Hypothesis: Anastomotic leaks following elective colorectal resections increase morbidity, mortality, and the need for additional interventions. An accurate understanding of risk factors would potentially reduce anastomotic leaks and/or allow appropriate selection of patients for diverting stomas.

Design: Prospective review of patient and operative characteristics that contribute to anastomotic leaks.

Setting: Fifty-one sites within the United States (May 2002-March 2005).

Patients: Six hundred seventy-two patients who participated in a trial comparing preoperative antimicrobials in elective open colorectal surgery.

Main Outcome Measures: Anastomotic leaks were diagnosed using clinical findings and were confirmed with imaging. We examined 20 variables possibly affecting anastomotic healing in univariate and multivariate analyses.

Results: There were 24 anastomotic leaks in 672 patients (3.6%) undergoing elective colorectal resection. There were 10 deaths (1.5%). A baseline albumin level of less than 3.5 g/dL (to convert to grams per liter, multiply by 10) (P = .04) and male sex (P = .03) were associated with anastomotic leaks in both univariate and multivariate analyses (adjusted odds ratios, 2.56 and 3.12, respectively). Increased duration of surgery (SD, 60 minutes; odds ratio, 1.53; 95% confidence interval, 1.06-2.22; P = .03) and steroid use at the time of surgery (odds ratio, 3.85; 95% confidence interval, 1.24-11.93; P = .02) were significant in univariate analysis. Surgical procedure with rectal resection; prophylaxis with ertapenem (vs cefotetan); or history of obesity, tobacco use, or diabetes was not associated with anastomotic leaks.

Conclusions: Significant risk factors for anastomotic leaks include low preoperative serum albumin level, steroid use, male sex, and increased duration of surgery. Appreciation of risk factors provides a rational basis for temporary diversion.

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of this study with regard to infection outcomes has been published previously. The study demonstrated a decreased incidence of postoperative surgical infections after 4 weeks of follow-up in patients who received ertapenem.

Of the 1002 randomized patients, 901 qualified for the modified intention-to-treat population and 672 were included in the evaluable population. To qualify, the patient was required to have undergone electively scheduled open colorectal surgery with completion of standard bowel preparation (sodium phosphate or polyethylene glycol) and received a complete dose of study medication. The antimicrobial drug must have been administered within 2 hours of incision and 6 hours of surgical closure. Patients were considered unvaluable if they were treated with delayed primary closure, developed a distant site infection, violated the 4-week follow-up, received prior antibiotic therapy, or had a study therapy dosing window violation. Patients were excluded because of a failure to meet surgical definition (n=60), a bowel preparation violation (n=8), a failure to meet follow-up guidelines (n=27), a distant site infection (n=67), a prior antibiotic violation (n=63), a study therapy dose violation (n=69), and/or other causes (n=14). Patients were recruited from 51 sites within the United States from May 2002 through March 2005. Each site obtained local institutional review board approval and informed consent from each patient. Anastomotic leaks were analyzed only in the 672 patients who were in the evaluable population. Patients were assessed for multiple clinical and laboratory parameters during their hospital stay and were observed for 4 weeks after treatment. Patients were examined for signs of infection at the surgical and other sites. Anastomotic leaks were diagnosed if sepsis was present. Evidence of the leak was confirmed radiologically. Subsequent treatment of anastomotic leaks was left to the judgment of the operating surgeon. Patients were older than 18 years. All operations were elective open colorectal resections. Laparoscopic and emergency colorectal operations were excluded. Elective colorectal procedures for revision of previous surgery (eg, colostomy closure or revision) and isolated rectal procedures were also excluded from the analysis.

We examined 20 variables in univariate and multivariate analyses. Patient characteristics (Table 1) included age, race, sex, tobacco use, obesity (body mass index [calculated as weight in kilograms divided by height in meters squared] >30), renal function (creatinine clearance <30 mL/min/1.73 m² [to convert to milliliters per second per meters squared, multiply by 0.0167]), history of diabetes, history of chronic obstructive pulmonary disease, preoperative albumin level (<3.0 g/dL [to convert to grams per liter, multiply by 10]), hematocrit level, and steroid use at time of surgery (0-40 mg/d). Operative variables (Table 2) comprised whether the procedure included rectal resection, indications for surgery, type of bowel preparation, whether the procedure required protective stoma or placement of drain, surgical duration, and whether gross spillage was encountered. Resections were not divided between right and left but whether or not they included the rectum. All patients received mechanical bowel preparation. No oral antibiotics were given with the bowel preparation. The decision to construct a protective colostomy or ileostomy or to place a drain was at the surgeon’s judgment.

Anastomotic leaks were suspected in patients who exhibited clinical signs of infection, including increasing pain, fever, tachycardia, and a distended abdomen. Anastomotic leaks were diagnosed by using evidence of fecal contamination draining externally or with imaging. Computed tomography was most frequently used, though a water-soluble contrast enema could also be used. A fluid collection adjacent to the anastomoses associated with extraluminal contrast confirmed anastomotic leaks on imaging studies.

Demographic characteristics were typical for patients undergoing colorectal surgery in North America. Mean patient age was 61 (SD, 14) years; 54% were male; and 77% were white. Half of the patients were tobacco users. Obesity was evident in 29% of our patients. Patients had evidence of malnutrition and chronic disease, demonstrated by albumin levels less than 3.5 g/dL (21%). Five percent of our patients were taking steroids at the time of surgery. Concomitant medical conditions included diabetes (18%), renal insufficiency (1.3%), and chronic obstructive pulmonary disease (6%). Rectal resection was required in 23% of our patients. However, we did not differentiate between left and right colon resections. Colon and rectal cancers were the most frequent indications for operation (47% and 17%, respectively), followed by diverticulitis (11%) and benign colonic neoplasm (9%). All patients underwent mecha-
Anastomotic leaks occurred in 3.6% of 672 patients after elective colorectal resection. This is within the range of prior series (2.7%-8%).11-15 Our patients were prospectively studied, and surgeons were asked to report evidence of anastomotic leaks based on clinical and radiological findings. Specific patient characteristics were collected, and follow-up was standardized so that all patients were examined at regular intervals during their hospital stay until 4 weeks after their operation. Since patients were recruited in 51 sites within the United States, this incidence of anastomotic leaks likely represents a reliable benchmark for this outcome in North America.

In the multivariate analysis, low serum albumin level (<3.5 g/dL) and male sex were significantly associated with anastomotic leaks. New Zealand surgeons have also confirmed male sex as a risk factor.16 We did not find other significant characteristics that led to leaks, eg, diabetes, tobacco use, alcohol use, duration of surgery, intraoperative fecal spillage, duration of operation, blood transfusion, or rectal anastomoses. Several of these characteristics, however, are associated with postoperative infection.17,18 Such patient and operative characteristics may serve as a guide to the surgeon as to whether he or she should construct a protective stoma. Construction of a protective stoma relies on the surgeon’s experience, particularly his or her ability to judge blood supply adequacy and perform a sound anastomosis in an adverse anatomic situation. We present our findings as additional data not only to guide the surgeon in operative decisions but also to aid in counseling patients regarding the likelihood of undergoing protective diversion. Men who were malnourished (serum albumin level <3.5 g/dL) or who were taking steroids long-term had a higher risk for leaks in our series; they should be told of this risk preoperatively and would benefit most from construction of a protective stoma.

Contrary to prior studies, we did not find anastomoses to the rectum to be more significantly associated with postoperative leaks. Several authors report an increased risk as high as 11%, particularly with low anastomoses.
Subclinical leaks have been described in colorectal right colectomies of 1.35% vs 5.20% for left colon resections. Right colectomies are usually less demanding technically; thus, the associated leak rates in right and left colon resections are significantly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal resections and their associations with anastomotic leaks have been published, but there are few published data that suggest that bowel preparation may reduce surgical site infections.

Increased duration of surgery was associated with leaks in this trial. Despite absence of oral antibiotics, our anastomotic leak rate was not different from those published in prior work. Also, there was no association between bowel preparation and leak rates. Prior studies indicate that there may be no significant benefits of using bowel preparation; however, we have recently published data that suggest that bowel preparation may reduce surgical site infections.

The anastomotic leak rate in this study may serve as a benchmark against which the rate in laparoscopic colorectal resections may be compared. Large series of laparoscopic colorectal resections and their associations with anastomotic leaks have been published, but there are few compared with studies of open surgical resections. We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.

The occurrence of inadvertent perforation or spillage was reported as a risk factor for anastomotic leakage. The published data that suggest that bowel preparation may reduce surgical site infections can also affect patient outcomes, though our study was not designed to detect minor leaks.19-21

Table 4. Univariate and Multivariate Analyses for Association Between Prespecified Risk Factors and Postoperative Anastomotic Leaks

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Baseline albumin level &lt; 3.5 g/dL</td>
<td>2.95 (1.26-6.87)</td>
<td>.01</td>
</tr>
<tr>
<td>Increased duration of surgery</td>
<td>1.53 (1.06-2.22)</td>
<td>.02</td>
</tr>
<tr>
<td>Steroid use at surgery, 0-40 mg/d</td>
<td>3.85 (1.24-11.83)</td>
<td>.02</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.39 (0.15-0.99)</td>
<td>.047</td>
</tr>
<tr>
<td>Occurrence of inadvertent perforation or spillage</td>
<td>3.59 (0.78-16.59)</td>
<td>.10</td>
</tr>
<tr>
<td>Other vs white race</td>
<td>0.47 (0.14-1.60)</td>
<td>.23</td>
</tr>
<tr>
<td>Surgical procedure without rectal resection vs rectal resection</td>
<td>2.13 (0.63-7.23)</td>
<td>.23</td>
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<tr>
<td>Procedure requiring ileostomy or colostomy</td>
<td>1.74 (0.68-4.50)</td>
<td>.25</td>
</tr>
<tr>
<td>Prophylaxis with ertapenem vs cefotetan</td>
<td>0.70 (0.31-1.59)</td>
<td>.39</td>
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<tr>
<td>Body mass index &gt; 30b</td>
<td>1.36 (0.56-3.27)</td>
<td>.51</td>
</tr>
<tr>
<td>History of chronic obstructive pulmonary disease</td>
<td>1.45 (0.33-6.42)</td>
<td>.62</td>
</tr>
<tr>
<td>Sodium phosphate vs polyethylene glycol bowel preparation</td>
<td>0.69 (0.30-1.56)</td>
<td>.37</td>
</tr>
<tr>
<td>Current tobacco user vs nonuser</td>
<td>1.27 (0.46-3.51)</td>
<td>.88</td>
</tr>
<tr>
<td>Ex-tobacco user vs nonuser</td>
<td>0.92 (0.35-2.42)</td>
<td>.69</td>
</tr>
<tr>
<td>Time from dosing of prophylaxis to skin incision</td>
<td>0.88 (0.58-1.34)</td>
<td>.56</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.66 (0.19-2.25)</td>
<td>.51</td>
</tr>
<tr>
<td>Increased baseline hematocrit</td>
<td>1.29 (0.83-2.00)</td>
<td>.26</td>
</tr>
<tr>
<td>Age</td>
<td>0.89 (0.60-1.33)</td>
<td>.57</td>
</tr>
<tr>
<td>Creatinine clearance &lt; 30 vs ≥30 mL/min/1.73</td>
<td>1.11 (0.43-2.84)</td>
<td>.83</td>
</tr>
<tr>
<td>No surgical drains used</td>
<td></td>
<td></td>
</tr>
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Abbreviations: CI, confidence interval; OR, odds ratio. SI conversion factors: To convert albumin to grams per liter, multiply by 10; creatinine clearance to milliliters per second per meters squared, multiply by 0.0167.

<8 cm from anal verge) and with preoperative chemoradiation.20 Our data did not specify exact level of rectal anastomoses, possibly leading us to miss this association. Furthermore, some studies have described different leak rates in right and left colon resections. Right colon resections are usually less demanding technically; therefore, lower associated leak rates would be expected. For example, Veyrie et al2 report leak rates for right colectomies of 1.35% vs 5.20% for left colon resections. Subclinical leaks have been described in colorectal surgery, exist in a higher percentage of patients, and have been found in 14% of patients who are followed up for evidence of radiological leakage.21 Minor clinical anastomotic leaks can also affect patient outcomes, though our study was not designed to detect minor leaks.21-23

The anastomotic leak rate in this study may serve as a benchmark against which the rate in laparoscopic colorectal resections may be compared. Large series of laparoscopic colorectal resections and their associations with anastomotic leaks have been published, but there are few compared with studies of open surgical resections. We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24 We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24 We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24 We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24 We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24 We expect the same patient and operative characteristics that are significantly associated with a leak after an open operation to be similarly associated with leaks in laparoscopic surgery. The laparoscopic approach to colorectal surgery has not been as universally adopted as open operation; therefore, lower associated leak rates would be expected.22-24
Previous Presentations: This paper was presented at the 2008 Annual Meeting of the Pacific Coast Surgical Association; February 17, 2008; San Diego, California; and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

REFERENCES

26. Rose J, Schneider C, Yhridin C, Geers P, Scheidbach H, Köckerling F. Compli...
8. Meta-analysis has shown that surgical drains are not necessary or beneficial in elective colorectal surgery. Can the authors comment on the use of drains on this study?

Dr Wilson: Gender, of course, makes a difference, as has also been observed by the New Zealand group. The narrow male pelvis makes a low anastomosis more technically difficult and therefore leak more likely.

With regard to the dose of prednisone, in clinical trials of antimicrobials for surgical infection, patients with a 15 mg per day dose or higher are often excluded on the basis of a presumed immunosuppressive effect on outcome. I do not think you should have a hard and fast rule because other factors weigh in, such as nutrition, anatomical difficulty, blood supply, and the inflammatory nature of the process.

I take serum albumin into consideration in 2 ways. One, it may be an opportunity to nutritionally improve the patient preoperatively for an elective operation; and second, a low serum albumin can help make an intraoperative decision with regard to diversion more objective.

Concerning level of anastomosis, we recognize that leak rates have been reported as much as 4 times higher after low anterior resection than after right colon resection. Often, reports divide leak rates into left colon vs right colon resection so you do not actually know where the level of resection is. For the purposes of this data collection, we decided to analyze by colectomy vs colorectal anastomosis, and, as you point out, there was no difference in leak rates.

The 10 deaths in the 672 patients (1.5%) were: 3 patients had respiratory failure, 3 had cardiac deaths, 1 pulmonary embolus, 1 small-bowel obstruction with complications, 1 aspiration pneumonia, and, somewhat surprisingly, only 1 death due to leak. The percentage of patients who had operations for causes other than cancer or diverticulitis was approximately 15% and included patients with polypoid lesions, rectal prolapse, recurrent volvulus, stricture, and other causes.

We did not recognize clinically detectable leaks in the 17% of our patients who had an ileostomy or colostomy for diversion; however, it is quite possible there were “subclinical” leaks. In fact, some surgeons suggest that the postoperative “subclinical” leak rate is actually twice that clinically appreciated. Approximately 30% of our patients had drains placed, but we did not find a difference in leak rate or, for that matter, a difference in infection rates with drains.

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