Risk-stratified surveillance protocol improves cost effectiveness after radical nephroureterectomy in patients with upper tract urothelial carcinoma

M. Momota¹, S. Hatakeyama¹, H. Yamamoto¹, Y. Tobisawa¹, T. Yoneyama¹, Y. Hashimoto¹, T. Koie¹, I. Iwabuchi², M. Ogasawara², T. Kawaguchi² and C. Ohyama¹

1) Department of Urology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan 2) Department of Urology, Aomori Prefectural Central Hospital, Aomori, Japan

Background:
To develop a surveillance protocol with improved cost-effectiveness after radical nephroureterectomy (RNU), as the cost-effectiveness of oncological surveillance after RNU remains unclear.

Methods:
We retrospectively evaluated 426 patients with RNU for upper tract urothelial carcinoma (UTUC) without distant metastasis at 4 hospital. Patients with routine oncological follow-up were stratified into normal-, high- and very high-risk groups according to a pathology-based protocol utilizing pathological stage, lymphovascular invasion (LVI) and surgical margin (SM). Cost-effectiveness of the pathology-based protocol was evaluated, and a risk score-based protocol was developed to optimize cost-effectiveness. Risk scores were calculated by adding risk factors independently associated with recurrence-free survival. Patients were stratified by low-, intermediate- and high-risk score. Estimated cost per recurrence detected by pathology-based and risk score based protocols was compared.

Results:
Of 426 patients, 109 (26%) and 113 (27%) experienced visceral and intravesical recurrences, respectively. The pathology-based protocol found significant differences in recurrence-free survival in the visceral recurrence but not in the intravesical recurrence. The medical costs per visceral recurrence detected were high, especially in normal-risk (≤pT2N0, LVI-, SM-) patients. We developed a risk score associated with visceral recurrence using Cox regression analysis. The risk score-based protocol was significantly more cost-effective than the pathology-based protocol. Estimated cost differences reached $747,929 per visceral recurrence detected, a suggested 55% reduction.

Conclusions:
A risk score-stratified surveillance protocol has the potential to reduce over investigation after RNU without adverse effects on medical.

Background of patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>P value</th>
<th>HR</th>
<th>95% CI</th>
<th>Risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor in ureter</td>
<td>&lt;0.001</td>
<td>2.25</td>
<td>1.44-3.52</td>
<td>1</td>
</tr>
<tr>
<td>Hydrenephrosis</td>
<td>&lt;0.001</td>
<td>2.83</td>
<td>1.76-4.56</td>
<td>1</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>&lt;0.001</td>
<td>3.13</td>
<td>1.97-4.97</td>
<td>2</td>
</tr>
<tr>
<td>Preoperative CKD</td>
<td>&lt;0.001</td>
<td>3.49</td>
<td>2.17-5.62</td>
<td>2</td>
</tr>
<tr>
<td>pT3-4</td>
<td>&lt;0.001</td>
<td>4.52</td>
<td>2.96-6.89</td>
<td>2</td>
</tr>
<tr>
<td>LVI+</td>
<td>&lt;0.001</td>
<td>4.68</td>
<td>3.18-6.89</td>
<td>2</td>
</tr>
<tr>
<td>SM+</td>
<td>&lt;0.001</td>
<td>8.85</td>
<td>4.78-16.4</td>
<td>2</td>
</tr>
</tbody>
</table>

Multivariate analysis for risk score calculation

Risk score-based protocol

- **Low risk (0-2)**
  - urological, and chest X-ray
  - Urine analysis, cytology and cystoscopy
- **Intermediate risk (3-5)**
  - CT scan of chest/abdomen/ pelvis
- **Very high risk (6-12)**
  - Low-risk (0-2)
  - Intermediate-risk (3-5)
  - Very high-risk (6-12)

Estimated screening cost (Pathology-based protocol)

- Normal-risk
- High-risk
- Very high-risk

Estimated screening cost (Risk score-based protocol)

- Low-risk
- Intermediate-risk
- Very high-risk

Total surveillance cost for 5 years

- Pathology-based
- Risk score-based

$747,929
(55% reduction)