Prediction of late-onset pouch failure in patients with restorative proctocolectomy with a nomogram

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Abstract

Background: A proportion of UC patients with restorative proctocolectomy and IPAA develop pouch failure. Accurate risk assessment is critical for making proper evaluation and treatment. Information on factors that may reliably predict pouch failure for the patients requiring referral to a specialized care unit is minimal.

Aim: We sought to develop and internally validate a nomogram for the prediction of late-onset pouch failure.

Methods: The study cohort included all eligible UC patients with restorative proctocolectomy and IPAA at the subspecialty Pouchitis Clinic from 2002 to 2009. Inclusion criteria were patients having: 1) inflammatory bowel disease; 2) ileal pouches; and 3) regular follow-up at the Pouchitis Clinic. Demographic and clinical variables were prospectively collected. Multivariable accelerated failure time regression model was developed to predict pouch failure defined as pouch excision or permanent diversion. Discrimination and calibration of the model were assessed following bootstrapping methods for correcting optimism, and the model was presented as a nomogram.

Results: A total of 921 patients were included for the model. The mean age for this cohort was 45.5 years old. The mean follow-up at the Pouchitis Clinic was 5.8 years. Kaplan–Meier analysis showed that the probabilities for pouch retention are 0.939, 0.916 and 0.907 at 3, 5 and 7 years, respectively. The predictor variables which were included in the nomogram were smoking,
1. Introduction

Approximately 30% of patients with ulcerative colitis (UC) eventually require colectomy. Ileal pouch–anal anastomosis (IPAA) has become the surgical treatment of choice for UC patients after colectomy. While the pouch surgery significantly improves patients’ quality of life, complications are common. Reported cumulative prevalence of pouch failure, defined as permanent diversion or pouch excision, ranged from 3.5% to 15.5% in large series. Early-onset pouch failure, i.e. failure within 12 months after ileostomy closure, is typically caused by surgery-associated complications, such as pelvic sepsis, anastomotic stricture and separation, pouch sinus, and fistula. On the other hand, late-onset pouch failure, i.e. pouch excision, revision or permanent diversion after 12 months of ileostomy closure, often resulted from chronic pouchitis, Crohn’s disease (CD) of the pouch, refractory cuffitis, pouch strictures, prolapse, and refractory pouch-vaginal fistula. Reported pre-, peri-, and post-operative risk factors for pouch failure were mucosectomy, anal pathology, abnormal anal manometry before surgery, and annual work load of colorectal surgeons performing the pouch surgery. The discrepancy in reported rates and in risk factors for pouch failure may be explained by intensity of pre-, peri-, and post-operative investigations, operative techniques, mode of follow-up, definition and diagnostic pouch-related variables and outcomes, and institutional expertise.

The burden for the identification and intervention of the risk factors for late-onset pouch failure lays on the shoulder of practicing gastroenterologists and colorectal surgeons. Accurate prediction of pouch outcome for each individual patient will have impact on clinical management of those patients. There were only few published prediction models for pouch failure in the literature. Even those existing models may not be readily applicable to clinical practice. Nomogram has been extensively used, particularly in oncology as a model for prediction. It creates a simple graphical representation of a statistical predictive model that generates a numerical probability of a clinical event. The ability of a nomogram to generate individualized predictions enables its use in the identification and stratification of patients in clinical trials. The combination of a user-friendly interface and widespread use of internet has contributed to their popularity among oncologists and patients themselves. We hypothesized that such type of statistical model would accurately predict late-onset pouch failure in patients with restorative proctocolectomy. The aim of the study was to develop a nomogram to predict late-onset pouch failure based on a prospective cohort.

2. Patients and methods

2.1. Patients

The Cleveland Clinic Institutional Review Board approved this historical cohort study, and informed consent was obtained from all patients. A total of 930 patients were seen in our Pouchitis Clinic staffed by an IBD specialist (B.S.) and participating colorectal surgeons from March 2002 to October 2009. All eligible patients were included in the study.

2.2. Inclusion and exclusion criteria

In order to qualify for the study, subjects needed to meet all of the following inclusion criteria: 1) having underlying IBD; 2) having an ileal pouch with ileostomy closure ≥ 12 months; and 3) regularly being followed up at our Pouchitis Clinic. Patients who had developed pouch failure prior to the initial Pouchitis Clinic visit were excluded. Pouch patients with familial adenomatous polyposis (FAP) were also excluded.

2.3. Diagnostic criteria

The 12-point modified Pouchitis Disease Activity Index (PDAI) scores were used for the diagnosis of pouchitis. Pouchitis was further classified as acute (antibiotic-responsive and antibiotic-dependent) and chronic (antibiotic-refractory) phenotypes. Cuffitis was defined as inflammation of the rectal cuff or anal transitional zone (ATZ) on endoscopy and histology without or with minimal concurrent inflammation of the pouch.

CD of the pouch was diagnosed based on our previously published criteria and algorithm. CD of the pouch was categorized into one of the three clinical phenotypes based on the modified Vienna Classification and Montreal Classification — inflammatory; fibrostenotic; and fistulizing CD. Inflammatory CD of the pouch was defined as ulcerated lesions of the small bowel or afferent limb without diffuse pouchitis (excluding backwash ileitis from diffuse pouchitis), with these ulcers persisting despite ≥ 4 weeks of antibiotic therapy. Fibrostenotic CD of the pouch was defined as the presence of ulcerated strictures at the small bowel, distal ileum, afferent limb, mid-pouch, or pouch inlet with concurrent ulcers or inflammation of the afferent limb. The diagnosis of inflammatory or fibrostenotic CD of the pouch was made after the exclusion of regular NSAID use at the time of the diagnosis. Fistulizing CD of the pouch was defined when a fistula developed at least 12 months after ileostomy closure in the absence of postoperative complications, such as pelvic sepsis, anastomotic stricture and separation, pouch sinus, and fistula. The discrepancy in reported rates and in risk factors for pouch failure may be explained by intensity of pre-, peri-, and post-operative investigations, operative techniques, mode of follow-up, definition and diagnostic pouch-related variables and outcomes, and institutional expertise.

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as abscess, leak, anastomotic separation, sinus, and pelvic sepsis. CD-associated fistulae included perianal, pouch-vaginal, pouch-bladder, entero- or pouch-cutaneous ones.

Late-onset surgical complications (occurring > 12 months after ileostomy closure) were defined as conditions which were attributed directly to surgical techniques. Those conditions included pouch sinus, non-CD severe anastomotic or small bowel strictures, pouch ischemia, and pouch prolapse. Irritable pouch syndrome was diagnosed based on the presence of active symptoms in the absence of endoscopic and histologic inflammation of the pouch.

2.4. Clinical practice of the Pouchitis Clinic

All eligible patients were evaluated with a standard protocol. A combined assessment of demographic, clinical, endoscopic, histologic, and in some cases, radiographic features was conducted. All patients underwent pouch endoscopy with biopsy. Examination under general anesthesia, retrograde water-soluble contrast pouchography, CT enterography, and MRI of the pelvis, were performed if the diagnosis of CD of the pouch and surgery-associated pouch strictures or sinusues was suspected. Routine laboratory tests were performed for patients with persistent symptoms despite medical (with or with endoscopic) therapy, including complete blood cell counts, complete metabolic panel, blood cytomegalovirus DNA, celiac disease serology (total IgA, IgG and IgA antigliadin, and IgG and IgA anti-tissue transglutaminase), and stool for Clostridium difficile toxins A and B. IBD serology evaluation has not been a part of our routine clinical practice.

All patients were followed for a minimum of 12 months after IPAA creation or ileostomy closure. Because of the nature of our Pouchitis Clinic, all patients whose pouches were constructed at the Cleveland Clinic or other institutions were periodically followed up. However, the interval between clinic visits varied from months to up to 2 years.

2.5. Definitions of variables

Demographic and clinical variables were defined as follows: “extensive colitis” — endoscopic, macroscopic or microscopic disease extending proximal to the splenic flexure; “indeterminate colitis (IC)” — a histopathological diagnosis on proctocolectomy specimens which defined a clear distinction between CD and UC; “Crohn’s colitis” — colitis with granulomas in the absence of perianal, small bowel and upper gastrointestinal lesions related; “pre-operative use of biologics” — any pre-colectomy use infliximab, adalimumab, or certolizumab pegol for IBD or concurrent autoimmune disorders; “post-IPAA use of biologics” — any use of infliximab, adalimumab, or certolizumab pegol for the pouch or concurrent autoimmune disorders after pouch construction. Pouch failure was defined as dysfunctional pouch requiring in pouch resection, redo, or permanent diversion.

2.6. Outcome measurement

The primary outcomes were the assessment of association between demographic and clinical factors and pouch failure, and development and validation of a nomogram model for late-onset pouch failure.

2.7. Statistical analysis

Estimates of the probability of pouch survival were calculated by the Kaplan–Meier method. Multivariable analysis was performed with the accelerated failure time (AFT) regression method. Continuous variables were modeled with restricted cubic splines to relax linearity assumptions. For model validation, we assessed both discrimination and calibration for model performance. Discrimination referred to the ability of the nomogram to rank patients by their risk, such that patients with a higher predicted risk should be more likely to develop pouch failure. Discrimination was measured by concordance index, which was similar to the area under the receiver operating characteristic (ROC) curve for binary outcome, was applicable to time-to-event data. Concordance index takes value from 0.5 (coin flip) to 1 (perfect prediction). We used the method of Harrell et al. to compute the concordance index with over-fitting bias corrected through bootstrap, in which a large number of bootstrapping re-samples (B=1000) were drawn from the original data set. A new model with the same model setting was built thereafter on each bootstrapping resample and made a prediction on patients who did not show in the resample. An optimism factor was then calculated over the 1000 new models, which was subtracted from the concordance index directly calculated from the original model to reach the bias-corrected one. Calibration referred to the accuracy of nomogram comparing with the observed outcomes in our dataset, which was assessed with visual inspection of the calibration curve. If the curve laid on the 45° curve, the model had a perfect prediction. All statistical analyses were performed using S-Plus software (S-plus 2000; Insightful Corp., Redmond, Wash) or open source software R version 2.8.1 with design package added.

3. Results

A total of 930 patients were evaluated and 72 of them developed pouch failures. Nine of 72 patients who had had pouch failure before their initial Pouchitis Clinic visit were excluded. Therefore, 920 patients, including 63 with pouch failures which occurred more than 12 months after ileostomy closure, were eligible for the study. Demographic and clinical characteristics were shown in Table 1. The mean age for this cohort was 45.5 years old. The mean follow-up at the Pouchitis Clinic was 4.0 years.

3.1. Pouch survival

Kaplan–Meier analysis showed that the pouch retaining probabilities are 0.939, 0.916 and 0.907 at 3, 5 and 7 years, respectively (Fig. 1). Survival time ratios were shown in Table 2. Baseline pouch diagnosis and post-operative use of biologics were shown to be significant predictors for pouch failure. Post-operative use of biologics would be expected to be associated with a 93% decrease in the pouch survival time. Patients with surgical complications, one of the categories of pouch diagnoses, would be expected to experience a pouch survival time 98% shorter than those without adverse diagnosis conditions.
### 3.2. Causes of late-onset pouch failure

The causes for pouch failure in the 72 patients after the inception at the Pouchitis Clinic visit were depicted in a pie graph (Fig. 2), in which 9 patients were excluded from the statistical analysis. The main causes for late-onset pouch failure were surgical complications, CD of the pouch, and chronic pouchitis. Of the 28 patients with pouch failure from CD, 24 (85.7%) had fistulizing phenotype and 4 (14.3%) had fibrostenotic phenotype. The causes of surgical complications resulting in pouch failure in 21 patients were pouch sinus (N=8, 38.1%), stricture (N=4, 19.0%), pouch ischemia (N=2, 9.5%), pouch prolapse (N=2, 9.5%), non-CD-related pouch-vaginal fistula (N=1, 4.8%), twisted pouch (N=1, 4.8%), infected mesh (N=1, 4.8%), short cuff (N=1, 4.8%) and fistula from a Barnett continent ileal reservoir (N=1, 4.8%).

### 3.3. Nomogram prediction model for pouch survival

The nomogram was generated using the AFT survival regression model (Fig. 3). The predictor variables which were included in the nomogram were smoking, duration of the pouch, preoperative and postoperative use of biologics, and baseline pouch diagnosis at the first Pouchitis Clinic visit. The postoperative nomogram predicted the 7-year pouch survival (Fig. 3).

The nomogram was used by first locating the position on each predictor variable scale according to the patient’s predictor values. Each scale position had corresponding prognostic points (top axis). Point values for all the predictor variables were determined consecutively and summed to arrive at a total point value. This value was then located on
the total point axis, from which a straight line was drawn down to determine the probability of maintaining pouch at 7 years. An illustration of the nomogram calculation was given for two hypothetical patients in Table 3.

The nomogram was internally validated by calculation of the concordance index, which achieved an excellent accuracy of 0.824, indicating that the nomogram was correct 82.4% of the time in identifying which patient had higher risk among all possible comparable patient pairs. In addition, calibration plot for predicting the pouch retention probability at 7 years was presented in Fig. 4. The predicted and the actual probabilities had a good agreement for the whole range within 95% confidence interval (CI), although the CI was quite wide.

A web-based calculator for the risk of late-onset pouch failure was designed (Fig. 5).

4. Discussion

Taking advantage of our subspecialty Pouchitis Clinic, we have prospectively diagnosed, managed, and monitored a large cohort of patients. At our tertiary referral center, patients with a variety of complications of IPAA were seen. The ability to predict risk for pouch failure, when such patients had a post-IPAA visit, remains challenging. Our study design has several advantages: 1) the involvement of a large number of patients; 2) the inclusion of multiple pre- and post-operative variables; 3) the establishment of the nomogram with an excellent predictive accuracy which was internally validated through bootstrapping; and 4) graphical presentation of the multivariable regression model as an easy-use nomogram. This nomogram will be included with others as an online clinical calculator for facilitating its

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### Table 2  Survival time ratio (N=920).

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Survival time ratio (95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td>Ex-smoker vs. non-smoker</td>
<td>0.47 (0.16,1.37)</td>
</tr>
<tr>
<td></td>
<td>Active smoker vs. non-smoker</td>
<td>0.55 (0.14,2.22)</td>
</tr>
<tr>
<td>Duration from pouch construction to the 1st Pouch Clinic visit</td>
<td>1:0**</td>
<td>1.08 (0.99,1.18)</td>
</tr>
<tr>
<td>Baseline pouch diagnosis</td>
<td>Irritable pouch syndrome vs. nil</td>
<td>0.72 (0.02,25.82)</td>
</tr>
<tr>
<td></td>
<td>Acute pouchitis vs. nil</td>
<td>0.43 (0.01,13.58)</td>
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<tr>
<td></td>
<td>Refractory pouchitis vs. nil</td>
<td>0.06 (0.00*,1.72)</td>
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<tr>
<td></td>
<td>Crohn's pouch vs. nil</td>
<td>0.05 (0.00*,1.57)</td>
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<tr>
<td></td>
<td>Cuffitis vs. nil</td>
<td>0.03 (0.00*,0.93)</td>
</tr>
<tr>
<td></td>
<td>Surgical complications vs. nil</td>
<td>0.02 (0.00*,0.47)</td>
</tr>
<tr>
<td>Preop biologics</td>
<td>Yes vs. No</td>
<td>0.73 (0.22,2.45)</td>
</tr>
<tr>
<td>Postop biologics</td>
<td>Yes vs. No</td>
<td>0.07 (0.02,0.20)</td>
</tr>
</tbody>
</table>

** "1:0" means one more year after construction before being referred to the Pouchitis Clinic will increase 8% pouch retention time.
* Stands for values less than <0.01.

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Figure 2  Cause of pouch failure in patients with Crohn's disease of the pouch (N=28).
computation (available at www.clinicriskcalculators.org). The nomogram can be used as a simple scoring system for calculating the risk of ileal pouch failure at particular time intervals for patients with IPAA.

Pouch failure can be divided into those occurring immediately (<12 months) after ileostomy closure and those with late onset (>12 months after the ileostomy closure). The early-onset pouch failure is often associated with causes from the surgical procedure itself, such as anastomotic leak or separation, abscess, and pelvic sepsis,4,9 while late-onset pouch failure frequently results from inflammatory complications, such as CD of the pouch and chronic pouchitis. Commonly reported pre- and peri-operative risk factors for short-term (or early-onset) pouch failure include hand-sewn anastomosis,16 tension on the anastomosis, and pouch construction without protective diverting ileostomy.27 Patients with hand-sewn anastomosis have been considered to have a higher frequency of anastomotic stricture, septic complications, bowel obstruction, and pouch failure, than those with stapled anastomosis.16 However, a meta-analysis showed no difference in pouch failure rate between the two anastomotic techniques.18 It has been reported that continent ileostomy had a similar pouch retention rate.9 In a study of 2491 patients from the UK National Pouch Registry with a median 54 months of follow-up, pouch failure rate was higher in salvaged IPAA (27.5%) than in primary IPAA (7.7%).7 While the pre-operative use of biological agents has been reported to be associated with an increased risk for post-operative infectious complications,29,30 it is not clear whether this particular factor increases the risk for late-onset pouch failure.

Our current study demonstrated that surgery-related complications can also be associated with late-onset pouch failure. Because of the nature of subspecialty Pouchitis Clinic, patients with the worst surgical complications that have otherwise failed all other treatments would tend to get referred, further increasing the chance of pouch failure. Most of these patients might have been more likely to have surgery with pouch excision, pouch revision or a redo pouch than those with inflammatory complications of IPAA (such as pouchitis and CD of the pouch) which were likely treated with medications.

CD-associated fistulae, abscesses, or sepsis are common causes for late-onset pouch failure. Our recent study showed that a diagnosis of the CD of the pouch was associated with a 5-fold increase in the risk for pouch failure.31 Reported rates of pouch failure from CD ranged from 25% to 100%, depending on the duration and intensity of follow-up, the use of medical or endoscopic therapy, and threshold of initiating pouch resection operation.2,11,13 The majority of those reports, however, had come prior to the era of routine use of biologics in CD. In the current study, we also found that the requirement of post-operative use of biologics was associated with an increased risk for pouch failure.

<table>
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<tr>
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<td>15</td>
<td>20</td>
<td>25</td>
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<tr>
<td>Diagnosis at First Pouch Clinic Visit</td>
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<td>Predicted 7-year pouch retention prob.</td>
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<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
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<td>0.7</td>
<td>0.8</td>
<td>0.9</td>
<td>0.95</td>
<td>0.98</td>
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</table>

Figure 3 Nomogram for prediction of pouch failure.
“highly motivated” patients with a preoperative diagnosis of Crohn’s colitis in whom IPAA was intentionally performed; 2) CD was also inadvertently found in colectomy specimens of patients with a pre-operative diagnosis of UC or IC on perioperative or postoperative histopathological examination, and 3) de novo CD of the pouch developed weeks or years after ileostomy take-down and a review of the proctocolectomy specimens may show no evidence of CD. CD of the pouch adversely affects outcomes and patients’ health-related quality of life, and it can lead to septic complications or pouch failure. Reported conservative treatment modalities for CD of the pouch include biologics and endoscopic balloon dilation of strictures. Surgical options were stricturoplasty, incision and drainage of abscess, seton placement, and conversion of J pouch to continent ileostomy.

In contrast to traditional scoring systems, prognostic nomograms have the ability to make predictions by simultaneously stratifying multiple factors, accurately accounting for continuous variables, and allocating greater influence to particular factors and graphical calculation of event probability. In the clinical practice, nomograms have been developed and widely implemented for predicting survivals for prostate, pancreatic, lung, hepatocellular, renal cell, and esophageal cancers and for predicting the probability of hyperlipidemia, hip fracture, and even vaginal birth after cesarean delivery. There are limitations to our study. First, there was referral bias, since all the patients in the current study were seen in our subspecialty Pouchitis Clinic where patients from around the US and abroad, with a variety of complex pouch disorders were diagnosed and managed. To overcome the pitfall, our study design mandated the inclusion of consecutive, eligible patients with a wide range of pouch conditions at the initial visits to the Pouchitis Clinic, including normal pouch, irritable pouch syndrome, acute and chronic pouchitis, CD of the pouch, cuffitis, and a combined category of surgery-associated complications. Therefore, our study encompassed almost all diseased conditions of the pouch. In addition, the initial diagnosis was included as a critical predictor in the nomogram for tailoring the predicted risk for various pouch conditions. We believe that the findings of our study and the nomogram model can readily be applied to clinicians’ daily practice in the diagnosis and management of pouch disorders. Another possible bias was that the patients with early-onset pouch failure within 12 months after ileostomy closure might not have been included in the study, as our inclusion criteria dictated the inclusion of those patients with ileostomy closure more than 12 months. The high prevalence of pouch disorders in this cohort did not reflect the true prevalence of these disorders in general pouch population. On the other hand, the current cohort of patients were accrued from 2002 to 2009. The results from this study may not be consistent with what had been published in 1980s and 1990s when operative technique was often different and experience of surgeons was less. Logistically, we had difficult in keeping incision point at the first Pouchitis Clinic standardized due to the natural of our practice pattern (e.g. 1, 5, or 10 years after pouch creation). The nomogram model may not be applicable to those with very “old” pouches. Moreover, our current nomogram model was based on the inception time of the first Pouchitis Clinic visit. Therefore, the current model may only be applied to the patients who have already had IPAA and the model was not designed for preoperative prediction for pouch failure. Furthermore, there were no established management algorithms for CD of the pouch. Variations among treating clinicians in the selection of medical regimens, determination on the duration of medical therapy, application of endoscopic therapy, threshold and choice for surgical modalities, might have resulted in different pouch failure rates. In addition, one of main challenges in the outcome research in IPAA population is that the diagnosis of pouch disease can be a moving target. For example,

<table>
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<tr>
<th>Predictor variables</th>
<th>Patient 1</th>
<th>Predictor value</th>
<th>Predictor point</th>
<th>Patient 2</th>
<th>Predictor value</th>
<th>Predictor point</th>
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<td>Never smoked</td>
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<td>92</td>
<td></td>
<td>–</td>
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<tr>
<td>7-year pouch retention probability</td>
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<td>0.80</td>
<td></td>
<td>–</td>
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</table>

Figure 4 Calibration plot.
a patient may be diagnosed with cuffitis at the initial visit, who can later on develop CD of the pouch. Finally, we will continue to follow this cohort of patients and periodically provide updated information on pouch outcome with a longer term follow-up.

In conclusion, the nomogram model appeared to predict late-onset pouch failure reasonably well with satisfactory concordance index and calibration curve. The nomogram is readily applicable for clinical practice in pouch patients.

5. Conflict of interest and disclosure

The authors declared no conflict of interest.

6. Authors’ contribution

Bo Shen assisted in the concept, patient recruitment, management of database, and preparation of manuscript.

Changhong Yu and Michael W. Kattan helped in the development of the statistical models.

Lei Lian contributed to the database management and critical review of manuscript.

Feza H. Remzi, Ravi P. Kiran and Victor W. Fazio performed the patient recruitment and critical review of manuscript.

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References


