Review Article

The role of parenteral nutrition in cancer in Indian settings

ABSTRACT

Background: Almost 50% of patients with cancer suffer from malnutrition during their first hospital visit. However, it is often overlooked and undiagnosed and is associated with morbidity, mortality, poor tolerance to treatment, and treatment outcomes. Guidelines recommend supportive nutrition from the early stages of cancertreatment. However, in clinical practice, nutritional support is often prescribed only as an end-of-life intervention or is not prescribed at all; moreover, the use of parenteral nutrition (PN) is not well-defined. There arelimited practical guidelines on the use of PN in patients with cancer.

Methods: A multidisciplinary group of specialists in India formulated this consensus to guide oncologists on the judicious use of PN in Indian settings. It includesgeneral and cancer-specific recommendations on the use of PN, supplemental PN (SPN), composition of PN, and monitoring patients to prevent adverse events associated with PN.

Recommendations: The risk of malnutrition should be assessed at the very first presentation of a patient with cancer. These patients' nutritional requirements are largely like those of the healthy population.Nutritional assessment of all cancer patients should begin at diagnosis and repeated regularly to initiate and monitor early nutritional intervention, before the general status is severely compromised.Oncologists and nutritionists need to be educated about using the appropriate nutrition support options according to the guidelines.While EN should be the preferred form of nutritional support, in specific circumstances PN might be a better option.Early PN in specific settings provides additional benefits, and is particularly important in some types of cancers. SPN as an additional nutritional support to EN can improve treatment tolerability and quality-of-life of patients with cancer.Education is also necessary for awareness about preventing and managing adverse effects of PN, which is the major reason for poor adoption of PN.

Keywords: *Parenteral nutrition, Total parenteral nutrition, Supplemental parenteral nutrition, Cancer*.

1. INTRODUCTION

The prevalence of malnutrition in patients with cancer ranges from 20% to more than 70%1It is seen in 15-20% of patients with early cancer, 80% of patients with advanced disease, and 80-90% of patients with terminal disease2In fact, malnutrition is present in >50% of patients with cancer during their first oncologic visit3 However, it often remains overlooked and undiagnosed; even if diagnosed, it remains untreated in about 50% of patients4The main causes for cancer-associated malnutrition are decreased nutrient intake and metabolicchanges caused by the disease leading totheactivationofproinflammatoryprocesses. The proinflammatory environment breaks down skeletal muscle proteins causing a loss of muscle mass5 Other causes include adverse effects of chemotherapy, such as nausea, vomiting, mucositis, or diarrhea, which preclude adequate oral intake6 Weight loss and sarcopenia is associated with morbidity and mortality, including poor quality of life (QoL), treatment-related toxicities, increased complications, and reduced tolerability, which in turn affect compliance to treatment. These subsequently lead to poor response to therapy, prolonged hospital stays, decreased survival, and higher healthcare costs. Even mild weight loss (>2.4%, or pre-cachexia) is significantly associated with decreased survival7

The European Society for Clinical Nutrition and Metabolism (ESPEN) 2021 guidelines recommend supportive nutrition if the diet intake is inadequate (i.e.,<50% of the daily requirement for >1 week or

only 50-75% of the requirement for >2 weeks). Supportive enteral nutrition (EN) is recommended if nutrition remains inadequate despite counseling andoral nutritional support (ONS);parenteral nutrition (PN)is recommended if EN is inadequate or not feasible8EN refers to the delivery of nutrients beyond the esophagus via feeding tubes9PNrefers to administering calories and nutrients through a vein. This could include carbohydrate calories delivered as simple sugar in an intravenous solution or all the required nutrients could be delivered including carbohydrates, protein, fat, vitamins, and trace elements10Total PN (TPN) is indicated when there is impaired gastrointestinal function and contraindications to enteral nutrition. TPN implies that the IV administered nutrition is the only source of nutrition the patient is receiving11Another modality is supplemental PN (SPN), which is the addition of PN when full EN is not possible or fails to meet caloric targets12SPN is less time-consuming, and the duration of infusion is shorter (usually 6–8 h for several days instead of 12–18 h every day)13

A recent study found that only 30%-60% of patients with cancer and at risk of malnutrition actually received nutritional support1Nutritional interventions are often provided in very advanced stages of cancer but not often used in patients who might benefit from early nutritional supplementation4PN is particularly reserved only for patients with a non-functional or compromised GI tract7Despite the guideline recommendations and evidence about the benefits of nutritional support in patients with cancer, data of the real-world clinical practice across various countries shows that cancer-related malnutrition is under-recognized and undertreated. Nutritional support is often prescribed as an end-of-life intervention or is not prescribed at all and the use of PN is quite delayed14-17

The benefits of oral nutrition, EN, and PNin terms of clinical outcomes are similar. Therefore, the clinical condition, risks, and benefits associated with each type of nutritional support and patient preferences should be considered7However, there is limited practical information regarding the use of PN in patients with cancer, which perhaps restricts its use at a more early stage e.g., in the form SPN. Hence, this consensus document has been prepared to provide cancer specialists and nutritionists in India with a reference framework regarding the use of PN for cancer-associated malnutrition.

2. MATERIALS AND METHODS

A multidisciplinary group comprising specialists in medical oncology, clinical hematology, nutrition specialists, surgical oncologists, and a gastro-surgeon jointly prepared this consensus document. The rationale for forming a multidisciplinary group was to be able to present cancer-specific recommendations for PNas all current recommendations do not specify the need and benefit of PN by type of cancer.The consensus was reached during a group meetingin April 2023, focusing on PN. International as well as Indian guidelines and the clinical experience of the group were considered in framing the consensus, which is summarized under ‘Results’.

3. RESULTS

3.1 Burden of cancer-associated malnutrition in India

The panel experts agreed that no large-scale studies on the burden of cancer-associated malnutrition in India have been conducted;hence, the exactburden is unknown. According to them, the general awareness about the guidelines on clinical nutrition for patients with cancer and their adoption among oncologists and dieticians in the country is very poor.

Indian patients with cancer are at a greater risk of protein malnutrition due to the predominance of a vegetarian diet18 A 2013 study reported an86% prevalence of malnutrition at the time of admission to intensive care in a tertiary care hospital. Other studies from India have also shown a high incidence rate of cancer-associated malnutrition, with the overall rate being up to 90%, with varying degrees of severity19-24 In one of these studies, 43% of patients stated that their food intake has changed, and 57% stated that their food intake was less than normal20 In another study, 90% of subjects suffered from weight loss after the first cycle of chemotherapy with a significant decrease in hemoglobin and albumin21However, most studies had a small sample size of less than 100 patients; hence, the wider prevalence remains unknown. Only a few accredited hospitals conduct nutrition screening at the time of reporting as a protocol. The timing of recognizing the presence of malnutrition or at-risk is very important to reverse the deteriorating nutritional status before it progresses to cachexia 25

3.2 Screening for cancer-associated malnutrition

According to the panel experts, the risk of malnutrition should be assessed at the very first presentation of the patient. The prevention and management of cancer-associated malnutrition

requires a stepwiseapproach with regular reassessment and follow-up. However, in practice, the daily calorie requirement of a patient undergoing cancer treatment is not calculated at almost 80 to 85% of centers in the country. The expert panel opined that among public hospitals in India, it was estimated 50 to 60% of patients with cancer are screened for malnutrition and close to 20% of hospitals have no dietician. Many hospitals with more than 100 beds have only one dietician. Moreover, even if screening is conducted and malnutrition is detected before initiating cancer treatment, there isinadequate time for correction of the malnutrition before surgery or chemotherapy.A recent survey of 443 hospitals in India, corroborated the experience shared by the experts. It was found that 26 non-accredited hospitals had no dietician service. For nutritional screening, 47.4% of accredited and 22.4 % of non-accredited hospitals used a single screening tool of choice. The dietician-patient ratio in accredited and non-accredited hospitals was 1:73, and 1:212 respectively26

While various validated tools suggested by the guidelines can be used for screening, the experts suggested that a quick in-clinic method could be measuring calfcircumference (CC). Serum albumin and a routine hemogram can indicate malnutrition. Another very useful tool to check for malnutrition in-clinic is a hand grip strength dynamometer.A recent study in India performed nutritional evaluation using Malnutrition Universal Screening Tool (MUST), Short Form of Mini Nutritional Assessment (MNA-SF), and CC in 206 patients. The performance of these tools in terms of accuracy of diagnosis was compared with the ESPEN criteria for malnutrition. It was found that a total of 28.6% were malnourished as per ESPEN criteria and 25.2% had CC less than the cut-off. CC had the highest specificity and positive predictive value for the total population (91.16%, 75% respectively)27

According to the ESPEN guidelines, nutritional assessment of all cancer patients should begin at diagnosis and repeated regularly to initiateand monitor early nutritional intervention, before the general statusisseverelycompromised5Screening assesses the risk of malnutrition rather than a diagnosis of malnutrition7 However, weight loss, body mass index (BMI), and low serum protein are not reliable measures of malnutrition when assessed individually, as they do not adequately indicate the metabolic and physiological changes in patients with cancer28 Several screening tools have been validated for use in cancer patients.The Nutrition Risk Screening (NRS-2002)tool considers weight loss, BMI, dietary intake, and severity of disease29 The Malnutrition Universal Screening Tool evaluates BMI, weight loss, and disease severity to calculate the risk30A recent global consensus (Global Leadership Initiative on Malnutrition (GLIM) proposed screening based on three phenotypic criteria (non-intentional weight loss, low BMI, and reduced muscle mass) and two etiologic criteria (decreased food consumption/ assimilation and inflammation/ disease burden). It recommended that one phenotypic and one etiologic criterion can diagnose malnutrition31 Other tools recommended by Indian guidelines (IAPEN INDIA) include the use of Patient-generated Subjective Global Assessment Scale (SGA) for literate population, to evaluate the malnutrition risk in both ambulatory and acute care settings. Radiological tools or bioimpedance analysis (BIA) can be used to assess decrease in muscle mass. Systemic inflammation can be determined by measuring serum C-reactive protein (CRP) and serum albumin25IAPEN also recommends a Malnutrition Self Screening Tool that can be used by patients (Table 1)25

Table 1: IAPEN INDIA Malnutrition Self Screening Tool (IMSST).

Conditions
Is there an unintentional weight loss in the last 3 months?
Is there unintentional reduced food intake?
Is there difficulty in chewing or swallowing of food?
Do you have ascites or edema?
Do you have any chronic disease e.g. diabetes, hypertension, cardiovascular disease, Thyroid, Renal, Liver disorders, etc.?
Are you severely overweight or underweight?

Further, experts at the meeting emphasized involving a qualified and trained nutritionist from the beginning of treatment. In their opinion, 60% of patients with cancer can be discharged in a well-nourished state if a nutritionist is involved from the outset.

3.3 Is there a need for an Indian consensus on PNand SPN in patients with cancer?

The expert panel agreed that there was a need for consensus on the use of PN in patients with cancer in the Indian context, due to various reasons. In the absence of guidelines there is a lack of uniformity in the practice and use of PN. An expert consensus might havewider acceptance and lead to uniformity in practice, besides preventing the non-judicious use of PN. The consensus would also reinforce the importance of baseline screening for malnutrition and having a nutritionist at centers treating these patients. It would help in guiding centers that do not have a nutritionist/dietician.Perhaps, the consensus would encourage hospitals to display uniform information about nutrition in oncology and discourage outdated practices. It would also increase awareness and knowledge about the importance of assessing individual patient requirements rather than initiation of a standard TPN composition for all patients requiring TPN. Another benefit of a consensus could be that it might aid arguments for including PN under insurance coverage as it is currently not covered, and cost is one of the major challenges in the wider adoption of PN. Further, there is very little awareness about SPN in the country and the consensus would help in increasing its awareness.

3.4 Indications for PN for patients with cancer

According to the panel experts, nutritional support should be initiated before patients are severely malnourished. The first step should be nutrition counseling to help manage symptoms and encourage the intake of protein and energy-rich foods and fluids. The addition of ONS should be considered when an enriched diet is ineffective in achieving nutritional goals.If <60% of the daily caloric requirement is met by oral feed, EN should be encouraged; however, if <60% of the requirement is met despite EN, PN should be encouraged. In the experts' experience, if it is assessed that the patient needs nutritional support for <1 month, EN is usually adequate. However, if support is required beyond 1 month, TPN is often necessary.Patients can be managed nutritionally with a feeding gastrostomy or jejunostomy.

According to the ESPEN guidelines, enteral nutrition (EN) is recommended if oralnutrition remains inadequate despite nutritional interventions(counseling, ONS), and PN if EN is not sufficient or feasible is also recommended in cases of severe intestinal insufficiency due to radiation enteritis, chronic bowel obstruction, short bowel syndrome, peritoneal carcinosis, or chylothorax. In intestinal failure, long-term PN should be offered, if EN is inadequate, expected survival is more than 2–3 months, and the patient desires this mode of nutritional support.PN can stabilize or improve the performance status and quality of life8 Studies have shown that some patients survive many months or even years exclusively on PN32,33 Data has shown benefits of home EN or PN in cancer patients with chronic poor dietary intake or absorption even in advanced cancer if survival of more than a few weeks is anticipated. It is important to evaluate the patient's cognitive and physical abilities before starting a home PN training program 8
According to the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines, PNshould be preferred in patients who need nutrition support but have contraindications to EN or cannot meet their needs with EN alone e.g., patients with severe hemodynamic instability, prolonged ileus, vomiting or diarrhea, or persistent gastrointestinal bleeding. PN should be initiated within 3–5 days in patients nutritionally at-risk and unlikely to achieve the desired oral intake or EN. However, initiation of PNshould be delayed in a patient with severe metabolic instability until the patient's condition has improved34

3.5 Indications for PN in different cancers

Patients undergoing surgery for cancer-Experts suggested that after an assessment for malnutrition malnourished patients should be provided nutritional support even if it requires postponement of surgery. Preoperative PN is not routinely indicated. However, if <60% of the daily caloric requirement is met by oral feed, EN should be encouraged and if <60% of the requirement is met despite EN, PN should be encouraged. Perioperative PN is also recommended by the ESPEN guidelines in malnourished patients, when EN is not possible8The IAPENINDIA guidelines also recommend appropriate preoperative nutritional support for 14 days (for poorly nourished) or at least for 5 days (for at risk or malnourished patients)., even if the surgery needs to be postponed18In a recent meta-analysis of 16 studies, most of them demonstrated benefits of preoperative PN on postoperative

outcomes, including reduced complications and length of hospital stay. It was suggested that when preoperative PN is indicated, patients should receive it at least for 7 days35A recent study suggested that post-surgical PN can also significantly improve the nutritional and psychological status, QoL, and immune function of patients operated for gastric cancer36In a study by Xu et al. in patients with esophageal cancer,those in the SPNgroupwere administered EN and PNon postoperative days 4 to 8. On postoperative day 7, prealbumin levels of the SPNgroup were significantly higher than those of the total EN group. The CRP level of the SPNgroup was significantly lower while IgA, IgG, and CD4 were significantly higher in the SPNgroup than in the total EN group37

3.5.1 Patients receiving Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

TPN is often necessary for few days after HIPEC, according to the clinical experience of experts. A recent meta-analysis found that malnutrition among patients with peritoneal carcinomatosis affects their eligibility and tolerance for HIPEC,increases postoperative infection rates, complicates wound healing, and increases the hospital stay. Moreover, compared to other gastrointestinal surgical procedures, HIPEC has been associated with longer postoperative ileus and inability to eat. TPN can improvepatients' nutritional status during various phases of treatment, such as, curative resection, palliative treatment, and supportive care38Elekonawo et al. reported that due to slow gastrointestinal recovery after HIPEC, postoperative TPN was often unavoidable39 In a study among 321 patients undergoing cytoreductive surgery and HIPEC, most patients required PN for more than 7 days. Further,poor pre-operative nutritional status and inability to achieve complete cytoreduction were predictors of prolonged PN requirements40

3.5.2 Patients with upper esophageal cancers, and upper gastric cancers

According to the panel experts, most of these patients are malnourished and might require TPN even before surgery.. The ESPEN and ASPEN guidelines recommend that in patients who have undergone major upper gastrointestinal (GI)tract surgery and EN is not feasible, PN should be initiated (only if the duration of therapy is anticipated to be more than 7 days)8,34A recent meta-analysis reported that patients undergoing upper GI surgeries most likely to benefit from preoperative PN are the ones least likely to be able to tolerate EN35A Cochrane study reported a substantial decrease in postoperative problems in patients receiving preoperative PNbefore GI surgery. A combination of EN and TPN might improve intestinal integrity and stimulate incretin production than TPN alone41SPNafter esophagectomy helps meet the daily calorie requirements, since large amounts of EN are not usually tolerated in the initial postoperative days42Ten days of preoperative and 9 days of postoperative PN decreased the mortality and complication risk by almost one-third in severely malnourished patients with GI cancer43

3.5.3 Lower GI and Gynecological cancer-

-According to the experts, PN is not indicated in patients with ovarian or colorectal cancer unless metastasis to the peritoneum leads to intestinal obstruction.In their experience, patients of gynecological cancer with long lesions often require TPN. Patients with ovarian cancer often have symptoms of obstruction for a considerable period before the obstruction is detected, by when they become intolerant to oral nutrition44Hence, early screening for malnutrition is important7Studies have also shown benefits of preoperative PN in these patients. In a study among 415 patients with advanced ovarian cancer, serum albumin level and Nutritional Risk Index were independent predictors of progression-free and overall survival. Among moderately and severely malnourished patients, those who received TPN had significantly shorter hospitalization period andsignificantly higher serum albumin levels after a week45Preoperative peripheral PNsupport with fat emulsion, multiple vitamins, and trace elements in patients undergoing colorectal cancer resection led to higher postoperative serum albumin levels, lower time to first ambulation, and shorter hospital stays compared to patients who did not receive preoperative peripheral PN. The rates of sepsis were 0% vs. 25% in the respective groups46

3.5.4 Cancers of the head, face, and neck (HFN)

Patientswith squamous cell carcinoma of the HFNdevelop malnutrition due to swallowing impairment related to the tumor site or treatment sequalae, and may needSPN in addition to oral feeding when EN is not feasible47In many patients receiving the docetaxel-cisplatin-fluorouracil regimen, the experts have often experienced that serum albumin level suddenly drops drastically in a week. Hence, it is difficult to administer the full dose in the following week. In such cases, PN might be useful. Nevertheless, if monitoring and guidance of a nutritionist is available from the outset, 60% of patients

can be managed with oral nutrition. However, before oral feed or EN through a Ryle's or PEG tube is initiated, the patient's swallowing and speaking ability should be assessed as there is a risk of aspirationin the absence of these reflexes.Based on the comprehensive review by Dinko Martinovic et al., PN is contraindicated in patients with a functional GI tract, those with no intravenous access, and those who need support for less than 5 days if they are not severely malnourished48 Many patients have intermittent hypophagia which allows only partial intake of oral food and supplements. For these patients, SPN can be combined with oral food/ONS49

3.5.5 Chemoradiation/chemotherapy

According to the experts, patients with ≥ grade 3 toxicity due to chemotherapy often require admission and TPN for a short duration. In cases of GI toxicity from chemotherapy or radiation therapy, short-term PN is usually better tolerated and is more efficient than EN to restore the intestinal function and prevent nutritional deterioration8According to the ESPEN guidelines, long-term PN in patients with sub-acute and chronic radiation enteropathy is very beneficial. If patients are malnourished or likely to face starvation for >1 week and EN is not feasible, PN is recommended. A common adverse effect of anticancer treatments such as 5-fluorouracil, irinotecan, or epithelial growth factor receptor monoclonal antibodies (e.g., cetuximab and panitumumab) is GI toxicity, manifesting as nausea, vomiting, mucositis, or diarrhea, which prevents adequate oral intake7

3.5.6 Patients with hematological cancers

According to the experts, bone marrow transplant (BMT)-associated chemotherapy causes nutritional impact due to changes in the gut microbiome, graft versus host disease (GVHD), and mucositis. Malnutrition is a negative prognostic factor for BMT and leads to longer engraftment time and higher risk of infection. These patients require short-term nutritional support, usually during the transplant period. Patients undergoing autologous BMT usually do not require TPN. Most patients with acute leukemias also do not require nutritional support, and with most BMTs moving to non-myeloablative type, the need for PN is decreasing. Those undergoing allogeneic BMT might require short-term PN during the transplant period. The risk of GVHD is high during the early period after BMT. About 30-40% of patients develop acute GVHD, of which 20% have severe GVHD and require TPN. Further, 10-30% of patients develop chronic GVHD and 15% develop severe chronic GVHD, requiring TPN. PN is initiated only in cases of severe mucositis, diarrhea, or vomiting which cause intolerance to EN. Even in patients on TPN, a minimal oral intake should be encouraged according to the experts.

ESPEN guidelines recommend that in Hematopoietic stem cell transplantation (HSCT) patients,PN should be reserved for those with severe mucositis, ileus, or intractable vomiting and should be withdrawn when patients are able to tolerate approximately 50% of their requirements enterally. However, the guidelines do not recommend the time for- introduction of PN in HSCT patients8

3.6 Role and indications for supplemental PN

According to the ESPEN guidelines, SPN is recommended if inadequate food and enteral intake (<60% of estimated energy expenditure) is anticipated for more than 10 days8SPNcan be considered from the time of hospital admission in severely malnourished patients who do not receive adequate nutrition. Conversely, in well-nourished patients, it should be considered later (days 5-7).Duringthe hospital stay based on the clinical course and adequacy of nutrition delivered12Early SPNcan improve compliance to cancer treatment and aid in maintaining the dose7For severely malnourished patients, SPN should be provided before surgery to reduce post-operative complications50 In patients withradiation enteritis or chemotherapy/radiation-induced diarrhea due to neoadjuvant therapy, short-term PN was better tolerated and more effective than EN in restoring intestinal function and preventing nutritional deterioration13 A recent randomized trial showed that supplemental home PN may prevent loss of muscle mass in patients with incurable GI cancer51 Qi et al. compared the clinical benefits of early SPN (within 72 hours of diagnosis of chemotherapy-induced severe granulocytopenia) with those of late SPN (over 72 hours after the diagnosis of granulocytopenia)in 182 patients with lung cancer who received insufficient nutrition through EN. Early initiation of SPN was associated with a lower risk of infection, higher rate of completion of chemotherapy, and shorter hospital stays and leukocyte recovery periods52

3.7 Calculating nutrient requirements and composition of PN

As mentioned in the guidelines8,18, the expert panel agreed that cancer patients' nutritional requirements are largely like those of the healthy population. The daily intake should be approximately

20–25 kcal/kg/day for bedridden and 25–30 kcal/kg/day for ambulatory patients. Protein deficiency is common in the Indian settings and protein requirements for a cancer patient should be calculated as 1.2-1.5 g/kg/day.However, it is not advisable to go beyond the recommended daily limits. This is also supported by theIAPENINDIA guidelines18Recent studies suggest a higher amount of proteinshould be provided to patients with cancer to help them tolerate the treatment53 The fluid intake should be calculated as 30–35 ml/kg/day and should be increased during fever and infection 54

Carbohydrate and fat metabolism are often altered in patients with cancer. Changes include impaired glucose tolerance55, increased cortisol secretion leading to decreased insulin: cortisol ratio, increased gluconeogenesis, and increased levels of triglycerides56 However, lipid oxidation might be normal or increased57 Hence, experts suggested increasing the fat/carbohydrate ratio in patients with cancer.Replacing glucose with lipids inPN regimens might reduce the risk of infection associated with hyperglycemia8 According to ESPEN guidelines, a higher than usual proportion of lipid (e.g., 50% of non-protein energy),might be beneficial in patients with frank cachexia who require prolonged PN8 Experts also recommended complex carbohydrates (such as grains, fruits, and vegetables), over simple carbohydrates (such as juices, packaged foods, and sugar) in patients with cancer because simple carbohydrates promote inflammation. In patients with insulin resistance,some proportion of carbohydrates should be replaced by fats. This is also supported by guidelines1,5,8,18The recommended daily allowance of vitamins, minerals, and trace elements can be provided through diet or supplementation (in case of inadequate intake). However, random high doses of micronutrients are not recommended unless a specific deficiency is detected18

3.8 Monitoring patients on PN and preventing adverse effects

- Hyperglycemia is the most common complication of PN according to the expert panel. To prevent hyperglycemia,PNshould be started slowly, and glucose levels should be monitored frequently. Other measures include limiting glucose and adding insulin to PN58 Another complication of PN is lipid overload. Hypertriglyceridemia can occur if the infusion rate ofintravenous lipid emulsionexceeds the capacity of plasma fat clearance or with glucose overfeeding. Therefore, energy requirements should be monitored and adjusted accordingly. Use of omega-3 fatty-acid enriched lipids is recommended to prevent hypertriglyceridemia59
- The most dangerous complication of PN is Refeeding syndrome (RS), which can also be fatal. According to the expert panel, most of the concerns about using PN relate to RS, and it is one of the major reasons for the underuse of PN. However, it is preventable. RS manifests as electrolyte imbalances during the beginning of nutritional support. It can develop within hours to days after initiation of nutritional support in a patient who has been malnourished for a prolonged period. According to ASPEN, hypophosphatemia is often considered the hallmark of this syndrome60 Other manifestations might include water retention, heart failure, pulmonary edema, and neuromuscular paralysis61The following patients are at moderate to high risk for developingRS: BMI < 18.5 kg/m^2; recent weight loss of 5% in 1 month or 7.5–10% in 3 to 6 months; none or negligible oral intake in the last 5–6 days; caloric intake <75% of estimated daily requirement for >5 days; caloric intake <75% of estimated daily requirement for >1 month; abnormal potassium, phosphorus, or magnesium serum concentrations; loss of subcutaneous fat; loss of muscle mass; comorbidities, such as alcoholism, eating disorders, cancer, and malabsorptive states60 It is useful to screen at-risk patients before initiating nutritional support to prevent RS.Fluid balance, cardiovascular function, and serum electrolytes should be monitored. It is critical to address serum electrolyte imbalance if any, especially phosphorus and potassium, before PN is initiated. Thiamine and vitamin B group deficiencies should also be corrected. A low caloric intake (10–20 kcal/kg/day or less in extreme cases) is recommended in patients at risk of RS, with a gradual increase over 4–7 days to meet the daily requirements60,61
- Other complications include PN-associated liver disease (PNALD), which can range from mild liver enzyme elevations to steatosis, fibrosis, or cirrhosis62 The cause is lack of enteral stimulation in the absence of oral feeding, whichweakens the bile flow and gallbladder contractility leading tobile stasis and gallstone formation. It usually occurs within 2 weeks of PN initiation63,64 Preventing excess energy administration and providing an appropriate ratio of glucose and fat is important for preventing PNALD. Early reintroduction of enteral feeding and lowering parenteral caloric intake, is also recommended to reduce the risk59
- Catheter-related bloodstream infection (CRBSI) is another common complication associated with PN. Following and implementing evidence-based guidelines for line care and placement is mandatory to minimize the risk ofCRBSI65

- Close monitoring of a patient on PNis importantto prevent and detection the complications. The frequency of monitoring depends on the patient's clinical status. Renal function tests, liver tests, glucose, serum electrolytes, and triglycerides should be checked daily until stable and then at least every week (more frequently in critically ill patients or patients at risk of RS)62

3.9 Current use of PN in real-world practice and challenges in the use of PN in India

According to the expert panel, early PN in specific settings provides additional benefits, and is particularly important in some types of cancers. There are several perceived barriers in the use of PN that need to be addressed. Some of these are as below:

1. The major barrier is the cost of PN itself and additional associated costs e.g., the need for a nurse is an important barrier. However, for increasing the use of PN when indicated, it is important to train patients' families with the help of trained nurses so that they can manage the patient, which might also reduce the cost.
2. According to the experts, in India even when PN is used, the patient selection might be inappropriate.
3. The knowledge about PN among the nursing staff is inadequate as most do not receive training on PN.
4. There is a lack of onco-nutritionists in the country.
5. Another challenge is a lack of awareness among the oncologists and nutritionists about the need to understand specific patient requirements and not recommend a standard composition TPN for all patients.
6. Other challenges include outdated practices such as neutropenic diet, incorrect use of supplements, use of simple carbohydrates such as fruit juices and coconut water to patients who refuse oral food. These need to be discouraged.
7. There is also a lack of awareness about the IAPENINDIA guidelines. These need to be widely communicated and shared by the healthcare industry and experts.
8. Cost of admission and availability of beds is also a major constraint leading to earlier discharge. Thus, nutritional management is not actively supervised, which is an area of concern.
9. There is a myth that patients on PN with a central venous line are at increased risk of infections (especially patients in the ICU). However, evidence shows that appropriate adherence to recommended care bundles for the insertion and maintenance of central venous access devices and control of blood glucose has successfully reduced infection rates and can prevent infections (66).

4. CONCLUSION

India has a high burden of cancer-associated malnutrition. However, early screening and intervention for malnutrition is uncommon and awareness of guidelines is poor. Only 30%-60% of patients with cancer and at risk of malnutrition receive nutritional support. Real-world data shows that nutritional support is often prescribed as an end-of-life intervention or is not prescribed at all and the use of PN is quite delayed. Cancer-associated malnutrition is associated with high costs of cancer treatment due to increased morbidity and poor tolerance to treatment. Oncologists and nutritionists need to be educated about using the appropriate nutrition modality according to the guidelines, so that there is uniformity in practice and non-judicious use can be prevented. Early and regular screening for cancer-related malnutrition needs to be emphasized and reinforced to mitigate the underuse of nutritional support including PN. Education is also necessary for awareness about preventing and managing adverse effects of PN, which is the major reason for poor adoption of PN. Education of surgical and medical residents about PN and EN is essential in the curriculum of their training. Simultaneously, training paramedics in caring for a patient on PN is important so that they can train patients' relatives about the same, which can also bring down the cost of PN. While EN should be the preferred form of nutritional support, in specific circumstances PN might be a better option, or SPN as an additional nutritional support can improve treatment tolerability and QoL.The benefit of PN needs to be weighed against patient, disease, and treatment-related factors. It can be immensely beneficial if used judiciously. However, unnecessary and non-judicious usecan lead to a burden on the healthcare system and the patient's family.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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