



Critical Care

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杨小蕾

1.The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: an observational cohort study

Introduction

The neutrophil-to-lymphocyte ratio (NLR) is a biological marker that has been shown to be associated with outcomes in patients with a number of different malignancies. The objective of this study was to assess the relationship between NLR and mortality in a population of adult critically ill patients.

Methods

We performed an observational cohort study of unselected intensive care unit (ICU) patients based on records in a large clinical database. We computed individual patient NLR and categorized patients by quartile of this ratio. The association of NLR quartiles and 28-day mortality was assessed using multivariable logistic regression. Secondary outcomes included mortality in the ICU, in-hospital mortality and 1-year mortality. An *a priori* subgroup analysis of patients with versus without sepsis was performed to assess any differences in the relationship between the NLR and outcomes in these cohorts.

Results

A total of 5,056 patients were included. Their 28-day mortality rate was 19%. The median age of the cohort was 65 years, and 47% were female. The median NLR for the entire cohort was 8.9 (interquartile range, 4.99 to 16.21). Following multivariable adjustments, there was a stepwise increase in mortality with increasing quartiles of NLR (first quartile: reference category; second quartile odds ratio (OR) = 1.32; 95% confidence interval (CI), 1.03 to 1.71; third quartile OR = 1.43; 95% CI, 1.12 to 1.83; 4th quartile OR = 1.71; 95% CI, 1.35 to 2.16). A similar stepwise relationship was identified in the subgroup of patients who presented without sepsis. The NLR was not associated with 28-day mortality in patients with sepsis. Increasing quartile of NLR was statistically significantly associated with secondary outcome.

Conclusion

The NLR is associated with outcomes in unselected critically ill patients. In patients with sepsis, there was no statistically significant relationship between NLR and mortality.

2.Optimal site for ultrasound-guided venous catheterisation in paediatric patients: an observational study to investigate predictors for catheterisation success and a randomised controlled study to determine the most successful site

Introduction

Venous catheterisation in paediatric patients can be technically challenging. We examined factors affecting catheterisation of invisible and impalpable peripheral veins in children and evaluated the best site for ultrasound-guided catheterisation.

Methods

Systolic pressure, age, sex, and American Society of Anaesthesiologists (ASA) physical status were determined in 96 children weighing less than 20 kg. Vein diameter and subcutaneous depth were measured with ultrasound. Logistic regression was used to evaluate the contribution of these factors to cannulation success with ($n = 65$) or without ($n = 31$) ultrasound guidance. Thereafter, we randomly assigned 196 patients for venous catheter insertion in the dorsal veins of the hand, the cephalic vein in the forearm, or the great saphenous vein. Success rates and vein diameters were evaluated by using Dunn tests; insertion time was evaluated by using Kaplan-Meier cumulative incidence analysis.

摘要

Results

Independent predictors of catheterisation were ultrasound guidance (odds ratio (OR) = 7.3, 95% confidence interval (CI) 2.0 to 26.0, $P = 0.002$), vein diameter (OR = 1.5 per 0.1 mm increase in diameter, 95% CI 1.1 to 2.0, $P = 0.007$), and ASA physical status (OR = 0.4 per status 1 increase, 95% CI 0.2 to 0.9, $P = 0.03$). Cephalic veins were significantly larger (cephalic diameter 1.8 mm, $P = 0.001$ versus saphenous 1.5 mm, $P < 0.001$ versus dorsal 1.5 mm). Catheterisation success rates were significantly better at the cephalic vein than either the dorsal hand or saphenous vein (cephalic 95%, 95% CI 89% to 100%, $P < 0.001$ versus dorsal 69%, 95% CI 56% to 82%, $P = 0.03$ versus saphenous 75%, 95% CI 64% to 86%).

Conclusions

The cephalic vein in the proximal forearm appears to be the most appropriate initial site for ultrasound-guided catheterisation in invisible and impalpable veins of paediatric patients.

3.Effects of glucose-dependent insulintropic polypeptide on gastric emptying, glycaemia and insulinaemia during critical illness: a prospective, double blind, randomised, crossover study

Introduction

Insulin is used to treat hyperglycaemia in critically ill patients but can cause hypoglycaemia, which is associated with poorer outcomes. In health glucose-dependent insulintropic polypeptide (GIP) is a potent glucose-lowering peptide that does not cause hypoglycaemia. The objectives of this study were to determine the effects of exogenous GIP infusion on blood glucose concentrations, glucose absorption, insulinaemia and gastric emptying in critically ill patients without known diabetes.

Methods

A total of 20 ventilated patients (Median age 61 (range: 22 to 79) years, APACHE II 21.5 (17 to 26), BMI 28 (21 to 40) kg/m²) without known diabetes were studied on two consecutive days in a randomised, double blind, placebo controlled, cross-over fashion. Intravenous GIP (4 pmol/kg/min) or placebo (0.9% saline) was infused between T = -60 to 300 minutes. At T₀, 100 ml of liquid nutrient (2 kcal/ml) containing 3-O-Methylglucose (3-OMG), 100 mcg of Octanoic acid and 20 MBq Tc-99 m Calcium Phytate, was administered via a nasogastric tube. Blood glucose and serum 3-OMG (an index of glucose absorption) concentrations were measured. Gastric emptying, insulin and glucagon levels and plasma GIP concentrations were also measured.

摘要

Results

While administration of GIP increased plasma GIP concentrations three- to four-fold (T = -60 23.9 (16.5 to 36.7) versus T = 0 84.2 (65.3 to 111.1); $P < 0.001$) and plasma glucagon (iAUC₃₀₀ 4217 (1891 to 7715) versus 1232 (293 to 4545) pg/ml.300 minutes; $P = 0.04$), there were no effects on postprandial blood glucose (AUC₃₀₀ 2843 (2568 to 3338) versus 2819 (2550 to 3497) mmol/L.300 minutes; $P = 0.86$), gastric emptying (AUC₃₀₀ 15611 (10993 to 18062) versus 15660 (9694 to 22618) %.300 minutes; $P = 0.61$), glucose absorption (AUC₃₀₀ 50.6 (22.3 to 74.2) versus 64.3 (9.9 to 96.3) mmol/L.300 minutes; $P = 0.62$) or plasma insulin (AUC₃₀₀ 3945 (2280 to 6731) versus 3479 (2316 to 6081) mU/L.300 minutes; $P = 0.76$).

Conclusions

In contrast to its profound insulinotropic effect in health, the administration of GIP at pharmacological doses does not appear to affect glycaemia, gastric emptying, glucose absorption or insulinaemia in the critically ill patient.

4、 Platelet mitochondrial dysfunction in critically ill patients: comparison between sepsis and cardiogenic shock

Introduction

Platelet mitochondrial respiratory chain enzymes are variably inhibited during human sepsis. Whether these changes occur even during other acute critical illness or is not known. The aims of this study were firstly to compare platelet mitochondrial respiratory chain enzymes activity between patients with sepsis and those with cardiogenic shock, and secondly to study the relationship between platelet mitochondrial respiratory chain enzymes activity and platelet responsiveness to agonists in patients with sepsis.

Methods

Platelets were isolated from venous blood of 16 patients with severe sepsis or septic shock (free from antiplatelet drugs) and 16 others with cardiogenic shock, within 48 hours from admission to Intensive Care. Platelet mitochondrial respiratory chain enzymes activity was measured with spectrophotometry and expressed relative to citrate synthase activity, a marker of mitochondrial density. Platelet aggregation and secretion in response to adenosine di-phosphate (ADP), collagen, U46619 and thrombin receptor activating peptide were measured with lumiaggregometry only in patients with sepsis. In total, 16 healthy volunteers acted as controls for both spectrophotometry and lumiaggregometry.

Results

Platelets of patients with sepsis or cardiogenic shock similarly had lower mitochondrial nicotinamide adenine dinucleotide dehydrogenase (NADH) ($P < 0.001$), complex I ($P = 0.006$), complex I and III ($P < 0.001$) and complex IV ($P < 0.001$) activity than those of controls. Platelets of patients with sepsis were generally hypo-responsive to exogenous agonists, both in terms of maximal aggregation ($P < 0.001$) and secretion ($P < 0.05$).

Conclusions

Several platelet mitochondrial respiratory chain enzymes are similarly inhibited during human sepsis and cardiogenic shock. In patients with sepsis, mitochondrial dysfunction is associated with general platelet hypo-responsiveness to exogenous agonists.

5、 Effect of high-dose dexamethasone on perioperative lactate levels and glucose control: a randomized controlled trial

Introduction

Blood lactate levels are increasingly used to monitor patients. Steroids are frequently administered to critically ill patients. However, the effect of steroids on lactate levels has not been adequately investigated. We studied the effect of a single intraoperative high dose of dexamethasone on lactate and glucose levels in patients undergoing cardiac surgery.

Methods

The Dexamethasone for Cardiac Surgery (DECS) trial was a multicenter randomized trial on the effect of dexamethasone 1 mg/kg versus placebo on clinical outcomes after cardiac surgery in adults. Here we report a pre-planned secondary analysis of data from DECS trial participants included at the University Medical Center Groningen. The use of a computer-assisted glucose regulation protocol—Glucose Regulation for Intensive care Patients (GRIP)—was part of routine postoperative care. GRIP aimed at glucose levels of 4 to 8 mmol/L. Primary outcome parameters were area under the lactate and glucose curves over the first 15 hours of ICU stay (AUC_{15}). ICU length of stay and mortality were observed as well.

Results

During the first 15 hours of ICU stay, lactate and glucose levels were significantly higher in the dexamethasone group than in the placebo group: lactate AUC_{15} 25.8 (13.1) versus 19.9 (11.2) mmol/L \times hour, $P < 0.001$ and glucose AUC_{15} 126.5 (13.0) versus 114.4 (13.9) mmol/L \times hour, $P < 0.001$. In this period, patients in the dexamethasone group required twice as much insulin compared with patients who had received placebo. Patients in the placebo group were more likely to stay in the ICU for more than 24 hours (39.2%) compared with patients in the dexamethasone group (25.0%, $P = 0.001$), and 30-day mortality rates were 1.6% and 2.4%, respectively ($P = 0.759$).

Conclusions

Intraoperative high-dose dexamethasone increased postoperative lactate and glucose levels in the first 15 hours of ICU stay. Still, patients in the dexamethasone group had a shorter ICU length of stay and similar mortality compared with controls.

6. Propofol increases morbidity and mortality in a rat model of sepsis

Introduction

Most patients require ventilatory support and propofol is commonly used to sedate mechanically ventilated patients. Volatile anesthetics have been shown to attenuate inflammation in a variety of different settings. We therefore hypothesized that volatile anesthetic agents may offer beneficial immunomodulatory effects during the course of long-term intra-abdominal sepsis in rats under continuous sedation and ventilation for up to 24 hours.

Methods

Sham operation or cecal ligation and puncture (CLP) was performed in adult male Wistar rats followed by mechanical ventilation. Animals were sedated for 24 hours with propofol (7 to 20 mg/kg/h), sevoflurane, desflurane or isoflurane (0.7 minimal alveolar concentration each).

Results

Septic animals sedated with propofol showed a mean survival time of 12 hours, whereas >56% of all animals in the volatile groups survived 24 hours ($P < 0.001$). After 18 hours, base excess in propofol + CLP animals (-20.6 ± 2.0) was lower than in the volatile groups (isoflurane + CLP: -11.7 ± 4.2 , sevoflurane + CLP: -11.8 ± 3.5 , desflurane + CLP -14.2 ± 3.7 ; all $P < 0.03$). Plasma endotoxin levels reached 2-fold higher levels in propofol + CLP compared to isoflurane + CLP animals at 12 hours ($P < 0.001$). Also blood levels of inflammatory mediators (tumor necrosis factor- α , interleukin-1 β , interleukin-10, CXCL-2, interferon- γ and high mobility group protein-1) were accentuated in propofol + CLP rats compared to the isoflurane + CLP group at the same time point ($P < 0.04$).

Conclusions

Results indicate that volatile anesthetics dramatically improved survival and attenuate systemic inflammation as compared to propofol. The main mechanism responsible for adverse propofol effects could be an enhanced plasma endotoxin concentration, leading to profound hypotension, which was unresponsive to fluid resuscitation.

7. Erythropoietin improves long-term neurological outcome in acute ischemic stroke patients: a randomized, prospective, placebo-controlled clinical trial

Introduction

This study tested the effect of erythropoietin (EPO) on long-term neurological outcome in patients after acute IS. This study aimed to evaluate the safety and efficacy of two consecutive doses of EPO (5,000 IU/dose, subcutaneously administered at 48 hours and 72 hours after acute IS) on improving the 90-day combined endpoint of recurrent stroke or death that has been previously reported. A secondary objective was to evaluate the long-term (that is, five years) outcome of patients who received EPO.

Methods

This was a prospective, randomized, placebo-controlled trial that was conducted between October 2008 and March 2010 in a tertiary referral center. IS stroke patients who were eligible for EPO therapy were enrolled into the study.

Results

The results showed that long-term recurrent stroke and mortality did not differ between group 1 (placebo-control; $n = 71$) and group 2 (EPO-treated; $n = 71$).

Long-term Barthel index of <35 (defining a severe neurological deficit) was lower in group 2 than group 1 ($P = 0.007$). Multiple-stepwise logistic-regression analysis showed that EPO therapy was significantly and independently predictive of freedom from a Barthel index of <35 ($P = 0.029$). Long-term major adverse neurological event (MANE; defined as: death, recurrent stroke, or long-term Barthel index < 35) was lower in group 2 than group 1 ($P = 0.04$). Log-Rank test showed that MANE-free rate was higher in group 2 than group 1 ($P = 0.031$).

Conclusion

EPO therapy significantly improved long-term neurological outcomes in patients after IS.

8. Neutralization of osteopontin attenuates neutrophil migration in sepsis-induced acute lung injury

Introduction

Sepsis refers to severe systemic inflammation leading to acute lung injury (ALI) and death. Osteopontin (OPN), a secretory glycoprotein produced by immune reactive cells, plays a deleterious role in various inflammatory diseases. We hypothesize that treatment with an OPN-neutralizing antibody protects mice against ALI during sepsis.

Methods

Sepsis was induced in 8-week-old male C57BL/6 mice by cecal ligation and puncture (CLP). Anti-OPN Ab or non-immunized IgG as control, at a dose of 50 µg/mouse, was intravenously injected at the time of CLP. After 20 hours, the expression of OPN and proinflammatory cytokines in tissues and plasma was examined by real-time PCR, Western blot, and ELISA. Plasma levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) and the lung myeloperoxidase (MPO) levels were determined by colorimetric assays. Lung damage and neutrophil infiltrations were determined by histological H&E and Gr-1 staining, respectively. The effect of recombinant mouse OPN (rmOPN) on human neutrophil-like cell (HL-60) migration was performed by Boyden chamber assays and the involvement of intracellular signaling molecules in HL-60 cells was revealed by Western blot.

摘要

Results

After 20 hours of sepsis, mRNA and protein levels of OPN were significantly induced in lungs, spleen, and plasma. Treatment with an anti-OPN Ab in septic mice significantly reduced the plasma levels of ALT, AST, and LDH, and the proinflammatory cytokines IL-6, IL-1 β and the chemokine MIP-2, compared with the vehicle group. Similarly, the lung mRNA and protein expressions of proinflammatory cytokines and chemokine were greatly reduced in anti-OPN Ab-treated animals. The lung histological architecture, MPO and neutrophil infiltration were significantly improved in anti-OPN Ab-treated mice compared with the vehicle animals. Treatment of rmOPN in HL-60 cells significantly increased their migration, *in vitro*. The neutrophils treated with rmOPN remarkably increased the levels of phospho focal adhesion kinase (pFAK), phospho extracellular signal-regulated kinase (pERK) and phospho p38.

Conclusions

Our findings clearly demonstrate the beneficial outcomes of anti-OPN Ab treatment in protecting against ALI, implicating a novel therapeutic strategy in sepsis.

9. Can yeast isolation be predicted in complicated secondary non-postoperative intra-abdominal infections?

Introduction

The aim of this study was to create a predictive score for yeast isolation in patients with complicated non-postoperative intra-abdominal infections (CNPIAI) and to evaluate the impact of yeast isolation on outcome.

Methods

All patients with a CNPIAI undergoing emergency surgery over a three-year period were included in the retrospective cohort (RC, n = 290). Patients with a yeast-positive peritoneal fluid culture (YP) were compared with patients with a yeast-negative culture (YN). Multivariate logistic regression was used to identify factors independently associated with yeast isolation and a predictive score was built. The score's performance was then established in the prospective cohort (PC, n = 152) over an 18-month period. Outcome of the whole cohort was evaluated and independent risks factors of mortality searched.

Results

In the RC, 39 patients (13.4%) were YP. Four factors were independently associated with the YP group: length of stay before surgery ≥ 48 h (odds ratio (OR) (95% confidence interval (CI)) = 3.1 (1.4 to 6.9), $P = 0.004$, 1 point), per-operative cardiovascular failure (2.4 (1.1 to 5.8), $P = 0.04$, 1 point), generalized peritonitis (6.8 (2.7 to 16.7), $P < 0.001$, 2 points) and upper gastrointestinal tract perforation (2.5 (1.2 to 5.6), $P = 0.02$, 1 point). In the PC, the area under the curve (95%CI) of the predictive score's receiver operating characteristic curve was 0.79 (0.72 to 0.86). For predicting an intra-abdominal candidiasis (IAC), a score ≥ 3 had a sensitivity of 0.60, a specificity of 0.84, a positive predictive value of 0.49 and a negative predictive value of 0.89. Furthermore, yeast isolation was associated with worse outcome and independently associated with mortality in the whole cohort (OR = 2.15; 95%CI (1.03 to 4.46), $P = 0.04$).

Conclusions

The new predictive score can be used to rule out intra-abdominal candidiasis and thus avoid the initiation of antifungal treatment. IAC is associated independently with an increased mortality in this population.

10. Early mobilization and recovery in mechanically ventilated patients in the ICU: a bi-national, multi-centre, prospective cohort study

Introduction

The aim of this study was to investigate current mobilization practice, strength at ICU discharge and functional recovery at 6 months among mechanically ventilated ICU patients.

Method

This was a prospective, multi-centre, cohort study conducted in twelve ICUs in Australia and New Zealand. Patients were previously functionally independent and expected to be ventilated for >48 hours. We measured mobilization during invasive ventilation, sedation depth using the Richmond Agitation and Sedation Scale (RASS), co-interventions, duration of mechanical ventilation, ICU-acquired weakness (ICUAW) at ICU discharge, mortality at day 90, and 6-month functional recovery including return to work.

Results

We studied 192 patients. Mortality at day 90 was 26.6% (51/192). We recorded the highest level of early mobilization. Despite the presence of dedicated physical therapy staff, no mobilization occurred in 1,079 (84%) of these episodes. Where mobilization occurred, the maximum levels of mobilization were exercises in bed (N = 94, 7%), standing at the bed side (N = 11, 0.9%) or walking (N = 26, 2%). In 94 of the 156 ICU survivors, strength was assessed at ICU discharge and 48 (52%) had ICU-acquired weakness. The MRC-SS score was higher in those patients who mobilized while mechanically ventilated (50.0 ± 11.2 versus 42.0 ± 10.8 , $P = 0.003$). Patients who survived to ICU discharge but who had died by day 90 had a mean MRC score of 28.9 ± 13.2 compared with 44.9 ± 11.4 for day-90 survivors ($P < 0.0001$).

Conclusions

Early mobilization of patients receiving mechanical ventilation was uncommon. More than 50% of patients discharged from the ICU had developed ICU-acquired weakness, which was associated with death between ICU discharge and day-90.

1. Diminished adrenal sensitivity to endogenous and exogenous adrenocorticotrophic hormone in critical illness: a prospective cohort study

2. Furosemide versus ethacrynic acid in pediatric patients undergoing cardiac surgery: a randomized controlled trial

3. Quantification of urinary TIMP-2 and IGFBP-7: an adequate diagnostic test to predict acute kidney injury after cardiac surgery?

4.The relationship between serum potassium, potassium variability and in-hospital mortality in critically ill patients and a before-after analysis on the impact of computer-assisted potassium control

5.Preload dependence indices to titrate volume expansion during septic shock: a randomized controlled trial

6.Rs1800625 in the receptor for advanced glycation end products gene predisposes to sepsis and multiple organ dysfunction syndrome in patients with major trauma



7. Epidemiology of invasive aspergillosis in critically ill patients: clinical presentation, underlying conditions, and outcomes

8. Preoperative intra-aortic balloon pump to reduce mortality in coronary artery bypass graft: a meta-analysis of randomized controlled trials

9. Integration of metabolic and inflammatory mediator profiles as a potential prognostic approach for septic shock in the intensive care unit



10.Reintubation in critically ill patients: procedural complications and implications for care

11.Dynamic arterial elastance predicts mean arterial pressure decrease associated with decreasing norepinephrine dosage in septic shock

12.Low-dose hydrocortisone reduces norepinephrine duration in severe burn patients: a randomized clinical trial



13. Gastric tonometry guided therapy in critical care patients: a systematic review and meta-analysis

14. Increasing the inspiratory time and I:E ratio during mechanical ventilation aggravates ventilator-induced lung injury in mice

15. Efficiency of hydrogen peroxide in improving disinfection of ICU rooms

16. Evaluation of sulfobutylether- β -cyclodextrin (SBECD) accumulation and voriconazole pharmacokinetics in critically ill patients undergoing continuous renal replacement therapy


17. A new two-tier strength assessment approach to the diagnosis of weakness in intensive care: an observational study

18. Successful treatment of severe sepsis and diarrhea after vagotomy utilizing fecal microbiota transplantation: a case report

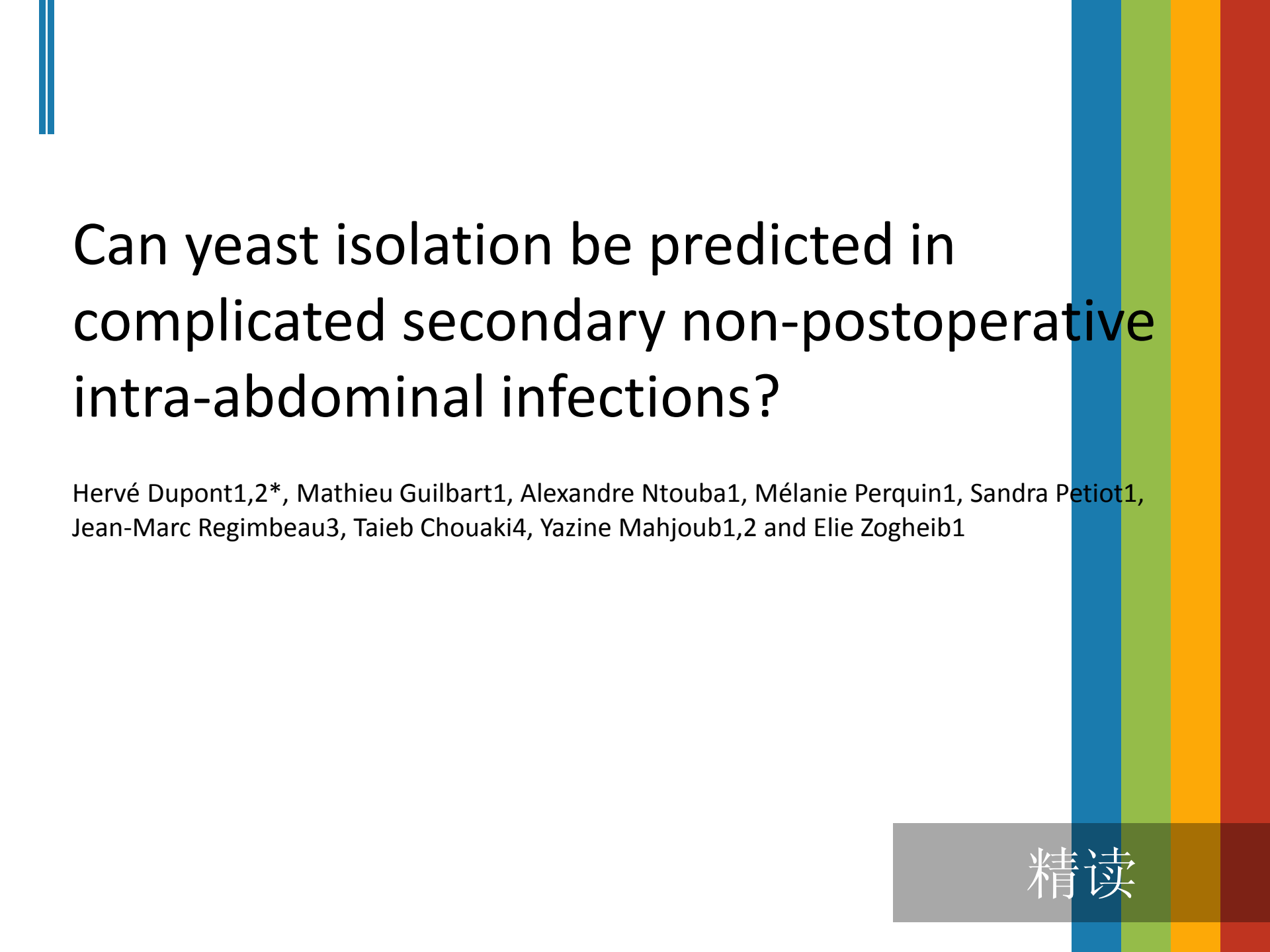
19. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study

20. Do corticosteroids reduce the mortality of influenza A (H1N1) infection? A meta-analysis

21. Prospective validation of pediatric disease severity scores to predict mortality in Ugandan children presenting with malaria and non-malaria febrile illness



22. Automated versus non-automated weaning for reducing the duration of mechanical ventilation for critically ill adults and children: a cochrane systematic review and meta-analysis



Can yeast isolation be predicted in complicated secondary non-postoperative intra-abdominal infections?

Hervé Dupont^{1,2*}, Mathieu Guilbart¹, Alexandre Ntomba¹, Mélanie Perquin¹, Sandra Petiot¹, Jean-Marc Regimbeau³, Taieb Chouaki⁴, Yazine Mahjoub^{1,2} and Elie Zogheib¹

introduction

A number of scores have been developed in order to predict the occurrence of candidemia in high-risk patients, including the colonization index, Leon et al.'s Candida score and a clinical rule. However, none of these scores is suitable for complicated intra-abdominal infections. Furthermore, each of these scores has a high negative predictive value (NPV) rather than a high positive predictive value (PPV).

Ten years ago, Dupont et al. developed a score for severe complicated intra-abdominal infections in the ICU. This is still the only available score with a moderately good PPV and NPV. However, it was developed in a severe population of ICU patients. There are few data on less severe patients having undergone emergency surgery.

The objectives of the present study were to build a predictive score for yeast isolation in the peritoneal fluid of patients with complicated non-postoperative intra-abdominal infections (CNPIAI) in a retrospective cohort of patients and validate the score in a separate prospective cohort. The new score will be compared with previously described scores. The relationship between intra-abdominal candidiasis (IAC) and the outcomes for patients with complicated CNPNIAIs was also evaluated.

Material and methods

Study design and patients

This study was conducted in three parts. In the first part (score construction), patients with a CNPIAI and having undergone emergency surgery in our tertiary university hospital were retrospectively included over a three-year period (from January 2009 to December 2011). Patients with yeast-positive (YP) peritoneal fluid culture were compared with patient with a yeast-negative (YN) culture. A predictive score was built by taking account of factors independently associated with IAC in the cohort.

In the second part of the study (score validation), patients were included in a prospective cohort over an 18-month period (from January 2012 to June 2013). The performance of the new score was compared with previously published predictive scores (Dupont et al. [13], Leon at al. [10] and Paphitou et al. [14]).



In the third part, the impact of IAC on outcome in the whole cohort was assessed.

Patients with infected acute pancreatitis, postoperative nosocomial infections, acute trauma perforation <6 hours and primary peritonitis (such as infected ascites) were not included in the study.

Surgery and microbiological management

Surgery was performed by an experienced, trained team in accordance with the above-mentioned guidelines for the treatment of complicated intra-abdominal infections. The definition of complicated intra-abdominal infection used is that presented in the Infectious Diseases Society of America (IDSA) guidelines: ‘Complicated intraabdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis’ [6]. Either laparoscopy or laparotomy was performed (depending on the diagnosis and the surgeon’s choice). All peritoneal fluid samples were sent for microbiological and mycological testing.

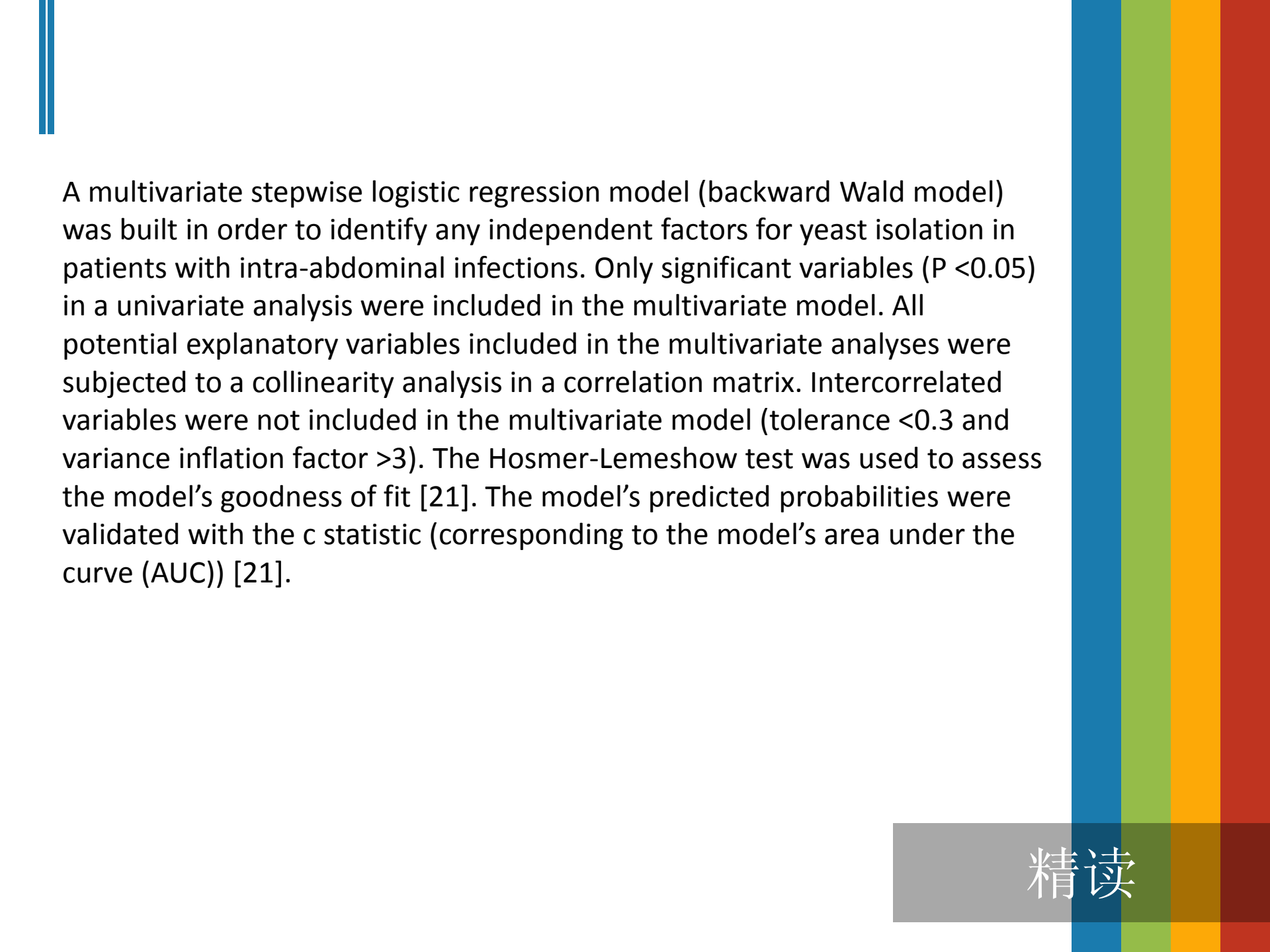
Definitions and data collection

The etiology of the intra-abdominal infection, the extent of the infection (generalized or localized) and the perforation site were recorded. The hospital length of stay before surgery was noted. A number of severity scores were calculated: the American Society of Anesthesiologist score [16], the Mannheim peritonitis index [17], APACHE II score [18], SAPS II and SOFA score [20]. Cardiovascular failure was defined by the need for norepinephrine during surgery (despite fluid challenge).

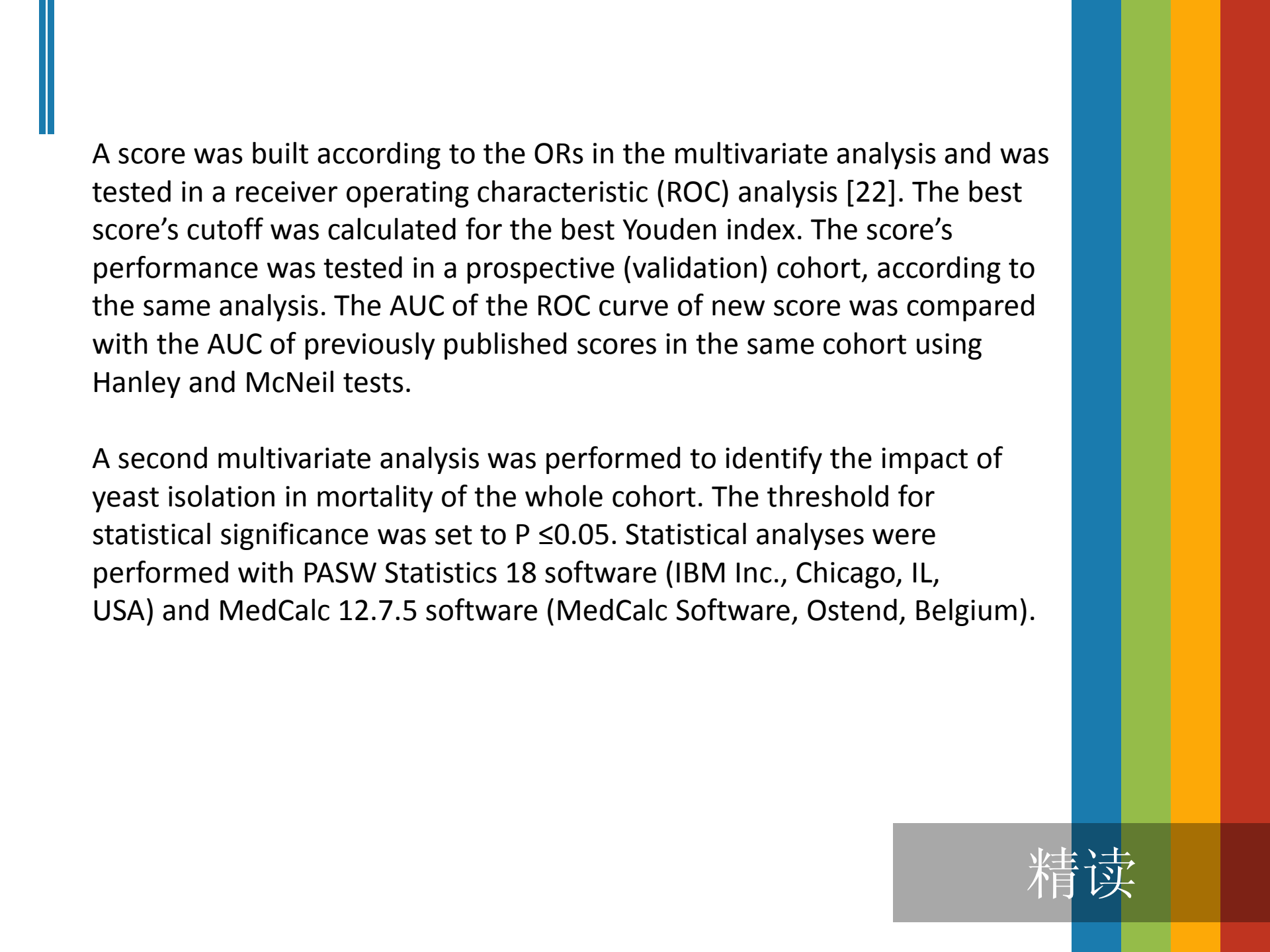
Respiratory failure was defined by the need for more than 24 hours of mechanical ventilation. The ICU admission rate, lengths of stay (in the ICU or a hospital ward) and in-hospital mortality were assessed.

Statistical analysis

Results are expressed as mean \pm standard deviation (SD) or number (proportion). First, patients in the YP group were compared with those in the YN group via a chi-squared test (with Yates' correction, if necessary) for qualitative variables and a two-sided t test for quantitative variables.

The slide features a white background with decorative vertical bars. On the left side, there are two thin blue vertical bars. On the right side, there are four wider vertical bars in blue, green, yellow, and red. A grey rectangular box is located in the bottom right corner, containing the Chinese characters '精读' (Jingdu) in white.

A multivariate stepwise logistic regression model (backward Wald model) was built in order to identify any independent factors for yeast isolation in patients with intra-abdominal infections. Only significant variables ($P < 0.05$) in a univariate analysis were included in the multivariate model. All potential explanatory variables included in the multivariate analyses were subjected to a collinearity analysis in a correlation matrix. Intercorrelated variables were not included in the multivariate model (tolerance < 0.3 and variance inflation factor > 3). The Hosmer-Lemeshow test was used to assess the model's goodness of fit [21]. The model's predicted probabilities were validated with the c statistic (corresponding to the model's area under the curve (AUC)) [21].

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A score was built according to the ORs in the multivariate analysis and was tested in a receiver operating characteristic (ROC) analysis [22]. The best score's cutoff was calculated for the best Youden index. The score's performance was tested in a prospective (validation) cohort, according to the same analysis. The AUC of the ROC curve of new score was compared with the AUC of previously published scores in the same cohort using Hanley and McNeil tests.

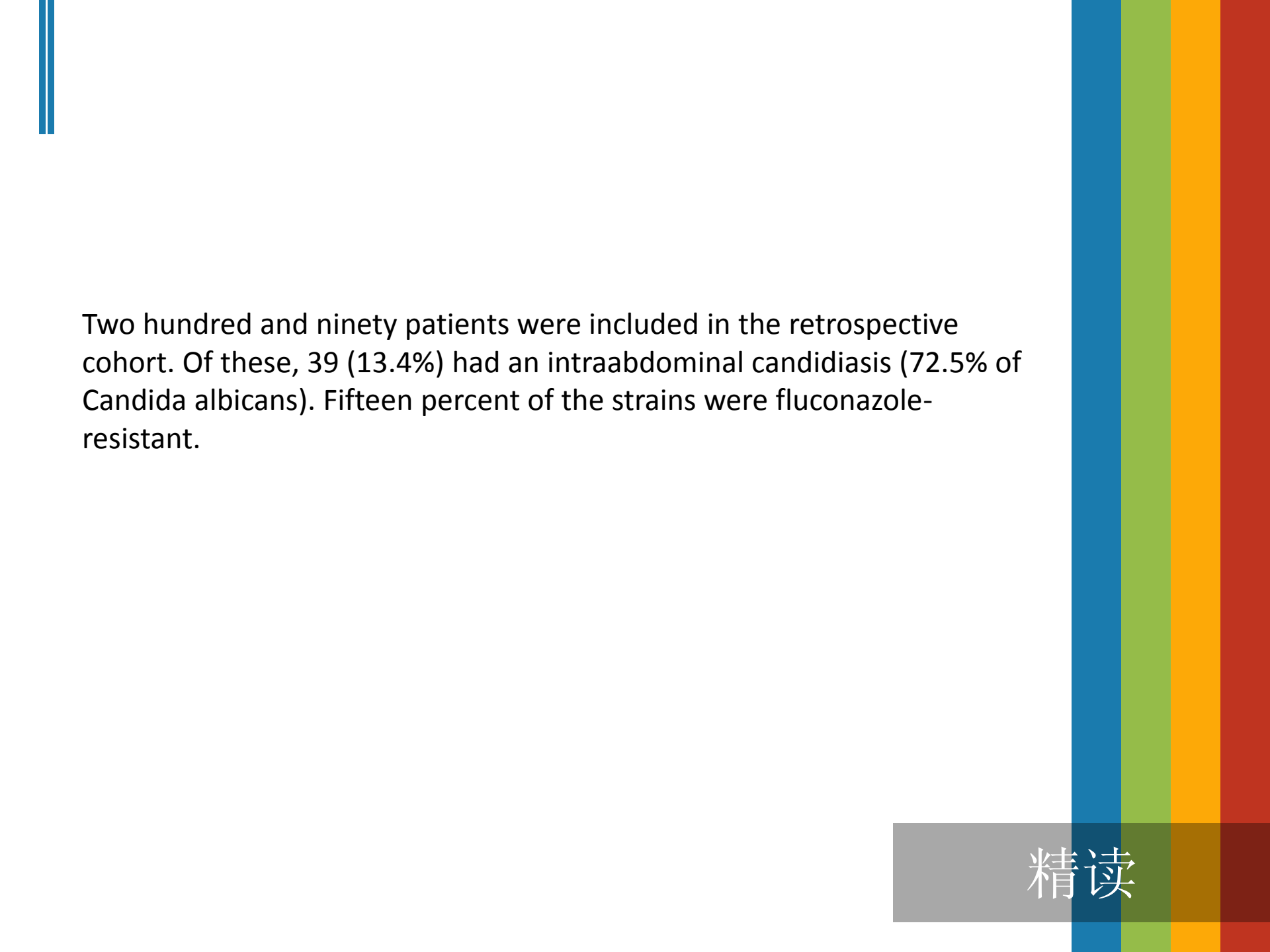
A second multivariate analysis was performed to identify the impact of yeast isolation in mortality of the whole cohort. The threshold for statistical significance was set to $P \leq 0.05$. Statistical analyses were performed with PASW Statistics 18 software (IBM Inc., Chicago, IL, USA) and MedCalc 12.7.5 software (MedCalc Software, Ostend, Belgium).

Results

Four hundred and forty-four patients were included in the study (290 in the retrospective cohort and 152 in the prospective cohort).

Table 1 Location and etiologies of complicated non-postoperative intra-abdominal infections in the whole cohort of patients

	Whole cohort (n = 442)
Lower gastrointestinal tract	312 (70.6)
Appendicitis	133 (30.1)
Diverticulitis	75 (17)
Inflammatory bowel disease	10 (2.3)
Malignancy	18 (4.1)
Ischemic	39 (8.8)
Miscellaneous	37 (8.4)
Upper intestinal tract	130 (29.4)
Biliary tract	76 (17.2)
Ulcer disease	43 (9.7)
Ischemic	6 (1.4)
Miscellaneous	5 (1.0)



Two hundred and ninety patients were included in the retrospective cohort. Of these, 39 (13.4%) had an intraabdominal candidiasis (72.5% of *Candida albicans*). Fifteen percent of the strains were fluconazole-resistant.

Table 3 Demographic data for the retrospective cohort according of the presence (yeast positive) or absence (yeast negative) of yeast in the peritoneal fluid culture

	Yeast positive (n = 39)	Yeast negative (n = 251)	P value
Age	65 ± 18	59 ± 22	0.08
Female gender	20 (51.3)	125 (49.8)	0.98
BMI (kg.m ⁻²)	26.6 ± 7.2	25.9 ± 5.7	0.95
Underlying diseases			
Prior abdominal surgery	7 (17.9)	46 (18.1)	0.87
Diabetes	7 (17.9)	40 (15.9)	0.93
Immunosuppression	7 (17.9)	12 (4.8)	0.006
Chronic cardiovascular disease	22 (56.4)	120 (47.8)	0.41
Chronic renal failure	3 (7.7)	9 (3.6)	0.15
ASA status	2.9 ± 0.6	2.5 ± 0.8	0.001
Mannheim peritonitis index score	22.9 ± 7.6	16.0 ± 8.1	<0.001
APACHE II score	14.6 ± 10.9	8.0 ± 7.9	<0.001
SAPS II score	36.2 ± 20.6	24.7 ± 15.2	<0.001
SOFA score	4.9 ± 6.5	1.9 ± 3	<0.001
Type of infection			
Community-acquired	19 (48.7)	196 (78.1)	<0.001
LOS ≥48 h before surgery	20 (51.3)	55 (21.9)	<0.001
Generalized peritonitis	31 (79.5)	95 (37.8)	<0.001
Upper gastrointestinal tract location	18 (46.2)	74 (29.6)	<0.001
Ongoing AB ≥48 h	12 (30.8)	35 (13.9)	0.01

The demographic characteristics of the YP and YN groups are summarized in Table 3. There were no significant intergroup differences other than a higher proportion of patients on immunosuppression in the YP group ($P = 0.006$). There were marked intergroup differences in the severity scores and types of infection. Patients in the YP group were significantly more likely to have worse severity scores ($P < 0.001$ for all), generalized infections (< 0.001), upper gastrointestinal tract perforation ($P < 0.001$) and ongoing antimicrobial therapy (≥ 48 hours) ($P = 0.01$).

Four independent factors were predictive of IAC: length of stay before surgery ≥ 48 h, per-operative cardiovascular failure, generalized peritonitis and upper gastrointestinal tract perforation. The model's Wald chi-squared statistic was 50.2 (df = 5, $P < 0.001$). The Hosmer-Lemeshow test statistic was 9.69 (df = 6, $P = 0.14$). The model's c statistic was 0.83 (0.77 to 0.89)

Table 4 Multivariate analysis of factors independently associated with an intra-abdominal candidiasis in the retrospective cohort with CAIs and NPNIAIs

Parameters	Adjusted OR	95%CI	P value
Per-operative cardiovascular failure	2.43	1.01 - 5.81	0.04
Upper gastrointestinal tract perforation	2.53	1.15 - 5.55	0.02
LOS ≥ 48 h before surgery	3.15	1.45 - 6.89	0.004
Generalized peritonitis	6.78	2.75 - 16.68	<0.001

CAIs, community-acquired infections; NPNIAIs, non-postoperative nosocomial intra-abdominal infections; OR, odds ratio; CI, confidence interval; LOS, length of stay.

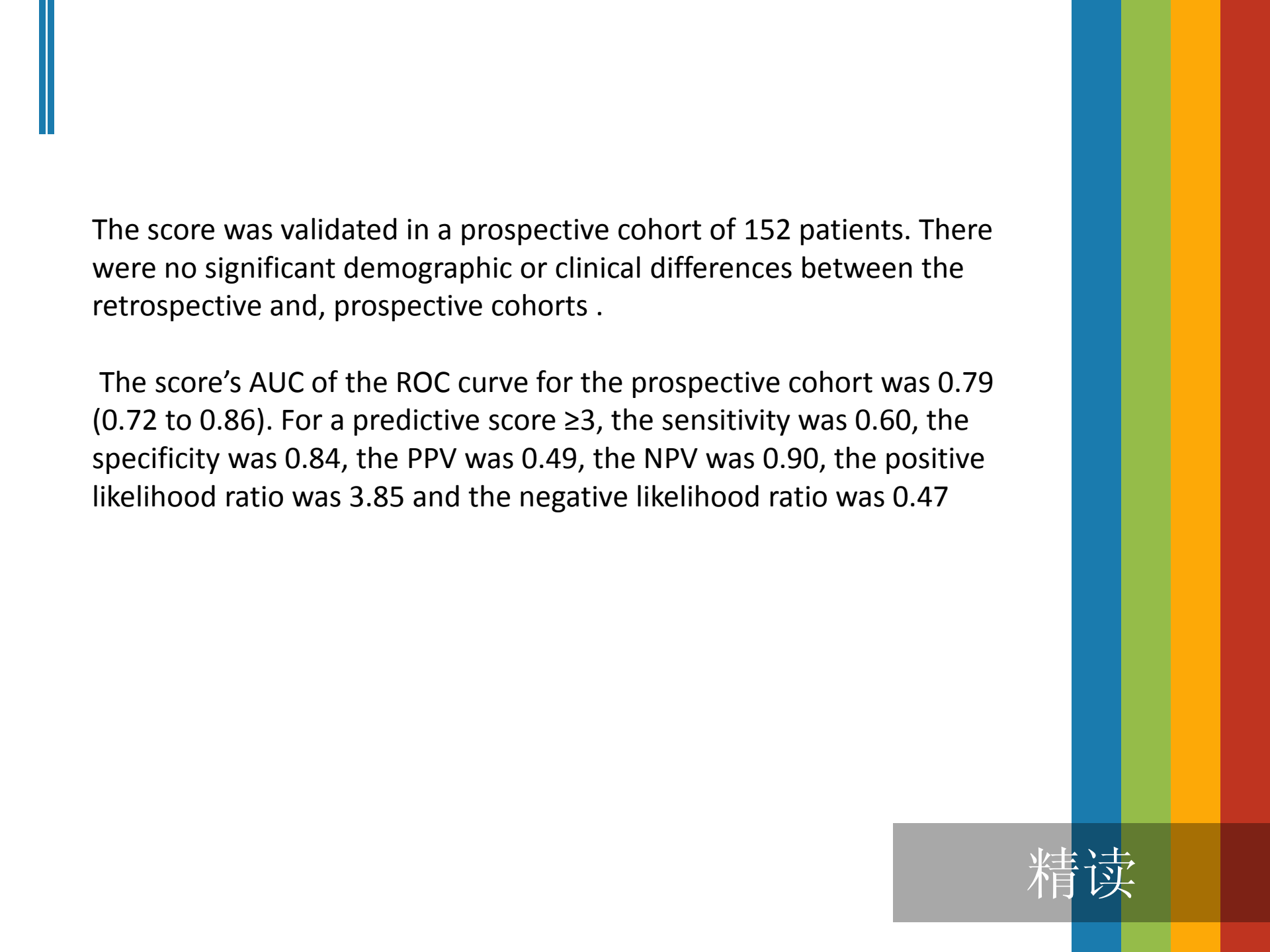
Construction and validation of the score

A predictive score was built according to the ORs in the multivariate analysis (Table 5). In the retrospective cohort, the area (95%CI) under the curve was 0.82 (0.73 to 0.90), yielding the following characteristics for a score ≥ 3 : sensitivity = 0.75; specificity = 0.77; PPV = 0.34; NPV = 0.95; positive likelihood ratio = 3.2; negative likelihood ratio = 0.34.

Table 5 Predictive score for intra-abdominal candidiasis in complicated non-postoperative intra-abdominal infections

Item	Value
LOS ≥ 48 h before surgery	1 point
Per-operative cardiovascular failure	1 point
Generalized peritonitis	2 points
Upper gastrointestinal tract perforation	1 point

LOS, length of stay.

The slide features a white background with decorative vertical bars. On the left, there are two thin blue vertical bars. On the right, there is a thick vertical bar composed of four colored segments: blue, green, yellow, and red. The text is centered on the page.

The score was validated in a prospective cohort of 152 patients. There were no significant demographic or clinical differences between the retrospective and, prospective cohorts .

The score's AUC of the ROC curve for the prospective cohort was 0.79 (0.72 to 0.86). For a predictive score ≥ 3 , the sensitivity was 0.60, the specificity was 0.84, the PPV was 0.49, the NPV was 0.90, the positive likelihood ratio was 3.85 and the negative likelihood ratio was 0.47

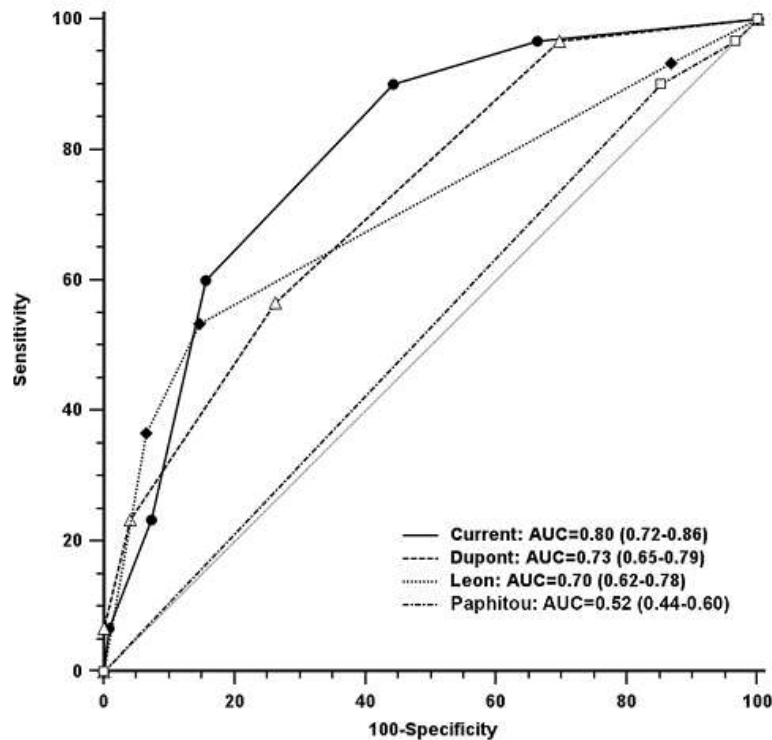


Figure 2 Comparison of receiver operating characteristic curves between the new score and previously published one in the prospective cohort (Dupont *et al.* [13], Leon *et al.* [10], Paphitou *et al.* [14]).

The AUC of the ROC curve of the new score is presented in comparison with previously published scores of Dupont *et al.* [13], Leon *et al.* [10] and Paphitou *et al.* in Figure 2. The new score had the best AUC when compared with other scores. However, no statistical differences were observed between the new score and Dupont's score ($P = 0.15$), the new score and Leon's score ($P = 0.17$). The former three scores were all significantly better than Paphitou's score ($P = 0.0001$; $P = 0.006$; $P = 0.02$, respectively).

Table 7 Comparison of outcomes between yeast-positive and yeast-negative groups with complicated non-postoperative intra-abdominal infections

Whole cohort (n = 442)	Yeast positive (n = 69)	Yeast negative (n = 373)	P value
Any complication	54 (63.8)	158 (42.4)	0.001
Infectious complication	32 (46.3)	98 (26.3)	0.001
Digestive	8	33	
Pneumonia	12	27	
Miscellaneous	12	38	
Transfusion	19 (27.5)	38 (10.2)	0.001
Relaparotomy	17 (24.6)	52 (13.9)	0.02
Cardiovascular failure	36 (52.2)	64 (17.2)	<0.001
Respiratory failure	35 (50.7)	81 (21.7)	<0.001
ICU admission	39 (56.5)	111 (29.8)	<0.001
Duration of mechanical ventilation (d)	10.7 ± 14.9	9.5 ± 14.7	0.69
ICU length of stay (d)	16.1 ± 16.4	11.6 ± 13.9	0.11
Hospital length of stay (d)	20.5 ± 22.4	13.2 ± 16.0	0.001
Mortality	19 (27.5)	31 (8.3)	<0.001

Briefly, patients with an IAC had more complications, had undergone more relaparotomies, and had more organ failure requiring ICU admission. Their hospital length of stay was twice as high and mortality three times higher (27.5% vs. 8.3%, $P < 0.001$).

Table 8 Predictive factors of mortality in the whole cohort of 442 patients with complicated non-postoperative intra-abdominal infections

Parameters	Univariate analysis			Multivariate analysis		
	OR	95%CI	<i>P</i> value	AOR	95%CI	<i>P</i> value
IAC	4.19	2.20-7.98	0.001	2.15	1.03-4.46	0.04
Ongoing AB \geq 48 h	3.52	1.83-6.79	0.001	-	-	-
MPI score \geq 17	7.96	3.31-19.10	0.001	3.22	1.26-8.25	0.02
ASA score \geq 3	19.42	5.95-63.47	0.001	7.56	2.21-25.78	0.001
SOFA score \geq 1	18.35	6.47-52.02	0.001	7.90	2.68-23.26	0.001
APACHE II score \geq 7	19.22	5.88-62.82	0.001	-	-	-

OR, odds ratio; CI, confidence interval; AOR, adjusted odds ratio; IAC, intra-abdominal candidiasis; AB, antimicrobial therapy; MPI, Mannheim peritonitis index; ASA, American Society of Anesthesiology; SOFA, Sepsis-related Organ Failure Assessment; APACHE II, Acute Physiology and Chronic Health Evaluation II.

Four independent factors of mortality in the whole cohort were evidenced: an IAC, a Mannheim peritonitis score \geq 17, an American Society of Anesthesiology (ASA) score \geq 3 and a SOFA score \geq 1.

Discussion

Our present results show that a YP peritoneal fluid culture is associated with worst outcomes and increased mortality in patients with CNPIAI. The prevalence of yeast isolation in this context is low (15.6%). The predictive score has a high NPV and thus can be used to rule out the presence of yeast in the peritoneal fluid. Hence, this score may constitute an easy-to-use bedside tool that enables the physician to avoid the initiation of inappropriate antifungal treatment .

In a case-control study, there was no significant difference in outcome between YP and YN CAIs . However, the study featured a small number of patients. In a study of patients with organ failure admitted to the ICU, a YP culture was found to be associated with elevated mortality [4]. Another study reported a significantly greater proportion of septic shock in CAIs when yeast was detected in the peritoneal fluid culture [23]. The overall prevalence of a YP culture in our study population (15.6%) is similar to the mean value reported in the literature (with values ranging from 4% to 43.4% in studies of CAIs)[2,24].

In the present study, four parameters were found to be independently associated with IAC of patients with a CNPIAI. Interestingly, upper gastrointestinal tract perforation and per-operative cardiovascular failure were previously included in a predictive score for severe intraabdominal infections in the ICU [4]. There are no literature data on why yeast isolation is more frequently associated with generalized peritonitis than with localized infection. It could be only due to the major impact of appendicitis infections in CAI.

The score developed in the present study has a good NPV. It may be important to avoid the inappropriate initiation of antifungal treatments that are costly and whose impact on resistance is not well known. Blood levels of β -glucan may be of value for the diagnosis of postoperative infections in high-risk surgical patients [28]. However, there are no data on the value of β -glucan levels in CAIs. We did not have access to a β -glucan assay during our study. The study was designed to assess the course of candidiasis in the ICU, rather than to predict the presence of candidiasis on admission.

A worse outcome associated with YP culture of the peritoneal fluid was evidenced in this study. Furthermore, it was independently associated with mortality. It is the first report in the literature of such impact in mild to moderate infections.

Our study had some potential limitations. First, this was a single-center study. The present study's results must be validated in multicenter trials. Recently, the sensitivity breakpoints for *Candida* spp. were modified according to the species [30]. This study used previously described breakpoints ($>32 \mu\text{g}\cdot\text{ml}^{-1}$) that could have underestimated the rate of strains resistant to fluconazole. Our study focused on the development of a predictive score and thus did not address the question of how best to treat IAC. Lastly, the use of the new score is not well calibrated for critical care patients because only one-third of the cohort was admitted to the ICU.

THANKS FOR YOUR WATCHING



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