Critical Care Medicine

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1、Abdominal Paracentesis Drainage Ahead of Percutaneous Catheter Drainage Benefits Patients Attacked by Acute Pancreatitis With Fluid Collections: A Retrospective Clinical Cohort Study

Objective: The efficacy and safety of ultrasound-guided abdominal paracentesis drainage ahead of percutaneous catheter drainage as the new second step of a step-up approach are evaluated.

Interventions: In this step-up approach, all patients subsequently received medical management, percutaneous catheter drainage (with or without previous abdominal paracentesis drainage), and necrosectomy if necessary according to indications. The patients were divided into two groups: 53 cases underwent abdominal paracentesis drainage followed by percutaneous catheter drainage (abdominal paracentesis drainage + percutaneous catheter drainage group) and 49 cases were managed only with percutaneous catheter drainage (percutaneous catheter drainage-alone group).

Main Results: The mortality rate was lower in the abdominal paracentesis drainage + percutaneous catheter drainage group (0%) than the percutaneous catheter drainage-alone group (8.2%) ($p = 0.050$). Compared with the percutaneous catheter drainage-alone group, the laboratory variables of the abdominal paracentesis drainage + percutaneous catheter drainage group decreased more rapidly, the mean number of failed organs was lower, and the interval from the onset of disease to further interventions was much longer. However, there was no significant difference in the prevalence and duration of infections between the two groups.

Conclusion: Application of abdominal paracentesis drainage ahead of percutaneous catheter drainage is safe and beneficial to patients by reducing inflammatory factors, postponing further interventions, and delaying or avoiding multiple organ failure.

2、Electroencephalogram Predicts Outcome in Patients With Postanoxic Coma During Mild Therapeutic Hypothermia

Objective: To assess the value of electroencephalogram for prediction of outcome of comatose patients after cardiac arrest treated with mild therapeutic hypothermia.

Measurements ：Continuous electroencephalogram was recorded during the first 5 days of ICU admission. Visual classification of electroencephalogram patterns was performed in 5-minute epochs at 12 and 24 hours after cardiac arrest by two independent observers, blinded for patients' conditions and outcomes. Patterns were classified as isoelectric, low voltage, epileptiform, burst-suppression, diffusely slowed, or normal. Burst-suppression was subdivided into patterns with and without identical bursts. Primary outcome measure was the neurologic outcome based on each patient's best achieved Cerebral Performance Category score within 6 months after inclusion.

Main Results: 67 patients (47%) had favorable outcome (Cerebral Performance Category, 1-2). In patients with favorable outcome, electroencephalogram patterns improved within 24 hours after cardiac arrest, mostly toward diffusely slowed or normal. At 24 hours after cardiac arrest, the combined group of isoelectric, low voltage, and "burst-suppression with identical bursts" was associated with poor outcome with a sensitivity of 48% (95% CI, 35-61) and a specificity of 100% (95% CI, 94-100). At 12 hours, normal or diffusely slowed electroencephalogram patterns were associated with good outcome with a sensitivity of 56% (95% CI, 41-70) and a specificity of 96% (95% CI, 86-100)

Conclusions: Electroencephalogram allows reliable prediction of both good and poor neurologic outcome of patients with postanoxic encephalopathy treated with mild therapeutic hypothermia within 24 hours after cardiac arrest.

3、Intracranial Pressure After Subarachnoid Hemorrhage

Objectives: To describe mean intracranial pressure after aneurysmal subarachnoid hemorrhage, to identify clinical factors associated with increased mean intracranial pressure, and to explore the relationship between mean intracranial pressure and outcome.

Measurements： Episodes of intracranial pressure greater than 20 mm Hg lasting at least 5 minutes and the mean intracranial pressure for every 12-hour interval were analyzed. The highest mean intracranial pressure was analyzed in relation to demographic characteristics, acute neurologic status, initial radiological findings, aneurysm treatment, clinical vasospasm, and ischemic lesion. Mortality and 6-month outcome (evaluated using a dichotomized Glasgow Outcome Scale) were also introduced in multivariable logistic models

Main Results: Eighty-one percent of patients had at least one episode of high intracranial pressure and 36% had a highest mean intracranial pressure more than 20 mm Hg. The number of patients with high intracranial pressure peaked 3 days after subarachnoid hemorrhage and declined after day 7. Highest mean intracranial pressure greater than 20 mm Hg was significantly associated with initial neurologic status, aneurysmal rebleeding, amount of blood on CT scan, and ischemic lesion within 72 hours from subarachnoid hemorrhage. Patients with highest mean intracranial pressure greater than 20 mm Hg had significantly higher mortality. When death, vegetative state, and severe disability at 6 months were pooled, however, intracranial pressure was not an independent predictor of unfavorable outcome 。

Conclusions: High intracranial pressure is a common complication in the first week after subarachnoid hemorrhage in severe cases admitted to ICU. Mean intracranial pressure is associated with the severity of early brain injury and with mortality.

4、Multicenter, Randomized, Placebo-Controlled Phase III Study of Pyridoxalated Hemoglobin Polyoxyethylene in Distributive Shock (PHOENIX)

Objective: To compare the effectiveness and safety of the hemoglobin-based nitric oxide scavenger, pyridoxalated hemoglobin polyoxyethylene, against placebo in patients with vasopressor-dependent distributive shock.

Patients: All patients admitted with distributive shock, defined as the presence of at least two systemic inflammatory response syndrome criteria, persisting norepinephrine dependence and evidence of organ dysfunction/ hypoperfusion despite adequate fluid resuscitation.

Interventions: Patients were randomized to receive 0.25 mL/kg/hr pyridoxalated hemoglobin polyoxyethylene (20 mg Hb/kg/hr) or an equal volume of placebo, infused for up to 150 hours, in addition to conventional vasopressor therapy.

Measurements and Main Results: The study was stopped after interim analysis showed higher mortality in the pyridoxalated hemoglobin polyoxyethylene group and an increased prevalence of adverse events. At this time, 377 patients had been randomized to pyridoxalated hemoglobin polyoxyethylene (n = 183) or placebo (n = 194). Age, gender, type of patient (medical/surgical), and Acute Physiology and Chronic Health Evaluation II scores were similar between groups. Twenty-eight-day mortality rate was 44.3% in the pyridoxalated hemoglobin polyoxyethylene group versus 37.6% in the placebo group (OR, 1.29; 95% CI, 0.85-1.95; p = 0.227). In patients with higher organ dysfunction scores (Sepsis-related Organ Failure Assessment > 13), mortality rates were significantly higher in the pyridoxalated hemoglobin polyoxyethylene group when compared with those in placebo-treated patients (60.9% vs 39.2%; p = 0.014). Survivors who received pyridoxalated hemoglobin polyoxyethylene had a longer vasopressor-free time (21.3 vs 19.7 d; p = 0.035).

Conclusions: In this randomized, controlled phase III trial in patients with vasopressor-dependent distributive shock, administration of a pyridoxalated hemoglobin solution decreased the need for vasopressors but was associated with a trend to increased mortality.

5、The Relationship Among Obesity, Nutritional Status, and Mortality in the Critically Ill

Introduction: The association between obesity and mortality in critically ill patients is unclear based on the current literature. To clarify this relationship, we analyzed the association between obesity and mortality in a large population of critically ill patients and hypothesized that mortality would be impacted by nutritional status.

Methods: Body mass index was determined at the time of dietitian consultation from the estimated dry weight or hospital admission weight and categorized a priori as less than 18.5 kg/m2 (underweight), 18.5-24.9 kg/m2 (normal/referent), 25-29.9 kg/m2 (overweight), 30-39.9 kg/m2 (obesity class I and II), and more than or equal to 40.0 kg/m2 (obesity class III). Malnutrition diagnoses were categorized as nonspecific malnutrition, protein-energy malnutrition, or well nourished. The primary outcome was all-cause 30-day mortality determined by the Social Security Death Master File.

Results: In the cohort, 5% were underweight, 36% were normal weight, 31% were overweight, 23% had class I/II obesity, and 5% had class III obesity. Nonspecific malnutrition was present in 56%, protein-energy malnutrition was present in 12%, and 32% were well nourished. The 30-day and 90-day mortality rate for the cohort was 19.1 and 26.6%, respectively. Obesity is a significant predictor of improved 30-day mortality following adjustment for age, gender, race, medical versus surgical patient type, Deyo-Charlson index, acute organ failure, vasopressor use, and sepsis: underweight odds ratio 30-day mortality is 1.09 (95% CI, 0.80-1.48), overweight 30-day mortality odds ratio is 0.93 (95% CI, 0.80-1.09), class I/II obesity 30-day mortality odds ratio is 0.80 (95% CI, 0.67-0.96), and class III obesity 30-day mortality odds ratio is 0.69 (95% CI, 0.49-0.97), all relative to patients with body mass index 18.5-24.9 kg/m2

Importantly, there is confounding of the obesity-mortality association on the basis of malnutrition. Adjustment for only nutrition status attenuates the obesity-30-day mortality association In a subset of patients with body mass index more than or equal to 30.0 kg/m2 (n = 1,799), those with either nonspecific or protein-energy malnutrition have increased mortality relative to well-nourished patients with body mass index more than or equal to 30.0 kg/m2: odds ratio of 90-day mortality is 1.67 (95% CI, 1.29-2.15; p < 0.0001), fully adjusted. In a cohort of propensity score matched patients (n = 3,554), the body mass index-mortality association was not statistically significant, likely from matching on nutrition status.

Conclusions: In a large population of critically ill adults, the association between improved mortality and obesity is confounded by malnutrition status. Critically ill obese patients with malnutrition have worse outcomes than obese patients without malnutrition.

6、International Study on Microcirculatory Shock Occurrence in Acutely Ill Patients*

Objectives: Microcirculatory alterations are associated with adverse outcome in subsets of critically ill patients. The prevalence and significance of microcirculatory alterations in the general ICU population are unknown. We studied the prevalence of microcirculatory alterations in a heterogeneous ICU population and its predictive value in an integrative model of macro- and microcirculatory variables.

Measurements : Demographic, hemodynamic, and laboratory data were collected in all ICU patients who were 18 years old or older. Sublingual Sidestream Dark Field imaging was performed to determine the prevalence of an abnormal capillary microvascular flow index (< 2.6) and its additional value in predicting hospital mortality

Main Results: In 501 patients with a median APACHEII score of 15 (10-21), a SOFAs score of 5 (2-8), and a hospital mortality of 28.4%, 17% exhibited an abnormal capillary microvascular flow index. Tachycardia (heart rate > 90 beats/min) (OR, 2.71; 95% CI, 1.67-4.39; p < 0.001), mean arterial pressure (OR, 0.979; 95% CI, 0.963-0.996; p = 0.013), vasopressor use (OR, 1.84; 95% CI, 1.11-3.07; p = 0.019), and lactate level more than 1.5 mEq/L (OR, 2.15; 95% CI, 1.28-3.62; p = 0.004) were independent risk factors for hospital mortality, but not abnormal microvascular flow index. In reference to microvascular flow index, a significant interaction was observed with tachycardia. In patients with tachycardia, the presence of an abnormal microvascular flow index was an independent, additive predictor for in-hospital mortality (OR, 3.24; 95% CI, 1.30-8.06; p = 0.011). This was not true for nontachycardic patients nor for the total group of patients.

Conclusions: In a heterogeneous ICU population, an abnormal microvascular flow index was present in 17% of patients. This was not associated with mortality. However, in patients with tachycardia, an abnormal microvascular flow index was independently associated with an increased risk of hospital death.

7、Failure of Anticoagulant Thromboprophylaxis: Risk Factors in Medical-Surgical Critically Ill Patients

Objectives: To identify risk factors for failure of anticoagulant thromboprophylaxis in critically ill patients in the ICU.

Interventions: All patients received anticoagulant thromboprophylaxis with low-molecular-weight heparin or unfractionated heparin at standard doses.

Measurements： : Independent predictors for venous thromboembolism, proximal leg deep vein thrombosis, and pulmonary embolism developing during critical illness were assessed.

Main Results ：A total of 289 patients (7.7%) developed venous thromboembolism. Predictors of thromboprophylaxis failure as measured by development of venous thromboembolism included a personal or family history of venous thromboembolism (hazard ratio, 1.64; 95% CI, 1.03-2.59; p = 0.04) and body mass index (hazard ratio, 1.18 per 10-point increase; 95% CI, 1.04-1.35; p = 0.01). Increasing body mass index was also a predictor for developing proximal leg deep vein thrombosis (hazard ratio, 1.25; 95% CI, 1.06-1.46; p = 0.007), which occurred in 182 patients (4.9%). Pulmonary embolism occurred in 47 patients (1.3%) and was associated with body mass index (hazard ratio, 1.37; 95% CI, 1.02-1.83; p = 0.035) and vasopressor use (hazard ratio, 1.84; 95% CI, 1.01-3.35; p = 0.046). Low-molecular-weight heparin (in comparison to unfractionated heparin) thromboprophylaxis lowered pulmonary embolism risk (hazard ratio, 0.51; 95% CI, 0.27-0.95; p = 0.034) while statin use in the preceding week lowered the risk of proximal leg deep vein thrombosis (hazard ratio, 0.46; 95% CI, 0.27-0.77; p = 0.004).

Conclusions: Failure of standard thromboprophylaxis using low-molecular-weight heparin or unfractionated heparin is more likely in ICU patients with elevated body mass index, those with a personal or family history of venous thromboembolism, and those receiving vasopressors. Alternate management or incremental risk reduction strategies may be needed in such patients.

8、Dysphagia-A Common, Transient Symptom in Critical Illness Polyneuropathy: A Fiberoptic Endoscopic Evaluation of Swallowing Study*.

Objectives: Critical illness polyneuropathy is a common disorder in the neurological ICU. Dysphagia is well known to deteriorate outcome in the ICU. The prevalence of dysphagia in critical illness polyneuropathy is not known. The aim of this study was to evaluate the prevalence of dysphagia in critical illness polyneuropathy using fiberoptic endoscopic evaluation of swallowing.

Interventions: Clinical swallowing examination and serial fiberoptic endoscopic evaluation of swallowing (days 3, 14, and 28 after admission).

Measurements：Swallowing of saliva, pureed consistencies, and liquids was tested using fiberoptic endoscopic evaluation of swallowing at three different time points. The penetration-aspiration scale by Rosenbek et al and the secretion severity rating scale by Murray et al were used for grading. Functional outcome after rehabilitation was assessed using the functional independence measure.

Main Results: Pathologic swallowing was found in 20 of 22 patients (91%). Hypesthesia of laryngeal structures was found in 17 of 22 patients (77%) during the first fiberoptic endoscopic evaluation of swallowing. Over the 4-week follow-up period, laryngeal hypesthesia resolved in 75% of affected cases. Pureed consistencies were swallowed safely in 18 of 22 cases (82%), whereas liquids and saliva showed high aspiration rates (13 of 17 [78%] and 10 of 22 [45%], respectively). Swallowing function recovered completely in 21 of 22 (95%) within 4 weeks.

Conclusions: Dysphagia is frequent among patients with critical illness polyneuropathy treated in the ICU. Old age, chronic obstructive pulmonary disease, the mode of mechanical ventilation, the prevalence of tracheal tubes, and behavioral "learned nonuse" may all be contributing factors for the development of dysphagia in critical illness polyneuropathy. Complete recovery occurs in a high percentage of affected individuals within 4 weeks.

9、Cytomegalovirus Seroprevalence as a Risk Factor for Poor Outcome in Acute Respiratory Distress Syndrome*.

Objective: Cytomegalovirus reactivation may complicate critical illness in latent carriers of the virus, even in patients who were previously immunocompetent. Patients with acute respiratory distress syndrome are considered to be prone for reactivation. Prophylactic antiviral therapy in immunocompetent cytomegalovirus seropositive patients admitted to the ICU with acute respiratory distress syndrome has therefore been proposed. We assessed cytomegalovirus seroprevalence as a risk factor for morbidity and mortality in patients with ARDS

Design: Prospective observational cohort study. We used the number of days alive and free of mechanical ventilation on day 28 as a composite outcome measure and used multivariable ordinal logistic regression analyses to adjust for potential confounders.

Patients: We included all newly admitted patients with acute respiratory distress syndrome who received mechanical ventilation for at least 4 days. Patients with known immunocompromise and those receiving antiviral treatment prior to ICU admission were excluded.

Measurements and Main Results: Over a 2-year period, 306 patients were included, 209 (68%) of whom were cytomegalovirus seropositive. Cytomegalovirus reactivation occurred in 53 of these cases (26%). One hundred patients (33%) died or continued to be mechanically ventilated by day 28. After adjustment for confounding, cytomegalovirus seroprevalence was not associated with the primary outcome (crude odds ratio, 1.09; 95% CI, 0.70-1.70; adjusted odds ratio, 1.01; 95% CI, 0.64-1.59). Seroprevalence was also not associated with poor outcome in any of the prespecified subgroup analyses. However, a significant association was found in a post hoc subgroup of patients who had developed acute respiratory distress syndrome in a setting of septic shock (adjusted odds ratio, 2.86; 95% CI, 1.32-6.23). The time course of pulmonary markers in survivors was comparable between the two serogroups.

Conclusions: Cytomegalovirus seroprevalence is not associated with prolonged mechanical ventilation or increased mortality in critically ill patients with acute respiratory distress syndrome, with possible exception of patients presenting with septic shock. Therefore, a prevention strategy targeting an unselected cohort of seropositive patients with acute respiratory distress syndrome is unlikely to show any meaningful benefit.

摘要

10. Novel Avian-Origin Influenza A (H7N9) in Critically Ill Patients in China

Objectives: In March 2013, human infection with a novel avian-origin reassortment influenza A (H7N9) virus was identified in China. A total of 26 cases were confirmed and treated in Jiangsu. All the patients had findings consistent with pneumonia and were admitted to an ICU, which pose a threat to human health. We aimed to provide the clinical features, treatment, and prognosis of the critically ill patients with H7N9 viral infection

Measurements and Main Results: Twenty-seven patients infected with H7N9 virus were identified in Jiangsu. Of these, 26 were hospitalized. The median age was 54.5 years, and 18 patients (69.2%) were men. The most common symptoms at the onset of illness were high fever and cough. White cell counts were normal or decreased. All the patients had findings consistent with pneumonia. Twenty-four patients (92.3%) developed acute respiratory distress syndrome, and 10 (38.5%) developed septic shock quickly after the onset of illness. Treatment with antiviral drugs was initiated in all the patients at a median of 8 days after the onset of illness. Mortality was 19.2% at 28 days and 30.8% at 90 days. Based on multiple logistic regression analysis, septic shock associated with severe hypoxemia was the only independent risk factor for mortality.

Conclusions: Infection with novel avian-origin reassortment influenza A (H7N9) virus is characterized by high fever, cough, and severe respiratory failure and is associated with a high mortality. These data provide some general understandings for the early identification, ICU treatment, and short-term prognosis of hospitalized critical patients with H7N9.

Clinical Investigations

Prevention of Ventilator-Associated Pneumonia and Ventilator-Associated Conditions: A Randomized Controlled Trial With Subglottic Secretion Suctioning

Influence of n-3 Polyunsaturated Fatty Acids Enriched Lipid Emulsions on Nosocomial Infections and Clinical Outcomes in Critically Ill Patients: ICU Lipids Study

Fluid Management With a Simplified Conservative Protocol for the Acute Respiratory Distress Syndrome*.

Hemodynamics and Vasopressor Support During Targeted Temperature Management at 33[degrees]C Versus 36[degrees]C After Out-of-Hospital Cardiac Arrest: A Post Hoc Study of the Target Temperature Management Trial*.

Clinical Investigations

The Association of Acute Kidney Injury in the Critically Ill and Postdischarge Outcomes: A Cohort Study*.

Is Copeptin Level Associated With 1-Year Mortality After Out-of-Hospital Cardiac Arrest? Insights From the Paris Registry*.

Postoperative Pro-Adrenomedullin Levels Predict Mortality in Thoracic Surgery Patients: Comparison With Acute Physiology and Chronic Health Evaluation IV Score*.

Early and Late Unplanned Rehospitalizations for Survivors of Critical Illness*.

A Systematic Review of Risk Factors for Delirium in the ICU*.

Xenon Improves Neurologic Outcome and Reduces Secondary Injury Following Trauma in an In Vivo Model of Traumatic Brain Injury

Epidemiology

Incidence Rate of Community-Acquired Sepsis Among Hospitalized Acute Medical Patients-A Population-Based Survey

Variations in Organism-Specific Severe Sepsis Mortality in the United States: 1999-2008

Pregnancy-Related ICU Admissions in France: Trends in Rate and Severity, 2006-2009

The Epidemiology of Chronic Critical Illness in the United States

Severe Sepsis in Hematopoietic Stem Cell Transplant Recipients*.

Special article

Surviving Sepsis Campaign: Association Between Performance Metrics and Outcomes in a 7.5-Year Study.

Methicillin-Resistant Staphylococcus aureus Prevention Strategies in the ICU: A Clinical Decision Analysis*.

Others

Comparing Observed and Predicted Mortality Among ICUs Using Different Prognostic Systems: Why Do Performance Assessments Differ?*.

Nonbeneficial Treatment Canada: Definitions, Causes, and Potential Solutions From the Perspective of Healthcare Practitioners*.

A Qualitative Investigation of Patients' and Caregivers' Experiences of Severe Sepsis*.

Development and Validation of Severe Hypoxemia Associated Risk Prediction Model in 1,000 Mechanically Ventilated Patients*

Coenrollment in a Randomized Trial of High-Frequency Oscillation: Prevalence, Patterns, Predictors, and Outcomes*

Inflence of n-3 Polyunsaturated Fatty Acids Enriched Lipid Emulsions on Nosocomial Infections and Clinical Outcomes in Critically Ill Patients: ICU Lipids Study*

Introduction：

During the last decade it has been recognized that lipidemulsions, administered within parenteral nutrition (PN) as a source of energy and polyunsaturatedfatty acids (PUFAs), exert an inflence on immune functions depending on their fatty acid (FA) composition, namely the contents of n-6 PUFAs (main source being soy bean oil) and n-3 PUFAs (derived from fih oil [FO]) Both n-6 and n-3 PUFAs are essential FAs, and besides their function as a source of energy, they are components of cellular membranes and are metabolized into bioactive mediators。

Several clinical trials have shown benefiial effects of parenteral FO supplementation in surgical patients, including modulation of inflmmatory markers, reduced length of hospital stay, and reduced infectious morbidity .Although these fidings suggest that critically ill patients may also benefi from potentially anti-inflmmatory properties of n-3 PUFAs, data derived from this patient population remain controversial .A recently published meta-analysis based on 23 studies extends the benefiial effects of parenteral n-3 PUFAs administration in surgical patients to ICU patients with respect to modulation of inflmmatory markers and reduced length of ICU and hospital stay.

MATERIALS AND METHODS:

Study Design

The study was designed as a prospective, multicenter, randomized, comparative, double-blind study in 17 Spanish ICUs.

Patient Population

Patients included (≥ 18 yr old, male and female, admitted t ICU with Acute Physiology and Chronic Health Evaluation [APACHE] II ≥ 13) were expected to require total PN (TPN) for at least 5 days according to the guidelines of the *American Society for Parenteral and Enteral Nutrition*

Exclusion criteria in detail Patients meeting one of the following criteria were excluded:

APACHE II score < 13

Cancer patients with metastasis and life expectancy less than 6 months

Morbid obesity (BMI ≥ 39)

Liver disease, defined as one of the following conditions:

o Portal hypertension with gastrointestinal bleeding at time of admission

o Clinically apparent hepatocellular ascites

o Hepatocellular bilirubin >3 mg/dL

o Serum albumin <30 g/l with portal hypertension

o Grade II or higher encephalopathy

o Clinical diagnosis of alcoholic hepatitis

Chronic renal insufficiency, defined by one of the following criteria:

o Plasma creatinine over 4 mg/dL

o Chronic peritoneal dialysis or hemodialysis

Patients with severe acquired or inherited hyperlipidemia (400 mg/day) of any type

TPN administration within 1 month prior to study enrolment

Continuous infusion treatment for over 24 hours with propofol or other pharmaceuticals that use lipid emulsions as a vehicle.

Chemotherapy or radiation therapy within 1 month prior to the study

Chronic treatment with corticoids within 1 month prior to ICU admission. (Patients who received treatment with corticoids after ICU admission due to septic shock were not excluded.)

Severe chronic neurological disease, defined by one of the following criteria:

o Cerebrovascular accident with persistent neurological deficit within the past 6 months

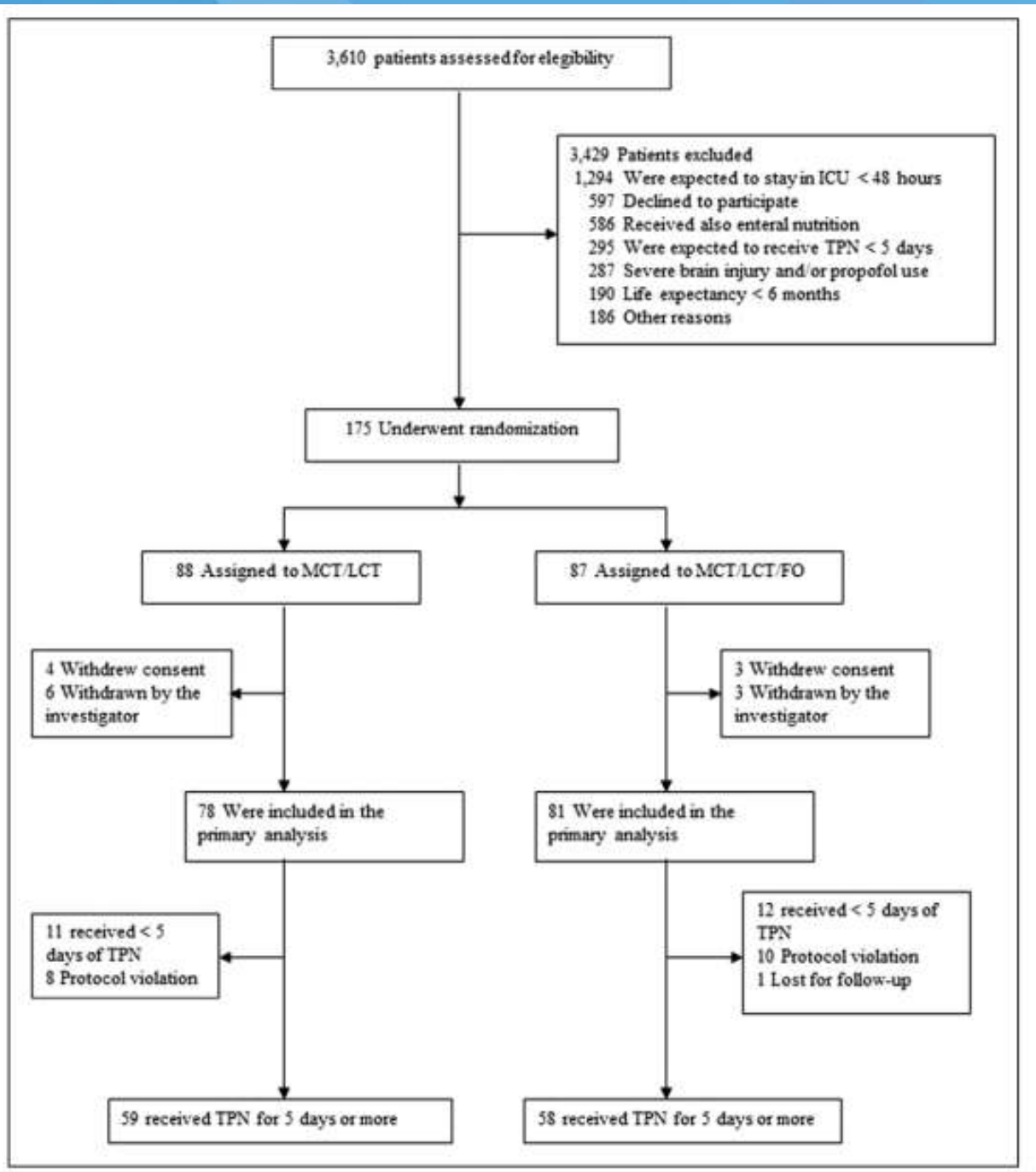
o Neurological deficit that requires chronic confinement

Infectious diseases transmitted by the blood, blood products, or urine: hepatitis B, C and HIV

Pregnancy

Enrollment in another clinical trial

Refusal to participate in the study


3,610 patients assessed for elegibility
3,429 Patients excluded
1,294 Were expected to stay in ICU < 48 hours
597 Declined to participate
586 Received also enteral nutrition
295 Were expected to receive TPN < 5 days
287 Severe brain injury and/or propofol use
190 Life expectancy < 6 months
186 Other reasons
175 Underwent randomization
88 Assigned to MCT/LCT
87 Assigned to MCT/LCT/FO
4 Withdrew consent
6 Withdrawn by the investigator
3 Withdrew consent
3 Withdrawn by the investigator
78 Were included in the primary analysis
81 Were included in the primary analysis
11 received < 5 days of TPN
8 Protocol violation
12 received < 5 days of TPN
10 Protocol violation
1 Lost for follow-up
59 received TPN for 5 days or more
58 received TPN for 5 days or more


精读

Interventions and Nutritional Regimen

Patients were randomly assigned to receive TPN either prepared with the study lipid emulsion (Lipoplus; BBraun Medical S.A.), containing 50% medium-chain triglycerides (MCT), 40% soybean oil (long-chain triglycerides, LCT), and 10% FO (MCT/LCT/FO), or prepared with the control lipid emulsion (Lipofundina; BBraun Medical S.A.), a standard lipid emulsion containing 50% MCT and 50% LCT (MCT/LCT). Randomization was computer-based, that is, randomization numbers were generated using an allocation program assuring balanced groups regarding prognostic factors (APACHE II score, < 20 and ≥ 20) and presence of sepsis at admission . Surveillance microbiological samples were taken at admission and every Monday and Thursday until discharge.

Primary Outcome

The primary endpoint was the prevalence of nosocomial infections (NIs) during 28 days of ICU stay (starting with the initiation of TPN, fialized before day 28 in the event of death or ICU discharge). Time free of infection (TFI) was calculated as timeframe between the fist treatment day and the onset of the fist episode of NI, death, or ICU discharge (maximal TFI, 28 d). Antibiotics-free time was also recorded

Secondary Outcomes

Secondary endpoints were ICU mortality, length of ICU stay,days of MV, nutritional effiacy, and liver function (concluded from adverse reactions [ARs] related to liver function and required action/medication). Hepatic dysfunctions were further differentiated into cholestasis, liver necrosis, and mixed injury (28) (Patients were followed 6 months after ICU discharge for length of hospital stay, hospital mortality, and 6-month mortality.

Data Management and Statistics

The prevalence of NIs, ICU mortality, hospital mortality, and 6-month mortality, as well as hepatic dysfunction and nutritional effiacy, were analyzed using the nonparametric Fisher exact test. Multivariate logistic regression was performed to investigate the relation between the prevalence of NIs and gender, age, prognostic variables, and nutritional regimen. Antibiotic-free days, length of MV, and ICU and hospital stay were analyzed using nonparametric Mann-Whitney test. TFI and survival time were estimated using Kaplan-Meier method and log-rank test was applied to test for statistical signifiance. TFI was estimated using the Kaplan-Meier method only including patients without signs of infection on the fist and second day after enrolment. For ICU mortality and the inverse relationship with NIs, we performed a competitive risk analysis

RESULTS:

TABLE 1. Baseline Characteristics of Study Groups

Variable	MCT/LCT (Control Group), *n* = 78	MCT/LCT/Fish Oil (Treatment Group), *n* = 81	*p*
Age	60.59 ± 16.37	60.70 ± 17.29	0.844
Gender, male/female (*n*)	54/24	62/19	0.372
Weight (kg)	76.6 ± 11.1	76.9 ± 11.9	0.957
Height (m)	1.68 ± 0.09	1.70 ± 0.08	0.175
Body mass index (kg/m^2)	27.1 ± 3.9	26.6 ± 4.0	0.358
Nutritional risk index[a]	71.4 ± 14.9	69.4 ± 15.3	0.445
Acute Physiology and Chronic Health Evaluation II score	21 ± 6	21 ± 5	0.742
Sequential Organ Failure Assessment score	7.0 ± 3.3	6.8 ± 3.6	0.553
Albumin[b]	2.41 ± 0.59	2.42 ± 0.81	0.902
C-reactive protein[c]	47.65 ± 85.27	46.39 ± 89.36	0.500
Patients with cancer (%)	8 (10.3)	6 (7.4)	0.585
Patients with sepsis (%)	37 (47.4)	36 (44.4)	0.752
Patients with septic shock (%)	23 (62.2)	23 (63.9)	1.000
Type of ICU patient (%)			0.751
Medical	36 (46.2)	40 (49.4)	
Surgical	42 (53.8)	41 (50.6)	
Urgent	35 (83.3)	35 (85.4)	1.000
Patients with injuries (%)	12 (15.4)	15 (18.5)	0.675
Patients with pancreatitis (%)	5 (6.4)	14 (17.3)	0.049
Patients with infections at enrollment and/or the subsequent 2 d (%)	10 (12.8)	10 (12.3)	1.000

MCT = medium-chain triglyceride, LCT = long-chain triglycerides.
[a]Calculated as 1.519 × serum albumin in g/L + 0.417 × (current/usual weight) × 100 (30).
[b]*n* (MCT/LCT) = 65, *n* (MCT/LCT/ fish oil [FO]) = 70.
[c]*n* (MCT/LCT) = 77, *n* (MCT/LCT/FO) = 81.

Prevalence of Nis:

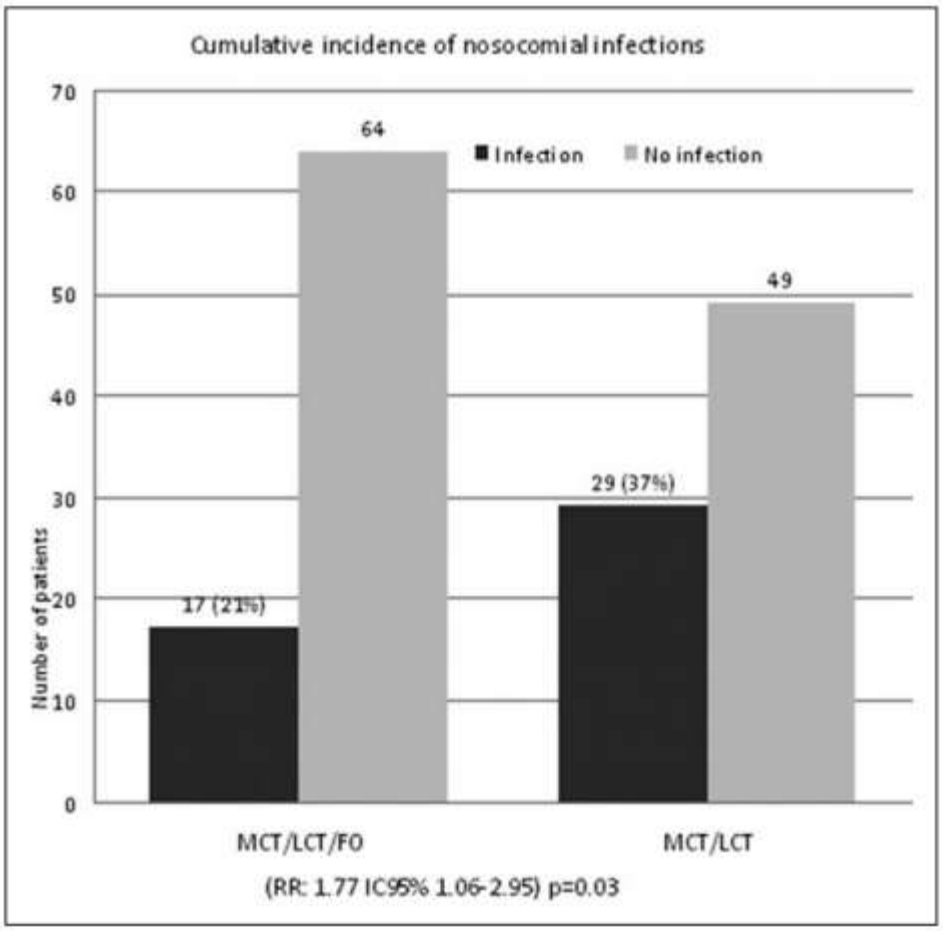


Figure 2. Cumulative prevalence of nosocomial infections. Bar chart showing the number of patients with and without infection in treatment (medium-chain triglyceride [MCT]/long-chain triglycerides [LCT]/fish oil [FO]) and control (MCT/LCT) groups. RR = risk ratio.

Prevalence of Nis:

TABLE 2. Prevalence of Nosocomial Infections

Variable	MCT/LCT, *n* (%)	MCT/LCT/Fish Oil, *n* (%)	*p*
Mechanical ventilation-associated pneumonia[a,b]	14/64 (21.9)	7/67 (10.5)	0.150
Bacteremia[a,c]	12/78 (15.4)	10/81 (12.4)	0.765
Surgical wound infection[a,d]	5/42 (11.9)	4/41 (9.8)	0.936
Intra-abdominal abscess[a,d]	4/42 (9.5)	1/41 (2.4)	0.247
Urinary tract infection[a,c]	3/78 (3.9)	4/81 (4.9)	0.679
Cumulative prevalence[e]	29/78 (37.2)	17/81 (21.0)	0.038
Antibiotic-free days	1.3±2.2	1.7±3.3	0.290

MCT = medium-chain triglyceride, LCT = long-chain triglycerides.

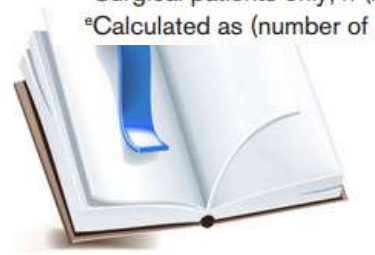
[a]Calculated as (number of infectious episodes)/(patients).

[b]Mechanically ventilated patients only; *n* (MCT/LCT) = 64, *n* (MCT/LCT/Fish Oil [FO]) = 67.

[c]All patients; *n* (MCT/LCT) = 78, *n* (MCT/LCT/FO) = 81.

[d]Surgical patients only; *n* (MCT/LCT) = 42, *n* (MCT/LCT/FO) = 41.

[e]Calculated as (number of patients with nosocomial infection(s))/(number of patients); *n* (MCT/LCT) = 78, *n* (MCT/LCT/FO) = 81.



TFI

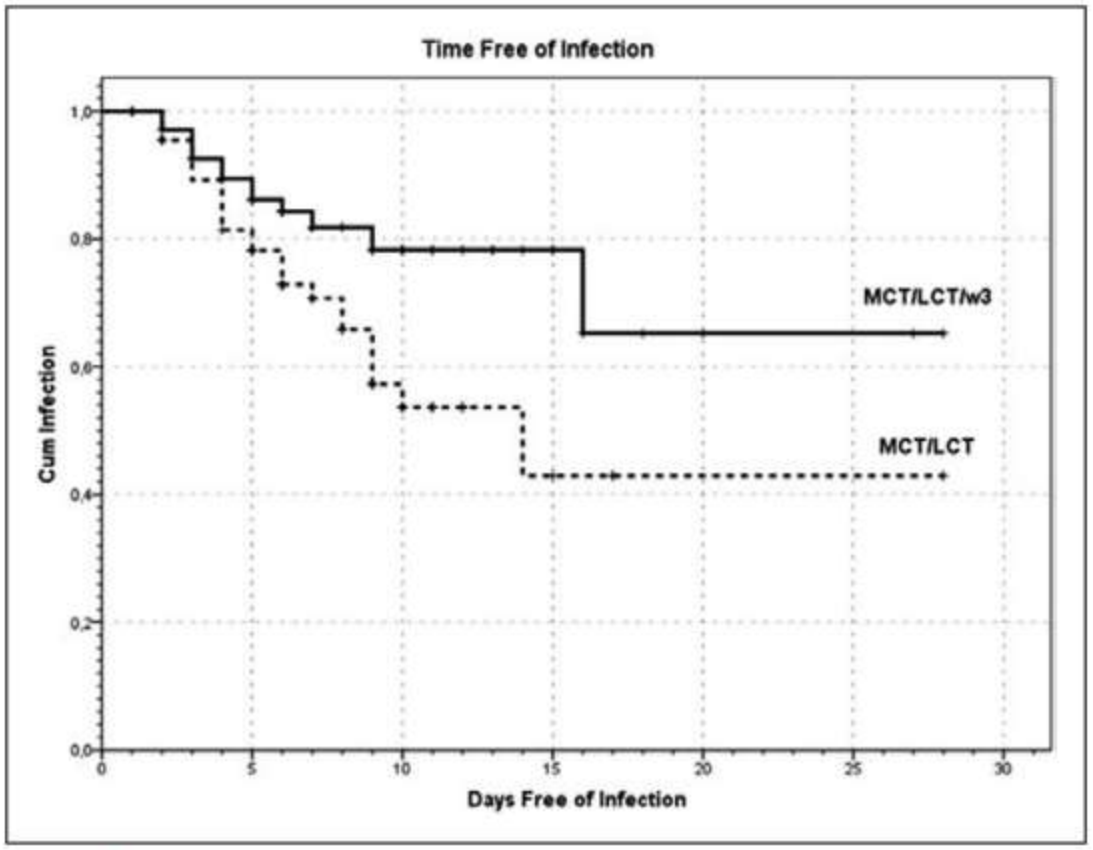


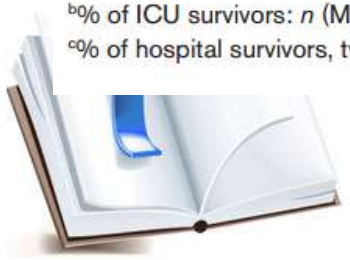
Figure 3. Time free of infection (TFI) in treatment (medium-chain triglyceride [MCT]/long-chain triglycerides [LCT]/fish oil [FO]) and control (MCT/LCT) groups. TFI was estimated for patients without signs of infection on 1st and 2nd days after study enrolment ($n = 68$) for treatment group and ($n = 71$) control group. TFI was significantly longer in the treatment group (21 vs 16 d, $p = 0.03$).

Other Clinical Outcomes

TABLE 3. Overview of Clinical Outcomes

Clinical Outcome	MCT/LCT ($n = 78$)	MCT/LCT/Fish Oil ($n = 81$)	p
Length of mechanical ventilation (d; median [interquartile range])	8 [8.5]	7 [6.0]	0.470
Length of ICU stay (d; median [interquartile range])	18 [13.25]	12 [18.5]	0.369
Length of hospital stay (d; median [interquartile range])	36.5 [34.0]	25 [34.5]	0.059
ICU mortality (n, %)[a]	16 (20.5)	26 (32.5)	0.106
Patients without pancreatitis	15 (19.2)	19 (23.8)	0.324
Patients with pancreatitis	1 (20.0)	7 (36.8)	0.338
Hospital mortality (n, %)[b]	6 (9.7)	6 (11.1)	1.000
6-month mortality (n, %)[c]	2 (3.6)	2 (4.3)	1.000
6-month survival (Kaplan-Meyer, d)	137.2 ± 7.6	117.7 ± 8.5	0.082

MCT = medium-chain triglyceride, LCT = long-chain triglycerides.
[a]One patient was lost to follow-up: n (MCT/LCT/ fish oil [FO]) = 80.
[b]% of ICU survivors: n (MCT/LCT) = 62, n (MCT/LCT/FO) = 54.
[c]% of hospital survivors, two patients were lost to follow-up for 6-month period: n (MCT/LCT) = 56, n (MCT/LCT/FO) = 46.



Safety of Administration

TABLE 4. Assessment of Hepatic Dysfunction

Variable	MCT/LCT	MCT/LCT/Fish Oil	*p*
Cholestasis (*n*, %)	66 (84.6)	67 (82.7)	0.832
Liver necrosis (*n*, %)	23 (29.5)	22 (27.2)	0.860
Mixed injury (*n*, %)	44 (56.4)	46 (56.8)	1
Measures taken: no action/retraction/ specific treatment/others (*n*)	51/1/4/4	53/0/4/3	0.920
Alterations concerning PN: none/reduction/ increase/interruption/cessation (*n*)	56/3/0/0/1	57/1/1/1/0	0.619

MCT = medium-chain triglyceride, LCT = long-chain triglycerides.

Nutritional Effiacy

TABLE 5. Caloric Intake, Lipid, and Protein Intake and Days of Total Parenteral Nutrition and Enteral Nutrition

Variable	MCT/LCT ($n = 78$)	MCT/LCT/FO ($n = 81$)	p
Parenteral energy intake (kcal/d)	1,782 ± 312[a]	1,737 ± 353	0.499
Parenteral nitrogen intake (g/d)	17.1 ± 2.1	17.5 ± 2.3	0.231
Protein delivery (g/kg BW/d)	1.41 ± 0.31	1.43 ± 0.11	0.221
Parenteral lipid intake (g/d)	80.0 ± 10.9	79.8 ± 13.1	0.806
Parenteral lipid intake [(g/kg BW)/d]	1.05 ± 0.13	1.04 ± 0.12	0.385
FO intake[b]	0	0.104 ± 0.012	Not done
Days of total PN	8.9 ± 5.4	8.8 ± 6.0	0.574
Initiation of enteral nutrition (n)	42	43	0.874
Days of total PN/days of nutritional support (%)	78.0 ± 26.4	78.1 ± 27.4	0.912

MCT = medium-chain triglyceride, LCT = long-chain triglycerides, FO = fish oil, BW = body weight.
[a]For one patient energy intake administered was not registered, $n = 77$.
[b]MCT/LCT/FO lipid emulsion only, FO content: 10%.

DISCUSSION

The main fiding of the current study is that administration of ~0.1 g FO/kg BW per day in combination with MCT and LCT in a lipid emulsion signifiantly reduced the risk of NIs (37.2% vs 21.0%) and signifiantly increased the predicted TFI for 5 days (16.2 vs 21.4 d) in medical and surgical ICU patients. This is in line with fidings of a study performed with 38 surgical intensive care patients that showed (although not signifiant) a reduced infection rate after FO supplementation (41.7% vs 27.8%) (31). Reduced infection rate found in the current study could not be attributed to a specifi type of NI. The risk of VAP in mechanically ventilated patients and the risk of intraabdominal abscess in surgical patients were reduced, but these fidings were not statistically signifiant. Sample size might be too small to allow differentiation between specifi types of NIs. The potentially reduced prevalence of VAP correlates well with fidings from other groups that showed improved respiratory function in critically ill patients receiving n-3 PUFA-enriched diets (32, 33). Also, there was a trend to more antibiotic-free days in the FO group. Probably, the systematic use of the selective digestive decontamination as a part of the pneumonia-zero campaign has led to misleading results because all mechanically ventilated patients received antibiotics in the fist 2 days after admission

The fidings of the current study are inconsistent with fidings of a large study with 166 medical ICU patients (43). Although, the amount of FO administered was similar (~0.1 g/kg/d) and the same type of lipid emulsion (MCT/LCT, 1:1) was used as control, the authors did not detect any benefiial effect of n-3 PUFAs administration. This might be due to differences in the patient population studied (critically ill medical patients vs critically ill medical and surgical patients) or the duration of FO administration. Although n-3 PUFAs were administered for 7 days in the previous study, patients in the current study received n-3 PUFAs as long as they required PN. It has been reported that levels of free n-3 PUFAs rapidly returned to baseline levels after cessation of infusion (36). Thus, it seems possible that prolonged administration of n-3 PUFAs might be necessary in critical illness to maintain a benefiial n-6/n-3 ratio.

In this study, no statistically signifiant differences were observed for other clinical outcomes, such as duration of MV, lengths of ICU and hospital stay, and mortality. However, in line with another study (33), length of hospital stay was reduced close to signifiance in the group that received n-3 PUFAs. Hospital mortality and 6-month mortality were almost equal between groups. A nonsignifiant higher mortality was found in the FO group. This is clearly related with a nonhomogeneous distribution of patients with pancreatitis in both groups. Despite there were no signifiant differences in mortality between both groups, deaths from pancreatitis were more than the 25% mortality in the FO group. Pancreatitis is a complex disease, and the prognosis is more related to the therapeutic approach, particularly the surgical approach, than the effect of any type of nutritional substrates.

ARs recorded did not differ between groups, and no serious or unexpected adverse events were reported confiming the fiding of a variety of clinical trials that FO-supplemented PN is safe in critically ill patients (3, 21). Nutritional effiacy was similar with or without FO supplementation.

The recruitment period of the study was longer than expected. This was caused by the diffiulties in obtaining informed consent in critically ill patients while having only a short time frame for enrollment since treatment has to be initiated early in the course of critical illness (3). As envisaged in the study protocol, an interim analysis maintaining blinding was performed after recruitment of 175 patients. This interim analysis indicated that the overall prevalence of Nis was lower than assumed for sample-size calculation. This is presumably attributed to the implementation of campaigns such as “Zero Bacteriemia” and “Pneumonia Zero” in Spanish ICUs. Considering the long recruitment period and the fiding that sample-size calculation was based on a no longer valid assumption, it was decided to terminate the study. Although the number of patients included into the study was therefore smaller than the sample size estimated in order to set up an adequately powered study able to detect a clinically relevant reduction of the prevalence of NIs by 20%, the number of patients at termination of the study is considered to be acceptable. This consideration is based on the fact that statistically signifiant results could be detected. Furthermore, the number of patients included is still large compared with the majority of studies available so far.

In conclusion, the study results presented here suggest that administration of ~0.1 g FO/kg BW per day in combination with MCT and LCT in a lipid emulsion reduces the risk of Nis and increases the predicted TFIs in critically ill medical and surgical ICU patients. Length of hospital stay was reduced close to signifiance. The administration of a MCT/LCT/FO parenteral lipid emulsion in critically ill patients was shown to be safe.

感谢聆听！