Preoperative serum lactate measurement as a prognostic biomarker for patients with primary brain tumor

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Background

High grade brain tumor is one of the most malignant cancer. The accurate diagnosis of high grade brain is sometimes difficult. Currently, there are several candidate for brain tumor or brain injury including glial neuron-specific biomarkers fibrillary acidic protein (GFAP), S100B, neuron-specific enolase (NSE), and neutrophil gelatinase-associated lipocalin (NGAL). In addition, Ramamani et al. demonstrated that serum lactate levels can potentially be used as a non-invasive biomarker of glioma which correlates with brain tumor grade. The goals of this study were (1) to determine which serum biomarker could serve as the diagnostic or prognostic biomarker for patients with primary brain tumor undergoing brain tumor resection, and (2) to determine the independent factor associated with high grade brain tumor.

Method

This study was conducted by retrospectively analysis of the data from a previous study investigating intraoperative goal-directed therapy for supratentorial brain tumor resection in NTUH, between 2013 and 2015. Data of 74 patients including patient demographics, comorbidities, tumor pathology, World Health Organization (WHO) grading of the tumor were analyzed (Table 1). pretreatment serum biomarkers, including lactate, lactate dehydrogenase, glial fibrillary acidic protein, S100β, neuron-specific enolase, and neutrophil gelatinase-associated lipocalin were measured and compared with postoperative outcomes including tumor grading, progression-free survival and overall survival.

Table 1. Patient characteristics in study cohort

Characteristic	Total (N=74)	High grade (N=20)	Low grade (N=54)	P Value
Age (years)	56.55±11.4	54.2±12.5	57.4±10.9	0.293
Male no. (%)	23 (31.1)	8 (40.0)	12 (27.8)	0.398
Body weight (kg)	60.40±9.6	58.9±8.7	60.9±9.9	0.455
Comorbidities, No. (%)				
Cadiovascular disease	6 (8.1)	2 (10.0)	4 (7.4)	0.659
Hypertension	14 (18.9)	5 (25.0)	9 (16.7)	0.308
Diabetes	7 (9.5)	3 (15.0)	4 (7.4)	0.379
Other cancer	5 (6.8)	1 (5.0)	4 (7.4)	0.589
Tumor size (cm)	4.39±1.75	4.50±1.78	4.31±1.73	0.450
Serium biomarkers				
Lactate (mmol/L)	1.38±0.92	1.91±1.06	1.19±0.78	0.011
LDH (mU/ml)	38.22±36.73	39.6±31.28	37.7±38.8	0.401
NGAL (ng/ml)	0.483±0.544	0.544±0.535	0.465±0.554	0.516
GFAP (mg/L)	0.243±0.483	0.14±0.35	0.28±0.52	0.097
NSE (ng/ml)	15.22±54.79	10.77±14.67	16.86±63.62	0.339
S100β (pg/ml)	87.06±128.95	93.61±131.76	84.59±129.06	0.353

Figure 1. Receiver operating characteristics analysis of serum lactate in discriminating high grade from low grade brain tumors

Result

- Multivariate Logistic regression revealed that only elevated serum lactate is the risk factor for high grade brain tumor ($p=0.0018$).
- Kaplan–Meier survival curves show significant difference in progression-free survival (PFS) time between patients with high or low lactate($p=0.021$, table 3), but no significant difference in survival (OS) ($p=0.093$)
- A multivariateoverall analysis showed higher lactate is associated with poor OS ($p = 0.048$). Higher lactate and male are factors associated with poor PFS ($p = 0.021$, $p = 0.023$, respectively, table 2)

Figure 2. Kaplan–Meier survival analysis of serum lactate measurement in association with patient survival.

Table 3. Univariate and multivariate cox regression analyses of overall survival and progression-free survival in primary brain tumor patients OS

Factor	univariate analysis			Multivariate analysis		
	HR	95% CI	P Value	HR	95% CI	P Value
Age (years)	1.041	0.973-1.114	0.247	—		
Gender (male:female)	4.349	1.037-18.247	0.045	3.785	0.903-15.859	0.0686
Body weight (kg)	0.994	0.925-1.070	0.881	—		
Tumor size (cm)	1.214	0.835-1.763	0.310	—		
Serium biomarkers						
Lactate (mmol/L)	2.046	1.078-3.886	0.029	2.049	1.0057-4.1747	0.0482
LDH (mU/mL)	1.013	0.998-1.028	0.084	—		
NGAL (ng/mL)	2.987	1.067-8.363	0.037	—		
GFAP (mg/L)	0.983	0.169-5.704	0.985	—		
NSE (ng/mL)	0.936	0.867-1.069	0.478	—		
S100β (pg/mL)	0.997	0.987-1.006	0.490	—		

Factor	univariate analysis			Multivariate analysis		
	HR	95% CI	P Value	HR	95% CI	P Value
Age (years)	1.0290	0.985-1.076	0.195	—		
Gender (male:female)	3.0190	1.192-7.645	0.020	2.951	1.161-7.496	0.0229
Body weight (kg)	1.0110	0.965-1.059	0.647	—		
Tumor size (cm)	1.1230	0.868-1.453	0.378	—		
Serium biomarkers						
Lactate (mmol/L)	1.6190	1.079-2.428	0.020	1.658	1.078-2.548	0.0211
LDH (mU/mL)	1.0090	0.999-1.019	0.067	—		
NGAL (ng/mL)	2.0620	0.993-4.279	0.052	—		
GFAP (mg/L)	1.2600	0.460-3.447	0.653	—		
NSE (ng/mL)	0.9980	0.989-1.008	0.740	—		
S100β (pg/mL)	1.0010	0.997-1.004	0.733	—		

Conclusion

An elevated pretreatment serum lactate level is a prognostic biomarker of high-grade primary brain tumors and is significantly associated with poor PFS in patients with supratentorial brain tumors undergoing tumor resection. By contrast, other serum biomarkers are not significantly associated with oncological outcomes.