The Impact of Tumor Resection on Survival and Functional Outcomes for Patients with Primary Central Nervous System Lymphoma

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Running title: Role of surgical resection in PCNSL

Supplementary Table 1 Univariate and multivariate analysis of potential predictive factors influencing overall survival of patients with PCNSLs

	Univariate Analysis		Multivariate Analysis[a]	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 60 years	2.68 (1.48-4.88)	0.002‡	1.63 (0.72-4.21)	0.274
Charlson Comorbidity Index ≥ 2	4.33 (2.33-8.07)	0.001‡	2.14 (0.60-7.90)	0.236
Preoperative KPS ≤ 70	3.36 (1.85-6.11)	<0.001‡	1.71 (0.67-4.26)	0.249
Preoperative mRS 3-5	3.91 (1.95-7.83)	<0.001‡	1.35 (0.56-3.44)	0.517
Chemotherapy	0.22 (0.07-0.71)	<0.001‡	0.74 (0.30-1.99)	0.538
Radiation therapy	0.27 (0.10-0.68)	<0.001‡	0.36 (0.16-0.84)	0.016‡
Serum LDH level> 260 U/L	1.78 (0.87-3.64)	0.071†	1.00 (0.65-1.47)	0.988
CSF protein level> 45 mg/dl	2.52 (1.16-5.47)	0.052†	1.99 (1.14-3.58)	0.018‡
Gross total resection	0.54 (0.24-1.23)	0.236		
Solitary lesion	1.04 (0.57-1.89)	0.899-		
Deep location	1.49 (0.78-2.84)	0.265		

CSF = cerebrospinal fluid; KPS = Karnofsky Performance Scale; LDH = lactate dehydrogenase; mRS = modified Rankin Scale.

† $p < 0.10$.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the Cox proportional hazards model.

Supplementary Table 2 Univariate and multivariate analysis of potential predictive factors influencing progression free survival of PCNSL patients with a solitary lesion

	Univariate Analysis		Multivariate Analysis[a]	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 60 years	1.64 (0.66-4.06)	0.299		
Charlson Comorbidity Index ≥ 2	1.60 (0.60-4.28)	0.377		
Preoperative KPS ≤ 70	2.89 (1.18-7.10)	0.032‡	1.18 (0.34-4.26)	0.790
Preoperative mRS 3-5	4.58 (1.34-15.7)	0.005‡	1.99 (0.48-8.20)	0.338
Chemotherapy	0.14 (0.03-0.64)	0.012‡	0.42 (0.09-2.02)	0.267
Radiation therapy	0.20 (0.05-0.75)	0.018‡	0.37 (0.11-1.51)	0.141
Serum LDH level > 260 U/L	1.38 (0.51-3.69)	0.523		
CSF protein level > 45 mg/dl	3.46 (1.16-10.34)	0.027‡	1.63 (0.77-3.64)	0.208
Gross total resection	0.25 (0.10-0.66)	0.045‡	0.13 (0.02-0.61)	0.023‡
Deep location	2.07 (0.84-5.10)	0.114		

CSF = cerebrospinal fluid; KPS = Karnofsky Performance Scale; LDH = lactate dehydrogenase; mRS = modified Rankin Scale.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the Cox proportional hazards model.

Supplementary Table 3 Univariate and multivariate analysis of potential predictive factors influencing overall survival of PCNSL patients with a solitary lesion.

	Univariate Analysis		Multivariate Analysis[a]	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥ 60 years	2.33 (0.99-5.47)	0.052†	0.80 (0.23, 3.69)	0.744
Charlson Comorbidity Index ≥ 2	2.92 (1.17-7.30)	0.022‡	3.72 (0.59, 24.4)	0.150
Perioperative KPS ≤ 70	2.57 (1.13-5.84)	0.024‡	1.09 (0.33-3.67)	0.884
Preoperative mRS 3-5	6.66 (1.90-23.3)	<0.001‡	4.08 (0.93-19.4)	0.065†
Chemotherapy	0.07 (0.01-0.33)	<0.001‡	1.12 (0.27-4.80)	0.876
Radiation therapy	0.12 (0.03-0.47)	0.002‡	0.47 (0.12-2.04)	0.279
Serum LDH level > 260 U/L	1.53 (0.62-3.75)	0.355		
CSF protein level > 45 mg/dl	2.59 (0.90-7.45)	0.078†	1.57 (0.69-3.67)	0.287
Gross total resection	0.56 (0.23-1.40)	0.214		
Deep location	1.68 (0.74-3.84)	0.215		
Maximal dimension ≥ 3cm[b]	2.21 (0.89, 5.50)	0.088†	1.57 (0.43, 7.50)	0.523

CSF = cerebrospinal fluid; KPS = Karnofsky Performance Scale; LDH = lactate dehydrogenase; mRS = modified Rankin Scale.

† $p < 0.10$.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the Cox proportional hazards model.

[b] In patients with multiple tumors, we measured the dominant tumor and recorded the maximal tumor dimension on the axial MRI images.

Supplementary Table 4 Univariate and multivariate analysis of potential predictive factors influencing overall survival of PCNSL patients with maximal tumor dimension ≥ 3 cm

	Univariate Analysis		Multivariate Analysis[a]	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age ≥60 years	1.87 (0.90-3.88)	0.102		
Charlson Comorbidity Index ≥ 2	3.28 (1.45-7.41)	0.030‡	1.94 (0.58-8.80)	0.323
Preoperative KPS ≤ 70	3.97 (1.91-8.25)	0.002‡	2.35 (0.70-8.52)	0.171
Preoperative mRS 3-5	4.13 (1.79-9.52)	<0.001‡	1.18 (0.40-3.60)	0.767
Chemotherapy	0.22 (0.06-0.79)	<0.001‡	0.22 (0.08-0.63)	0.003‡
Radiation therapy	0.22 (0.07-0.72)	<0.001‡	0.03 (0.11-0.78)	0.012‡
Serum LDH level > 260 U/L	2.06 (0.91-4.62)	0.051†	1.76 (0.91-3.27)	0.078†
CSF protein level > 45 mg/dl	1.59 (0.58-4.37)	0.413		
Gross total resection	0.67 (0.27-1.70)	0.451		
Gross total or partial tumor resection	0.53 (0.25-1.11)	0.083†	0.37 (0.15-0.87)	0.027‡
Solitary lesion	1.35 (0.64-2.87)	0.447		

CSF = cerebrospinal fluid; KPS = Karnofsky Performance Scale; LDH = lactate dehydrogenase; mRS = modified Rankin Scale.

† $p < 0.10$.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the Cox proportional hazards model.

Supplementary Table 5 Univariate and multivariate logistic regression analysis of potential predictive factors for poor functional outcome (mRS 3-6 at last follow-up)

	Univariate Analysis		Multivariate Analysis[a]	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age ≥60 years	3.34 (1.33-8.70)	0.010‡	16.9 (2.42, 186.2)	0.008‡
Charlson Comorbidity Index ≥ 2	2.88 (1.06-7.97)	0.039‡	0.29 (0.03-2.05)	0.237
Preoperative KPS ≤ 70	7.59 (2.84-22.4)	<0.001‡	4.97 (1.07-27.6)	0.049‡
Preoperative mRS 3-5	13.9 (3.70-91.1)	<0.001‡	3.11 (0.31-47.0)	0.360
Chemotherapy	0.13 (0.01-0.73)	0.016‡	0.16 (<0.01-8.06)	0.491
Radiation therapy	0.30 (0.07-1.02)	0.053†	0.10 (<0.01-0.70)	0.033‡
Gross total resection	0.18 (0.04-0.63)	0.007‡	0.32 (0.04, 2.47)	0.277
Gross total or partial tumor resection	0.62 (0.25-1.54)	0.303		
Solitary lesion	0.45 (0.18-1.13)	0.090†	0.48 (0.08-2.60)	0.399
Deep location	4.46 (1.68, 12.3)	0.003‡	3.34 (0.58-21.3)	0.180
Bilateral lesions	2.63 (1.01, 7.51)	0.049‡	0.39 (0.07-2.06)	0.277

KPS = Karnofsky Performance Scale; mRS = modified Rankin Scale.

† $p < 0.10$.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the multivariate logistic regression analysis model.

Supplementary Table 6 Univariate and multivariate logistic regression analysis of potential predictive factors for deterioration of functional outcome (mRS at last follow-up compared with pre-OP mRS)

	Univariate Analysis		Multivariate Analysis[a]	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age ≥60 years	1.97 (0.81-4.86)	0.133		
Charlson Comorbidity Index ≥ 2	1.79 (0.66-4.81)	0.252		
Preoperative KPS ≤ 70	3.94 (1.59-10.2)	0.003‡	2.63 (0.74, 10.4)	0.144
Preoperative mRS 3-5	0.27 (0.09-0.71)	0.008‡	0.99 (0.20-4.49)	0.991
Chemotherapy	0.26 (0.04-1.04)	0.057†	0.38 (0.05-1.99)	0.291
Radiation therapy	0.38 (0.10-1.17)	0.093†	0.38 (0.08-1.45)	0.179
Gross total resection	0.22 (0.05-0.76)	0.017‡	0.45 (0.08, 2.39)	0.357
Gross total or partial tumor resection	0.82 (0.34-2.00)	0.663		
Solitary lesion	0.65 (0.27-1.56)	0.337		
Deep location	2.71 (1.04, 7.16)	0.041‡	1.99 (0.51-8.03)	0.317
Bilateral lesions	1.64 (0.67, 4.22)	0.285		

KPS = Karnofsky Performance Scale; mRS = modified Rankin Scale.

† $p < 0.10$.

‡ $p < 0.05$.

[a] All factors with $p < 0.10$ in the univariate analysis were selected as covariates assessed in the multivariate logistic regression analysis model.

Supplementary Fig. 1 Analysis of progression free survival (a) and overall survival (b) stratified by PCNSL patients with a solitary lesion receiving gross total resection (GTR) versus those without GTR