A new prognostic scoring system for perforation peritonitis secondary to duodenal ulcers

Pages with reference to book, From 53 To 59

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Abstract

Objective: To identify prognostic factors for perforated duodenal ulcers and to devise and assess a new scoring system.
Methods: The observational prospective study was conducted at the Mayo Hospital, Lahore in two phases: from March 2010 to September 2011; and from October 2011 to July 2012. It included patients with duodenal ulcer perforation who were observed for identifying factors predicting 30-day prognosis. Each of the predictive factor was given a score based on its severity to devise a new scoring system. Chi-square was used for univariate analysis. Multivariate analysis was done using forward stepwise regression. Accuracy of the new scoring system was calculated using receiver operating curve analysis and its validity was evaluated in the second phase of the study.
Results: Predictors of poor prognosis included multiple gut perforations, size of largest perforation >0.5cm, amount of peritoneal fluid >1000ml, simple closure, development of complications, post-operative systemic septicaemia and winter/autumn season of presentation. Overall 30-day mortality rate was 32.3% (n=32) and morbidity rate was 21.2% (n=21). The mean score was higher in the ones with poor prognosis (p=0.001). Similarly, the mean score was greater in those with grave prognosis (p=0.001). The scoring system had an overall sensitivity of 85.12% and specificity of 80.67% and was favourably comparable to other scoring systems.
Conclusion: The new scoring system is a useful tool in predicting 30-day prognosis for perforated duodenal ulcers in acid peptic disease.
Keywords: Duodenal perforation, Ulcer, Prognosis. (JPMA 64: 50; 2014).

Introduction

Peritonitis due to perforation of the gastrointestinal tract is a common surgical emergency all over the world. The spectrum of etiology of perforation differs in the East from its Western counterpart.[1] Majority of the patients present late, with purulent peritonitis and septicaemia.[2] Surgical treatment of perforation peritonitis is highly demanding. Combination of improved surgical technique, anti-microbial therapy and intensive care support has improved the outcome of such cases.[3]
Peptic ulcer bleeding and perforation are common medical emergencies, with an in-hospital or 30-day mortality of 10% for bleeding ulcers and up to 25-40% for ulcer perforation.[4] Although perforated peptic ulcer frequently is considered a rather benign condition, but it is a life-threatening complication and is associated with an over-all mortality rate that still ranges between 10 and 15 per cent.[5]
Globally, the incidence of peptic ulcer disease has fallen in recent years. However, the number of patients admitted for emergency surgery after peptic ulcer perforation has not undergone a similar decline, and peptic ulcer perforation remains a substantial healthcare problem.[6] Suture closure of perforated duodenal ulcer is a contaminated emergency surgery. So, patients may frequently develop post-operative complications like wound sepsis, pneumonia, paralytic ileus, septicaemia, shock renal failure, electrolyte imbalance, duodenal fistula, intrabdominal abscess and/or burst abdomen.[7]

While several studies have investigated the impact of risk factors on morbidity after abdominal surgery, only a few have analysed their role in perforated peptic ulcer disease.6 Moreover, although intraoperative parameters have been recognised as significant predictors of mortality in duodenal perforation, but there is lack of an accurate scoring system to predict mortality.[8] A major limitation of these scoring systems is their dependence on sophisticated investigations that may not be easily available at every setup in developing countries.[9] We, therefore, felt the need for a cost-effective, simple yet accurate scoring system. The study was designed to recognise pre-operative, intraoperative and post-operative predictors of mortality and morbidity in duodenal perforation and to devise a statistically accurate scoring system.

Patients and Methods

This project was approved by the Ethical Review Board for Research, King Edward Medical University and Mayo Hospital, Lahore. All patients provided informed written consent. All the work was in accordance with the ethical standards of the responsible committee on human experimentation and with the latest (2008) version of Helsinki Declaration of 1975.

This prospective study included 99 consecutive patients with perforated duodenal ulcers who presented to South Surgical Unit, Mayo Hospital, Lahore, between March 2010 and September 2011. The identification of predictors for mortality and morbidity was done on an initial set of 99 patients prospectively. Using these predictors, the scoring system thus devised was validated on the next 50 consecutive patients between October 2011 and July 2012.

Diagnostic criteria included a detailed history suggestive of duodenal ulcer and acid peptic disease, evidence of peritonitis and pneumoperitoneum on erect X-ray abdomen confirmed by radiologist. All the patients regardless of age and gender fulfilling diagnostic criteria, haemodynamically stable and with absence of systemic sepsis on presentation were enrolled. Definitive diagnosis was made on explorative laparotomy by finding duodenal perforation. Other causes of perforation were ruled out by peritoneal biopsy, ascitic fluid examination and culture.[9-11] Only individuals with definitive diagnosis of duodenal perforation were eventually included in the study.

Pregnant and breastfeeding women, non-surgically treated patients, those with other causes of perforation and poorly controlled major medical illnesses (cardiorespiratory disease, renal failure, diabetes mellitus, and hepatic precoma) were excluded from the study.[10]

Pre-operative features possibly related to mortality or morbidity that were examined prospectively included gender, age, length of chronic ulcer symptoms and season of presentation. The intraoperative parameters included number of gut perforations, size of largest perforation, extent of peritoneal contamination and type of primary operation. Post-operative parameters included development of systemic sepsis and complications as separate predictors. All the patients were followed for at least 30 days post-procedure to evaluate their prognostic status defined in terms of morbidity and mortality. Those with higher mortality and morbidity risk were the ones with poor prognosis.

After adequate resuscitation, laparotomy was done through midline incision, perforation site was identified, parameters were recorded, and intervention was done. Biopsy was taken from the margins of ulcerated lesions for histopathology. Peritoneal biopsy and peritoneal fluid were obtained for examination and culture. The abdomen was closed layer by layer transversely with interrupted suture of 1/0 or 2/0 catgut. Meticulous post-operative care and followup were done in all the cases. Individuals getting complications and sepsis were managed accordingly.

Among pre-operative measures noted, season of presentation was categorised as winter/autumn (October-March) or summer/spring (April-September) on the basis of local climatic conditions.[12,13] Intraoperatively, the size of perforation was noted using diameter of lesion in centimetres via standard vernier caliper and categorised as <0.5cm or >0.5cm. The number of perforations was categorized as

being either single when one or multiple when >2. Extent of peritoneal contamination was based on amount of contaminated peritoneal fluid at laparotomy and labelled as < or > 1000ml with the latter identifying greater extent of contamination. The cut-off values specified were based on statistical analysis for each of these risk factors studied and were used to categorise them into the above mentioned groups. The type of primary operation was categorised as either simple closure or definitive surgery i.e., resection and end-to-end anastomosis of gut. The following parameters were used to assess the complications at surgery: pulmonary complications, cardiac complications, renal complications, profuse bleeding and haemodynamic instability. The following parameters were used to assess the complica-tions after surgery: Wound dehiscence, residual abscess, intestinal obstruction, paralytic ileus, wound infection, pulmonary complications, cardiac complications, renal complications, hepatic complications or urological complications, profuse bleeding and haemodynamic instability.[6]
Development of systemic sepsis was identified as a separate risk factor on the basis of standard definitions and categorised as either present or not.[14] It was recorded post-operatively. Period of stay in the hospital was recorded from the day of admission to the day of discharge, completion of 30 days or death. Morbidity was defined on the basis of generalized ill health, poor nutritional and hydration status, poor functional status, dependence on others for simple daily activities, bed-bound, development of deep venous thrombosis (DVT) and number of days away from work. Nutritional and hydration status were defined using standard parameters.[15,16] Mortality was defined as death within 30 days of surgery excluding other non-related causes of death.
During phase 1 of the study, positive predictors of outcome were used to create a predictive model. During phase 2, the model was applied on a set of 50 patients for validation. A non-consecutive non-probability sampling technique was used for patient selection. An observational prospective study design was used for phase 1, while phase 2 was a validation study.
Baseline characteristics were analysed using simple descriptive statistics. Pearson-Chi square test was used for univariate analysis. Multivariate analysis was done using stepwise logistic and linear regression analysis. All data was analysed with a probability value of <0.05 being statistically significant.
Using receiver operator curve (ROC) analysis, a cut-off value for mortality and morbidity was calculated for each risk factor. Using these values, dichotomous tables were constructed for each factor and tested using chi-square test. Subsequent logistic regression analysis identified the significant factors among the ones determined through chi-square that were then used to construct a new scoring system. This was done by assigning each of these factors a score based on their division according to the cutoff value. Using the statistically significant predictors of prognosis, the new scoring system model thus constructed defined prognosis in terms of morbidity and mortality. The terms PEDURS-M and PEDURS-m were used to describe the score on the basis of intraoperative parameters for mortality and morbidity respectively and were used to assess the risk at surgery. The terms PEDURSS-M and PEDURSS-m were used to describe the score both on the basis of intraoperative parameters plus development of post-operative sepsis for mortality and morbidity respectively and used post-operatively. The score so constructed was used to identify the patients as being low risk or high risk for mortality and morbidity by having a score value below or above the cutoff value respectively. The term PEDURS was used as an abbreviation for Perforated (PE) Duodenal (D) Ulcer (U) Risk (R) Stratification (S) score, while PEDURSS for Perforated (PE) Duodenal (D) Ulcer (U) Risk (R) Stratification (S) Sepsis (S) score. The notion 'M' was used to describe mortality whereas 'm' was used to denote morbidity. Combining the prognostic parameters for all, the score as a whole was named as PEDURS(S)-M/m scoring system. This scoring system was prospectively validated in the next 50 consecutive patients. The accuracy of the system was calculated using sensitivity and specificity. The sensitivity and specificity of the new [PEDURS(S)-M/m] scoring system were then compared with those of other scoring systems. ROC curves were constructed and area under the curve (AUC) was

calculated for both phases of the study and subsequently compared. All analyses were performed using SPSS version 16.

Results

Of the 99 patients in the first phase, 98 (99%) were male. Overall mean age was 46.96±17.67 years and the mean period of stay was 6.14±6.74 days. Pre-operatively, 93 (93.9%) individuals had <2months length of chronic ulcer symptoms, while 6 (6%) had > 2 months.

Intraoperatively, multiple gut perforations were seen in 97 (97%) individuals, while single perforation in 2 (2%). A perforation <0.5cm in size was observed in 45 (45.5%) patients whereas >0.5cm in 54 (54.5%). Amount of fluid was seen to be <1000ml in 32 (32.3%) individuals while >1000ml in 67 (67.7%). Besides, 48 (48.5%) individuals presented in winter/autumn, while 51 (51.5%) in summer/spring. Definitive surgery was performed in 9 (9.1%) whereas simple closure was done in 90 (90.9%). Moreover, 32 (32.3%) individuals developed complications. Post-operatively, 17 (17.2%) individuals had systemic septicaemia. The mean period of stay in hospital among non-survivors was 8.43±12.81 days. Among the ones with morbidity, mean period of stay in the hospital was 7.81±10.66 days.

Overall 30-day mortality rate for this population was calculated to be 21 (21.2%). Positive predictors of mortality included male gender (95.2%; n=20; p=0.001), multiple gut perforations (90.5%; n=19; p=0.005), size of largest perforation >0.5 cm (85.7%; n=18; p=0.01), greater extent of peritoneal contamination (81%; n=17; p<0.0005), use of simple closure rather than definitive surgery (76.2% ; n=16; p=0.002), winter/autumn season of presentation (22.9%; n=11; p=0.001), development of complications (100%; n=21; p<0.0005) and systemic septicaemia (71.4%; n=15; p<0.0005). On the other hand, length of chronic ulcer symptoms and age came out to be insignificant in predicting 30-day mortality (p>0.05). Positive predictors were the ones defining poor prognosis.

Overall 30-day rate of morbidity was 32 (32.2%). Positive predictors of morbidity included male gender (96.9%; n=31; p=0.001), multiple gut perforations (93.8%; n=30; p=0.005), size of largest gut perforation >0.5cm (87.7%; n=28; p=0.01), greater extent of peritoneal contamination (75%; n=24; p=0.02), simple closure rather than definitive surgery (78.1%; n=25; p=0.002), winter/autumn as the presenting season (53.1%; n=17; p=0.001), development of complications (100%; n=21; p<0.0005) and systemic septicaemia (53.1%; n=17; p<0.0005). Length of chronic ulcer symptoms and age were non-significant predictors (p>0.05). Positive predictors were the ones defining poor prognosis.

Using statistically significant predictors of mortality and morbidity with cutoff value for each risk factor, the cutoff value for PEDURS-M and PEDURS-m score was calculated to be 5 for both. All the individuals with a score <5 were regarded as low-risk, whereas the ones >5 as high-risk. The high-risk individuals were the ones with poor prognosis. The mean PEDURS-M score among non-survivors was 5.28 and among the survivors was 2.7 with significant difference between the two (p=0.001). Similarly, the mean PEDURS-m score among morbidity group was 4.96 and among the non-morbidity group was 2.49 with significant difference (p=0.001). Using the above mentioned cutoff values, the PEDURS-M system had a sensitivity of 90.5% and specificity of 60.3%. Similarly, the PEDURS-m system had a sensitivity of 87.5% and specificity of 67.2% (Table 1 and 2).

Table-1: Scoring system model for predicting 30-day prognosis.

Parameter	PEDURS-M/ PEDURS-m (intra-operatively)		PEDURS(S)-M/ PEDURS(S)-m (post-operatively)	
Number of gut perforations	Single	Multiple	Single	Multiple
	0	2	0	2
Size of largest perforation	≤0.5 cm	>0.5 cm	≤0.5 cm	>0.5 cm
	0	2	0	2
Amount of peritoneal fluid	≤1000 ml	>1000ml	≤1000 ml	>1000ml
	0	1	0	1
Simple closure vs definitive surgery	Simple closure	Definitive surgery	Simple closure	Definitive surgery
	2	0	2	0
Development of complications	Yes	No	Yes	No
	2	0	2	0
Post-operative systemic septicemia	-	-	Yes	No
	-	-	3	0
Total score	out of 9	out of 12		
Interpretation	Low Risk = ≤5 High Risk =>5	Mortality =low/high Morbidity =low/high	Low Risk = ≤7 High Risk =>7	Mortality =low/high Morbidity =low/high

The new [PEDURS(S)-M/m] scoring system; a score has been allocated to each of the risk factors; the sum of the individual scores defines the total score in the respective category and thus stratify patients as low or high risk within the respective category for predicting mortality and morbidity.

Table-2: Comparison of different scoring systems.

Scoring system (%)	Sensitivity (%)	Specificity
Modified MPI	73	90
Hacettepe	66	73
Boey et al	86	78
Modified APACHE II	73	87
Jabalpur score	87	85
Jabalpur score for co-efficient	86	68
PEDURS(S)-M/m	85.1	80.6%
" PEDURS-M	90.5	60.3
" PEDURSS-M	90.5	94.9
" PEDURS-m	87.5	67.2
" PEDURSS-m	72	100

Comparison of accuracy of different scoring systems used to predict prognosis in abdominal surgeries. Some of them are particular to peptic ulcer perforation, while others are not. PEDURS(S)-M/m scoring system has comparable accuracy with other scoring systems while using simple parametres.

Likewise, the cutoff value for PEDURSS-M & PEDURSS-m was calculated to be 7 for both. All the individuals with a score <7 were regarded as low-risk, whereas the ones >7 as high-risk. The high-risk individuals were the ones with poor prognosis. The mean PEDURSS-M score among non-survivors was 7.57 and among the survivors was 2.06 with significant difference between the two (p=0.001). Similarly, the mean PEDURSS-m score among the morbidity group was 6.68 and among the non-morbidity group was 1.58 with significant difference (p=0.001). Using the above mentioned cutoff values, the PEDURSS-M system had a sensitivity of 90.5% and specificity of 94.9%. On the other hand, PEDURSS-m system had a sensitivity of 72% and specificity of 100%.

The AUC for all the four components of the model and its validation phase ranged from good to excellent test results. The AUC for PEDURS-M model was 0.88 and that for PEDURSS-M, 0.95. The AUC for PEDURS-m model was 0.95, while that for PEDURSS-M was 0.91. In the validation phase, the AUC for PEDURS-M was 0.87 and that for PEDURSS-M was 0.94. The AUC for PEDURS-m for this phase was 0.94, while that for PEDURSS-M was 0.97. Combining all the four components of the system, the PEDURS(S)-M/m scoring system had an overall sensitivity of 85.12% and specificity of 80.67%. The ROC curves for all the components of both phases were compared which showed quite consistent results (Figure).

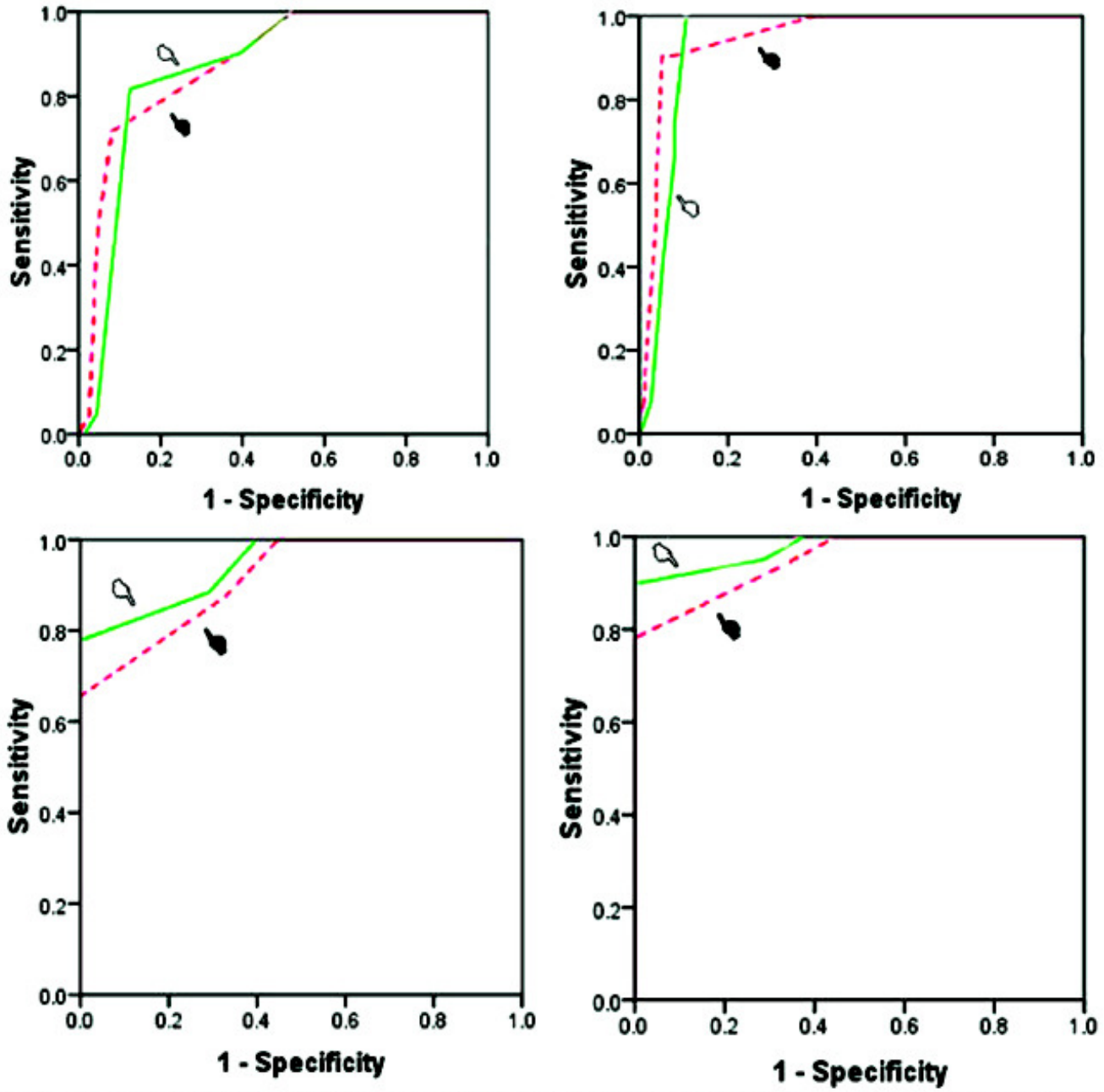

Figure: Roc curves for the PEDURS(S)-M and PEDURS-m scoring model (Black hand pointers) and their comparison with ROC curves drawn for the validation phase (White hand pointers). 1a: PEDURS(S)-M score; 1b: PEDURS(S)-M score; 1c: PEDURS(S)-m score; 1d: PEDURS(S)-m score.

Discussion

The identification of various predictors for prognosis in duodenal perforation can help in risk stratification of individuals and thus signify the need of early prompt therapeutic measures in such individuals.[9] The present study showed an overall 30-day mortality rate of 21.2% (n=21) that is comparable to the findings of Thomsen RW et al.[4] Overall, 32.3% patients had post-operative morbidities that was comparable to that reported by Mattingly SS et al.[17]

In our study, male gender was found to be a positive predictor for both mortality and morbidity (p=0.001 for both). This is in contrast to the results of Kim JM et al who proposed female gender to be

a significant predictor.[6] However, it must be noted that our study was a case series and therefore limited by predominant induction of males unintentionally in the process. Therefore, gender was not taken into account for devising the scoring system. The mean age in the non-survivors was 44.38±15.9 years and that in the individuals with morbidity was 46.96±17.67 years. These were both much lower than the ones identified by Wakayama T et al and Kim JM et al respectively.[6,18] Age was not identified as a prognostically significant predictor in our study ($p>0.05$). Although it has been postulated that mortality is higher in older patients, but Boeys J et al found that age itself has no effect on patient's outcome, but they did find concurrent medical illness to have a significant detrimental effect. This indicates that higher mortality in old age might be due to associated medical illness.[11] That is why we excluded patients with associated medical illnesses from our study. Age, however, was not found to be a positive predictor. Regarding season of presentation, most of the individuals presented during summer/spring (51.5%), but winter/autumn was identified to be associated with worse prognosis ($p=0.001$ for both mortality and morbidity). Past documentation on duodenal ulcer seasonality showed variations in season of presentation.[19,20] Therefore, despite being a significant predictor of prognosis, this parameter was not used in the new scoring system because of seasonal variations among regions. Multiple gut perforations were found to be statistically significant for both mortality and morbidity ($p=0.005$) and therefore included in the scoring system. Size of largest perforation was found to be a significant predictor for both ($p=0.01$) and consistent with findings of Nakano A et al & Chiarugi M et al. [21,22] Greater extent of peritoneal contamination defined by greater amount of contaminated peritoneal fluid was found to be a significant predictor in our series, accounting for 81% ($p<0.0005$) in mortality group and 75% ($p=0.02$) among the morbid ones. This was consistent with the results of Boey J et al.11 Intraoperatively, simple closure was related with greater mortality and morbidity than definitive surgery ($p=0.002$). Although there has been much debate in literature on the type of procedure to be used in this particular set of patients, but our results are supported by Rizoli SB et al.[23] Development of complications and systemic septicaemia were both recognised as significant predictors of both mortality and morbidity ($p<0.0005$ for each) and comparable to the findings of Chiarugi M et al.[22]

The identification and validation of various factors like the ones mentioned above for predicting prognosis in perforated duodenal ulcers have been made previously as evident by the work of Boey J et al.[22] However, the scoring systems used so far for this set of patients in particular have been claimed not to have precise results as noticed by Buck DL et al.[8] In fact, they found that Boey score, the American Society of Anaesthesiologists (ASA) score, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and the sepsis score predict mortality poorly in patients with perforated peptic ulcers. Therefore, we devised a new PEDURS(S)-M/m scoring system and validated it prospectively via ROC analysis. The AUC for all the four components of the model and its validation phase ranged from good to excellent test results. The ROC curves for all the components of both phases were compared which showed quite consistent results. The scoring model had an overall sensitivity of 85.12% and specificity of 80.67%. This is quite comparable to the previous scoring systems and in fact, somewhat better in certain regards statistically (Table-2). Yet it is based on simple and easily recordable parameters with quite an accurate predicting power.

Like most studies, our work also has some limitations. While keeping level of significance at 5%, power of test at 95% and anticipated population proportion for 30-day mortality at 25%, the sample size for the study was 300.[4,25] As the study aimed at development of a new diagnostic tool and is limited to 99 patients due to the restraints like time limitation and difficulties in patient followup, this study is limited with regards to the sample size and further validation of this model needs to be evaluated in future projects.

Conclusion

PEDURS(S)-M/m scoring system has comparable accuracy with other systems and can assist in risk stratification for perforated duodenal ulcers in acid peptic disease. The use of this system can help delineate high-risk patients and thus identify the need of early intervention and prompt treatment for better patient outcomes.

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