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Machine learning improves early prediction of organ failure in hyperlipidemia acute pancreatitis using clinical and abdominal CT features

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A B S T R A C T

Background: This study aimed to investigate and validate machine-learning predictive models combining computed tomography and clinical data to early predict organ failure (OF) in Hyperlipidemic acute pancreatitis (HLAP).
Methods: Demographics, laboratory parameters and computed tomography imaging data of 314 patients with HLAP from the First Affiliated Hospital of Wenzhou Medical University between 2017 and 2021, were retrospectively analyzed. Sixty-five percent of patients (n = 204) were assigned to the training group and categorized as patients with and without OF. Parameters were compared by univariate analysis. Machine-learning methods including random forest (RF) were used to establish model to predict OF of HLAP. Areas under the curves (AUCs) of receiver operating characteristic were calculated. The remaining 35% patients (n = 110) were assigned to the validation group to evaluate the performance of models to predict OF.
Results: Ninety-three (45.59%) and fifty (45.45%) patients from the training and the validation cohort, respectively, developed OF. The RF model showed the best performance to predict OF, with the highest AUC value of 0.915. The sensitivity (0.828) and accuracy (0.814) of RF model were both the highest among the five models in the study cohort. In the validation cohort, RF model continued to show the highest AUC (0.820), accuracy (0.773) and sensitivity (0.800) to predict OF in HLAP, while the positive and negative likelihood ratios and post-test probability were 3.22, 0.267 and 72.85%, respectively.
Conclusions: Machine-learning models can be used to predict OF occurrence in HLAP in our pilot study. RF model showed the best predictive performance, which may be a promising candidate for further clinical validation.

1. Introduction

Acute pancreatitis (AP) is an abdominal emergency characterized by acute attack and rapid deterioration. Hyperlipidemia is currently the third leading cause of acute pancreatitis, following gallstones and alcohol abuse [1,2]. The incidence of Hyperlipidemia AP (HLAP) is growing during the decades [3]. Compared with non-HLAP, HLAP has a worse mortality [4] and progress more frequently and rapidly to necrotizing pancreatitis and Organ failure (OF) [5].

OF is a severe complication in about 20% of AP patients. It is a hallmark manifestation in mild severe AP (MSAP) and severe AP (SAP), which increased the mortality rate to as high as 30% [6]. Currently, there is no robust parameter to predict the clinical

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outcome of AP before the occurrence of. Therefore, it is of clinical significance to find a predictive models for OF at early time, thus ensuring more intensive care and corresponding intervention.

HLAP was defined in AP patients when the serum TGs >11.3 mmol/L; or milky serum with 5.65 ≤ TGs ≤11.3 mmol/L [7]. Excessive TG is the key driver in the pathogenesis of HLAP. Some studies have indicated that obesity is associated with the poor prognosis of AP [8], while radiological parameters of body composition are associated with the severity of the disease. Multiple studies have confirmed that HLAP patients with high visceral adipose tissue (VAT) correlate with high incidence of, MOF syndrome, and even death [9]. Adiposity distribution is linked to the occurrence of SAP in AP patients [10]. Although mostly not needed to establish the diagnosis of AP, abdominal computed tomography (CT) is commonly ordered early on for suspected AP in some hospitals to rule out other acute abdomen. CT can also reliably assess fat distribution and delineate adipose tissues. However, few studies have evaluated the performance of lipid metabolism-related clinical data in combination with CT features to predict OF in HLAP in the Chinese population.

The modified Marshall grading system has been suggested to evaluate severity of in AP [11]. The Ranson score, and the Acute Physiology and Chronic Health Evaluation II (APACHE II), showed only modest value of predicting potential OF. However, these scoring systems are based on parameters dynamically accessed in clinic and are cumbersome to calculate [11]. Therefore, there is unmet need to develop an effective and simplified method that can reliably predict OF in the early phase.

The application of machine learning algorithms (MLAs) has enabled the analyses of a larger number of predictors, and is advantageous to establish more optimal models as compared to traditional methods. The aim of this study was to develop and validate a robust MLA to predict the development of in patients with an episode of HLAP from a larger number of predictors that include lipid metabolism-related clinical and abdominal CT features.

2. Methods

2.1. Patients

The complete clinical data from the 314 patients with HLAP , who were admitted to First Affiliated Hospital of Wenzhou Medical University between July 2017 and August 2021,were retrospectively analyzed. Revised Atlanta Definitions of AP was employed to diagnose AP [11]. HLAP was defined in AP patients when the serum TGs >11.3 mmol/L; or milky serum with 5.65 ≤ TGs ≤11.3 mmol/L, with no other known etiology of AP. Confirmed HLAP patients who had undergone abdominal CT investigation in 72 h upon abdominal pain were included in our study. Those patients with poor abdominal CT imaging, with known etiology of AP (biliary, alcoholic, autoimmune, etc.), or being concomitant with liver cirrhosis, pancreatic cancer, coagulation system disease or pregnancy, were excluded. The design of our study has been approved by the ethics committee of the First Affiliated Hospital of Wenzhou Medical University (KY2019–011).

2.2. Data extraction

Clinical features and laboratory results upon the admission were obtained from the Electronic Health Record System (Table 1). The levels of TGs, white blood cells (WBC), C-reactive protein (CRP), albumin and calcium were categorized as high and low, using 22.4 mmol/L, 12 × 10^9/L, 90 mg/L, 35 g/L and 2 mmol/L as the cutoffs, respectively [12]. Systematic inflammatory response syndrome (SIRS), Ranson, APACHE II, BISAP and scorings were evaluated when feasible.

Table 1
Univariate analysis of clinical characteristics associated with OF in HLAP in the training cohort.

Characteristics	OF Group	Non-OF Group	*P* value
General information			
No. of patients [n(%)]	93(45.6)	111(54.4)	
Sex [n(%)]			0.086
male	66(71.0)	89(80.2)	
Age [years, n(%)]			0.096
≥40	40(43.0)	59(53.2)	
BMI [n(%)]			0.069
≥25	49(52.7)	71(64)	
Laboratory examination			
TG (μmol/L)			**< 0.001**
≥ 22.4	42(45.2)	21(18.9)	
WBC (× 10^9/L)			0.148
≥ 12	62(66.7)	65(58.6)	
CRP (mg/L)			0.494
≥ 90	58(62.4)	68(61.3)	
Abumin (g/L)			**<0.001**
<35	58(62.4)	25(22.5)	
Calcium (mmol/L)			**<0.001**
<2	54 (58.1)	11(9.9)	
HDL-C (mmol/L)	0.53 (0.40–0.67)	0.68 (0.58–0.85)	**<0.001**
LDL-C (mmol/L)	1.92 (1.52–2.75)	2.17 (1.73–2.99)	0.058
Apo-AI (g/L)	0.79 (0.68–0.89)	0.90 (0.77–1.14)	**<0.001**
Apo-B (g/L)	0.84 (0.44–0.98)	0.84 (0.74–1.21)	**0.008**
Lipoprotein (mg/L)	49.0 (21.0–92.5)	52.0 (33.0–116.0)	**0.020**
Amylase (U/L)	211 (93.5–463.0)	109 (61.0–221.0)	**<0.001**
Lipase (U/L)	334 (167.0–761.5)	210 (112.0–382.0)	**<0.001**

Data were expressed as n (%) or median (interquartile range). P < 0.05 were considered statistically significant and highlighted in bold. Aapo-AI, apolipoprotein AI; apo-B, apolipoprotein B; BMI, body mass index; TG, triglyceride; CRP, customer realized price; HDL-C, high-density lipoprotein cholesterol; HLAP, hyperlipidemia acute pancreatitis; LDL-C, low-density lipoprotein cholesterol; OF, organ failure; WBC, white blood cell.

A total of 224 (71.3%) patients has undergone Contrast-enhanced CT scanning of abdomen due to deterioration of the disease. Parenchymal necrosis and pancreatic collections were assessed by modified CT severity index (MCTSI) in those patients, otherwise by CT severity index (CTSI) with non-enhanced CT scanning. Non-enhanced CT scanning are exploited to assess body composition features. Image J software were used to highlight the muscle and adipose tissue at the transverse plane of third lumbar vertebra [13]. Muscle, subcutaneous fat and VAT were delineated in area from −29 to 150 Hounsfield units (HU), from− 190 to − 30 HU, and from −150 to 50 HU, respectively. The region of interest (ROI) area were evaluated automatically. Waist circumference (WC) was calculated at the navel plane. The visceral adiposity index (VAI), which includes WC, BMI, TG levels and HDL-C, is indicative of visceral adiposity function [14]. The VAI was calculated to be WC(cm)/(39.68 + 1.88 × BMI) × TG/1.03 × 1.31/HDL-C in male, and WC(cm)/(36.58 + 1.89 × BMI) × TG/0.81 × 1.52/HDL-C in female. Fatty liver (FL) was diagnosed when liver to spleen density ratio (L/S) is less than 1.0 in the unenhanced CT scanning, and was further categorized as mild (0.7<L/S < 1.0), moderate (0.5<L/S ≤ 0.7) and severe (L/S ≤ 0.5). Liver spontaneous attenuation was defined as the mean measurements of the liver less than 40 HU in the unenhanced CT images, including one ROI in the left side and two in the right side [15]. The below factors alone or in combination are regarded as liver dysfunction: Serum total bilirubin≥34 μmol/L, and serum alanine aminotransferase level exceeds 2 of the normal value. CT measurements were conducted by two experienced radiologists blinded to the clinical features exploiting a post processing station (GE Healthcare Advantage Workstation, version 4.6).

2.3. Study outcomes

The outcome of the study was the progression of HLAP to OF during hospitalization. The OF was evaluated in the cardiovascular, respiratory, and renal systems. The modified Marshall scoring system, a simple and universally applicable approach that can objectively define disease severity, was employed to determine OF if one of these three organ systems scores more than 2 [11].

2.4. Machine learning model

Patients were randomly assigned to the training cohort (65%) or a validation cohort (35%) using a seed of 45 while the gender and age maintained proportional between these 2 cohorts. Data from the training cohort was aimed to teach the MLAs to determine OF. The validation cohort was a separate data that was used to assess the performance of the trained MLAs. Note that the data in the validation cohort was not included during training of MLAs. Before analyses, the median values were used to replace missing values before the data were standardized. The inputting variables showing significant differences ($p < 0.05$) in univariate analysis were included in the MLAs models to predict the risk of OF in HLAP. Then, GBDT methodology, a process of feature selection, was exploited to capture the most representative features and increase the specificity and sensitivity of prediction. Five MLAs were selected: decision tree (DT), k-nearest neighbors (KNN), logistic regression (LR), naive bayes (NB), and random forest (RF) [16]. The hyperparameters applied in the final RF model were obtained by a 5-fold cross-validation. The n_ estimators, max_ depth, min_ samples split values were 20, 10, and 20, respectively. Finally, the widely used scoring systems, SIRS, Ranson, APACHE II and BISAP , were compared.

2.5. Statistical analysis

Statistical analysis was conducted by SPSS18.0 (IBM. SPSS Statistics for Windows, USA). Continuous variates were compared by two independent samples *t*-test or Mann-Whitney U test, while categorical variates were compared by chi-square test. In order to identify early risk factors of OF-related events in HLAP, univariate logistic regression analyses were exploited to calculate odds ratios (OR) and 95% confidence intervals (CIs). Those variables showing significant correlation with OF were further subjected to MLAs. $P < 0.05$ was considered to be statistically different two groups. ROC curve was depicted to assess the performance of the machine learning model; the sensitivity, specificity, accuracy, positive and negative likelihood ratios, and area under curve (AUC) were also calculated. All statistical analyses were handled with R 3.5.1, Python 3.5.6 and SPSS18.0 (IBM. SPSS Statistics for Windows, USA).

3. Results

3.1. Baseline characteristics

A total of 314 patients with HLAP were included in this study. OF occurred in 143 of the 314 patients (45.54%) in the whole cohort. The 204 HLAP cases assigned to the training sample have 93 (45.59%) patients presenting OF; whereas the 110 HLAP cases in the validation cohort have 50 (45.45%) patients presenting OF. The characteristics of the included HLAP patients in the training sample with and without OF were summarized in Tables 1–2. The age ranged from 10 to 67 years, with a median age of 40 years. 77% of the patients were male and 40% of all the patients were obese ($BMI \geq 25$ kg/m^2). Clinical parameters including TG, albumin, calcium, HDL-C, apo-AI, apo-B, amylase and lipase were significantly different between HLAP patients with and without OF ($P < 0.05$). Abdominal CT features including VAI, fatty liver, liver disfunction and CTSI also showed significant difference between the two groups ($P < 0.05$). Unexpectedly, no statistical differences were observed in the other belly fat signs of CT images between the two groups ($P > 0.05$). Besides, there were no statistical differences in gender, age, and BMI between the two groups ($P > 0.05$).

3.2. Models

With the study sample, the LR, NB, KNN, DT and RF models were established and the AUCs were 0.838, 0.824, 0.853, 0.897, and 0.915, respectively (Fig. 1). RF model showed the highest AUC to predict OF in patients with HLAP, which also had the highest sensitivity (0.828) and accuracy (0.814) among the five models (Table 3). The validation cohort obtained AUCs of 0.806, 0.804, 0.811, 0.807, and 0.820, respectively. The positive likelihood ratios of the LR, NB, KNN, DT and RF models were 3.04, 3.50, 3.046, 3.491 and 3.22, respectively, while the negative likelihood ratios of these modeds were 0.32, 0.375, 0.434, 0.441 and 0.267, respectively. In the validation study, RF model continued to show the highest AUC (0.820), accuracy (0.773) and sensitivity (0.800) to predict OF in HLAP, while the pre-test probability and post-test probability were 45.45% and 72.85%, respectively. The decision curve and precision-recall (PR) curve of the five models are presented in Figs. 2 and 3. The confusion matrix of all the models, except that of NB, performed well. In the GBDT methodology, the most representative features were HDL-C, low calcium, amylase, VAI, apo-AI and lipase. The best feature predictors were HDL-C and Calcium (Fig. 4).

To further assess the accuracy of RF, the new model was compared with the existing scoring systems used in clinics, including SIRS, Ranson, APACHE-II and BISAP in the validation cohort. The ROC curves of SIRS and those scoring systems were shown in Fig. 5. The AUCs of these scoring systems are all significantly lower than the 5 MLAs.

4. Discussion

In this study, we developed several MLAs to predict those HLAP patients who potentially progressed to OF at an early phase. All these five models yielded satisfactory predictive performance. We demonstrated that RF model had the best performance, with an AUC over 0.90 and both specificity and sensitivity over 0.80. Besides, the RF model outperformed the clinical scoring system. These findings showed that the application of an RF model may be advantageous to predict OF in HLAP patients. This may positively trigger more intensive monitoring the disease.

Early recognition of is crucial in the emergent management of AP patients, and has essential impact on the MSAP and SAP patients' immediate and long-term survival. Studies have revealed that patients with HLAP are more likely to progress to OF due to existence of large amount of FFA in serum, which is produced from excessive TG levels through the process of pancrelipase hydrolysis [17]. Meanwhile, OF increases the risk of infected pancreatic necrosis and is associated with a worse mortality rate as high as 30% [18]. The existing approaches to diagnose OF usually take more than 48 h, while some are cumbersome to score and determine. Therefore, there is an unmet need of tools to early predict OF in HLAP patients. Machine-learning techniques are informative approaches and can select the most significant parameters for model construction [19]. Three MLAs had been proposed to predict multiple OF in MSAP and SAP, of which a neural network-based model outperformed support vector machine and LR methods [20]. An artificial neural networks model has also showed highest performance for prediction of in-hospital mortality of AP patients by

Table 2
Univariate analysis of abdominal CT Features associated with OF in HLAP in the training cohort.

CT Features	OF Group ($n = 93$)	Non-OF Group ($n = 111$)	P Value
Belly fat signs			
WC(cm)	90.1 (83.0–101.6)	90.2 (83.9–100.5)	0.927
Muscle area(cm^2)	158.8 (121.0–198.2)	171.4 (143.4–199.5)	0.070
SATA (cm^2)	152.3 (104.1–224.7)	136.1 (93.2–194.2)	0.164
VAFA (cm^2)	166.1 (115.2–255.0)	188.2 (141.3–255.3)	0.130
TATA (cm^2)	302.7 (248.4–370.2)	292.6 (248.0–371.6)	0.983
VAI	64.0 (32.8–217.0)	27.4 (13.0–62.5)	**<0.001**
Liver signs			
Liver CT value (HU)	36.0 (25.0–49.0)	40.0 (32.0–49.0)	0.193
Fatty liver	48(51.6)	35(31.5)	**0.003**
LSA (HU)			0.094
< 40	74(79.6)	97(87.4)	
Liver dysfunction	28(30.1)	20(18.0)	**0.031**
CTSI			**<0.001**
≥ 4	86(92.5)	61(55.5)	

CTSI, CT severity index; HLAP, hyperlipidemia acute pancreatitis; OF, organ failure; SATA, subcutaneous fat area; TATA, total fat area; LSA, liver spontaneous attenuation; VAI, visceral adiposity index; VATA, visceral fat area; WC, waist circumference. Data were expressed as n (%) or median (interquartile range). $P < 0.05$ were considered statistically significant and highlighted in bold.

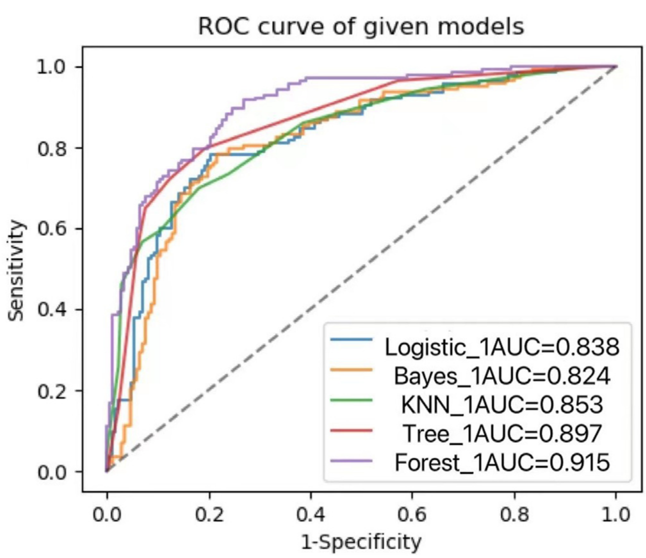

Fig. 1. ROC curve for five machine-learning models to predict the development of organ failure in hyperlipidemic acute pancreatitis. ROC: receiver operating characteristic; AUC, area under the curve. Logistic: logistic regression; Bayes: naive bayes; KNN: k-nearest neighbors; Tree: decision tree; Forest: random forest.

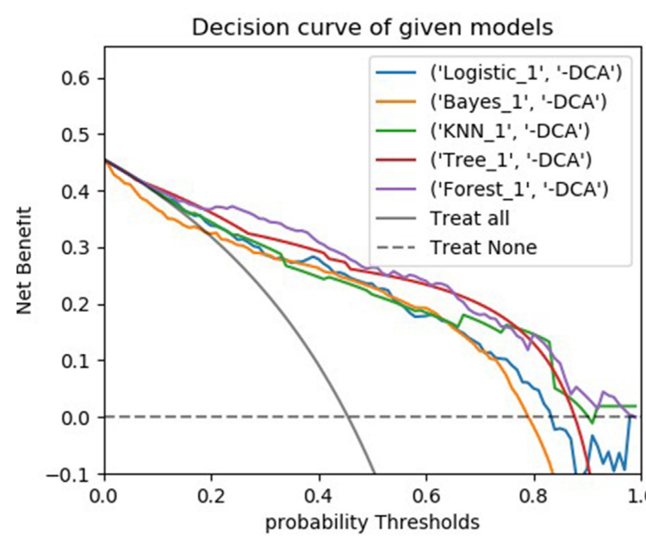

Fig. 2. Decision curve of five machine-learning models to predict the development of organ failure in hyperlipidemic acute pancreatitis. Logistic: logistic regression; Bayes: naive bayes; KNN: k-nearest neighbors; Tree: decision tree; Forest: random forest.

Table 3
The predictive performance of different types of machine learning in OF occurrence in HLAP patients.

Machine learning	AUC	Accuracy	Sensitivity	Specificity	Positive Prediction	Negative prediction	Positive likelihood ratio	Negative likelihood ratio
training cohort								
Logistic regression	0.838	0.804	0.785	0.820	0.785	0.820	4.356	0.262
naive Bayes	0.824	0.784	0.699	0.856	0.802	0,772	4.849	0.352
k-nearest neighbors	0.853	0.784	0.688	0.865	0.810	0.768	5.092	0.361
decision tree	0.897	0.813	0.656	0.982	0.968	0.773	36.403	0.35
random forest	0.915	0.814	0.828	0.802	0.778	0.848	4.177	0.215
validation Cohort								
Logistic regression	0.806	0.755	0.760	0.750	0.717	0.789	3.04	0.32
naive Bayes	0.804	0.755	0.700	0.800	0.745	0.762	3.50	0.375
k-nearest neighbors	0.811	0.727	0.660	0.783	0.717	0.734	3.046	0.434
decision tree	0.807	0.736	0.640	0.817	0.744	0.731	3.491	0.441
random forest	0.820	0.773	0.800	0.750	0.727	0.818	3.22	0.267

AUC, area under curve; HLAP, hyperlipidemia acute pancreatitis; OF, organ failure.

machine learning [21]. In this study, MLAs can also be exploited to predict OF in patients with HLAP at an early phase, which outperformed the complicated score systems. Although remains to be further validated in other centers, this machine learning-based

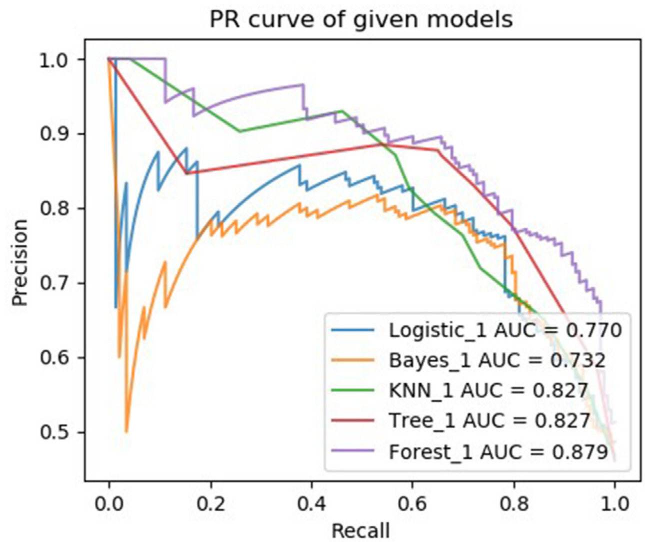

Fig. 3. Precision-recall curve of five machine-learning models to predict the development of organ failure in hyperlipidemic acute pancreatitis. PR: precision-recall; AUC, area under the curve. Logistic: logistic regression; Bayes: naive bayes; KNN: k-nearest neighbors; Tree: decision tree; Forest: random forest.

RF model is suggested by our study to be implemented in clinical settings.

BMI and waist-to-hip ratio have been shown to serve as markers of obesity to predict the severity of HLAP and its complications [22]. Nevertheless, BMI is not able to distinguish trunk obesity from visceral obesity. VAT has been suggested to highly correlate with AP-related OF and necrosis [23]. These findings indicate that fat distribution may play a significant role in the prognosis of HLAP. Xia et al. has found that the VAI is a favorable predictor of the severity of HLAP which outperformed classical indicators including BMI, VAT and WC [24]. This study has identified various lipid metabolism related abdominal CT features, reflecting the close association between fat distribution and OF among HLAP patients. Using sophisticated machine learning methods, we also found that only VAI, a sex-dependent index based on BMI, TG, WC and HDL-C, was associated with OF. The VAI alone achieved the high AUC (0.697) to early predict of HLAP by ROC curves. Thus, VAI can be identified as an applicable indicator to predict OF in HLAP patients in the early stage. Intriguingly, none of other CT parameters of belly fat were entered into the five predicted models for OF in HLAP patients. Our previous study also found no association between lipid metabolism-related body composition and the severity of HLAP [25].

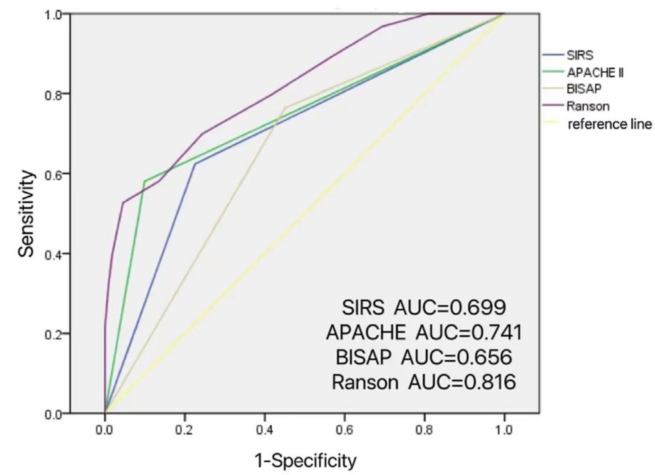

Fig. 5. ROC curve for SIRS, Ranson, APACHE-II and BISAP to predict the development of organ failure in hyperlipidemic acute pancreatitis in the validation cohort. ROC, receiver operating characteristic; AUC, area under the curve.

Our previous research found apo-AI was associated with the severity of HLAP and length of hospital stay [25]. This study also recognized that the effect of apo-AI levels on OF in HLAP. There has been studies showing that the levels of apo-AI, HDL-C, and combinations of apo-AI and scoring systems are valuable predictors of persistent OF in AP [26]. Several parameters, including the HDL-C, calcium and lactate dehydrogenase, have been suggested to

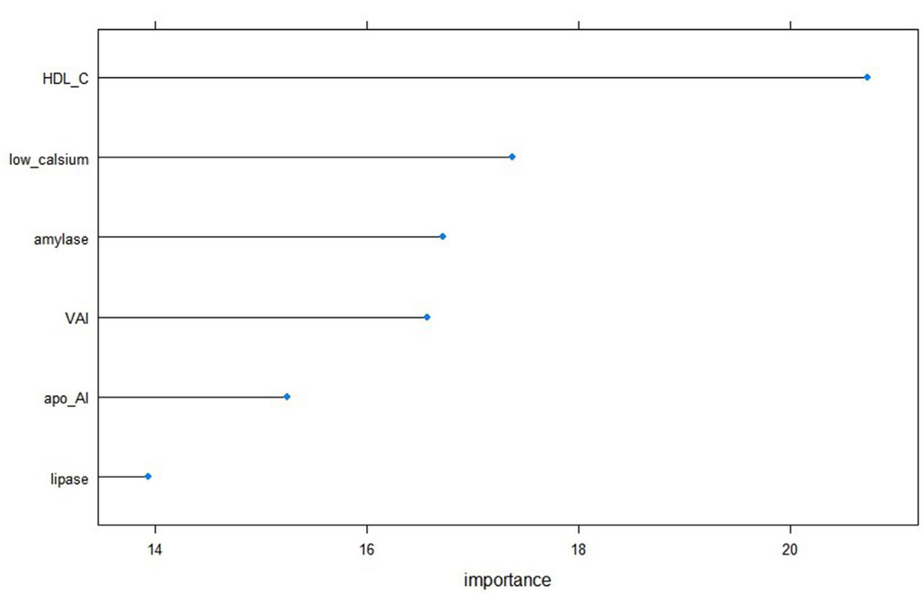

Fig. 4. Feature importance derived from the machine-learning based RF model for predictors for OF in HLAP in the training cohort. RF: random forest; OF: organ failure; HLAP: hyperlipidemia acute pancreatitis.

predict persistent OF in AP [26]. In this study, we found that the five main clinical features for OF prediction were HDL-C, low calcium, amylase, apo-AI and lipase. It is worth noting that the five clinical features were tested in venous blood, which is relatively safe and accessible in HLAP patients. Moreover, the machine-learning technique enable the model to be conducted easily, repeatedly and as early as the blood sample were taken upon admission.

FL is thought to be a hepatic metabolic disorder, and is a growing public health problem worldwide, which is increasingly recognized as an important cause of abnormal liver function tests. Moreover, the problem of hepatocytes being “fatty” also increases the risk for chronic kidney disease, cardiovascular disease, some malignancy and death. It is closely related to metabolic syndrome [27]. Recent study has suggested that liver spontaneous attenuation in CT correlates with the severity of pancreatitis [28]. In the current study, although FL and liver disfunction failed to predict of HLAP in the five predicted models, they were more common in HLAP patients with OF. A high prevalence of hepatic steatosis (260 of 314 patients [82.8%]) and a deeper degree of steatosis in HLAP patients with OF (median CT value 33 HU vs 46 HU, $P = 0.009$) was found. Therefore, more investigation may be of help to determine the predictive role of FL for OF in HLAP.

There were some limitations of the present research. Firstly, the study was designed retrospectively and patients with HLAP were enrolled in a single hospital with a limited sample size. Ethnical and/or regional discrepancy has been suggested in the etiology and epidemiology of HLAP patients [29,30]. Therefore, extensive studies including prospective patients from multiple centers are needed to validate and refine the RF model to predict OF in HLAP patients. Secondly, OF in our study is determined as a binomial factor (present or absent), which cannot differentiate existence of multiple OF or OF grade. This to some extent neglected the dynamic development of. Thirdly, the current study only confines to HLAP patients, while our finding cannot be extended to the AP patients with other etiologies. Lastly, some parameters from the RF model, such as Apo-AI, Apo-B and lipoprotein, may not available in some clinical centers, limiting its wide clinical application.

5. Conclusions

Our study showed that, by exploiting clinical and abdominal CT features, machine learning can be applied to predict of HLAP. As a result, RF model outperformed other models and clinically used scoring systems to predict OF occurrence in HLAP. This RF model may allow the individualized management and implement early interventions in those HLAP patients with high risk of early-stage OF. Besides, machine learning revealed that VAI and apo-AI may serve as novel predictive biomarkers for OF occurrence. Collaborations with multi-centers and prospective studies on HLAP are needed to validate the usefulness of our models and predictors.

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Declaration of competing interest

The authors declare no conflicts of interest.

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Not applicable.

References

[1] Yang AL, McNabb-Baltar J. Hypertriglyceridemia and acute pancreatitis. Pancreatology 2020;20:795–800.
[2] Pothoulakis I, Paragomi P, Archibugi L, Tuft M, Talukdar R, Kochhar R, et al. Clinical features of hypertriglyceridemia-induced acute pancreatitis in an international, multicenter, prospective cohort (APPRENTICE consortium). Pancreatology 2020;20:325–30.
[3] Jin M, Bai X, Chen X, Zhang H, Lu B, Li Y, et al. A 16-year trend of etiology in acute pancreatitis: the increasing proportion of hypertriglyceridemia-associated acute pancreatitis and its adverse effect on prognosis. J Clin Lipidol 2019;13:947–953.e1.
[4] Rashid N, Sharma PP, Scott RD, Lin KJ, Toth PP. All-cause and acute pancreatitis health care Costs in patients with severe hypertriglyceridemia. Pancreas 2017;46:57–63.
[5] Qiu L, Sun RQ, Jia RR, Ma XY, Cheng L, Tang MC, et al. Comparison of existing clinical scoring systems in predicting severity and Prognoses of hyperlipidemic acute pancreatitis in Chinese patients: a retrospective study. Medicine (Baltim) 2015;94:e957.
[6] Schepers NJ, Bakker OJ, Besselink MG, Ahmed Ali U, Bollen TL, Gooszen HG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut 2019;68:1044–51.
[7] Xiang JX, Hu LS, Liu P, Tian BY, Su Q, Ji YC, et al. Impact of cigarette smoking on recurrence of hyperlipidemic acute pancreatitis. World J Gastroenterol 2017;23:8387–94.
[8] Premkumar R, Phillips AR, Petrov MS, Windsor JA. The clinical relevance of obesity in acute pancreatitis: targeted systematic reviews. Pancreatology 2015;15:25–33.
[9] Yashima Y, Isayama H, Tsujino T, Nagano R, Yamamoto K, Mizuno S, et al. A large volume of visceral adipose tissue leads to severe acute pancreatitis. J Gastroenterol 2011;46:1213–8.
[10] Kuan LL, Dennison AR, Garcea G. Association of visceral adipose tissue on the incidence and severity of acute pancreatitis: a systematic review. Pancreatology 2020;20:1056–61.
[11] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[12] Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH, et al. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2012;97:2969–89.
[13] Girish V, Vijayalakshmi A. Affordable image analysis using NIH Image/ImageJ. Indian J Cancer 2004;41:47.
[14] Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, et al. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care 2010;33:920–2.
[15] Zver T, Calame P, Koch S, Aubry S, Vuitton L, Delabrousse E. Early prediction of acute biliary pancreatitis using clinical and abdominal CT features. Radiology 2022;302:118–26.
[16] Zhu Y, Zhang J, Wang G, Yao R, Ren C, Chen G, et al. Machine learning prediction models for Mechanically ventilated patients: analyses of the MIMIC-III database. Front Med 2021;8:662340.
[17] Tsuang W, Navaneethan U, Ruiz L, Palascak JB, Gelrud A. Hypertriglyceridemic pancreatitis: presentation and management. Am J Gastroenterol 2009;104:984–91.
[18] Petrov MS, Shanbhag S, Chakraborty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology 2010;139:813–20.
[19] Balyen L, Peto T. Promising artificial intelligence-machine learning-deep learning algorithms in ophthalmology. Asia Pac J Ophthalmol (Phila) 2019;8:264–72.
[20] Qiu Q, Nian YJ, Guo Y, Tang L, Lu N, Wen LZ, et al. Development and validation of three machine-learning models for predicting multiple organ failure in moderately severe and severe acute pancreatitis. BMC Gastroenterol 2019;19:118.
[21] Ding N, Guo C, Li C, Zhou Y, Chai X. An artificial neural networks model for early predicting in-hospital mortality in acute pancreatitis in MIMIC-III. BioMed Res Int 2021;2021:6638919.
[22] Yang L, Liu J, Xing Y, Du L, Chen J, Liu X, et al. Correlation of body mass index and waist-hip ratio with severity and complications of hyperlipidemic acute pancreatitis in Chinese patients. Gastroenterol Res Pract 2017;2017:6757805.
[23] Natu A, Stevens T, Kang L, Yasinow S, Mansoor E, Lopez R, et al. Visceral adiposity predicts severity of acute pancreatitis. Pancreas 2017;46:776–81.
[24] Xia W, Yu H, Huang Y, Yang Y, Shi L. The visceral adiposity index predicts the severity of hyperlipidaemic acute pancreatitis. Intern Emerg Med 2022;17:417–22.
[25] Chen L, Huang Y, Yu H, Pan K, Zhang Z, Man Y, et al. The association of parameters of body composition and laboratory markers with the severity of hypertriglyceridemia-induced pancreatitis. Lipids Health Dis 2021;20:9.
[26] Zhou CL, Zhang CH, Zhao XY, Chen SH, Liang HJ, Hu CL, et al. Early prediction of persistent organ failure by serum apolipoprotein A-I and high-density lipoprotein cholesterol in patients with acute pancreatitis. Clin Chim Acta 2018;476:139–45.
[27] Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clin Med 2018;18(3):245–50.

[28] Roussey B, Calame P, Revel L, Zver T, Konan A, Piton G, et al. Liver spontaneous hypoattenuation on CT is an imaging biomarker of the severity of acute pancreatitis. Diagn Interv Imaging 2022;103:401–7.
[29] Fan J, Ding L, Lu Y, Zheng J, Zeng Y, Huang C. Epidemiology and etiology of acute pancreatitis in urban and suburban areas in Shanghai: A retrospective study. Gastroenterol Res Pract 2018;2018:1420590.
[30] Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:175–84.