ABSTRACT

Introduction
Morbidity after pancreaticoduodenectomy (PD) still remains high. Postoperative pancreatic fistula (POPF) is the most common cause of increased morbidity after PD. Assessment of predictability of risk score for severe postoperative complications was the objective of this study.

Methods
This was a retrospective observational study. Patients undergoing pancreaticoduodenectomy at Tribhuvan University Teaching Hospital (TUTH) between January 2017 to December 2017 were included in the study. Variables were recorded from case sheets of the patients. The “Risk Score” was calculated using the pancreatic duct diameter and body mass index (BMI). Association of risk score and severe postoperative complications were analyzed.

Results
A total number of patients were 43, including 23 (53.5%) males and 20 (46.5%) females. The mean age was 57.09 ± 11.85 years ranges from 29 years to 76 years. The POPF and delayed gastric emptying (DGE) was 23.3% (10/43); and post-pancreaticoduodenectomy hemorrhage (PPH) was 11.6% (5/43). Severe postoperative complications were present in 13.9% (6/43) patients. In univariate analysis, pancreatic duct diameter (p=0.045) and Risk Score (p=0.02) were significantly associated with severe postoperative complications after PD. However none of them were significant in multivariate analysis.

Conclusion
Risk score failed to predict severe postoperative complication after pancreaticoduodenectomy.

Keywords
Pancreaticoduodenectomy, postoperative pancreatic fistula, severe postoperative complications
INTRODUCTION

Pancreatectoduodenectomy (PD) is associated with high morbidity due to the development of a severe postoperative complication. Severe postoperative complications after PD are still not decreased even after establishing different surgical techniques like pancreaticogastrostomy, pancreatic duct stenting, early removal of drain, prophylactic use of octreotide. Most of the studies have been focused on identifying the predictor of postoperative pancreatic fistula (POPF). The risk score was also evaluated to predict POPF after PD. Statistical model was constructed to calculate risk score using pancreatic duct diameter and body mass index (BMI) which were independently correlated with POPF negatively and positively, respectively. Similarly, small pancreatic duct diameter and BMI have also been identified as predictors of severe postoperative complications. POPF is the most significant postoperative complication which results in increased morbidity.

This study was conducted to evaluate the predictive role of a risk score to predict severe postoperative complications after PD.

METHODS

This was a retrospective observational study conducted in the Department of GI and General Surgery, Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal. All patients who had undergone pancreatectoduodenectomy (PD) from January 2017 to December 2017, were included in the study. There were overlap of study period of this study and other study in patients who were undergone pancreatectoduodenectomy. Patients with age <16 years were excluded from the study because those patients were managed in the department of GI and general surgery by Pediatric Surgeons. The primary objective of the study was to evaluate the role of “Risk Score” in predicting severe postoperative complications after PD. The secondary objective of the study was to assess the association of other variables (age, BMI, serum albumin, pancreatic duct size, risk score, pancreatic texture, ASA grade, duration of surgery, intraoperative blood loss, pathological diagnosis) with development of severe postoperative complications. All variables (demography, clinical features, body mass index, ASA grade, main pancreatic duct diameter, serum albumin, serum amylase on 3rd postoperative day, duration of surgery, intra-operative blood loss, POPF, delayed gastric emptying (DGE), post-pancreatectoduodenectomy hemorrhage (PPH), overall post-operative complication according to Clavien Dindo classification, and pathological diagnosis) were recorded from data. Overall postoperative complications were graded according to Clavien Dindo classification, and grade III and above were defined as severe postoperative complications. The risk score was calculated by entering the value of the main pancreatic duct diameter in millimeter (mm) and body mass index (BMI) and risk score value for each patient were recorded. POPF was defined as an output via an operatively placed drain (or a subsequently placed, percutaneous drain) of any measurable volume of drain fluid on or after POD 3, with drain fluid amylase level >3 times the upper normal serum value of the institute. Revised classification and grading of POPF by the International Study Group for Pancreatic Surgery (ISGPS) was used to classify POPF. PPH and DGE were defined according to ISGPS. Perioperative mortality was defined as death within the same hospital admission or 30 days of surgery. Biliary leakage (fistula) was defined as bilirubin concentration in the drain fluid at least three times the serum bilirubin concentration on or after postoperative day three.

The results were expressed in mean±SD for the quantitative (continuous) data and differences between the 2 groups were compared using the Mann–Whitney U-Test. The categorical data was expressed in number (percentage) and differences between the 2 groups were compared using Chi-square test or Fisher’s exact test. The p-value <0.05 was taken as statistically significant. All data were analysed using SPSS (version 25.0).

RESULTS

There were 43 cases studied during the study period. There were 23 (53.5%) males and 20 (46.5%) females. The mean age was 57.09 ± 11.85 years ranges from 29 years to 76 years. There were 8 (18.6%) underweight (BMI <18.5), 9 (20.9%) pre-obese (BMI 25 to 29.9) and 2 (4.7%) obese (≥30) patients in the study. There were 18 (41.9%) patients with hypoalbuminemia (serum albumin <3.5 g/dL).

Severe postoperative complications (Clavien Dindo classification ≥3) were developed in 6 (13.9%) patients including one mortality due to pneumonia. POPF was developed in 10 (23.3%) patients among them, one patient had grade C POPF and the remaining nine patients had grade B POPF (Table 1). The most common indication for PD was ampullary adenocarcinoma which included 18 (41.9%) patients (Figure 1).

Small pancreatic duct diameter, and risk score were associated with the development of severe postoperative complications (p = 0.02) in univariate analysis (Table 2). However neither small pancreatic duct diameter (p=0.87) nor risk score (p=0.17) were significantly associated with development of severe postoperative complication in multivariate analysis (Table 3).
DISCUSSION

Pancreateicoduodenectomy (PD) includes complex surgical steps including multiple organ resection and multiple anastomosis. Therefore it is associated with increased perioperative morbidity.\textsuperscript{12}

There are several scoring systems used to predict postoperative complications e.g. Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM), Estimation of Physiologic Ability and Surgical Stress (E-PASS). POSSUM underestimate low-risk patients and over-estimate high-risk patients for the development of postoperative complications after PD. The predictability of POSSUM to predict postoperative complication is poor.\textsuperscript{13,14} E-PASS was initially studied for risk assessment of patients undergoing general gastrointestinal surgery. E-PASS has poor predictive value for PD.\textsuperscript{15} Studies demonstrated predictability of Surgical Apgar

Table 1. Postoperative complications

| Complications                                      | Frequency (%) |
|---------------------------------------------------|--------------|
| Procedure-related                                 |              |
| POPF                                              | 10 (23.3%)   |
| DGE (Grade A)                                     | 10 (23.3%)   |
| PPH (Mild, intraluminal)                          | 5 (11.6%)    |
| Severe complications (Clavien-Dindo)              | 6 (13.9%)    |
| Others postoperative complications                |              |
| Surgical site infection                           | 8 (18.6%)    |
| Biliary fistula                                   | 4 (9.3%)     |
| Intra-abdominal abscess                           | 1 (2.3%)     |
| Wound dehiscence                                  | 4 (9.3%)     |

Table 2. Association of different variables with severe postoperative complications (n=43)

| Variables                                     | Severe postoperative complications |
|-----------------------------------------------|-----------------------------------|
|                                               | Present                           | Absent                           | p-value  |
| Age                                           | 58.33 ± 11.15                     | 56.89 ± 12.09                     | 0.75     |
| BMI *                                         | 0                                 | 8 (100%)                         | 0.45     |
| < 18.5                                        | 4 (16.7%)                         | 20 (83.3%)                       |          |
| 23 to 24.9                                    | 2 (18.2%)                         | 9 (81.8%)                        |          |
| Serum albumin, g/dl                           | 3.9 (± 0.5)                       | 3.5 (± 0.6)                      | 0.15     |
| Pancreatic duct size (mm)                     | 3.25 (± 2.4)                      | 4.8 (± 2.3)                      | 0.045    |
| Risk score                                    | 13.66 (± 6.4)                     | 7.6 (± 5.7)                      | 0.02     |
| ASA grade                                     | 4 (16.0%)                         | 21 (84.0%)                       | 1.00     |
| 1                                             | 2 (11.1%)                         | 16 (88.9%)                       |          |
| Pancreatic texture                             |                                    |                                  |          |
| Soft                                          | 2 (11.1%)                         | 16 (88.9%)                       | 1.00     |
| Hard                                          | 4 (16%)                           | 21 (84%)                         |          |
| Duration of surgery (min)                     | 412 (± 42)                        | 403 (± 76)                       | 0.83     |
| Intra-op blood loss (ml)                      | 466.7 (± 294.4)                   | 400.0 (± 174)                    | 0.86     |
| Pathological diagnosis ‡                      |                                    |                                  |          |
| Pancreatic origin                              | 3 (18.8%)                         | 13 (81.3%)                       | 0.66     |
| Non-pancreatic origin                         | 3 (11.1%)                         | 24 (88.9%)                       |          |

Fig 1. Indications of pancreaticoduodenectomy by pathological diagnosis

Table 3. Multivariate analysis of variables to predict severe postoperative complication

| Variables              | Odd ratio (95% CI) | p-value |
|------------------------|--------------------|---------|
| Pancreatic duct size   | 0.518-2.189        | 0.87    |
| Risk score             | 0.709-1.063        | 0.17    |
Score (SAS) for morbidity after PD which includes intraoperative variables. However, SAS does not include variables of pancreatic morphology. 16, 17 Chen et al also established a simplified scoring system for predicting postoperative complications after pancreaticoduodenectomy which includes intra/post-operative variables (postoperative 24 hours urine output, arterial pH, serum Na+, and WBC). It also does not includes organ-specific variables. 12 Preoperative prediction of postoperative complications after PD has added advantage of explaining patients and their relatives about the risk associated with PD before surgery. We can take extra measures intraoperatively (e.g. multiple drain placement at pancreaticojejunostomy, feeding jejunostomy) in high-risk patients and the high-risk patient can be monitored carefully to act on time in the presence of abnormal clinical signs and laboratory findings in the early postoperative period.

Severe postoperative complications (Clavien Dindo ≥3) developed in 6 (13.9%) patients including one mortality. Among these, three patients had all three procedure-specific complications (POPF, DGE, and PPH), one had POPF and one mortality. Mortality was due to the development of pneumonia without associated procedure-specific complications. This explains that, both procedure-specific as well as non-procedure specific complications may increase morbidity after PD.

Roberts et al studied “Risk Score” as a predictor of POPF, that included both organ-specific risk factor (pancreatic duct diameter) and general risk factor (BMI) which can be calculated preoperatively. 4 Small pancreatic duct diameter and high BMI are associated with increased risk of development of severe postoperative complications. 5, 6 Moreover, increased severe postoperative complications after PD is because of the development of POPF in most of the cases (61.5%). 18 Therefore we assumed Risk Score can predict severe postoperative complications. Though POPF related severe postoperative complications were developed in 5/6 (83.3%) cases in our study, Risk Score has failed to predict severe postoperative complications.

There are few limitations to the study. First, this risk score can not stratify the type of complications. Second, this is a retrospective single-center study with a small number of cases with severe postoperative complications. Thus, prospective study with larger sample size is needed to evaluate role of risk score in predicting severe post-operative complications.

**CONCLUSION**

In this study “Risk Score” has failed to predict severe postoperative complications after pancreaticoduodenectomy.

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