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Infectious complications associated with parenteral nutrition in intensive care unit and non-intensive care unit patients

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ABSTRACT

Introduction: Malnutrition is associated with an increased risk of complications in hospitalized patients, and parenteral nutrition (PN) is used when oral or enteral feeding is not possible. This study aimed at analyzing associations between PN characteristics and infectious complications in hospitalized patients.
Material and methods: This was a retrospective cohort study conducted in a tertiarycare university hospital. Data from consecutive adult patients submitted to PN (January 2016 to December 2017; ICU and ward) were reviewed by means of an electronic database. Patient's clinical characteristics, PN prescription and catheter insertion procedure data were extracted and analyzed. The main outcome was the development of central line–associated bloodstream infection (CLABSI). The secondary outcomes were other infectious complications and mortality, as well as factors associated with CLABSI.
Results: We analyzed 165 patients and 247 catheters used for parenteral nutrition infusion. The CLABSI rate was 6.47 per 1000 catheter-days. In the univariable analysis, CLABSI was associated with longer hospitalization time, longer PN time, longer catheter time, catheter insertion performed by a surgeon or a surgical resident, and procedures performed outside the ICU. In an extended time-dependent Cox regression, no variable was associated with a higher risk of CLABSI, and additional PN days did not increase the rate of CLABSI. The overall mortality rate was 24.8%. Only the patients' comorbidity index was associated with death in the multivariable analysis.

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Discussion: In our study, patients who needed PN had an overall CLABSI rate of 6.47 per 1000 catheter-days. These outcomes were not associated with PN and catheter characteristics studied after adjustment for catheter time. The overall mortality rate was 24.8% and it was not associated with PN in multivariable analyses, only with Charlson comorbidity index.

Introduction

Malnutrition is associated with an increased risk of complications, higher mortality rate, longer hospital stays, and higher hospitalization costs.[1] Nutritional support is an alternative to overcome this problem, and it is indicated for patients unable to feed orally.[2] There are two available options: enteral nutrition, usually chosen to preserve the patient's gastrointestinal transit,[3] and parenteral nutrition (PN), used when it is impossible to achieve partial or full enteral nutrition (EN) requirements. A pragmatic multicenter randomized clinical trial evaluated PN versus EN in ICU patients of developed countries and found no difference in both nutritional strategies in terms of number of treated infectious complications or 90-day mortality.[4]

The infection rate related to a central venous catheter (CVC) used for PN varies according to the definition used. This rate can reach up to 18 infectious events per 1000 catheter-days,[5,6] a higher rate compared with central catheter infections in devices not used for PN (two infectious events per 1000 catheter-days in US intensive care units (ICUs) and 6.8 infectious events per 1000 catheter-days in developing countries' ICUs[7]). However, most central line infection data come from developed countries where resources differ (including the types of PN available and the device used for PN nutrition) from emerging countries.[8] A multicentric Brazilian publication reported 10.22 bloodstream infections per 1000 catheters/day, and the risk factors for infection were multiple–lumen catheters, duration of catheterization and length of stay in the ICU, but PN was not evaluated as a variable in that study.[9] Indeed, another study performed in the same country showed that PN was a risk factor for central venous catheter infection.[10]

Most studies on infection rates of PN refer to specific populations, such as critically ill, cancer or trauma patients.[5] Few studies evaluated different diseases, non-critically-ill patients, catheter bundles and physicians experience to insert CVC, using a recently inserted versus an already used catheter for nutrition purposes. Studying this more heterogeneous cohort may infer more associations with the route of nutrition itself and not regarding specific groups. Furthermore, characteristics of the vascular access correlated with increased odds of infection in PN users are unknown, and the recommendations regarding the best vascular access to PN have low to very low quality of evidence.[11] Therefore, the aim of the present study was to examine mediators of PN and central line–associated bloodstream infection (CLABSI) in a tertiary-care-level hospital. The secondary aim was to analyze the rate of other complications in patients submitted to PN.

Materials and methods

A retrospective cohort study was conducted in an 800-bed tertiary-care university hospital in the south of Brazil through review of electronic medical records of all adult inpatients submitted to PN in the period of January 2016 to December 2017. Patients who received PN for less than 72 h were excluded from the analyses, as were those who received PN through a long-term catheter (LTC) due to their out-of-hospital use and possibility of lack of notification or even occurrence of an outcome in another institution. A peripherally inserted central catheter (PICC) were used in the hospital during the study only in experimental situations and they were not analyzed because of the possibility of bias due to differentiated care related to a new technology/device in the population. The study was approved by the local research ethics committee.

The assistant physician (based on local protocol and current guidelines) defined the choice for the total or supplementary PN.[2,3] All of the prescribed solutions were two-in-one (2:1), combining glucose and amino acids, separately from intravenous lipid emulsion. The available solutions and the products used were Fresenius Kabi—Germany, Aminoven 10%, Lipovenos MCT 20%, and glucose 50%, with electrolytes, vitamin K, trace elements, and addition of multivitamins. Glycemic control during hospitalization was an attribution of the attending physician, as was the CVC installation, although both are standardized procedures. The local protocol about care with central lines includes qualified personnel and a bundle for best care of CVC.[12] According to our hospital protocol, all physicians were encouraged to start enteral or oral diet and discontinue the PN solution as soon as possible and the device should be removed, since it would be no longer necessary.

Demographics characteristics, clinical data,[13–15] and aspects of CVC insertion were reviewed. Daily records from the insertion of the first CVC used for PN until discharge or death were revised. Patients were classified according to the indication for PN: total PN, when there was contraindication or intolerance to any amount of enteral or oral diet or supplemental PN, when it was not possible to achieve the nutritional goal only with enteral or oral diet. For each patient, total hospitalization time, total PN time, total time with CVC in use, and time between the CVC insertion and start of PN were calculated.

The main outcome was development of central line–associated bloodstream infection (CLABSI), defined as CVC with clinical signs of infection and no other source of bacteremia, except the catheter up to 48 h after the CVC's withdrawal, plus 1) one positive blood culture for a known pathogen or 2) two positive blood cultures for skin pathogen.[16]
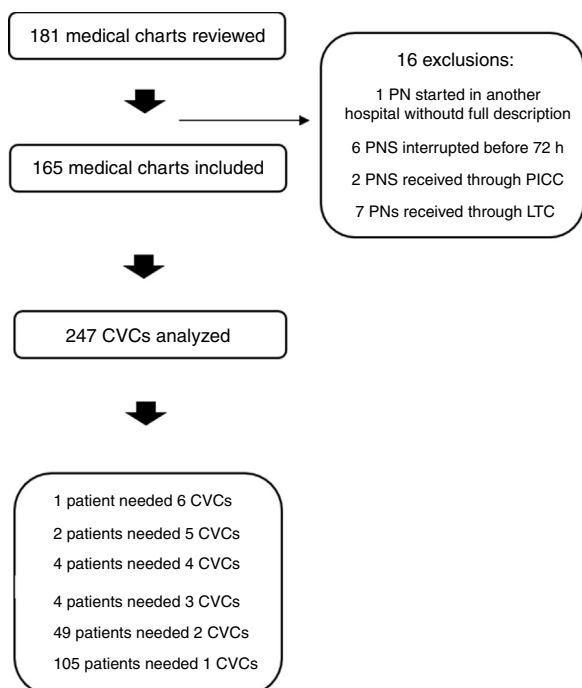
Fig. 1 – Flowchart of Included and Excluded Patients. CVC, central venous catheter; LTC, long-term catheter; PICC, peripherally inserted central catheter.

We also recorded as secondary outcomes other infections (pulmonary infection, abdominal infection, bacteremia not related to CVC, fungemia, urinary infection, operative wound infection based on clinical diagnosis), death, and hyperglycemia, as well as factors associated with CLABSI. Hyperglycemia was arbitrarily defined as at least four episodes of capillary glucose >200 mg/dl during PN infusion; a need for a regular insulin prescription to achieve glycemic control; or a description of decompensated diabetes.

Sample size calculation, considering 18.3% cumulative incidence of CLABSI as found in a study performed in a similar population in the same hospital,[10] was estimated in 231 catheters evaluation to identify factors associated with CVC infection, considering a power of 95% and a margin of error of 5%.

Statistic analyses were conducted as appropriated. Continuous variables were reported as mean and standard deviation, median and interquartile range, or number of patients and percentages. The differences between the groups were analyzed with Student's t-test, Mann-Whitney U-test, or χ^2, as appropriate. Generalized estimating equations were used for comparison in relation to CVC (more than one device per patient is possible). In multivariable analysis independent variables were included in the model according to their significance in the univariate analysis ($p < 0.05$) or their biological importance. The results were expressed as hazard ratio (HR) with their respective 95% confidence intervals (CI). For analysis of CVC infection, Cox regression adjustments were performed for time-dependent covariables (CVC time in days) until the occurrence of the patient's first event. The other catheters inserted after the occurrence of CLABSI

Table 1 – Characteristics of the included patients (n = 165).

Characteristics	Value
Age (years)	56.3 (±16.6)
Male sex	92 (55.8%)
Weight (kg)	70.15 (±16.6)
BMI (kg/m^2)	25.42 (±5.6)
Surgical admission	132 (80%)
Abdominal surgery	119 (72.1%)
PN started in the ICU	71 (43%)
Hospitalization time (days)	43 (27.5−64.5)
Charlson (comorbidity index)	4 (2−6)
SAPS 3[a]	63.4 (±14.5)
SOFA[a]	5 (3−7)
Vasoactive drugs[a]	21 (12.7%)
PN time (days)	15 (9−25)
Total PN	125 (75.7%)
Supplemental PN	40 (24.2%)
Comorbidities	
DM	35 (21.2%)
Coronary artery disease	16 (9.7%)
Heart failure	6 (3.6%)
Stroke	16 (9.7%)
Pulmonary disease	20 (12.1%)
Hepatic disease	8 (4.8%)
Cancer	73 (44.2%)
Chronic kidney disease	13 (7.9%)
PN daily prescription	
Calories (kcal)	1598 (±423.3)
Calories (kcal/kg)	25.2 (20.2−27.6)
Protein (g/kg)	1.5 (1.24−1.61)
Glucose (g/kg)	3.08 (2.52−3.52)
Lipids (g/kg)	0.8 (0.58−0.91)
Outcomes	
Mortality	41 (24.8%)
Hyperglycemia	62 (37.6%)
Any infection	107 (64.8%)
Pulmonary infection	28 (17%)
Abdominal infection	60 (36.4%)
Operative wound infection	7 (4.2%)
Urinary infection	9 (5.5%)
Bacteremia not related to CVC	7 (4.2%)
CLABSI	24 (14.5%)
Fungemia	12 (7.3%)

N represents the number of patients (and percentage). Mean (± standard deviation) or median (interquartile range). BMI, body mass index; ICU, intensive care unit; SAPS 3, simplified acute physiology score 3; SOFA, sequential organ failure assessment; PN, parenteral nutrition; DM, diabetes mellitus; CVC, central venous catheter; and CLABSI, central line–associated bloodstream infection.

[a] Only collected in the 71 patients who started PN in the ICU.

were excluded from this analysis. The data were stored and analyzed in the statistical programs SPSS 22.0 (IBM SPSS Statistics for Windows, Armonk, NY) and R version 3.5.1 (Foundation for Statistical Computing, Vienna, Austria). In all analyses, a p-value <0.05 was considered as statistically significant. The study was conducted in accordance with local regulations and with the current guidelines for observational studies.[17] All data were analyzed anonymously.

Table 2 – Univariable analysis for evolution to CLABSI at hospitalization.

Variables:	CLABSI (24 patients)	No-CLABSI (141 patients)	*p-value*
Age (years)	55.9 ± 16.1	56.4 ± 16.7	.77
BMI (kg/m^2)	26.4 ± 5.7	25.2 ± 5.6	.36
Charlson (comorbidity index)	5.5 (2−6)	4 (2−6)	.29
Postoperative	18 (75%)	113 (80.1%)	1
Hospitalization time (days)	66 (53.5−82)	38 (27−59)	.0001
PN time (days)	30 (11.5−43)	14 (9−23)	.003
DM	5 (20.8%)	30 (21.3%)	1
Hyperglycemia	8 (33.3%)	54 (38.3%)	.81
PN started in ICU	9 (37.5%)	61 (43.9%)	.719
Supplemental PN	2 (8.3%)	38 (27%)	0.09
Calories infused/day (kcal)	1537 ± 402.7	1608 ± 427	.448
Proportion of calories from glucose (%)	45 (42–47.5)	45 (42–48)	.74
Procedure performed by a surgeon[a,b]	81 ± 7.9% (61−92%)	56 ± 3.7% (49−64%)	.025
Procedure performed in ICU[b]	16 ± 7.4% (6−36%)	39 ± 3.6% (32−46%)	.03
CVC time (days)[b]	20.6 ± 1.6 (17.4−23.7)	17.27 ± 0.8 (15.7−18.8)	.034
Double-lumen[b]	96 ± 3.5% (78−100%)	95 ± 1.5% (91−97%)	.741
Subclavian-site[b]	39 ± 8.5% (24−56%)	38 ± 3.3% (32−45%)	.933
Ultrasound-guided[b]	37 ± 8.3% (23−54%)	52 ± 3.6% (45−59%)	.123
PN infused in a recently inserted (<48 h) CVC[b]	82 ± 7.5% (63−93%)	77 ± 2.8% (71−82%)	.55

BMI is body mass index; ICU, intensive care unit; PN, parenteral nutrition; DM, diabetes mellitus; CVC, central venous catheter; and CLABSI, central line–associated bloodstream infection. The cells represent N (%), mean ± SD or median (interquartile range).

[a] Surgeon or a surgical resident.

[b] Estimated marginal mean ± standard error and 95% Wald confidence interval, through analysis by GEE (log-gamma distribution).

Results

A total of 181 medical charts of patients who received PN between January 2016 and December 2017 (24 consecutive months) were reviewed. Sixteen patients were excluded leaving 165 patients and 247 CVCs (Fig. 1).

Description of study cohort

Table 1 summarizes the main characteristics of the included patients. Most patients were male, 56.3 ± 16.6 years old, overweight, median Charlson index was 4, and the most frequent comorbidity was cancer. Mean nutritional prescription, caloric and proteic, was adequate. Overall mortality rate was 24.8%. The most prevalent outcome was any infectious complication during PN administration, mainly due to abdominal infection.

Clinical outcomes

Table 2 summarizes the findings associated with CLABSI. There were 28 episodes of CLABSI (11.3% of 247 CVCs), but some events occurred in the same patient. At least one episode of bloodstream infection occurred in 24 patients (14.5% of 165 patients). Considering the time used for each CVC, the CLABSI index was 6.47 per 1000 CVC-days. In the univariable analysis, CLABSI was associated with longer hospitalization time, longer PN time, longer CVC time, catheter insertion performed by a surgeon or a surgical resident, and procedures performed outside the ICU. No association was found with total calories of PN, proportion of macronutrients, hyperglycemia, supplemental PN, use of ultrasound or comorbidities at the beginning of PN. Furthermore, no CLABSI occurred in less than 5 days of CVC use (median of 15 days), and using a recently inserted device (with less than 48 h of use) when starting PN was not

associated with a lower rate of CLABSI. In an extended time-dependent Cox regression, no variable was associated with a higher risk of CLABSI in the univariable and multivariable analysis (Table 3). Additional information about the 247 CVC insertion procedures is available in Supplementary Table.

Regarding CLABSI epidemiology, coagulase-negative staphylococci were present in 13 cases (46.4%), followed by fungal infections (*Candida*) in eight cases (28.6%) and *Staphylococcus aureus* in two cases (7.1%). *Klebsiella*, *Enterococcus*, *Pseudomonas*, *Enterobacter*, and *Escherichia* were responsible for one case of CLABSI each (3.6%). The median time for blood culture positivity in CLABSI cases was 13.9 h (12−24 h) for peripheral blood cultures and 12.2 h (9.9–19.8 h) for blood cultures collected from the PN pathway.

Overall mortality rate was 24.8% in this study. Higher Charlson index, starting PN in ICU, development of any infection during PN administration and development of abdominal infection during PN administration were related to death (Table 4). In multivariate analysis with these variables, only the Charlson comorbidity index remained significantly associated with mortality (HR 1.175; CI 1.052–1.312; p = .004).

Discussion

In this study, a large sample of patients submitted to PN over a two-year period in a university hospital of the South of Brazil was analyzed. To the best of our knowledge, this is one of the largest cohorts identified in the literature analyzing patients receiving PN both in the general ward and in the ICU settings. The rate of infectious complications in these individuals is high. Patients who needed PN had a higher incidence of CLABSI compared to patients with CVC and without PN in the literature,[18,19] but no characteristics of PN studied were asso-

Table 3 – Evolution to CLABSI in a time-dependent Cox regression.

	HR	95% CI	p-value
Univariable time-dependent			
Procedure performed by a surgeon[a]	2.235	0.82–6.07	.11
Number of previous CVC needed for PN	1.148	0.42–1.76	.7
PN time until current CVC	1.002	0.94–1.05	.92
Total time of PN	0.991	0.99–1.02	.15
Hospitalization time until current CVC	1.001	0.97–1.02	.91
Total time of hospitalization	0.995	0.99–1.01	.42
Multivariable time-dependent			
Procedure performed by a surgeon[a]	2.215	0.81–6.01	.11
Total time of PN	1.009	0.99–1.02	.16

Extended Cox model for time-dependent covariates, through Ršurvival package. HR: Hazard Ratio; CI: 95% confidence interval. R square = 0.019. Concordance = 0.566. Likelihood ratio test = 4.38. Wald test 4.28. Logrank test 4.54 p = 0.1.
[a] Surgeon or a surgical resident.

Table 4 – Univariable analysis for evolution to death at hospitalization.

Variables	Death (41 patients)	Discharge (124 patients)	p-value
Age (years)	60.2 ± 17.1	55.06 ± 16.3	.087
BMI (kg/m^2)	24.1 ± 3.9	25.8 ± 6	.099
Charlson (comorbidity index)	5 (4−7)	3 (2−6)	.001
Postoperative	33 (80.5%)	99 (79.8%)	1
Hospitalization time (days)	43 (29−67)	43 (27−63.75)	0.76
PN time (days)	17 (9−25)	15 (9−24.5)	.815
DM	12 (29.3%)	23 (18.5%)	.21
Hyperglycemia	19 (46.3%)	43 (34.7%)	.25
PN started in ICU	26 (63.4%)	45 (36.3%)	.003
Any infection during PN	33 (80.5%)	74 (59.7%)	.026
Abdominal infection during PN	21 (51.2%)	39 (31.5%)	.036
Pulmonary infection during PN	10 (24.4%)	18 (14.5%)	.22
CLABSI during PN	5 (12.2%)	19 (15.3%)	.8
Supplemental PN	7 (17.5%)	33 (26.6%)	.3
Calories infused/day (kcal)	1521.5 ± 383.6	1623.4 ± 434.1	.18
Proportion of calories from glucose (%)	45 (43−48)	45 (41.2−48)	.79

BMI represents body mass index; ICU, intensive care unit; PN, parenteral nutrition; DM, diabetes mellitus; CVC, central venous catheter; and CLABSI, central line–associated bloodstream infection. The cells represent N (%), mean ± SD or median (interquartile range).

ciated with CLABSI and additional days of PN did not increase the rate of CLABSI in multivariate analyses in our study.

In an earlier study conducted in the same hospital almost 20 years earlier,[10] PN was shown to be independently associated with CLABSI in multivariate analysis. That study differs from the present investigation for including only ICU patients, and because microbiological analyses of all patients (blood culture or catheter tip) were performed. The association between PN and infection could be due to colonization of the device. Probably for the same reason, a two-fold higher rate of CLABSI per 1000 catheter days was identified in comparison with the current study, although improvements in procedures and in catheter care that have been established over time may have also influenced this difference.

The high incidence of CLABSI found in our study (6.47 per 1000 CVC-days or 11.7% of all CVCs) when compared to patients with CVC and without PN in the literature[18–20] is still within the range (which reaches 18.8 per 1000 CVC-days) of the international literature for PN-associated CVC infection[6]). In a time-dependent Cox regression, PN time was not an independent factor that could justify a higher incidence of CLABSI in this population. It is difficult to identify reasons for this inci-

dence, since the study was conducted in a university hospital accredited by the Joint Commission[21] and specific bundles for CVC care are available in our hospital. Nevertheless, Brazil is an emerging country and data about catheter infection, especially in patients receiving PN, are scarce.

Dissanaike et al.[22] found an association between CLABSI and higher total calorie infusion, which was not observed in our cohort. Most of the patients in Dissanaike's study received more than 30−40 kcal/kg/day, in contrast with the current study, where the local protocol encouraged a goal of 22−25 kcal/kg/day and few patients received more than 30 kcal/kg/day, in accordance with recent guidelines.[3] We believe that such findings indicate that avoiding hyperalimentation may reduce the rate of CLABSI and other unfavorable outcomes, as already demonstrated by studies that limited total calories and compared parenteral and enteral nutrition using the same caloric target.[4] One possible explanation for the high CLABSI rate in our study was the use of two-in-one bags separated from intravenous lipid emulsion that are supposed to be associated with an increased risk of infection, through CVC manipulation. However, this evidence is

still limited and not sufficient to endorse or refute such an association.[23]

The present study did not identify lower rates of CLABSI when a new CVC was installed after indication of PN, thus not justifying the need for a new device or replacement of the CVC when initiating such therapy. Other catheter-related factors, such as the number of lumens, were also not associated with higher chance of infection in our study, although the analysis was not robust enough because of the low prevalence of mono-lumen catheters (less than 5%) used in our hospital. Therefore, it is impossible to refute this association found in the literature,[24] and although recommended, there is a paucity of evidence regarding PN-dedicated lumens.[25]

Our mortality rate was high, and the age-adjusted Charlson comorbidity index indicates that our sample of patients was sicker than population in other PN studies, probably justifying the higher mortality.[26,27] This comorbidity metrics is the most commonly studied prognostic measure of illness burden in clinical research[28] and is probably related to increased rates of chronic disease and mortality.[29–31] Our study failed to identify prolonged hospitalization or PN time as independent factors to justify this rate. Only greater number of comorbidities was associated with mortality in the multivariate analysis.

Among the limitations, the study methodology does not allow for cause-effect inference, although it is possible to generate hypotheses. Multivariate analysis and logistic regression were performed to mitigate bias and confounding. Furthermore, our high rate of infection does not invalidate the finding that CLABSI was not associated with specifics of PN or vascular access characteristics. In addition, the retrospective design may hinder outcome recovery and related factors due to underreporting in the medical records. To counteract underreporting, we chose laboratory results and the outcome of hospitalization (death or discharge) as the main outcomes. The study was not powered to detect mortality difference a priori, and this aspect should be considered when analyzing data.

The exclusion of LTC and PICC from the analyses is also a limitation. LTC may lead to underreporting due to their out-of-hospital use and possibility of lack of notification or even occurrence of an outcome in another institution. It has already been stated that PICC were used in the hospital during the study only in experimental situations and they were not analyzed because of the possibility of bias due to differentiated care involving a new technology. As a mitigating factor, less than 10 of these devices (seven LTC and two PICC) were used for PN in the hospital in the study period (3.6% of all catheters used for PN), possibly not affecting the results.

In conclusion, patients who needed PN in our study had a considerable rate of CLABSI and other infectious complications. No variable was associated with higher risk of CLABSI in the univariate and multivariate analyses after adjustment for catheter time. The mortality rate was high and not associated with PN in multivariate analyses, only with Charlson comorbidity index.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.bjid.2020.02.002.

REFERENCES

1. Correia MI, Waitzberg DL. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr. 2003;22:235–9.
2. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN-Parenter Enter. 2016;40:159–211.
3. Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients, 2009. JPEN-Parenter Enter. 2009;33:255–9.
4. Harvey SE, Parrott F, Harrison DA, Bear DE, Segaran E, Beale R, et al. Trial of the route of early nutritional support in critically ill adults. New Engl J Med. 2014;371:1673–84.
5. Gavin NC, Button E, Keogh S, McMillan D, Rickard C. Does parenteral nutrition increase the risk of catheter-related bloodstream infection? A systematic literature review. JPEN-Parenter Enter. 2017;41:918–28.
6. Yilmaz G, Koksal I, Aydin K, Caylan R, Sucu N, Aksoy F. Risk factors of catheter-related bloodstream infections in parenteral nutrition catheterization. JPEN-Parenter Enter. 2007;31:284–7.
7. Rosenthal VD, Bijie H, Maki DG, Mehta Y, Apisarnthanarak A, Medeiros EA, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control. 2012;40:396–407.
8. Hajjej Z, Nasri M, Sellami W, Gharsallah H, Labben I, Ferjani M. Incidence, risk factors and microbiology of central vascular catheter-related bloodstream infection in an intensive care unit. J Infect Chemother. 2014;20:163–8.
9. Bicudo D, Batista R, Furtado GH, Sola A, Medeiros EASd. Risk factors for catheter-related bloodstream infection: a prospective multicenter study in Brazilian intensive care units. Brazi J Infecti Dis. 2011;15:328–31.
10. Beghetto MG, Victorino J, Teixeira L, Azevedo MJ. Parenteral nutrition as a risk factor for central venous catheter–related infection. JPEN-Parenter Enter. 2005;29:367–73.
11. Kovacevich DS, Corrigan M, Ross VM, McKeever L, Hall AM, Braunschweig C. American Society for Parenteral and Enteral Nutrition Guidelines for the selection and care of central venous access devices for adult home parenteral nutrition administration. JPEN-Parenter Enter. 2019;43:15–31.
12. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52:e162–93.

13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chron Dis. 1987;40:373–83.

14. Moralez GM, Rabello LSCF, Lisboa TC, Lima MFA, Hatum RM, De Marco FVC, et al. External validation of SAPS 3 and MPM(0)-III scores in 48,816 patients from 72 Brazilian ICUs. Ann Intensive Care. 2017;7:53.

15. Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: A systematic review. Crit Care. 2008;12:R161.

16. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36:309–32.

17. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61:344–9.

18. Parienti JJ, Mongardon N, Megarbane B, Mira JP, Kalfon P, Gros A, et al. Intravascular complications of central venous catheterization by insertion site. N Engl J Med. 2015;373:1220–9.

19. Lin K-Y, Cheng A, Chang Y-C, Hung M-C, Wang J-T, Sheng W-H, et al. Central line-associated bloodstream infections among critically-ill patients in the era of bundle care. J Microbiol Immunol. 2017;50:339–48.

20. Rosenthal VD, Al-Abdely HM, El-Kholy AA, AlKhawaja SAA, Leblebicioglu H, Mehta Y, et al. International Nosocomial Infection Control Consortium report, data summary of 50 countries for 2010-2015: device-associated module. Am J Infect Control. 2016;44:1495–504.

21. Joint Commission on Accreditation of Healthcare Organizations & Joint Commission Resources. Jt Comm J Qual Saf. 2005.

22. Dissanaike S, Shelton M, Warner K, O'Keefe GE. The risk for bloodstream infections is associated with increased parenteral caloric intake in patients receiving parenteral nutrition. Crit Care. 2007;11:R114.

23. Slattery E, Rumore MM, Douglas JS, Seres DS. 3-in-1 vs 2-in-1 parenteral nutrition in adults: a review. Nutr Clin Pract. 2014;29:631–5.

24. Templeton A, Schlegel M, Fleisch F, Rettenmund G, Schobi B, Henz S, et al. Multilumen central venous catheters increase risk for catheter-related bloodstream infection: prospective surveillance study. Infection. 2008;36:322–7.

25. Gavin NC, Button E, Castillo MI, Ray-Barruel G, Keogh S, McMillan DJ, et al. Does a dedicated lumen for parenteral nutrition administration reduce the risk of catheter-related bloodstream infections? A systematic literature review. J Infus Nurs. 2018;41:122–30.

26. Adjemian D, Arendt BM, Allard JP. Assessment of parenteral nutrition prescription in Canadian acute care settings. Nutrition. 2018;49:7–12.

27. Akbar T. Catheter-related bloodstream infections in adults receiving parenteral nutrition: does the time taken to report blood cultures impact on clinical management? Clin Med. 2019;19:40.

28. de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity: a critical review of available methods. J Clin Epidemiol. 2003;56:221–9.

29. Peterson JC, Paget SA, Lachs MS, Reid MC, Charlson ME. The risk of comorbidity. Ann Rheum Dis. 2012;71:635–7.

30. Fraccaro P, Kontopantelis E, Sperrin M, Peek N, Mallen C, Urban P, et al. Predicting mortality from change-over-time in the Charlson Comorbidity Index: A retrospective cohort study in a data-intensive UK health system. Medicine. 2016;95:e4973.

31. Özbilgin S, Hanci V, Ömür D, Özbilgin M, Tosun M, Yurtlu S, et al. Morbidity and mortality predictivity of nutritional assessment tools in the postoperative care unit. Medicine. 2016;95:e5038.