Initiation of nutritional support is delayed in critically ill obese patients: a multicenter cohort study\textsuperscript{1–3}

Anne-Laure Borel, Carole Schwebel, Benjamin Planquette, Aurélien Vésin, Maïté Garrowste-Orgées, Christophe Adrie, Christophe Clec'h, Elie Azoulay, Bertrand Souweine, Bernard Allaouchiche, Dany Goldgran-Toledano, Samir Jamali, Michael Darmon, and Jean-François Timsit

ABSTRACT

Background: A high catabolic rate characterizes the acute phase of critical illness. Guidelines recommend an early nutritional support, regardless of the previous nutritional status.

Objective: We aimed to assess whether the nutritional status of patients, which was defined by the body mass index (BMI) at admission in an intensive care unit (ICU), affected the time of nutritional support initiation.

Design: We conducted a cohort study that reported a retrospective analysis of a multicenter ICU database (OUTCOMEREA) by using data prospectively entered from January 1997 to October 2012. Patients who needed orotracheal intubation within the first 72 h and $>$3 d were included.

Results: Data from 3257 ICU stays were analyzed. The delay before feeding was different according to BMI groups ($P = 0.035$). The delay was longer in obese patients [BMI (in kg/m$^2$) $\geq 30$; $n = 663$] than in other patients with either low weight (BMI $< 20$; $n = 501$), normal weight (BMI $\geq 20$ and $< 25$; $n = 1135$), or overweight (BMI $\geq 25$ and $< 30$; $n = 958$). The association between nutritional status and a delay in nutrition initiation was independent of potential confounding factors such as age, sex, and diabetes or other chronic diseases. In comparison with normal weight, the adjusted RR (95% CI) associated with a delayed nutrition initiation was 0.92 (0.86, 0.98) for patients with low weight, 1.00 (0.94, 1.05) for overweight patients, and 1.06 (1.00, 1.12) for obese patients ($P = 0.004$).

Conclusions: The initiation of nutritional support was delayed in obese ICU patients. Randomized controlled trials that address consequences of early compared with delayed beginnings of nutritional support in critically ill obese patients are needed. \textit{Am J Clin Nutr} 2014;100:859–66.

INTRODUCTION

The acute phase of critical illness is characterized by a high catabolic rate that mobilizes body fat and provokes a net breakdown of skeletal muscle proteins (1). The loss of body tissue, when the critical illness is prolonged, may induce a depletion of the nutritional status that leads to a variety of clinical events including an immunosuppression characterized by an increased frequency of nosocomial infections (2), a decrease or delay in wound healing and tissue repair (3), and a loss of muscle strength and diminished activity (4). Muscle weakness may be reflected in the patient’s inability to be weaned from a mechanical ventilator, but it also contributes to complications related to extended bed rest, such as thrombophlebitis and pulmonary embolism. In the long term, these clinical events limit the ability of patients to care for themselves, prolong convalescence, and impede the return to health of patients.

Guidelines favor an early nutritional support. Enteral nutrition is the first option and should be initiated 24–48 h after admission to an intensive care unit (ICU) (5). There has been a growing concern, particularly in the United States where the obesity prevalence in ICU is high, about the specific needs of obese patients hospitalized in an ICU. It was underlined that a bias against feeding these patients exists, secondary to the perception that an enormous quantity of calories is stored in adipose tissue (6). The most challenging questions were how to assess energy requirements of obese patients and whether hypocaloric (permissive) underfeeding should be used (7). Indeed, hypocaloric, high-protein enteral or parenteral nutrition has allowed the achievement of a net protein anabolism and avoidance of overfeeding complications such as hyperglycemia, with fat weight loss as a welcome secondary benefit (8). Instead, hypocaloric,
low-protein nutrition has led to adverse outcome in obese patients. Recent guidelines have been provided by the American Society for Parenteral and Enteral Nutrition (9) regarding the specific nutritional support for obese patients in an ICU. The conclusions were that a nutritional support should be initiated for obese patients within the first 48 h and could use hypocaloric, high-protein enteral or parenteral nutrition.

In regard to these recent recommendations, the main objective of the current study was to address the current routine clinical practice regarding the nutritional support initiation according to the BMI (in kg/m²) of critically ill patients. The secondary objective was to look for a potential association between the nutrition initiation delay and mortality in critically ill obese patients.

SUBJECTS AND METHODS

Study design and data source

A retrospective analysis was conducted in a multicenter database named OUTCOMEREA by using data prospectively entered from January 1997 to October 2012 (10). The database is generated by 12 French ICUs and contains data on admission features and diagnosis, daily disease severity, iatrogenic events, nosocomial infections, and vital status. The different ICUs of the OUTCOMEREA group have enrolled either consecutive patients admitted to an ICU or some patients sampled in consecutive admissions or all admissions to predefined ICU beds. Data included in the OUTCOMEREA database have been collected by senior physicians or research monitors of participating ICUs. For each patient, data were first entered into an electronic case-report form by using VIGIREA and RHEA data-capture software programs (OUTCOMEREA), and all case-report forms were entered into the OUTCOMEREA data warehouse. At entry in the database, the data-capture software automatically conducts multiple checks for the internal consistency of most variables. Queries generated by these checks are resolved before the incorporation of new data in the database. For each participating ICU, the data quality is controlled by a senior physician from another participating ICU who checked a 2% sample of the study data at random. A 1-d coding course is organized annually with study investigators and clinical research monitors.

According to French law, this database study, which collected data from routine clinical practice, did not require informed consent; however, whenever possible, patients or their family were informed of the study and could refuse to be included in the database. The study was approved by the Institutional Ethics Committee of the Clermont-Ferrand University Hospital, Clermont-Ferrand, France (Institutional Review Board no. 5891).

Study population

All patients who needed orotracheal intubation within the first 72 h of ICU stay and >3 d were included to select patients with a theoretical indication of artificial nutrition (5, 11–13). Patients were excluded if BMI was not available. Patients who were <16 y old and those who did not survive the first 3 d of ICU stay were also excluded (see Figure 1 for a flow chart).

Data collection

The following data were collected at admission and daily if appropriate: age; sex; admission category (medical, emergency surgery, or scheduled surgery); admission main symptom; whether the patient was transferred from a hospital ward (defined as a stay in an acute-bed ward that lasted >24 h immediately before ICU admission); body weight and height assessed objectively at the bedside allowing the calculation of BMI; co-morbidities assessed by the using Charlson’s comorbidity score (14); severity of illness at ICU admission assessed by using the simplified acute physiology score II (15); severity of underlying condition assessed by the presence of chronic diseases and McCabe’s score (16); type of nutritional support that could be parenteral, enteral, and oral, excluding the intravenous infusion of glucose; orotracheal intubation; lengths of ICU stay; nosocomial infections; therapeutic limitation; and vital status at discharge from the ICU and hospital.

![Flowchart. ICU, intensive care unit.](https://academic.oup.com/ajcn/article-abstract/100/3/859/4576502/10.1093/ajcn/nqz294/Figure1)
Definitions

Patients were classified into subgroups of nutritional status according to their BMI. Patients with BMI <20 were defined as low weight, patients with BMI ≥20 and <25 were defined as normal weight, patients with BMI ≥25 and < 30 were defined as overweight, and patients with BMI ≥30 were defined as obese (Figure 1). Of note, a group that was low weight was preferred to a group of underweight patients with BMI <18.5 to better balance the number of patients and the range of BMI within different subgroups (17).

The period before feeding was defined as the number of days between the first day of orotracheal intubation and the first day of parenteral or enteral or oral nutrition. Nosocomial infections were defined as either nosocomial ventilator-associated pneumonia or bacteremia or a surgery-site deep infection. Overall deaths were all deaths that occurred after ICU admission until hospital discharge. Deaths at 30 d were all deaths that occurred before the 30th day after ICU admission.

Statistical analysis

Descriptive analyses

Patients’ characteristics were shown by using the frequency and percentage for qualitative variables and the median and IQR for quantitative variables. Comparisons were made by using the Kruskal-Wallis test for quantitative variables and the chi-square for qualitative variables. When the Kruskal-Wallis test was significant, post hoc analyses were conducted to compare one BMI group with the other 3 groups by using a Wilcoxon’s rank test. A Bonferroni correction was performed to take into account multiple comparisons. The specific incidence rate for nosocomial infections was calculated as the ratio of the number of infectious events related to the number of ICU days. Differences in specific incidence rates between BMI groups were tested by using negative binomial regression including the number of ICU days as the offset variable. Kaplan-Meier estimates were used to plot 30-d survival curves according to BMI groups, and the log-rank test was used to test for survival differences between groups.

Main objective

Patients’ characteristics that were associated with the time interval before nutrition initiation were tested by using the Kruskal-Wallis test. Variables that met the 20% P value in the univariate analysis were entered in a multivariate negative binomial model. Backward elimination was performed until all variables met the 5% threshold in the multivariate context.

Secondary objective

In the subgroup of obese patients, the effect of the time interval before the initiation of nutrition on the 30-d mortality of obese patients was tested by using a Cox model with consideration of day 4 as time 0. The time interval before the initiation of nutrition in the first 3 d was tested as dummy variables, whereas the delay of nutrition initiation since day 4 was tested as a time-dependent variable by taking the value one as soon as the patient started nutrition. An adjustment on independent risk factors of 30-d mortality in obese patients was performed. All statistical analyses were performed with SAS 9.3 software (SAS Institute Inc).

RESULTS

From 3427 ICU stays with patients who had orotracheal intubation within the first 72 h and >3 d, 170 ICU stays were never fed. Comparisons of ICU stays in which patients were fed with ICU stays where patients were unfed are reported in the online supplement (see Online supplemental table 1 under “Supplemental data” in the online issue). ICU stays in which patients were unfed were characterized by a more severe Simplified Acute Physiology Score II, more frequent decision of a therapeutic limitation, and a high mortality rate. These ICU stays were excluded from additional analyses.

Descriptive analyses

Patients’ characteristics are reported in Table 1. Subgroups defined by the range of BMI were different for age, sex distribution, admission category, and main symptom at admission. Charlson’s comorbidity score, McCabe’s score, the prevalence of diabetes, and other chronic diseases (chronic cardiovascular diseases, chronic hepatic diseases, chronic renal diseases, and chronic respiratory diseases) were also different between subgroups, whereas the severity of patients at ICU admission, which was estimated by using the Simplified Acute Physiology Score II, was not different between groups. The delay for nutrition initiation was different between BMI groups (P = 0.035). Post hoc analyses showed that only obese patients had a longer delay before feeding than that of the 3 other BMI groups (P = 0.012).

Outcomes of patients according to BMI subgroups were characterized by a progressive decrease of mortality rates from patients with low weight and normal weight to overweight and obese patients (32.1%, 29.6%, 24.8%, and 22.2% of deaths at 30 d, respectively, P < 0.001). The survival of patients according to BMI groups is reported by Kaplan-Meier estimates in Figure 2. Nosocomial infection (pneumonia, bacteremia, and deep surgery-site infection)–specific incidence rates were not statistically different between BMI subgroups.

Main objective

After univariate analyses (see Online supplemental table 2 under “Supplemental data” in the online issue), we identified independent factors associated with the delay of nutrition initiation (Table 2) in a multivariate analysis. BMI subgroups remained independently associated with a delayed nutrition initiation, and adjusted RRs associated with the delay of nutrition initiation according to patient BMI groups are reported in Figure 3.

Secondary objective

Effects of the delay of nutrition initiation on 30-d mortality in obese patients are reported in Table 3. The start of nutrition at day 1 after orotracheal intubation compared with after day 1 tended to be associated with lower risk of mortality (P = 0.09) in an unadjusted analysis, but this tendency weakened in the adjusted analysis (P = 0.5). The initiation of nutrition at day 2 or 3 or after day 4 after orotracheal intubation was not associated with 30-d mortality.
DISCUSSION

The current study addressed current habits in the ICU routine clinical practice regarding the delay to initiate a nutritional support in critically ill patients according to their BMI. Patients who were never fed during their ICU stay were considered to represent the most severe patients, with an impaired short-term prognosis that could explain the lack of nutrition in a context of a therapeutic limitation. Therefore, these ICU stays were excluded from additional analyses.

The delay before feeding was delayed in obese patients independently of other factors. This delay in nutrition initiation was not associated with the mortality outcome in obese patients.
Factors remained independently associated with the delay in younger patients had an increased delay; however, none of these were not associated with the delay before feeding, whereas univariate analyses showed that sex and the presence of diabetes age and sex distributions were different according BMI groups.

Injury that lead to specific nutritional needs. In the current study, strategy in an ICU because of specific responses to acute illness or sex (21) of patients are taken into account in the nutritional

Nutritional support in obese patients. In addition, the age (20) and hyperglycemia instead of the nutritional status that led to delay of withholding lipids, and use intensive insulin therapy to achieve a marker of nutritional status. Patients received kilocalories per day per kilogram was lower in obese than low-weight patients (<20). Of note, the time (in h) before the initiation of enteral nutrition in these patients was progressively longer than for low-weight to obese patients. The observational design of this study could not prove causality; however, an association was shown between the amount of nutrition received in the first 12 d and subsequent 60-d mortality, particularly in patients with low BMI (<25) and high BMI (>35) but with little evidence of a treatment effect in patients in with midrange BMI (25–35). Our current results are in accordance with this study. The routine clinical practice seems characterized by a spontaneous attitude toward the delay of the initiation of nutritional support in patients with higher BMI. This spontaneous attitude occurs, although to

<table>
<thead>
<tr>
<th>Variable and items</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Center</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 compared with others</td>
<td>0.83 (0.78, 0.89)</td>
<td></td>
</tr>
<tr>
<td>2 compared with others</td>
<td>1.38 (1.29, 1.48)</td>
<td></td>
</tr>
<tr>
<td>3 compared with others</td>
<td>1.80 (1.57, 2.05)</td>
<td></td>
</tr>
<tr>
<td>4 compared with others</td>
<td>1.24 (1.14, 1.35)</td>
<td></td>
</tr>
<tr>
<td>5 compared with others</td>
<td>1.04 (0.92, 1.17)</td>
<td></td>
</tr>
<tr>
<td>6 compared with others</td>
<td>0.88 (0.79, 0.98)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Low compared with normal weight</td>
<td>0.92 (0.86, 0.98)</td>
<td></td>
</tr>
<tr>
<td>Overweight compared with normal weight</td>
<td>1.00 (0.94, 1.05)</td>
<td></td>
</tr>
<tr>
<td>Obese compared with normal weight</td>
<td>1.06 (1.00, 1.12)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay before ICU admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 d compared with direct admission</td>
<td>0.92 (0.86, 0.99)</td>
<td>0.001</td>
</tr>
<tr>
<td>2–4 d compared with direct admission</td>
<td>0.91 (0.85, 0.97)</td>
<td></td>
</tr>
<tr>
<td>&gt;4 d compared with direct admission</td>
<td>0.81 (0.76, 0.86)</td>
<td></td>
</tr>
<tr>
<td>Admission category</td>
<td></td>
<td>0.030</td>
</tr>
<tr>
<td>Medical compared with scheduled surgery</td>
<td>0.90 (0.83, 0.99)</td>
<td></td>
</tr>
<tr>
<td>Emergency surgery compared with scheduled surgery</td>
<td>1.00 (0.91, 1.09)</td>
<td></td>
</tr>
<tr>
<td>Main symptom</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>MOF/shocks compared with others</td>
<td>1.04 (0.96, 1.12)</td>
<td></td>
</tr>
<tr>
<td>ARDS/COPD exacerbation compared with others</td>
<td>0.94 (0.86, 1.01)</td>
<td></td>
</tr>
<tr>
<td>Coma compared with others</td>
<td>1.04 (0.95, 1.14)</td>
<td></td>
</tr>
<tr>
<td>SAPS II</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>30–44 compared with &lt;30</td>
<td>1.06 (0.98, 1.16)</td>
<td></td>
</tr>
<tr>
<td>45–59 compared with &lt;30</td>
<td>1.12 (1.03, 1.22)</td>
<td></td>
</tr>
<tr>
<td>≥60 compared with &lt;30</td>
<td>1.17 (1.08, 1.28)</td>
<td></td>
</tr>
<tr>
<td>Chronic diseases</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Chronic hepatic disease</td>
<td>1.17 (1.08, 1.27)</td>
<td></td>
</tr>
</tbody>
</table>

1 A multivariate negative binomial model was built that included all variables associated with the delay in nutrition initiation in a univariate regression with P < 0.2. Backward elimination was performed until all variables met the 5% threshold in the multivariate context. ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; MOF, multorgan failure; SAPS II, Simplified Acute Physiology Score II.
our knowledge, no previous study has clearly addressed the question of the potential deleterious or beneficial effect of early nutrition for the prognosis of obese patients.

Traditional measures of nutritional assessment, such as BMI and serum albumin, do not accurately predict sarcopenia in ICU patients. The resting energy expenditure measured by using indirect calorimetry is increased in the proportion of fat-free mass and might be an indirect way to address the nutritional status in the ICU with the welcome benefit to permit the precise calculation of energy needs. Such an assessment of the daily energy requirement by using indirect calorimetry has been recommended for obese patients whenever available in the clinical setting (9).

Obese patients had a lower mortality rate than that of other patients. This result was already shown and published in a previous work from the OUTCOMEREA database (22). Thus, results from the actualized database confirmed these previous analyses. Such a protective effect of obesity regarding mortality under critical illness has already been observed in other studies. A majority of studies concluded that obese ICU patients have equivalent (23) or improved mortality than that of their nonobese counterparts. With an analysis of overall data, 3 meta-analyses drew similar conclusions when obese patients were compared with either normal-weight patients (24, 25) or patients who were of normal weight or underweight (26). Obesity also represents a survival advantage in hemodialyzed patients (27), patients with chronic heart failure (28), and patients with chronic respiratory diseases (29). This survival advantage of obese patients who have a critical illness or chronic diseases shows a reversal epidemiology compared with in the general population in which obesity is associated with an increased all-cause mortality (30). Such discrepancy has been called the “obesity paradox” and is likely to be explained by the increased lean body mass that characterizes obese patients as shown by their high resting energy expenditure measured by using indirect calorimetry (31).

Such a nutritional reserve is nevertheless challenged by acute diseases and the hospital setting. In the Australasian Nutrition Care Day Survey 2010 (n = 3122), 18% of the overweight and obese participants (BMI >25) were assessed as being malnourished (32). A multicenter study conducted in 17 French comprehensive cancer centers (n = 1545 patients) showed that preexisting obesity was independently associated with risk of malnutrition, which suggested that preexisting obesity could drive the misidentification of nutritional needs or delay the nutrition support in this category of patients (33). In hospitalized elderly patients, Mudge et al (34) showed that higher BMI was independently associated with inadequate caloric intake. Similar results were shown in other studies (35, 36). One hypothesis is that obese patients have frequent exposure to unintentional weight loss and malnutrition because of a lack of attention given by patients themselves and caregivers to this loss. The consequence of such weight losses in hypermetabolic contexts is risk of developing sarcopenia with a persistent obesity, which would be associated with increased metabolic and functional risks (37). In the current study, the mean difference in delay before feeding was ∼0.5 d when low-weight were compared with obese patients. In the majority of patients, the delay before feeding ranged between 1 and 4 d. Although the difference was of small amplitude, it could have had a clinical impact to reach nutritional support goals. Indeed, patients are often exposed to an energy deficit during their ICU stay, with the nutritional support failing to reach energy needs (17). It has been shown by Wandrag et al (38) that several factors were independently associated with such a deficit in energy, including the number of days before the initiation of nutritional support. In addition, a delay in the initiation of enteral nutrition (1 d compared with 4 d before feeding) has been reported to reduce the small-intestinal glucose absorption and prolong the mechanical ventilation and length of ICU stay (39).

In conclusion, current guidelines recommend initiating a nutritional support within the 24–48 first hours of ICU stay. In the current study, we observed that the initiation of nutritional support was delayed in obese patients, possibly because of the subjective thought that their nutritional reserve was sufficient. However, the lose of lean body mass could be prejudicial in obese patients, thereby challenging their metabolic health and

TABLE 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutrition since day 1 compared with after day</td>
<td>0.6 (0.4, 1.08)</td>
<td>0.09</td>
</tr>
<tr>
<td>Nutrition since day 2 compared with after day</td>
<td>1.3 (0.8, 2.0)</td>
<td>0.3</td>
</tr>
<tr>
<td>Nutrition since day 3 compared with after day</td>
<td>1.1 (0.7, 1.8)</td>
<td>0.6</td>
</tr>
<tr>
<td>Adjusted analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutrition since day 1 compared with after day</td>
<td>0.8 (0.5, 1.4)</td>
<td>0.5</td>
</tr>
<tr>
<td>Nutrition since day 2 compared with after day</td>
<td>1.1 (0.7, 1.8)</td>
<td>0.6</td>
</tr>
<tr>
<td>Nutrition since day 3 compared with after day</td>
<td>1.0 (0.6, 1.6)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

1 Effect of the time interval before the initiation of nutrition on the 30-d mortality of obese patients was tested by using Cox model with consideration of day 4 as time zero. The Time interval before the initiation of nutrition in the first 3 d was tested as dummy variables, whereas the delay of nutrition initiation since day 4 was tested as a time-dependent variable by taking the value one as soon as the patient started nutrition.

Adjusted for the Simplified Acute Physiology Score severity score, hepatic and cardiovascular chronic diseases, McCabe’s score, and therapeutic limitation in 48 h.
functional recovery. Randomized controlled trials that address the issue of the consequences of an early compared with delayed beginning of nutritional support in critically ill obese patients are needed to progress in the specific nutritional care of obese patients in the ICU.

We thank Céline Feger for her editorial assistance and the following participants in the OUTCOMEREA study group—scientific committee: J-FT (Hôpital Bichat-Claude Bernard and Unité mixte de Recherche 1137 Infection, Antimicrobials, Modelling, Evolution Team5, Paris, France), EA (Medical Intensive Care Unit (ICU), Hôpital Saint Louis, Paris, France), Yves Cohen (ICU, Hôpital Avicenne, Bobigny, France), MG-O (ICU Hôpital Saint-Joseph, Paris, France), Lilou Soufr (ICU, Hôpital Saint-Joseph, Paris, France), Jean-Ralph Zahar (Microbiology Department, Hôpital Necker, Paris, France), Christophe Adrie (ICU, Hôpital Delafontaine, Saint Denis, and Physiology, Cochin Hospital, Paris, France), MD (Medical ICU, University hospital St Etienne, St Etienne, France), Corinne Alberti (Robert Debré Hospital, Paris, France), and CC (ICU, Hôpital Avicenne, Bobigny, and INSERM U823, Grenoble, France); biostatistical and informatics expertise: J-FT (Hôpital Albert Michallon and Integrated Research Center U823, Grenoble, France), Corinne Alberti (Medical Computer Sciences and Biostatistics Department, Robert Debré, Paris, France), Adrien François (Integrated Research Center U823, Grenoble, France), Aurélien Vesin (Integrated Research Center U823, Grenoble, France), Stephane Ruckly INSERM U823, Grenoble, France), CC (ICU, Hôpital Avicenne, Bobigny, and INSERM U823, Grenoble, France), Frederik Lecorre (Supelec, France), and Didier Nakache (Conservatoire National des Arts et Métiers, Paris, France), Aurélien Vannieuwenhuyze (Tourcoing, France); investigators of the OUTCOMEREA database: CA (ICU, Hôpital Delafontaine, Saint Denis, France and Physiology, Hôpital Cochin, Paris, France), BA (Surgical ICU, Edouard Herriot Hospital, Lyon, France), Claire Ara-Somohano [Centre Hospitalier Universitaire (CHU) A Michallon, Grenoble, France], Laurent Argault (medical ICU Edouard Herriot Hospital, Lyon, France), Agnès Bonadona (CHU A Michallon, Grenoble, France), ALB (Nutrition, CHU A Michallon, Grenoble, France), Caroline Bornstain (ICU, Hôpital de Montfermeil, Montfermeil, France), Lila Bouadma (ICU, Bichat Claude Bernard Hospital, Paris, France), Alexandre Boyer (ICU, Hôpital Pellegrin, Bordeaux, France), Christine Cheval (Hôpital d’Hyères, Hyères, France), Jean-Pierre Colin (ICU, Hôpital de Dourdan, Dourdan, France), MD (ICU, CHU Saint Etienne, France), Anne-Sylvie Dumenil (Hôpital Antoine Bécère, Clamart France), Adrien Descours-Declere (Hôpital Antoine Bécère, Clamart France), Jean-Philippe Fosse (ICU, Hôpital Avicenne, Bobigny, France), Rebecca Hamidifar-Roy (CHU A Michallon, Grenoble, France), SJ (ICU, Hôpital de Dourdan, Dourdan, France), Hatem Khalife (ICU, Cayenne General Hospital, Cayenne, France), Christian Laplace (ICU, Hôpital Kremlin-Bicêtre, Bicêtre, France), Alexandre Lauerttte (ICU, CHU G Montpiéd, Clermont-Ferrand, France), Thierry Lazard (ICU, Hôpital de la Croix Saint-Simon, Paris, France), Eric Le Merc (ICU, Hôpital Louis Mourier, Colombes, France), Guillaume Marcotte (Surgical ICU, Edouard Herriot Hospital, Lyon, France), Montesino (ICU, Hôpital Bichat, Paris, France), Bruno Mourvillier (ICU, Hôpital Bichat, Paris, France), Benoît Missset (ICU, Hôpital Saint-Joseph, Paris, France), Delphine Moreau (ICU, Hôpital Saint-Louis, Paris, France), Etienne Piguet (ICU, Hôpital Louis Mourier, Colombes, France), BS (ICU, CHU G Montpiéd, Clermont-Ferrand, France), CS (CHU A Michallon, Grenoble, France), Gilles Troché (Hôpital Antoine Bécère, Clamart France), Marie Thuong (ICU, Pontoise Hospital, Pontoise, France), Guillaume Thierry (ICU, Hôpital Saint-Louis, Paris, France), Dany Toledano (Centre Hospitalier Gonesse, Gonesse, France), and Eric Vantalon (Surgical ICU, Hôpital Saint-Joseph, Paris, France); and study monitors: Caroline Tournegros, Loic Ferrand, Nadira Kaddour, Boris Berthe, Kaouttar Mellouk, Sophie Letrou, Igor Theodose, Julien Fournier, and Veronique Deiler.

The authors’ responsibilities were as follows—A-LB: analyzed data and wrote the manuscript; CS, MG-O, CA, CC, EA, BS, BA, DG-T, SJ, and MD: conducted research and had substantial involvement in the manuscript revision before submission; BP: acquired data and had substantial involvement in the manuscript revision before submission; AV: performed the statistical analysis; J-FT: conducted and designed the research, had substantial involve-

REFERENCES


