External validation and revision of Penn incisional hernia prediction model: A ~~retrospective cohort study~~large-scale retrospective cohort of abdominal operations

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Highlights

- The original Penn model yielded fair discrimination in external validation cohort
- Adding new predictor variables improved model performance
- Age, immunosuppressive medication, ostomy reversal, and transfusion were added
- BMI, chronic liver disease, and open surgery remained in the revised model

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Abstract

Background: Incisional hernia (IH) manifests in 10 % to 15 % of abdominal surgeries and patients at elevated risk of this complication should be identified for prophylactic intervention. This study aimed to externally validate the *Penn hernia risk calculator*.

Methods: The Ramathibodi abdominal surgery cohort was constructed by linking relevant hospital databases from 2010 to 2021. Penn hernia risk scores were calculated according to the original model which was externally validated using a seven-step approach. An updated model which included four additional predictor variables (i.e., age, immunosuppressive medication, ostomy reversal, and transfusion) added to those of the three original predictors (i.e., body mass index, chronic liver disease, and open surgery) was also evaluated. The area under the receiver operating characteristic curve (AUC) was estimated and calibration performance compared using the Hosmer-Lemeshow goodness-of-fit method for the observed/expected (O/E) ratio.

Results: A total of 12,155 abdominal operations were assessed. The original Penn model yielded fair discrimination with an AUC (95% confidence interval (CI)) of 0.645 (0.607, 0.683). The updated model that included the additional predictor variables achieved an acceptable AUC (95% CI) of 0.733 (0.698, 0.768) with the O/E ratio of 0.968 (0.848, 1.088).

Conclusion: The updated model achieved improved discrimination and calibration performance, and should be considered for the identification of high-risk patients for further hernia prevention strategy.

Keywords: Abdominal surgery; External validation; Incisional hernia; Prediction score.

Introduction

Incisional hernia (IH), a protrusion of visceral tissue at the area of an incision due to incomplete surgical wound healing, occurs in approximately 10-15% of post-surgical procedures.[1] Control group evidence from randomized controlled trials (RCTs) investigating prophylactic mesh placement during fascia closure suggested an 11.4-52.3% risk of IH in high-risk patients.[2-4] Data from cost analysis of IH repair indicated that reduced IH incidence could represent significant cost savings.[5] As such, accurate identification of high risk IH patients in need of prevention interventions is essential.

Many risk factors associated with IH have been identified, including type of surgery, high body mass index (BMI), and surgical site infection (SSI).[6, 7] However, accurate identification of high risk IH patients is important in order for them to receive prophylaxis intervention. We completed a systematic review and reported several prediction models developed for this purpose following general abdominal surgery.[8-11] Of these models,[8-11] the number of predictor variables ranged from 3 to 17, and their discriminatory performance ranged from 0.77 to 0.92 in terms of concordance statistics; the *Penn Hernia Risk Calculator*[11] was the most recent and available as a mobile phone application. This model can be applied to all types of abdominal surgery and is considered to offer clinical utility, although it remains to be externally validated.

Prediction models generally perform well in the discovery test cohort but are less specific and sensitive when validated externally. As such, every prediction model should be externally validated and revised before their application in different populations.[12, 13] This study aims to validate the Penn Hernia Risk Calculator in the Thai Ramathibodi abdominal surgical dataset and improve model performance, as appropriate, to better identify high risk IH patients for targeted prophylactic intervention.

Materials and Methods

Study design

We constructed a retrospective cohort of adult abdominal surgical patients in Ramathibodi Hospital from January 2010 to August 2021. This cohort was compared with the original Penn cohort, which included 29,739 patients undergoing intra-abdominal operations from January 2005 to June 2016.[11] The data were retrieved from different sources using International Statistical Classification of Diseases and Related Health Problems (ICD) codes for operation and diagnosis (ICD-10), laboratory, medication, and billing data using linked encrypted patient identification (i.e., hospital and admission number). Eligible patients were identified using ICD-9-CM for intra-abdominal operations if they were 18 years or older, not pregnant or in the postpartum period, and underwent intra-abdominal surgery not related to abdominal wall hernia, see Supplementary Fig.1. Patients whose IH was diagnosed before their operation were also excluded. This study adhered to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) reporting guidelines.[14]

Only records with complete data for the Penn IH model's predictors were included for external validation. Sixteen predictor variables were included in the original Penn IH model, two of which were not considered as only Thai nationals were included and the Elixhauser comorbidity score was not performed as part of routine patient assessment. The 14 remaining predictor variables were available and used for validation, including 8 preoperative factors (i.e., BMI, smoking status, chronic obstructive pulmonary disease (COPD), chronic liver disease, cancer, history of chemotherapy/radiation therapy, antiplatelet/anticoagulant use, previous abdominal surgery) and 6 intra-operative factors (i.e., open approach, emergency surgery, emergency vascular

surgery, laparoscopic hysterectomy, concurrent ostomy procedure, and small bowel obstruction). The outcome of interest was any IH post-surgery, which was identified by incisional hernia diagnosis (ICD-10) or incisional hernia repair (ICD-9-CM).

The following data were retrieved: patients' baseline characteristics (age, sex, BMI), American Society of Anesthesiologists (ASA) physical status classification, smoking status, underlying diseases (i.e., COPD, chronic liver disease, and diabetes), cancer, chemotherapy and radiation therapy, concurrent medication (i.e., antiplatelet/anticoagulant and immunosuppressive medication), history of abdominal surgery, history of incisional hernia repair, surgical factors (i.e., wound classification, open approach, emergent laparotomy, emergent vascular procedure, concurrent ostomy procedure, ostomy reversal, colorectal procedure, laparoscopic hysterectomy, small intestinal obstruction, and inflammation pathology), transfusion, intensive care unit admission, post-operative complications (i.e., SSI, wound complication, pneumonia), and IH occurrence.

Statistical analysis

Data were described by frequency and percentage for categorical variables, mean and standard error (SD) or median and interquartile range (IQR) for continuous data. Summary characteristics and risk factors were compared between the Ramathibodi and Penn cohorts[11] using Chi-square tests. Predictor variables were regressed on IH occurrence using univariate and multivariate logistic equations, and the coefficients and 95% confidence intervals (95% CIs) estimated. The Penn model was validated as follows (additional details are provided in Appendix 1)[13]: 1) Composite risk scores were calculated based on the original model,[11] then against the IH outcome by logistic regression to assess the original model performance in the Ramathibodi

dataset. 2) Model coefficient revision was performed by adding each original model predictor variable individually to the model containing only the risk score, and only significant predictors were retained. 3) Potential predictors, not considered in the original model but that were significantly associated with IH occurrence were added to the original model. 4) All original predictors were re-fitted on IH outcome in multivariate logistic regression to re-estimate $\boldsymbol{\beta}$-coefficients based on the Ramathibodi cohort data. 5) Only significant predictors from step 4 were retained in the model. 6) Only predictors identified in step 3 and 5 were simultaneously considered and only significant predictors were retained. 7) As per step 6, with only pre-operative and intra-operative predictors considered.

Discrimination performance was assessed by estimating concordance statistics (i.e., the area under the receiver operating characteristic curve (AUC)). Hosmer-Lemeshow goodness-of-fit chi-square tests of the observed/expected outcome (O/E) ratio, and the O/E plot, were used to assess calibration performance.

The best model was selected on the basis of both discrimination and calibration performance. A composite risk score was constructed based on coefficients for the selected model, and was further categorized based on the distribution frequencies at 25^{th}, 50^{th}, and 75^{th} percentiles as a cut-off. Then, sensitivity, specificity, positive and negative predictive values (PPV and NPV), and likelihood ratios were estimated for each cut-off. Significance was considered for p-value < 0.05. Stata version 17 (StataCorp, Texas, USA) was used for all statistical analyses.

Results

Characteristics of patients

A total of 423,704 operations were recorded in the Ramathibodi Surgery databases for the period January 2010 to August 2021, see Supplementary Fig.1. Of these, 18,358 were identified as abdominal surgeries using ICD-9-CM codes for various kinds of intra-abdominal procedures. Of the 18,358 abdominal surgeries, 16,731 records met our inclusion criteria, although only 12,155 records (11,617 patients) had complete data and were included for external validation of the Penn IH model. The median follow-up time (IQR) was 23.4 (6.3 – 52) months. The mean age (SD) was 57 (16.1) years, and 38.4% of patients were male. Biliary surgery was the most frequently performed procedure (41.5%), followed by gastrointestinal (24%), colorectal (19.5%), and gynecologic procedures (10.2%). A total of 178 out of 12,155 patients had IH occurrence with an incidence (95% CI) of 1.5% (1.3%, 1.7%).

Predictive factors

Significant differences between the Ramathibodi patients and the Penn cohort were observed, see Table 1. Among 14 predictor variables included in the Penn model, two predictors (i.e., emergency vascular surgery and laparoscopic hysterectomy) had no IH occurrence, and therefore their coefficients could not be estimated leaving the 12 remaining predictors to calculate a Penn risk score. Of these, six predictors (i.e., BMI, chronic liver disease, antiplatelet/anticoagulant use, open surgery, concurrent ostomy, and previous abdominal surgery) were significantly associated with IH in the Ramathibodi data, see Supplementary Table 1. All significant predictors had the same directions of association as in the Penn cohort. Two of these 6 predictor variables (i.e., open surgery and previous abdominal surgery) had similar coefficients in both the Ramathibodi and Penn datasets, 0.36 versus 0.35 and 0.82 versus 0.85, respectively, in contrast to the remaining coefficients which were substantially different.

Performance of Penn model

External validation of the Penn model was based on the original weighted score and predictor variable coefficients as previously reported,[11] see Table 2. The original model provided fair discrimination for both coefficient and weighted score approaches (step 1) with AUCs (95% CI) of 0.634 (0.595, 0.674) and 0.645 (0.607, 0.683), respectively.

Model revision

Model revision (step 2, 4, and 5) focused on the original predictors and showed little improved performance with AUCs (95% CI) of 0.679 (0.641, 0.717), 0.692 (0.655, 0.729), and 0.689 (0.652, 0.726), respectively. Additional predictors significantly associated with IH identified from univariate regression (Supplementary Table 2) were included in the model (step 3), with improved discrimination performance of 0.729 (0.693, 0.765). Step 6, which simultaneously considered the original significant predictors from step 5 and additional predictors from step 3, improved the AUC to 0.743 (0.707, 0.778). Finally, step 7, which considered only pre- and intra-operative predictors and excluded SSI from the model, resulted in an AUC of 0.733 (0.698, 0.768). All models demonstrated good calibration performance, where the O/E ratio ranged from 0.968 to 1.031. More details from each validation step are described in Appendix 2.

The final model (step 7) included only pre- and intra-operative data and may prove more clinically applicable, given its acceptable discrimination and calibration performance (Table 2 and Fig.1). The following equation was constructed based on the predictor variable coefficients derived from step 7 (Supplementary Table 3).

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -5.71 + 1.11x(Age\ 45-65) + 1.63x(Age > 65) -$$

$$0.39x(BMI < 18) - 0.57x(BMI\ 18-25) + 0.64x(BMI > 30) +$$

$$0.92x(Cirrhosis) + 0.74x(Immunosuppressive\ drug) + 0.50x(Open\ surgery)$$

$$+ 2.06x(Ostomy\ reversal) + 0.60x(Transfusion)$$

The risk scores calculated based on predictor variable coefficients ranged from –6.28 to 1.38, which were stratified into very low, low, moderate, and moderate-high based on thresholds of –5.17, –4.60, and –4.07 representing the 25th, 50th, and 75th percentiles, see Table 3. Sensitivity, specificity, PPV, and likelihood ratios are presented in Table 3.

Discussion

The original Penn[11] score provided reasonable discriminatory performance in their original dataset with an AUC of 0.84 but its performance decreased when evaluated in the Ramathibodi data (AUC = 0.645). There may be several reasons to explain the difference observed. First, IH incidence in the Ramathibodi data was approximately 2-fold lower than in the Penn data,[11] i.e., 1.5% vs 3.8%. Second, there were significant differences in the characteristics and risk factors between both cohorts, see Table 1. As such, only six out of the 14 original predictor variables were significant in the Ramathibodi dataset; all had the same direction of association in both cohorts. However, only three of the 16 original predictors were retained in the revised/updated models. In addition, the significant original predictor variables (i.e., emergency surgery which was the most significant), emergent vascular procedure, and laparoscopic hysterectomy were not significantly associated with IH in the Ramathibodi data, which were likely significant contributors to the

variation in model performance observed across both datasets. These findings support the need for model revision and validation in external independent datasets.

Additional predictor variables were considered in revision steps if they were identified from other IH prediction models[8,10,15] or fascial dehiscence[16-18] or were significantly associated with IH in univariate logistic regression (Supplementary Table 2). Even though the Elixhauser comorbidity score was not available, ASA classification which captures patient's status was considered in this step. However, it was removed from the model during stepwise selection. Integration of the new predictor variables, including age, immunosuppressive medication, ostomy reversal, SSI, and transfusion significantly improved the Ramathibodi model performance with an AUC of 0.743 and the O/E ratio of 0.967 (step 6). Given the reported 178 IH cases in the Ramathibodi dataset and the rule of thumb that requires ten events per predictor variable, the model derived in step 6 was less likely to suffer from model overfitting.

Surgical techniques incorporated during abdominal fascia closure such as small-bite fascial suturing[22] and mesh reinforcement can minimize IH incidence.[2-4] Unfortunately, information for neither small-bite fascial closure nor prophylactic mesh placement was available in our electronic databases. Recent meta-analyses[20-22] have provided evidence of the benefits associated with mesh on hernia prevention, especially with regard to onlay and retromuscular placement.[20, 22, 23] Therefore, identification of patients at higher IH risk based on information available before or during surgery (step 7) would be clinically helpful for fascia-enhanced prophylactic intervention allocation. As such, incorporation of post-operative predictors such as SSI may offer limited value to enable IH prophylactic intervention. Nevertheless, although SSI was removed from the risk prediction model, its importance should not be overlooked as opportunities to reduce post-operative SSI would likely result in lower IH risk.

Our model performance was less than that reported for the HERNIA score,[9] and Fischer et al.'s models,[10] which yielded AUCs of 0.77,[9, 10] and much lower than that of Veljkovic et al.[8] (AUC = 0.92). The Veljkovic model was based on data from 603 patients and included only 4 predictor variables (BMI, suture length to incision length ratio, time to suture removal or complete epithelialization, and SSI) with relatively short follow-up time (6.9 ± 2.1 months),[8] representing one pre-operative, one intra-operative, and two post-operative factors.

The HERNIA score is a well-known IH prediction model derived from data from 428 patients using only 3 predictor variables (BMI, COPD, and surgical approach [laparotomy or hand-assisted laparoscopy]).[9] Given that current procedures tend to be limited to minimally invasive laparoscopic techniques, hybrid procedures such as hand-assisted laparoscopy is relatively unpopular, which perhaps makes the HERNIA score model less applicable.

The *Penn hernia risk calculator* was derived from the original Fischer et al. model by the same group[10] using Cox regression on data from 12,373 patients. Seventeen predictors were originally included in the model; six related to surgical procedures (bariatric surgery, small bowel resection, proctectomy, partial colectomy, ostomy creation, and ostomy reversal). Unlike the *Penn hernia risk calculator*,[11] Fischer's model focused solely on patients undergoing elective open abdominal surgery. Thus, generalizability of this model to laparoscopic surgery or acute procedures is questionable. Of the four IH models, only the HERNIA score has been externally validated and revised, although model performance measures such as concordance statistics or calibration plots were not reported.[24] Given the HERNIA score[9] may be less clinically applicable, we did not validate it. Lack of data for suture length to incision length ratio and time to suture removal or complete epithelialization also precluded us from evaluating the Veljkovic model.[8]

Our study had several limitations. First, not all predictor variables were considered in the external validation for the following reasons: Elixhauser comorbidity scores were not available and race/ethnicity was not applicable as our data were based solely in a Thai setting. Second, BMI was missing in 27.4 % of all subjects and therefore external validation was undertaken in only those cases with complete data (12,155 records), which may have resulted in some degree of bias. Third, some clinically insignificant IHs might not be detected because imaging was not routinely used for hernia detection in actual clinical practice at our settings. Finally, this externally validated updated model focused solely on abdominal surgery as other surgery-specific models could not be evaluated given the restrictions of the data collected.

Conclusion

Although the original *Penn hernia risk calculator* did not perform well in the Ramathibodi IH surgical cohort, a revised model achieved improved discrimination and calibration performance. This revised model included age, BMI, chronic liver disease, immunosuppressive medication, open surgery, ostomy reversal, and transfusion, which helped identify those patients at increased risk of IH and those most in need of targeted intervention thus guiding and improving clinical care.

Author contributions

This study was conceptualized by A.Ta. and S.T. under supervision of P.N., P.S., and A.T. Data was linked to construct study cohort by H.T., A.P., and P.P. Data cleaning was performed by H.T., A.Ta., A.P., and N.P. A.Ta. performed data analysis under supervision of P.N. and A.T. Manuscript was drafted by A.Ta. and revised by G.MK., J.A., and A.T. All authors have read and approved this manuscript before submission.

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Study registration: Thai Clinical Trials Registry (TCTR20220704001), 4 July 2022, retrospectively registered.

Ethical approval: This study was approved by the Ramathibodi Human Research Ethics Committee (MURA2022/224) before data retrieval.

Consent to participate: Not applicable.

Consent for publication: Not Applicable

Patient and Public involvement: No patient and public involved.

Data statement: Access to the dataset from the current study is available from the corresponding author upon reasonable request and approval.

Disclosure information: All authors declared no conflict of interest.

List of abbreviations

ASA – American Society of Anesthesiologists

AUC – Area under the receiver operating characteristic curve

BMI – Body mass index

CI – Confidence interval

COPD – Chronic obstructive pulmonary disease

IH – Incisional hernia

IQR – Interquartile range

NPV – Negative predictive value

O/E ratio – The observed/expected ratio

PPV – Positive predictive value

RCT – Randomized controlled trial

SD – Standard error

SSI – Surgical site infection

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Figure legend

Fig.1 Revised incisional hernia prediction model performance for abdominal surgery a) Receiver operating characteristic curve b) Calibration plot

Electronic Supplementary Material

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Fig.1 Ramathibodi surgical data extraction

Table 1. Estimation of Penn model predictor coefficients based on Ramathibodi surgical cohort data

Table 2. Additional predictor variables significantly associated with incisional hernia occurrence in Ramathibodi surgical cohort data

Table 3. Final validation step multivariable predictor coefficients and 95% confidence intervals

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Appendix 1: Seven steps of external validation

Appendix 2: Equations for each of the seven steps

Table 1

Table 1. Summary characteristics for Ramathibodi and Penn cohorts

Predictors, n (%)	Penn cohort (N = 29,739)	Ramathibodi cohort (N = 12,155)	P-value
Incisional hernia	1,127 (3.8)	178 (1.5)	< 0.001
Race, Caucasian	18,702 (62.8)	NA	
Age, years			
< 45	8,837 (29.7)	2,887 (23.8)	< 0.001
45 – 65	13,895 (46.7)	5,168 (42.5)	
> 65	7,007 (23.5)	4,100 (33.7)	
Sex, male	10,894 (36.6)	4,667 (38.4)	0.001
BMI, kg/m^2			
< 18	1,103 (3.7)	662 (5.5)	< 0.001
18 – 25	8,021 (26.9)	6,811 (56.0)	
> 25 – 30	9,928 (33.4)	3,451 (28.4)	
> 30	10,687 (35.9)	1,231 (10.1)	
Smoker	8,102 (27.2)	27 (0.2)	< 0.001
COPD	8,632 (29.0)	207 (1.7)	< 0.001
Hypertension	14,776 (49.6)	3,798 (31.3)	< 0.001
Diabetes	5,720 (19.2)	1,463 (12.0)	< 0.001
Cirrhosis	NA	206 (1.7)	NA
2+ Elixhauser comorbidity score	18,711 (62.9)	NA	NA
Cancer	6,654 (22.3)	3,853 (31.7)	< 0.001
Chemotherapy/Radiotherapy	1,306 (4.4)	1,954 (16.1)	< 0.001
Antiplatelet/Anticoagulant	3,016 (10.1)	1,572 (12.9)	< 0.001
Emergency surgery	3,523 (11.8)	3,434 (28.3)	< 0.001
Open surgery	11,628 (39.1)	5,431 (44.7)	< 0.001
Concurrent Ostomy	NA	753 (6.2)	NA
Ostomy reversal	NA	56 (0.5)	NA
Small bowel resection	NA	416 (3.4)	NA
Large bowel surgery			
Partial colectomy	NA	1,902 (15.7)	NA
Proctectomy	NA	288 (2.4)	NA
Emergency vascular procedure	354 (1.2)	2 (0.02)	< 0.001
Laparoscopic hysterectomy	2,446 (8.2)	92 (0.8)	< 0.001
History of abdominal surgery	3,781 (12.7)	652 (5.4)	< 0.001
Small bowel obstruction	3,561 (11.9)	508 (4.2)	< 0.001
Wound complication	NA	660 (5.4)	NA

BMI body mass index, COPD chronic obstructive pulmonary disease, NA not available

Table 2. Penn model performance validation in the Ramathibodi cohort data

Step	Model	AUC (95% CI)	O/E (95% CI)
1	Coefficient	0.634 (0.595, 0.674)	1.031 (0.930, 1.132)
	Weighted score	0.645 (0.607, 0.683)	1.021 (0.897, 1.145)
2	Coefficient	0.646 (0.607, 0.684)	1.026 (0.919, 1.134)
	Weighted score	0.679 (0.641, 0.717)	1.006 (0.906, 1.106)
3	Coefficient	0.727 (0.691, 0.763)	0.984 (0.847, 1.120)
	Weighted score	0.729 (0.693, 0.765)	0.984 (0.894, 1.074)
4		0.692 (0.655, 0.729)	0.978 (0.875, 1.081)
5		0.689 (0.652, 0.726)	0.995 (0.891, 1.100)
6		0.743 (0.707, 0.778)	0.967 (0.861, 1.072)
7		0.733 (0.698, 0.768)	0.968 (0.848, 1.088)

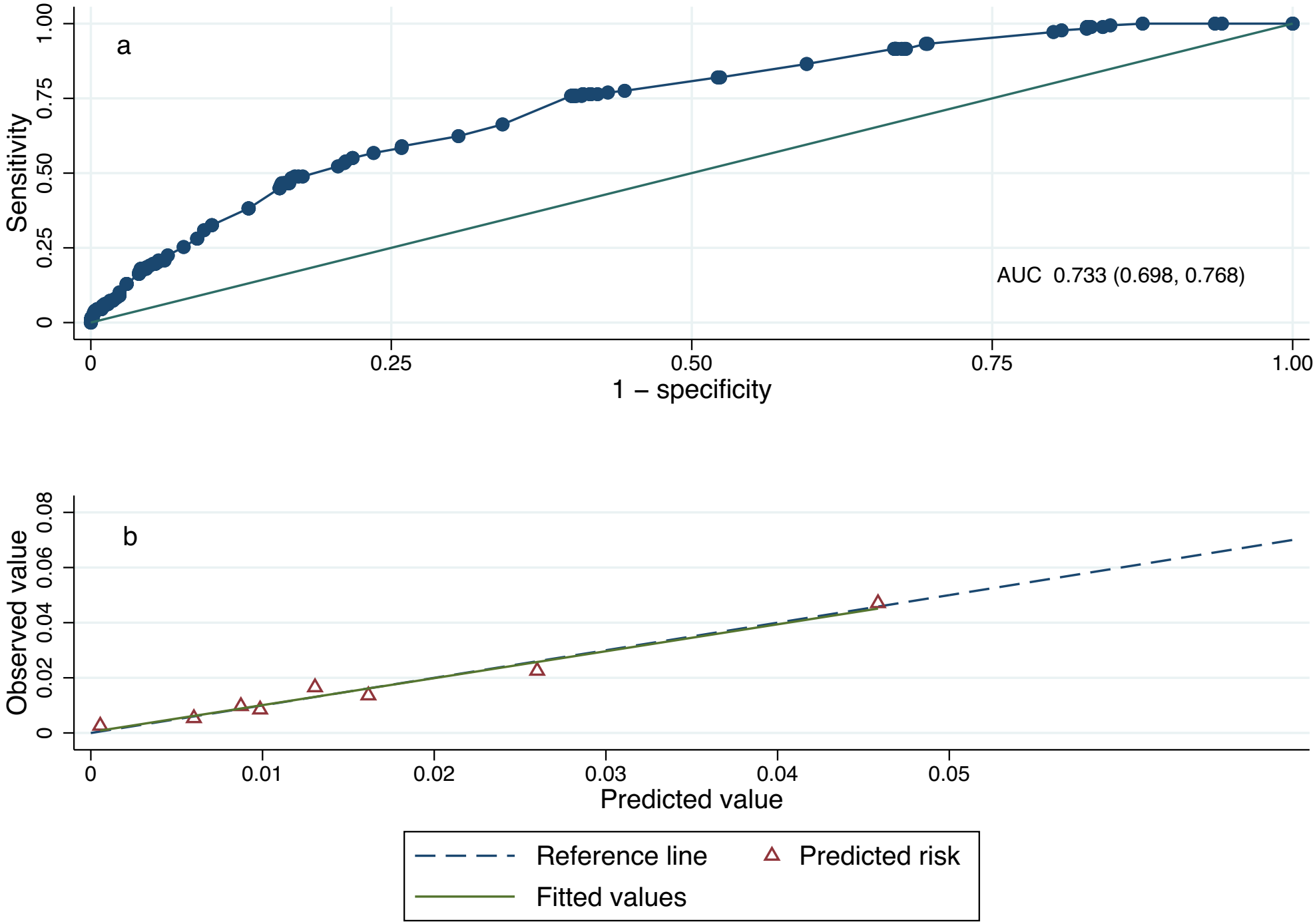
AUC the area under the receiver operating characteristic curve, CI confidence interval, O/E the observed/expected outcome ratio

Table 3. Revised Ramathibodi incisional hernia risk classification score using only pre- and intra-operative predictor variables

Thresholds	Sensitivity (%)	Specificity (%)	PPV (%)	LR (+)
-6.28	100 (97.9, 100)	5.9 (5.5, 6.3)	1.6 (1.3, 1.8)	1.06 (1.06, 1.07)
-5.17	97.2 (93.6, 99.1)	19.9 (19.2, 20.6)	1.8 (1.5, 2.1)	1.21 (1.18, 1.25)
-4.60	77.5 (70.7, 83.4)	55.6 (54.7, 56.5)	2.5 (2.1, 3.0)	1.75 (1.61, 1.89)
-4.07	58.4 (50.8, 65.8)	74.1 (73.3, 74.9)	3.3 (2.7, 3.9)	2.26 (1.99, 2.57)

LR likelihood, PPV positive predictive value, 95% confidence intervals are shown in parentheses

Figure 1


a
Sensitivity
0
0.25
0.50
0.75
1.00
1 – specificity
AUC 0.733 (0.698, 0.768)
b
Observed value
0
0.02
0.04
0.06
0.08
Predicted value
0.01
0.03
0.05
Reference line
Predicted risk
Fitted values

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Ammarin Thakkinstian declares all support for the present manuscript the National Research Council of Thailand (NRCT #N42A640323). The sponsor had no role in the design or conduct of the study.

All remaining authors have no conflicts to delare

TRIPOD Checklist: Prediction Model Validation

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	3
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	3
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	4
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	4
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	4
	5b	Describe eligibility criteria for participants.	4
	5c	Give details of treatments received, if relevant.	4
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	4-5
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	4-5, appendix
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	4
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	4
Statistical analysis methods	10c	For validation, describe how the predictions were calculated.	5-6
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	5-6
	10e	Describe any model updating (e.g., recalibration) arising from the validation, if done.	5-6
Risk groups	11	Provide details on how risk groups were created, if done.	6
Development vs. validation	12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	4
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	6-7, supplement
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	7
	13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	7, Table 1, Supplement
Model performance	16	Report performance measures (with CIs) for the prediction model.	7-8, Table 2
Model-updating	17	If done, report the results from any model updating (i.e., model specification, model performance).	7-8, Table 2
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11
Interpretation	19a	For validation, discuss the results with reference to performance in the development data, and any other validation data.	9, 10
	19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	9-11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	11-12
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	13
Funding	22	Give the source of funding and the role of the funders for the present study.	13

External validation and revision of Penn incisional hernia prediction model: A large-scale retrospective cohort of abdominal operations

Supplementary Figures

Supplementary Tables

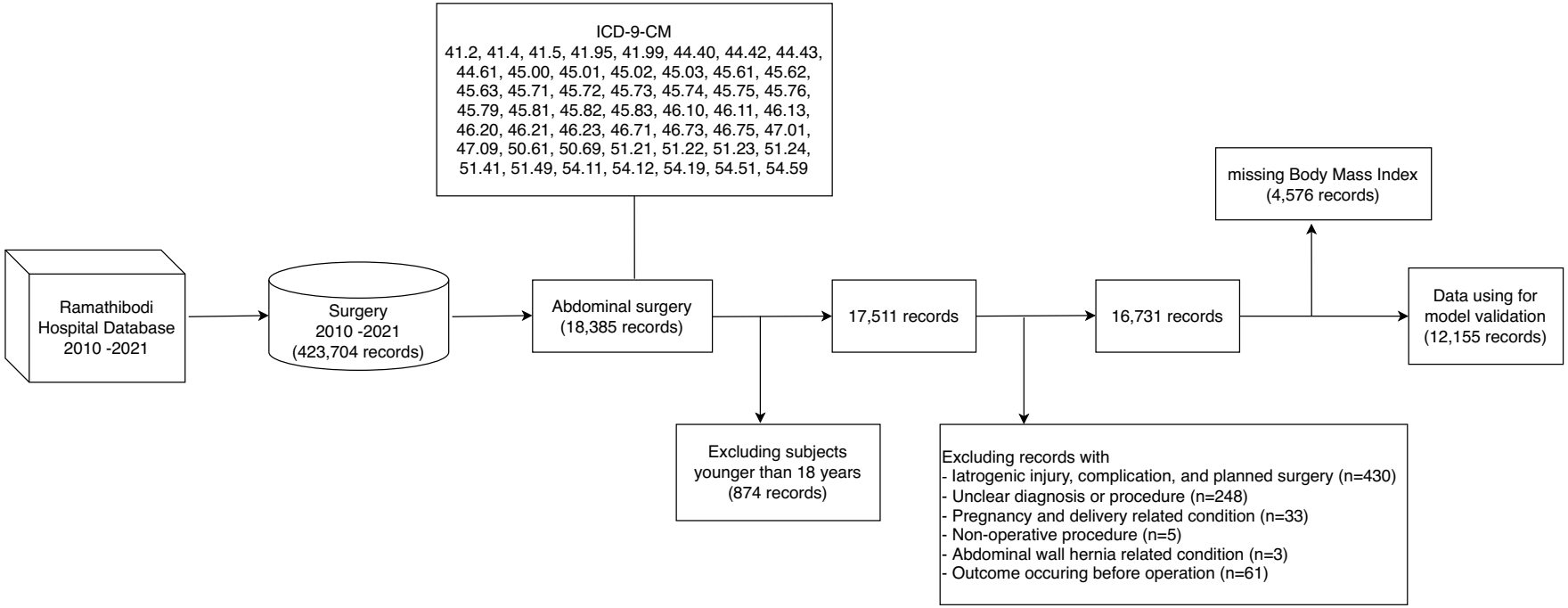


Fig.1 Ramathibodi surgical data extraction

Table 1. Estimation of Penn model predictor coefficients based on Ramathibodi surgical cohort data

Variables, n (%)	Ramathibodi data						Penn IH prediction model			
	IH		Univariate		Multivariate					
	Yes N = 178	No N = 11,977	Coef (95% CI)	p-value	Coef (95% CI)	p-value	% IH	Coef (95% CI)	OR (95% CI)	Score
Caucasian										
Yes							4.5	0.67 (0.49, 0.84)	1.95 (1.63, 2.32)	2
No							2.7	0	1	0
BMI, kg/m^2										
< 18	9 (1.4)	653 (98.6)	-0.27 (-0.97, 0.44)	0.458	-0.52 (-1.23, 0.20)	0.154	1.8	-1.61 (-2.21, -0.99)	0.20 (0.11, 0.37)	-4
18-25	74 (1.1)	6,737 (98.9)	-0.49 (-0.84, -0.15)	0.005	-0.60 (-0.94, -0.25)	0.001	2.9	-0.65 (-0.87, -0.45)	0.52 (0.42, 0.64)	-2
25-30	61 (1.8)	3,390 (98.2)	0		0		-	0	1	0
> 30	34 (2.8)	1,197 (97.2)	0.46 (0.03, 0.88)	0.035	0.52 (0.10, 0.95)	0.017	5.1	0.35 (0.16, 0.54)	1.42 (1.17, 1.72)	1
Smoker										
Yes	1 (3.7)	26 (96.3)	0.95 (-1.05, 2.96)	0.350	0.96 (-1.06, 2.97)	0.353	6.7	0.50 (0.34, 0.66)	1.65 (1.40, 1.94)	1
No	177 (1.5)	11,951 (98.5)	0		0		2.7	0	1	0
COPD										
Yes	6 (2.9)	201 (97.1)	0.71 (-0.11, 1.54)	0.09	0.38 (-0.46, 1.23)	0.378	6.3	0.22 (0.05, 0.38)	1.24 (1.05, 1.46)	1
No	172 (1.4)	11,776 (98.6)	0		0		2.8	0	1	0
Chronic liver disease										
Yes	10 (4.9)	196 (95.2)	1.27 (0.62, 1.93)	< 0.001	1.13 (0.46, 1.80)	0.001	NA	0.31 (0.11, 0.50)	1.36 (1.12, 1.65)	1
No	168 (1.4)	11,781 (98.6)	0		0		NA	0	1	0
2+ Elixhauser score										
Yes							5.1	0.41 (0.17, 0.65)	1.51 (1.18, 1.91)	1
No							1.6	0	1	0
Cancer										
Yes	71 (1.8)	3,782 (98.2)	0.36 (0.06, 0.67)	0.019	0.30 (-0.09, 0.69)	0.127	5.7	0.29 (0.10, 0.47)	1.34 (1.11, 1.60)	1
No	107 (1.3)	8,195 (98.7)	0		0		3.2	0	1	0
Chemo/RT										
Yes	35 (1.8)	1,919 (98.2)	0.25 (-0.12, 0.62)	0.190	-0.18 (-0.61, 0.26)	0.427	9.6	0.29 (0.01, 0.57)	1.33 (1.01, 1.76)	1
No	143 (1.4)	10,058 (98.6)	0		0		3.5	0	1	0
Antiplatelet/anticoagulant										
Yes	43 (2.7)	1,529 (97.3)	0.78 (0.43, 1.13)	< 0.001	0.58 (0.21, 0.94)	0.002	8.2	0.25 (0.04, 0.31)	1.28 (1.04, 1.36)	1
No	135 (1.3)	10,488 (98.7)	0		0		3.3	0	1	0
Emergency surgery										
Yes	62 (1.8)	3,372 (98.2)	0.31 (-0.001, 0.62)	0.050	0.27 (-0.10, 0.63)	0.155	15.8	1.54 (1.36, 1.71)	4.65 (3.90, 5.55)	4
No	116 (1.3)	8,605 (98.7)	0		0		2.2	0	1	0
Open surgery										
Yes	101 (1.9)	5,330 (98.1)	0.49 (0.19, 0.79)	0.001	0.36 (0.02, 0.70)	0.039	6.3	0.35 (0.17, 0.54)	1.42 (1.18, 1.72)	1
No	77 (1.2)	6,647 (98.9)	0		0		2.2	0	1	0
Ostomy										
Yes	21 (2.8)	732 (97.2)	0.72 (0.26, 1.18)	0.002	0.52 (0.03, 1.02)	0.039	NA	0.25 (0.02, 0.46)	1.28 (1.02, 1.59)	1
No	157 (1.4)	11,245 (98.6)	0		0		NA	0	1	0

Emergency vascular surgery										
Yes	0 (0)	2 (100)	NA	NA	NA	NA	11.9	0.79 (0.33, 1.25)	2.21 (1.39, 3.50)	2
No	178 (1.5)	11,975 (98.5)	NA		NA		3.7	0	1	0
Laparoscopic hysterectomy										
Yes	0 (0)	92 (100)	NA	NA	NA	NA	0.8	-0.58 (-1.11, -0.05)	0.56 (0.33, 0.95)	-2
No	178 (1.5)	11,885 (98.5)	NA		NA		4.1	0	1	0
History of abdominal surgery										
Yes	23 (3.5)	629 (96.5)	0.98 (0.54, 1.43)	< 0.001	0.82 (0.34, 1.29)	0.001	11.1	0.85 (0.67, 1.03)	2.33 (1.95, 2.79)	2
No	155 (1.4)	11,348 (98.7)	0		0		2.7	0	1	0
Small bowel obstruction										
Yes	10 (2.0)	498 (98.0)	0.32 (-0.33, 0.96)	0.336	-0.02 (-0.71, 0.67)	0.954	10.7	0.51 (0.32, 0.69)	1.66 (1.38, 2.00)	1
No	168 (1.4)	11,479 (98.6)	0		0		2.8	0	1	0

BMI, body mass index; Chemo/RT, chemotherapy or radiation therapy; CI, confidence interval; Coef, coefficient; COPD, chronic obstructive pulmonary disease; IH, incisional hernia; NA, not available; OR, odds ratio

Table 2. Additional predictor variables significantly associated with incisional hernia occurrence in Ramathibodi surgical cohort data

Variables	Univariate analysis	
	Coefficient (95% CI)	p-value
Age, years		
< 45	0	
45 - 65	1.18 (0.56, 1.79)	< 0.001
> 65	1.76 (1.16, 2.36)	< 0.001
ASA classification		
Class 1	0	
Class 2	-0.28 (-0.71, 0.16)	0.215
Class 3 - 5	0.70 (0.34, 1.05)	< 0.001
Diabetes	0.83 (0.48, 1.18)	< 0.001
Immunosuppressive drug	0.99 (0.53, 1.45)	< 0.001
Small bowel resection	1.12 (0.61, 1.63)	< 0.001
Colorectal procedure	0.60 (0.28, 0.92)	< 0.001
Ostomy reversal	2.12 (1.26, 2.98)	< 0.001
Wound classification		
Clean and Clean-contaminated	0	
Contaminated and Dirty	0.65 (0.06, 1.24)	0.032
Wound complication	1.45 (1.07, 1.84)	< 0.001
Surgical site infection	1.35 (0.93, 1.77)	< 0.001
Transfusion	0.88 (0.56, 1.19)	< 0.001
ICU stay	0.85 (0.52, 1.19)	< 0.001

ASA, American Society of Anesthesiologist; CI, confidence interval; ICU, intensive care unit

Table 3. Final validation step multivariable predictor coefficients and 95% confidence intervals

Variables	Coefficient (95% CI)	p-value
Age, years		
< 45	0	
45 - 65	1.11 (0.49, 1.73)	< 0.001
> 65	1.63 (1.03, 2.24)	< 0.001
BMI, kg/m^2		
< 18	-0.39 (-1.11, 0.33)	0.285
18 – 24.9	-0.57 (-0.91, -0.22)	0.001
25 – 29.9	0	
> 30	0.64 (0.21, 1.07)	0.004
Cirrhosis	0.92 (0.25, 1.59)	0.007
Immunosuppressive drug	0.74 (0.27, 1.22)	0.002
Open surgery	0.50 (0.19, 0.81)	0.002
Ostomy reversal	2.06 (1.18, 2.95)	< 0.001
Transfusion	0.60 (0.26, 0.93)	< 0.001
Constant term	-5.17 (-6.35, -5.07)	< 0.001

BMI, body mass index; CI, confidence interval

External validation and revision of Penn incisional hernia prediction model: A large-scale retrospective cohort of abdominal operations

Appendixes

Appendix 1: Seven steps of external validation

Step 1: Model performance

The original Penn IH prediction scores were calculated based on coefficients (1.1) and weighted scores (1.2) as follows:

(1.1) $$[\text{Score 1.1}] = -\ 1.61 \text{ x (BMI } < 18) - 0.65 \text{ x (BMI } 18-25) + 0.35 \text{ x (BMI } > 30) + 0.50 \text{ x (Smoking)} + 0.22 \text{ x (COPD)} + 0.31 \text{ x (Cirrhosis)} + 0.29 \text{ x (Cancer)} + 0.29 \text{ x (Chemotherapy or RT)} + 0.25 \text{ x (Antiplatelet or Anticoagulant)} + 1.54 \text{ x (Emergency)} + 0.35 \text{ x (Open surgery)} + 0.25 \text{ x (Ostomy)} + 0.85 \text{ x (Previous surgery)} + 0.51 \text{ x (SBO)}$$

(1.2) $$[\text{Score 1.2}] = -\ 4 \text{ x (BMI } < 18) - 2 \text{ x (BMI } 18-25) + 1 \text{ x (BMI } > 30) + 1 \text{ x (Smoking)} + 1 \text{ x (COPD)} + 1 \text{ x (Cirrhosis)} + 1 \text{ x (Cancer)} + 1 \text{ x (Chemotherapy or RT)} + 1 \text{ x (Antiplatelet or Anticoagulant)} + 4 \text{ x (Emergency)} + 1 \text{ x (Open surgery)} + 1 \text{ x (Ostomy)} + 2 \text{ x (Previous surgery)} + 1 \text{ x (SBO)}$$

Then, these scores were fitted on the IH outcome with the following equations:

Model 1.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.1]}$$

Model 1.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.2]}$$

Step 2: Model revision

Model coefficient revision was performed by adding each predictor variable individually to the original model containing the risk score; only significant predictor variables were retained. The equations used were:

Model 2.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.1]} + \sum_i b_i x_i$$

Model 2.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.2]} + \sum_i b_i x_i$$

Step 3: Model update

Potential predictors, not included in the original model but significantly associated with IH occurrence in Ramathibodi data were added to the original model. The equations used were as follows:

Model 3.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.1]} + \sum_i b_i z_i$$

Model 3.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \mathrm{b}_1 \text{ x [Score 1.2]} + \sum_i b_i z_i$$

Step 4: Model update

All original predictors were re-fitted on IH outcome to re-estimate $\boldsymbol{\beta}$-coefficients based on Ramathibodi data. The equation used was as follows:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 - b_1 \text{ x (BMI } < 18) - b_2 \text{ x (BMI } 18-25) + b_3 \text{ x (BMI } > 30)$$
$$+ b_4 \text{ x (Smoking)} + b_5 \text{ x (COPD)} + b_6 \text{ x (Cirrhosis)}$$
$$+ b_7 \text{ x (Cancer)} - b_8 \text{ x (Chemotherapy or RT)}$$
$$+ b_9 \text{ x (Antiplatele or Anticoagulant)} + b_{10} \text{ x (Emergency)}$$
$$+ b_{11} \text{ x (Open surgery)} + b_{12} \text{ x (Ostomy)}$$
$$+ b_{13} \text{ x (Previous surgery)} - b_{14} \text{ x (SBO)}$$

Step 5: Model update

Same as the model in step 4 but only significant predictor variables were retained. The equation used was as follows:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \sum_i b_i x_i$$

Where x_i are only significant predictors

Step 6: Model update

Only predictors identified from step 3 and 5 were simultaneously considered and only significant predictor variables were retained. The equation used was as follows:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = b_0 + \sum_i b_i x_i + \sum_i b_i z_i$$

Where x_i are the only significant predictors from step 5

Step 7: Model update

As for step 6, only the pre-operative and intra-operative predictor variables were considered.

Appendix 2: Equations for each of the seven steps

Step 1: Model performance

Model 1.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.52\ +\ 0.48 \text{ x [Score 1.1]}$$

Model 1.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.55\ +\ 0.19 \text{ x [Score 1.2]}$$

Step 2: Model revision

Model 2.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.54\ +\ 0.47 \text{ x [Score 1.1]} + 1.08 \text{ x (Cirrhosis)}$$

Model 2.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 4.50\ +\ 0.30 \text{ x [Score 1.2]} + 0.87 \text{ x (Cirrhosis)} - 0.89 \text{ x (Emergency)}$$

Step 3: Model update

Model 3.1:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 5.84\ +\ 0.41 \text{ x [Score 1.1]} + 1.14 \text{ x (Age } 45-65) +\ 1.64 \text{ x (Age} >\ 65)$$
$$+\ 0.96 \text{ x (SSI)} +\ 0.74 \text{ x (Immunosuppression)} +\ 1.89 \text{ x (Ostomy reversal)}$$

Model 3.2:

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -\ 5.84\ +\ 0.16 \text{ x [Score 1.2]} + 1.13 \text{ x (Age } 45-65) +\ 1.61 \text{ x (Age} >\ 65)$$
$$+\ 0.94 \text{ x (SSI)} +\ 0.73 \text{ x (Immunosuppression)} +\ 1.91 \text{ x (Ostomy reversal)}$$

Step 4: Model update

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -4.57 - 0.52 \text{ x (BMI } < 18) - 0.60 \text{ x (BMI } 18-25) + 0.52 \text{ x (BMI } > 30)$$
$$+ 0.96 \text{ x (Smoking)} + 0.38 \text{ x (COPD)} + 1.13 \text{ x (Cirrhosis)}$$
$$+ 0.30 \text{ x (Cancer)} - 0.18 \text{ x (Chemotherapy or RT)}$$
$$+ 0.58 \text{ x (Antiplatele or Anticoagulant)} + 0.27 \text{ x (Emergency)}$$
$$+ 0.36 \text{ x (Open surgery)} + 0.52 \text{ x (Ostomy)}$$
$$+ 0.82 \text{ x (Previous surgery)} - 0.02 \text{ x (SBO)}$$

Step 5: Model update

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -4.49 - 0.48 \text{ x (BMI } < 18) - 0.58 \text{ x (BMI } 18-25) + 0.52 \text{ x (BMI } > 30)$$
$$+ 1.13 \text{ x (Cirrhosis)} + 0.62 \text{ x (Antiplatelet or Anticoagulant)}$$
$$+ 0.49 \text{ x (Open surgery)} + 0.81 \text{ x (Previous surgery)} + 0.56 \text{ x (Ostomy)}$$

Step 6: Model update

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -5.72 - 0.37 \text{ x (BMI } < 18) - 0.56 \text{ x (BMI } 18-25) + 0.63 \text{ x (BMI } > 30)$$
$$+ 1.09 \text{ x (Age } 45-65) + 1.61 \text{ x (Age } > 65) + 0.93 \text{ x (Cirrhosis)}$$
$$+ 0.69 \text{ x (Immunosuppression)} + 0.46 \text{ x (Open surgery)}$$
$$+ 1.96 \text{ x (Ostomy reversal)} + 0.50 \text{ x (Transfusion)} + 0.96 \text{ x (SSI)}$$

Step 7: Model update

$$\ln\left[\frac{P_{IH}^{+}}{(1-P_{IH}^{+})}\right] = -5.71 - 0.39 \text{ x (BMI } < 18) - 0.57 \text{ x (BMI } 18-25) + 0.64 \text{ x (BMI } > 30)$$
$$+ 1.11 \text{ x (Age } 45-65) + 1.63 \text{ x (Age } > 65) + 0.92 \text{ x (Cirrhosis)}$$
$$+ 0.74 \text{ x (Immunosuppression)} + 0.50 \text{ x (Open surgery)}$$
$$+ 2.06 \text{ x (Ostomy reversal)} + 0.60 \text{ x (Transfusion)}$$