

Table S2. Detailed commentaries and references.

Recommendation 1: Parenteral nutrition (PN) is indicated in patients who are unable to meet their nutritional needs orally and/or enterally as a result of suboptimal function of the gastrointestinal tract (GIT) or in whom the GIT is not accessible.

Commentary: PN provides essential nutrients intravenously and bypasses the GIT. It can be used to provide complete nutritional requirement (total parenteral nutrition) or partial nutritional requirement (supplemental PN) to supplement oral and/or enteral feeding. PN should only be considered when it is not possible to meet individuals' nutritional needs orally and/or enterally due to suboptimal function of the GIT or when GIT is not accessible. The 5 broad categories of conditions that may require PN are impaired absorption and/or loss of nutrients, mechanical bowel obstruction, clinical need for bowel rest, bowel motility disorders and inability to achieve or maintain enteral access.⁵

In a meta-analysis of studies in the critical care setting,⁶ the use of enteral nutrition (EN) was found to significantly reduce infectious complications and length of stay in the intensive care unit (ICU) when compared to PN. Similar findings were also observed in other studies with non-ICU patients⁷⁻¹¹ where EN was associated with lower rates of infection and postoperative complications, and reduced length of hospital stay. In a landmark technical review of 82 randomised controlled trials (RCTs)¹², PN was not found to improve survival, total complications or length of stay compared to standard therapy. Besides, some studies¹³ found that PN resulted in more harm such as increased risk of infection, poorer response to cancer treatment and higher mortality. Hence, whenever possible, oral and/or EN should be optimised before initiating PN as they are physiologically more advantageous, cost-effective and associated with fewer complications. PN should not be started until all pragmatic approaches to improve tolerance to oral or EN have been attempted.

Recommendation 2a: For patients who are well-nourished on initial assessment, initiating PN can be considered after 5-7 days of not achieving 60% or more of estimated total energy requirement.

Recommendation 2b: For patients who are severely malnourished or at high risk of malnutrition, consider initiating PN earlier than 5 days of not achieving 60% or more of estimated total energy requirement.

Commentary: The optimal time to initiate PN remains debated and unclear. Due to large heterogeneity in studies, recommendations made in clinical practice guidelines are fundamentally based on expert opinions. The European Society of Parenteral and Enteral Nutrition (ESPEN) 2019 guideline suggested that supplemental PN should be initiated in all critically ill patients 3 days after admission if oral and/or EN is below 60% of the energy requirement, regardless of nutritional status. In contrast, the American Society of Parenteral and Enteral Nutrition (ASPEN) and Society of Critical Care Medicine (SCCM) 2016 guideline¹⁴ recommended initiating PN only after 7 days of ICU admission, as supplemental PN in the first week of ICU stay does not improve clinical outcomes and may even cause potential harm.¹⁵ These recommendations made, however, were criticised as it was based on data that did not consider the nutritional status of the patients.

Although some studies¹⁶⁻¹⁸ found no significant difference in mortality when comparing early PN and late PN, the EPaNIC study¹⁹ observed that late PN initiation 7 days after admission was associated with lower incidence of infections, earlier recovery from organ failure and shorter hospital stay compared to early PN initiation before 7 days. On the other hand, findings of a recent retrospective analysis where surgical patients were stratified based on their nutritional risk¹⁹ revealed that those with high risk of malnutrition who received early supplemental PN within 48 hours after emergency surgery had a better survival when compared to those who did not receive PN earlier. A favourable finding was also demonstrated in another RCT where early supplemental PN in patients undergoing major abdominal surgery with high nutritional risk²⁰ was associated with reduced nosocomial infections.

Hence, taking all the above-mentioned into consideration, we recommend initiating PN after 5-7 days for well-nourished patients who have not been able to achieve 60% or more of estimated total energy requirement and earlier than 5 days for patients who are severely malnourished or at high risk of malnutrition.

Recommendation 3a: Contraindications to PN include patients with critical electrolytes abnormalities, specifically serum potassium (K) <2.5 mmol/L, serum sodium (Na) <125 mmol/L, serum phosphate (PO₄) <0.4 mmol/L or serum magnesium (Mg) <0.5 mmol/L.

Commentary: Metabolic complications can occur during PN administration due to intracellular shifts of glucose, electrolytes and fluid. Refeeding syndrome is a potentially fatal condition that may occur when artificial nutrition is introduced after prolonged starvation or minimal nutrient intake. Rapid feeding may worsen electrolyte derangement and exacerbate pathophysiological complications that adversely affect muscular, cardiac, respiratory, neurological, haematological and hepatic systems.

Severe and life-threatening electrolyte abnormalities are defined as serum K <2.5 mmol/L, serum Na <125 mmol/L, serum PO₄ <0.4 mmol/L and serum Mg <0.5 mmol/L.²¹⁻²⁴ There is a lack of RCTs and observational studies to guide the threshold for electrolytes at which PN could be started or withheld. Hence, it is not recommended to start PN for patients who have critical electrolyte abnormalities until it has been adequately corrected.^{25,26} PN should only be initiated after electrolytes are at an acceptable level after replacement. Due to lack of evidence on this matter, we recommend that PN should be initiated with caution when electrolytes are replaced and rechecked to an acceptable level of at least K >3 mmol/L, Na >125 mmol/L, Phos >0.6 mmol/L and Mg >0.6 mmol/L.

Recommendation 3b: Contraindications to PN include patients who have suffered irreversible brain injury or terminal illness where there is a lack of therapeutic goal to prolong life in the inevitable death.

Commentary: PN is not encouraged for patients with irreversible brain injury or terminal illness due to its potential complications, cost and futility. Besides, PN therapy may lead to unnecessary prolongation of suffering. PN may, however, be considered in a subgroup of terminally ill cancer patients who have reasonable functional status (Eastern Cooperative Oncology Group <3, Karnofsky status >50) and with an expected survival of more than 3 months when oral and/or EN is not feasible due to intestinal obstruction or high output fistula.²⁷

Recommendation 3c: Contraindications to PN include patients who have no suitable venous access for PN.

Commentary: The preferred delivery of PN is through central venous access (inserted either peripherally or centrally), especially for those who require longer-term PN support.^{28,29} Delivery of PN through central venous access allows solutions of higher osmolality and volume to be infused as compared to delivery of PN through peripheral venous access. A dedicated catheter for PN delivery is recommended. These catheters should be handled using aseptic technique all the time. Withdrawal of blood via these catheters should be avoided. When catheter-related sepsis or blockage happens, catheter removal may be required. However, if all possible routes for central venous access have been exhausted, PN delivery through the peripheral route may be considered.

Recommendation 4: Patients on PN support in hospital should be managed by a nutrition support service consisting of a team of trained physician, nurse, dietitian and pharmacist.

Commentary: PN is a complex and specialised form of nutrition support. Inappropriate use and prescription of PN may lead to severe electrolyte disturbances, metabolic complications and even death.³⁰ Consulting a multidisciplinary team of HCPs dedicated to PN support has been demonstrated to enhance the quality of care, promote appropriate use of PN, improve clinical outcomes and reduce the incidence of adverse PN-related complications.³¹⁻³⁴

Dietitians play a pivotal role in conducting individualised nutritional assessments to determine patients' specific nutritional needs. They develop and implement personalised nutrition care plans and monitor the effectiveness of interventions. They are also responsible in identifying and preventing metabolic complications, such as refeeding syndrome. Pharmacists are integral to the safe administration of parenteral nutrition. They are tasked with designing, compounding and dispensing PN formulations tailored to patients' needs. They ensure the safety and quality of PN preparations by adhering to stability, compatibility and aseptic standards. Nurses are responsible for managing and maintaining central venous access devices used for PN administration. This includes monitoring for and preventing complications, such as catheter-related bloodstream infections and thrombosis. The physician is responsible in determining the indication for PN, conducting accurate assessment, overseeing the monitoring for complications, as well as ensuring safe and effective use of PN.

In Singapore, each hospital has its own governance regarding qualification of nutrition support team member. Ideally, the nutrition support team should acquire the relevant clinical experience and attain relevant course pertaining to nutrition support service such as the National Board for Nutrition Support Certificate (ASPEN) before being inducted into nutrition support team.

Recommendation 5a: All patients should have a baseline biochemical assessment prior to initiation of PN.

Recommendation 5b : After establishing a patient on PN, the frequency of biochemical monitoring should be adjusted according to patient's clinical progress, nutritional status and stage of PN therapy.

Commentary: Biochemical monitoring is essential for the detection of potential metabolic complications. Common complications associated with PN are electrolyte imbalances, hyperglycaemia, refeeding syndrome, metabolic bone disease and hepatobiliary disorders.²⁵ Regular biochemical monitoring and early detection enables timely management of these abnormalities, thereby mitigating the risk of complications associated with PN.

Before initiating PN, it is essential to conduct baseline tests assessing renal function (including sodium, potassium, creatinine, urea, bicarbonate and chloride levels), bone metabolism (such as calcium, phosphate, magnesium), liver function (including alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transferase, bilirubin) and lipid profile. The time interval for biochemical surveillance after PN initiation depends on the patient's clinical progress and nutritional status, as well as the stage of PN therapy that he/she is at. The stages of therapy include the initiation, maintenance and transition phases. The initiation phase is where there is a gradual increase of caloric delivery based on the patient's status and tolerance. The maintenance phase is where the patient is being provided a full, stable nutrition to meet its nutritional goals after being stabilised from the initial acute illness or postoperative phase. The transition phase is where the patient has adequate nutritional intake through oral or enteral feeding and parenteral nutrition are being gradually reduced.

Biochemical parameters should be reviewed daily for the first few days, and subsequent monitoring can be less frequent depending on patient's clinical status and stability of the biochemical parameters measured. There is currently no evidence to guide the timing of laboratory monitoring. Hence, the recommendation made here is based on the opinions and institutional practices of the authors of this guideline.

Recommendation 6a: Energy expenditure for patients requiring PN should ideally be measured using indirect calorimetry. However, if indirect calorimetry is not available, providing 25-30 kcal/kg/day or using validated predictive equations, taking into account physical activity and stress factor, are acceptable to calculate energy requirement.

Commentary: Inappropriate delivery of PN can have detrimental effects on patients' clinical outcomes. Excessive PN has been associated with complications such as hyperglycaemia, liver dysfunction and weight gain. On the other hand, inadequate PN can lead to macro- and micro-nutrient deficiencies and weight loss. Hence, accurate measurement or calculation of energy requirement is important so that adequate calories can be provided.

Energy requirements are not only highly variable between individuals, it also varies widely during different phases of the disease or clinical conditions for each individual. Therefore, regular assessment of energy requirement is recommended to ensure PN prescriptions are adjusted accordingly. Indirect calorimetry is the gold standard for determining resting energy expenditure (REE). REE is calculated using the adjusted Weir's equation ($3.941 \times \text{VO}_2 \text{ (L/min)}/\text{RQ} + 1.106 \times \text{VCO}_2 \text{ (L/min)} \times 1440$) based on measurements of oxygen consumption and carbon dioxide production. Even though indirect calorimetry is a well-established method to measure REE, it is often underutilised due to cost, lack of trained personnel and measurements can be time-consuming. Furthermore, many hospitals do not have a metabolic cart.

In the absence of indirect calorimetry, predictive equations such as Harris-Benedict, Schofield and Mifflin St-Jeor can be used to estimate REE. However, concerns regarding their applicability in patients with increased metabolic rates associated with injury, inflammation and disease were raised as these equations were initially developed to predict REE of healthy individuals. Moreover, large discrepancies were recorded between estimates obtained from predictive equations and measurements taken using indirect calorimetry, with differences ranging from ± 10 –90% of measured REE.^{35–38}

To date, 7 RCTs and cohort studies^{39–45} had compared estimated REE using predictive equations against measured REE using indirect calorimetry for patients on PN. Findings from early studies observed that estimates calculated using the Harris-Benedict equation were not significantly different from the measured REE for both hospitalised and healthy ambulatory patients on PN.^{39,43} There was also no difference reported for patients on cyclic and continuous PN regimens.³⁹ These findings, however, were not replicated in subsequent studies. For critically ill patients on PN, 2 studies^{40,41} found that the Harris-Benedict equation significantly underestimated measured REE using indirect calorimetry. While in non-critically ill patients, 1 study⁴² demonstrated that half of the predicted REEs using the Harris-Benedict equation overestimated the measured REE by >10%.

In summary, in the absence of indirect calorimetry, predictive equations are acceptable, but no equation can confidently estimate REE due to various compounding factors. A practical alternative using standard caloric intake ranges 25–30 kcal/kg/day with adjustments based on individual clinical conditions has also been recommended by ESPEN as a reasonable estimate of energy requirement.⁴⁶ The nutrition support team will need to exercise clinical judgement when using predictive equations or standard caloric ranges as they may under- or overestimate the true caloric requirement.

Recommendation 6b: Protein requirements for patients requiring PN should be tailored to individual needs, ranging from 1 to 2 g/kg/day. Higher protein doses may be required for the critically ill, cancer and elderly patients.

Commentary: Protein requirements for patients requiring PN vary depending on the clinical condition, nutritional status and metabolic stress. In general, patients receiving PN should have protein intake adjusted to their individual needs to promote recovery, prevent muscle wasting, and improve outcomes. The protein requirement for adults in the acute care setting typically ranges from 1.0 to 2.0 g/kg/day, with higher amounts for patients in severe catabolic states.

In a randomised control trial⁴⁷ that evaluated the effect of protein intake through parenteral nutrition on muscle strength and clinical outcomes in critically ill patients, those who received higher protein intake (1.2 g/kg/day) showed improved handgrip strength, greater muscle thickness and less fatigue during the first week of ICU as compared to those who received less protein intake (0.8 g/kg/day). Similarly, in a large retrospective observational study⁴⁸ that assessed the association between protein intake and mortality in non-critically ill older patients receiving PN, higher protein intake (≥ 0.8 g/kg/day) was found to be significantly associated with better survival outcomes. These findings highlight the importance of ensuring adequate protein provision in this vulnerable population to improve clinical outcomes. Additionally, in another study⁴⁹ among non-critically ill patients with advanced cancer receiving PN for more than 3 weeks, patients treated with high protein PN (1.5 g/kg/day) had a significantly higher

body weight as compared with patients treated with standard protein PN (1 g/kg/day). High protein PN appeared to be safe with no adverse effect on liver function.

While the studies discussed above provide valuable insights into protein intake and clinical outcomes for patients requiring PN, there is a pressing need to expand the scope of research in other patient population groups to further validate this recommendation. In summary, protein requirements should be individualised, with higher protein goals for patients with higher catabolic states, such as critical illness, malnutrition or cancer. Regular monitoring and adjustment of protein requirement are essential to ensure adequate protein intake while avoiding complications such as renal overload in specific conditions.

Recommendation 7: There is currently no nutritional assessment tool developed specifically for patients requiring PN. Validated assessment tools, such as Subjective Global Assessment (SGA), are recommended for the diagnosis and determination of the severity of malnutrition.

Commentary: Nutritional assessment is the collection of in-depth information pertaining to individuals' nutritional status carried out by trained HCPs. The assessment made will enable HCPs to formulate appropriate nutritional therapy tailored to the individual's needs. Commonly used nutritional assessment tools, such as SGA, Patient-Generated SGA and Mini Nutritional Assessment, have been validated in both hospital and community settings.⁵⁰⁻⁵³ Only 2 studies^{54,55} have assessed the sensitivity and validity of nutritional assessment tools used in the local acute care settings. One of the 2 studies found that 7-point SGA is more sensitive in detecting changes in nutritional status over time, in comparison to conventional SGA.⁵⁵ While findings from another study have shown that although modified Nutrition Risk in Critically Ill Score tool has a prognostic ability to predict mortality in the critical care setting, it has a poor agreement with SGA.⁵⁴

No specific nutritional assessment tool has been developed or validated among patients requiring PN thus far. Hence, based on current literature, SGA can be used until other validated nutritional assessment tools become available. In addition, the nutrition support team should perform a comprehensive assessment of the patient's baseline anthropometry, biochemistry, clinical signs and symptoms and diet history as part of the nutrition care process for all patients requiring PN.

Recommendation 8: It is recommended to start at 15-20 kcal/kg/day on day 1 and increasing it progressively to target for non-critically ill patients. Patient's nutritional status and risk of refeeding should be considered when initiating and advancing PN infusion rate.

Commentary: Twenty-six studies^{15-17,56-78} were included in the analysis of this question. Of these studies, 20 studies were conducted among ICU patients,^{15,17,56-66,71-74,77,78} 4 studies among surgical patients,^{69,70,75,76} 1 study among patients undergoing stem cell transplant⁶⁷ and 1 study that included exclusively patients who required PN.⁶⁸ There were vast differences in methodological quality and intervention design among these studies. The methods used to determine energy expenditure were also different. Some studies measured energy expenditure using indirect calorimetry,⁵⁷⁻⁶⁰ while others were based on predictive equations^{17,61-63,72} or weight-based estimates.^{15,17,64-66} In addition, the discrepancy between prescribed calories versus (vs) calories received by patients

was likely present as not all studies have provided information on actual calories delivered.

Only 7 out of all included studies^{17,63,66-70} compared the clinical effects of different PN dosages (high-calorie vs low-calorie) for patients who were solely on PN support, while other studies^{57, 60, 61, 63, 65, 71-75} included patients who were on both PN and EN support. The impact of EN on clinical outcomes in these studies was difficult to establish.

In the critical care setting, most of these studies^{15,17,57,60-63,72} did not find any significant difference in mortality, length of stay in hospital and in ICU, number of mechanically ventilated days, incidence of organ failure and infection rate when comparing patients in the high-calorie group and patients in the low-calorie group. Four studies^{15,62,71,73} reported that providing lower amounts of calories was more advantageous as it was associated with a lower rate of infection and fewer days of mechanical ventilation. Other favourable clinical outcomes included improved survival rates (with a higher number of patients discharged alive from ICU), increased survival at day 60, and reduced length of stay in ICU and hospital.^{15,71,72,78} In contrast, 1 study⁶⁰ found a higher number of nosocomial infections in the hypocaloric group. The outcome might be attributed to the relatively low provision of protein (0.4 g/kg/day). On the other hand, in the non-ICU setting, little insight could be gained due to the heterogeneity of studies.^{67-70,75,76} Therefore, based on our consensus, calorie intake may start with 15-20 kcal/kg/day on day 1 and increase progressively to target by day 3 or day 4 for non-critically ill patients, while critically ill patients may necessitate a more cautious approach to calorie progression.

Recommendation 9: PN can be reduced and discontinued when the patient is receiving more than 60% of target energy requirement from enteral nutrition and/or oral diet.

Commentary: There is no available data thus far to determine the cut-off point when PN can be discontinued. Clinical judgement is still required, especially for malnourished patients and patients with a complicated hospital course. These patients may require a longer period of PN support and should demonstrate a higher enteral and/or oral intake before PN is discontinued. Patients with severe gastrointestinal diseases, such as short bowel syndrome, may never be weaned off PN and will require long-term home PN support.

The ASPEN and SCCM guideline¹⁰ suggested that when tolerance to enteral nutrition is evident, PN should be weaned off when more than 60% of the patient's needs are met orally or enterally. Other studies^{15,20,79,80} used 50-80% as the cut-off points to discontinue PN.

Recommendation 10: Fish oil (FO) containing injectable lipid emulsion (ILE) should be used as part of the lipid component of PN.

Commentary: ILE should be included in PN formulation to provide a dense source of non-protein energy as well as a source of essential and conditionally essential fatty acids to prevent essential fatty acid deficiency. A variety of ILEs are currently available in Singapore, from conventional soy-based-ILE to newer fourth generation ILE containing soybean oil (SO), medium and long chain triglyceride (MCT/LCT), olive oil (OO) and FO.

Seven original studies⁸¹⁻⁸⁷ and 9 systematic reviews and meta-analyses⁸⁸⁻⁹⁶ were evaluated to determine the most favourable type of ILE to be used in PN therapy. Among the 7 original studies, 6 studies^{81-85, 87} compared FO-ILE against non-FO-ILE (namely SO-ILE, OO-ILE and a combination of SO and OO ILE), while 1 study⁸⁶ compared FO-ILE against lipid-free PN, SO-ILE, MCT/LCT and OO-ILE. Among the benefits of FO demonstrated in these studies were improvements in biochemical parameters indicating preservation of liver functions,^{81,82, 84} as well as improvement in clinical outcomes such as shorter length of hospital stay⁸⁴ and reduced rate of nosocomial infections.⁸⁷ The benefit of reduced length of stay was demonstrated in certain patient groups such as postoperative patients and critically ill patients. A reduction in all-cause mortality was demonstrated in a study of critically ill patients with sepsis.⁸³ Among the 9 systematic reviews and meta-analyses, the patient population was mostly postoperative and critically ill patients.

Most of the studies, which were of moderate to high quality of evidence,^{88,91-94,97,99} demonstrated that the use of FO-ILE was associated with reduced mortality, shorter length of hospital stay, fewer mechanical ventilated days, and lower infection rate compared to non-FO-ILE. However, there were conflicting data suggesting that there was no mortality advantage with FO-ILE.^{89,90,95} Taking into consideration the strengths and limitations of the studies included, the authors recommended using FO-ILE as part of the lipid component of PN.

Recommendation 11a: Multivitamins are recommended in patients initiated on PN. In patients at risk of refeeding syndrome, additional intravenous thiamine supplementation for 3-5 days is recommended.

Commentary: Vitamins are essential micronutrients required for normal cell function, growth and development. They function as enzyme cofactors that play important roles in energy metabolism, protein synthesis, wound healing and maintenance of proper immune function. Inadequate intake of vitamins can lead to deficiencies with negative clinical outcomes.

Serum levels of various vitamins decrease in the presence of inflammatory response. This has been observed among postoperative patients and patients with sepsis. The addition of multivitamins to PN formulation for postoperative patients has been found to reduce traumatic stress and improve the metabolic transition from catabolism to anabolism.¹⁰¹ Due to a nationwide shortage of multivitamins in the US in 1997, multiple cases of adverse clinical outcomes related to vitamin deficiency were also reported.^{102,103} Therefore, daily supplementation of multivitamins should be provided to all patients on PN support, especially to those who are malnourished with/without underlying acute illness. Patients who are at risk of refeeding syndrome will require higher doses of intravenous thiamine supplementation of 250 mg/day for 3-5 days to prevent the development of Wernicke's encephalopathy.¹⁰⁴

Recommendation 11b: Trace elements are recommended in patients initiated on PN.

Commentary: Trace elements are minerals that are required in small amounts and function primarily as catalysts in enzymatic reactions. Some trace elements are nutritionally essential as they are vital for normal growth and development, whereas some trace elements are non-essential. Common essential trace elements added to PN formulation are chromium, copper, iron, manganese, selenium and zinc.

Case studies of trace element deficiencies were more frequently reported among patients receiving long-term PN support. There is currently no high-quality RCT that has evaluated the clinical outcomes of patients on PN who had received trace elements compared to those who did not. In addition, standardised laboratory measurement of the various trace elements serum levels is still lacking, hence making it difficult to confirm the presence of deficiencies. Most of the available studies¹⁰¹⁻¹¹⁵ suggested that all adult patients on PN support should receive daily supplementation of trace elements.

Deficiencies of trace elements have been predominantly reported in patients receiving long-term PN. For patients newly initiated on PN, especially those without pre-existing deficiencies or critical illness, the clinical impact of omitting trace elements remains unclear. As such, findings from the literature and expert consensus suggest that trace elements may be omitted for the first month of PN therapy in this subgroup of patients.¹¹⁶⁻¹¹⁸ After this period, or in cases of pre-existing deficiencies or critical illness, supplementation with standard daily dose of trace elements is recommended.

While most studies suggest universal supplementation, the low quality of evidence and lack of clear deficiency markers emphasise the importance of clinical judgement. Limitations of evidence revolve around 3 consideration points: (1) lack of high-quality RCTs comparing outcomes of patients receiving PN with and without trace elements, (2) reported deficiencies are more common in long-term PN patients and may not be applicable to short-term PN use in acute care settings, and (3) the absence of standardised tests for serum levels of trace elements limits the ability to confirm or categorise deficiencies reliably.¹¹⁶⁻¹¹⁸

While all adult patients on PN are recommended to receive daily supplementation of trace elements, this should be guided by clinical judgement, particularly in the first month of therapy for patients without pre-existing deficits or critical illness. The inclusion of trace elements should be re-evaluated based on clinical context, duration of PN, and availability of reliable laboratory assessments.

Recommendation 12a: Additional supplementation of vitamin C is recommended for patients who are critically ill and patients who have had gastrectomy or colorectal resection.

Commentary: Vitamin C, also known as ascorbic acid, is an antioxidant that protects the body cells from harmful free radicals. It is essential for the synthesis of collagen, carnitine and neurotransmitters. Prolonged deficiency of vitamin C can result in defective collagen synthesis, blood vessel fragility and, in severe cases, scurvy. Classical manifestations of scurvy include easy bruising, gum bleeding, poor wound healing and extracutaneous haemorrhage.

Two RCTs^{111,112} had reported that high-dose supplementation of vitamin C was associated with decreased postoperative oxidative stress and improved wound healing among patients who had undergone gastric or colorectal resection. Serum vitamin C level was observed to drop significantly shortly after major gastrointestinal surgeries, but it was quickly restored with high dose of intravenous vitamin C supplementation. Therefore, special consideration for additional supplementation of intravenous vitamin C of up to 500 mg/day, on top of a standard dose of multivitamins, should be given to critically ill patients and those who have undergone gastric or colorectal resection. The

additional supplementation should be administered peripherally instead of being added to PN admixtures as high doses of vitamin C may affect PN stability.¹¹²⁻¹¹⁴

Recommendation 12b: Additional supplementation of zinc (Zn) is recommended for patients with high GIT losses. For every 1L of GIT losses via fistula or stoma, an additional 12-17 mg of Zn should be provided.

Commentary: Zn is an important cofactor for many enzymatic reactions and plays a vital role in cell division and growth, protein and deoxyribonucleic acid synthesis, wound healing, immunity and regulation of the central nervous system. Zn deficiency can lead to a range of skin disorders, impaired gastrointestinal digestion and absorption, immune dysregulation and impaired cognitive function.

In a study of patients with gastrointestinal disease,¹¹⁵ a Zn replacement equation was derived using a regression analysis. Based on the equation, Zn replacement can be accurately calculated using measured GIT losses. In studies with burns patients (>20% total body surface area),¹¹⁹⁻¹²¹ it was observed that these patients experienced significant exudative Zn losses hence higher dosage of Zn should be added to PN. Zn supplementation up to 40 mg/day for 3 weeks was found to be safe and demonstrated clinical benefits, especially in wound healing.¹¹⁹⁻¹²¹

Recommendation 13: Additional supplementation of glutamine is not recommended in patients initiated on PN.

Commentary: Glutamine, a conditionally essential amino acid, is the most abundant amino acid in the blood. In normal healthy individuals, glutamine can be produced in sufficient amount and does not need to be supplemented in the diet. However, during critical illness when utilisation is high, the body may not be able to produce sufficient amount of glutamine to meet requirement hence causing a depletion in glutamine level making it a conditionally essential amino acid.¹²²

Eleven studies¹²³⁻¹³³ and 8 systematic reviews and meta-analyses¹³⁴⁻¹⁴¹ were reviewed to evaluate the benefits of adding glutamine into PN. There is significant heterogeneity in the quality of studies and patient population, making it challenging to make a recommendation. Studies had also reported that PN with glutamine supplementation was associated with a reduction in infection rates, length of hospital stay and days on mechanical ventilation in critically ill and post-surgical patients^{126,127,130,134-138,140,141} as well as in patients with acute pancreatitis.^{127,128,131,132,139} Early studies observed reduced mortality in critically ill patients or those with acute pancreatitis; however, these studies and reviews had small sample sizes and were of low to moderate methodological quality.^{128,129,131,138,139} Subsequent high-quality, large sample multicentre RCT study¹²³ showed that glutamine supplementation was associated with increased mortality for critically ill patients with multi-organ failure. Other studies and reviews with moderate to high methodological quality^{133-136,140} also did not show mortality benefits. Thus, in view of conflicting data and high heterogeneity of studies as well as a lack of recommendations in the international guidelines, the authors do not recommend additional glutamine supplementation in PN.

Recommendation 14: Peripherally inserted central catheter (PICC) with a dedicated lumen is recommended for PN administration. However, an existing central venous access device (CVAD) in the internal jugular vein can be used for up to 14 days.

Commentary: The choice of venous access for the administration of PN is of paramount importance.¹⁴² PN should be delivered through a CVAD. CVAD is defined as a catheter with its distal tip located at the junction of the superior vena cava and the right atrium.^{143,144} Common sites of venepuncture for CVAD placement include the subclavian, jugular, cephalic and basilic veins.

PICC is a CVAD placed in the antecubital fossa and is suitable for hospitalised patients requiring PN infusion. PICC is the preferred choice of vascular access for PN therapy as it is cost-effective and is associated with fewer catheter-related complications such as infection, obstruction, dislocation and venous thrombosis.^{142,145} However, there is no clear data showing significant advantages of PICC over other CVADs for hospitalised patients on PN therapy.^{142,146}

Femoral catheters, on the other hand, are not recommended for the administration of PN due to their association with increased risk for contamination, infection and venous thrombosis. Hence, PICC is a relatively safe device for the administration of long-term PN as it preserves the integrity of the venous system.¹⁴⁷ Nevertheless, PICC should be avoided for patients with renal failure where venous access for dialysis takes priority.¹⁴⁵

Recommendation 15: CVADs should be flushed using normal saline after each use, or weekly if not in use, to maintain catheter patency.

Commentary: Most CVADs can be safely flushed and locked with normal saline solution when not in use. Although the use of heparin flush to maintain CVAD patency has been recommended in some nursing guidelines, the evidence to support this practice was based on low-quality studies.¹⁴⁸ Several systematic reviews^{146,147,150} have shown that heparin flushes have no significant benefit over normal saline flushes in maintaining catheter patency. Therefore, taking into account all the above-mentioned reasons, the flushing of CVADs with normal saline solution is recommended.

Current recommendations pertaining to how frequent CVADs should be flushed are conflicting and based on weak evidence.^{151,152} The most appropriate flushing frequency is after each use or weekly if not in use. In addition, several flushing techniques can minimise the risk of CVAD occlusion. For example, flushing with a push-pause motion causes turbulence of flow which may prevent build-up of deposits.¹⁵³ Additionally, clamping the catheter while injecting the last 0.5 ml of fluid will prevent blood from being drawn back into the catheter tip.

Recommendation 16a: PPN can be used as supplemental PN where oral or EN is suboptimal.

Recommendation 16b: The duration of PPN therapy should not exceed 14 days due to an increased risk of complications related to peripheral intravenous catheters.

Commentary: High-quality studies evaluating the benefits of PPN therapy are limited. Most studies are either small in sample size or based on retrospective data.¹⁵⁴⁻¹⁵⁶ In view of the high volume and low nutritional content of PPN, PPN alone is unlikely to be adequate to meet individual's nutritional requirement. Therefore, PPN can be used as a short-term therapy to bridge the nutritional gap during transition periods until CVAD is inserted or as a supplement to oral and/or EN until GIT regains full function.

Peripheral intravenous catheters typically have a short dwell time as the risk of complications increases for every day it is left in place.^{156,157} Consequently, there is a need to change the venous access site every 48–72 hours or earlier if local complications such as infection, subcutaneous infiltration of infusate or thrombophlebitis develop. The risk of thrombophlebitis has been reported to range from 14% to 28% with the use of PPN.^{154,158,159} Thus, the authors do not recommend the use of PPN for more than 14 days. It is important to assess the adequacy of the patient's venous access prior to starting PPN. The access site must be examined daily for signs of local complications.

Recommendation 17: Osmolarity of PPN therapy should be maintained at less than 900 mOsm/L to minimise the risk of catheter-related complications.

Commentary: PPN is usually reserved for short-term use because the infusion of hypertonic solution into peripheral veins may cause phlebitis and thrombosis. Hence, the osmolarity of the solution should be kept low and this can be achieved by lowering nutrient content and increasing fluid volume of the PPN solution. The osmolarity of less than 900 mOsm/L in PPN has been shown to be well tolerated.^{160,161}

Recommendation 18a: Patients who are at risk of refeeding syndrome are required to have their serum electrolytes monitored daily for the first few days, following which frequency of monitoring can be reduced when serum electrolytes stabilise.

Recommendation 18b: Serum electrolyte abnormalities should be promptly recognised and corrected.

Commentary: Refeeding syndrome is a potentially fatal condition that may occur when artificial nutrition is introduced in malnourished patients who have undergone prolonged fasting or minimal oral/enteral intake. It is characterised by serum electrolyte disturbances (predominantly hypokalaemia, hypophosphataemia and hypomagnesaemia), thiamine deficiency and shift in body fluids.^{162,163} When nutrition is introduced after a prolonged period of fasting, nutrient utilisation in the body shifts from endogenous protein and fat stores to exogenous carbohydrates. This process leads to increase in insulin production and utilisation of potassium, phosphate, magnesium and thiamine as glucose is transported into cells to be converted to energy stores in the form of adenosine triphosphate. Consequently, rapid depletion of extracellular electrolytes and thiamine can ensue, which may cause serious clinical complications, such as cardiac dysfunction, respiratory failure, neurological and haematological disorders.

Individuals who are at high risk of refeeding syndrome include those who have prolonged fasting, are severely malnourished and have history of chronic alcoholism. The incidence of refeeding syndrome in patients requiring PN has been reported to be high, with a study¹⁶⁴ reporting approximately 84% of patients developed biochemical characteristics of refeeding syndrome after commencement of PN.

Although refeeding syndrome is associated with severe and life-threatening complications, it is preventable through close monitoring, early detection and timely replacement of serum electrolytes and vitamins. Therefore, serum electrolytes should be monitored daily during the first few days of PN therapy and corrected promptly as

refeeding syndrome tends to occur within the first 72 hours after initiation of nutrition therapy.^{165,166} Vital signs, hydration status and blood glucose should be monitored when PN is initiated. The frequency of monitoring can be reduced subsequently depending on the clinical status, trend of serum electrolyte levels and fluid balance of the patient. Preventive measures through initial controlled hypocaloric feeding have also been found to be associated with reduced risk of refeeding syndrome and improved overall survival.^{72,167} Hence, it is recommended that PN therapy should be started at a lower infusion rate and gradually escalating to target nutritional needs for those who are at risk of refeeding syndrome. Additionally, prophylactic supplementation of thiamine (250 mg/day) should be provided prior to starting PN therapy.

Recommendation 19: Blood glucose levels should be measured every 6 hourly at least for the initial 48 hours after initiation of PN therapy.

Commentary: Hyperglycaemia and hypoglycaemia are common complications in hospitalised patients receiving PN and are independently associated with adverse clinical outcomes.¹⁶⁸ Hyperglycaemia is reported to occur in more than half of the patients receiving PN regardless of pre-existing diabetes mellitus.¹⁶⁹ The increase in blood glucose level results from a combination of factors such as increased stress hormones and insulin resistance due to underlying acute illness, surgery or trauma, as well as delivery of glucose and gluconeogenic substrates through PN.¹⁷⁰ It is well reported that hyperglycaemia increases the length of hospital stay and the risk of complications such as systemic infections, organ dysfunction and death.¹⁷¹ Hypoglycaemia, on the other hand, tends to result from tight glycaemic control with insulin therapy, abrupt discontinuation of PN, tapering doses of corticosteroids or vasopressors, and improved glycaemic control upon recovery from acute illness or organ failure.¹⁷¹

A retrospective study¹⁷² reported that there was no association between the frequency of glucose monitoring and mortality. There is also insufficient evidence to demonstrate that less frequent blood glucose monitoring results in worse glycaemic control or poorer outcomes.¹⁷² However, guidelines from various international societies^{14,173,174} recommended that blood glucose levels should be monitored every 6 hours for the first 48 hours after PN initiation. Glucose monitoring may be discontinued in non-diabetic patients who are normoglycaemic without insulin therapy after 48 hours of achieving target nutrition infusion.

Recommendation 20: A target blood glucose ranging between 7.8-10 mmol/L is recommended for patients receiving PN.

Commentary: Both hypoglycaemia and hyperglycaemia are associated with poorer outcomes for patients receiving PN with or without pre-existing diabetes.^{172,175} Patient's medical condition, PN formulation, insulin therapy and medication administered must be considered when controlling blood glucose level.

An early RCT¹⁷⁶ reported that in critically ill patients, tight glycaemic control (4.4-6.1 mmol/L) using continuous intravenous insulin infusion reduced length of stay and morbidity but not mortality. However, findings from the NICE-SUGAR study¹⁷⁷ revealed that ICU patients with tight glycaemic control (4.5-6.0 mmol/L) had a higher mortality of 10.1% compared to those on conventional blood glucose control (<10 mmol/L). Subsequent meta-analyses and systemic reviews¹⁷⁸⁻¹⁸¹ concurred that there was no

evidence that tight glycaemic control with intensive insulin therapy reduced mortality but instead, it increased the risk of hypoglycaemia which was associated with worse outcomes.

Multiple international societies including ASPEN,¹⁸² American Association of Clinical Endocrinologists,¹⁸³ American Diabetes Association¹⁸³ and Endocrine Society¹⁷¹ recommended a target blood glucose ranging 7.8–10.0 mmol/L for adult patients admitted in the acute care setting.

Recommendation 21: Subcutaneous insulin is preferred over the addition of insulin to PN admixtures for glycaemic control. At the discretion of the nutrition support team and guided by local institution practices, short-acting insulin may be added to PN admixture in patients whose clinical conditions and PN requirements are stable.

Commentary: Insulin therapy is the choice of treatment to correct hyperglycaemia in both diabetic and non-diabetic patients receiving PN.¹⁸⁴ Insulin can be administered subcutaneously, intravenously or added to PN admixture. The addition of short-acting insulin into PN admixture has the advantage of delivering a steady rate of insulin, which has been reported to provide a smoother glycaemic control without increasing risk of hypoglycaemia.¹⁸⁵ On the other hand, subcutaneous administration of long-acting insulin is associated with reduced glycaemic variability and facilitates the transition to basal-bolus regimens when PN is reduced or discontinued.¹⁸⁶

Multiple studies¹⁸⁷⁻¹⁹⁰ have shown that both methods of insulin administration, subcutaneous insulin and insulin added to PN admixture, are safe and provided similar effects on glycaemic control. Findings from the INSUPAR trial,¹⁹¹ a multicentre RCT where diabetic patients receiving PN therapy were randomised to 1 of the 2 insulin regimens (100% short-acting insulin added to PN or 50% subcutaneous basal long-acting insulin with 50% short-acting insulin added to PN), revealed that there were no significant differences in mean blood glucose levels, infectious complications, length of hospital stay and mortality between both groups. Patients who received a mix of subcutaneous insulin and intravenous insulin infusion from PN had better glycaemic control after PN interruption. However, the incidence of non-severe hypoglycaemia was higher and the duration to achieve mean blood glucose <10 mmol/L was longer.

There is also concern pertaining to insulin availability after it is added into PN admixtures with a reported range of 10–95%.¹⁹² The availability of insulin is affected by differing PN compositions such as macronutrient content, presence of vitamins, trace elements and pH of the PN admixture.^{193,194} Flow rates and contact time between insulin with the PN bag and intravenous tubes can also affect insulin availability.¹⁹⁵⁻¹⁹⁷ The variability of insulin availability may result in unpredictable blood glucose levels and increases the risk of hypoglycaemia.

Although adding insulin to PN is more convenient and leads to better glycaemic control, the concern pertaining to the variability of insulin availability after it is added to PN admixture cannot be disregarded.¹⁹⁸ Hence, the addition of insulin to PN admixture is not recommended in patients whose medical conditions and PN requirements are unstable. For these patients, the use of subcutaneous insulin for glycaemic control while receiving PN is recommended. The addition of short-acting insulin into PN admixture may be considered at the discretion of the nutrition support team and guided by local institution practices. It should only be provided to patients whose medical conditions

and PN requirements are stable and have achieved adequate glycaemic control on PN.¹⁸⁵

Recommendation 22: Baseline liver function tests (LFTs) should be obtained prior to initiation of PN. LFTs should be monitored on a weekly basis, with a reduction in frequency of monitoring subsequently depending on clinical progress.

Commentary: Derangement of LFTs is common among patients receiving PN. The aetiology is usually multi-factorial and frequently caused by non-PN-related factors, such as pre-existing liver disease, sepsis, underlying acute illness and drug-related factors. A study reported that 34% of patients had underlying abnormal LFTs prior to starting PN therapy.¹⁹⁹ Hence, it is pertinent to obtain baseline LFTs before PN is initiated and it should be monitored on a weekly basis. Frequency of LFTs monitoring can subsequently be reduced if it is normal.

Recommendation 23: Non-PN-related causes of abnormal LFTs should first be identified and managed accordingly. Overfeeding of PN may also cause abnormal LFTs, hence adjustment of dextrose and/or lipid content of PN admixture may be necessary.

Commentary: PN-related deranged LFTs typically occur after 2–4 weeks of PN therapy.^{200,201} Among patients who were already receiving PN, 1 study²⁰² reported raised aspartate aminotransferase, alkaline phosphatase and bilirubin concentrations in 27%, 32% and 31% of patients, respectively. However, most LFT abnormalities were mild and transient, and usually resolved after PN was discontinued and oral nutritional intake was commenced.²⁰³

The initial management of abnormal LFTs should always include the identification and management of possible non-PN-related causes, such as biliary obstruction, hepatitis and sepsis.²⁰⁴ The use of hepatotoxic drugs, especially antibiotics, should be minimised or avoided. Besides, overfeeding patients with PN therapy can also lead to liver dysfunction. Excessive dextrose infusion can cause hepatic steatosis, where a build-up of fats occurs in hepatocytes due to an imbalance between fatty acid synthesis and oxidation.²⁰⁵ Excessive lipid infusion, on the other hand, may result in lipid overload overwhelming the body's lipid clearance capacity. Therefore, adjustments to dextrose and lipid content in PN admixture are necessary if liver dysfunction is related to overfeeding. The ASPEN recommends that dextrose content should not exceed 7 g/kg/day and lipid content not greater than 1 g/kg/day for adults.²⁰⁶ Nonetheless, clinical judgement is still necessary to prevent worsening of LFTs.

Recommendation 24: Cyclic PN can be started when patient is clinically stable and satisfactory glycaemic control is maintained during a fasted state without PN.

Commentary: PN is commonly administered through continuous infusion over 24 hours. The duration of PN infusion can gradually be reduced hourly over a period of days or weeks once the patient has achieved target nutritional goals and has remained clinically and biochemically stable. The tolerance of a higher PN flow rate should be frequently assessed, as it is administered over a shorter period of time. Blood glucose levels should be closely monitored for sudden fluctuations, particularly during the first hour following PN initiation and PN discontinuation.²⁰⁷

Cyclic PN has been associated with a lower incidence of PN-related liver disease, as it mimics the physiological function of nutrient metabolism of oral feeding.^{208,209} During the fasting period of cyclic PN, carbohydrate oxidation reduces while lipid oxidation increases, hence improving the clearance of free fatty acids and suppressing lipogenesis in the liver. When compared with continuous PN, cyclic PN resulted in higher net hepatic lipid oxidation and lower net hepatic lipogenesis.²⁰⁹ Cyclic PN is advantageous for patients who require prolonged PN support, as it also allows daytime ambulation and activities when they are not receiving PN. Potential metabolic side effects associated with cyclic PN include fluctuations in blood glucose level and fluid imbalance.²¹⁰

Recommendation 25: Serum triglyceride should be maintained below 4.6 mmol/L.

Commentary: Hypertriglyceridaemia is a complication associated with the use of PN, with reported incidence ranging from 6% to 38%.^{211,212} It occurs as a result of alteration in lipid metabolism caused either by overloading of dextrose or lipid. Persistent hypertriglyceridaemia may lead to adverse effects such as decreased pulmonary gas diffusion, impaired immune response and acute pancreatitis, especially when serum triglyceride level exceeds 11.3 mmol/L.^{205,206} As the risk of adverse effects increases when serum level exceeds 4.6 mmol/L, it is recommended that serum triglyceride should be maintained ≤ 4.6 mmol/L during PN therapy.²¹³

Recommendation 26: If serum triglyceride is more than 4.6 mmol/L, dextrose load in PN should be reduced followed by a reduction in ILE if serum triglyceride level does not improve. PN should be discontinued if serum triglyceride is more than 11.4 mmol/L.

Commentary: Dextrose overload is usually the primary cause of hypertriglyceridaemia in patients receiving PN. When the body receives a large amount of dextrose, lipogenesis occurs as excess dextrose is converted to fatty acids, which are then transported to the liver as triglyceride-rich lipoproteins. Therefore, when hypertriglyceridaemia develops, the amount of dextrose in PN should be reduced. On the other hand, hypertriglyceridaemia induced by excessive ILE infusion occurs due to a reduction in lipoprotein lipase (LPL) activity. LPL promotes the hydrolysis of circulating triglycerides into fatty acids. When LPL activity becomes saturated and reaches maximal capacity, typically at serum triglyceride levels between 3.4 and 4.5 mmol/L, lipid clearance is impaired resulting in lipid accumulation. Hence, reducing the dosage of ILE in PN could enhance lipid clearance if hypertriglyceridaemia does not improve after the amount of dextrose in PN is reduced.

Besides PN therapy, other non-PN-related causes should be considered when managing hypertriglyceridaemia. Clinical conditions that predispose patients to hypertriglyceridaemia are sepsis, diabetes, liver failure, renal failure, multiorgan failure, obesity, alcoholism and pancreatitis.²¹⁴⁻²¹⁶ Medications such as steroids, antipsychotics, immunosuppressants, antiretroviral agents and beta-blockers may interfere with lipid metabolism and increase the risk of hypertriglyceridaemia. Additionally, propofol, which is infused in 10% lipid emulsion, can cause dose-dependent and duration-dependent hypertriglyceridaemia.^{217,218} In cases of severe hypertriglyceridaemia where serum triglyceride level exceeds 11.3 mmol/L, PN should be withheld until level normalises.^{214,215}

Recommendation 27: The use of thrombolytic agents and anticoagulation treatment is recommended for catheter-related thrombosis (CRT), with removal of CVAD if complete resolution from these measures is not achieved.

Commentary: CRT is a relatively common complication of CVAD use in PN therapy, with an incidence of 5% for symptomatic CRT and 15% for asymptomatic CRT when screened by venography.^{219,220} Multiple risk factors for the development of CRT have been identified and it includes patient's underlying disease, type of CVAD and technique used for CVAD insertion. Patients with hypercoagulable states, such as cancer, critical illness, sepsis, renal failure and thrombophilic conditions are at increased risk of CRT. In relation to catheter-related factors, catheters with higher number of lumens and larger lumen diameter are associated with a higher risk of CRT.²²¹⁻²²³ Catheters made of polyvinylchloride or polyethylene were found to be more thrombogenic compared with those made of polyurethane or silicone.²²⁴ With regard to insertion technique, improper positioning of the catheter tip, subclavian venepuncture insertion, left-sided insertion and multiple insertion attempts were associated with increased risk of CRT.²²⁵

In order to minimise the risk of CRT, smaller diameter single lumen CVAD made of polyurethane or silicone should be used. In addition, the International Society of Thrombosis and Haemostasis guideline²²⁶ recommends that CVAD should be inserted into the right jugular vein with the tip located at the junction of the superior vena cava and right atrium. The routine use of anticoagulants to prevent CRT is not recommended.

Although the removal of blocked CVADs is common practice, some causes of catheter occlusion may be rectified through simple measures. Occluded CVAD caused by build-up of lipid emulsion residue may be cleared by instilling a solution of 70% ethanol into the catheter.²²⁷ For occlusion caused by an intraluminal clot or fibrin sheath, thrombolytic agents such as urokinase or alteplase may be used to restore lumen patency.^{228,229} In symptomatic CRT, systemic anticoagulation for at least 3 months is recommended if the existing CVAD remains in-situ. Low molecular weight heparin is the preferred choice of anticoagulation for cancer patients.²³⁰ The treatment of CRT should include thrombolysis for acute symptomatic cases and anticoagulation therapy for subacute and chronic symptomatic cases. CVAD should be removed if all measures to achieve complete patency fails.

Recommendation 28a: In the event that catheter related-bloodstream infection (CRBSI) is suspected, 2 sets of blood cultures should be obtained from both the CVAD and peripheral vein before initiation of antimicrobial therapy.

Recommendation 28b: In complicated CRBSI, the CVAD should be removed for source control. In uncomplicated CRBSI or in patients with limited vascular access, discussion with an infectious disease specialist is recommended to explore possibility of CVAD salvage.

Commentary: Paired blood cultures should be drawn from both the CVAD and a peripheral vein for suspected CRBSI before the initiation of antimicrobial therapy. In a retrospective cohort study,²³¹ obtaining blood cultures before initiation of antimicrobial therapy was associated with better pathogen detection rates. The initial choice of antimicrobial therapy depends on the severity of the patient's clinical presentation, risk factors for infection and types of potential pathogens suspected.²³²

Complicated CRBSI refers to those that are associated with severe suppurative thrombophlebitis, endocarditis and blood infection that continues despite more than 72 hours of appropriate antimicrobial therapy, or infection due to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, fungi and mycobacteria.²³² Under such circumstances, CVAD should be removed to prevent undesirable complications such as septic shock and death.²³²⁻²³⁴ Reinsertion of CVAD should be deferred until after appropriate antimicrobial therapy has begun and/or after a repeat blood culture is negative. Discussion with an infectious disease specialist is recommended to guide how soon a new CVAD can be inserted.

Retrospective studies showed that CVAD salvage is possible in uncomplicated CRBSI, especially if the pathogen is coagulase-negative *S. aureus* and both antimicrobial lock and systemic antimicrobial therapy are used.^{233,235} As the reinfection rate was approximately 3 folds higher in salvaged CVAD,²³⁵ consultation with an infectious disease specialist is prudent.

Recommendation 29: It is not necessary to withhold PN during surgery.

Commentary: Concerns regarding the safety of continuous administration of PN during operative procedures when patients are under metabolic stress of surgery have been raised. Excessive use of fluids intraoperatively can put patients at risk of fluid overload, acid-based imbalance, renal impairment and cardio-respiratory compromise. Currently, there are no studies that have examined the metabolic effects of intraoperative administration of PN and patient outcomes. In view of a lack of evidence to support withholding PN during surgery, the authors recommend that it is not necessary to practice it.

Recommendation 30: Tapering of PN or administration of intravenous dextrose solution after abrupt termination of PN may not be necessary unless the patient is on insulin therapy.

Commentary: Gradual tapering of PN before cessation is a common practice to prevent rebound hypoglycaemia. However, it has been shown that the body adapts quickly to decreased glucose levels and subsequent need for insulin.^{46,236,237} In an RCT,²³⁷ which compared the metabolic effects of patients who had abrupt discontinuation of PN and those who had tapered discontinuation of PN, no difference was found in mean levels of glucose, insulin and counter-regulatory hormones such as glucagon, cortisol, growth hormone, epinephrine and norepinephrine. No patients had symptomatic hypoglycaemia throughout the study. Other studies^{238,239} also demonstrated that blood glucose response was rapid and returned to normal values within 60 minutes after the abrupt termination of PN, even in diabetic patients.

Although ESPEN recommended that tapering of PN is not necessary,⁴⁶ tapering of PN may be a safety precaution for patients who are susceptible to hypoglycaemia or on insulin therapy. PN infusion rate can be reduced by 50% for 1-2 hours before discontinuation with concurrent close monitoring of blood glucose levels. Alternatively, the initial PN infusion rate can be reduced by 50% for the first hour followed by a further reduction in infusion rate by another 50% over the second hour. In the event of unforeseen abrupt discontinuation of PN, intravenous dextrose solution may be administered, and blood glucose levels should be monitored.

REFERENCES

1. Wischmeyer PE, Klek S, Berger MM, et al. Parenteral nutrition in clinical practice: International challenges and strategies. *Am J Health Syst Pharm* 2024;81:S89-101.
2. Wong AT, Ong JP, Han HH. The Use of Parenteral Nutrition Support in an Acute Care Hospital and the Cost Implications of Short-term Parenteral Nutrition. *Ann Acad Med Singap* 2016;45:237-44.
3. Business Market Insights. Asia-Pacific Parenteral Nutrition Market. <https://www.businessmarketinsights.com/reports/asia-pacific-parenteral-nutrition-market>. Accessed 20 January 2025.
4. Chuah SW, Ng DHL, Liu P, et al. The use of parenteral nutrition in an acute care hospital. *Ann Acad Med Singap* 2013;42:395-400.
5. Worthington P, Balint J, Bechtold M, et al. When Is Parenteral Nutrition Appropriate? *JPEN J Parenter Enteral Nutr* 2017;41:324-77.
6. Elke G, van Zanten AR, Lemieux M, et al. Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. *Crit Care* 2016;20:117.
7. Aiko S, Yoshizumi Y, Sugiura Y, et al. Beneficial effects of immediate enteral nutrition after esophageal cancer surgery. *Surg Today* 2001;31:971-8.
8. Boelens PG, Heesakkers FFBM, Luyer MDP, et al. Reduction of postoperative ileus by early enteral nutrition in patients undergoing major rectal surgery: prospective, randomized, controlled trial. *Ann Surg* 2014;259:649-55.
9. Bozzetti F, Braga M, Gianotti L, et al. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: a randomised multicentre trial. *Lancet* 2001;358:1487-92.
10. Gupta R, Patel K, Calder PC, et al. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II > or =6). *Pancreatology* 2003;3:406-13.
11. Petrov MS, Kukosh MV, Emelyanov NV. A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition. *Dig Surg* 2006;23:336-44; discussion 344-5.
12. Koretz RL, Lipman TO, Klein S. AGA technical review on parenteral nutrition. *Gastroenterology* 2001;121:970-1001.
13. Lewis SR, Schofield-Robinson OJ, Alderson P, et al. Enteral versus parenteral nutrition and enteral versus a combination of enteral and parenteral nutrition for adults in the intensive care unit. *Cochrane Database Syst Rev* 2018;6:Cd012276.
14. McClave SA, Taylor BE, Martindale RG, 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 J Parenter Enteral Nutr* 2016;40:159-211.
15. Casaer MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med* 2011;365:506-17.
16. Doig GS, Simpson F, Sweetman EA, et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. *JAMA* 2013;309:2130-8.
17. Shah S, Hollands JM, Pontiggia L, et al. Impact of the Time to Initiation of Parenteral Nutrition on Patient Outcomes in Critically Ill Adults. *Nutr Metab Insights* 2019;12:1178638819859315.

18. Wan X, Gao X, Tian F, et al. Early parenteral nutrition alone or accompanying enteral nutrition in critically ill patients: a systematic review and meta-analysis. *Asia Pac J Clin Nutr* 2015;24:227-33.
19. Sim J, Hong J, Na EM, et al. Early supplemental parenteral nutrition is associated with reduced mortality in critically ill surgical patients with high nutritional risk. *Clin Nutr* 2021;40:5678-83.
20. Gao X, Liu Y, Zhang L, et al. Effect of Early vs Late Supplemental Parenteral Nutrition in Patients Undergoing Abdominal Surgery: A Randomized Clinical Trial. *JAMA Surg* 2022;157:384-93.
21. Kardalas E, Paschou SA, Anagnostis P, et al. Hypokalemia: a clinical update. *Endocr Connect* 2018;7:R135-46.
22. Amanzadeh J, Reilly RF, Jr. Hypophosphatemia: an evidence-based approach to its clinical consequences and management. *Nat Clin Pract Nephrol* 2006;2:136-48.
23. Rafat C, Flamant M, Gaudry S, et al. Hyponatremia in the intensive care unit: How to avoid a Zugzwang situation? *Ann Intensive Care* 2015;5:39.
24. Pham PCT, Pham PAT, Pham SV, et al. Hypomagnesemia: a clinical perspective. *Int J Nephrol Renovasc Dis* 2014;7:219-30.
25. Sobotka L, Camilo ME. Basics in clinical nutrition: Metabolic complications of parenteral nutrition. *e-SPEN journal* 2009;4:e120-2.
26. Dounousi E, Zikou X, Koulouras V, et al. Metabolic acidosis during parenteral nutrition: Pathophysiological mechanisms. *Indian J Crit Care Med* 2015;19:270-4.
27. Gutman M, Singer P, Gimmon Z. [Is there an indication for parenteral nutrition support in the terminally ill cancer patient?]. *Harefuah* 2008;147:224-8, 278, 277.
28. British Association for Parenteral and Enteral Nutrition. Access Routes <https://www.bapen.org.uk/education/nutrition-support/parenteral-nutrition/access-routes/2016>. Accessed 14 October 2024.
29. Dietitians Association of Australia. Parenteral nutrition manual for adults in health care facilities 2018. https://aci.health.nsw.gov.au/__data/assets/pdf_file/0010/159805/ACI-Parenteral-nutrition-pocketbook.pdf. Accessed 1 September 2024.
30. Ayers P, Adams S, Boullata J, et al. A.S.P.E.N. parenteral nutrition safety consensus recommendations. *JPEN J Parenter Enteral Nutr* 2014;38:296-333.
31. Reber E, Strahm R, Bally L, et al. Efficacy and Efficiency of Nutritional Support Teams. *J Clin Med* 2019;8:1281.
32. Naylor CJ, Griffiths RD, Fernandez RS. Does a multidisciplinary total parenteral nutrition team improve patient outcomes? A systematic review. *JPEN J Parenter Enteral Nutr* 2004;28:251-8.
33. Sriram K, Cyriac T, Fogg LF. Effect of nutritional support team restructuring on the use of parenteral nutrition. *Nutrition* 2010;26:735-9.
34. Nehme AE. Nutritional support of the hospitalized patient. The team concept. *JAMA* 1980;243:1906-8.
35. Cioffi I, Marra M, Pasanisi F, et al. Prediction of resting energy expenditure in healthy older adults: A systematic review. *Clin Nutr* 2021;40:3094-103.
36. Madden AM, Mulrooney HM, Shah S. Estimation of energy expenditure using prediction equations in overweight and obese adults: a systematic review. *J Hum Nutr Diet* 2016;29:458-76.
37. Mazzo R, Ribeiro FB, Vasques ACJ. Accuracy of predictive equations versus indirect calorimetry for the evaluation of energy expenditure in cancer patients with solid tumors - An integrative systematic review study. *Clin Nutr ESPEN* 2020;35:12-9.

38. Tatucu-Babet OA, Ridley EJ, Tierney AC. Prevalence of Underprescription or Overprescription of Energy Needs in Critically Ill Mechanically Ventilated Adults as Determined by Indirect Calorimetry: A Systematic Literature Review. *JPEN J Parenter Enteral Nutr* 2016;40:212-25.
39. Just B, Messing B, Darmaun D, et al. Comparison of substrate utilization by indirect calorimetry during cyclic and continuous total parenteral nutrition. *Am J Clin Nutr* 1990;51:107-11.
40. Flancbaum L, Choban PS, Sambucco S, et al. Comparison of indirect calorimetry, the Fick method, and prediction equations in estimating the energy requirements of critically ill patients. *Am J Clin Nutr* 1999;69:461-6.
41. Koea JB, Wolfe RR, Shaw JH. Total energy expenditure during total parenteral nutrition: ambulatory patients at home versus patients with sepsis in surgical intensive care. *Surgery* 1995;118:54-62.
42. Quiroz-Olguín G, Medina-Vera I, Serralde-Zúñiga AE, et al. Accurate determination of energy requirements in hospitalised patients with parenteral nutrition. *J Hum Nutr Diet* 2018;31:810-7.
43. Quebbeman EJ, Ausman RK. Estimating energy requirements in patients receiving parenteral nutrition. *Arch Surg* 1982;117:1281-4.
44. Ławiński M, Singer P, Gradowski Ł, et al. Predicted versus measured resting energy expenditure in patients requiring home parenteral nutrition. *Nutrition* 2015;31:1328-32.
45. Skallerup A, Nygaard L, Olesen SS, et al. Can We Rely on Predicted Basal Metabolic Rate in Patients With Intestinal Failure on Home Parenteral Nutrition? *JPEN J Parenter Enteral Nutr* 2017;41:1139-45.
46. Braga M, Ljungqvist O, Soeters P, et al. ESPEN Guidelines on Parenteral Nutrition: surgery. *Clin Nutr* 2009;28:378-86.
47. Ferrie S, Allman-Farinelli M, Daley M, et al. Protein Requirements in the Critically Ill: A Randomized Controlled Trial Using Parenteral Nutrition. *JPEN J Parenter Enteral Nutr* 2016;40:795-805.
48. Tamiya H, Yasunaga H, Hosoi T, et al. Association between protein intake and mortality in older patients receiving parenteral nutrition: a retrospective observational study. *Am J Clin Nutr* 2021;114:1907-16. Erratum in: *Am J Clin Nutr* 2023;117:838.
49. Goodrose-Flores C, Schedin A, Nelander J, et al. High-protein compared with standard parenteral nutrition in palliative cancer care. *BMJ Support Palliat Care* 2022;12:332-8.
50. da Silva Fink J, de Mello PD, de Mello ED. Subjective global assessment of nutritional status - A systematic review of the literature. *Clin Nutr* 2015;34:785-92.
51. Hu Y, Yang H, Zhou Y, et al. Prediction of all-cause mortality with malnutrition assessed by nutritional screening and assessment tools in patients with heart failure: a systematic review. *Nutr Metab Cardiovasc Dis* 2022;32:1361-74.
52. Steenson J, Vivanti A, Isenring E. Inter-rater reliability of the Subjective Global Assessment: a systematic literature review. *Nutrition* 2013;29:350-2.
53. Xu YC, Vincent JL. Clinical measurement properties of malnutrition assessment tools for use with patients in hospitals: a systematic review. *Nutr J* 2020;19:106.
54. Lew CCH, Cheung KP, Chong MFF, et al. Combining 2 Commonly Adopted Nutrition Instruments in the Critical Care Setting Is Superior to Administering Either One Alone. *JPEN J Parenter Enteral Nutr* 2017;148607117726060.
55. Lim SL, Lin XH, Daniels L. Seven-Point Subjective Global Assessment Is More Time Sensitive Than Conventional Subjective Global Assessment in Detecting Nutrition Changes. *JPEN J Parenter Enteral Nutr* 2016;40:966-72.

56. Müller TF, Müller A, Bachem MG, et al. Immediate metabolic effects of different nutritional regimens in critically ill medical patients. *Intensive Care Med* 1995;21:561-6.
57. Allingstrup MJ, Kondrup J, Wiis J, et al. Early goal-directed nutrition versus standard of care in adult intensive care patients: the single-centre, randomised, outcome assessor-blinded EAT-ICU trial. *Intensive Care Med* 2017;43:1637-47.
58. Berg A, Rooyackers O, Bellander BM, et al. Whole body protein kinetics during hypocaloric and normocaloric feeding in critically ill patients. *Crit Care* 2013;17:R158.
59. Frankenfield DC, Smith JS, Cooney RN. Accelerated nitrogen loss after traumatic injury is not attenuated by achievement of energy balance. *JPEN J Parenter Enteral Nutr* 1997;21:324-9.
60. Petros S, Horbach M, Seidel F, et al. Hypocaloric vs Normocaloric Nutrition in Critically Ill Patients: A Prospective Randomized Pilot Trial. *JPEN J Parenter Enteral Nutr* 2016;40:242-9.
61. Hausmann D, Mosebach KO, Caspari R, et al. Combined enteral-parenteral nutrition versus total parenteral nutrition in brain-injured patients. A comparative study. *Intensive Care Med* 1985;11:80-4.
62. Ichimaru S, Sono M, Seo R, et al. Energy intake in the first week in an emergency intensive care unit may not influence clinical outcomes in critically ill, overweight Japanese patients. *Asia Pac J Clin Nutr* 2017;26:1016-20.
63. Owais AE, Kabir SI, McNaught C, et al. A single-blinded randomised clinical trial of permissive underfeeding in patients requiring parenteral nutrition. *Clin Nutr* 2014;33:997-1001.
64. Charles EJ, Petroze RT, Metzger R, et al. Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care unit: a randomized controlled trial. *Am J Clin Nutr* 2014;100:1337-43.
65. Ridley EJ, Davies AR, Parke R, et al. Supplemental parenteral nutrition versus usual care in critically ill adults: a pilot randomized controlled study. *Crit Care* 2018;22:12.
66. Ahrens CL, Barletta JF, Kanji S, et al. Effect of low-calorie parenteral nutrition on the incidence and severity of hyperglycemia in surgical patients: a randomized, controlled trial. *Crit Care Med* 2005;33:2507-12.
67. Cetin T, Arpacı F, Dere Y, et al. Total parenteral nutrition delays platelet engraftment in patients who undergo autologous hematopoietic stem cell transplantation. *Nutrition* 2002;18:599-603.
68. McCowen KC, Friel C, Sternberg J, et al. Hypocaloric total parenteral nutrition: effectiveness in prevention of hyperglycemia and infectious complications--a randomized clinical trial. *Crit Care Med* 2000;28:3606-11.
69. Sevette A, Smith RC, Aslani A, et al. Does growth hormone allow more efficient nitrogen sparing in postoperative patients requiring parenteral nutrition? A double-blind, placebo-controlled randomised trial. *Clin Nutr* 2005;24:943-55.
70. Liu C, Du Z, Lou C, et al. Enteral nutrition is superior to total parenteral nutrition for pancreatic cancer patients who underwent pancreaticoduodenectomy. *Asia Pac J Clin Nutr* 2011;20:154-60.
71. Xiong W, Qian K. Low-Protein, Hypocaloric Nutrition with Glutamine versus Full-Feeding in the Acute Phase in ICU Patients with Severe Traumatic Brain Injury. *Neuropsychiatr Dis Treat* 2021;17:703-10.
72. Doig GS, Simpson F, Heighes PT, et al. Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial. *Lancet Respir Med* 2015;3:943-52.

73. Fan M, Wang Q, Fang W, et al. Early Enteral Combined with Parenteral Nutrition Treatment for Severe Traumatic Brain Injury: Effects on Immune Function, Nutritional Status and Outcomes. *Chin Med Sci J* 2016;31:213-20.
74. Hui L, Zang K, Wang M, et al. Comparison of the Preference of Nutritional Support for Patients With Severe Acute Pancreatitis. *Gastroenterol Nurs* 2019;42:411-6.
75. Braga M, Vignali A, Gianotti L, et al. Benefits of early postoperative enteral feeding in cancer patients. *Infusionsther Transfusionsmed* 1995;22:280-4.
76. Hwang TL, Mou SC, Chen MF. The importance of a source of sufficient protein in postoperative hypocaloric partial parenteral nutrition support. *JPEN J Parenter Enteral Nutr* 1993;17:254-6.
77. Choban PS, Burge JC, Scales D, et al. Hypoenergetic nutrition support in hospitalized obese patients: a simplified method for clinical application. *Am J Clin Nutr* 1997;66:546-50.
78. Hartl WH, Bender A, Scheipl F, et al. Calorie intake and short-term survival of critically ill patients. *Clin Nutr* 2019;38:660-7.
79. Perinel J, Mariette C, Dousset B, et al. Early Enteral Versus Total Parenteral Nutrition in Patients Undergoing Pancreaticoduodenectomy: A Randomized Multicenter Controlled Trial (Nutri-DPC). *Ann Surg* 2016;264:731-7.
80. Wischmeyer PE, Hasselmann M, Kummerlen C, et al. A randomized trial of supplemental parenteral nutrition in underweight and overweight critically ill patients: the TOP-UP pilot trial. *Crit Care* 2017;21:142.
81. Klek S, Chambrier C, Singer P, et al. Four-week parenteral nutrition using a third generation lipid emulsion (SMOFlipid)--a double-blind, randomised, multicentre study in adults. *Clin Nutr* 2013;32:224-31.
82. Piper SN, Schade I, Beschmann RB, et al. Hepatocellular integrity after parenteral nutrition: comparison of a fish-oil-containing lipid emulsion with an olive-soybean oil-based lipid emulsion. *Eur J Anaesthesiol* 2009;26:1076-82.
83. Umpierrez GE, Spiegelman R, Zhao V, et al. A double-blind, randomized clinical trial comparing soybean oil-based versus olive oil-based lipid emulsions in adult medical-surgical intensive care unit patients requiring parenteral nutrition. *Crit Care Med* 2012;40:1792-8.
84. Mertes N, Grimm H, Fürst P, et al. Safety and efficacy of a new parenteral lipid emulsion (SMOFlipid) in surgical patients: a randomized, double-blind, multicenter study. *Ann Nutr Metab* 2006;50:253-9.
85. Wichmann MW, Thul P, Czarnetzki HD, et al. Evaluation of clinical safety and beneficial effects of a fish oil containing lipid emulsion (Lipoplus, MLF541): data from a prospective, randomized, multicenter trial. *Crit Care Med* 2007;35:700-6.
86. Edmunds CE, Brody RA, Parrott JS, et al. The effects of different IV fat emulsions on clinical outcomes in critically ill patients. *Crit Care Med* 2014;42:1168-77.
87. Grau-Carmona T, Bonet-Saris A, García-de-Lorenzo A, et al. Influence of n-3 polyunsaturated fatty acids enriched lipid emulsions on nosocomial infections and clinical outcomes in critically ill patients: ICU lipids study. *Crit Care Med* 2015;43:31-9.
88. Manzanares W, Dhaliwal R, Jurewitsch B, et al. Parenteral fish oil lipid emulsions in the critically ill: a systematic review and meta-analysis. *JPEN J Parenter Enteral Nutr* 2014;38:20-8.
89. Manzanares W, Langlois PL, Dhaliwal R, et al. Intravenous fish oil lipid emulsions in critically ill patients: an updated systematic review and meta-analysis. *Crit Care* 2015;19:167.
90. Wei C, Hua J, Bin C, et al. Impact of lipid emulsion containing fish oil on outcomes of surgical patients: systematic review of randomized controlled trials from Europe and Asia. *Nutrition* 2010;26:474-81.

91. Chen B, Zhou Y, Yang P, et al. Safety and efficacy of fish oil-enriched parenteral nutrition regimen on postoperative patients undergoing major abdominal surgery: a meta-analysis of randomized controlled trials. *JPEN J Parenter Enteral Nutr* 2010;34:387-94.
92. Tian H, Yao X, Zeng R, et al. Safety and efficacy of a new parenteral lipid emulsion (SMOF) for surgical patients: a systematic review and meta-analysis of randomized controlled trials. *Nutr Rev* 2013;71:815-21.
93. Pradelli L, Klek S, Mayer K, et al. Omega-3 fatty acid-containing parenteral nutrition in ICU patients: systematic review with meta-analysis and cost-effectiveness analysis. *Crit Care* 2020;24:634.
94. Pradelli L, Mayer K, Klek S, et al. ω -3 Fatty-Acid Enriched Parenteral Nutrition in Hospitalized Patients: Systematic Review With Meta-Analysis and Trial Sequential Analysis. *JPEN J Parenter Enteral Nutr* 2020;44:44-57.
95. Pradelli L, Mayer K, Muscaritoli M, et al. n-3 fatty acid-enriched parenteral nutrition regimens in elective surgical and ICU patients: a meta-analysis. *Crit Care* 2012;16:R184.
96. Palmer AJ, Ho CK, Ajibola O, et al. The role of ω -3 fatty acid supplemented parenteral nutrition in critical illness in adults: a systematic review and meta-analysis. *Crit Care Med* 2013;41:307-16.
97. Bae HJ, Lee GY, Seong JM, et al. Outcomes with perioperative fat emulsions containing omega-3 fatty acid: A meta-analysis of randomized controlled trials. *Am J Health Syst Pharm* 2017;74:904-18.
98. Dai YJ, Sun LL, Li MY, et al. Comparison of Formulas Based on Lipid Emulsions of Olive Oil, Soybean Oil, or Several Oils for Parenteral Nutrition: A Systematic Review and Meta-Analysis. *Adv Nutr* 2016;7:279-86.
99. Li NN, Zhou Y, Qin XP, et al. Does intravenous fish oil benefit patients post-surgery? A meta-analysis of randomised controlled trials. *Clin Nutr* 2014;33:226-39.
100. Manzanares W, Dhaliwal R, Jurewitsch B, et al. Alternative lipid emulsions in the critically ill: a systematic review of the evidence. *Intensive Care Med* 2013;39:1683-94.
101. Li ZJ, Chen W, Jiang H, et al. Effects of Postoperative Parenteral Nutrition Enhanced by Multivitamin on Metabolic Phenotype in Postoperative Gastric Cancer Patients. *Mol Nutr Food Res* 2018;62:e1700757.
102. Lactic acidosis traced to thiamine deficiency related to nationwide shortage of multivitamins for total parenteral nutrition -- United States, 1997. *MMWR Morb Mortal Wkly Rep* 1997;46:523-8.
103. Da Silva YS, Horvat CM, Dezfulian C. Thiamin Deficiency as a Cause of Persistent Hyperlactatemia in a Parenteral Nutrition-Dependent Patient. *JPEN J Parenter Enteral Nutr* 2015;39:604-6.
104. Francini-Pesenti F, Brocadello F, Manara R, et al. Wernicke's syndrome during parenteral feeding: not an unusual complication. *Nutrition* 2009;25:142-6.
105. Plogsted S, Adams SC, Allen K, et al. Parenteral Nutrition Trace Element Product Shortage Considerations. *Nutr Clin Pract* 2016;31:843-7.
106. Akutsu Y, Kono T, Uesato M, et al. Are additional trace elements necessary in total parenteral nutrition for patients with esophageal cancer receiving cisplatin-based chemotherapy? *Biol Trace Elem Res* 2012;150:109-15.
107. Stehle P, Stoffel-Wagner B, Kuhn KS. Parenteral trace element provision: recent clinical research and practical conclusions. *Eur J Clin Nutr* 2016;70:886-93.
108. Jin J, Mulesa L, Carrilero Rouillet M. Trace Elements in Parenteral Nutrition: Considerations for the Prescribing Clinician. *Nutrients* 2017;9:440.

109. Carr AC, Rosengrave PC, Bayer S, et al. Hypovitaminosis C and vitamin C deficiency in critically ill patients despite recommended enteral and parenteral intakes. *Crit Care* 2017;21:300.
110. Shen H, Mei Y, Zhang K, et al. The Effect of Vitamin D Supplementation on Clinical Outcomes for Critically Ill Patients: A Systemic Review and Meta-Analysis of Randomized Clinical Trials. *Front Nutr* 2021;8:664940.
111. Fukatsu K, Shineha R, Kawauchi Y, et al. Optimizing Vitamin and Trace Element Profiles in Blood after Gastrointestinal Tract Surgery by a New Parenteral Nutrition Formula. *Ann Nutr Metab* 2019;74:189-99.
112. Yamazaki E, Horikawa M, Fukushima R. Vitamin C supplementation in patients receiving peripheral parenteral nutrition after gastrointestinal surgery. *Nutrition* 2011;27:435-9.
113. Stawny M, Gostyńska A, Olijarczyk R, et al. Stability studies of parenteral nutrition with a high dose of vitamin C. *J Oncol Pharm Pract* 2020;26:1894-902.
114. Gibbons E, Allwood MC, Neal T, et al. Degradation of dehydroascorbic acid in parenteral nutrition mixtures. *J Pharm Biomed Anal* 2001;25:605-11.
115. Wolman SL, Anderson GH, Marliss EB, et al. Zinc in total parenteral nutrition: requirements and metabolic effects. *Gastroenterology* 1979;76:458-67.
116. Plogsted S, Adams SC, Allen K, et al. Parenteral Nutrition Trace Element Product Shortage Considerations. *Nutr Clin Pract* 2016;31:843-7.
117. Akutsu Y, Kono T, Uesato M, et al. Are additional trace elements necessary in total parenteral nutrition for patients with esophageal cancer receiving cisplatin-based chemotherapy? *Biol Trace Elem Res* 2012;150:109-15.
118. Stehle P, Stoffel-Wagner B, Kuhn KS. Parenteral trace element provision: recent clinical research and practical conclusions. *Eur J Clin Nutr* 2016;70:886-93.
119. Berger MM, Binnert C, Chiolerio RL, et al. Trace element supplementation after major burns increases burned skin trace element concentrations and modulates local protein metabolism but not whole-body substrate metabolism. *Am J Clin Nutr* 2007;85:1301-6.
120. Berger MM, Cavadini C, Bart A, et al. Cutaneous copper and zinc losses in burns. *Burns* 1992;18:373-80.
121. Berger MM, Shenkin A. Trace element requirements in critically ill burned patients. *J Trace Elem Med Biol* 2007;21 Suppl 1:44-8.
122. Vanek VW, Matarese LE, Robinson M, et al. A.S.P.E.N. position paper: parenteral nutrition glutamine supplementation. *Nutr Clin Pract* 2011;26:479-94.
123. Heyland D, Muscedere J, Wischmeyer PE, et al. A randomized trial of glutamine and antioxidants in critically ill patients. *N Engl J Med* 2013;368:1489-97. Erratum in: *N Engl J Med* 2013;368:1853. Dosage error in article text.
124. Powell-Tuck J, Jamieson CP, Bettany GE, et al. A double blind, randomised, controlled trial of glutamine supplementation in parenteral nutrition. *Gut* 1999;45:82-8.
125. Morlion BJ, Stehle P, Wachtler P, et al. Total parenteral nutrition with glutamine dipeptide after major abdominal surgery: a randomized, double-blind, controlled study. *Ann Surg* 1998;227:302-8.
126. Estívariz CF, Griffith DP, Luo M, et al. Efficacy of parenteral nutrition supplemented with glutamine dipeptide to decrease hospital infections in critically ill surgical patients. *JPEN J Parenter Enteral Nutr* 2008;32:389-402.
127. Sahin H, Mercanligil SM, Inanç N, et al. Effects of glutamine-enriched total parenteral nutrition on acute pancreatitis. *Eur J Clin Nutr* 2007;61:1429-34.
128. Xian-li H, Qing-jiu M, Jian-guo L, et al. Effect of total parenteral nutrition (TPN) with and without glutamine dipeptide supplementation on outcome in severe acute pancreatitis (SAP). *Clinical Nutrition Supplements* 2004;1:43-7.

129. da Gama Torres HO, Vilela EG, da Cunha AS, et al. Efficacy of glutamine-supplemented parenteral nutrition on short-term survival following allo-SCT: a randomized study. *Bone Marrow Transplant* 2008;41:1021-7.
130. Grau T, Bonet A, Miñambres E, et al. The effect of L-alanyl-L-glutamine dipeptide supplemented total parenteral nutrition on infectious morbidity and insulin sensitivity in critically ill patients. *Crit Care Med* 2011;39:1263-8.
131. Liu X, Sun XF, Ge QX. The role of glutamine supplemented total parenteral nutrition (TPN) in severe acute pancreatitis. *Eur Rev Med Pharmacol Sci* 2016;20:4176-80.
132. Ockenga J, Borchert K, Rifai K, et al. Effect of glutamine-enriched total parenteral nutrition in patients with acute pancreatitis. *Clin Nutr* 2002;21:409-16.
133. Ziegler TR, May AK, Hebbar G, et al. Efficacy and Safety of Glutamine-supplemented Parenteral Nutrition in Surgical ICU Patients: An American Multicenter Randomized Controlled Trial. *Ann Surg* 2016;263:646-55.
134. Stehle P, Ellger B, Kojic D, et al. Glutamine dipeptide-supplemented parenteral nutrition improves the clinical outcomes of critically ill patients: A systematic evaluation of randomised controlled trials. *Clin Nutr ESPEN* 2017;17:75-85.
135. Chen QH, Yang Y, He HL, et al. The effect of glutamine therapy on outcomes in critically ill patients: a meta-analysis of randomized controlled trials. *Crit Care* 2014;18:R8.
136. Tao KM, Li XQ, Yang LQ, et al. Glutamine supplementation for critically ill adults. *Cochrane Database Syst Rev* 2014;2014:Cd010050.
137. Zheng YM, Li F, Zhang MM, et al. Glutamine dipeptide for parenteral nutrition in abdominal surgery: a meta-analysis of randomized controlled trials. *World J Gastroenterol* 2006;12:7537-41.
138. Wischmeyer PE, Dhaliwal R, McCall M, et al. Parenteral glutamine supplementation in critical illness: a systematic review. *Crit Care* 2014;18:R76.
139. Yong L, Lu QP, Liu SH, et al. Efficacy of Glutamine-Enriched Nutrition Support for Patients With Severe Acute Pancreatitis: A Meta-Analysis. *JPEN J Parenter Enteral Nutr* 2016;40:83-94.
140. Bollhalder L, Pfeil AM, Tomonaga Y, et al. A systematic literature review and meta-analysis of randomized clinical trials of parenteral glutamine supplementation. *Clin Nutr* 2013;32:213-23.
141. Wang Y, Jiang ZM, Nolan MT, et al. The impact of glutamine dipeptide-supplemented parenteral nutrition on outcomes of surgical patients: a meta-analysis of randomized clinical trials. *JPEN J Parenter Enteral Nutr* 2010;34:521-9.
142. Pittiruti M, Hamilton H, Biffi R, et al. ESPEN Guidelines on Parenteral Nutrition: central venous catheters (access, care, diagnosis and therapy of complications). *Clin Nutr* 2009;28:365-77.
143. Michele M. Gottschlich MHD, P. Guenter. The A.S.P.E.N. nutrition support core curriculum: a case-based approach: the adult patient. Gottschlich MM, editor: American Society for Parenteral and Enteral Nutrition; 2007
144. Smith RN, Nolan JP. Central venous catheters. *BMJ* 2013;347:f6570.
145. Gorski LA, Hadaway L, Hagle ME, et al. Infusion Therapy Standards of Practice, 8th Edition. *J Infus Nurs* 2021;44:S1-224.
146. Micic D, Semrad C, Chopra V. Choosing the Right Central Venous Catheter for Parenteral Nutrition. *Am J Gastroenterol* 2019;114:4-6.
147. Randolph AG, Cook DJ, Gonzales CA, et al. Benefit of heparin in peripheral venous and arterial catheters: systematic review and meta-analysis of randomised controlled trials. *BMJ* 1998;316:969-75.

148. López-Briz E, Ruiz-García V. [Effectiveness of heparin versus NaCl 0.9% in central venous catheter flushing. A systematic review]. *Farm Hosp* 2005;29:258-64.
149. Peterson FY, Kirchhoff KT. Analysis of the research about heparinized versus nonheparinized intravascular lines. *Heart Lung* 1991;20:631-40.
150. Goode CJ, Titler M, Rakel B, et al. A meta-analysis of effects of heparin flush and saline flush: quality and cost implications. *Nurs Res* 1991;40:324-30.
151. Bishop L, Dougherty L, Bodenham A, et al. Guidelines on the insertion and management of central venous access devices in adults. *Int J Lab Hematol* 2007;29:261-78.
152. Green E, Macartney G, Zwaal C, et al. ONLINE Special Article Managing central venous access devices in cancer patients: A practice guideline. *Can Onco Nurs J* 2008;18.
153. Gabriel J. Vascular device occlusion: causes, prevention and management. *Nurs Stand* 2011;25:49-55.
154. Liu MY, Tang HC, Hu SH, et al. Influence of preoperative peripheral parenteral nutrition with micronutrients after colorectal cancer patients. *Biomed Res Int* 2015;2015:535431.
155. Hsieh CE, Lin KH, Lin CC, et al. Comparative factor analysis of the effect of postoperative peripheral parenteral nutrition on recovery of right lobe liver donors. *Exp Clin Transplant* 2015;13:157-62.
156. Maki DG, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters. A randomized controlled trial. *Ann Intern Med* 1991;114:845-54.
157. Infusion Nurses Society. Infusion Nursing Standards of Practice. *J Infus Nurs* 2006;29:S1-92.
158. Thomas DR, Zdrodowski CD, Wilson MM, et al. A prospective, randomized clinical study of adjunctive peripheral parenteral nutrition in adult subacute care patients. *J Nutr Health Aging* 2005;9:321-5.
159. Rubino M, Jin J, Gramlich L. Safety and impact of peripheral parenteral nutrition on nutrient delivery in patients with nutrition risk: A prospective observational study. *Nutr Clin Pract* 2022;37:1162-71.
160. Isaacs JW, Millikan WJ, Stackhouse J, et al. Parenteral nutrition of adults with a 900 milliosmolar solution via peripheral veins. *Am J Clin Nutr* 1977;30:552-9.
161. Hoffmann E. A randomised study of central versus peripheral intravenous nutrition in the perioperative period. *Clin Nutr* 1989;8:179-80.
162. Klein S. A primer of nutritional support for gastroenterologists. *Gastroenterology* 2002;122:1677-87.
163. Btaiche IF, Khalidi N. Metabolic complications of parenteral nutrition in adults, part 1. *Am J Health Syst Pharm* 2004;61:1938-49.
164. Pantoja F, Fragkos KC, Patel PS, et al. Refeeding syndrome in adults receiving total parenteral nutrition: An audit of practice at a tertiary UK centre. *Clin Nutr* 2019;38:1457-63.
165. Ambrose T, De Silva A, Naghibi M, et al. Refeeding risks in patients requiring intravenous nutrition support: Results of a two-centre, prospective, double-blind, randomised controlled trial. *Clin Nutr ESPEN* 2021;41:143-52.
166. Bistran BR. Update on total parenteral nutrition. *Am J Clin Nutr* 2001;74:153-4.
167. Olthof LE, Koekkoek WACK, van Setten C, et al. Impact of caloric intake in critically ill patients with, and without, refeeding syndrome: A retrospective study. *Clin Nutr* 2018;37:1609-17.

168. Umpierrez GE, Isaacs SD, Bazargan N, et al. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab* 2002;87:978-82.
169. Pleva M, Mirtallo JM, Steinberg SM. Hyperglycemic events in non-intensive care unit patients receiving parenteral nutrition. *Nutr Clin Pract* 2009;24:626-34.
170. Dungan KM, Braithwaite SS, Preiser JC. Stress hyperglycaemia. *Lancet* 2009;373:1798-807.
171. Umpierrez GE, Hellman R, Korytkowski MT, et al. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2012;97:16-38.
172. Lee H, Koh SO, Park MS. Higher dextrose delivery via TPN related to the development of hyperglycemia in non-diabetic critically ill patients. *Nutr Res Pract* 2011;5:450-4.
173. Singer P, Berger MM, Van den Berghe G, et al. ESPEN Guidelines on Parenteral Nutrition: intensive care. *Clin Nutr* 2009;28:387-400.
174. Gosmanov AR, Umpierrez GE. Management of hyperglycemia during enteral and parenteral nutrition therapy. *Curr Diab Rep* 2013;13:155-62.
175. Pasquel FJ, Spiegelman R, McCauley M, et al. Hyperglycemia during total parenteral nutrition: an important marker of poor outcome and mortality in hospitalized patients. *Diabetes Care* 2010;33:739-41.
176. Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006;354:449-61.
177. Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1283-97.
178. Kansagara D, Fu R, Freeman M, et al. Intensive insulin therapy in hospitalized patients: a systematic review. *Ann Intern Med* 2011;154:268-82.
179. Wiener RS, Wiener DC, Larson RJ. Benefits and risks of tight glucose control in critically ill adults: a meta-analysis. *JAMA* 2008;300:933-44.
180. Griesdale DE, de Souza RJ, van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. *CMAJ* 2009;180:821-7.
181. Marik PE, Preiser JC. Toward understanding tight glycemic control in the ICU: a systematic review and metaanalysis. *Chest* 2010;137:544-51.
182. McMahon MM, Nystrom E, Braunschweig C, et al. A.S.P.E.N. clinical guidelines: nutrition support of adult patients with hyperglycemia. *JPEN J Parenter Enteral Nutr* 2013;37:23-36.
183. Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Diabetes Care* 2009;32:1119-31.
184. Jakoby MG, Nannapaneni N. An insulin protocol for management of hyperglycemia in patients receiving parenteral nutrition is superior to ad hoc management. *JPEN J Parenter Enteral Nutr* 2012;36:183-8.
185. McCulloch A, Bansiya V, Woodward JM. Addition of Insulin to Parenteral Nutrition for Control of Hyperglycemia. *JPEN J Parenter Enteral Nutr* 2018;42:846-54.
186. Oghazian MB, Javadi MR, Radfar M, et al. Effectiveness of regular versus glargine insulin in stable critical care patients receiving parenteral nutrition: a randomized controlled trial. *Pharmacotherapy* 2015;35:148-57.
187. Hakeam HA, Mulia HA, Azzam A, et al. Glargine Insulin Use Versus Continuous Regular Insulin in Diabetic Surgical Noncritically Ill Patients Receiving Parenteral Nutrition: Randomized Controlled Study. *JPEN J Parenter Enteral Nutr* 2017;41:1110-8.

188. Ramos A, Rabasa F, Mendoza L, et al. Differences in Glycemic Control in Diabetic and Non-diabetic Patients with Parenteral Nutrition Using a Basal plus Correction Insulin Regimen: An Observational, Retrospective Study. *Diabetes Ther* 2018;9:1359-67.
189. Neff K, Donegan D, MacMahon J, et al. Management of parenteral nutrition associated hyperglycaemia: a comparison of subcutaneous and intravenous insulin regimen. *Ir Med J* 2014;107:141-3.
190. Verçoza Viana M, Verçoza Viana L, Tavares AL, et al. Insulin Regimens to Treat Hyperglycemia in Hospitalized Patients on Nutritional Support: Systematic Review and Meta-Analyses. *Ann Nutr Metab* 2017;71:183-94.
191. Oliveira G, Abuín J, López R, et al. Regular insulin added to total parenteral nutrition vs subcutaneous glargine in non-critically ill diabetic inpatients, a multicenter randomized clinical trial: INSUPAR trial. *Clin Nutr* 2020;39:388-94.
192. Forchielli ML, Bongiovanni F, Platé L, et al. Insulin Instability in Parenteral Nutrition Admixtures. *JPEN J Parenter Enteral Nutr* 2018;42:907-12.
193. Henry H, Lannoy D, Maboudou P, et al. Addition of Regular Insulin to Ternary Parenteral Nutrition: A Stability Study. *Pharmaceutics* 2021;13:458.
194. Ichikawa E, Kimura M, Mori H, et al. Apparent increase of insulin peak area in HPLC analysis of a preparation consisting of a mixture of insulin and total parenteral nutrition. *Chem Pharm Bull (Tokyo)* 2006;54:1196-9.
195. Christianson MA, Schwartz MW, Suzuki N. Determinants of insulin availability in parenteral nutrition solutions. *JPEN J Parenter Enteral Nutr* 2006;30:6-9.
196. Yu KH, Tsao HL, Lin SJ, et al. Quantitative analysis of insulin in total parenteral nutrition bag in Taiwan. *J Food Drug Anal* 2016;24:214-9.
197. Marcuard SP, Dunham B, Hobbs A, et al. Availability of insulin from total parenteral nutrition solutions. *JPEN J Parenter Enteral Nutr* 1990;14:262-4.
198. Schönenberger KA, Reber E, Dürig C, et al. Management of Hyperglycemia in Hospitalized Patients Receiving Parenteral Nutrition. *Front Clin Diabetes Healthc* 2022;3:829412.
199. Baker ML NJ. Abnormal liver function tests and parenteral nutrition. *Clinical Nutrition* 2004;23:864-5.
200. Gabe SM, Culkin A. Abnormal liver function tests in the parenteral nutrition fed patient. *Frontline Gastroenterol* 2010;1:98-104.
201. Grant JP, Cox CE, Kleinman LM, et al. Serum hepatic enzyme and bilirubin elevations during parenteral nutrition. *Surg Gynecol Obstet* 1977;145:573-80.
202. Clarke PJ, Ball MJ, Kettlewell MG. Liver function tests in patients receiving parenteral nutrition. *JPEN J Parenter Enteral Nutr* 1991;15:54-9.
203. Quigley EM, Marsh MN, Shaffer JL, et al. Hepatobiliary complications of total parenteral nutrition. *Gastroenterology* 1993;104:286-301.
204. Nanji AA, Anderson FH. Sensitivity and specificity of liver function tests in the detection of parenteral nutrition-associated cholestasis. *JPEN J Parenter Enteral Nutr* 1985;9:307-8.
205. Btaiche IF, Khalidi N. Metabolic complications of parenteral nutrition in adults, Part 2. *Am J Health Syst Pharm* 2004;61:2050-7; quiz 2058-9.
206. Mueller C, Lord LM, Marian M, American Society for P, et al. The ASPEN adult nutrition support core curriculum. 3rd Ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017
207. Suryadevara S, Celestin J, DeChicco R, et al. Type and prevalence of adverse events during the parenteral nutrition cycling process in patients being prepared for discharge. *Nutr Clin Pract* 2012;27:268-73.

208. Hwang TL, Lue MC, Chen LL. Early use of cyclic TPN prevents further deterioration of liver functions for the TPN patients with impaired liver function. *Hepatogastroenterology* 2000;47:1347-50.
209. Arenas Villafranca JJ, Nieto Guindo M, Álvaro Sanz E, et al. Effects of cyclic parenteral nutrition on parenteral-associated liver dysfunction parameters. *Nutr J* 2017;16:66.
210. Stout SM, Cober MP. Metabolic effects of cyclic parenteral nutrition infusion in adults and children. *Nutr Clin Pract* 2010;25:277-81.
211. Miles JM, Park Y, Harris WS. Invited Review: Lipoprotein Lipase and Triglyceride-Rich Lipoprotein Metabolism. *Nutr Clin Prac* 2001;16:273-9.
212. Trujillo EB, Young LS, Chertow GM, et al. Metabolic and monetary costs of avoidable parenteral nutrition use. *JPEN J Parenter Enteral Nutr* 1999;23:109-13.
213. Mirtallo JM, Ayers P, Boullata J, et al. ASPEN Lipid Injectable Emulsion Safety Recommendations, Part 1: Background and Adult Considerations. *Nutrition in Clinical Practice* 2020;35:769-82.
214. Samra JS, Summers LKM, Frayn KN. Sepsis and fat metabolism. *Br J Surg* 1996;83:1186-96.
215. Garber AJ, Vinik AI, Crespín SR. Detection and management of lipid disorders in diabetic patients. A commentary for clinicians. *Diabetes Care* 1992;15:1068-74.
216. Hiasa Y, Nakanishi K, Tada K, et al. Alcoholic hypertriglyceridemia with decreased activity of lipoprotein lipase and hepatic triglyceride lipase. *Intern Med* 1993;32:490-3.
217. Eddleston JM, Shelly MP. The effect on serum lipid concentrations of a prolonged infusion of propofol--hypertriglyceridaemia associated with propofol administration. *Intensive Care Med* 1991;17:424-6.
218. Barrachina F, Mateu-de Antonio J. Propofol and hypertriglyceridemia: no problem? *Crit Care Med* 1999;27:224-5.
219. Wall C, Moore J, Thachil J. Catheter-related thrombosis: A practical approach. *J Intensive Care Soc* 2016;17:160-7.
220. Verso M, Agnelli G. Venous thromboembolism associated with long-term use of central venous catheters in cancer patients. *J Clin Oncol* 2003;21:3665-75.
221. Bonizzoli M, Batacchi S, Cianchi G, et al. Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. *Intensive Care Med* 2011;37:284-9.
222. Zochios V, Umar I, Simpson N, et al. Peripherally inserted central catheter (PICC)-related thrombosis in critically ill patients. *J Vasc Access* 2014;15:329-37.
223. Liem TK, Yanit KE, Moseley SE, et al. Peripherally inserted central catheter usage patterns and associated symptomatic upper extremity venous thrombosis. *J Vasc Surg* 2012;55:761-7.
224. Pinelli F, Balsorano P, Mura B, et al. Reconsidering the GAVeCeLT Consensus on catheter-related thrombosis, 13 years later. *J Vasc Access* 2021;22:501-8.
225. Saber W, Moua T, Williams EC, et al. Risk factors for catheter-related thrombosis (CRT) in cancer patients: a patient-level data (IPD) meta-analysis of clinical trials and prospective studies. *J Thromb Haemost* 2011;9:312-9.
226. Debourdeau P, Farge D, Beckers M, et al. International clinical practice guidelines for the treatment and prophylaxis of thrombosis associated with central venous catheters in patients with cancer. *J Thromb Haemost* 2013;11:71-80.

227. Werlin SL, Lausten T, Jessen S, et al. Treatment of central venous catheter occlusions with ethanol and hydrochloric acid. *JPEN J Parenter Enteral Nutr* 1995;19:416-8.
228. Murray J, Precious E, Alikhan R. Catheter-related thrombosis in cancer patients. *Br J Haematol* 2013;162:748-57.
229. Deitcher SR, Fesen MR, Kiproff PM, et al. Safety and efficacy of alteplase for restoring function in occluded central venous catheters: results of the cardiovascular thrombolytic to open occluded lines trial. *J Clin Oncol* 2002;20:317-24.
230. Kearon C, Kahn SR, Agnelli G, et al. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133:454S-545S.
231. Scheer CS, Fuchs C, Gründling M, et al. Impact of antibiotic administration on blood culture positivity at the beginning of sepsis: a prospective clinical cohort study. *Clin Microbiol Infect* 2019;25:326-31.
232. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009;49:1-45.
233. Raad I, Narro J, Khan A, et al. Serious complications of vascular catheter-related *Staphylococcus aureus* bacteremia in cancer patients. *Eur J Clin Microbiol Infect Dis* 1992;11:675-82.
234. Strinden WD, Helgerson RB, Maki DG. *Candida* septic thrombosis of the great central veins associated with central catheters. Clinical features and management. *Ann Surg* 1985;202:653-8.
235. Dibb MJ, Abraham A, Chadwick PR, et al. Central Venous Catheter Salvage in Home Parenteral Nutrition Catheter-Related Bloodstream Infections: Long-Term Safety and Efficacy Data. *JPEN J Parenter Enteral Nutr* 2016;40:699-704. Epub 20140915.
236. Sanderson I, Deitel M. Insulin response in patients receiving concentrated infusions of glucose and casein hydrolysate for complete parenteral nutrition. *Ann Surg* 1974;179:387-94.
237. Krzywda EA, Andris DA, Whipple JK, et al. Glucose response to abrupt initiation and discontinuation of total parenteral nutrition. *JPEN J Parenter Enteral Nutr* 1993;17:64-7.
238. Wagman LD, Newsome HH, Miller KB, et al. The effect of acute discontinuation of total parenteral nutrition. *Ann Surg* 1986;204:524-9.
239. Nirula R, Yamada K, Waxman K. The effect of abrupt cessation of total parenteral nutrition on serum glucose: a randomized trial. *Am Surg* 2000;66:866-9.