

Computed tomography-based prediction of pancreatitis following biliary metal stent placement with the convolutional neural network



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ABSTRACT

Background and study aims Pancreatitis is a potentially lethal adverse event of endoscopic transpapillary placement of a self-expandable metal stent (SEMS) for malignant biliary obstruction (MBO). Deep learning-based image recognition has not been investigated in predicting pancreatitis in this setting.

Patients and methods We included 70 patients who underwent endoscopic placement of a SEMS for nonresectable distal MBO. We constructed a convolutional neural network (CNN) model for pancreatitis prediction using a series of pre-procedure computed tomography images covering the whole pancreas ($\geq 120,960$ augmented images in total). We examined the additional effects of the CNN-based probabilities on the following machine learning models based on clinical parameters: logistic regression, support vector machine with a linear or RBF kernel, random forest classifier, and gradient boosting classifier. Model performance was assessed based on the area under the curve (AUC) in the receiver operating characteristic analysis, positive predictive value (PPV), accuracy, and specificity.

Results The CNN model was associated with moderate levels of performance metrics: AUC, 0.67; PPV, 0.45; accuracy, 0.66; and specificity, 0.63. When added to the machine learning models, the CNN-based probabilities increased the performance metrics. The logistic regression model with the CNN-based probabilities had an AUC of 0.74, PPV of 0.85, accuracy of 0.83, and specificity of 0.96, compared with 0.72, 0.78, 0.77, and 0.96, respectively, without the probabilities.

Conclusions The CNN-based model may increase predictability for pancreatitis following endoscopic placement of a biliary SEMS. Our findings support the potential of deep learning technology to improve prognostic models in pancreatobiliary therapeutic endoscopy.

Introduction

In parallel with recent advances in high-performance computing technologies, machine learning algorithms have opened opportunities for reliable predictions of clinical outcomes of diseases by modeling linear and nonlinear contributions of and interactions between multiple parameters. Convolutional neural network (CNN)-based image recognition has emerged as a platform of artificial intelligence, which is increasingly utilized as a means of extracting abstract data from a series of medical images in an unbiased fashion [1, 2, 3, 4, 5]. In the field of diagnostic endoscopy for pancreatobiliary diseases, emerging evidence suggests the potential for a computer-assisted diagnosis system based on the CNN platform for endoscopic ultrasound (EUS) images to accurately identify incidental pancreatic cancer [6] or intraductal papillary mucinous neoplasm-derived carcinoma [7]. However, the utility of machine learning algorithms including CNN-based technologies has not been explored in clinical research on interventional endoscopy for pancreatobiliary diseases.

Endoscopic transpapillary deployment of a self-expandable metal stent (SEMS) has been the mainstay of nonsurgical palliative management of distal malignant biliary obstructions (MBOs) [8, 9, 10], given a longer functional time compared with plastic stents [11]. Pancreatitis has been a common adverse event (AE) of this procedure with potentially fatal outcomes [12, 13]. Therefore, a substantial number of studies have investigated risk factors for this AE, including stent mechanical properties, non-pancreatic cancer tumors, and contrast injection to the pancreatic duct during endoscopic retrograde cholangiopancreatography (ERCP) [14, 15, 16, 17]. Given evidence linking baseline morphological features of the pancreas to risk of pancreatitis following endoscopic SEMS placement [18], it is considered that there are ample opportunities for imaging information to facilitate risk prediction. However, the utility of deep learning algorithms (e.g., CNN) for pre-procedure cross-sectional images has not been investigated in this context.

To better predict risk of pancreatitis following endoscopic SEMS placement for nonresectable distal MBO, we developed machine learning-based models using not only clinical parameters but also the probabilities predicted via the CNN model using pre-procedure computed tomography (CT) images. We assessed the predictabilities of the models and examined the potential of CNN-based metrics to increase model performance for prediction of post-ERCP pancreatitis.

Patients and methods

Study design

The current study aimed to construct a CT-based CNN model to predict post-ERCP pancreatitis following endoscopic SEMS placement for nonresectable distal MBO and evaluated the additive effect of the CNN-based probabilities on the machine learning models based on clinical parameters (► **Fig. 1a**). We compared the models using the performance metrics including area under the curve (AUC) in the receiver operating character-

istic (ROC) analysis, positive predictive value (PPV), accuracy, and specificity. Given the pilot nature of this feasibility study based on pancreatic morphology, we analyzed a single type of SEMS placed for nonresectable distal MBO (WallFlex; Boston Scientific, Massachusetts, United States) to exclude the possibility of differential pancreatitis risks by stent mechanical properties [17, 19]. This SEMS was one of the widely used SEMSs worldwide during the study period, and its properties and clinical outcomes were well documented [20, 21, 22].

Informed consent for research use of the data was obtained from all participants on an opt-out basis given the retrospective nature of the study. This study was designed and conducted according to the guidelines in the Helsinki Declaration (the latest version updated in 2013). The study was approved by the Ethics Committee at The University of Tokyo (Tokyo, Japan; approval number, #2058).

Study population

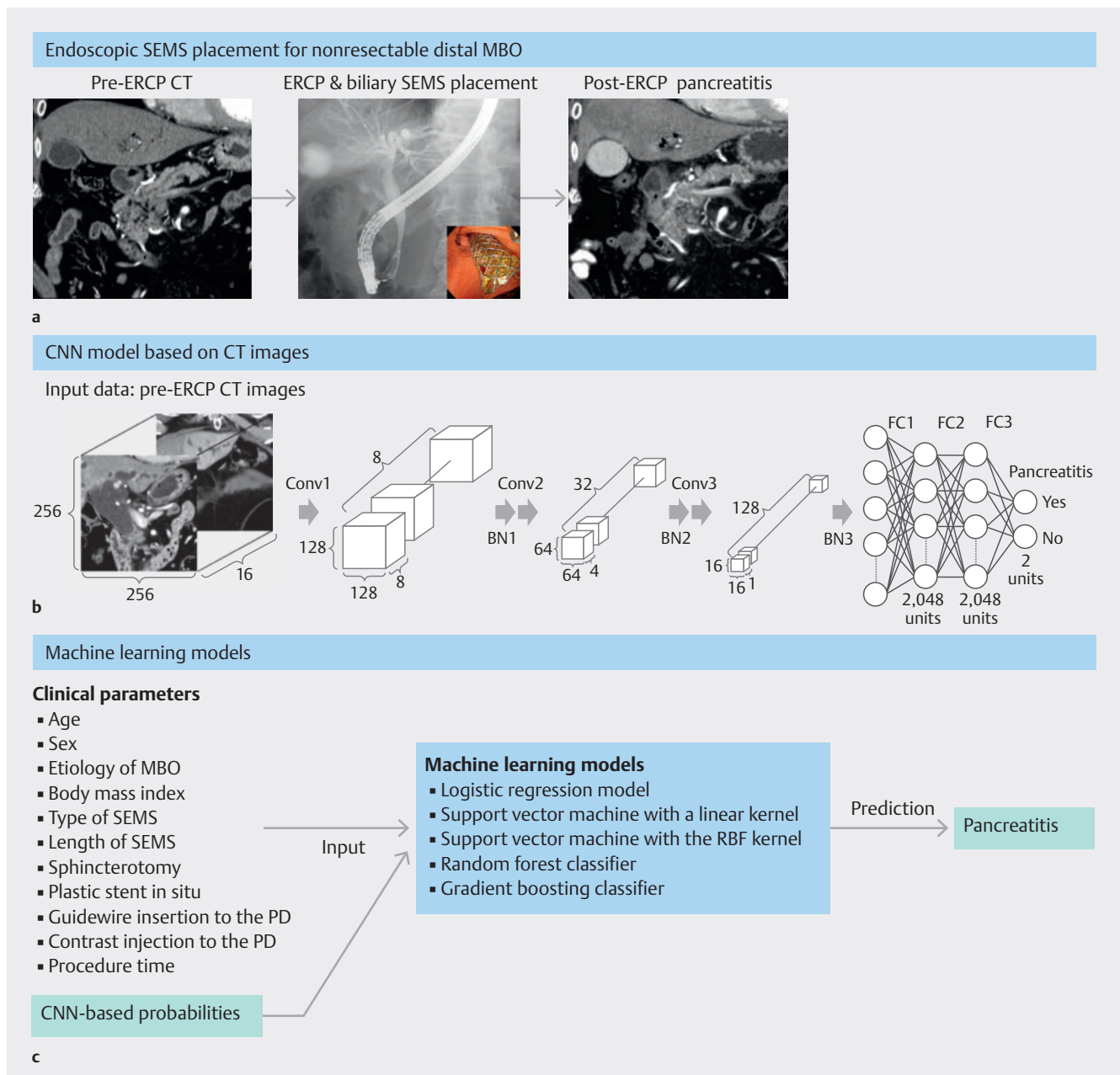
We screened consecutive patients who received initial SEMS placement for nonresectable distal MBO at The University of Tokyo Hospital (Tokyo, Japan) between March 2009 and March 2021 (► **Fig. 2**). We only included cases with available stent-native CT images. We excluded patients with a history of biliary SEMS placement and patients without available CT images. Distal MBO was defined as a malignant biliary stricture located ≥ 2 cm from communication of the bilateral hepatic ducts. All SEMS placement procedures were conducted on an inpatient basis, and the patients were followed every 2 to 4 weeks after discharge on an outpatient basis and through telephone interviews by study physicians until death or June 30, 2023, whichever came first.

Assessment of post-ERCP pancreatitis

The primary study endpoint was post-ERCP pancreatitis following biliary SEMS placement, which was defined as follows: 1) new or worsened abdominal pain; 2) prolonged hospitalization for at least 2 days; and 3) an elevated level of serum amylase (above three times the upper limit of normal), measured > 24 hours after ERCP [23, 24]. We routinely evaluated serum levels of amylase and pancreatic amylase 3 hours after ERCP and the following day. When pancreatitis was suspected based on clinical symptoms (e.g., abdominal pain, nausea) or blood tests, abdominal CT was conducted. We included pancreatitis events occurring within 14 days of the index ERCP procedure. Pancreatitis severity was graded according to the American Society of Gastrointestinal Endoscopy lexicon guidelines [25].

Endoscopic procedures

SEMSs were deployed via ERCP in a standard manner [26]. Cholangiography along with intraductal ultrasonography was performed to assess the status of biliary stricture and confirm the absence of accessory bile ducts. Sphincterotomy was carried out at the discretion of the endoscopist [27]. SEMSs were placed with the distal end being 5 to 10 mm in the duodenum. Prophylactic nonsteroidal anti-inflammatory drugs were not used routinely because the medications had not been approved for this indication during the study period in Japan. A prophy-



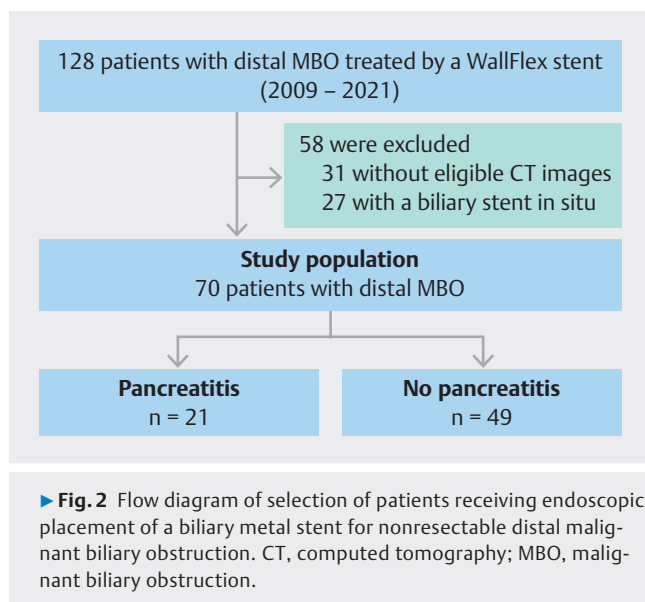
► **Fig. 1** Schematic overview of the current study. **a** Clinical scenario of endoscopic placement of a SEMS for nonresectable distal MBO. **b** Simplified structure of the CNN model. The CNN model based on pre-procedure CT images was constructed to calculate the predicted probabilities for post-ERCP pancreatitis. **c** Machine learning models for the prediction of post-ERCP pancreatitis. BN, batch normalization; CNN, convolutional neural network; Conv, convolutional layer; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; FC, fully connected layer; MBO, malignant biliary obstruction; PD, pancreatic duct; RBF, radial basis function; SEMS, self-expandable metal stent.

lactic pancreatic duct stent was not placed in any of the patients. Procedure time was defined as the duration from the insertion to withdrawal of an endoscope.

CNN model based on pre-procedure CT images

The deep CNN model was constructed using a series of pre-procedure CT images of the pancreas as input data (the model structure is summarized in ► **Fig. 1b**). The study population ($n = 70$) was randomly split into five groups ($n = 14$ each) with the number of pancreatitis cases balanced between the groups. We

trained the CNN model in a combined cohort of four groups and computed predictive probabilities of post-ERCP pancreatitis for each case in the remaining group. This procedure was repeated using each of the five groups as a validation set. A study radiologist (K.Y.) blinded to other clinical data conducted the image processing and model construction. The CNN models were constructed using Python (version, 3.8; Python Software Foundation, Wilmington, Delaware, United States) and the Chainer library. Image processing (i.e., cropping and augmentation) was performed using the Pillow library.



Contrast-enhanced (late arterial-phase) coronal-plane CT images (384 × 384 pixels) were extracted in the DICOM (Digital Imaging and Communications in Medicine) format. For each case, a consecutive series of 16 images (2 mm thick) covering the pancreas were selected, and 256 × 256 pixels well delineating the pancreatic parenchyma with the pancreatic duct were cropped from each image. Therefore, the shape of the input data for the CNN model was 256 × 256 × 16 pixels. The CNN model consisted of three convolutional layers and three batch normalizations, followed by three fully connected layers. The number of kernels for the convolutional layers were 8, 32, and 128. At each convolutional layer, 3 × 3-pixel kernels were convolved with a slide of two pixels for the first two convolutional layers and four pixels for the last convolutional layer, and the zero-padding. The number of units for the fully connected layers were 2,048, 2,048, and 2. Other hyperparameters used in the CNN model were as follows: optimizer, AdaGrad; error function, softmax cross entropy; batch size, 20; and the number of epochs, 20. The image data in the training process were augmented: i. e., parallel-shifted, rotated, flipped, contrast-changed, or brightness-changed images were generated for each original image (≥ 1,728 augmented images per case and ≥ 120,960 images in total).

Statistical analyses including other machine learning models

We utilized five machine learning algorithms that have been extensively validated and widely used for prediction of clinical outcomes of diseases [28, 29]: i. e., the logistic regression model, support vector machine (SVM) with a linear or radial basis function (RBF) kernel, random forest classifier, and gradient boosting classifier (► **Fig. 1c**). For the logistic regression model and SVM with a linear kernel, continuous variables were standardized. We assessed the importance of variables in a random forest classifier including the following variables: age (continuous), sex (male vs. female), etiology of MBO (pancreatic cancer

vs. bile duct cancer vs. lymph node metastasis), body mass index (BMI, continuous), SEMS type (fully covered vs. partially covered vs. uncovered), SEMS length (continuous), endoscopic sphincterotomy (not performed vs. performed during a previous session vs. performed during the index session), a plastic stent in situ (absent vs. present), number of guidewire insertions to the pancreatic duct (continuous), contrast injection to the pancreatic duct (absent vs. present), and procedure time (continuous) as well as CNN-based probabilities. In addition to the CNN-based probabilities, we selected four variables with the highest feature importance for the final models: i. e., BMI, procedure time, age, and MBO etiology (**Supplementary Fig. 1**). We confirmed that inclusion of the whole set of covariates did not improve model performance (data not shown). Hyperparameters were determined using the grid search with 5-fold cross-validation (**Supplementary Table 1**). With a leave-one-out cross-validation, we computed the predicted probability of post-ERCP pancreatitis for each case in all models. Using the optimal threshold of probability determined based on the Youden index, we calculated performance metrics for the models. In secondary analyses, we assessed model performance stratified by BMI levels (which exhibited the highest feature importance) or other relevant parameters. All machine learning analyses were conducted using Python 3.11 and the Scikit-learn and xgboost libraries.

To compare clinical characteristics between patients with and without post-ERCP pancreatitis, we used Student's *t*-test for continuous variables and the chi-square or Fisher's exact test, as appropriate, for categorical variables. Two-sided *P* < 0.05 was considered statistically significant. Given multiple comparisons, the results were interpreted cautiously. These statistical analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, North Carolina, United States).

Results

Among 70 patients with available coronal-plane images of pre-procedure CT, 21 patients (30%) developed post-ERCP pancreatitis with mild, moderate, and severe grades in 14, six, and one patient(s), respectively (► **Fig. 2**). **Supplementary Table 2** summarizes treatment and outcomes of patients with moderate- or severe-grade pancreatitis. Compared with patients with no pancreatitis, patients with pancreatitis were more likely to have higher BMI and non-pancreatic cancer as an etiology of distal MBO (► **Table 1**).

In an analysis of the CNN-based probabilities, PPV, accuracy, and specificity were 0.45, 0.66, and 0.71, respectively (► **Table 2**). In the ROC analysis, the CNN-based probabilities yielded an AUC of 0.67. When integrated into machine learning models, the CNN-based probabilities were associated with higher model performance (► **Table 2**). Taking an example of the logistic regression model yielding the largest AUC value based only on clinical parameters, the addition of the CNN-based probabilities was associated with increases in AUC (0.72 to 0.74), PPV (0.78 to 0.85), and accuracy (0.77 to 0.83). However, the addition resulted in no increase in specificity. The ROC curves are illustrated in **Supplementary Fig. 2**. In contrast, the addition of

► **Table 1** Demographic and procedure characteristics of patients receiving endoscopic placement of a biliary metal stent for nonresectable distal malignant biliary obstruction, overall or by the presence of post-procedure pancreatitis.

Characteristic*	Post-ERCP pancreatitis			P
	All cases	Absent	Present	
	(n = 70)	(n = 49)	(n = 21)	
Demographics				
Mean age ± SD, years	68.1 ± 11.1	69.0 ± 10.7	66.0 ± 11.8	0.30
Sex				0.53
▪ Male	36 (51%)	24 (49%)	12 (57%)	
▪ Female	34 (49%)	25 (51%)	9 (43%)	
Cause of biliary obstruction				0.011
▪ Pancreatic cancer	65 (93%)	48 (98%)	17 (81%)	
▪ Bile duct cancer	3 (4.3%)	0	3 (14%)	
▪ Lymph node metastasis	2 (2.9%)	1 (2.0%)	1 (4.8%)	
Mean body mass index ± SD, kg/m ²	21.5 ± 3.4	20.9 ± 2.9	23.0 ± 3.9	0.015
Procedure characteristics				
Type of SEMS				0.61
▪ Fully covered	47 (67%)	31 (63%)	16 (76%)	
▪ Partially covered	21 (30%)	16 (33%)	5 (24%)	
▪ Uncovered	2 (2.9%)	2 (4.1%)	0	
Length of SEMS				0.15
▪ 40 mm	4 (5.7%)	1 (2.0%)	3 (14%)	
▪ 60 mm	35 (50%)	26 (53%)	9 (43%)	
▪ 80 mm	31 (44%)	22 (45%)	9 (43%)	
Diameter of SEMS				NA
▪ 10 mm	70 (100%)	49 (100%)	21 (100%)	
Endoscopic sphincterotomy				0.82
▪ No	10 (14%)	7 (14%)	3 (14%)	
▪ Yes (during a previous session)	23 (33%)	15 (31%)	8 (38%)	
▪ Yes (during the index session)	37 (53%)	27 (55%)	10 (48%)	
Plastic stent in situ				0.79
▪ Absent	35 (50%)	25 (51%)	10 (48%)	
▪ Present	35 (50%)	24 (49%)	11 (52%)	
Guidewire insertion to the PD				0.21
▪ None	48 (69%)	36 (73%)	12 (57%)	
▪ 1–5 times	17 (24%)	11 (22%)	6 (29%)	
▪ 6–10 times	5 (7.1%)	2 (4.1%)	3 (14%)	
PD injection				0.16
▪ Absent	58 (83%)	43 (88%)	15 (71%)	
▪ Present	12 (17%)	6 (12%)	6 (29%)	
Median procedure time (IQR), minutes	33 (20–53)	35 (25–50)	26 (18–57)	0.61

► **Table 1** (Continuation)

Characteristic ^a	Post-ERCP pancreatitis			P
	All cases	Absent	Present	
	(n = 70)	(n = 49)	(n = 21)	
Prophylactic rectal diclofenac				0.30
▪ Absent	69 (99%)	49 (100%)	20 (95%)	
▪ Present	1 (1.4%)	0	1 (4.8%)	

^aPercentage indicates the proportion of cases with a specific characteristic in all cases or each stratum of post-ERCP pancreatitis. Total percentages may not equal 100% due to rounding.
ERCP, endoscopic retrograde cholangiopancreatography; IQR, interquartile range; NA, not available; PD, pancreatic duct; SD, standard deviation; SEMS, self-expandable metal stent.

► **Table 2** Performance metrics of the models for prediction of pancreatitis following endoscopic placement of a biliary metal stent, with or without convolutional neural network (CNN)-based probabilities.

Model	Performance metric			
	AUC ^a	PPV	Accuracy	Specificity
CNN-based probabilities	0.67	0.45	0.66	0.63
Model without CNN-based probabilities				
▪ Logistic regression model	0.72	0.78	0.77	0.96
▪ Support vector machine (linear kernel)	0.72	0.78	0.77	0.96
▪ Support vector machine (RBF kernel)	0.59	1.00	0.79	1.00
▪ Random forest classifier	0.64	0.55	0.73	0.82
▪ Gradient boosting classifier	0.68	0.53	0.71	0.84
Model with CNN-based probabilities				
▪ Logistic regression model	0.74	0.85	0.83	0.96
▪ Support vector machine (linear kernel)	0.71	0.82	0.80	0.96
▪ Support vector machine (RBF kernel)	0.59	1.00	0.79	1.00
▪ Random forest classifier	0.65	0.53	0.71	0.84
▪ Gradient boosting classifier	0.67	0.56	0.73	0.84

^aThe AUC values were calculated using the receiver operating characteristic analysis.
AUC, area under the curve; CNN, convolutional neural network; PPV, positive predictive value; RBF, radial basis function.

the CNN-based probabilities was not associated with higher performance of the other machine learning models for prediction of post-ERCP pancreatitis (► **Table 2**).

We conducted secondary analyses stratified by the parameters that might affect risk of post-ERCP pancreatitis. Compared with patients with lower BMI, patients with higher BMI were more likely to experience post-ERCP pancreatitis (40% vs. 20%, respectively; $P = 0.068$). In an analysis stratified by BMI levels (► **Table 3**), the logistic regression model was associated with the highest AUC in the ROC analysis in both strata (0.70 and 0.68 for low and high levels of BMI, respectively). In the logistic

regression model, all performance metrics examined were higher in the BMI-low group than in the BMI-high group. In an analysis stratified by age (**Supplementary Table 3**) or presence of a plastic stent in situ (**Supplementary Table 4**), the logistic regression model yielded the highest AUC in the ROC analysis in generally high-risk patients (i.e., younger patients and patients without a plastic stent) but not in low-risk patients. In addition, an analysis limited to covered SEMS yielded consistent results with the highest AUC in the ROC analysis in the logistic regression model (**Supplementary Table 5**).

► **Table 3** Performance metrics of the models with convolutional neural network-based probabilities for prediction of pancreatitis following endoscopic placement of a biliary metal stent, stratified by body mass index.

Model	Performance metric			
	AUC [*]	PPV	Accuracy	Specificity
Body mass index, low (n = 35)[†]				
▪ Logistic regression	0.70	1.00	0.86	1.00
▪ Support vector machine (linear kernel)	0.59	0.67	0.83	0.96
▪ Support vector machine (RBF kernel)	0.13	1.00	0.86	1.00
▪ Random forest classifier	0.45	0	0.74	0.93
▪ Gradient boosting classifier	0.51	0	0.77	0.96
Body mass index, high (n = 35)[†]				
▪ Logistic regression	0.68	0.58	0.66	0.76
▪ Support vector machine (linear kernel)	0.62	0.55	0.63	0.76
▪ Support vector machine (RBF kernel)	0.31	0.80	0.69	0.95
▪ Random forest classifier	0.67	0.54	0.63	0.71
▪ Gradient boosting classifier	0.62	0.47	0.57	0.62

^{*}The AUC values were calculated using the receiver operating characteristic analysis.

[†]Body mass index was dichotomized at the median value.

AUC, area under the curve; PPV, positive predictive value; RBF, radial basis function.

Discussion

In a consecutive series of patients with nonresectable distal MBO managed via endoscopic SEMs placement, the CNN-based profiling of pre-procedure CT images provided a modest predictive ability for post-ERCP pancreatitis. Adding the CNN-based probabilities to machine learning models resulted in increases in performance metrics (e.g., PPV and accuracy) without a decrease in specificity. The findings appeared to be robust in subpopulations classified by the most influential factor BMI. Our data support the potential for unbiased information extraction via the deep learning algorithm in facilitating prediction of post-ERCP pancreatitis in this patient population.

Utilizing pre-procedure CT images of pancreatic morphology under the deep CNN framework, we attempted to better predict risk of post-ERCP pancreatitis associated with endoscopic SEMs placement for distal MBO. In an investigation using pre-procedure CT images [18], estimated volume of the pancreatic parenchyma was well correlated with risk of post-ERCP pancreatitis in this setting. Using axial-plane CT images, the researchers manually measured the thickness of the pancreatic parenchyma (excluding the main pancreatic duct) at three pre-specified pancreatic regions and found a positive association of the sum of the thickness values with pancreatitis risk. Despite its simplicity, this approach was limited by bias due to the non-automated and thus operator-dependent measurement. The CNN captures the morphological information about the pan-

creatic ductal system, parenchymal texture, and pancreatic nodularity in a comprehensive unbiased fashion. Contrast-enhanced CT is routinely examined before biliary SEMs placement to evaluate the location and resectability of MBO and exclude the possibility of an accessory hepatic duct, and therefore, data on CT images are readily available in clinical practice. Therefore, predictive models via a deep learning approach for CT images may characterize risk of post-ERCP pancreatitis at no additional material cost in contrast to biomarker-based prediction approaches. Our data suggest that CNN-based probabilities per se may only provide a modest predictive ability for post-ERCP pancreatitis. However, in some of the widely utilized machine learning models, CNN-based probabilities contributed to reasonable model performance, working synergistically with relevant clinical parameters. Taken together, there may be ample opportunities for CNN-based pattern recognition to facilitate our prediction of post-ERCP pancreatitis.

Post-ERCP pancreatitis has been associated with substantial morbidity and mortality among patients receiving endoscopic biliary interventions [12, 13]; therefore, a large number of studies have investigated clinical parameters as potential risk factors as well as preventive measures for this procedure-related AE [30]. Risk stratification based on factors related to patients, procedures, and operators would help personalize peri-procedure care for patients receiving the treatment. Preventive measures (e.g., prophylactic pancreatic stent, nonsteroidal anti-inflammatory drugs, and hydration [31]) can be undertak-

en for patients who are predicted to be at high risk of developing post-ERCP pancreatitis. In randomized controlled trials of patients with nonresectable distal MBO [32,33], researchers have demonstrated the feasibility of EUS-guided choledochoduodenostomy using a lumen-apposing metal stent with a higher technical success rate and comparable stent patency compared with ERCP-based SEMS placement. During EUS-guided drainage, the mechanical burden on the pancreatic ductal system and resultant pancreatic inflammation may be minimized. Given the risks of specific AEs associated with EUS-guided drainage (e.g., bile leak), further research is warranted to determine the most appropriate drainage strategy for patients with distal MBO overall. Nonetheless, EUS-guided drainage may be a reasonable alternative to endoscopic transpapillary drainage in patients who are predicted to be at high risk of post-ERCP pancreatitis based on the CNN-based pipeline. Further research is warranted to optimize drainage strategies for distal MBO according to the CNN-based risk prediction for post-ERCP pancreatitis. A much larger number of patients receive ERCP for various indications, and prevention of post-ERCP pancreatitis in this population may have a substantial impact on burdens to patients and the health care system. Therefore, the utility of CNN-based stratification of risk of post-ERCP pancreatitis should be investigated in patients receiving ERCP overall. In addition, scoring systems based on different sets of clinical parameters from the current study have been reported for prediction of post-ERCP pancreatitis [34,35]. Therefore, future research is warranted to investigate whether integration of deep learning-based image recognition with these scoring systems improves predictive ability.

We acknowledge the potential limitations of the current investigation. First, we analyzed a single type of SEMS with the same diameter. This inclusion criterion excluded the influence of differential risks of post-ERCP pancreatitis associated with mechanical properties of the SEMSs [17,19] while allowing us to focus on clinical parameters and morphological signatures of the pancreas in risk stratification of post-ERCP pancreatitis. Nonetheless, external validation including various types of SEMSs is required to ensure the generalizability of our conclusions. Second, despite our extensive efforts in data augmentation during construction of the CNN model, the small sample size of the total study population might limit the robustness of our findings. In the machine learning models (e.g., SVM), the small sample size of cases and events compared with the number of variables might result in model overfitting, thereby reducing the predictive abilities in the validation sets. Therefore, further investigation of the machine learning models using multicenter data with an external test set is desirable.

Conclusions

In conclusion, the deep CNN model based on pre-procedure CT images appeared to synergize with clinical parameters in risk stratification for pancreatitis following endoscopic SEMS placement for nonresectable distal MBO. There may be opportunities for the deep learning platform to contribute to refinement

of prognostic models in therapeutic endoscopy for pancreaticobiliary diseases.

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T.H. and K.Y. contributed equally as co-first authors.

Conflict of Interest

Y.N. and H.I. receive research funding and honoraria from Boston Scientific Japan. This work was not funded by this company. No other conflicts of interest exist. The other authors declare that they have no conflicts of interest.

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