Risk factors for peristomal pyoderma gangrenosum complicating inflammatory bowel disease☆,☆☆

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KEYWORDS
Crohn's disease; Inflammatory bowel disease; Peristomal pyoderma gangrenosum; Ulcerative colitis

Abstract

Background and aims: Risk factors for peristomal pyoderma gangrenosum (PPG) are not well defined. The aim of this study was to evaluate risk factors associated with development of PPG.

Methods: Both PPG patients and controls were obtained by searching a database of the Cleveland Clinic using the ICD-9 code from March 2005 to May 2011. The control group was selected by matching for underlying diseases and type of stoma in a ratio of 3:1. Univariate and multivariate analyses were performed.

Results: A total of 15 PPG cases and 45 controls were included. The mean age at the time of PPG diagnosis was 46.0±14.4 years. The underlying disease was Crohn's disease in 7 patients (46.7%), ulcerative colitis in 7 (46.7%) and indeterminate colitis in 1 (6.7%). Eleven patients (73.3%) had end ileostomy, 3 (20.0%) had loop ileostomy and 1 (6.7%) had colostomy. Eleven patients (73.3%) had active intestinal disease. In multivariate analysis, female gender, the presence of concurrent autoimmune disorders, and a high body mass index (BMI) were significantly associated with the presence of PPG, with odds ratios of 8.385 (95% confidence interval [CI]: 1.496–46.982, p =0.015), 6.882 (95% CI:1.438–32.941, p =0.016), and 9.895 (95% CI: 1.970–43.704, p= 0.005), respectively. After a median follow-up of 12.8 (interquartile range: 7.9–20.1) months with appropriate therapy, PPG healed in 8 patients (53.3%) and improved in 7 (46.7%) patients, after treatment.

Abbreviations: BMI, body mass index; CD, Crohn's disease; CI, confidence interval; EIM, extraintestinal manifestations; IBD, inflammatory bowel disease; IC, indeterminate colitis; IQR, interquartile range; IRB, institutional review board; OR, odds ratio; PPG, peristomal pyoderma gangrenosum; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.

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1. Introduction

Pyoderma gangrenosum is an ulcerative, cutaneous condition, initially described in 1930. The characteristic lesions are chronic and recurrent ulcerations with a well-defined, undermined, violaceous border. Fifty percent of cases are found to be associated with underlying systemic diseases, most commonly inflammatory bowel diseases (IBD), arthritis, polyarthritis and malignancy. Lower extremities are the most frequently affected area, though other parts of the body can also be involved. Pyoderma gangrenosum often starts with a painful nodule or pustule, and healing typically results in a weblike cribriform atrophic scar, which is vulnerable to further breakdown with minor irritation or trauma.

As an uncommon subtype, peristomal pyoderma gangrenosum (PPG) develops close to an abdominal stoma, comprising about 15% of all cases of pyoderma gangrenosum. Similar to pyoderma gangrenosum, PPG is often a diagnosis of exclusion. Cultures typically do not reveal pathogenic organisms, and histologic evaluation often demonstrates nonspecific inflammatory reaction characterized by dermal infiltration of neutrophils. Other etiologies can also result in peristomal ulceration, resembling PPG, such as stitch abscess, contact dermatitis, extension of underlying Crohn’s disease (CD) and irritation from leaking feces. Differential diagnosis of a peristomal ulceration sometimes is difficult, and misdiagnosis of PPG is not uncommon. Studies evaluating predictors for the development of PPG are warranted to improve the diagnosis and management of PPG.

Previously reported potential risk factors associated with PPG included female gender, active underlying disease and extra-intestinal manifestations (EIM) of IBD. However, the majority of the data are based on case reports and risk factors for PPG have not been systematically studied. The aim of this study was to evaluate the risk factors associated with PPG in IBD patients.

2. Materials and methods

2.1. Patients

This study was approved by the Cleveland Clinic Institutional Review Board (IRB). All eligible patients were identified by searching the database using the ICD-9 codes from March 2005 to May 2011. Both paper charts and electronic medical records were carefully reviewed to extract patients’ demographic information, clinicopathological variables and outcomes of PPG.

2.2. Patient groups

In this case-control study, a consecutive of 15 PPG patients were identified as cases. The controls were selected by matching for underlying disease and type of stoma with a study to control ratio of 1:3.

2.3. Inclusion and exclusion criteria

In order qualify for the study, PPG patients needed to meet all the following inclusion criteria: (1) having peristomal ulcers caused by pyoderma gangrenosum; (2) having underlying IBD; and (3) regular follow up at our institution. Patients whose peristomal ulcers were caused by other etiologies, such as stitch abscess and contact dermatitis, were excluded.

Controls needed to meet all the following inclusion criteria: (1) having a stoma; (2) being consistent with the matching criteria; and (3) regularly being followed up at our institution. Patients with a history of pyoderma gangrenosum were excluded.

2.4. Diagnosis and treatment of PPG

As shown by a previous study from our institution, the diagnosis of PPG has predominantly been clinical and based on a classic presentation of painful, undermined peristomal ulceration. Biopsy of the ulcers was performed for the purpose of exclusion.

The choice of the treatment modality and the use of type of pharmaceutical agents were at the discretion of treating physicians/colorectal surgeons. However, the common practice pattern in our institution was that local wound care with intra-lesional injection of corticosteroids was used in localized, non-aggressive form of PPG; and additional systemic medication (corticosteroids and/or immunosuppressive agents) was often administered for PPG refractory to local therapy or for an extensive and aggressive form of PPG. If the patient failed the first-line topical and systemic therapy, anti-TNF biological agents (infliximab, adalimumab, or certilizumab pegol) were used.

2.5. Demographic and clinical variables

Demographic and clinical variables evaluated in the study included age at the diagnosis of IBD, age at stoma construction, duration of IBD, duration of stoma, body mass index (BMI), gender, history of smoking or, excessive alcohol use, type of IBD, type of stoma, family history of IBD, concurrent autoimmune disorders, extraintestinal manifestations (EIM), significant comorbidities, history of drug allergy, history of tonsillectomy, pre-operation use of immunosuppressives, pre-operation use of biologics, pre-operation high platelet counts, indication for surgery, stoma complications and activity of underlying IBD.

Duration of IBD was defined as the time interval from the date of IBD diagnosis (i.e. preoperative diagnosis of ulcerative colitis [UC], indeterminate colitis [IC] or CD) to the date of stoma construction. Duration of stoma was defined as the time interval from the date of stoma construction to the diagnosis of PPG for cases, and to the date of stoma closure or last follow-up for controls. Indeterminate colitis (IC) was defined as histopathological diagnosis on proctocolectomy specimens.
that defied a clear distinction between CD and UC. Family history of IBD was defined as first degree relatives having CD and/or UC. Autoimmune disorders included asthma, psoriasis, type 1 diabetes, rheumatoid arthritis, autoimmune thyroid diseases (including Grave’s disease and Hashimoto’s thyroiditis), systemic lupus erythematosus, autoimmune hemolytic anemia, vitiligo, celiac disease, pernicious anemia, idiopathic thrombocytopenic purpura, and multiple sclerosis. EIM included arthralgia or arthropathy, erythema nodosum, IBD-related ocular lesions, thromboembolic events, and primary sclerosing cholangitis (PSC).

2.6. Outcome measurement

The primary outcome of this study was the assessment of risk factors which were associated with the development of PPG.

2.7. Statistical analysis

Comparisons of the distribution of patient characteristics between cases and controls were made using the 2-sample t test (or the Wilcoxon rank sum test as appropriate) for continuous variables and the chi-square test (or the Fisher exact test as appropriate) for categorical variables. A multivariate conditional Logistic regression analysis using the forward stepwise method with an entry criterion of \( p < 0.05 \) and a removal criterion of \( p > 0.10 \) was applied to assess the risk factors associated with PPG. All statistical analyses were performed with the open source software R version 2.8.1 with design package added. \( p \) value less than 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 15 consecutive PPG patients met inclusion criteria and were included in the study (Fig. 1). Three patients (20.0%) were male and 12 (80.0%) were female. The mean age at the time of PPG diagnosis was 46.0 ± 14.4 years (Table 1). The underlying systemic diseases were CD in 7 patients (46.7%), UC in 7 (46.7%) and IC in 1 (6.7%). Eleven patients (73.3%) had end ileostomy, 3 (20.0%) had loop ileostomy and 1 (6.7%) had colostomy (Table 1). Active intestine disease was identified in 11 patients (73.3%) when PPG developed. Five patients had a retained rectum after total abdominal colectomy as the first stage of an ileal pouch anal anastomosis for UC, three patients with CD had active small bowel disease and three (2 CD and 1 IC) had active perianal disease.

All PPG cases in the study were diagnosed predominantly based on the clinical presentation. Biopsy of the ulcers was performed in 13 patients (86.7%) for the purpose of exclusion. A painful peristomal ulceration was the main complaints for all of the 15 patients, with a mean diameter of 5.1 ± 3.9 cm (Table 1). Three patients (20%) had synchronous pyoderma gangrenosum at other areas, including 2 in the lower extremities and 1 at multiple locations. The median time to onset of PPG was 7.0 (interquartile range, [IQR]: 1.0–26.4) months after stoma construction, and the median follow-up duration was 12.8 (IQR: 7.9–20.1) months.

3.2. Risk factors for PPG

Forty-five patients were selected as controls by matching for underlying disease and type of stoma with the cases. When compared with controls, patients in the study group had a female predominance, with women accounting for 80.0% of cases and 42.2% of controls (\( p = 0.011 \)) (Table 2). The mean body mass index was 30.3 ± 6.5 kg/m² for cases vs. 25.4 ± 5.0 kg/m² for controls (\( p = 0.004 \)) (Table 2). The study group had more patients with autoimmune disorders and EIM than the control group, with 60.0% vs. 22.2% and 60.0% vs. 24.4% in the study and control groups, respectively (\( p = 0.010 \) and \( p = 0.011 \)) (Table 2). The study group also tended to have more patients with a history of drug allergy, but this did not reach statistical significance (\( p = 0.068 \)) (Table 2). No difference was detected between the two groups in terms of other demographic and clinicopathological factors (\( p > 0.05 \)) (Table 2).

![Figure 1](https://academic.oup.com/ecco-jcc/article-abstract/7/5/e171/378168) Clinical appearance of peristomal pyoderma gangrenosum.
To evaluate the risk factors for PPG, a multivariate conditional logistic regression model was constructed. This analysis showed that all factors identified from the univariate analysis, except for EIM, were confirmed to be risk factors in the multivariate analysis, with odds ratios (OR) of 8.813 (95% confidence interval [CI]: 1.496–46.982, \( p = 0.015 \)), 9.895 (95% CI: 1.970–43.704, \( p = 0.005 \)) and 6.882 (95% CI: 1.438–32.941, \( p = 0.016 \)) for female gender, high BMI and the presence of concurrent autoimmune disorders, respectively (Table 3).

### 3.3. Management of PPG

All the 15 patients underwent debridement and unroofing of undermined ulcers under local anesthesia, followed by the intra-lesional injection with corticosteroids. Two patients (13.3%) either completely (\( n = 1 \)) or partially (\( n = 1 \)) responded to the local therapy. Systemic medications in the form of corticosteroids, 6-mercaptopurine/azathioprine, cyclosporine, or dapsone were used in 13 patients (86.7%). And the combination therapy of local treatment and systemic medical therapy resulted in a complete response of PPG in 5 patients (38.5%), partial response in 4 (30.8%) and no response in 4 (30.8%). Infliximab (\( n = 3 \)) or adalimumab (\( n = 1 \)) was used in the 4 patients (26.7%) who had no response to the combination therapy, PPG was completely healed in 2 patients and partially healed in 2 at the last follow-up. Of note, relocation of stoma was done in 2 patients (13.3%), both had a recurrence of PPG at the new stoma site. Twelve patients (80.0%) had

### Table 2 Univariate analysis of risk factors associated with peristomal pyoderma gangrenosum a.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All cases</th>
<th>Controls</th>
<th>Cases</th>
<th>( p ) b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>60</td>
<td>45</td>
<td>15</td>
<td>0.214 c</td>
</tr>
<tr>
<td>Age at diagnosis of IBD, yrs</td>
<td>31.8±15.2</td>
<td>30.4±15.0</td>
<td>36.1±15.4</td>
<td>0.736 c</td>
</tr>
<tr>
<td>Age at stoma construction, yrs</td>
<td>41.6±15.4</td>
<td>41.2±15.2</td>
<td>42.8±16.5</td>
<td>0.085 d</td>
</tr>
<tr>
<td>Duration of IBD, months</td>
<td>87.1 (33.6–173.4)</td>
<td>98.3 (37.1–195.1)</td>
<td>37.9 (16.0–157.2)</td>
<td>0.011</td>
</tr>
<tr>
<td>Duration of stoma, months</td>
<td>11.9 (4.4–34.4)</td>
<td>13.1 (5.7–39.1)</td>
<td>7.0 (1.0–26.4)</td>
<td>0.011</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.6±5.8</td>
<td>25.4±5.0</td>
<td>30.3±6.5</td>
<td>0.004 c</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>29</td>
<td>26 (57.8%)</td>
<td>3 (20.0%)</td>
<td>0.011</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>24</td>
<td>19 (43.2%)</td>
<td>5 (33.3%)</td>
<td>0.503</td>
</tr>
<tr>
<td>History of alcohol use, n (%)</td>
<td>15</td>
<td>10 (22.2%)</td>
<td>5 (33.3%)</td>
<td>0.497 e</td>
</tr>
<tr>
<td>Family history of IBD, n (%)</td>
<td>15</td>
<td>13 (31.7%)</td>
<td>2 (14.3%)</td>
<td>0.304 e</td>
</tr>
<tr>
<td>Concurrent autoimmune disorders, n (%)</td>
<td>19</td>
<td>10 (22.2%)</td>
<td>9 (60.0%)</td>
<td>0.010 e</td>
</tr>
<tr>
<td>Rheumatoid arthritis, n (%)</td>
<td>8</td>
<td>6 (13.3%)</td>
<td>2 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Asthma, n (%)</td>
<td>5</td>
<td>1 (2.2%)</td>
<td>4 (26.7%)</td>
<td></td>
</tr>
<tr>
<td>Type 1 diabetes, n (%)</td>
<td>4</td>
<td>2 (4.4%)</td>
<td>2 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Autoimmune thyroid disorders, n (%)</td>
<td>3</td>
<td>1 (2.2%)</td>
<td>2 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Ankylosing spondylitis, n (%)</td>
<td>1</td>
<td>0</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Psoriatic arthritis, n (%)</td>
<td>1</td>
<td>0</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus, n (%)</td>
<td>1</td>
<td>1 (2.2%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Extraintestinal manifestations, n (%)</td>
<td>20</td>
<td>11 (24.4%)</td>
<td>9 (60.0%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Arthralgia/arthritis, n (%)</td>
<td>10</td>
<td>4 (8.9%)</td>
<td>6 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>Thromboembolic events, n (%)</td>
<td>6</td>
<td>4 (8.9%)</td>
<td>2 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Ocular lesions, n (%)</td>
<td>3</td>
<td>1 (2.2%)</td>
<td>2 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Mouth ulcers, n (%)</td>
<td>2</td>
<td>2 (4.4%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Primary sclerosing cholangitis, n (%)</td>
<td>1</td>
<td>0 (0.0%)</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Significant comorbidity, n (%)</td>
<td>13</td>
<td>11 (25.0%)</td>
<td>2 (13.3%)</td>
<td>0.482 e</td>
</tr>
<tr>
<td>History of any drug allergy, n (%)</td>
<td>36</td>
<td>24 (53.3%)</td>
<td>12 (80.0%)</td>
<td>0.068</td>
</tr>
<tr>
<td>History of tonsillectomy, n (%)</td>
<td>10</td>
<td>6 (13.3%)</td>
<td>4 (26.7%)</td>
<td>0.426 e</td>
</tr>
<tr>
<td>Pre-operation use of immuno-suppressives, n (%)</td>
<td>32</td>
<td>26 (59.1%)</td>
<td>6 (46.2%)</td>
<td>0.409</td>
</tr>
<tr>
<td>Pre-operation use of biologics, n (%)</td>
<td>25</td>
<td>20 (45.5%)</td>
<td>5 (38.5%)</td>
<td>0.655</td>
</tr>
<tr>
<td>Pre-operation high platelet counts, n (%)</td>
<td>14</td>
<td>9 (20.5%)</td>
<td>5 (41.7%)</td>
<td>0.258 e</td>
</tr>
<tr>
<td>Indication for surgery, n (%)</td>
<td></td>
<td>0.671</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory IBD</td>
<td>25</td>
<td>18 (40.0%)</td>
<td>7 (46.7%)</td>
<td></td>
</tr>
<tr>
<td>Steroid dependent IBD</td>
<td>8</td>
<td>7 (15.6%)</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>27</td>
<td>20 (44.4%)</td>
<td>7 (46.7%)</td>
<td></td>
</tr>
<tr>
<td>Stoma complication, n (%)</td>
<td>12</td>
<td>7 (15.6%)</td>
<td>5 (33.3%)</td>
<td>0.262 e</td>
</tr>
<tr>
<td>Active intestine disease, n (%)</td>
<td>39</td>
<td>28 (62.2%)</td>
<td>11 (73.3%)</td>
<td>0.435</td>
</tr>
</tbody>
</table>

a Due to missing data, cases may total less than 60 for some variables.
b p value calculated using chi-square test.
c p value calculated using t test.
d p value calculated using Mann–Whitney test.
e p value calculated using Fisher’s exact test.
at least 1 relapse of PPG after initial healing, and a parallel course with PPG occurred in 3 patients (20.0%).

4. Discussion

This case control study that evaluated the risk factors for the development of PPG included a total of 60 patients, 15 cases and 45 controls. Female gender, the presence of concurrent autoimmune disorders and a high BMI were strong and independent factors associated with the development of PPG in IBD patients. The majority of our cases were managed conservatively, with PPG having either healed or improved in all patients after a median follow-up of 12.8 (IQR: 7.9–20.1) months. Stoma relocation was undertaken in two patients, and PPG recurred in both.

PPG occurs in approximately 2%–4.3% IBD patients who have had stoma surgery,19–21 with an annual incidence rate of 0.6% among all abdominal stoma patients.22 Evidence suggests that incidence of PPG is increasing.9,23,24 Although the clinical appearance and course of PPG have been well characterized, the pathogenesis is unknown. Diagnosis of PPG remains largely based on clinical suspicion, and the primary objective of biopsy is to rule out other causes of ulceration. PPG is associated with high morbidity. The ulcers are quite destructive and can expand by 1 to 2 cm over the course of a single day.8 The rapidity of the development of the lesion is considered the hallmark of the disease, and delayed and/or inappropriate treatment often necessitates hospitalization.23 A case of peristomal small bowel evisceration as a result of PPG has been reported.14 Defining risk factors for the development of PPG after stoma creation can help lead to early diagnosis, hence to early management, which may be effective for promoting the healing of PPG.21

While 15% to 50% of cases of pyoderma gangrenosum are associated with IBD, almost all cases of PPG that have been reported have occurred in patients with underlying IBD.8,9,11,17,21,26–28 Other rare associated systemic disorders that have been described include diverticulitis, abdominal malignancy, and neurologic dysfunction. Whether PPG is more common in patients with CD than UC is still controversial,16–18 while results from our study support that PPG has no predominance of either type of IBD. The mean age of our patients at the time of PPG diagnosis was 46.0±14.4 years, which is consistent with studies that have shown that PPG most commonly affects young and middle aged adults.5,29 Similar to the clinicopathological presentations of classic pyoderma gangrenosum, painful ulceration was reported by all of our patients, and biopsies of the specimens revealed a nonspecific inflammatory reaction consisting of a mixture of neutrophils, lymphocytes, and histiocytes in most patients. Another interesting finding of our study is that more than 70% of PPG patients had the stoma configuration of end ileostomy, similar to a previous report from Japan.21

Previous studies have shown that PPG was more likely to occur in female patients,16–18 a phenomenon that was also found in our study. Although the underlying mechanisms for the female predominance of PPG are not clear, sex hormones might play a role as evidenced by the studies which have shown that oral contraceptive use was associated with an increased risk of disease relapse in IBD patients.30,31 And the fact that female patients suffer a higher incidence of other autoimmune disorders in comparison with males lends further weight to our findings.32,33 Furthermore, our study showed that the presence of autoimmune disorders was more common among patients in the study group than that in the control group, suggesting that PPG and other autoimmune disorders might share similar autoimmune-mediated mechanisms in the process of pathogenesis.7,8 In addition, we also found that PPG patients had a significantly higher BMI than the controls. As to whether a high BMI predisposes patients with stomas to the development of PPG has not been reported, however obese individuals have been reported to produce higher levels of pro-inflammatory chemokines compared with lean persons.34 A connection between obesity and autoimmune disorders has also been reported.34,35 Binus et al.36 have reported that the mean BMI value for patients with pyoderma gangrenosum was 30.6±9.0 kg/m², a value very close to that for our patients (30.3±6.5 kg/m²).

Although controversy exists, stoma hernia as well as other stoma related complications are thought to trigger the development of PPG.22,37–39 In our study, patients in the study group did tend to have more stoma related complications than those in the control group, although the difference between the two groups did not reach statistical significance. Similar to other studies, EIM was risk factor in the univariate analysis in our study.15 However, the predictive value of EIM lost its significance after adjusting for other variables. Previous studies have also suggested that the presence of active intestinal disease might play a role in the development of PPG.8,16,18 Indeed, the majority of cases (73.3%) in our study had active bowel disease. This was however not identified as a risk factor for PPG, probably due to type II error of the study caused by the small sample size of enrolled cases (n =15).

Management of PPG is empiric for most cases, although at general consensus has been reached. Once PPG is diagnosed, a multidisciplinary team consisting of gastroenterologist, dermatologist, surgeon and stoma therapist should be involved. Despite the fact that cases of successful surgical management of pyoderma gangrenosum have been reported,18,40 medical therapy remains the mainstay.3,41–44 Since PPG has both systemic and local wound components, a combination therapy consisting of local wound care, topical agents and systemic use

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Table 3  Risk factors associated with peristomal pyoderma gangrenosum: multivariate conditional logistic regression analysis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>p valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female vs. male)</td>
<td>8.385</td>
<td>1.496–46.982</td>
<td>0.015</td>
</tr>
<tr>
<td>Mean body mass index, kg/m² (≥26.6 vs. &lt;26.6)</td>
<td>9.895</td>
<td>1.970–43.704</td>
<td>0.005</td>
</tr>
<tr>
<td>Concurrent autoimmune disorders (yes vs. no)</td>
<td>6.882</td>
<td>1.438–32.941</td>
<td>0.016</td>
</tr>
</tbody>
</table>

a p value calculated using multivariable conditional logistic regression analysis.
of corticosteroids, immunosuppressants, or even biologics is often necessary. Consistent with the previous report from our group, local wound care with intra-lesional injection of corticosteroids and systemic corticosteroids or immunosuppressive agents were administered in the majority of patients in this cohort, resulting in an overall response rate of 73.3%. Biological agents were applied in the remaining 4 patients who failed the therapy, and two of these patients completely healed at the last follow-up. Early diagnosis and management might also have contributed to the overall good outcome, since as a tertiary referral center we are more acquainted with this disorder. However, the course of PPG is still unpredictable and complicated, about 80.0% of cases have at least one relapse as shown by our study. Stoma relocation was done in two UC patients in our series, and PPG recurred at the new stoma for both. Since pathergy can coincide in 25–50% cases, management of PPG by relocating the stoma is not recommended based on our experience and that of previous the literature.

The findings of our current study have several clinical implications. It has previously been estimated that approximately 10% of skin ulcers are misdiagnosed as pyoderma gangrenosum. Management of peristomal ulcers caused by PPG and other disorders is different, misdiagnosis can lead to substantial complications as well as deterioration of the cutaneous ulceration. Critical to the proper management of PPG is the establishment of a correct diagnosis, since this which can be improved by defining the related risk factors. Our study reveals associated risk factors, the presence of which may aid in the early diagnosis of PPG. Patients who develop the condition should be closely monitored by colorectal surgeon, gastroenterologist, and stoma nurses. PPG needs to be suspected once ulcers develop around the stoma area in these patients. Since BMI and the presence of autoimmune disorders are significant predictors for PPG in IBD patients in our study, weight loss and treatment of autoimmune disorders, especially for female patients when stoma construction is inevitable, might help decrease the likelihood of developing PPG.

There are some limitations to our study. Firstly, not all the lesions in our study were biopsied. However, the value of biopsy is to rule out other causes of peristomal ulceration rather than to make a diagnosis. Further, the diagnosis of PPG in all of our patients was made through a combination of efforts from a multidisciplinary team. Thus, the possibility of a misdiagnosis should be small. Secondly, the number of PPG cases in our study was small and only a limited number of variables were introduced into the conditional logistic regression model. However, PPG is a rare condition, and a prospective study with a large sample size would not be feasible. Furthermore, a review of published literature suggested that although there are some data currently available regarding the risk factors associated with PPG, most of the conclusions from the studies were made based on a simple description of cases without controls.

In conclusion, the results obtained from this study establish that female gender, the presence of autoimmune disorders and a greater BMI are strong and independent risk factors associated with the development of PPG in IBD patients. Pyoderma gangrenosum should be considered in all patients who have a peristomal ulceration, especially when they have one or more of these risk factors. Once the diagnosis of PPG is confirmed, a combination therapy consisting of both local wound care and systemic medication administration is preferred due to the aggressive nature of the disorder.

Conflict of interest

We have no conflict of interest to declare.

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XRW contributed to study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript. SM, RPK, FHR and BS contributed to study concept and design, analysis and interpretation of data and critically revised the manuscript. JH conducted statistical analysis. All authors read and approved the final manuscript.

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