

Supplementary Materials

Supplementary Definition

The definition and severity classification of acute pancreatitis was based on the determinant-based classification¹. Severe acute pancreatitis (SAP) was defined as infected pancreatic necrosis (IPN) or persistent (≥ 48 h) organ failure, and critical acute pancreatitis (CAP) was defined as IPN and persistent (≥ 48 h) organ failure². The criteria for organ failure was defined as a score of 2 or more for 1 of these 3 organ systems (respiratory, cardiovascular, and renal) using the modified Marshall Score². Multiple organ failure (MOF) was defined as the failure of at least 2 organ systems. IPN was defined as the positive culture of pancreatic necrosis or fluid obtained during the first drainage or necrosectomy. Multidrug-resistant organisms (MDRO) infection was defined as microorganisms not susceptible to at least 1 agent in at least 3 microbial categories³. MDROs in this study mainly included Carbapenem-resistant *Acinetobacter baumannii* (CRAB), *Escherichia coli* producing extended-spectrum beta-lactamase (ESBLp), Carbapenem-resistant *Klebsiella pneumoniae* (CRKP), Carbapenem-resistant *Citrobacter freundii*, Carbapenem-resistant *Enterobacter cloacae*, Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), Methicillin-resistant *Staphylococcus aureus* (MRSA). Bloodstream infection (BSI) was defined per modified CDC/NHSN criteria: ≥ 1 positive blood culture for a recognised pathogen, or ≥ 2 sets within 48 h yielding the same common skin commensal from separate venipunctures; candidemia and *S. aureus* bacteraemia required one positive set. Peripancreatic fungal infection was defined as the detection of fungal pathogens (e.g., *Candida* spp.) in peripancreatic fluid or necrotic tissue, confirmed by culture. Hemorrhage was defined as intraabdominal or retroperitoneal massive bleeding requiring radiologic, endoscopic, or surgical intervention. Gastrointestinal fistula was defined as the secretion of digestive juice or fecal material from drains or necrotic tissue cavities confirmed by imaging or during surgery. Pancreatic fistula was defined as the amylase content of fluid obtained from the drains > 3 times the serum amylase level. Complications were defined as having at least one of the following pre-existing conditions: hypertension, diabetes, or coronary heart disease. Step-up approach was defined as percutaneous catheter drainage (PCD) performed as the initial step, followed by minimally invasive retroperitoneal pancreatic necrosectomy (MARPN) if necessary, and open pancreatic necrosectomy (OPN) performed only for cases of uncontrolled infection or lethal complications after minimally invasive interventions. Conversely, the step-down approach prioritized OPN as the first choice of surgical intervention.

The score details of Acute Physiology and Chronic Health Examination II (APACHE II) and Bedside Index of Severity in Acute Pancreatitis (BISAP) were as follows^{4,5}: (1) APACHE II score: It evaluates various physiological parameters, including temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, arterial pH, serum sodium, potassium, creatinine, hematocrit, white blood cell count, and Glasgow Coma Scale score. Scores range from 0 to 71, with higher scores indicating greater severity of illness. Higher scores correlate with increased risk of mortality. (2) BISAP score: It assesses five clinical parameters, including blood urea nitrogen, level > 25 mg/dL, impaired mental status, systemic inflammatory response syndrome, age > 60 years, and presence of pleural effusion. Scores range from 0 to 5, with 1 point assigned for each parameter present. Higher scores indicate increased severity, with scores ≥ 3 associated with higher mortality risk.

Reference

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2. Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis. *Gastroenterology*. Jan 2020;158(1):67-75 e1. doi:10.1053/j.gastro.2019.07.064
3. Cheng G, Wang D, Zhu P, et al. Clinical Characteristics of Acute Pancreatitis Patients with Multidrug-Resistant Bacterial Infection. *Infect Drug Resist*. 2022;15:1439-1447. doi:10.2147/IDR.S354347
4. Larvin M, McMahon MJ. APACHE-II score for assessment and monitoring of acute pancreatitis. *Lancet*. Jul 22 1989;2(8656):201-5. doi:10.1016/s0140-6736(89)90381-4
5. Mederos MA, Reber HA, Girgis MD. Acute Pancreatitis: A Review. *JAMA*. Jan 26 2021;325(4):382-390. doi:10.1001/jama.2020.20317

Supplementary Methods S1. Data encoding and harmonisation

All isolated pathogens were incorporated in constructing the clustering matrix. Per-patient microbiology was encoded as a binary presence with absence matrix (columns, bacterial/fungal taxa; rows, patients). To avoid undefined binary dissimilarities, we removed never-observed taxa (all-zero columns) and patients without any positive isolates (all-zero rows).

Supplementary Methods S2. Dissimilarity and clustering

Pairwise dissimilarities were computed using the Jaccard distance in binary space. We applied agglomerative hierarchical clustering with Ward's minimum-variance linkage on the Jaccard distance matrix. No outcome variables were used during clustering.

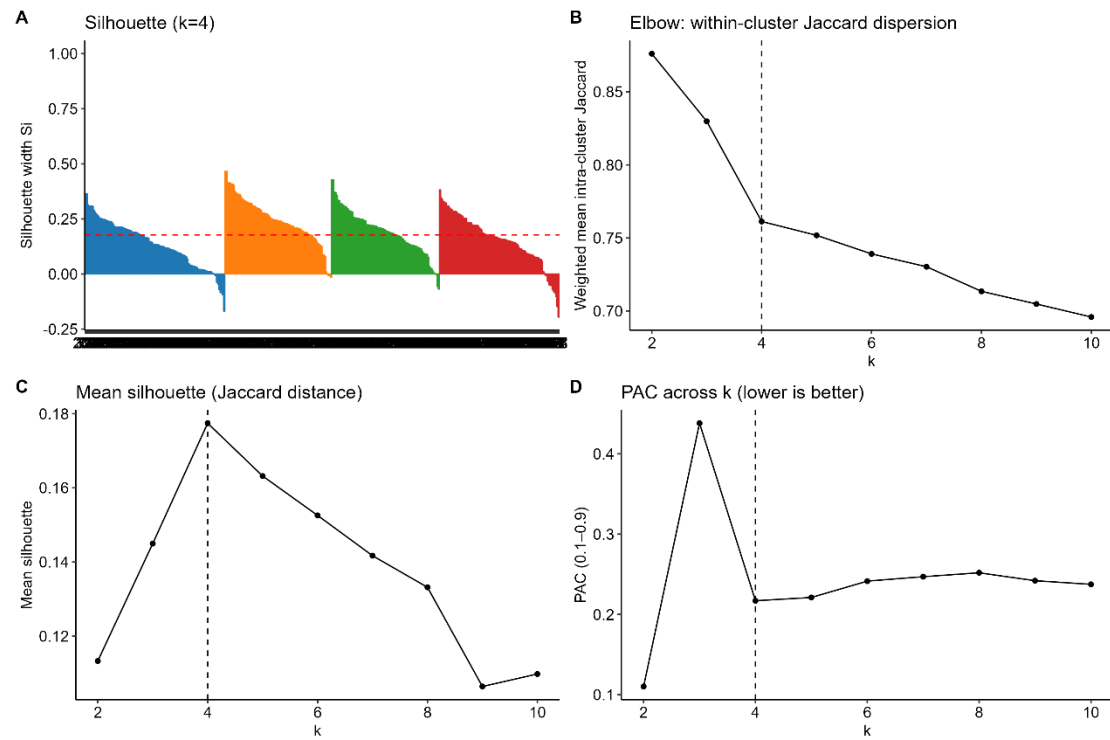
Supplementary Methods S3. Determination of the number of clusters

Candidate k values were prespecified as $k=2-10$. We used three complementary internal criteria, all computed in the Jaccard space: (i) the elbow in within-cluster Jaccard dispersion; (ii) the mean silhouette curve; and (iii) subsampling consensus, with selection favouring the smallest k that satisfied elbow/peak-silhouette/low-ambiguity.

Supplementary Methods S4. Subsampling consensus and PAC

Cluster stability was quantified by subsampling consensus to construct a consensus matrix and compute the proportion of ambiguous clustering (PAC)—the fraction of co-assignments in an intermediate range; lower values indicate greater stability. Subsampling used 80% resamples, repeated 500 times with a fixed random seed. Convergence checks showed negligible change in PAC when increasing iterations (300–800).

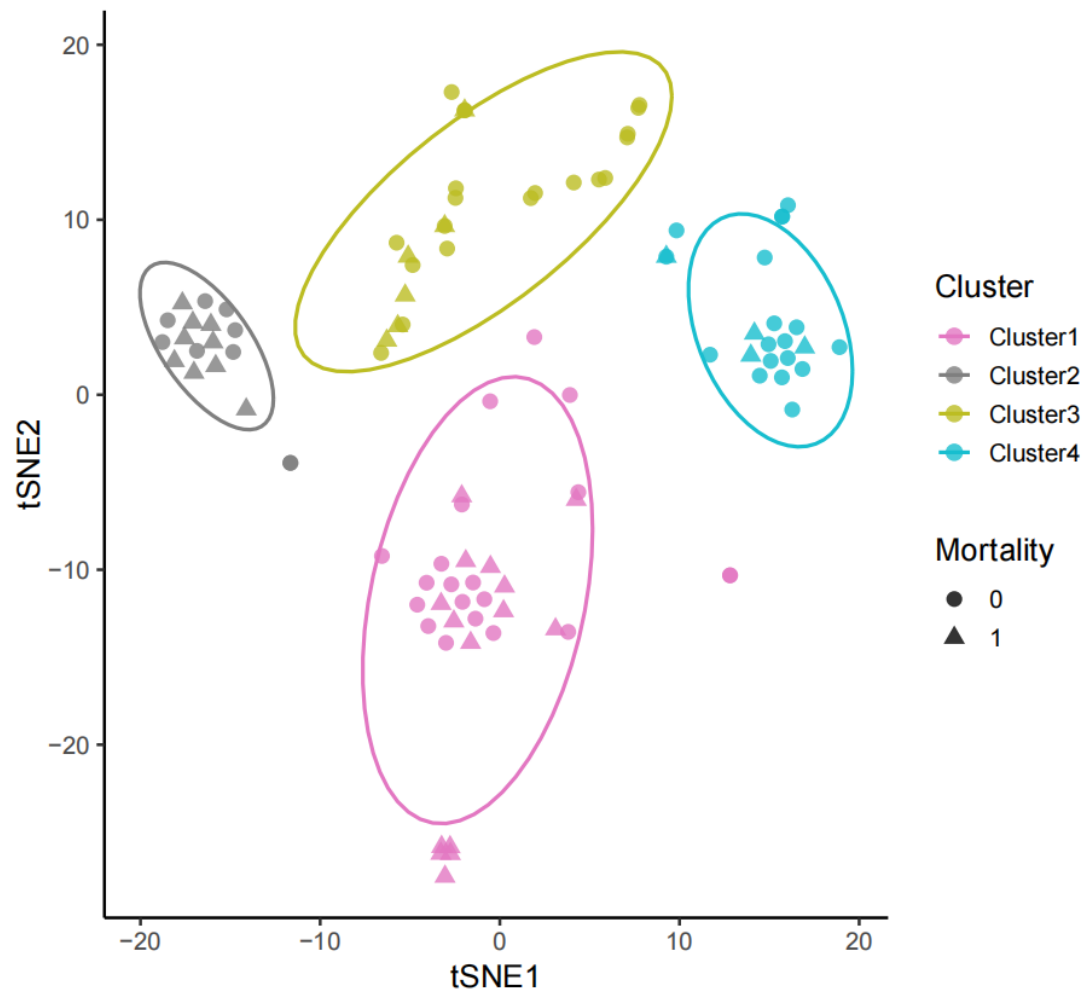
Figure



Supplementary Figure 1. Internal validation composite. (A) Silhouette distribution at $k=4$ (dashed line, mean). (B) Elbow in within-cluster Jaccard dispersion across k . (C) Mean silhouette across k . (D) PAC across k .



Supplementary Figure 2. The distribution of pathogens in 4 clusters in the derivation cohort. Heatmap showing frequency of pathogen in each cluster. Hierarchical clustering groups IPN patients into separate clusters based on pathogen.

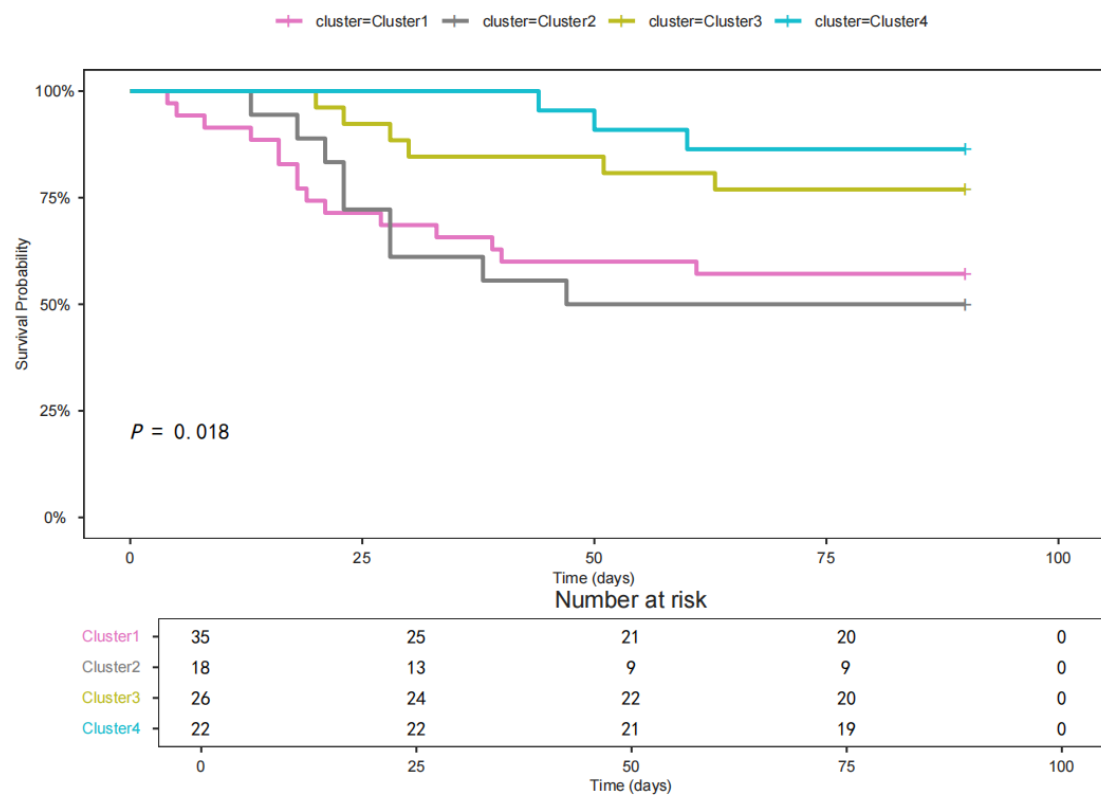


Supplementary Figure 3. t-SNE plot in the validation cohort.

The main purpose of t-SNE plot is the visualization of high-dimensional data. In t-SNE plot, circles represent individual patients.



Supplementary Figure 4. The distribution of pathogens in 4 clusters in the validation cohort. Heatmap showing frequency of pathogen in each cluster. Hierarchical clustering groups IPN patients into separate clusters based on pathogen.



Supplementary Figure 5. Kaplan-Meier survival analysis of the validation cohort. All show significant differences in 90-days mortality by clusters ($P=0.018$)

Table

Supplementary Table 1 Baseline characteristics of patients with infected pancreatic necrosis in the derivation cohort

Characteristics	levels	
Age	Median (IQR)	48.0 (38.0 to 55.0)
Gender	Female	102 (25.8%)
	Male	294 (74.2%)
Complications	No	275 (69.4%)
	Yes	121 (30.6%)
Smoking or drinking	No	229 (57.8%)
	Yes	167 (42.2%)
Etiology	Biliary	197 (49.7%)
	Hypertriglyceride mia	121 (30.6%)
	Alcoholic	19 (4.8%)
	Other	59 (14.9%)
Severity classification	Severe acute Pancreatitis	396 (100%)
	Critical acute Pancreatitis	212 (53.5%)
APACHE II score	Median (IQR)	8.0 (5.0 to 15.0)
BISAP score	Median (IQR)	2.0 (2.0 to 3.0)
Number of organ failures	No	178 (44.9%)

Characteristics	levels	
	Single organ failure	83 (21.0%)
	Multiple organ Failure	135 (34.1%)
Respiratory failure	No	206 (52.0%)
	Yes	190 (48.0%)
Renal failure	No	256 (64.6%)
	Yes	140 (35.4%)
Circulation failure	No	304 (76.8%)
	Yes	92 (23.2%)
ICU stay	No	120 (30.3%)
	Yes	276 (69.7%)
Duration of ICU stay	Median (IQR)	6.0 (0.0 to 18.0)
Surgery approach	Step-up approach	336 (84.8%)
	Step-down approach	60 (15.2%)
The number of surgery intervention	Median (IQR)	3.0 (2.0 to 5.0)
Invasive ventilator	No	231 (58.3%)
	Yes	165 (41.7%)

Characteristics		levels
CRRT	No	303 (76.5%)
	Yes	93 (23.5%)
CVC indwelling	No	229 (57.8%)
	Yes	167 (42.2%)
Vasopressor administration	No	265 (66.9%)
	Yes	131 (33.1%)
Hemorrhage	No	307 (77.9%)
	Yes	87 (22.1%)
Pancreatic fistula	No	237 (60.5%)
	Yes	155 (39.5%)
Gastrointestinal fistula	No	332 (84.3%)
	Yes	62 (15.7%)
Bloodstream infection	No	286 (72.2%)
	Yes	110 (27.8%)
Peripancreatic polymicrobial infection	No	155 (39.1%)
	Yes	241 (60.9%)
Pancreatic infection	MDRO No	184 (46.5%)

Characteristics		levels	
Pancreatic infection	fungal	Yes	212 (53.5%)
		No	297 (75.0%)
Death		Yes	99 (25.0%)
		No	308 (77.8%)
		Yes	88 (22.2%)

APACHE II score, Acute Physiology and Chronic Health Examination II score; BISAP score, Bedside Index of Severity in Acute Pancreatitis score; CRRT, continuous renal replacement therapy; CVC: Central Venous Catheter; MDRO, Multidrug-resistant organisms; ICU, Intensive care unit; IQR, Interquartile range.

Supplementary Table 2 The distribution of the pathogens in four clusters

Pathogens	Overall	Cluster α	Cluster β	Cluster γ	Cluster δ	P-value
n	396	112	78	152	54	
Enterococcus faecium (%)	111 (28.03)	51 (45.54)	0 (0.00)	60 (39.47)	0 (0.00)	<0.001
Staphylococcus haemolyticus (%)	9 (2.27)	5 (4.46)	0 (0.00)	4 (2.63)	0 (0.00)	0.134
Escherichia coli (%)	95 (23.99)	1 (0.89)	63 (80.77)	31 (20.39)	0 (0.00)	<0.001
Klebsiella pneumoniae (%)	145 (36.62)	0 (0.00)	16 (20.51)	129 (84.87)	0 (0.00)	<0.001
Proteus mirabilis (%)	23 (5.81)	6 (5.36)	3 (3.85)	13 (8.55)	1 (1.85)	0.238
Enterobacter cloacae (%)	34 (8.59)	19 (16.96)	5 (6.41)	10 (6.58)	0 (0.00)	0.001
Acinetobacter baumannii (%)	106 (26.77)	22 (19.64)	10 (12.82)	34 (22.37)	40 (74.07)	<0.001
Staphylococcus aureus (%)	32 (8.08)	0 (0.00)	16 (20.51)	16 (10.53)	0 (0.00)	<0.001
Burkholderia cepacia (%)	12 (3.03)	9 (8.04)	0 (0.00)	3 (1.97)	0 (0.00)	0.003
Escherichia coli inactive (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
Klebsiella oxytoca (%)	8 (2.02)	1 (0.89)	2 (2.56)	2 (1.32)	3 (5.56)	0.201
Staphylococcus epidermidis (%)	12 (3.03)	6 (5.36)	2 (2.56)	3 (1.97)	1 (1.85)	0.399
Staphylococcus xylosus (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
Pseudomonas aeruginosa (%)	47 (11.87)	4 (3.57)	11 (14.10)	29 (19.08)	3 (5.56)	0.001
Candida glabrata (%)	23 (5.81)	3 (2.68)	2 (2.56)	7 (4.61)	11 (20.37)	<0.001
Enterobacter aerogenes (%)	8 (2.02)	4 (3.57)	0 (0.00)	4 (2.63)	0 (0.00)	0.224
Klebsiella ornithinolytica (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
Acinetobacter haemolyticus (%)	2 (0.51)	0 (0.00)	1 (1.28)	1 (0.66)	0 (0.00)	0.604
Streptococcus salivarius (%)	4 (1.01)	0 (0.00)	1 (1.28)	3 (1.97)	0 (0.00)	0.367
Citrobacter freundii (%)	15 (3.79)	4 (3.57)	1 (1.28)	6 (3.95)	4 (7.41)	0.346
Raoultella planticola (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
Enterococcus gallinarum (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
Myroides odoratimimus (%)	1 (0.25)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.85)	0.096

<i>Corynebacterium urealyticum</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.85)	0.096
<i>Enterococcus casseliflavus</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Streptococcus haemolyticus</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Monomorphus bacterium</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Streptococcus mitis</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Streptococcus intermedius</i> (%)	2 (0.51)	0 (0.00)	1 (1.28)	0 (0.00)	1 (1.85)	0.238
<i>Pseudomonas putida</i> (%)	2 (0.51)	0 (0.00)	2 (2.56)	0 (0.00)	0 (0.00)	0.042
<i>Candida parapsilosis</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	0 (0.00)	1 (1.85)	0.327
<i>Streptococcus constellatus</i> (%)	6 (1.52)	0 (0.00)	5 (6.41)	1 (0.66)	0 (0.00)	0.001
<i>Stenotrophomonas maltophilia</i> (%)	30 (7.58)	12 (10.71)	4 (5.13)	12 (7.89)	2 (3.70)	0.331
<i>Aeromonas caviae</i> (%)	6 (1.52)	1 (0.89)	0 (0.00)	2 (1.32)	3 (5.56)	0.059
<i>Candida albicans</i> (%)	24 (6.06)	15 (13.39)	3 (3.85)	6 (3.95)	0 (0.00)	0.001
<i>Enterococcus faecalis</i> (%)	17 (4.29)	7 (6.25)	1 (1.28)	7 (4.61)	2 (3.70)	0.416
<i>Streptococcus pneumoniae</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Streptococcus agalactiae</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Streptococcus anginosus</i> (%)	6 (1.52)	0 (0.00)	3 (3.85)	3 (1.97)	0 (0.00)	0.132
<i>Streptococcus oralis</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	1 (0.66)	0 (0.00)	0.783
<i>Alcaligenes faecalis</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Staphylococcus hominis</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Candida tropicalis</i> (%)	7 (1.77)	3 (2.68)	0 (0.00)	3 (1.97)	1 (1.85)	0.577
<i>Achromobacter xylosoxidans</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Staphylococcus warneri</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	0 (0.00)	1 (1.85)	0.327
<i>Enterobacter asburiae</i> (%)	7 (1.77)	4 (3.57)	0 (0.00)	1 (0.66)	2 (3.70)	0.125
<i>Serratia marcescens</i> (%)	9 (2.27)	2 (1.79)	2 (2.56)	5 (3.29)	0 (0.00)	0.549
<i>Streptococcus sanguinis</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Morganella morganii</i> (%)	8 (2.02)	0 (0.00)	2 (2.56)	6 (3.95)	0 (0.00)	0.094

<i>Acinetobacter hospitalis</i> (%)	6 (1.52)	2 (1.79)	2 (2.56)	2 (1.32)	0 (0.00)	0.682
<i>Burkholderia multivorans</i> (%)	4 (1.01)	3 (2.68)	0 (0.00)	1 (0.66)	0 (0.00)	0.199
<i>Corynebacterium jeikeium</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Bacteroides thetaiotaomicron</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	1 (0.66)	0 (0.00)	0.783
<i>Bacteroides nordii</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Bacteroides ovatus</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Enterococcus avium</i> (%)	2 (0.51)	0 (0.00)	1 (1.28)	1 (0.66)	0 (0.00)	0.604
<i>Veillonella parvula</i> (%)	4 (1.01)	2 (1.79)	1 (1.28)	1 (0.66)	0 (0.00)	0.689
<i>Candida krusei</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	1 (0.66)	0 (0.00)	0.783
<i>Enterobacter kobei</i> (%)	5 (1.26)	3 (2.68)	1 (1.28)	1 (0.66)	0 (0.00)	0.401
<i>Aeromonas jandaei</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Pseudomonas alcaligenes</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Staphylococcus capitis</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Klebsiella aerogenes</i> (%)	14 (3.54)	4 (3.57)	1 (1.28)	2 (1.32)	7 (12.96)	0.001
<i>Candida lusitaniae</i> (%)	2 (0.51)	1 (0.89)	0 (0.00)	0 (0.00)	1 (1.85)	0.327
<i>Pseudomonas otitidis</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Proteus hauseri</i> (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
<i>Corynebacterium striatum</i> (%)	3 (0.76)	3 (2.68)	0 (0.00)	0 (0.00)	0 (0.00)	0.053
<i>Enterobacter bugandensis</i> (%)	2 (0.51)	1 (0.89)	1 (1.28)	0 (0.00)	0 (0.00)	0.509
<i>Raoultella ornithinolytica</i> (%)	2 (0.51)	0 (0.00)	0 (0.00)	1 (0.66)	1 (1.85)	0.394
<i>Kluyvera ascorbata</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	1 (0.66)	0 (0.00)	0.657
<i>Aeromonas hydrophila</i> (%)	2 (0.51)	0 (0.00)	1 (1.28)	0 (0.00)	1 (1.85)	0.238
<i>Acinetobacter calcoaceticus</i> (%)	1 (0.25)	1 (0.89)	0 (0.00)	0 (0.00)	0 (0.00)	0.468
<i>Enterococcus hirae</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.85)	0.096
<i>Bacteroides fragilis</i> (%)	2 (0.51)	0 (0.00)	2 (2.56)	0 (0.00)	0 (0.00)	0.042
<i>Citrobacter koseri</i> (%)	1 (0.25)	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.85)	0.096

Klebsiella variicola (%)	2 (0.51)	1 (0.89)	0 (0.00)	1 (0.66)	0 (0.00)	0.783
Fusobacterium necrophorum (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252
Haemophilus parainfluenzae (%)	1 (0.25)	0 (0.00)	1 (1.28)	0 (0.00)	0 (0.00)	0.252

Supplementary Table 3. Baseline of clusters in the validation cohort.

Characteristics	Levels	Cluster1 (N=35)	Cluster2 (N=18)	Cluster3 (N=26)	Cluster4 (N=22)	P-value
Age	Mean $\pm$ SD	46.5 $\pm$ 13.7	46.8 $\pm$ 14.7	49.2 $\pm$ 14.1	41.2 $\pm$ 10.4	0.222
Gender	Female	13 (37.1%)	8 (44.4%)	7 (26.9%)	9 (40.9%)	0.636
	Male	22 (62.9%)	10 (55.6%)	19 (73.1%)	13 (59.1%)	
Complications	No	20 (57.1%)	9 (50%)	9 (34.6%)	15 (68.2%)	0.119
	Yes	15 (42.9%)	9 (50%)	17 (65.4%)	7 (31.8%)	
Smoking or drinking	No	26 (74.3%)	15 (83.3%)	18 (69.2%)	12 (54.5%)	0.225
	Yes	9 (25.7%)	3 (16.7%)	8 (30.8%)	10 (45.5%)	
Etiology	Alcoholic	5 (14.3%)	0 (0%)	3 (11.5%)	1 (4.5%)	0.680
	Biliary	16 (45.7%)	9 (50%)	8 (30.8%)	8 (36.4%)	
	Hypertriglyceridemia	10 (28.6%)	6 (33.3%)	10 (38.5%)	10 (45.5%)	
	Other	4 (11.4%)	3 (16.7%)	5 (19.2%)	3 (13.6%)	
Severity classification	Critical acute pancreatitis	29 (82.9%)	11 (61.1%)	16 (61.5%)	14 (63.6%)	0.198
APACHE II score	Median (IQR)	9.0 (5.0 to 17.5)	7.0 (3.0 to 16.0)	8.5 (5.0 to 17.0)	7.0 (4.0 to 10.0)	0.705
BISAP score	Median (IQR)	3.0 (2.0 to 3.0)	2.0 (1.0 to 3.0)	2.0 (2.0 to 3.0)	2.0 (2.0 to 2.0)	0.133
Number of organ failures	Multiple organ Failure	18 (51.4%)	10 (55.6%)	11 (42.3%)	11 (50%)	0.215
	No	6 (17.1%)	7 (38.9%)	10 (38.5%)	8 (36.4%)	
	Single organ failure	11 (31.4%)	1 (5.6%)	5 (19.2%)	3 (13.6%)	
ICU stay	No	5 (14.3%)	5 (27.8%)	4 (15.4%)	8 (36.4%)	0.179

Characteristics	Levels	Cluster1 (N=35)	Cluster2 (N=18)	Cluster3 (N=26)	Cluster4 (N=22)	P-value
	Yes	30 (85.7%)	13 (72.2%)	22 (84.6%)	14 (63.6%)	
Duration of ICU stay	Median (IQR)	14.0 (4.0 to 24.0)	17.0 (0.0 to 32.0)	11.5 (5.0 to 23.0)	6.5 (0.0 to 21.0)	0.619
Surgery approach	Step-up approach	7 (20%)	1 (5.6%)	6 (23.1%)	5 (22.7%)	0.452
	Step-down approach	28 (80%)	17 (94.4%)	20 (76.9%)	17 (77.3%)	
Hemorrhage	No	26 (74.3%)	14 (77.8%)	19 (73.1%)	16 (72.7%)	0.983
	Yes	9 (25.7%)	4 (22.2%)	7 (26.9%)	6 (27.3%)	
Pancreatic fistula	No	24 (68.6%)	13 (72.2%)	18 (69.2%)	18 (81.8%)	0.715
	Yes	11 (31.4%)	5 (27.8%)	8 (30.8%)	4 (18.2%)	
Gastrointestinal fistula	No	31 (88.6%)	14 (77.8%)	21 (80.8%)	16 (72.7%)	0.490
	Yes	4 (11.4%)	4 (22.2%)	5 (19.2%)	6 (27.3%)	
Bloodstream infection	No	28 (80%)	8 (44.4%)	19 (73.1%)	16 (72.7%)	0.058
	Yes	7 (20%)	10 (55.6%)	7 (26.9%)	6 (27.3%)	
Peripancreatic polymicrobial infection	No	20 (57.1%)	15 (83.3%)	5 (19.2%)	13 (59.1%)	<0.001
	Yes	15 (42.9%)	3 (16.7%)	21 (80.8%)	9 (40.9%)	
Pancreatic infection	fungal	No	29 (82.9%)	15 (83.3%)	21 (95.5%)	0.532
	Yes	6 (17.1%)	3 (16.7%)	3 (11.5%)	1 (4.5%)	
Pancreatic infection	MDRO	No	11 (31.4%)	4 (22.2%)	12 (46.2%)	0.030

Characteristics	Levels	Cluster1 (N=35)	Cluster2 (N=18)	Cluster3 (N=26)	Cluster4 (N=22)	P-value
Death	Yes	24 (68.6%)	14 (77.8%)	14 (53.8%)	8 (36.4%)	0.068
	No	20 (57.1%)	9 (50%)	20 (76.9%)	18 (81.8%)	
	Yes	15 (42.9%)	9 (50%)	6 (23.1%)	4 (18.2%)	

APACHE II score, Acute Physiology and Chronic Health Examination II score; BISAP score, Bedside Index of Severity in Acute Pancreatitis score; MDRO, Multidrug-resistant organisms; ICU, Intensive care unit; IQR, Interquartile range.

Supplementary Table 4 Statistical test results of 90-days mortality among the clusters in validation cohort

Outcome	General	Statistical test <i>P</i>					
		Pairwise					
		1 vs. 2	1 vs. 3	1 vs. 4	2 vs. 3	2 vs. 4	3 vs. 4
90-days mortality	0.018	1.000	0.456	0.045	0.264	0.036	1.000