SURGICAL RISK PROFILE OF PERFORATED PEPTIC ULCER IN SOUTH YEMEN

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Abstract

There is increasing evidence that preoperative risk factors are associated with increased patient morbidity and mortality after surgery for perforated peptic ulcer. On the basis of currently available evidence, the effect of these factors on outcomes in Yemeni patients with perforated peptic ulcer remains largely undefined. We performed this prospective study to estimate the impact of preoperative prognostic factors on surgical outcomes in terms of mortality and morbidity in these patients. Between July 2014 and June 2019, 50 consecutive patients were operated for perforated peptic ulcer in two hospitals. The prognostic impact was evaluated by univariate and multivariate analyses. With regard to the surgical outcomes, the overall morbidity rate was 30%. Univariate and multivariate analyses successfully demonstrated that in presence of preoperative shock, gastric ulcers, comorbidities, and surgical delay < 48 hours as risk factors for morbidity. Univariate and multivariate analyses failed to identify the previous ulcer history, current smoker, age, gender, ulcer size, amount of fluid and non-steroidal anti-inflammatory drugs use as risk factors for morbidity. The overall mortality rate was 10%. Univariate and multivariate analyses successfully demonstrated that in presence of complications, gastric ulcers, shock, age ≥ 40 years, comorbidities, and surgical delay > 48 hours as significant prognostic factors for deaths. Univariate and multivariate analyses failed to identify the current smoker, non-steroidal anti-inflammatory drugs, gender, previous ulcer history, amount of fluid and ulcer size as significant prognostic factors for deaths. The preoperative risk factors are determinants of surgical outcomes after perforated peptic ulcer surgery. The preoperative

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knowledge of "at risk" patients could greatly influence which steps are taken to reduce the morbidity and mortality. Our work needs validation by other large groups.

Keywords: Perforated peptic ulcer, Preoperative risk factors, Surgical outcomes

Introduction

The incidence of peptic ulcer disease (PUD) has been estimated at around 1.5% to 3 % (Chung and Shelat, 2017). Globally, its incidence has fallen in recent years (Chalya *et al*., 2o11; Ugochukwu *et al*., 2013; Almeida *et al*., 2016). Perforated peptic ulcer (PPU) is life threatening complication of PUD (Shah and Panchal, 2016). It is estimated that 2% to 10% of patients with PUD (Bertleff and Lange, 2010; Chalya *et al*., 2o11; Almeida *et al*., 2016; Gulzar *et al*., 2016; Chung and Shelat, 2017). It is associated with short-term mortality in up to 30% of patients and morbidity in up to 50 % (Søreide *et al*., 2015; Chung and Shelat, 2017).

Risk factor is considered a significant if patients present with it preoperatively in patients with PPU. Any surgeon will testify that preoperative risk factors are more important in determining postoperative morbidity and mortality. The fact little is known about the role of preoperative risk factors and it's the actual effect in Yemeni patients presenting with PPU undergoing surgery. Clearly, studies are needed to identify these patients at high risk for a poor surgical outcome and to foster progress in research. The present study therefore aimed to estimate the impact of preoperative prognostic factors on surgical outcomes in these patients. This would help us adapt the postoperative strategy.

Methods

This study was designed as a prospective aimed for to looking at any association between preoperative risk factors and outcomes in terms of mortality and morbidity after surgery for PPU. All patients underwent emergency exploratory laparotomy at Al-Gamhouria

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Modern General Hospital and Basuheeb Military General Hospital in South Yemen from July 2014 to June 2019. All patients or their representatives gave informed consent.

PPU was diagnosed by history, physical examination, plain abdominal and chest radiographs. All patients received intravenous fluids, antibiotics, anti-ulcer drugs and placed nasogastric tube. In brief, surgical access was achieved via midline incision. Identified perforated ulcer location then repaired by simple closure with reinforced pedicled omental patch (Graham's omentopexy).

The data were estimated for preoperative risk was based on the age, gender, duration of perforation , shock, previous history of PUD, smoking , non-steroidal anti-inflammatory drugs (NSAIDs) use, and comorbidities. Intraoperative variables related to disease risk factors were ulcer location, ulcer size, and amount of intraperitoneal fluid. Risk factors were defined as a factor that is believed to increase the probability of postoperative outcomes. Preoperative shock was defined as a permanent deterioration in systolic blood pressure below 90 mmHg. Duration of perforation (surgical delay) was defined as time interval from onset of symptoms till surgery. Mortality was defined according to current guidelines as death in hospital prior to discharge or within 30 days of surgery (regardless of location). Complications were defined as any life-threatening conditions (morbidities) occurring before discharge or within 30 days of surgery (regardless of location).

Study outcomes end points: Primary endpoint was postoperative mortality rate within 30 days. Secondary endpoints were postoperative complications rates within 30 days.

Statistical analysis

Continuous variables are presented as mean ± standard deviation or medians. Categorical variable are described as numbers and percentages.

Analysis of the preoperative and disease risk factors for postoperative mortality and complications were performed using univariate and multivariable analyses. The x^2 test or

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Fisher's exact test were used in Univariate analyses. Logistic regression was used in multivariate analyses. Confidence interval (95% CI) was used to estimate the strength of association between these factors and postoperative outcomes. Statistical analyses were performed using SPSS version 17.0 (SPSS, Inc, Chicago, IL, USA) and values of $p \leq 0.05$ were considered significant.

Factors	Complicated N (%)	OR	95% CI	P-value

Results

Fifty patients underwent emergency laparotomy for PPU. Our population was of 29 (58%) males and 21 (42%) females (M/F ratio of 1.4:1). The average age was 40.5 ± 8.5 (range, 11 – 70) years with median of 36 years. Most of patients, 31 (62%) were younger than 40 years of age. Overall postoperative complications were 15 (30%) for all cases (Table 1). Among the 15 patients, wound infections occurred in 7 (46.7%).

Table 1: Postoperative complications

Complications	N (%)
Wound infections	7 (46.7)
Post-operative pyrexia	5 (33.3)
Pulmonary infection	4 (26.7)
Intra-abdominal abscess	3 (20)
Wound dehiscence	3 (20)
Septic shock	2 (13.3)
Enterocutaneous fistula	2 (13.3)
Cardiopulmonary arrest	1 (6.7)
Acute renal failure	1 (6.7)
Paralytic ileus	1 (6.7)

In univariate analysis (Table 2), the risk of postoperative complications were significantly higher in cases with preoperative shock [Odds ratio (OR): 2.37, 95% CI: 1.84 to 3.05, $P = $ **0.001**], and in gastric ulcer cases [OR: 1.63, 95% CI: 1.14 to 2.31, $P = $ **0.01**]. Otherwise, postoperative complications significantly increased in comorbidities patients [OR: 3.54, 95% CI: 1.33 to 5.87, $P = $ **0.012**], and in delay in surgical intervention less than 48 hours patients [OR: 1.06, 95% CI: 1.01 to 5.45, $P = $ **0.021**].

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Total (n = 50)	15 (30%)			
Preoperative factors				
Age (year)				
≥40 (n =19)	6 (31.6)	3.91	0.94 to 5.23	0.167
<40 (n = 31)	9 (29)			
Gender				
Male (n = 29)	8 (27.6)	1.87	0.22 to 4.88	0.334
Female (n = 21)	7 (33.3)			
Duration of perforation (hours)				
<48 (n =12)	9 (75)	1.06	1.01 to 5.45	**0.021**
≥48 (n = 38)	6 (15.8)			
Preoperative shock				
Yes (n = 22)	13 (59.1)	2.37	1.84 to 3.05	**0.001**
No (n = 28)	2 (7.1)			
Previous ulcer				
Yes (n = 15)	5 (33.3)	0.21	0.11 to 1.78	0.051
No (n = 35)	10 (28.6)			
Current smoker				
Yes (n = 32)	10 (31.2)	3.11	0.44 to 5.23	0.145
No (n = 18)	5 (27.8)			
NSAIDs use				
Yes (n = 6)	2 (33.3)	1.98	0.99 to 3.91	0.923
No (n = 44)	13 (29.5)			
Comorbidities				
Yes (n = 4)	3 (75)	3.54	1.33 to 5.87	**0.012**
No (n = 46)	12 (26.1)			
Disease factors				
Ulcer location				
Duodenum (n = 46)	13 (28.3)	1.63	1.14 to 2.31	**0.01**
Gastric (n = 4)	2 (50)			
Ulcer size (cm)				
<5 mm (n = 10)	4 (40)	0.848	0.354 to 2.031	0.711
≥5 mm (n = 40)	11 (27.5)			
Amount of fluid (ml)				
<200 (n = 12)	3 (25)	0.902	0.353 to 2.304	0.829
≥200 (n = 38)	12 (31.6)			

Finally, there was no significant influence in the univariate analysis of previous ulcer history ($P = 0.051$), current smoker ($P = 0.145$), age ($P = 0.167$), gender ($P = 0.334$), ulcer size ($P = 0.711$), amount of fluid ($P = 0.829$), and NSAIDs use ($P = 0.923$).

Table 2: Univariate analysis of predictive factors for postoperative complication

In multivariate analysis (Table 3), showed preoperative shock remained a significant prognostic factor related to postoperative complications [OR: 1.46, (95% Cl: 1.15 to 1.86), $P = $ **0.002**]. Otherwise, delay in surgical intervention less than 48 hours [OR: 0.23, (95% Cl: 0.11 – 0.95), $P = $ **0.003**], gastric ulcer [OR: 1.37, (95% Cl: 1.10 to 1.69), $P = $ **0.004**], and the

presence of comorbidities [OR: 5.28, (95% Cl: 2.39 – 6.82), *P* = **0.007**] significantly increased the risk of postoperative complications. Finally, amount of fluid (*P* = 0.079), NSAIDs use (*P* = 0.123), current smoker (*P* = 0.334), ulcer size (*P* = 0.37), age (*P* = 0.786), previous ulcer history (*P* = 0.786), and gender (*P* = 0.937) did not have a significant influence on postoperative complications.

Table 3: Multivariate analysis of predictive factors for postoperative complication

Factors	OR	95% CI	*P*-value
Preoperative Factors			
Age (year): ≥40 vs <40	1.23	0.93 to 2.34	0.786
Gender: male vs female	3.32	0.45 to 4.66	0.937
Duration of perforation (hour): <48 vs ≥48	0.23	0.11 to 0.95	**0.003**
Preoperative shock: yes vs no	1.46	1.15 to 1.86	**0.002**
Previous ulcer: yes vs no	1.65	0.32 to 2.89	0.786
Current smoker: yes vs no	3.02	0.99 to 4.56	0.334
NSAIDs use: yes vs no	1.02	0.78 to 3.90	0.123
Comorbidities: yes vs no	5.28	2.39 to 6.82	**0.007**
Disease factors			
Ulcer location: duodenum vs gastric	1.37	1.10 to 1.69	**0.004**
Ulcer size (cm) : <5 mm vs ≥5 mm	0.79	0.56 to 1.10	0.37
Amount of fluid (ml): <200 vs ≥200	0.49	0.21 to 1.09	0.079

The overall mortality rate was 5 (10%). On univariate analysis (Table 4), showed postoperative death was significantly high in patients with postoperative complications [OR: 1.98, (95% Cl: 1.54 to 7.93), *P* = **0.005**]. Gastric ulcer was associated with significantly increased mortality [OR: 5.81, (95% Cl: 3.33 to 6.92), *P* = **0.012**], and preoperative shock was associated with significantly increased mortality [OR: 7.9, (95% Cl: 3.98 to 9.88), *P* = **0.022**]. There was a significant correlation between patients aged 40 years or older and postoperative death (*P* = **0.032**). The presence of comorbidities (*P* = **0.039**) and delay in surgical intervention more than 48 hours (*P* = **0.044**) having a univariate association with postoperative deaths. However, univariate analysis for other predictors revealed that preoperative current smoker (*P* = 0.140), NSAIDs use (*P* = 0.39), gender (*P* = 0.896),

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previous ulcer history (P = 0.896), amount of fluid (P = 0.982), and ulcer size (P = 0.987) were not associated with postoperative mortality.

On multivariate analysis (Table 5), identified significant high correlation was seen between patients age equal to or greater than 40 years and postoperative mortality [OR: 4.61, (95% Cl: 2.72 to 7.91), P = **0.002**]. Preoperative shock was identified as prognostic factor for mortality [OR: 3.74, (95% Cl: 2.11 to 7.76), P = **0.005**]. Moreover, a multivariate analysis identified presence of complications (P = **0.011**), comorbidities (P = **0.017**), gastric ulcer (P = **0.018**) and delay in surgical intervention more than 48 hours (P = **0.028**) as significant factors determining postoperative deaths. Finally, a multivariate analysis showed that amount of fluid (P =0.067), previous ulcer history (P = 0.345), current smoker (P = 0.37), NSAIDs use (P = 0.43), ulcer size (P = 0.453), and gender (P = 0.983) were not associated with increased postoperative deaths.

Table 4: Univariate analysis of predictive factors for postoperative mortality

Factors	Death N (%)	OR	95% CI	P-value
Total (n = 50)	5 (10%)			
Preoperative Factors				
Age (year)				
≥40 (n =19)	4 (21.1)	2.33	1.25 to 3.42	**0.032**
<40 (n = 31)	1 (3.2)			
Gender				
Male (n = 29)	3 (10.3)	1.25	0.32 to 3.56	0.896
Female (n = 21)	2 (9.5)			
Duration of perforation (hours)				
<48 (n =12)	1 (8.3)	2.87	2.11 to 7.21	**0.044**
≥48 (n = 38)	4 (10.5)			
Preoperative shock				
Yes (n = 22)	4 (18.2)	7.9	3.98 to 9.88	**0.022**
No (n = 28)	1 (3.6)			
Previous ulcer				
Yes (n = 15)	2 (13.3)	1.75	0.76 to 4.34	0.896
No (n = 35)	3 (8.6)			
Current smoker				
Yes (n = 32)	3 (9.4)	1.98	0.80 to 4.93	0.140
No (n = 18)	2 (11.1)			
NSAIDs use				
Yes (n = 6)	1(16.7)	0.68	0.26to 1.60	0.39
No (n = 44)	4(9.1)			
Comorbidities				
Yes (n = 4)	2 (50)	6.21	1.49 to 7.01	**0.039**
No (n = 46)	3 (6.5)			
Disease factors				
Ulcer location				
Duodenum (n = 46)	3 (6.5)	5.81	3.33 to 6.92	**0.012**
Gastric (n = 4)	2 (50)			
Ulcer size (cm)				
<5 mm (n = 10)	1 (10)	1.98	0.45 to 3.82	0.987
≥5 mm (n = 40)	4 (10)			
Amount of fluid (ml)				
<200 (n = 12)	1 (8.3)	0.67	0.23to 4.65	0.982
≥200 (n = 38)	4 (10.5)			
Complications				
Yes (n = 15)	4 (26.7)	1.98	1.54 to 7.93	**0.005**
No (n = 35)	1 (2.9)			

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Table 5: Multivariate analysis of predictive factors for postoperative mortality

Factors	OR	95% CI	*P*-value
Preoperative Factors			
Age (year): ≥40 vs <40	4.61	2.72 to 7.91	**0.002**
Gender: male vs female	2.93	0.94 to 3.81	0.983
Duration of perforation (hour): <48 vs ≥48	2.91	1.22 to 6.66	**0.028**
Preoperative shock: yes vs no	3.74	2.11 to 7.76	**0.005**
Previous ulcer: yes vs no	3.11	0.98 to 4.88	0.345
Current smoker: yes vs no	1.23	0.78 to 1.95	0.37
NSAIDs use: yes vs no	0.63	0.20 to 2.04	0.43
Comorbidities: yes vs no	3.78	2.98 to 7.90	**0.017**
Disease factors			
Ulcer location: duodenum vs gastric	1.35	1.11 to 3.86	**0.018**
Ulcer size (cm) : <5 mm vs ≥5 mm	3.13	0.99 to 4.89	0.453
Amount of fluid (ml): <200 vs ≥200	1.61	0.89 to 2.73	0.067
Complications: yes vs no	2.86	2.22 to 6.45	**0.011**

Discussion

This is the first prospective study that sought to figure out the relationship between preoperative risk factors and outcomes in Yemeni patients with PPU undergoing surgery. It seems to be evident from the data that the higher preoperative risk profile in these patients translates into a higher mortality and morbidity after surgery. The effect of these factors on surgical outcomes is complex and contradictory results have been reported. Our results highlight the challenges faced by Yemeni surgeons when presented with a patient who has PPU.

In the last decades, focus has shifted from mortality to more interest on morbidity in surgical procedures. If morbidity is reduced, the risk of mortality will expectedly follow. In our study, overall postoperative morbidity rate was 30%. Our result is strikingly very similar to the study by Chalya *et al*., (2011). Our result is lower than result reported in the local study by Bin-Talb *et al*., (2008), and by other studies (Ugochukwu *et al*., 2013; Shah and Panchal, 2016; Gulzar *et al.*, 2016). Our result is higher than result reported in study by Gona *et al*., (2016).

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However, mortality is the main quality marker analysed in surgery for PPU. The postoperative mortality in our patients was 10%. A study by Chalya *et al*., (2011) reported very similar to our result. Our result is higher than result reported by Bin-Talb *et al*., (2008), and lower than result reported by Gona *et al*., (2016), and Gulzar *et al.*, (2016).

Several current studies (Chalya *et al*., 2011; Buck *et al*., 2013; Saverio *et al*., 2014; Anbalakan *et al*., 2015; Gona *et al*., 2016; Gulzar *et al*., 2016) have shown preoperative shock can have a negative impact on outcome. Our study strongly corroborated this negative effect of preoperative shock. It demonstrated a striking association between preoperative shocks with the development of postoperative complications and mortality in both the univariate and multivariate analysis.

In studies (Jordan *et al*., 1974; Zittel *et al*., 2000; Sivri, 2004; Harbison and Dempsey, 2005; Bertleff and Lange, 2010; Leeman *et al*., 2013; Vijian *et al*., 2016; Shah and Panchal, 2016) have shown that gastric ulcers are associated with a two to threefold increased morbidity and mortality risk. This observation was confirmed in our univariate and multivariate analysis. This can be explained by the increased risk of developing hemorrhage and obstruction to be side perforation. Another explanation gastric ulcer being associated with larger ulcer sizes, that means, causes more peritoneal contamination result in death.

According to previous studies (Zittel *et al*., 2000; Makela *et al*., 2002; Harbison and Dempsey, 2005; Bertleff and Lange, 2010; Chalya *et al*., 2011; Anbalakan *et al*., 2015; Shah and Panchal, 2016; Chung and Shelat, 2017) the presence of preoperative comorbidities has been reported as a predictor of mortality and morbidity. Our study clearly demonstrates that presence comorbidities are prognostic factor for morbidity and mortality in univariate and multivariate analysis.

Among the various indices used for the evaluation of the preoperative risk factors, delayed surgical treatment has been identified as the most valuable predictor of adverse

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postoperative outcomes. Our observation is in consonance with previous studies (Bertleff and Lange, 2010; Chalya *et al*., 2011; Buck *et al*., 2013; Moses *et al*., 2015; Shah and Panchal, 2016) confirmed in univariate and multivariate analysis. This effect can be explained by the increased risk of developing severe sepsis. The cornerstones in the treatment of sepsis are administered intravenous broad-spectrum antibiotic therapy within the first hour of diagnosis and sepsis source control, which synonymous with surgery (Bertleff and Lange, 2010; Buck *et al*., 2013).

Although previous reports (Feliciano *et al*., 1984; Bertleff and Lange, 2010; Søreide *et al*., 2014; Moses *et al*., 2015; Chung and Shelat, 2017) have shown that risk of morbidity and mortality is closely related to the age older than 40 year. In contrast to these literatures, we observed that morbidity was no significantly influenced by the age in univariate and multivariate analysis. In paired univariate and multivariate analysis, we observed that a downward trend on the mortality. This can be explained by the occurrence of concomitant medical diseases but also by difficulties in making the right diagnosis resulting in a delay of >24 hour.

In recent time, attention was drawn to the importance of addressing gender. Our study has shown that patient sex has no effect on morbidity and mortality. A same finding was reported in study by Chalya *et al*., (2011). In contrast to our finding, other studies (Noguiera *et al*., 2003; Kocer *et al*., 2007; Anbalakan *et al*., 2015) showed that morbidity and mortality influenced by female sex. Both biological and gender-related differences can influence the outcome of men and women. This effect can be explained by the males and females have different disease profiles, probably more than genetic or hormonal factors.

As previously described by other authors (Jordan *et al*., 1974; Svanes, 2000; Harbison and Dempsey, 2005; Vijian *et al*., 2016; Gona *et al*., 2016; Chung and Shelat, 2017), the larger size of perforation and the amount of peritoneal fluid are associated with higher postoperative

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mortality and morbidity. This effect can be explained by the gastroduodenal contents cause more peritoneal contamination, directly contributing to increased mortality rate.

In study by Ishiguro *et al*., (2014) believed that amount of accumulated intraperitoneal fluid by computed tomography (CT) scan will be useful for predicting the severity of postoperative complications and also helpful for treatment decision-making. On the other hand, recent evidence suggests that young age group with a smaller ulcer sizes has been better outcome in study by Vijian *et al*., (2016). Even though one could reasonably expect adverse outcome in patients with larger size of ulcer and larger the amount of peritoneal fluid, we could not observe any relationship between these two variables and adverse outcome in our univariate and multivariate analysis.

Not surprisingly and like other previous publications (Chalya *et al*., 2011; Ugochukwu *et al*., 2013; Shah and Panchal, 2016; Gona *et al*., 2016), we observed that, NSAIDs use, smoking, and previous history of PUD had a not significant impact on morbidity and mortality on univariate and multivariate. Although, in some studies (Noguiera *et al*., 2003; Kocer *et al*., 2007 Søreide *et al*., 2014) have found correlations between smoking and NSAIDs use and morbidity and mortality.

However, complications and mortality indicators measure only one aspect of the quality of care. Different surgical outcomes may differ; reflecting differences in the rate of surgical risk for PPU from one country to another. In this regard, the findings of our study may be a reflection of local characteristics of surgical care. To provide optimal care and allocate resources, it is important to stratify patients into high and low risk of mortality, ideally before the surgery. Careful evaluation of preoperative risk factors is imperative to guide appropriate surgical management. By this we also hoped that our results could shed light on our surgical practice.

Finally, early diagnosis, prompt resuscitation and urgent surgical intervention are essential to improve outcomes. Our study has the limitation that the sample size was small and thus larger studies are needed to confirm these findings.

Conclusions

PPU represent uncommon but fatal complications in our setting. In the setting of emergency surgical patients with PPU, our results have good outcomes. Based on our results, we consider that preoperative shock, gastric ulcer, presence of comorbidities and surgical delay are significant risk factors related to increase the surgical outcomes in terms of morbidity and mortality. Also the presence of postoperative complications and age ≥ 40 years are significant risk factors related to increased mortality risk. The present study adds further evidence on the detrimental role of preoperative risk factors in the development of complications and mortality after surgery for PPU. We recommend development and validation local standard surgical risk estimators "Calculator" model for predicting postoperative morbidity and mortality in Yemeni patients with PPU.

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