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ORIGINAL ARTICLE

Preoperative factors influencing mortality and morbidity in peptic ulcer perforation

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Abstract
Purpose Perforated peptic ulcer is one of the most common surgical emergencies worldwide. With the improvement in medical therapy for peptic ulcers, the number of elective surgical procedures has come down. However, the incidence of perforated peptic ulcer is still increasing and remains as a substantial health problem with significant postoperative morbidity and mortality. This study aimed to find out the association between various preoperative and intraoperative factors with the postoperative mortality and morbidity in patients operated for peptic ulcer perforation.
Methods This prospective observational study had a time based sample of 101 perforation peritonitis cases admitted to the surgical wards of a tertiary care center from February 2015 to January 2016 who underwent laparotomy, diagnosed to have peptic ulcer perforation and underwent simple closure with an omental patch. Data regarding age, gender, presenting complaints, time elapsed from the onset of symptoms to surgery, physical examination findings, comorbid diseases, laboratory and imaging findings, intraoperative findings, length of hospital stay, postoperative morbidity, and mortality were recorded and analyzed.
Results Female gender, older age group, perforation surgery interval more than 36 h, and size of perforation more than 1 cm^2 were found to be significant factors influencing postoperative mortality and morbidity. Postoperative morbidity was also associated with comorbid diseases. Abnormal renal function on presentation was identified as an additional risk factor for postoperative morbidity and longer hospital stay.
Conclusions An understanding of these factors, identification of patients at risk and early intervention can help in reducing the postoperative morbidity and mortality in peptic ulcer perforation.

Keywords Peptic ulcer perforation · Perforation peritonitis · Peptic ulcer · Mortality—morbidity—peptic ulcer perforation

Introduction

Peptic ulcer perforation still remains as one of the most common surgical emergencies worldwide, especially in developing countries, in spite of the improvements in medical therapy for peptic ulcer disease [1]. The choice of treatment for peptic ulcer perforation remains to be surgery [2]. Currently, the most preferred surgical method is simple closure and omental patch repair. In spite of the better understanding of disease, effective resuscitation and prompt surgery under modern anesthesia techniques, there is still high postoperative morbidity (20–50%) and mortality (3–40%) [3, 8] The high incidence of postoperative complications necessitates the identification of factors associated with the morbidity and mortality. Factors, such as concomitant diseases, shock on admission, delayed surgery (>24 h), resection surgery, and postoperative abdominal and wound infections, have been associated with increased morbidity and mortality in perforated ulcer patients [4].

In the last few decades, several studies have evaluated the various risk factors associated with postoperative mortality and morbidity in peptic ulcer perforation. Most of these studies have equated postoperative morbidity to

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the occurrence of any of the postoperative complications. However, many of the patients have more than one postoperative complication and each of these vary in its magnitude. There is a need to analyze the risk factors associated with individual postoperative complication. None of the previous studies available have analyzed the associations of individual postoperative complications. Only very few studies are available from the Asian population. Our study aims in evaluating the association between various preoperative factors with postoperative mortality and morbidity in patients operated for peptic ulcer perforation in a tertiary care center.

Methods

This is a prospective observational study with a time-based sample of 101 perforation peritonitis cases admitted to the surgical wards of a tertiary care center from February 2015 to January 2016 who underwent laparotomy, diagnosed to have peptic ulcer perforation and underwent simple closure with an omental patch. Clearance certificate from the Human Ethics Committee (Medical College Thiruvananthapuram, India) (IEC.No.01/37/2014/MCT.) was obtained prior to the study. Informed consent was obtained from all individual participants included in the study. Patients who underwent previous abdominal surgeries or diagnosed postoperatively to have malignant ulcer perforations were excluded from the study.

The oral intake of patients who were diagnosed with perforation peritonitis was discontinued, and urinary catheters and nasogastric tubes were placed. Relevant history and examination findings were recorded, and blood samples were collected. Following adequate fluid resuscitation, the patients were taken for surgery. Antibiotics were started preoperatively according to the institutional protocol. It included a third generation cephalosporin (cefotaxime or ceftriaxone) plus metronidazole intravenously. The same regimen was continued postoperatively for 5 days and stopped in uncomplicated cases. In complicated cases, antibiotics were changed as per the culture and sensitivity results. Laparotomy was performed in all the patients. The consultant surgeon in charge of emergency theatre assisted by a senior and a junior surgery resident trainee performed the laparotomy. With an intraoperative finding of a gastric or duodenal peptic ulcer perforation which warrants only a simple omental patch repair, the enrollment to the study was confirmed. Edge biopsy was taken in suspicious cases and those with a pathological diagnosis of malignancy were later excluded from the study. After aspiration of the free gastrointestinal content in the abdomen and saline irrigation, the perforation was closed with an omental patch. Relevant intraoperative findings were recorded. The nasogastric tubes were withdrawn after 3–4 days. On postoperative day 4 or 5, the patients were started on oral fluids. Postoperative antibiotic treatment was maintained for 7–10 days and proton pump inhibitors were continued for 1 month. Postoperative intensive care was provided when indicated based on the institutional protocols.

Data on relevant preoperative, intraoperative, and postoperative variables were compiled using semi-structured questionnaire-based interview, clinical examination, investigation reports, intraoperative findings, and postoperative follow-up. Age, gender, onset of symptoms, comorbid diseases, physical examination findings, investigation reports, time elapsed from the onset of symptoms to surgery, and site and size of perforation were taken as the study variables. Postoperative mortality, individual postoperative complications, and total duration of hospital stay were taken as outcome variables. Postoperative mortality was defined as death of the patient in hospital during the same admission period. Postoperative complications, such as wound infection, chest infection, renal failure, cardiac failure, septic shock, or need for mechanical ventilation during the same admission period, were analyzed.

Statistical Package for Social Sciences 16.0 (SPSS Inc., Chicago, IL, USA) software for Windows was used for statistical analysis. Age and gender distribution, prevalence of comorbid diseases, pattern of presenting symptoms, and nature of perforation and postoperative complications were analyzed. Analysis was performed on the preoperative and intraoperative variables, and their relationship with the mortality, each postoperative complication, and duration of hospital stay was evaluated. The relative risk with 95% confidence intervals (CI) for each independent variable was calculated. The level of significance (p value) and confidence interval was evaluated using Pearson's Chi-squared test. A p value less than 0.05 was considered statistically significant.

Results

The demographic and clinical characteristics of enrolled patients are depicted in Table 1. A total of 101 consecutive cases were analyzed. The mean age of presentation was 48 (15–80) years with a standard deviation of 16. Of these, 92 were males (91.1%) and 9 were females (8.9%). All the patients had abdominal pain on presentation, of which 34 (33.7%) presented between 24 and 36 h of onset of pain. 34 (33.7%) cases had fever and 49 (48.5%) cases had vomiting on presentation. Diabetes Mellitus (20.8%), Systemic Hypertension (13.9%), Chronic Obstructive Pulmonary Disease (6.9%), and Coronary Artery Disease (5%) were the major comorbidities of our study population. Of the 101 patients, 6 (5.9%) had an ASA score of 1, 53

Table 1 Demographic and clinical features

	Number of patients (%)
Age distribution, years	
<30	17 (16.8)
30–44	23 (22.8)
45–59	31 (30.7)
>50 y	30 (29.7)
Gender	
Males	92 (91.1)
Females	9 (8.9)
Duration of abdominal pain on presentation, h	
<12	8 (7.9)
12–24	27 (26.7)
24–36	34 (33.7)
>36	32 (31.7)
Comorbid diseases	
Diabetes mellitus	21 (20.8)
Systemic hypertension	14 (13.9)
Chronic obstructive pulmonary disease	7 (6.9)
Coronary artery disease	5 (5.0)
Addictions	
Smoking	54 (53.5)
Alcoholism	42 (41.6)
ASA score	
1	6 (5.9)
2	53 (52.5)
3	37 (36.6)
4	5 (5.0)
Onset of abdominal pain to surgery interval, h	
<12	4 (4.0)
12–24	27 (26.7)
24–36	38 (37.6)
>36	32 (31.7)
Size of perforation, cm^2	
≤1	73 (72.3)
>1	28 (27.7)
Site of perforation	
Antrum	89 (88.1)
Duodenum	12 (11.9)
Postoperative complications	
Wound infection	14 (13.9)
Chest Infection	38 (37.6)
Cardiac failure	8 (7.9)
Renal failure	17 (16.8)
Needed mechanical ventilation	26 (25.7)
Reopening	1 (1.0)

(52.5%) an ASA score of 2, 37 (36.6) an ASA score of 3, and 5 (5.0%) an ASA score of 4. Majority (33.7%) of the patients presented within 24–36 h of onset of symptoms. On laparotomy, the site of perforation was located mostly in the antrum (88.1%) and 72.3% cases had a perforation of size less than 1 cm^2.

Among 101 patients operated on for peptic ulcer perforation, 66 (65.3%) experienced complications and 11 (10.8%) died. Nearly, one out of four patients (25.7%) required mechanical ventilation during the initial postoperative period, but majority were stabilized and weaned off early. Wound infection including minor skin infection to wound dehiscence was found in 14 (13.9%) cases. Postoperative renal dysfunction was present in 17% and cardiac dysfunction in 7.9%. One patient required reopening due to re-perforation. Mean duration of postoperative hospital stay was 11.6 days (standard deviation of 7.3). The maximum duration of hospital stay was 46 days.

Analysis was performed to identify risk factors of postoperative mortality, postoperative morbidities, and longer duration of hospital stay. Relative risk for each variable was calculated, and the level of significance (p value) and confidence interval was evaluated using Pearson's Chi-squared test. An age above 65 years ($p<0.001$), female gender ($p=0.033$), perforation to surgery interval more than 36 h (<0.001), and size of perforation more than 1 cm^2 ($p=0.035$) were associated significantly with postoperative mortality (Table 2).

Need for postoperative ventilator support, renal failure, chest infection, and a duration of postoperative hospital stay more than 2 weeks were taken as outcome variables suggestive of postoperative morbidity. On univariate analysis, female gender ($p=0.003$), age more than 65 years ($p=0.002$), comorbidities—Chronic obstructive pulmonary disease ($p=0.004$), preoperative blood urea level >30 mg/dl ($p<0.001$), preoperative serum creatinine level >1.5 mg/dl ($p=0.001$), perforation to surgery interval more than 36 h ($p=0.005$), and size of perforation more than 1 cm^2 ($p=0.015$) were significantly associated with the need for postoperative ventilator support (Table 3).

Postoperative chest infection was found to have significant association with age more than 50 years ($p<0.001$) and size of perforation more than 1 cm^2 ($p=0.012$) (Table 4).

Female gender ($p=0.029$), age more than 50 years (<0.001), comorbidities—diabetes mellitus ($p=0.001$), preoperative serum creatinine level more than 1.5 mg/dl ($p<0.001$), perforation to surgery interval more than 36 h ($p=0.016$), and size of perforation more than 1 cm^2 ($p=0.004$) had significant association with postoperative renal failure (Table 5).

The duration of hospital stay was taken a marker of postoperative morbidity. An age more than 50 years ($p=0.003$), preoperative blood urea level more than 30 mg/dl ($p=0.004$), preoperative serum creatinine level of more than 1.5 mg/dl ($p=0.016$), and size of perforation more

Table 2 Analysis of correlation between study variables and mortality

Variables	All patients ($n=101$)	Mortality		RR	95% CI	p value
		Yes ($n=11$) (10.8%)	No ($n=90$) (89.1%)			
Gender						
Female	9	6 (66.7%)	3 (33.3%)	12.267	4.652–32.344	<0.001
Male	92	5 (5.4%)	87 (94.6%)			
Perforation to surgery interval, h						
>36	32	9 (28.1%)	23 (71.9%)	9.703	2.223–42.359	<0.001
≤36	69	2 (2.9%)	67 (97.1%)			
Size of perforation, cm^2						
>1	28	6 (21.4%)	22 (78.6%)	3.129	1.037–9.436	0.035
≤1	73	5 (6.8%)	68 (93.2%)			
Age, years						
>65	21	5 (23.8%)	16 (76.2%)	3.175	1.073–9.379	0.033
≤65	80	6 (7.5%)	74 (92.5%)			

Table 3 Analysis of correlation between study variables and need for postoperative ventilator support

Variables	All patients ($n=101$)	Need for postoperative ventilator support		RR	95% CI	p value
		Yes ($n=26$) (25.7%)	No ($n=75$) (74.2%)			
Gender						
Female	9	6 (66.7%)	3 (33.3%)	3.067	1.678–5.605	0.003
Male	92	20 (21.7%)	72 (78.3%)			
Age, years						
>65	21	11 (52.4%)	10 (47.6%)	2.794	1.515–5.151	0.002
≤65	80	15 (18.8%)	65 (81.2%)			
Comorbidity—COPD						
Yes	7	5 (71.4%)	2 (28.6%)	3.197	1.752–5.834	0.004
No	94	21 (22.3%)	73 (77.7%)			
Preoperative blood urea level, mg/dl						
>30	55	24 (43.6%)	31 (56.4%)	10.036	2.504–40.228	<0.001
≤30	46	2 (4.3%)	44 (95.7%)			
Preoperative serum creatinine level, mg/d						
>1.5 l	26	13 (50.0%)	13 (50.0%)	2.885	1.542–5.395	0.001
≤1.5	75	13 (17.3%)	62 (82.7%)			
Perforation—surgery interval, h						
>36	32	14 (43.8%)	18 (56.2%)	2.516	1.317–4.805	0.005
≤36	69	12 (17.4%)	57 (82.6%)			
Size of perforation, cm^2						
>1	28	12 (42.9%)	16 (57.1%)	2.235	1.183–4.222	0.015
≤1	73	14 (19.2%)	59 (80.8%)			

Table 4 Analysis of correlation between study variables and postoperative chest infection

Variables	All patients ($n=101$)	Postoperative chest infection		RR	95% CI	p value
		Yes ($n=38$) (37.6%)	No ($n=63$) (62.4%)			
Age, years						
>50	48	27 (56.2%)	21 (43.8%)	2.710	1.514–4.851	<0.001
≤50	53	11 (20.8%)	42 (79.2%)			
Size of perforation, cm^2						
>1	28	16 (57.1%)	12 (42.9%)	1.896	1.180–3.047	0.012
≤1	73	22 (30.1%)	51 (69.9%)			

Table 5 Analysis of correlation between study variables and postoperative renal failure

Variables	All patients ($n=101$)	Postoperative renal failure		RR	95% CI	p value
		Yes ($n=18$) (17.8%)	No ($n=83$) (82.1%)			
Gender						
Female	9	4 (44.4%)	5 (55.6%)	2.921	1.217–7.009	0.029
Male	92	14 (15.2%)	78 (84.8%)			
Age, years						
>50	48	16 (33.3%)	32 (66.7%)	8.833	2.141–36.441	<0.001
≤50	53	2 (3.8%)	51 (96.2%)			
Comorbidity—diabetes mellitus						
Yes	21	9 (42.9%)	12 (57.1%)	3.810	1.730–8.387	0.001
No	80	9 (11.2%)	71 (88.8%)			
Preoperative serum creatinine level, mg/dl						
>1.5	26	12 (46.2%)	14 (53.8%)	5.769	2.411–13.806	<0.001
≤1.5	75	6 (8.0%)	69 (92.0%)			
Size of perforation, cm^2						
>1	28	10 (35.7%)	18 (64.3%)	3.259	1.433–7.409	0.004
≤1	73	8 (11.0%)	65 (89.0%)			
Perforation—surgery interval, h						
>36	32	10 (31.2%)	22 (68.8%)	2.695	1.175–6.180	0.016
≤36	69	8 (11.6%)	61 (88.4%)			

than 1 cm^2 ($p=0.030$) were found to have significant association with a postoperative hospital stay more than 2 weeks (Table 6).

Discussion

The prevalence of peptic ulcer disease is estimated to be 1500–3000 per 100,000 people [5]. The lifetime possibility for a person to develop peptic ulcer disease is approximately 5% [6]. The use of proton pump inhibitors for the treatment of peptic ulcer disease has resulted in a decrease in elective ulcer surgery [1]. However, in spite of these developments, the rate of perforation remains as high as 7% per year in peptic ulcer disease [7]. Peptic ulcer perforation is frequently seen in the fourth and fifth decades, while the mean age of our patients was 48 in a way similar to the literature [8]. The male-to-female ratio in our study was 10.2:1.0. Arveen et al. [9] report that in their series, the male-to-female ratio was 10.3:1.0. Especially in Eastern countries, other studies also report a similar ratio [10].

All the cases had abdominal pain, 34 (33.7%) cases had fever, and 49 (48.5%) cases had vomiting on presentation. In a similar study, Taş et al. [11] reported abdominal pain

Table 6 Analysis of correlation between study variables and postoperative hospital stay

Variables	All patients ($n=101$)	Postoperative hospital stay		RR	95% CI	p value
		>2 weeks ($n=16$) (15.8%)	≤2 weeks ($n=85$) (84.2%)			
Age, years						
>50	48	13 (27.1%)	35 (72.9%)	4.785	1.451–15.777	0.003
≤50	53	3 (5.7%)	50 (94.3%)			
Preoperative blood urea level, mg/dl						
>30	55	14 (25.5%)	41 (74.5%)	5.855	1.403–24.438	0.004
≤30 mg/dl	46	2 (4.3%)	44 (95.7%)			
Preoperative serum creatinine level, mg/dl						
>1.5	26	8 (30.8%)	18 (69.2%)	2.885	1.205–6.903	0.016
≤1.5	75	8 (10.7%)	67 (89.3%)			
Size of perforation, cm^2						
>1	28	8 (28.6%)	20 (71.4%)	2.607	1.084–6.272	0.030
≤1	73	8 (11.0%)	65 (89.0%)			

as presentation in 100% and nausea-vomiting in 32.4%. Surapaneni et al. [12] in a case series of 150 patients reported that 65 patients (43.3%) presented within 24 h of the onset of severe abdominal pain (Group A), 27 patients (18%) presented between 24 and 48 h (Group B), and 58 patients (38.6%) presented after 48 h (Group C). In our study, out of the 101 patients, 4% presented within 12 h, 26.7% within 12–24 h, 37.6% within 24–36 h, and 31.7% after 36 h. Majority of patients (37.6%) were operated between 24 and 36 h of onset of abdominal pain. The most common comorbid disease was Diabetes Mellitus followed by Systemic Hypertension which is similar to the comorbidity profile reported by other Asian studies [13].

On laparotomy, the site of perforation was located mostly in the antrum (88.1%) and 72.3% cases had a perforation of size less than 1 cm^2. Study by Taş et al. [11] reported the site of perforation as Pre-pyloric in 68.2% and Duodenum in 31.8%. Anbalakan et al. [13] reported a size of peptic ulcer range from 1 to 50 mm with a mean of 9.5 mm and median of 5 mm.

The postoperative mortality rate in peptic ulcer perforation ranges between 4 and 30% [3, 8]. The mortality rate in our study was 10.8%. An age above 65 years, female gender, perforation to surgery interval more than 36 h, and size of perforation more than 1 cm^2 were associated significantly with mortality in our study. Koçer et al. [8] stated that mortality was 1.4% below the age of 65, while it was 37.3% above 65 years of age. Testini et al. [14] also revealed that patients over 65 years have a significantly higher mortality rate after surgery for perforated peptic ulcer than younger patients because of the more frequent presence of comorbid diseases. Boey et al. [15] stated that a delay of surgery after onset of symptoms for more than 48 h, shock upon admission, and a high degree of comorbidity were associated with a 100% mortality when all factors where present. Eventually, the delay of surgery was adjusted to 24 h, and the scoring system was validated in a cohort study [16]. Apart from factors described in previous studies and literature, the size of perforation more than 1 cm^2 and female gender were also found to be significantly related to mortality in our study on univariate analysis. Kim et al. [17] in a study reported female gender as a significant factor associated with morbidity. A perforation diameter more than 0.5 cm was found to be associated with mortality by Taş et al. [11].

The postoperative morbidity ranges from 20 to 50% [3, 8]. Our study group had a postoperative morbidity of 65.3% which was higher than in the literature. Parallel with the literature, our patients were identified to have morbidity spectrum of wound site infections, renal, cardiac, and pulmonary complications. The postoperative requirement of mechanical ventilation was taken as an indicator of morbidity, but same was not studied previously. 25.7% required mechanical ventilation during the initial postoperative period. Wound infection including minor skin infection to wound dehiscence was found in 13.9% cases. Mean duration of postoperative hospital stay was 11.6 days with a standard deviation of 7.3. The maximum duration of hospital stay was 46 days. In a similar study from South Asia by Arveen et al. [9], the mean hospital stay was 10.9 ± 6.8 days. Taş, et al. [11] reported a mean hospital stay of 8.7 ± 4.6 days with a maximum duration of 44 days which was similar to our study. The duration of hospital stay more than 2 weeks was taken as an indicator of morbidity.

Unlike previous studies, where the comorbidity or postoperative complication was analyzed as a single outcome factor, we independently tested each comorbidity for its association with preoperative and intraoperative risk factors. Each postoperative complication had a different spectrum of risk factors but with significant overlap with the other (Tables 3, 4, 5, 6). Taş et al. [11] reported that patients above the age of 60, with a time to presentation longer than 24 h, presence of shock at the time of presentation, concomitant diseases, and a perforation diameter wider than 0.5 cm were at a high risk for postoperative morbidity. Kim et al. [17] stated that age above 60 and female gender constituted the risk factors that influenced postoperative morbidity. As reported in the literature, comorbidities, such as Chronic Obstructive Pulmonary Disease and Diabetes Mellitus, were found to be important risk factors for morbidity in our study [18, 19]. Hirsch and McGill [20] and Stagnaro-Green [21] observed that patients with diabetes mellitus who underwent surgery had an increased risk of postoperative morbidity.

Factors, such as older age, female gender, perforation to surgery interval more than 36 h, and size of perforation more than 1 cm^2 affected both mortality and morbidity. Postoperative morbidity was also associated with comorbid diseases. Abnormal renal function on presentation was identified as an additional risk factor for postoperative morbidity and longer hospital stay. These findings could be used as a guide by surgeons to monitor patients with peptic ulcer perforation for a better outcome after surgical intervention.

Conclusion

Peptic ulcer perforation remains a serious surgical problem with significant mortality and morbidity in spite of the better understanding of disease, effective resuscitation, and prompt surgery under modern anesthesia techniques. Female gender, older age group, perforation surgery interval more than 36 h, and size of perforation more than 1 cm^2 were found to be significant factors influencing

postoperative mortality and morbidity. Postoperative morbidity was also associated with comorbid diseases. Abnormal renal function on presentation was identified as an additional risk factor for postoperative morbidity and longer hospital stay. An understanding of these factors and identification of patients under risk can help in reducing the postoperative morbidity and mortality rates.

Compliance with ethical standards

Conflict of interest Sivaram P and Sreekumar A declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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References

1. Mäkelä J, Laitinen S, Kairaluoma MI. Complications of peptic ulcer disease before and after the introduction of H2 receptor antagonists. Hepatogastroenterology. 1992;39:144–8.
2. Crofts TJ, Park KG, Steele RJ, et al. A randomized trial of non-operative treatment for perforated peptic ulcer. New Eng J Med. 1989;320:970–3.
3. Lau JY, Sung J, Hill C, et al. Systematic review of the epidemiology of complicated peptic ulcer disease: incidence, recurrence, risk factors and mortality. Digestion. 2011;84(2):102–13.
4. Moller MH, Adamsen S, Thomsen RW, et al. Multicentre trial of a perioperative protocol to reduce mortality in patients with peptic ulcer perforation. Br J Surg. 2011;98(6):802–10.
5. Zittel TT, Jehle EC, Becker HD. Surgical management of peptic ulcer disease today indication, technique and outcome. Langenbecks Arch Surg. 2000;385:84–96.
6. Vaira D, Menegatti M, Miglioli M. What is the role of Helicobacter pylori in complicated ulcer disease? Gastroenterology. 1997;113:78–84.
7. Casali JJ, Franzon O, Kruel NF, et al. Epidemiological analysis and use of rapid urease test in patients with perforated peptic ulcers. Rev Col Bras Cir. 2012;39:93–8.
8. Koçer B, Sürmeli S, Solak C, et al. Factors affecting mortality and morbidity in patients with peptic ulcer perforation. J Gastroenterol Hepatol. 2007;22:565–70.
9. Arveen S, Jagdish S, Kadambari D. Perforated peptic ulcer in South India: an institutional perspective. World J Surg. 2009;33(8):1600–4.
10. Gupta S, Kaushik R, Sharma R, et al. The management of large perforations of duodenal ulcers. BMC Surg. 2005;5:15.
11. Taş, Ülger BV, Önder A, et al. Risk factors influencing morbidity and mortality in perforated peptic ulcer disease. Ulus Cerrahi Derg 2014;31(1):20–5.
12. Surapaneni S, Rajkumar S, Vijaya bhaskar Reddy A. Perforation-operation time interval; an important mortality indicator in peptic ulcer perforation. J Clin Diagn Res. 2013;7(5):880–2.
13. Anbalakan K, Chua D, Pandya GJ, Shelat VG. Five year experience in management of perforated peptic ulcer and validation of common mortality risk prediction models—are existing models sufficient? A retrospective cohort study. Int J Surg. 2015;14:38–44.
14. Testini M, Portincasa P, Piccinni G, et al. Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer. World J Gastroenterol. 2003;9:2338–40.
15. Boey J, Wong J, Ong GB. A prospective study of operative risk factors in perforated duodenal ulcers. Ann Surg. 1982;195(3):265–9.
16. Boey J, Choi SK, Poon A, et al. Risk stratification in perforated duodenal ulcers. A prospective validation of predictive factors. Ann Surg. 1987;205(1):22–6.
17. Kim JM, Jeong SH, Lee YJ, et al. Analysis of risk factors for postoperative morbidity in perforated peptic ulcer. J Gastric Cancer. 2012;12:26–35.
18. Noguiera C, Silva AS, Santos JN, et al. Perforated peptic ulcer: main factors of morbidity and mortality. World J Surg. 2003;27(7):782–7.
19. Montalvo-Jav´e EE, Corres-Sillas O, Athi´e-Guti´errez C. Factors associated with postoperative complications and mortality in perforated peptic ulcer. Cir Cir. 2011;79(2):141–8.
20. Hirsch IB, McGill JB. Role of insulin in management of surgical patients with diabetes mellitus. Diabetes Care. 1990;13:980–91.
21. Stagnaro-Green A. Perioperative glucose control: does it really matter? Mt Sinai J Med. 1991;58:299–304.