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Original Article

Development and Pilot Testing of an Online Calculation Tool for Relapse Risk Prediction in Ulcerative Colitis

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Abstract

Background: Ulcerative colitis (UC) is a relapsing gastrointestinal disease. Identifying patients at a high risk of UC relapse and initiating preventive treatment can reduce the risk of UC recurrence and its dangerous side effects. The present study was performed to design and pilot test an online calculation tool for relapse risk prediction in UC.

Methods: This study is based on our previous prospective study on 157 patients with UC in-remission UC. We designed an online website rooted in our pre-developed equation to calculate relapse risk scores. Then, 280 patients with UC who were not in relapse were randomly selected from our database, and the required information was filled in on the website accordingly. Finally, the indicators were manually calculated using the formula and compared with online-calculated data.

Results: The developed bilingual website is available at http://www.ucrelapserisk.com. Of the 280 patients with UC, 151 (53.9%) were male. 88 patients were at high risk of relapse in the following year. There were no differences between the manually and online calculated Seo index, UC risk score, and probability of relapse in one year.

Conclusion: This online tool is now available for patients and clinicians and provides an accurate relapse risk prediction for UC patients.

Keywords: Ulcerative colitis, Risk score, Online calculation tool

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Introduction

Inflammatory bowel diseases (IBDs) are a class of chronic and relapsing gastrointestinal conditions mainly represented by two types, including ulcerative colitis (UC) and Crohn's disease (CD).[1] The incidence and prevalence of IBDs are increasing over time, and these diseases are becoming pervasive worldwide.[2] The main causes of IBD and its recurrence remain unclear. Nonetheless, environmental and genetic factors, as well as the immune system, are among the most contributing factors in the etiology of the disease.[3]

Frequent episodes of exacerbations (relapses) are the hallmarks of UC.[4] Recurrence of UC is the result of severe inflammation in the affected parts of the patient's gastrointestinal tract, which manifests itself with symptoms such as severe diarrhea, feeling of incontinence, and rectal bleeding.[5] In many cases, recurrence can lead to severe and fatal complications such as mega-colonialism and perforation of the intestine, which will result in a mortality rate of 40%.[6] According to a study by Huber et al, recurrence, perforation, and electrolyte imbalance are the reason for 44% of hospitalization of patients with IBD in intensive care units.[7] It is obvious that whenever the symptoms recur, along with healthcare expenditure, the quality of the patient's personal and professional lives will decrease. Predicting the recurrence of UC leads to identifying and managing high-risk patients who need intensive medication plans and more follow-up care.[8]

Data mining is a multidisciplinary field that is used to extract information from large volumes of data. It is an interdisciplinary field that includes areas such as machine learning, statistics, pattern recognition, artificial intelligence, and data visualization. Such data must be converted into useful information that can be used in various applications (apps) such as market analysis, telecommunications, and healthcare apps. Data mining techniques have been used in various medical fields to improve medical diagnosis, including predicting diabetes and heart disease by discovering relationships between clinical and pathological data.[9]

Today, apps are widely used to analyze research and improve healthcare systems.[10] Numerous apps have been developed for diabetes, depression, cardiovascular disease, and lifestyle changes.[11,12] There are some apps related to health and fitness, with about 11 000 (Google Play for Android) to 20 000 (App Store for Apple iOS) variety, and medical apps range from 5000 (Google Play) to 14 000 (App Store). (11) However, too dater, no app has been designed to predict the risk score for UC recurrence. Therefore, this study was performed to design and pilot

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test an online calculation tool for relapse risk prediction in patients with UC.

Materials and Methods

UC Relapse Risk Score

The UC relapse risk score can predict the disease recurrence risk in the following year based on an equation developed in our previous prospective study.[13] Briefly, we randomly selected 157 patients with UC with clinical and endoscopic remission and no relapse activity for at least 3 months before the enrollment from the Gastroenterohepatology Research Center Registry at Shiraz, Fars Province, Iran. We then evaluated the patients' clinical and laboratory information every three 3 months. All participants were followed for 12 months or until relapse. Finally, 154 participants completed the study, and 74 patients experienced relapse. According to univariate logistic regression analysis, age, cigarette smoking, hemoglobin, albumin, erythrocyte sedimentation rate (ESR), white blood cell count, Seo index, fecal calprotectin, pre-study disease, and remission duration were significantly associated with the risk of UC relapse and were used for subsequent analyses. Quantitative variables were converted to two-state qualitative variables using receiver operating characteristic (ROC) curve analysis for inclusion in the multiple logistic regression model. The results of logistic regression showed that fecal calprotectin ≥ 341 μg/g, previous relapses ≥ 2, age ≤ 42.5 years, and Seo index ≥ 148.3 contributed to the highest risk of UC relapse. The regression coefficient for each variable was used to generate the risk-score formula. The Seo calculation formula and developed risk score formula are provided below: The risk score could be between 0-9.[13]

Seo Index = (60 * number of bloody stool/day) + (13 * number of bowel movements/day) + (0.5* ESR) - (4 * hemoglobin) - (15 * albumin) +200

UC relapse risk score = (4 * Seo Index) + (2 * number of previous relapses) + (2 * fecal calprotectin) + (1 * age)

In the next step, the relapse risk score was calculated for all patients, and acceptable discriminate validity and goodness of fit were detected for this measure. ROC curve analysis also demonstrated that UC patients with a risk score ≥ 6.5 were at high risk of recurrence within one year (sensitivity = 80% and specificity = 97.1%) (Figure 1). The probability of relapse for each of the calculated scores was estimated using logistic regression (Table 1).

Development of the Online UC Relapse Risk Score System/Website

We designed an online website to facilitate the accessibility of patients and clinicians to the UC relapse risk score calculator. In this calculator, the server performs the calculations using a hypertext preprocessor (PHP) and a My Structured Query Language (MySQL) database to store the data.

Table 1. Probability of ulcerative colitis relapse in each of the risk scores

Score	Probability
0	0.01316
1	0.03595
2	0.09442
3	0.22573
4	0.44909
5	0.69506
6	0.86438
7	0.94687
8	0.98033
9	0.99287

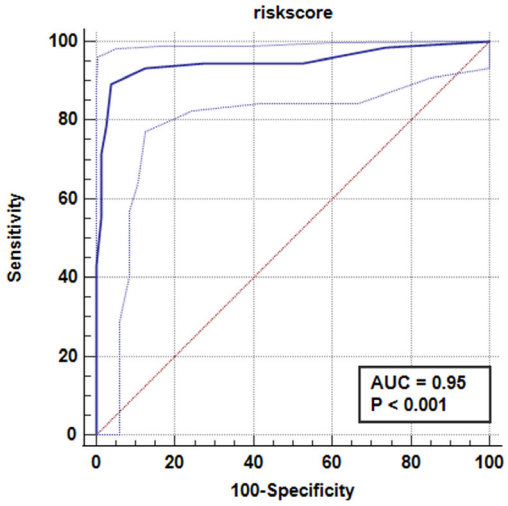

Figure 1. ROC curve analysis for relapse risk score

Pilot Testing of the Online UC Relapse Risk Score

For pilot testing of the online UC relapse risk score, we randomly selected recorded data related to 280 patients with UC referred to the Shahid Motahhari Digestive Disease Clinic, Shiraz, Iran, who were not in relapse. Accordingly, we filled in all the required information on the designed website to calculate the UC relapse risk score. We then calculated the indicators manually using the formula and compared them with the online-calculated data.

The distribution of data was evaluated using the Kolmogorov-Smirnov test. Parametric, non-parametric, and qualitative variables are reported as mean ± standard deviation, median (range), and frequency (percentage), respectively. Between-group comparisons were conducted using the Chi-square test for qualitative variables and the Mann–Whitney U test for non-parametric variables. Data analysis was performed using SPSS software version 25.

Results

Design of the Online UC Relapse Risk Score Website

The developed bilingual website (English and Persian)

is available at http://www.ucrelapserisk.com, which predicts the recurrence risk of patients with UC. The website consists of two main sections for inputting general information (i.e., name, father's name, ID number, sex (mandatory), age at diagnosis (mandatory), telephone, and province) and the medical data (including fecal calprotectin, hemoglobin, ESR, albumin, number of previous relapses, number of bowel movements, and number of bloody stools (all are mandatory)). Furthermore, a guidance note on how to use the tool, as well as advice to patients suffering from the active phase of the disease at the form completion time to consult the doctor, is provided in a separate section. The architecture of the designed website is shown in Figure 2. After completing the required parts and clicking on "calculate", the Seo index, UC relapse risk score, and the probability of relapse in the following year (from the time of form completion) are calculated for each patient with UC. Then, patients are guided to continue taking previously prescribed drugs if their risk score and relapse probability are < 4 and < 40%, respectively. However, they are advised to consult with their doctors if the values are above the cutoff points. These values were estimated according to the Mayo score criteria.[14]

Pilot Testing

Participants' characteristics are presented in Table 2. The mean age of participants was 44.5 years. Patients at a high risk of UC recurrence were more likely to be female. Furthermore, they had significantly lower age, hemoglobin, and albumin levels but higher ESR, fecal calprotectin, and the number of bloody stools, bowel movements, and previous relapses than low-risk patients.

As indicated in Table 3, the median of the UC relapse risk score and probability of relapse in one year were 5.00 and 70%. According to the ROC curve analysis, 88 patients (31.5 %) were at high risk of relapse in the following year. There were no differences between the manually and online calculated Seo index, UC risk score, or probability of relapse in the following year.

Figure 2. Website's overall structure. The sections for inputting general information (a) and the medical data (b), a guidance note on how to use the tool (c)

Table 2. Characteristics of the participants in the pilot study

Variables	Total	High-risk patients (n=88)	Low-risk patients (n=192)	*P* value
Sex (Male), n (%)	151 (53.93)	35 (39.80)	116 (60.40)	0.001
Age (year)	42.00 (33.00-52.00)	38.00 (31.00-47.00)	45.50 (35.50-54.00)	<0.001
Hemoglobin (g/L)	13.40 (11.60-15.80)	12.40 (11-20-14.60)	13.90 (12.00-16.00)	0.001
Albumin (g/L)	4.60 (4.22-5.00)	4.10 (3.90-4.70)	4.70 (4.50-6.00)	<0.001
ESR (mm/h)	16.00 (8.00-23.00)	19.00 (10.25-35.5)	13.00 (7.00-20.00)	<0.001
Fecal calprotectin (µg/g)	163.90 (39.40-458.00)	490.25 (158-1209.62)	98.40 (30.00-270.00)	<0.001
Number of bowel movements/day	4.00 (3.00-6.00)	6.00 (4.00-10.75)	3.00 (2.00-5.00)	<0.001
Number of bloody stools/day	1.00 (0.00-3.00)	3.00 (1.00-7.00)	1.00 (0.00-2.00)	<0.001
Number of previous relapses	2.00 (1.00-5.00)	5.00 (3.00-8.00)	2.00 (1.00-3.00)	<0.001

Abbreviations: ESR: erythrocyte sedimentation rate; IQR: interquartile range. All quantitative variables are reported as median and IQR. Sex was compared by Chi-squared test between high-risk and low-risk patients, and other variables were compared by Mann–Whitney U test.

Table 3. The Seo index, UC relapse risk score, and probability of relapse in participants included in the pilot study

Seo index, median (IQR) [a]	UC relapse risk score, median (IQR) [a]	Probability of relapse in one year, median (IQR) [a]
191.95 (113.10-332.90)	5.00 (3.00-7.00)	70.00 (23.00-95.00)

UC, ulcerative colitis; IQR, interquartile range.
[a] All values were similar between manual and online calculations.

Discussion

Most patients with UC have low adherence to drug treatment and are at a high risk of relapse.[15] To the best of our knowledge, this is the first website about relapse risk prediction in patients with UC. This tool helps physicians make informed decisions about prescribing pre-ordered drugs, or conducting preventive medical treatment and rigorous monitoring according to the relapse risk score of each patient. Furthermore, this website is helpful for patients with UC guiding them regarding taking previously prescribed drugs or consulting with their doctors and reducing the number of unnecessary visits to doctors or hospitals. This online tool provides accurate results compared with manual calculations.

Based on our pilot study, it was found that female patients and those who were younger had a higher risk of UC recurrence in the following year. These results are similar to the study by Jang et al, which reported that an age lower than 45 years is an independent predictor for UC relapse.[16] Nonetheless, data regarding the influence of sex on UC relapse is controversial.[17,18] More studies should be conducted to clarify the association between sex and UC relapse risk.

Mobile phone apps or websites may provide useful adjuncts to IBD monitoring and management. Several apps targeting patients with IBD with different contents and functions are commercially available. Some apps have diary functionalities that allow patients with IBD to track their symptoms or dietary intake. These apps may also suggest potential triggers for symptomatic episodes based on the user input. Some other apps provide disease information.[19] However, these applications have shortcomings in terms of adherence to clinical guidelines and validation. Nonetheless, no app or website has been designed yet for UC relapse risk prediction and offering related guidance.

Online risk-scoring tools provide a potential avenue for subjects to find their risk of disease or predict their disease outcomes and complications for adaptation of risk-reducing behaviors.[20] Therefore, several online clinical scoring systems that are relevant to different health conditions have become popular. Framingham Risk Score is one of these tools with seven components, including age, sex, total cholesterol, cigarette smoking, high-density lipoprotein cholesterol, systolic blood pressure, and medication for hypertension that estimates the 10-year cardiovascular risk of a given individual.[21,22] FRAX (Fracture Risk Assessment Tool) score is also a computer-based algorithm for the estimation of the patient's 10-year probability of major osteoporotic fractures, including clinical spine, forearm, hip, or shoulder fractures.[23] Q fracture, Burch-Wartofsky Score, and non-alcoholic fatty liver disease (NAFLD) score are other risk calculators engines used to estimate an individual's future risk of osteoporotic fractures, probability of thyroid storm, and degree of liver fibrosis with varying degrees of accuracy.

Despite some available scoring tools on other health outcomes that their accuracy needs to be evaluated,[20] our online calculator is accurate, evidence-based, and driven by a prospective cohort study.[13] This tool originated from data of patients from Shiraz, southern Iran, so its results may not be generalizable to other populations with differences in ethnicity, age, and distribution of risk factors.

Conclusion

Our designed website is an accurate and practical tool for prognostication of UC relapse risk and is now online available for patients and clinicians.

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Authors' Contribution

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Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

This study was evaluated and approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1400.693).

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