Colonoscopic ultrasound is associated with a learning phenomenon despite previous rigid probe experience

Pulathis N. Siriwardana · Shivanthi J. De S. Hewavisenthi · Arunasalam Pathmeswaran · Kemal I. Deen

Abstract
Colonoscopic ultrasound (CUS) enables total colonoscopic examination combined with staging of tumor. Rigid probe transrectal ultrasound (TRUS) is reliable in assessing rectal cancer. Both the modalities are associated with an initial learning curve. We evaluated the predictability CUS in pre-operative staging of rectal cancer during the learning curve, despite experience with TRUS. Forty-four patients with non-obstructing rectal cancer were assessed by colonoscopy and colonic ultrasound using a 7.5 MHz rotating transducer. Accuracy of ultrasound staging was compared with pathological staging. Tumor staging and nodal staging at pathology and ultrasound were named pT, pN and uT, uN, respectively. The pathological staging was pT1 in two (4.5%), pT2 in 16 (36%), pT3 in 21 (48%) and pT4 in five (11.5%) rectal cancer specimens. CUS understaged the tumor in 11 cases and overstaged it in 10 cases. Overall, the positive predictive value was 61%, negative predictive value 73%, sensitivity 61%, and specificity 73%. Lymph nodes were not visualized in 14. The overall un-weighted kappa of CUS staging of RC was 0.18 (poor). The predictive value in tumor staging of CUS is suboptimal in the learning phase, despite previous experience with TRUS.

Keywords Learning experience · Preoperative staging · Rectal cancer

Introduction
Management of rectal cancer involves a multidisciplinary approach. Pre-operative staging helps predict outcome and survival. Whilst T1 tumors are amenable to local excision, neo-adjuvant chemoradiation is advocated for stages T3 or T4. The overall accuracy of computerized tomography (CT), magnetic resonance imaging (MRI) and MRI with endorectal coil in predicting tumor stage is 80%, 74% and 81%, respectively and that for nodal staging is 66%, 74% and 82% respectively. Endorectal ultrasound assessment is increasingly being used for management decisions in rectal cancer.

Although rigid probe endosonography for rectal cancer is reliable in predicting mural extent of tumor in the lower and mid-rectum, examination of tumor proximal to the mid-rectum requires colonoscopic endosonography. An added advantage of colonoscopic ultrasound (CUS) is its ability to perform total colonoscopy at the same time.

Transrectal ultrasound (TRUS) has a recognized learning curve which requires at least 50 examinations to overcome. CUS is also likely to be associated with a learning curve in initial examinations. We evaluated the efficacy of CUS performed by a person experienced in rigid probe ultrasound in predicting tumor stage in patients with rectal cancer.

Methods
Patients presenting with non-obstructing rectal cancer were initially evaluated by colonoscopy and, at the same time, by endoluminal ultrasound (EUS) using an ultrasound colonoscope with a 7.5-mHz rotating transducer (CF UM-20; Olympus, Tokyo, Japan). All the CUS examinations were performed by a single operator (KID), who has had previous experience with rigid probe endosonography. Patients who had received neo-adjuvant radiotherapy were excluded from this study. The study design was approved by the Ethics committees of the National Research Council and University of Kelaniya, Sri Lanka.
Bowel preparation was achieved by using polyethylene glycol. Patients received midazolam and fentanyl, and were monitored with pulse oximetry. The procedure was performed with the patient in the left lateral position. After colonoscopy, the lesion was assessed endonsonographically and acoustic contact with the tumor was ensured by filling the rectal balloon with degassed normal saline. Evaluation of mural stage of tumor was based on the five-layer model, where stage was assigned T0/T1–T4 based on the Union Internacional Contra la Cancrum (UICC) system. Nodal involvement was predicted only if para-rectal nodes were visualized endonsonographically – hypoechoic, round rather than oval, non-branching, discrete lesions with no continuity with the tumor. Pathology stage and ultrasound stage for tumor and lymph nodes were named pT, pN and uT, uN, respectively.

Laparotomy and surgical excision was performed on all patients by a qualified colorectal surgeon (KID) and the resected specimens were assessed by a trained colorectal pathologist who was blinded to the ultrasound stage of the tumor (SJDH).

The ultrasound stage of each tumor was compared with its corresponding pathology stage and, sensitivity, specificity, negative and positive predictive values were analyzed by an independent reviewer (PNS). Furthermore kappa (k) statistic was calculated to assess percent measure of agreement between TRUS and final pathology. In order to assess the degree of scatter a weighted k value was used. Correlation of (k) statistics was performed according to Landis and Koch (<0.2, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent).

In order to assess the effect of operator experience on CUS accuracy, examinations were reanalyzed in four sequential blocks of 10 patients.

**Results**

Forty-four patients (median age 64 years [range 32–88]; 21 men) were assessed by CUS. Seventeen (39%) tumors were in the upper rectum, 9 in mid- and 18 in lower rectum. There was no procedure-related morbidity or mortality. Total colonoscopy was achieved in all the patients.

While it was possible to predict wall stage of tumors in 44 patients using ultrasound, para-rectal nodes were seen only in 30 patients. In the remaining 14, para-rectal nodes were not visualized by ultrasound based on standard criteria. CUS prediction of tumor stage and the corresponding pathology stage for this series of patients is shown in Table 1. Eleven (25%) tumors (pT3 – 6, pT4 – 5) were under-staged by colonoscopic ultrasound. Of these, four (9%) tumors were predicted as uT3 but were found to be pT4 on pathology staging. Although CUS under-staged these tumors, the predictions did not result in under-treatment because both pT3 and pT4 tumors qualified for neo-adjuvant therapy. Hence, only seven (16%) patients would have been deprived of neo-adjuvant treatment based on CUS prediction. None of the pT2 tumors were understaged by CUS. It was possible to predict the requirement for neo-adjuvant chemoradiation or no therapy in 84% of ultrasound examinations. Ten (23%) tumors were overstaged by colonoscopic ultrasound. Nine (20%) of these tumors (pT1 – 1, pT2 – 8) would have been over-treated based on this staging.

Overall results of predictability for the nodes were poor; PPV 61%, NPV 73%, sensitivity 73% and specificity 61%. Nodes were not visualized in 14 patients on ultrasound; 5 of them were pN +ve.

There was a steady increase in accuracy in the prediction of colonoscopic tumor stage according to k statistics from poor to good (un-weighted k: –0.07, 0.08, 0.24, and 0.64; weighted k: –0.06, 0.13, 0.3, and 0.67) in the sequential blocks of 10 patients (Table 2).

**Discussion**

In this series with CUS staging, the prediction of the need for neo-adjuvant chemoradiation was accurate in 84% of

<table>
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<th>Pathology staging</th>
<th>pT1</th>
<th>pT2</th>
<th>pT3</th>
<th>pT4</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound staging(n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>uT1</td>
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<td>0</td>
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<td>0</td>
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</tr>
<tr>
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<td>8</td>
<td>6</td>
<td>1</td>
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<tr>
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<td>4</td>
<td>28</td>
</tr>
<tr>
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<td>0</td>
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<td>0</td>
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<tr>
<td>Total</td>
<td>2</td>
<td>16</td>
<td>21</td>
<td>5</td>
<td>44</td>
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<td>Sensitivity (%)</td>
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<td>71.4</td>
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<tr>
<td>Specificity (%)</td>
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<td>71.4</td>
<td>43.5</td>
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<td>Negative predictive value (%)</td>
<td>0.95</td>
<td>71.4</td>
<td>62.5</td>
<td>88.6</td>
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</tbody>
</table>

Colonoscopic ultrasound accuracy: Weighted kappa = 0.18, unweighted kappa = 0.15
cases. In this study, over-treatment by chemoradiation for T1 and T2 tumors was in the order of 20% (pT1 – 1, pT2 – 8). The majority of predictive errors (18%) in staging occurred in lesions that were ultrasound stage T3 but pathology stage T2. Peritumoral inflammation has been indicated as a possible explanation. A factor leading to over-treatment is operator bias towards over staging, particularly amongst those who have not overcome the learning curve. Another factor is operator tendency to overstage, which is reflected in this series as well.

Under-staging was seen mainly in pT3 tumors, which were ultrasonically staged uT2. This may be due to microscopic extension of tumor beyond the muscularis mucosa, which is not visualized by ultrasonography. Mackay et al. proposed that an uT2 tumor with extensive infiltration into the muscularis propria be considered uT3, by which understaging of T3 tumors may be reduced by 9.5%. None of the pT1 (5%) tumors were predicted accurately by CUS in this series. This is probably due to the sub-optimal accuracy of superficial layer visualization by the lower frequency probes (7.5 mHz). Likewise, none of the pT4 tumors was diagnosed by CUS preoperatively. Lateral lymph node involvement in rectal cancer is an indicator for neo-adjuvant therapy or lateral node dissection. Endosonographic prediction would have resulted in under treatment of lymph nodes in 16% of our patients. Endoluminal ultrasound-guided biopsy of lymph nodes seen at ultrasound may require further evaluation as a method of improving accuracy of nodal stage. The most important factor for accurate prediction in EUS is operator experience. Despite previous rigid probe experience, a new learning curve could be demonstrated for the flexible scope ultrasound examinations. The overall kappa in the rigid probe series for rectal cancer staging was 0.94 (excellent) compared to 0.18 (poor) in this series. In this learning curve experience of CUS, an improved predictive value was found in subsequent patients.

In this study, the greatest limitation for wall staging of rectal tumors was seen in T1 and T4 tumors. For lymph nodes, whilst overall accuracy was 64%, the greatest limitation was lack of visualization of nodes by ultrasound. Hence, at least in the learning phase of CUS, it would be beneficial to compliment ultrasound staging of rectal tumors with other modalities such as magnetic resonance or computerized tomography.

Acknowledgment

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References