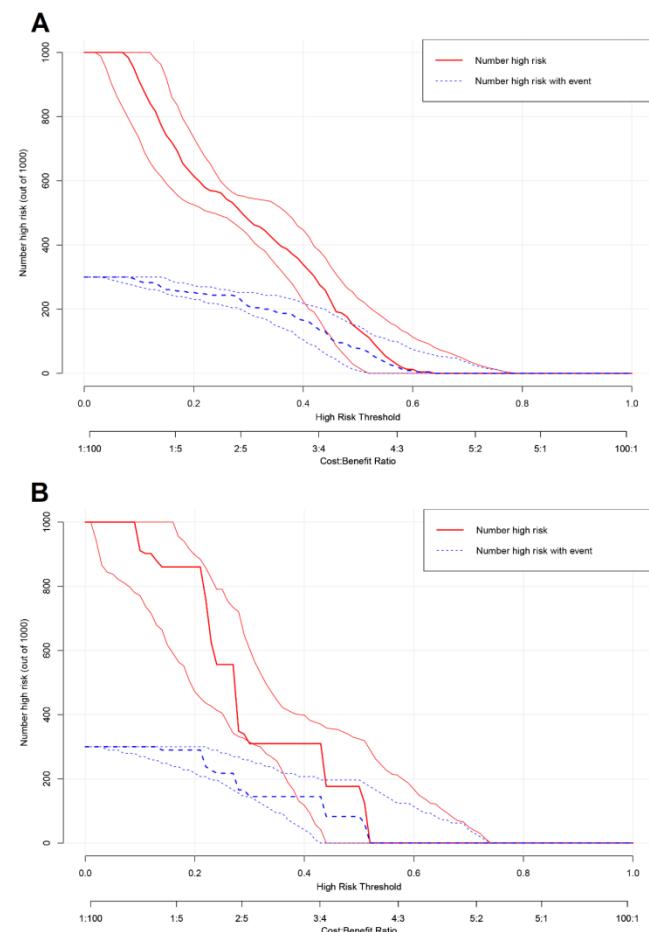


Supplementary Figure 1 Prediction performance of RFC model via CIC. A. Training set.B. Validation set.

Notes. The blue line predicts the probability of poor POPF, and the red line shows the possibility that the patient is at high risk of POPF.



Supplementary Table 1. The candidate variables screening associated with POPF via RFC algorithm.

| Variables                | Mean decrease accuracy | Mean decrease Gini |
|--------------------------|------------------------|--------------------|
| Gender                   | 7.95E-36               | 6.64E-16           |
| Age                      | 1.734295532            | 0.006570824        |
| Smoking                  | -1.000500375           | 6.44E-16           |
| Drinking_history         | 4.00E-20               | 1.18E-15           |
| BMI                      | 7.752857419            | 1.160603853        |
| Diabetes                 | 1.876120666            | 0.197624078        |
| Hypertension             | -1.000500375           | 2.31E-15           |
| Abdominal_operation      | 1.000500375            | 1.44E-15           |
| AGR                      | 1.401790734            | 0.112733826        |
| Blood_transfusion        | -4.46E-37              | 1.47E-15           |
| Anemia                   | 1.59E-36               | 2.11E-15           |
| Lesion_size              | -3.07E-36              | 4.73E-16           |
| WBC                      | 1.000500375            | 0.006128946        |
| ASA                      | -2.82E-37              | 2.86E-15           |
| CRP                      | 16.20252423            | 10.79150889        |
| Pancreatic_duct_diameter | 5.391957774            | 0.248305508        |
| PCT                      | 14.58641932            | 7.795556509        |
| Remnant_texture          | 7.993763406            | 1.008267889        |
| NLR                      | 2.493084773            | 0.031696064        |
| Neutrophil_count         | 4.449507859            | 0.426070013        |
| Lymphocyte_count         | 6.573470217            | 0.768947958        |
| Platelet_count           | 4.678255669            | 0.199639767        |
| Monocyte_count           | 3.262890782            | 0.036517628        |

|            |             |             |
|------------|-------------|-------------|
| Hemoglobin | 1.414839013 | 0.010591206 |
| PLR        | 12.89456443 | 4.433346142 |
| NAR        | 27.4710452  | 25.70052591 |
| LMR        | 3.46372971  | 0.099760135 |
| PNI        | 9.251421528 | 1.740339183 |
| HALP       | 28.62807236 | 27.76215888 |

Abbreviations: POPF. postoperative pancreatic fistula. BMI. body mass index. ASA.American Society of Anesthesiologists. CRP. C-reactive protein. WBC.white blood cell. PCT. Procalcitonin. AGR. albumin-to-globulin ratio. PNI. prognostic nutrition index. NLR. neutrophil-to-lymphocyte ratio. NAR. neutrophil-to-albumin ratio. PLR. platelet-to-lymphocyte ratio. LMR. lymphocyte-to-monocyte ratio. HALP. hemoglobin level \* albumin level \* lymphocyte count / platelet count ratio.

Supplementary Table 1 The predictive performances of different models associated with POPF

| GL model         | Multivariate analysis |         | Discrimination |                |         |     |
|------------------|-----------------------|---------|----------------|----------------|---------|-----|
|                  | OR(95%CI)             | P-value | Brier          | R <sup>2</sup> | C-index | AIC |
| <b>Model1</b>    |                       |         |                |                |         |     |
| Sex              |                       |         |                |                |         |     |
| (Male vs Female) | 1.25(0.68-1.82)       | <0.05   |                |                |         |     |
| Age*,y           | 1.12(0.57-1.67)       | <0.01   |                |                |         |     |
| Remnant texture  |                       |         |                |                |         |     |
| (soft vs hard)   | 1.14(0.59-1.69)       | <0.01   |                |                |         |     |

|                                |                 |       |      |      |       |    |      |
|--------------------------------|-----------------|-------|------|------|-------|----|------|
| Lesion size, cm<br>(> 3 vs ≤3) | 0.78(0.23-1.33) | <0.01 | 0.07 | 0.08 | 0.757 | 50 | 349. |
| PNI                            | 1.25(0.74-1.76) | <0.01 |      |      |       |    |      |
| NAR                            | 1.35(0.82-1.88) | <0.01 |      |      |       |    |      |
| HALP                           | 1.21(0.68-1.74) | <0.05 |      |      |       |    |      |
| NLR                            | 1.59(1.06-2.12) | <0.01 |      |      |       |    |      |

### **Model2**

|                                   |                 |       |      |      |       |    |      |
|-----------------------------------|-----------------|-------|------|------|-------|----|------|
| Sex<br>(Male vs Female)           | 1.32(0.79-1.85) | <0.01 |      |      |       |    |      |
| BMI,kg/m <sup>2</sup>             | 1.07(0.50-1.64) | <0.01 |      |      |       |    |      |
| PCT                               | 1.14(0.57-1.71) | <0.01 |      |      |       |    |      |
| Remnant texture<br>(soft vs hard) | 1.66(1.09-2.23) | <0.01 | 0.06 | 0.08 | 0.786 | 50 | 367. |
| NAR                               | 1.17(0.68-1.66) | <0.05 |      |      |       |    |      |
| PLR                               | 1.46(0.97-1.95) | <0.01 |      |      |       |    |      |
| LMR                               | 1.49(0.98-2.00) | <0.01 |      |      |       |    |      |

### **Model3**

|                                   |                 |       |      |      |       |      |  |
|-----------------------------------|-----------------|-------|------|------|-------|------|--|
| Sex<br>(Male vs Female)           | 1.02(0.51-1.53) | <0.01 |      |      |       |      |  |
| BMI                               | 1.31(0.80-1.82) | <0.05 |      |      |       |      |  |
| Remnant texture<br>(soft vs hard) | 1.57(1.01-2.13) | <0.01 |      |      |       |      |  |
| Pancreatic duct diamet            | 0.95(0.39-1.51) | <0.01 | 0.07 | 0.08 | 0.795 | 371. |  |

|                     |                 |       |
|---------------------|-----------------|-------|
| er,mm<br>(<3 vs ≥3) |                 | 50    |
| PNI                 | 1.18(0.62-1.74) | <0.01 |
| NAR                 | 1.12(0.56-1.68) | <0.01 |
| PLR                 | 1.32(0.76-1.88) | <0.05 |

Notes. \*. Continuous variable. AIC: Akaike information criterion. GL model: generalize linear model. OR: odds ratio. 95%CI: 95% confidence lev el.

Supplementary Table 3 The predictive ability and parameter inclusion of prediction models reported in previous literature

| Title   | Author   | Parameters  | Predicting outcomes  | Methods  | Predictive power  |
|---|--|---|--|--|---|
| Risk Factors of Postoperative Clinically Relevant Pancreatic Fistula following Distal Pancreatectomy with Stapler Closure.    | Ozyazici S, Erdogan O.2021                     | Age, Sex, Body mass index, Preoperative serum albumin, Disease, ASA level   | Operative time, Intraoperative blood loss, Pancreatic texture, Type of surgery, Closure type | Chi-square test, Fisher's Exact test, Logistic regression test                                   | Clinically relevant POPF rate 31.6%. The soft pancreatic texture is an independent risk factor for clinically relevant POPF(OR: 0.016, p = 0.039) |
| Abdominal drain amylase on the first day after pancreatectomy: a predictive factor for pancreatic fistula                     | Rosa, Pablo Henrique Brito da et al.2021       | Age, Sex, Histopathological diagnosis, Complications, Abdominal collection, Deaths, Readmission, Number of days with drain, Number of days hospitalized, Surgical procedure, The drain on the first postoperative day | The diagnosis of PF exclusion  | Fisher's exact test, the Chi-square test, Student's T-test, the Mann-Whitney non-parametric test | The 444 U/L value was the most satisfactory cutoff point: CI 0.690–0.941 (with a sensitivity of 94.4% and a specificity of 60%)                   |
| Preoperative risk stratification of postoperative pancreatic fistula: A risk-tree predictive model for pancreateoduodenectomy | Perri G, Marcegiani G, Partelli S, et al. 2021 | Sex, Body mass index, Age at diagnosis, Smoker, Alcohol abuse, Diabetes, Weight los, ASA score, MPD diameter  | 3 risk groups with significantly different postoperative pancreatic fistula risks            | regression risk-tree model, the independent sample t tes, the MannWhitney test                   | AUC 0.65 (95% CI, 0.59-0.71)  |

|   |                                 |  |  |  |  |
|---|---------------------------------|--|--|--|--|
| Comprehensive Diagnostic Nomogram for Predicting Clinically Relevant Postoperative Pancreatic Fistula After Pancreatoduodenectomy                                       | Li B, Pu N, Chen Q, et al. 2021 | MPD diameter, operation time, intraoperative bleeding, red blood cells (RBC), hemoglobin (HGB), white blood cells (WBC), platelets (PLT), neutrophils (NEUT), lymphocytes (LYM), monocytes (MO), CRP, PCT, albumin (ALB), total bilirubin (TBil), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gammaglutamyl transferase (g-GT), alkaline phosphatase (ALP), Creatinine (Cr), blood urea nitrogen (BUN), operative area drainage (OAD), and drain AMY | concordance index (C-index), calibration curve, decision curve analysis (DCA), and clinical impact curve (ClC) | Chi-square test, Fisher's exact test, Student's t-test, Mann-Witney U test                       | predictive value concordance index 0.814 (95% CI, 0.736–0.892)                         |
| Use of alternative pancreatic fistula risk score system for patients with clinical relevant postoperative pancreatic fistula after laparoscopic pancreaticoduodenectomy | Niu, C Y et al. 2021            | Age, Sex, Body mass index, CA19-9, CA125, pancreatic texture, main pancreatic duct diameter  | incidence of CR-POPF   | Univariate analysis and multivariate Logistic regression analysis                                | AUC 0.735(95%CI:0.668-0.799)   |
| Risk factors and prevention of postoperative pancreatic fistula after insulinoma enucleation:a retrospective study from a high-volume center                            | Xu Q, Xie Q, Ge C, et al. 2021  | Age, Sex, Surgery duration, Blood loss, Tumor size, Ki67 index, POPF Grading, Maximum drainage, Drainage time  | incidence of CR-POPF   | multivariable logistic regression model, Chi-square test, Fisher's exact test, Shapiro-Wilk test | distance from insulinoma to MPD ≤2 mm ( $p = 0.003$ , OR = 6.011, 95% CI 1.852–19.512) |

|   |                                  |  |                                   |  |  |
|---|----------------------------------|--|-----------------------------------|--|--|
| The value of serum amylase and drain fluid amylase to predict postoperative pancreatic fistula after pancreatectoduodenectomy: a retrospective cohort study | van Dongen, Jelle C et al. 2021  | Age, Male sex, BMI, ASA status, Diabetes mellitus, Neoadjuvant therapy, pathology, Preoperative biliary drainage, Pancreatic duct diameter, pancreatic texture, Intra-operative blood loss, CRP on POD 3, Days to drain removal in days, Length of hospital stay | Risk of grade B/C POPF            | T-test, Mann-Whitney U test, the chi-squared test, Fisher's exact test,  | AUC: 0.82  |
| Drain output volume after pancreaticoduodenectomy is a useful warning sign for postoperative complications  | Fukui, Taro et al.2021           | Age, Gender, Diseases, BMI, Preoperative biliary drainage, Preoperative hemoglobin,  | incidence of CR-POPF              | Mann-Whitney U test, Spearman's rank correlation coefficient analysis, multivariable logistic regression analysis                | AUC 0.655, 95% CI: 0.587–0.724   |
| Predictive nomogram for postoperative pancreatic fistula following pancreaticoduodenectomy: a retrospective study   | Shen J, Guo F, Sun Y, et al.2021 | Age, Sex, Body mass index, Smoking, Drinking, Biliary drainage, Diabetes, Hypertension, Epigastric operation history, Total bilirubin, Albumin, Operative time, Pancreas duct size, Pancreas texture, Pathology, Tumour location, Data on POD 1                  | POPF rate                         | t-test, Mann-Whitney U test, chi-squared test, Fisher's exact test, Lasso regression, multivariable logistic regression analysis | AUC 0.87, 95% CI: 0.81–0.94  |
| Preoperative prediction of clinically relevant postoperative pancreatic fistula after pancreaticoduodenectomy   | Lin, Ziying et al.2021           | Age,Gender, Diabetes mellitus, Hypertension, Smoking history, Alcohol consumption, surgical procedures, Pathological diagnosis, Clinical   | preoperative prediction of CRPOPF | Independent t test, chi-square test, ROC analysis  | radiomics model:AUC 0.871 (95 %CI 0.816,0.926), combined model:AUC 0.869 (95 % CI 0.779,0.958) |

|  |                              | outcome   |                                   |  |   |
|--|------------------------------|---|-----------------------------------|--|---|
| Post-operative procalcitonin and C-reactive protein predict pancreatic fistula after laparoscopic pancreatoduodenectomy          | Ma, Jie et al. 2021          | Age, Gender, BMI, Diabetes, History of abdominal operation, Obstructive jaundice, Pre-operative biliary drainage, Serum albumin, Hemoglobin, Operation time, Operation time, Pathology, Pancreatic gland texture, Pancreatic duct diameter, Pathologic type | CRPF development                  | Mann-Whitney U test, Chi-square test, Fisher's exact test, Logistic regression analysis        | POD 3 (AUC 0.951; sensitivity 88.2%, specificity 92.9%, P<0.001)  |
| A simple preoperative stratification tool predicting the risk of postoperative pancreatic fistula after pancreatoduodenectomy    | Lapshyn, Hryhoriy et al.2021 | Age, Gender, BMI, PVR, Pancreatic texture, Pancreatic anastomosis, Histological diagnosis, 90 days postoperative mortality,   | risk of developing grade B/C POPF | Chi-squared test, Fisher's exact test, Mann-Whitney-U-test                                     | training cohort: AUC 0.808 (95%CI 0.726e0.874), independent test cohort: AUC 0.756 (95%CI 0.669-0-830)  |
| Predictive factors of postoperative pancreatic fistula after laparoscopic pancreatoduodenectomy                                  | Jin, Jikuan et al.2021       | Gender, Age, BMI, Preoperative comorbidities, Pancreatitis history, Abdominal surgery history, Preoperative biliary drainage, Pathology   | POPF rate, morbidity incidence    | Chi-squared test, Fisher's exact test, Mann-Whitney U-test                                     | pancreatic texture: AUC =0.854, pancreatic texture + pancreatic duct width: AUC =0.904  |
| Dynamic prediction for clinically relevant pancreatic fistula: a novel prediction model for laparoscopic pancreaticoduodenectomy | Liu, Runwen et al.2021       | Operation age, Gender, Body mass index, Smoking, Drinking, History of hypertension, History of diabetes, Total bilirubin, Albumin, Blood urea nitrogen, ASA grading, Operation time, Preoperative biliary drainage, Intraoperative blood loss,              | Risk of POPF                      | chi-squared test, independent t-test, Mann-Whitney U rank-sum test, logistics regression model | AUC of postoperative days 2, 3, and 5 was 0.866 (95% CI 0.737–0.996), 0.896 (95% CI 0.814–0.978), and 0.888 (95% CI 0.806–0.971), respectively. |

|  |   |  |  |
|--|---|--|--|
|  | Dissection and reconstruction of vessels, Texture of pancreas, Pancreatic Duct's diameter |  |  |
|--|---|--|--|