Role of Plasma Pancreastatin in Predicting Prognosis Following R0/R1 Surgical Cytoreduction in Small Bowel Neuroendocrine Tumors

Eugene A. Woltering, MD, FACS; Brianne A. Voros, MS; Ramcharan Thiagarajan, MD, FACS; David T. Beyer, BS; Robert A. Ramirez, DO, FACP; Gregg Mamikunian, MS; and Philip Boudreaux MD, FACS

Abstract

Background

Pancreastatin (PST), a post-translational fragment of chromogranin A, has shown to be a reliable biomarker for small bowel neuroendocrine tumors (NETs). Elevated PST levels are associated with worse survival. Based on our experience, we hypothesized that patients with elevated PST levels despite undergoing R0 (100%) or R1 (90–99%) resection have a poor prognosis.

Methods

Data were analyzed from patients who underwent surgical cytoreduction for NETs of the small bowel, ileum, or jejunum. All patients received standard of care following surgical cytoreduction. Only patients who had serial preoperative PST (PreopPST) and postoperative PST (PostopPST) levels were included in this study (Normal <135 pg/ml, InterScience Institute, Inglewood, Calif). Patients were sorted into groups to assess the response of their PST level to surgery. Overall survival (OS) was calculated from date of surgery to date of death or end of study (December 31, 2017).

Results

RO/R1 resection was performed in 211 patients with small bowel NETs. Group 1 included 65 patients (31%) who had normal PreopPST and PostopPST levels. Group 2 included 75 patients (36%) with an elevated PreopPST level but a normal PostopPST level. Group 3 included 71 patients (34%) with either a normal or elevated PreopPST level and an elevated PostopPST level. Comparable survival rates were observed in Groups 1 and 2 while significantly worse survival was observed in Group 3 despite RO/R1 resection (P < 0.001). Kaplan-Meier 5-year and 10-year OS rates were as follows: Group 1 – 96% and 93%; Group 2 – 92% and 70%; and Group 3 – 70% and 40% (Table 1 & Figure 1).

Conclusions

Plasma PST levels and the extent of resection seem to be complimentary in predicting outcome following surgical cytoreduction in small bowel NETs. Serial monitoring of PST levels can identify patients who have a poor prognosis despite undergoing RO/R1 resection.

Table 1. Survival Following RO/R1 Resection by PreopPST/PostopPST Group (N=211)

<table>
<thead>
<tr>
<th>PreopPST/PostopPST Group</th>
<th>N</th>
<th>Mean OS ± SD (in months)</th>
<th>5-Year OS</th>
<th>10-Year OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>65</td>
<td>131 ± 3</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>Group 2</td>
<td>75</td>
<td>120 ± 5</td>
<td>92%</td>
<td>70%</td>
</tr>
<tr>
<td>Group 3</td>
<td>71</td>
<td>86 ± 8</td>
<td>70%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Abbreviations: PreopPST, Preoperative pancreastatin level; PostopPST, Postoperative pancreastatin level; SD, standard deviation; OS, overall survival

Role of Plasma Pancreastatin in Predicting Prognosis Following R0/R1 Surgical Cytoreduction in Small Bowel Neuroendocrine Tumors

Eugene A. Woltering, MD, FACS1,2,3, Brianne A. Voros, MS1,2,3, Ramcharan Thiagarajan, MD, FACS1,2,3, David T. Beyer, BS1,2,3, Robert A. Ramirez, DO, FACP1,3, Gregg Mamikunian, MS4, J. Philip Boudreaux MD, FACS1,2,3

1The New Orleans Louisiana Neuroendocrine Tumor Specialists, New Orleans, LA; 2Louisiana State University Health Sciences Center – New Orleans, Department of Surgery, Neuroendocrine Tumor Program, New Orleans, LA; 3Ochsner Medical Center, Neuroendocrine Tumor Clinic, Kenner, LA; 4InterScience Institute, Inglewood, CA


Background

- Pancreastatin (PST), a post-translational fragment of chromogranin A, has shown to be a reliable biomarker for small bowel neuroendocrine tumors (NETs).

- Elevated PST levels are associated with worse survival. Based on our experience, we hypothesized that patients with elevated PST levels despite undergoing R0 (100%) or R1 (90–99%) resection have a poor prognosis.
Methods

• Data were analyzed from patients who underwent surgical cytoreduction for NETs of the small bowel, ileum, or jejunum.

• All patients received standard of care following surgical cytoreduction. Only patients who had serial preoperative PST (PreopPST) and postoperative PST (PostopPST) levels were included in this study (Normal <135 pg/ml, InterScience Institute, Inglewood, Calif).

• Patients were sorted into 3 groups to assess their response to surgical cytoreduction.
  • **Group 1** included patients with normal PreopPST and PostopPST levels.
  • **Group 2** included patients with an elevated PreopPST level and a normal PostopPST level.
  • **Group 3** included patients who had a normal or elevated PreopPST level and an elevated PostopPST level.

• Overall survival (OS) was calculated from date of surgery to date of death or end of study (December 31, 2017).
Role of Plasma Pancreastatin in Predicting Prognosis Following R0/R1 Surgical Cytoreduction in Small Bowel Neuroendocrine Tumors

Eugene A. Woltering, MD, FACS, Brianne A. Voros, MS, Ramcharan Thiagarajan, MD, FACS, David T. Beyer, BS, Robert A. Ramirez, DO, FACP, Gregg Mamikunian, MS, J. Philip Boudreaux MD, FACS

1The New Orleans Louisiana Neuroendocrine Tumor Specialists, New Orleans, LA; 2Louisiana State University Health Sciences Center – New Orleans, Department of Surgery, Neuroendocrine Tumor Program, New Orleans, LA; 3Ochsner Medical Center, Neuroendocrine Tumor Clinic, Kenner, LA; 4InterScience Institute, Inglewood, CA


Results

R0/R1 resection was performed in 211 patients with small bowel NETs.

Small Bowel NETs (N=516)

R0/R1 Resection & Serial PST Levels (N=211)

Group 1
Normal PreopPST
Normal PostopPST (N=65)

Group 2
Elevated PreopPST
Normal PostopPST (N=75)

Group 3
Elevated PreopPST
Elevated PostopPST (N=71)
Role of Plasma Pancreastatin in Predicting Prognosis Following R0/R1 Surgical Cytoreduction in Small Bowel Neuroendocrine Tumors

Eugene A. Woltering, MD, FACS1,2,3, Brianne A. Voros, MS1,2,3, Ramcharan Thiagarajan, MD, FACS1,2,3, David T. Beyer, BS1,2,3, Robert A. Ramirez, DO, FACP1,3, Gregg Mamikunian, MS4, J. Philip Boudreaux MD, FACS1,2,3

1The New Orleans Louisiana Neuroendocrine Tumor Specialists, New Orleans, LA; 2Louisiana State University Health Sciences Center – New Orleans, Department of Surgery, Neuroendocrine Tumor Program, New Orleans, LA; 3Ochsner Medical Center, Neuroendocrine Tumor Clinic, Kenner, LA; 4InterScience Institute, Inglewood, CA


Survival Analysis

- Comparable survival rates were observed in Groups 1 and 2 while significantly worse survival was observed in Group 3 despite R0/R1 resection ($P < 0.001$).
- Kaplan-Meier 5-year and 10-year OS rates were as follows: Group 1 – 96% and 93%; Group 2 – 92% and 70%; and Group 3 – 70% and 40% (Figure 1 & Table 1).

Figure 1. Kaplan-Meier survival stratified by pancreastatin level group (N=211).

Table 1. Survival Following R0/R1 Resection by PreopPST/PostopPST Group (N=211)

<table>
<thead>
<tr>
<th>PreopPST/PostopPST Group</th>
<th>N</th>
<th>Mean OS ± SD (in months)</th>
<th>5-Year OS</th>
<th>10-Year OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>65</td>
<td>131 ± 3</td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td>Group 2</td>
<td>75</td>
<td>120 ± 5</td>
<td>92%</td>
<td>70%</td>
</tr>
<tr>
<td>Group 3</td>
<td>71</td>
<td>86 ± 5</td>
<td>70%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Abbreviations: PreopPST, Preoperative pancreastatin level; PostopPST, Postoperative pancreastatin level; SD, standard deviation; OS, overall survival
CONCLUSIONS

- Plasma PST levels and the extent of resection seem to be complimentary in predicting outcome following surgical cytoreduction in small bowel NETs.

- Serial monitoring of PST levels can identify patients who have a poor prognosis despite undergoing R0/R1 resection.