Absorbable Mesh Sling Prevents Radiation-Induced Bowel Injury During “Sandwich” Chemoradiation for Rectal Cancer

Brad E. Waddell, MD; R. Jeffery Lee, MD; Miguel A. Rodriguez-Bigas, MD; Thomas K. Weber, MD; Nicholas J. Petrelli, MD

Hypothesis: Absorbable mesh slings can prevent radiation-induced bowel injury when adjuvant pelvic radiotherapy is given in the early postoperative period. We hypothesized that the mesh sling technique is similarly effective during “sandwich” sequence adjuvant chemoradiation.

Design: Retrospective review.

Setting: Tertiary care comprehensive cancer center.

Patients: Nonrandomized series of 19 consecutive patients who underwent abdominoperineal resection and received postoperative sandwich sequence chemoradiation at Roswell Park Cancer Institute, Buffalo, NY, between January 1994 and September 1999.

Interventions: Twelve patients had an absorbable mesh sling placed at the completion of abdominoperineal resection. Seven patients did not have an absorbable mesh sling placed.

Main Outcome Measures: Radiotherapy dose and gastrointestinal toxic effects.

Results: All 12 patients in the “mesh” group were able to receive full-dose radiotherapy with tumor bed boost (total dose, 54 Gy, 11 patients; 59.4 Gy, 1 patient). Only 3 of 7 patients in the “no mesh” group were able to receive a tumor bed boost (total dose, 46.8 Gy, 1 patient; 50.4 Gy, 3 patients; 54 Gy, 3 patients). Acute gastrointestinal toxic effects were minimal in the mesh group (grade 1, 10 patients; grade 2, 2 patients) compared with the no mesh group (grade 2, 6 patients; grade 3, 1 patients). None of the patients in the mesh group have shown evidence of late gastrointestinal toxic effects. One patient in the no mesh group required surgery for complications of chronic radiation enteritis.

Conclusions: The protective effects of an absorbable mesh sling extend beyond the life expectancy of the mesh itself. Sandwich sequence chemoradiation should not preclude the use of the mesh sling technique.

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In the United States, the standard adjuvant treatment for stage II and stage III rectal adenocarcinoma is combined-modality therapy consisting of fluorouracil (5-FU)-based chemotherapy and pelvic radiotherapy (RT). Most commonly, this adjuvant therapy is given in the postoperative setting. Concurrent chemotherapy and RT are usually started within several weeks of surgery, and systemic chemotherapy alone may follow for some time. More recently, “sandwich” sequence schedules of chemoradiation have been devised. In a typical sandwich regimen, systemic chemotherapy is given for 6 cycles, with RT being given concurrently with cycles 3 and 4. Hence, the period of concurrent chemoradiation is “sandwiched” between 2 cycles of chemotherapy given alone.

Unfortunately, adjuvant chemoradiation therapy for rectal cancer is not without risk. The potential adverse effects of 5-FU–based chemotherapy are well known. In addition, radiation-induced bowel injury, which is also known as radiation enteritis, remains a problem. Various approaches to prevent or ameliorate radiation-induced bowel injury associated with pelvic RT have been reported in the literature. In a recent publication from our institution, we reviewed these techniques. They include abdominopelvic partitioning procedures, modifications to RT planning and/or treatment delivery, and radioprotective agents. Abdominopelvic partitioning describes a variety of procedures designed to exclude the small bowel from the pelvis and thus prevent radiation-induced bowel injury. These procedures may use native tissues (eg, omentum) or prosthetic materials (eg, absorbable mesh or saline-filled tissue expanders) to keep the small bowel out of the pelvic radia-
PATIENTS AND METHODS

The medical records of all patients with stage II and stage III rectal adenocarcinoma who underwent abdominoperineal resection and received postoperative sandwich sequence adjuvant chemoradiation at our institution between January 1994 and September 1999 were retrospectively reviewed. Patients who had surgery at our hospital but received adjuvant treatment at other facilities were excluded. Likewise, patients who received adjuvant chemoradiation in any schedule other than a sandwich sequence were excluded. Nineteen patients were identified and included in our review. Twelve of these patients had absorbable mesh slings placed at the time of abdominoperineal resection. The remaining 7 patients did not have a mesh sling placed. Placement of the mesh sling was at the discretion of the attending surgeon.

Postoperatively, the patients received 5-FU-based chemotherapy and pelvic RT in 1 of 3 regimens: (1) an intravenous bolus of 5-FU before, during, and after RT; (2) an intravenous bolus of 5-FU pre-RT and post-RT with continuous infusion of 5-FU during RT; or (3) continuous infusion of 5-FU before, during, and after RT. Choice among these regimens depended on the preference of the treating medical oncologist and whether the patient was a participant in a clinical trial.

Radiotherapy was begun during the third cycle of chemotherapy and was given 5 days per week in 1.8-Gy fractions. Patients were treated in the prone position with bladder distention. All patients underwent simulation with small bowel contrast prior to beginning RT. Patients with mesh in place underwent a second simulation at the end of the standard course of RT. If the small bowel was adequately excluded from the tumor bed during the second simulation, then a booster dose of radiation was given (Figure 2). Patients without a mesh sling did not undergo a second small bowel contrast simulation study. Acker and Marks12 have shown that small bowel location and mobility do not change significantly during a standard course of pelvic RT in patients who have not undergone abdominopelvic partitioning. Therefore, we used the initial simulation studies to determine whether these patients were eligible for a tumor bed boost of RT (Figure 3).

For this study, we sought to determine what proportion of each group of patients (‘mesh’ group vs ‘no mesh’ group) was able to receive a tumor bed boost of RT. We also evaluated the acute gastrointestinal toxic effects experienced by each group using the Radiation Therapy Oncology Group acute radiation morbidity scoring system as outlined in Table 1. Statistical analysis was performed using SPSS for Windows, version 9.0 (Statistical Products and Services Solutions Inc, Chicago, Ill).

Figure 1. Absorbable mesh sling holds the small bowel above pelvic inlet. Reprinted with permission from J Am Coll Surg.4 Copyright 1999, Elsevier Science.
effects of the technique. The purpose of this study was to assess the effectiveness of the absorbable mesh sling technique in patients receiving adjuvant postoperative sandwich sequence chemoradiation.

**RESULTS**

The clinical characteristics and timing of RT treatment are summarized in Table 2. The results of our review are summarized in Table 3. The study population consisted of 19 patients (15 men and 4 women) with a median age of 60 years. Five patients had stage II rectal cancer while the remaining 14 patients had stage III disease. The median time interval from surgery to the start of RT for all patients was 103 days (range, 85-134 days). The median duration of RT for all patients was 42 days (range, 36-49 days). There were no significant differences between the 2 groups with respect to age, sex distribution, stage of disease, or timing of RT.

In the mesh group, all 12 patients (100%) were able to receive full-dose RT including a tumor bed boost. Eleven patients received a total dose of 54 Gy. The remaining patient had a T4 tumor with sacral involvement and received a second boost to the tumor bed for a total dose of 59.4 Gy. In the no mesh group, significantly fewer patients received a tumor bed boost of radiation. Only 3 (43%) of 7 patients received full-dose RT (54 Gy). Three of the remaining patients did not receive a tumor bed boost because of the findings of the small bowel contrast simulation study (total dose received, 50.4 Gy). The final patient in the no mesh group experienced grade 3 gastrointestinal toxic effects that did not respond to several treatment breaks and 5-FU dose reductions. Ultimately, her adjuvant treatment was discontinued, with the final RT dose being 46.8 Gy.

![Figure 2. Small bowel contrast study (lateral view) taken after a 50.4-Gy dose in a patient from the mesh group. Small bowel is still sufficiently excluded from the pelvis; therefore, a boost dose of radiation was given.](image)

![Figure 3. Small bowel contrast study (lateral view) in a patient from the no mesh group. The volume of the small bowel in the pelvis precludes a tumor bed boost of radiation.](image)

**Table 1. Radiation Therapy Oncology Group Acute Radiation Morbidity Scoring Criteria**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Effects on the Lower Gastrointestinal Region, Including the Pelvis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No change</td>
</tr>
<tr>
<td>1</td>
<td>Increased frequency or change in quality of bowel habits not requiring medication</td>
</tr>
<tr>
<td></td>
<td>Rectal discomfort not requiring analgesics</td>
</tr>
<tr>
<td>2</td>
<td>Diarrhea requiring parasympatholytic drugs (e.g., atropine sulfate)</td>
</tr>
<tr>
<td></td>
<td>Mucous discharge not necessitating sanitary pads</td>
</tr>
<tr>
<td>3</td>
<td>Diarrhea requiring parenteral support</td>
</tr>
<tr>
<td></td>
<td>Severe mucus or blood discharge necessitating sanitary pads</td>
</tr>
<tr>
<td></td>
<td>Abdominal distention (flat plate radiograph demonstrates distended bowel loops)</td>
</tr>
<tr>
<td>4</td>
<td>Acute or subacute obstruction, fistula, or perforation</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal bleeding requiring transfusion</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain or tenesmus requiring tube decompression or bowel diversion</td>
</tr>
</tbody>
</table>

**Table 2. Clinical Characteristics and Timing of Postoperative Radiotherapy**

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Mesh Group (n = 12)</th>
<th>No Mesh Group (n = 7)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (range)</td>
<td>61 (31-78)</td>
<td>60 (54-71)</td>
<td>.90</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of males</td>
<td>10</td>
<td>5</td>
<td>.60</td>
</tr>
<tr>
<td>No. of females</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. at stage II</td>
<td>4</td>
<td>1</td>
<td>.60</td>
</tr>
<tr>
<td>No. at stage III</td>
<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Median time to start of RT, d (range)</td>
<td>104 (93-134)</td>
<td>102 (85-125)</td>
<td>.43</td>
</tr>
<tr>
<td>Median duration of RT, d (range)</td>
<td>42 (39-49)</td>
<td>40 (36-44)</td>
<td>.07</td>
</tr>
<tr>
<td>Median time to end of RT, d (range)</td>
<td>150 (133-177)</td>
<td>140 (123-166)</td>
<td>.34</td>
</tr>
</tbody>
</table>

*RT indicates radiotherapy. For patients’ sex and stage, the Fisher exact test was used for comparison. For all other characteristics, the Mann-Whitney test was used.

†P values were not statistically significant.

**Table 3. Results of Patient Review**

<table>
<thead>
<tr>
<th>Mesh Group (n = 12)</th>
<th>No Mesh Group (n = 7)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT tumor bed boost</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Not given</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>GI toxic effects, grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

*RT indicates radiotherapy; GI, gastrointestinal. For all comparisons, the Fisher exact test was used.
Acute gastrointestinal toxic reactions were minimal in the mesh group. Ten (83%) of 12 patients experienced only grade 1 toxic effects. The remaining 2 patients experienced grade 2 toxic effects. In contrast, 6 (86%) of 7 patients in the no mesh group experienced grade 2 toxic effects. More importantly, the remaining patient in the no mesh group experienced grade 3 toxic effects as described earlier, and did not complete the course of adjuvant chemoradiation. None of the patients in the mesh group have shown evidence of late gastrointestinal toxic reactions. One patient in the no mesh group developed a high-grade small-bowel obstruction 6 months after completion of his adjuvant treatment. Contrast small bowel study showed chronic radiation enteritis. On surgical exploration, the distal small bowel was “frozen” in the pelvis owing to dense adhesions. Resection of the obstructing site was not felt to be safe and a jejunocolic bypass was performed.

**COMMENT**

The natural history of radiation-induced bowel injury makes it challenging to evaluate strategies designed to prevent or ameliorate this complication of RT. Chronic radiation enteritis usually manifests within 1 to 2 years after therapy, but some cases may not become evident for several decades. Previous studies have shown that the absorbable mesh sling technique is an effective means of preventing radiation injury to the bowel in patients receiving adjuvant RT in the early postoperative period. Likewise, studies have shown that the use of pretreatment small bowel contrast studies is beneficial in these patients. We sought to evaluate the effectiveness of the mesh sling technique in patients receiving sandwich sequence chemoradiation. The 2 sets of small bowel contrast studies done in the mesh sling patients serve as an objective means of evaluating the exclusion of the small bowel from the pelvis during RT. The fact that all 12 of these patients had satisfactory exclusion of the small bowel throughout RT substantiates our belief that the mesh technique is a viable option for patients receiving sandwich sequence adjuvant treatment. Furthermore, the more severe gastrointestinal toxic effects (acute and chronic) experienced by the no mesh group illustrates the value of small bowel exclusion from the pelvis during RT.

It is simple to understand the value of an intact mesh sling. When properly placed, the sling will not allow any small bowel to fall into the pelvis. However, as the mesh dissolves, it is easy to assume that the small bowel will immediately fall into the pelvis and become at risk for radiation-induced bowel injury. It is generally accepted that the mesh dissolves in 90 to 120 days. Patients treated with sandwich sequence chemoradiation typically undergo their RT during this exact period. Therefore, it is easy to appreciate why some authors have suggested that the mesh sling technique is not a sensible option for abdominopelvic partitioning in these patients. Based on the results of our study we contend that the mesh sling technique is indeed a viable alternative. We offer 2 possible explanations for this statement. First, in the early postoperative period, while the mesh sling holds the small bowel in the upper abdomen, adhesions may form that continue to hold the small bowel out of the pelvis after the mesh dissolves. Second, no adhesions may form, and the small bowel may be completely mobile in the abdomen. With simple techniques such as prone positioning and full bladder, the small bowel can be kept out of the pelvis during RT. It is also quite possible that both of these mechanisms could be involved at the same time in any given patient (Figure 4 and Figure 5).

The common thread connecting these 2 hypotheses is the absence of adhesions that trap the small bowel in the pelvis. The inherent mobility of the small bowel is one of the most significant factors able to protect the small bowel from radiation injury. It is well known that patients with a history of previous intra-abdominal surgery are at significantly higher risk for radiation-induced injury of the small bowel than patients without a history of sur-

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**Figure 4.** Top, Prone posteroanterior view. Bottom, Prone lateral view. Small bowel contrast study performed 3 years after mesh sling placement. With prone positioning and full bladder, the small bowel is completely excluded from the pelvis.
This is, in large part, why pretreatment small bowel contrast studies are beneficial. These studies allow radiation oncologists to identify areas where the small bowel is at increased risk and plan their treatment portals accordingly. Unfortunately, the use of contrast studies to minimize the risk of radiation-induced bowel injury may come at the expense of tumor control because these studies often force the radiation oncologists to limit their field size and/or dose. As shown earlier, we use this information to determine if patients are candidates for a tumor bed boost of radiation.

There is support in the literature for both theories suggested above. Devereux et al. first evaluated the absorbable mesh technique in a small animal model and published their results in 1984. Animals were humanely killed 30, 60, 90, and 120 days after mesh placement. The authors noted that “absorption of the mesh was complete by 60 days,” but they went on to point out that “at 120 days . . . the small bowel remains fixed in the upper abdominal position.” The same authors next evaluated the mesh sling technique in a primate model. One animal each was killed 6 months and 12 months after mesh placement, respectively. Neither had evidence of residual mesh at necropsy. In the animal killed at 6 months, “there were filmy adhesions maintaining the small bowel in its upper abdominal position.” In the animal killed at 12 months, there were no intraabdominal adhesions seen, and the small bowel was freely mobile. Similar results have been seen in humans undergoing additional surgery 4 to 14 months after mesh placement. It is from these studies that we have come to accept that the natural life of an absorbable mesh sling is 90 to 120 days. It is indeed ironic that the very same studies offer logical explanations for why the benefit of the mesh technique may extend beyond the life expectancy of the mesh itself.

In conclusion, postoperative adjuvant chemoradiation is of proven benefit in patients with resected stage II and stage III rectal adenocarcinoma. However, the optimal combined modality regimen has yet to be determined. Sandwich sequence chemoradiation is a reasonable option and is the subject of several ongoing clinical trials. Unfortunately, radiation-induced bowel injury remains a threat. The absorbable mesh sling technique is an excellent option that can be used in many patients to prevent radiation-induced bowel injury. We believe that sandwich sequence adjuvant chemoradiation should not preclude the use of the mesh sling technique.

Corresponding author: Nicholas J. Petrelli, MD, Division of Surgical Oncology, Roswell Park Cancer Institute, Elm and Carlton streets, Buffalo, NY 14263 (e-mail: nicholas.petrelli@roswellpark.org).

REFERENCES


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ARCHIVES OF INTERNAL MEDICINE

The Aneurysm Detection and Management Study Screening Program: Validation Cohort and Final Results

Frank A. Lederle, MD; Gary R. Johnson, MS; Samuel E. Wilson, MD; Edmund P. Chute, MD; Robert J. Hye, MD; Michel S. Makaroun, MD; Gary W. Barone, MD; Dennis Bandyk, MD; Gregory L. Moneta, MD; Raymond G. Markhoul, MD; and the Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators

Background: We previously reported the prevalence and associations of abdominal aortic aneurysm (AAA) in 73431 veterans aged 50 to 79 years who underwent ultrasound screening.

Objective: To understand the prevalence of and principal positive and negative risk factors for AAA, and to assess reproducibility of our previous findings.

Methods: In the new cohort of veterans undergoing screening, 52745 subjects aged 50 to 79 without history of AAA underwent successful ultrasound screening for AAA, after completing a questionnaire on demographics and potential risk factors.

Results: We detected AAA of 4.0 cm or larger in 613 participants (1.2%; compared with 1.4% in the earlier cohort). The direction and magnitude of the important associations reported in the first cohort were confirmed. Respective odds ratios for the major associations with AAA for the second and for the combined cohorts were as follows: 1.81 and 1.71 for age (per 7 years), 0.12 and 0.18 for female sex, 0.59 and 0.53 for black race, 1.94 and 1.94 for family history of AAA, 4.45 and 5.07 for smoking, 0.50 and 0.52 for diabetes, and 1.60 and 1.66 for atherosclerotic diseases. The excess prevalence associated with smoking accounted for 75% of all AAAs of 4.0 cm or larger in the total population of 126196. Associations for AAA of 3.0 to 3.9 cm were similar but tended to be somewhat weaker.

Conclusions: Our findings confirm our previous cohort findings. Age, smoking, family history of AAA, and atherosclerotic diseases remained the principal positive associations with AAA, and female sex, diabetes, and black race remained the principal negative associations. (2000;160:1425-1430)

Reprints: Frank A. Lederle, MD, Minneapolis Veterans Affairs Medical Center, Department of Medicine (III-0), One Veterans Drive, Minneapolis, MN 55417.