Is serum lactate a potential biomarker of malignancy in patients with high grade brain tumors – A Retrospective review.
RamamaniMariappan M.D., Gelareh Zadeh M.D., Ph.D. FRCSC, Shalini Cynthia M.D., L Venkatraghavan M.D., F.R.C.P.C.
Department of Anesthesia & Neurosurgery, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Canada
Department of Anesthesia, Christian Medical College, Vellore, Tamil Nadu, India.

Introduction
Lactate - product of anaerobic metabolism, an indicator of poor tissue perfusion, measures the severity of the illness.
Hyperlactemia (>4 mmol/L) and metabolic acidosis with clinical signs of tissue hypoxia. Hyperlactemia can occur without tissue hypoxia or hypoxia perfusion (Type B).
High grade brain tumor such as GBM utilize high levels of glucose at a rapid rate with concomitant lactic acid production even in the presence of adequate oxygen - aerobic glycolysis or the Warburg effect. This lactic acid is effluxed into tumor microenvironment for its survival.
We have observed high baseline serum lactate levels (>2 mmol/L) and further rise during the tumor resection (>3 mmol/L) with subsequent decline to normal level during the post operative period, in patients undergoing craniotomy for brain tumor resection, without an obvious cause.
The aim of the present study is to determine possible correlations between high grade brain tumors and the pre/intraoperative serum lactate elevation in patients undergoing craniotomy for tumor resection.

Materials and Methods
Institutional review and ethics board clearance obtained.
Retrospective review of charts of 50 patients who underwent craniotomy for tumor resection from January 2012 to February 2013.
Inclusion criteria: Patients who had primary and metastatic brain tumors, from two institutions (Toronto Western Hospital, Toronto, Canada and Christian Medical college, Vellore, India) were included in the study.
Exclusion criteria: 1. Patients with congestive heart failure, renal or liver dysfunction during the preoperative period.
2. Patients who needed isotropic support to maintain the blood pressure.
3. Patient who had more than 4 units of red blood cell transfusion during the intraoperative period.
Data collection: Demographics, co-morbidities, tumor pathology, World Health Organization (WHO) grading of the tumor, location and the size of the tumor, total amount of fluids given and blood loss during the intraoperative period, the use of mannitol, patient position during surgery and the blood gas results including the base deficit, serum lactate and the electrolytes.
Statistical analysis: Bivariate (Pearson correlation coefficient) and multivariate regression analysis were performed to determine the correlation between serum lactate and the variables that can potentially increase the serum lactate during the pre and intraoperative period.
After determining the significant correlation between the tumor grade and serum lactate, the sensitivity, specificity, positive and negative predictive values were also calculated.
Statistical analyses were performed using SPSS software version 15. P value < 0.05 was considered statistically significant.

Glycolysis in normal tissue and tumor tissue

Results - Demography

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline lactate elevation present</th>
<th>Baseline lactate elevation absent</th>
<th>Odds Ratio with CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Grade 1-Low 2-High</td>
<td>16</td>
<td>22</td>
<td>11</td>
<td>32</td>
</tr>
<tr>
<td>Age</td>
<td>1&lt;-60yrs 2&gt;60 yrs</td>
<td>12</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>Sex</td>
<td>1-Male 2-Female</td>
<td>11</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>Tumor size 1:&lt;5cm 2&gt;5.1 cm</td>
<td>12</td>
<td>5</td>
<td>20</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intraop lactate elevation present</th>
<th>Intraop lactate elevation absent</th>
<th>Odds Ratio with CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Grade 1-Low 2-High</td>
<td>2</td>
<td>18</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>Base deficit</td>
<td>1:&lt;4, 2&gt;=4</td>
<td>2</td>
<td>7</td>
<td>28</td>
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<tr>
<td>Blood loss</td>
<td>1:&lt;500 ml 2&gt;500 ml</td>
<td>12</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Duration of Sx</td>
<td>1:&lt;5 hrs 2&gt;5 hrs</td>
<td>5</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>BMI</td>
<td>1:&lt;25 2&gt;25</td>
<td>12</td>
<td>8</td>
<td>17</td>
</tr>
</tbody>
</table>

There was a significant correlation between baseline serum lactate level and high grade malignant brain tumors (p value 0.000). (Table 1)
There were no correlations between the baseline serum lactate and age, sex, tumor size or tumor location. (Table 1)
There was a significant correlation between intraoperative serum lactate level and high grade malignant brain tumors (p value 0.000). (Table 2)
There were correlations between blood loss and duration of surgery (p value 0.000), also between the blood loss and the tumor size (p value 0.018). (Table 2)
There were no correlations between intraoperative lactate elevation with increased BMI, duration of surgery or blood loss. (Table 2)
There was a significant correlation between baseline serum lactate level and high grade malignant brain tumors.
Further prospective studies are needed to see whether serum lactate can be used as a biomarker in patients with high grade brain tumour for assessing the tumor progression and recurrence.

Conclusion