1.6%)	45 (8.7%)	
Not reported	30 (15.5%)	62 (12.0%)	
Radiation therapy type			
Photon	180 (92.8%)	502 (97.1%)	0.010
Proton	14 (7.2%)	15 (2.9%)	

contemporary national database revealed no apparent influence of the degree of resection or CSI dose on OS. Chemotherapy may be associated with improved OS in select patients, although it appeared that concurrent CRT did not offer additional benefits with sequential CRT.

Although several smaller retrospective reports demonstrated improved outcomes with greater extent of resection [16–18], this has not been the case in other case series [8,19] and in reviews when medulloblastoma patients were stratified by molecular status [20]. Our study carries biases regarding the NCDB's limited granularity of the degree of resection, the lack of molecular infor-

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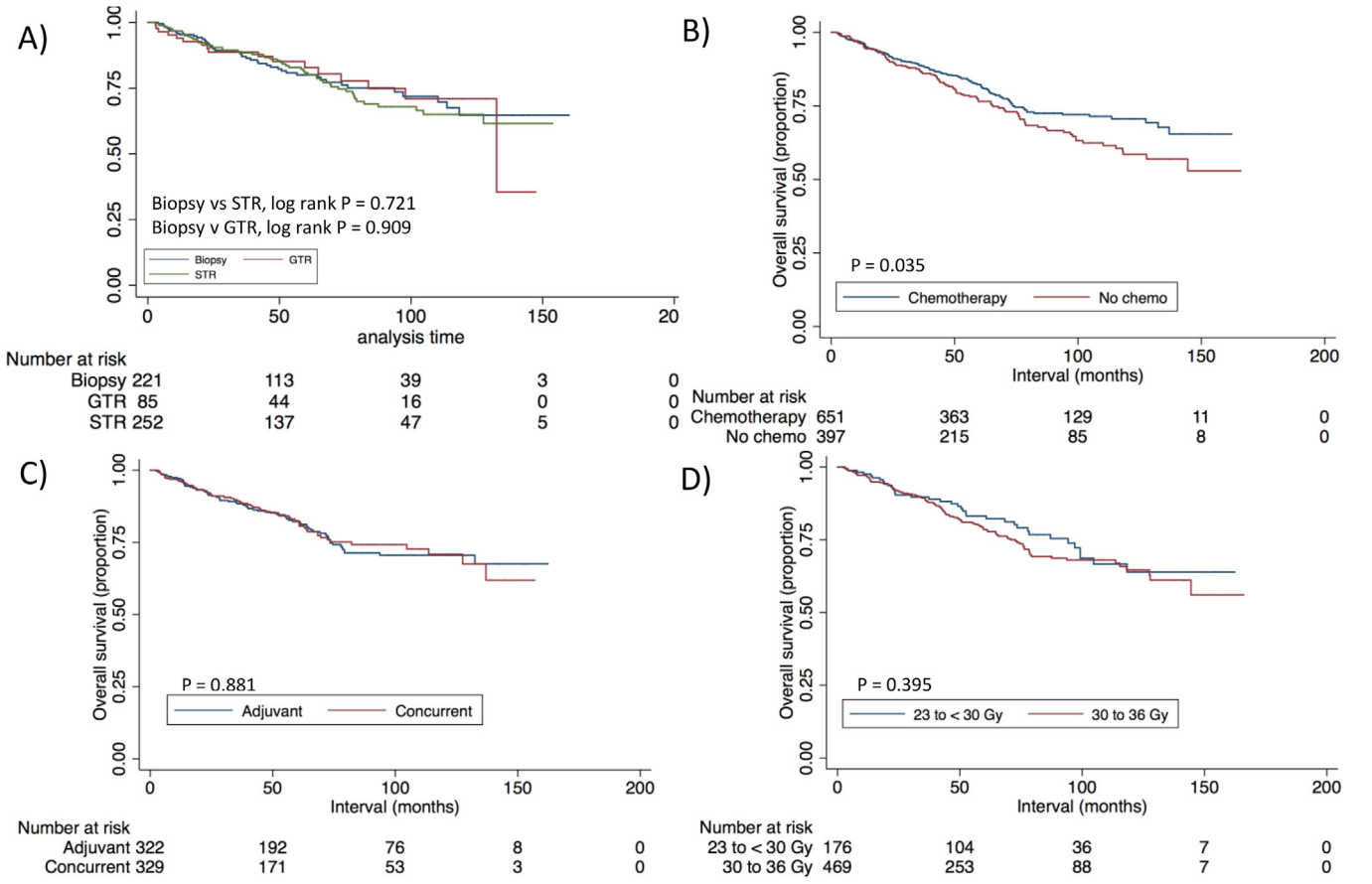

Fig. 1. Kaplan-Meier curves comparing overall survival based on the extent of resection (A), delivery of chemotherapy (B), sequencing of chemotherapy (C), and radiotherapy dose (D).

mation, and the smaller proportion of GTR cases than other reports [16,17,19]. However, studies that correlate the extent of resection with survival likely also carry a bias, in the sense that more infiltrative and/or deeply invasive tumors (which may be a surrogate for aggressive behavior) may be less likely to undergo GTR. Hence, the degree of resection may not be a "cause" of improved OS, but rather an "effect" of biological factors and local aggressiveness.

Our results regarding chemotherapy support a large meta-analysis showing an OS improvement [21]. The trend (rather than a significant finding) on Cox multivariate analysis likely reflects that not all patients benefit from an equal extent from chemotherapy. Higher-risk patients likely benefit to a greater extent from chemotherapy, which has also been posited by the findings of Call and colleagues [9]. However, despite the corroborative data mentioned above, retrospective biases of NCDB investigations regarding the "fitness" to receive chemotherapy as a confounding variable cannot be eliminated.

Additionally, particularly interesting was the finding that sequential CRT seemed to be associated with similar OS as concurrent cases. A logical argument is that if chemotherapy remains controversial for AM, then it should be even more controversial whether concurrent chemotherapy is indeed required. Both CSI and chemotherapy can cause neuro-cognitive sequelae in these patients, which is especially concerning because AM generally occurs in younger adults with long expected lifespans [3]. Although delivering concurrent CRT generally increases toxicities (compared to sequential therapy) in most neoplasms, it is possible that (if better proven in AM) avoiding concurrent CRT could better allow for preserved neuro-cognitive function and an improved quality of life. Given that NCDB investigations evaluating concurrent versus sequential CRT carry biases relating to some degree of preferential delivery of concurrent CRT in "higher-risk" or more aggressive cases with a poorer prognosis [22–24], continuing to prospectively study sequential CRT regimens as done elsewhere [11–13] is essential, including evaluation of neuro-cognition and quality of life.

RT dose was also not associated with OS, despite the caveat that only two groups were assessed, rather than more finely separating the groups. This was primarily owing to the distribution of prescribed CSI doses being largely patterned after pediatric medulloblastoma cases (i.e. 23.4 Gy or 36 Gy). Thus, this investigation cannot adequately assess whether CSI dose reduction is effective for AM. The results of the randomized pediatric ACNS0331 study showed that reduced-dose (18 Gy) CSI produced inferior event-free and OS [25], but whether this can be extrapolated to AM remains questionable.

The NCDB is a unique and novel resource to study rare neoplasms such as AM, but carries several recognized limitations in addition to those mentioned above [26]. These are not limited to the definition of GTR/STR, chemotherapy agents and cycles, RT fields and technique, molecular classification, as well as the lack of other non-OS endpoints. The NCDB does not offer information on clinical workup, clinical rationale for a particular therapy, or salvage management. There is also no information on the degree (cm^3) of residual disease and hence calculation of risk status; however, multiple studies have questioned whether risk group predicts for survival in AM [11,27]. Lastly, we also did not have adequate sample size for adequate subgroup analysis, and additionally did not encompass other proposed prognostic factors such as the time between resection and start of RT, or

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Table 5
Cox proportional hazards modeling for factors associated with overall survival.

	Univariate analysis			Multivariate analysis		
Characteristic	Hazard ratio	95% confidence interval	P-value	Hazard ratio	95% confidence interval	P-value
Radiation type						
Photon	1 (reference)			–	–	–
Proton	0.590	0.219–1.590	0.297	–	–	–
Age						
18–20	1 (reference)			1 (reference)		
21–30	0.861	0.577–1.286	0.465	0.854	0.569–1.285	0.451
31–40	0.961	0.627–1.471	0.854	0.912	0.588–1.414	0.679
41–50	1.247	0.780–1.994	0.356	1.258	0.775–2.043	0.353
50+	2.111	1.297–3.437	0.003	1.946	1.158–3.269	0.012
Sex						
Male	1 (reference)			–	–	–
Female	0.935	0.721–1213	0.612	–	–	–
Race						
White	1 (reference)			–	–	–
African American	1.165	0.789–1.721	0.442	–	–	–
Other/not recorded	0.991	0.565–1.737	0.975	–	–	–
Charlson-Deyo comorbidity score						
0	1 (reference)			1 (reference)		
1	0.834	0.527–1.320	0.439	0.734	0.461–1.167	0.191
2	2.418	1.072–5.454	0.033	2.392	1.044–5.481	0.039
≥3	1.809	0.578–5.659	0.308	1.429	0.450–4.545	0.545
Practice type						
Academic	1 (reference)			–	–	–
Non Academic	1.482	0.924–2.378	0.103	–	–	–
Not recorded	0.746	0.514–1.084	0.124	–	–	–
Insurance status						
Medicare	1 (reference)			1 (reference)		
Private	0.326	0.181–0.590	<0.001	0.413	0.224–0.763	0.005
Medicaid	0.492	0.263–0.920	0.026	0.698	0.362–1.346	0.283
Not insured	0.315	0.155–0.642	0.001	0.434	0.208–0.905	0.026
Other government/not recorded	0.442	0.195–1.002	0.050	0.497	0.216–1.144	0.100
Extent of resection						
Biopsy only	1 (reference)			–	–	–
Sub total resection	1.374	0.678–2.782	0.378	–	–	–
Gross total resection	1.314	0.698–2.473	0.397	–	–	–
Surgery NOS	1.357	0.768–2.397	0.293	–	–	–
Craniospinal radiation dose						
23 to <30 Gy	1 (reference)			1 (reference)		
30 to 36 Gy	1.522	0.990–2.340	0.056	1.347	0.862–2.106	0.191
Other/not reported	2.012	1.312–3.086	0.001	1.815	1.172–2.811	0.008
Chemotherapy						
Concurrent	1 (reference)			1 (reference)		
Yes, non- concurrent	0.981	0.691–1.391	0.913	1.001	−0.703–1.426	0.995
No	1.437	1.055–1.957	0.021	1.329	0.965–1.830	0.082
Socioeconomic status						
<$63,000	1 (reference)			–	–	–
$63,000 +	0.956	0.729–1.252	0.741	–	–	–
Not reported	0.674	0.094–4.848	0.695	–	–	–
Distance from facility (miles)						
0–<20	1 (reference)			–	–	–
20–50	0.878	0.635–1.214	0.432	–	–	–
>50	1.040	0.740–1.463	0.820	–	–	–
Not reported	0.680	0.095–4.865	0.701	–	–	–
M stage						
M0	1 (reference)			1 (reference)		
M1-3	1.558	1.043–2.328	0.031	1.494	0.98902.255	0.056
Not reported	0.536	0.252–1.138	0.104	0.503	0.235–1.077	0.077

the total RT treatment time [28]. These shortcomings should allow for an understanding that causation is not implied in this study.

5. Conclusions

This study of a large, contemporary national database of adult medulloblastoma revealed no apparent influence of the degree of resection or CSI dose on OS. Chemotherapy may be associated with improved OS in select patients, although it appeared that concurrent CRT did not offer additional benefits with sequential CRT. These results do not imply causation, and careful patient selection is still recommended.

Funding

There was no research support for this study.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Please cite this article as: W. Haque, V. Verma, E. Brian Butler et al., Prognostic role of chemotherapy, radiotherapy dose, and extent of surgical resection in adult medulloblastoma, Journal of Clinical Neuroscience, https://doi.org/10.1016/j.jocn.2020.04.002

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2020.04.002.

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Please cite this article as: W. Haque, V. Verma, E. Brian Butler et al., Prognostic role of chemotherapy, radiotherapy dose, and extent of surgical resection in adult medulloblastoma, Journal of Clinical Neuroscience, https://doi.org/10.1016/j.jocn.2020.04.002