Consensus on Surgical Pharmacy Practice of Parenteral and Enteral Nutrition

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Nutrition support therapy, which is referred to as nutrition support, is the process of providing appropriate nutrients via parenteral or enteral routes for patients who cannot eat normally. Parenteral and enteral nutrition (PEN) is the study of the basic theory and clinical practice of nutrition support. In 2015, Guangdong Pharmaceutical Association (GPA) coined the term "surgical pharmacy" to standardize the roles and responsibilities of surgical pharmacists, and nutrition support is one of its core components. Perioperative nutrition support can prevent and treat malnutrition, improve patients' tolerance to surgical trauma, and enable their quick recovery.

In healthcare settings, nutrition support is usually delivered by an interdisciplinary team comprised of physicians, dietitians, pharmacists, nurses and other medical service providers. Nutrition support pharmacy (NSP) is a specialty that focuses on ensuring optimal medication therapy outcomes, and is responsible for ensuring the safety and efficacy of parenteral and enteral nutrition preparations, confirming the stability and compatibility of total nutrient admixture, providing consultation on the interaction between drugs and nutrients, conducting a comprehensive evaluation of clinical nutrition preparations and assisting in the development of individualized nutrition support programs[1].

To advance the work of NSP, GPA released the *Consensus on Clinical Pharmacy of Enteral Nutrition*[2] and *Consensus on Clinical Pharmacy of Parenteral Nutrition*[3] for the first time in China in 2012 and 2015, respectively, and updated these two consensuses in 2017[4,5]. As the work of surgical pharmacy and NSP has progressed in recent years, we have summarized the standard procedures of nutrition support for surgical pharmacy practice. This consensus was finally reached through two rounds of extensive consultation, and focuses on clinical practice standards of NSP, aiming to promote the practical ability of surgical pharmacists.

1. Metabolic changes in surgical patients

Surgical patients are prone to malnutrition, especially the elderly, patients with malignant tumors, gastrointestinal diseases and neurological disorders. During the perioperative period, a series of stress reactions of the body are rapidly triggered by surgery and injury, the most important of which is the release of stress hormones and cytokines. The intensity of these responses is proportional to the amount of stress imposed. With increasing levels of stress, increasingly intense reactions result in more pronounced catabolic reactions. Central to all these reactions and subsequent metabolic states is the loss of normal synthesis of insulin, such as insulin resistance. The changes of insulin sensitivity are related to the degree of surgical trauma.

Excessive catabolism usually brings no benefits to the body, and the depletion of energy reserves and the continuous breakdown of muscle tissue in catabolism state lengthen the time required for recovery. Therefore, the key to a rapid recovery after surgery is to reduce catabolism and restore the metabolic balance of patients as soon as possible. The maintenance of an adequate energy and protein balance is key to the success of this process. Accordingly, nutrition is essential for recovery in perioperative care.

2. Definition and terminology

Nutrition support therapy provides the body with nutrients to ensure normal metabolism. Clinical nutrition supply includes oral nutrition supplement, enteral tube feeding (enteral nutrition) and parenteral nutrition. In an effort to standardize clinical nutrition diagnosis and treatment, the European Society for Parenteral and Enteral Nutrition (ESPEN) officially published the definition guidelines for clinical nutrition in 2017[6]. In 2019, the book entitled *Terminology of Parenteral and Enteral Nutrition* was published in China[7]. The most frequently used terms are listed as follows:

2.1. Oral nutritional supplement (ONS)

ONS is a nutrition support therapy that uses enteral nutrition preparation or foods for special medical purposes (FSMPs) for oral supplement when the energy and protein provided by diet are 50%-75% of the target demand.

2.2. Enteral tube feeding/enteral nutrition (EN)
EN is a nutrition support therapy that provides nutrition to patients who are unable to eat but have functioning gastrointestinal tract by indwelling catheter through nasogastric or nasointestinal pathway or through the way of creating stoma such as stomach or jejunum.

2.3. Parenteral nutrition (PN)
PN is a nutrition support therapy that provides basic nutrients for metabolism through parenteral (intravenous) administration.

2.3.1. Total parenteral nutrition (TPN)
TPN is a nutrition support therapy, in which all essential nutrients needed by patients are taken through intravenous administration, but not gastrointestinal tract.

2.3.2. Supplemental parenteral nutrition (SPN)
SPN is a nutrition support therapy that replenishes nutrients intravenously when enteral nutrition is insufficient to meet the patient's energy needs.

2.3.3. All-in-one solution/total nutrition admixture (TNA)
In a specific place (ultra-clean dispensing center), various components of a patient's PN prescription, such as glucose, amino acids, lipid emulsion, electrolytes, trace elements, water-soluble vitamins and fat-soluble vitamins, are mixed into an infusion bag by trained professionals in a clean environment that meets the requirements of relevant laws and regulations according to a certain proportion and prescribed procedures, and then the parenteral nutrition mixture is administered into the patient through the peripheral or central veins.

2.3.4. Two-in-one solution
The parenteral nutrition components except fat emulsion are transferred into an infusion bag under specific conditions to prepare a mixed intravenous solution.

2.3.5. Triple-chambered bag (TCB)
A special soft bag filled with lipid emulsion, amino acid and glucose, separated into three relatively independent chambers. When in use, squeeze the soft bag, open the middle space, and quickly and fully mix the three liquids.

2.3.6. Dual-chambered bag (DCB)
A special soft bag filled with various amino acid electrolyte solutions and glucose electrolyte solutions, separated into two relatively independent chambers. When in use, squeeze the soft bag, open the middle space, and fully mix the two liquids.

3. Surgical pharmacy practice of nutrition support
Nutritional diagnosis and treatment includes four steps, namely, nutritional risk screening, nutritional assessment and diagnosis, nutritional intervention and nutritional monitoring. As shown in Figure 1, surgical pharmacy practice of nutrition support is closely aligned with the diagnosis and treatment process, including two parts: identifying patients requiring nutrition support and pharmaceutical practice of nutrition support.

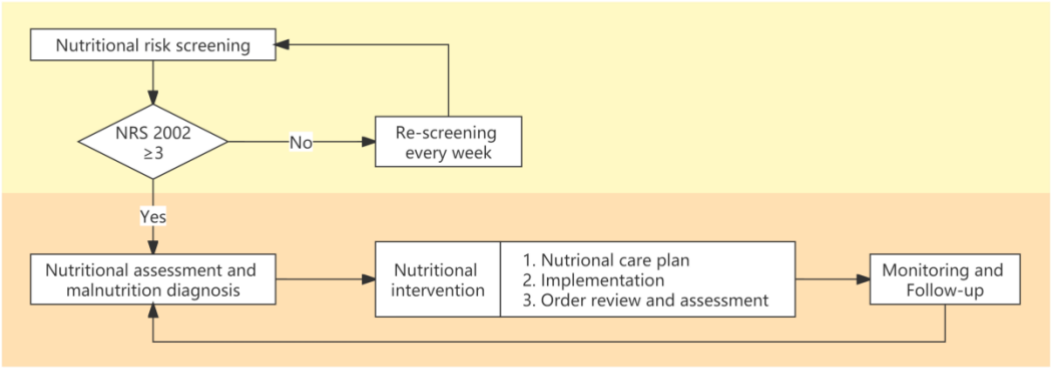

Figure 1. The process of surgical pharmacy practice of nutrition support

3.1. Nutritional risk screening

Nutrition risk refers to the adverse effects on patients' clinical outcomes due to nutrition-related factors instead of malnutrition, including infection-related complications, ideal and actual hospital days, quality-adjusted life years and survival time.. The first step of nutrition support is to identify patients' nutrition-related risks with nutrition screening tools.

In 2021, ESPEN Surgical Nutrition Guidelines[8] recommend nutritional risk screening 2002 (NRS 2002) for surgical patients because it takes into account the changes of nutritional status and the severity of diseases. NRS 2002 is evidence-based and has been validated in retrospective and prospective clinical studies in patients aged 18-90 who have been hospitalized for more than 24 hours (including oncology patients), but not recommended for minors. Currently, it is reported that NRS 2002 can be applied to patients over 90 years old, outpatients and the elderly in nursing homes, but further confirmatory research is still needed.

The NRS 2002 scale consists of three parts, namely, nutritional status score, disease severity score, and an age score. The first two parts include three grades of 1-3 points, with the highest score according to the scoring standard. The final score is the sum of the three parts, with a maximum of 7 points. If the score $\geqslant$3, a patient is considered to be at nutritional risk.

In 2018, the Chinese Society of Parenteral and Enteral Nutrition (CSPEN) released the consensus of experts on clinical application of NRS 2002[9] in an effort to further standardize its implementation. The consensus is favorable and provides a detailed analysis of how NRS 2002 can be applied, including the evaluation of reduced food intake, body mass acquisition, body mass index, albumin levels, and comparable diseases, which makes NRS 2002 easier to use.

In 2018, the American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative recommended a special perioperative nutrition screening tool (PONS) in their ERAS series of expert consensus[10]. PONS refers to the relevant indexes and variables in NRS 2002, and is easier to use. Nevertheless, the efficacy of the PONS scoring system remains to be further validated by clinical studies.

3.2. Nutritional assessment and malnutrition diagnosis

Nutritional assessment, which is referred to as malnutrition or undernutrition assessment, is a method for determining the nutritional status of inpatients who are at nutritional risk. The purpose of a nutritional assessment is to diagnose malnutrition, develop nutrition support plans, make nutritional orders and monitor progress. The assessment should be performed independently or cooperatively by NST members, and it consists of two steps: a) The part of medical history related to malnutrition assessment, which includes liver and kidney function, blood glucose, blood lipids, serum electrolytes, acid-base balance indicators, etc. These are routinely collected for inpatients and are necessary for developing a nutrition support plan, making nutritional orders and monitoring progress. b) If there remains doubt about whether the patient needs nutrition support, a malnutrition diagnosis should be performed in accordance with the Global Leadership Initiative on Malnutrition (GLIM) evaluation standard consensus[11] in September 2018. GLIM consensus does not recommend subjective global assessment (SGA) scale or patient-generated

subjective global assessment (PG-SGA) scale for the assessment or diagnosis of malnutrition.

The diagnosis of malnutrition in the GLIM consensus is generally divided into three steps, namely, nutritional risk screening, malnutrition diagnosis and determination of malnutrition severity, as shown in Figure 2[11–13].

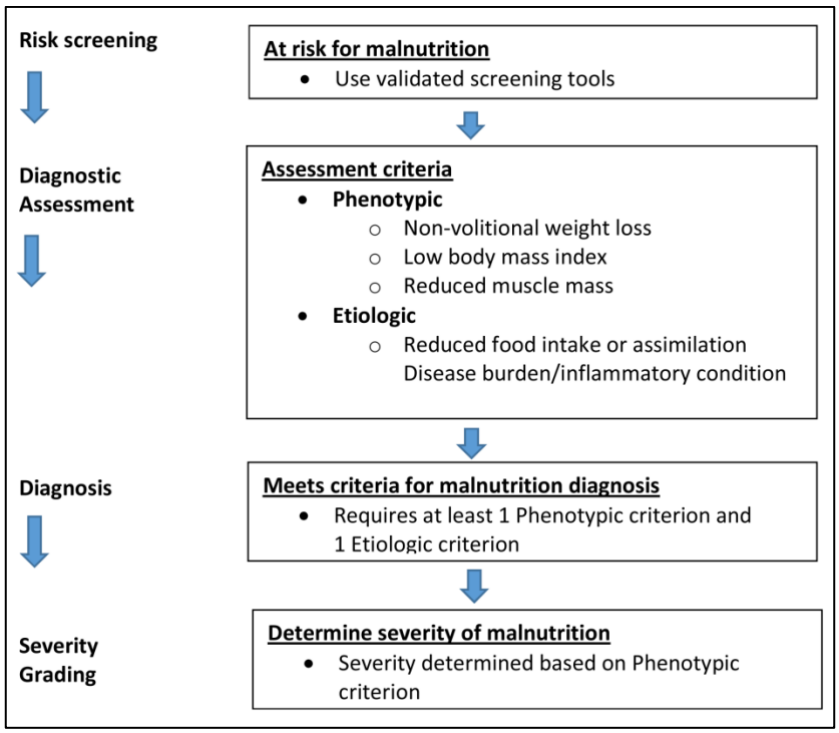

Figure 2. Malnutrition diagnosis process

The first step in malnutrition diagnosis is screening for nutritional risk using nutritional screening tools that have been prospectively validated in the country where it is administered. NRS 2002 tools are recommended for screening in China[12]. Patients who screen positive for nutritional risk are diagnosed with or without malnutrition according to the second step of GLIM. The diagnosis of malnutrition needs to meet at least one phenotypic criterion (including unintentional weight loss, a low body mass index, or decreased muscle mass) and one etiologic criterion (including decreased dietary intake or absorption, disease burden or inflammatory state). Patients who meet the GLIM criteria and are diagnosed as malnourished can be graded in severity according to the phenotypic indicators in the third step.

Despite the presence of three phenotypic criteria in GLIM criteria, due to the lack of grading data of Asian population for low body mass index, the assessment tools and cut-off values of decreased muscle mass have not been confirmed[13,14]. Only two phenotypic indicators, including involuntary weight loss and low body mass index, are currently used (see Table 1), and only involuntary weight loss is used to grade the severity of malnutrition (see Table 2).

Table 1. Phenotypic and etiologic criteria of GLIM malnutrition

	Indicators	Criteria
Phenotypic	Involuntary weight loss	> 5% within the past 6 months, or > 10% beyond 6 months.
	Low body mass index	< 18.5kg/m^2 with impaired general condition
Etiological	Reduced food intake or assimilation	≤ 50% of energy requirements for more than 1 week, or any reduction for more than 2 weeks, or any chronic gastrointestinal symptoms that adversely impacts food assimilation or absorption.
	Inflammatory	Acute disease or injury, or chronic disease-related.

Table 2. The severity grading of GLIM malnutrition

Severity grading	Performance indicators	Grading Criteria
Severe malnutrition (meet any of these)	Involuntary weight loss	>10% within the past 6 months, or >20% beyond 6 months.
	Low body mass index	< 18.5kg/m^2 with impaired general condition

The improvement, verification, and popularization of the GLIM malnutrition diagnostic criteria will contribute to the application of nutrition support therapy in the context of diagnosis related groups (DRG) and big data diagnosis-intervention packet (DIP).

3.3. Nutritional intervention

Nutritional intervention refers to the process of developing and implementing nutrition support plans for patients with malnutrition or at risk of malnutrition according to the results of nutrition screening and nutritional assessment. It includes nutrition consultation, fortified diet and artificial nutrition; the latter mainly refers to PN and EN.

Fundamental to perioperative nutritional intervention is meeting the nutritional needs for energy, protein, fluid, electrolytes, and micronutrients, and the ultimate goal is to regulate metabolic disorders, enhance immunity, control disease, improve life quality and prolong survival time. Nutritional intervention should follow the five-step treatment principle[15] (see Figure 3): The first choice is nutritional education, and then ONS, EN, SPN or TPN in turn.

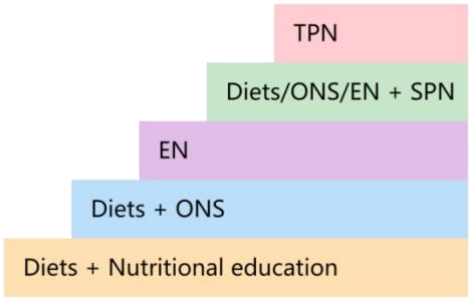

Figure 3. Five-step model of nutritional intervention

3.3.1. Forms and timing of nutritional intervention[8]

ONS or EN should be the first choice for nutrition support if the patient is expected to be unable to eat for more than 5 days or to be unable to maintain more than 50% of the recommended intake for more than 7 days. If ONS and EN cannot meet the requirements, SPN should be used in combination. When patients need nutrition support, but there are EN contraindications, such as intestinal obstruction, TPN should be administered as soon as possible.

3.3.1.1. Preoperative nutrition support

Tumor patients with malnutrition or high-risk patients (such as elderly patients with sarcopenia) undergoing major abdominal surgery should be given ONS before operation for 5-7 days continuously. If patients' preoperative normal diet can't meet their energy needs, regardless of their nutritional status, they are encouraged to be given ONS preoperatively, so as to shorten the hospital stay and reduce the incidence of

nosocomial infection. EN or PN is only suitable for patients with malnutrition or high nutritional risk before operation, and ONS cannot meet the energy needs. It recommends to use EN or PN for 7-14 days before operation.

Enhanced recovery after surgery (ERAS) has been widely developed in different professional fields, and its preoperative preparation is obviously different from traditional surgery. Shortening the time of fasting and water prohibition before operation and proper administration of carbohydrates have been proved to regulate metabolism, reduce insulin resistance, relieve anxiety of patients, and have the possibility of improving clinical outcomes. The measures mainly include fasting for 6 hours before operation, having a clear liquid diet 2 hours before operation, and having 50-100g carbohydrate drinks 2-3 hours before operation, which should be taken within 5-10 minutes to induce insulin secretion. There are still some problems in the recognition and implementation of the above measures in clinical practice, and it is the key for specialists to understand and reach a consensus on ERAS concept.

3.3.1.2. Postoperative nutrition support

Surgical injury induces a cascade of responses, including the release of stress hormones and inflammatory mediators in the early postoperative period, resulting in impaired nutrient utilization and an increase in catabolism, which generates some endogenous heat. Therefore, achieving nutritional requirements during the first three postoperative days is not emphasized for patients without preoperative malnutrition, and fluid therapy or a liquid diet can meet the patient's needs and stabilize the internal environment. 4-7 days after operation, patients should gradually return to a normal diet or a diet combined with ONS that is close to the required amount.

Early EN (within 24 hours) should be initiated in patients in whom early oral nutrition cannot be started, or oral intake will be inadequate for more than 7 days, especially tumor patients undergoing major head and neck or gastrointestinal surgery, patients with severe trauma (including brain injury) and patients with obvious malnutrition during surgery. EN should be initiated at a low flow rate (e.g., 10-20mL/h) and increased gradually the flow rate according to the patient's intestinal tolerance. The time to reach the target intake varies from person to person and may take 5-7 days.

Despite the current emphasis on ONS and EN for postoperative nutrition support, PN should not be overlooked. Clinical studies have found no difference between EN and PN in terms of postoperative outcomes, and yet PN is superior in terms of supply speed and dose accuracy. SPN or TPN is required when postoperative oral or enteral nutrition are intolerable, nutrient requirements cannot be met, or postoperative complications (i.e., impaired gastric emptying and intestinal obstruction) affect gastrointestinal function and render gastrointestinal route nutrition impossible. EN combined reasonably with PN is a good choice for clinical practice in surgery.

3.3.2. Nutritional requirements

The energy requirement is determined according to the energy expenditure (EE) measured by indirect calorimetry. If indirect calorimetry is unavailable, the energy requirement is estimated based on body weight, that is, 25–30kcal/kg per day. Patients with severe malnutrition for a long time should be given low energy at first to avoid refeeding syndrome. The estimated daily protein requirement is 1.5g/kg/d, and patients with renal insufficiency need to adjust the supply of protein according to specific diseases[16,17].

The daily fluid requirement of adults is generally 30–40mL/kg, but it can also be calculated according to age or weight[4]. Patients with cardiac and renal insufficiency need to adjust the fluid amount accordingly. Electrolyte supply is generally based on daily dietary reference intake (DRI) and adjusted according to serum electrolyte level. Micronutrients, including vitamins and trace elements, are very important and easily overlooked parts of nutritional support, and are generally given according to DRI.

3.3.3. Characteristics and selection of enteral formulas

The enteral nutrition drugs sold in China are all adult formulas, including powder, suspension and emulsion. The parameters of the preparation are shown in Figures 4 and 5 respectively. Powder is regularly used in ONS and can also be used in EN, whereas suspension and emulsion are frequently used in EN and can also be used in ONS.

Formulas		ENSURE			NUTRISON			PEPTISORB
		per can	per standard	per spoon	per can	per standard	per spoon	per bag
Standard brewing method		Add 6 spoons(55.8g) of this formulas to 200ml of warm boiled water and mix thoroughly.			Add 9 spoons(43g) of this formulas to 200ml of warm boiled water and mix thoroughly.			Add 1 bag(125g) of this formulas to 500ml of warm boiled water and mix thoroughly.
Feature		Total Protein(TP)			Total Protein(TP)			Short Peptide(SP)
Content	g	400.00	55.80	9.30	320.00	43.00	4.78	125.00
Energy	kcal	1800.00	251.10	41.85	1478.40	198.66	22.08	502.50
Density of energy	kcal/ml	1.06			1.00			1.00
Carbohydrate	g	242.80	33.87	5.65	180.48	24.25	2.70	88.75
Carbohydrate	%	54.02			48.68			70.45
Fat	g	63.60	8.87	1.48	58.24	7.83	0.87	8.38
Fat	%	31.84			35.35			14.96
Protein	g	63.60	8.87	1.48	59.20	7.96	0.88	18.38
Protein	%	14.15			15.97			14.59
Energy nitrogen ratio		152:1			132:1			146:1
Glucose lipid ratio		63:37			58:42			82.5:17.5
Fibre	g	——			——			——

Figure 4. Main parameters of EN powder sold in China

Formulas		RuiSu	NengQuan Li1.0	NengQuan Li1.5	RuiXian	RuiGao	BaiPuLi	KangQuan Gan	JEVITY	RuiDai	KangQuan Li	GLUCERNA	RuiNeng
		Enteral Nutritional Emulsion	Enteral Nutritional suspension	Enteral Nutritional suspension	Enteral Nutritional Emulsion	Enteral Nutritional Emulsion	Enteral Nutritional suspension	Enteral Nutritional suspension	Enteral Nutritional suspension	Enteral Nutritional Emulsion	Enteral Nutritional suspension	Enteral Nutritional suspension	Enteral Nutritional Emulsion
Feature		TP	TPF	TPF	TPF	TP-HE	SP	TP-MCT	TPF-FOS	TPF-D	TPF-DM	TPF-D	TPF-T
Content	ml	500	500	500	500	500	500	500	500	500	500	500	500
Energy	kcal	500	500	750	750	750	500	500	535	450	375	505	650
Density of energy	kcal/ml	1	1	1.5	1.5	1.5	1	1	1.07	0.9	0.75	1.01	1.3
Carbohydrate	g	69	61.5	92.5	94	85	88	63	70.25	60	42	40.7	52
Carbohydrate	%	54.65	49.10	49.15	50.20	45.27	69.22	50.17	54.34	53.10	44.68	33.14	32.05
Fat	g	17	19.45	29.2	29	29	8.5	16.7	17.35	16	16	27.2	36
MCT	g	6	0	0	0	16.5	0	10.1	0	0	0	0	0
Fat	%	30.30	34.94	34.91	34.85	34.75	15.04	29.92	30.19	31.86	38.30	49.84	49.92
Protein	g	19	20	30	28	37.5	20	25	20	17	16	20.9	29.25
Protein	%	15.05	15.97	15.94	14.95	19.97	15.73	19.91	15.47	15.04	17.02	17.02	18.03
Energy nitrogen ratio		158	123	145	148	134	405	147	113	141	93	41	62
Glucose lipid ratio		64.3:35.7	58.4:41.6	58.5:41.5	59:41	56.6:43.4	82:18	63:37	64:36	62.5:37.5	54:46	40:60	39:61
Fibre	g	0	7.5	7.5	10	0	0	0	8.8	7.5	7.5	7.2	6.5
Osmotic pressure	mOsm/L	250	250	300	320	300	NA	NA	NA	320	225	NA	350

Figure 5. Main parameters of EN suspensions and emulsions sold in China

In clinical practice, EN drugs are generally classified as follows:

- Total Protein (TP)
- Total Protein and Fibre (TPF)
- Total Protein-High Energy (TP-HE)
- Short Peptide (SP)
- Total Protein-Middle Chain Triglyceride (TP-MCT)
- Total Protein and Fibre-Diabetes (TPF-D)
- Total Protein and Fibre-Tumor (TPF-T)
- Total Protein and Fibre-Fructooligosaccharide (TPF-FOS)

The composition of a standard formula is based on the maintenance diet for a healthy subject. Consequently, standard formulas are sufficient for the majority of patients, but situations of metabolic changes must be taken into account, and a specific formula may be needed[18].

The standard energy formulas (TP or TPF) are complete nutritionally. 15-20% of energy is derived from whole protein; approximately 30% of energy is from lipid (primarily long-chain triglycerides, LCT); 50–55% of energy is from carbohydrates (primarily of low glycemic index); 10–20mg/mL fibre or fibre-free; a full complement of vitamins and trace elements; approximately 85% water; nearly 1kcal/mL of energy density, and 200~350mOsm/kg of osmolality.

High-energy formulas (TP-HE and some TPF) are derived from the standard formulas with a reduction in water (70–75%), giving the formulation an energy density of 1.2–1.5kcal/mL. These formulations are recommended for patients with fluid restriction, such as those with heart or kidney diseases, and are occasionally administered to those with electrolyte disorders. However, high-energy formulas have a higher osmolality than standard ones, which can increase the risk of osmotic diarrhea.

Pre-digested peptide-based formulas, also known as short peptide (SP) formulas, predominantly contain

nitrogen in peptide form (chains of 2-50 amino acids). At least a portion of lipids are provided as medium-chain triglycerides (MCTs). Likewise, the carbohydrate content will have less expansive polymerization. There will be no fiber. Since, they are easier to absorb than other formulas. Few patients need a SP formula. The indications for SP are when whole protein formulas are not tolerated but EN is still indicated; when capacity for absorption is severely impaired; in the initial phase after prolonged starvation; when administration is to the jejunum (in critical care and in severe acute pancreatitis); in selected patients with short bowel syndrome; in selected patients with enterocutaneous fistulae. In addition, because short peptides are better absorbed and have a lower osmolality than free amino acids, formulas based on free amino acids are rarely used in adults.

The MCT-rich formulas (TP-MCT) contain a proportion of lipids as MCTs. MCT absorption does not require bile salts or pancreatic lipase, and they bypass the lymphatic system with direct uptake into the portal circulation. Consequently, TP-MCT is indicated for patients with lipid metabolic disorders.

There are two broad categories of diabetes formulas available. First, the traditional diabetes formulas closely resemble standard formulas. There may be a small amount of fructose and a higher proportion of polysaccharides in traditional diabetes formulas, but the differences are negligible. Subsequently, a newer generation of diabetes formulas has been developed, with polymeric formulas modified to contain up to 35% of their energy in the form of monounsaturated fatty acids (MUFA), a higher total amount of fat, and fewer carbohydrates. A systematic review[19] demonstrates that diabetic patients taking the high MUFA formula had lower HbA1c levels.

Higher energy, more lipids, and fewer carbohydrates are the main differences between the TPF-T and the standard formula. Other than that, TPF-T typically refers to immune-modulating formulas. According to the product label, it contains omega-3 fatty acids, vitamin A, vitamin C, and vitamin E. However, the actual amount of these nutrients is not indicated.

Fructose oligosaccharides are considered a source of prebiotics, which can regulate the intestines and improve tolerance. Formulas containing prebiotics contain a portion of carbohydrates and fiber as fructose oligosaccharides (TPF-FOS).

3.3.4. Characteristics and selection of parenteral solutions

Parenteral solutions, which are typically administered intravenously and are intended to provide energy and nutrients rather than hydration alone, contain glucose, lipid emulsions, amino acids, water, electrolytes, trace elements, and vitamins as required. These solutions may be administered using separate bottles, but compounding or ready-to-mix bags are preferred. All-in-one solutions and two-in-one solutions are typically provided by pharmacies, whereas ready-to-mix bags, such as TCB and DCB, are typically manufactured by industry. In any case, parenteral solutions must be mixed in accordance with Standard Operating Procedure (SOP) [20]. Almost all commercially available parenteral preparations in China are included in Table 3.

Table 3. Commercially available parenteral preparations in China

Ingredients	Preparations
Glucose	Glucose injection(10%, 50%).
Lipid	Soybean oil long chain fat emulsion injection(SO), Medium and long chain fat emulsion injection(MCT/LCT), Structural fat emulsion injection(STG), Olive oil long chain fat emulsion injection(OO), Fish oil long chain fat emulsion injection(FO), Multi-oil fat emulsion injection(SMOF).
Amino acids	Compound amino acid injection(3AA, 6AA, 9AA, 15AA, 18AA, 20AA, etc.), Paediatric compound amino acid injection, Alanyl glutamine injection.
Water	Sterile water for injection, Sodium chloride injection(0.9%), Glucose injection(5%), Glucose sodium chloride injection, etc.

Electrolytes	Concentrated sodium chloride injection, Potassium chloride injection, Calcium gluconate injection, Calcium chloride injection, Magnesium sulphate injection, Potassium aspartate and magnesium aspartate injection, Sodium glycerophosphate injection, Composite potassium hydrogen phosphate injection.
Trace elements	Multi-trace elements injection.
Vitamins	Water-soluble vitamins for injection, Fat-soluble vitamins for injection, Multivitamins for injection, Multivitamins for injection(12).
Pre-mixed	Fat emulsion, amino acid and glucose injection.

The only carbohydrate in the PN is glucose, the primary source of energy for human body. All cells can use glucose, and some are glucose-dependent, including those lacking mitochondria, such as red blood cells; cells in a hypoxic state, such as bone marrow, and rapidly proliferating cells. In addition, the brain also preferentially oxidizes glucose for energy supply due to the low permeability of the blood-brain barrier to fatty acids. However, the oxidation of glucose is limited and is related to the body's energy expenditure. The maximum rate of glucose oxidation in adults is 4-5mg/kg/min. Commercial glucose solutions contain glucose in water for injection at different concentrations; different concentrations of glucose injections should be selected based on the patient's fluid requirements.

Fat is the body's important energy substrate and the main energy reserve. Intravenous fat emulsion is a two-phase system with lecithin as emulsifier to disperse tiny oil droplets uniformly in the aqueous phase, and its average particle size should be 0.5μm or less. Unstable systems can cause an increase in the particle size of the fat emulsion, which can lead to irreversible "coalescence" or "oiling out" and other lethal adverse reactions. The stabilities are different in the various types of fat emulsions[21]. The fat emulsion currently used in clinical practice and its characteristics are shown in Table 4. The origins, compositions, and physiological properties of various fat emulsions should be considered prior to selection.

Generally, FO should be used in conjunction with other fat emulsions due to its lack of essential fatty acids. However, some researches have shown that FO can be used alone in certain circumstances, such as when a patient has an allergy to soy oil or when a neonate or child has parenteral nutrition-associated cholestasis (PNAC)[22,23].

Table 4. Characteristics of fat emulsion

Fat emulsion	Composition	Physiological characteristics
SO	C14~24, composed of 100% soybean oil with a small amount of glycerin and lecithin.	It offers a plentiful source of essential fatty acids, which are crucial for a variety of biofilms and bioactive compounds to function properly. Metabolites promote inflammatory responses.
MCT/LCT	C6~24 or C8~24, composed of 50% MCT and 50% SO with a small amount of glycerol and lecithin, some preparations contain the antioxidant α-tocopherol.	MCT has a small molecular weight, rapid and complete hydrolysis, short half-life, no storage in adipose tissue when given parenterally, and less hepatic fat infiltration, particularly for those who cannot utilize LCT due to a lack of or reduced activity of the carnosine transporter enzyme; additionally, MCT has a greater ketogenic effect than LCT.
STG	C6 to 24, composed of 75% mixed chain triglycerides and small amounts of LCT and MCT, with small amounts of glycerol and lecithin.	Theoretically, the hydrolysis and esterification of fatty acids to randomly bind various MCTs and LCTs on the three carbon chains of the same glycerol molecule is more consistent with the physiological metabolism of the body.
OO	C14~24, composed of 80% olive oil and 20% soybean oil with a small amount of glycerin and lecithin.	Rich in MUFA. Metabolites are immuno-neutral.
FO	C12~24, composed of 100% fish oil with a small amount of glycerin, lecithin and the antioxidant α-tocopherol.	Rich in omega-3 fatty acids. Metabolites inhibit inflammatory responses.
SMOF	Composed of 30% soybean oil, 30% medium chain triglycerides,	A physical mixture of SO, MCT, OO, and FO in certain proportions ensures a supply of essential fatty acids and also

25% olive oil and 15% fish oil with a small amount of glycerin and lecithin.	acts as an immune regulator.

Amino acids are crystalline units of proteins after they are hydrolyzed. Human proteins are composed of 20 amino acids, eight of which are essential amino acids (EAA) for adults. Commercial compound amino acid injections contain a mixture of various concentrations and profiles of crystalline amino acids. The compound amino acid injection 18AA is the most commonly used because of its balanced profile. Other specific amino acid solutions have been developed for neonates or children, as well as for patients with liver or renal diseases. When selecting compound amino acid injections, their components and concentrations should be considered. Lastly, it should be noted that the compound amino acid injection 9AA contains only EAA and is not recommended for patients with chronic kidney disease who have received renal replacement therapy.

Glutamine, a non-essential amino acid, is one of the 20 amino acids that make up human protein. In the presence of infection, inflammation, metabolic stress, or malnutrition, glutamine becomes conditionally essential. Due to its instability and low solubility, glutamine is added separately as a dipeptide, such as alanyl glutamine, for intravenous administration. Remarkably, alanyl glutamine injection is contraindicated for patients with severe hepatic or renal dysfunction who do not receive replacement therapy. In addition, it is contraindicated in unstable and complex ICU patients[24], as well as in neonates and children younger than 2 years of age[25].

Water and electrolytes are the primary components of body fluids. Fluid equilibrium provides the interior milieu necessary for normal cellular metabolism and is essential for maintaining the life of the body and the physiological functions of the organs. According to the distribution characteristics and physiological functions of different electrolytes in the body, fluid and electrolyte disorders must be considered from three perspectives: intakes, losses, and redistributions. When selecting electrolyte preparations, attention should be paid to the conversion of units and doses of the various electrolyte preparations, and the supply should be adjusted according to the laboratory tests.

Micronutrients and vitamins are essential micronutrients that support the body's efficient utilization of energy substrates and amino acids. They are required in relatively small amounts but cannot be synthesized or are insufficiently synthesized within the body, necessitating external supplementation. Microelements are inorganic micronutrients, six of which (chromium, copper, iron, manganese, selenium, and zinc) are necessary for maintaining the body's physiological functions[26]. Vitamins are organic micronutrients and can be divided into two categories: fat-soluble (vitamins A, D, E, and K) and water-soluble (vitamins B family and C). Commercial micronutrient preparations usually conform to the DRI. Notably, multivitamins for injection (12) are devoid of vitamin K, and it is crucial to be aware of vitamin K deficiency with long-term use[27].

3.3.5. Review and evaluation of nutrition prescription

Order review is the quality control before prescription dispensing, and order evaluation is the analysis and improvement after prescription dispensing. Review and evaluation of nutritional orders should follow the *Regulations for Order Review in Medical Institutions*[28] and *Management Standards for Order Evaluation in Medical Institutions*[29] in combination with the characteristics of the EN and PN formulas (as mentioned in 3.3.3 and 3.3.4). The review and evaluation of EN orders should include the indications and contraindications of drug use, whether nutritional risk screening has been performed, the appropriateness of drug selection, dosages, and administration routes, and drug-nutrition interactions. The review and evaluation of PN orders should include the indications and contraindications of drug use, the appropriateness of drug selection, dosages, and administration routes, especially for fish oil fat emulsion injection, alanyl glutamine injection, and multivitamins for injection (12), drug-nutrition interactions, and the stability and compatibility of the PN admixtures. Guidance for the order review of TNA can be found in Table 5.

Table 5. Guidance for orders review of parenteral nutrition admixture[30]

	Review Index	Limitation	Review Level	Rationale	Treatment measures
1	Monovalent cation	≤150mmol/L	**Compulsory**	The stability of the fat emulsions in TNA cannot be guaranteed.	Reducing the supply of sodium or potassium is advised, and the calculator should be used to determine the cut-off values to guide physicians.
2	Divalent cation	≤10mmol/L	**Compulsory**	The stability of the fat emulsions in TNA cannot be guaranteed.	Reducing the supply of calcium or magnesium is advised, and the calculator should be used to determine the cut-off values to guide physicians.
3	Amino acids	>0g	**Compulsory**	The stability of the fat emulsions in TNA cannot be guaranteed.	The addition of amino acid injections or fat emulsions alone is recommended.
4	Vitamin C	Without calcium	**Compulsory**	In a nutrient bag, vitamin C can degrade into oxalic acid, which binds calcium ions in TNA to produce calcium oxalate precipitate.	It is suggested that vitamin C be administered via alternative routes.
5	Potassium ion concentration	≤3g/L	**Compulsory,conditional**	The main adverse effects of intravenous potassium infusion are phlebitis, cardiac arrhythmias, and hyperkalaemia. Potassium should not exceed 40 mmol(3g) per litre(L) of infusion when administered via a peripheral vein. Potassium can be administered through a central vein, which permits complete dilution of potassium through the blood, thereby reducing the risk of extravasation and avoiding pain and phlebitis associated with peripheral infusions, with a maximum concentration of 400 mmol/L (30 g/L) and continuous cardiac monitoring.	It is recommended to reduce the supply of potassium and the calculator should be used to determine the cut-off values to guide physicians.
6	Glutamine	Without other amino acids or with 9AA alone	**Forced**	Glutamine is a conditionally essential amino acid. There are no instances in which the body requires only glutamine and no other amino acids. Therefore, glutamine must be combined with a compounded amino acid. The exception is the compounded amino acid(9AA), which is a formulation containing only essential amino acids and is administered to patients with chronic kidney disease who require a low-protein diet. Glutamate is not suitable for such conditions.	It is recommended that glutamine be combined with a compounded amino acid but not a compounded amino acid(9AA).
7	The percentage of glutamine in amino acids	≤30%	**Reminder**	It is stated in the European product label.	The proportion of glutamine to total amino acids should not exceed 30%, and the calculator should be used to determine the cut-off values to guide physicians.
8	Fish oil	Without other fat emulsion	**Compulsory,conditional**	Fish oil fat emulsion is low in essential fatty acids. Use it alone only in patients with a clear allergy to soybean oil fat emulsion.	First, determine whether the patient is allergic to soybean oil fat emulsion. If so, instruct the physician to document the reason in the patient's medical records (for review). If not, do not recommend single-use (since it lacks sufficient essential fatty acids).
9	The percentage of fish oil in fat emulsions	≤20%	**Reminder**	It is stated in the Chinese product label.	The proportion of fish oil to total fat emulsions should not exceed 20%, and the calculator should be used to determine the cut-off values to guide physicians.
10	Calorie ratio of fat to non-protein	≤60%	**Reminder**	The probability of developing fat clearance disorders is high.	It is recommended to adjust the glycose lipid ratio, and the calculator should be used to determine the cut-off values to guide physicians. If necessary, it is recommended to monitor blood triglycerides.
11	Multivitamins(12)	Without vitamin K	**Reminder**	It is devoid of vitamin K. Consider the risk of vitamin K deficiency with long-term use.	Additional vitamin K supplementation or switching to a multivitamin preparation containing vitamin K is recommended.

3.4. Monitoring

Perioperative nutritional monitoring includes the monitoring of the effects and complications of nutrition support. The effect monitoring includes all nutrition-related complaints, symptoms, signs, anthropometric indicators, laboratory test indicators and disease conditions in patients. The complications monitored include gastrointestinal complications, mainly in EN; metabolic complications, mainly in PN; infectious complications; and mechanical complications associated with the delivery route. Refer to Table 6 for details.

Table 6. Basic indicators and frequency of nutrition monitoring

	Indicators	Unstable	Stable
Complaints, symptoms and signs	Clinical condition	2-3 times/day	1 time/day
	Catheter position	1 time/day	1 time/day
	Gastrointestinal motility	1 time/2-4 hours	1 time/8 hours
	Intake and output volume	1 time/day	1 time/week
Anthropometrics	Body weight	1 time/week	1 time/week
	Calf circumference	1 time/week	1 time/week
	Handgrip strength	If necessary	If necessary
	6-metre walk	If necessary	If necessary
	Body composition analysis	If necessary	If necessary
Laboratory tests (blood)	Routine	2 times/week	1 time/week
	Liver function	1-2 times/week	1 time/week
	Kidney function	1-2 times/week	1 time/week
	Albumin	1 time/week	1 time/week
	Pre-albumin	1 time/week	1 time/week
	Glucose	1-2 times/day	1-2 times/week
	Triglyceride	1-2 times/week	1 time/week
	Sodium, potassium, chloride	1-2 times/day	1-2 times/week
	Calcium, magnesium, phosphorus	2-3 times/week	1 time/week
	C-reactive protein	If necessary	If necessary
	Calcitoninogen	If necessary	If necessary
Laboratory tests (urine)	Routine	If necessary	If necessary
Laboratory tests (faeces)	Routine	If necessary	If necessary
Laboratory tests (drainage fluid)	Electrolytes and nitrogen	If necessary	If necessary

3.5. Documentation

Documentation is an integral part of clinical pharmacy practice. In the surgical pharmacy practice of nutrition support, identifying patients in need of nutrition support and providing such support to patients with diagnosed malnutrition should be documented separately.

Patients should first undergo a thorough nutritional evaluation (a worksheet can be referred to Figure 6). Nutritional evaluation consists of a nutritional risk screening (NRS 2002) and a diagnosis of malnutrition. Patients with an NRS 2002 score <3 are not at nutritional risk, but those with a score ≥3 may be diagnosed with malnutrition and graded according to the GLIM diagnostic criteria.

Malnourished patients at nutritional risk should receive nutritional care (see Figure 7 for the worksheet). According to the diagnosis of malnutrition, the monitoring frequency can be

determined, and graded nutritional care can be carried out. The content of nutritional care includes the patient's general state, disease features, various testing indicators, the target requirements of nutrition support and specific nutritional prescriptions. According to the nutritional status of patients, review the nutritional plan, put forward pharmaceutical professional opinions, and carry out pharmaceutical intervention and patient education when necessary.. After each nutritional care, the follow-up date should be indicated, and the next monitoring should be carried out as planned.

Nutritional Assessment

1. Nutritional risk screening: ☐No risk (<3) ☐At risk (≥3)

NRS2002	Score 1 (anyone below)	Score 2 (anyone below)	Score 3 (anyone below)
Severity of disease	☐Chronic patients, in particular with acute complications: ☐cirrhosis, ☐COPD. ☐Hip fracture ☐Diabetes ☐Chronic hemodialysis ☐Oncology ☐Comparable disease:	☐Major abdominal surgery ☐Stroke ☐Severe pneumonia ☐Hematologic malignancy ☐Comparable disease:	☐Head injury ☐Bone marrow transplantation ☐Intensive care patients (APACHE II > 10) ☐ Comparable disease:
Impaired nutritional status	☐Weight loss >5% in 3 months.	☐Weight loss >5% in 2 months.	☐Weight loss >5% in 1 months. ☐Weight loss >15% in 3 months. ☐BMI<18.5kg/m^2 and impaired general condition
	☐Food intake 50-75% of normal requirement in preceding week.	☐Food intake 25-50% of normal requirement in preceding week.	☐Food intake 0-25% of normal requirement in preceding week.
Age	☐≥70 years		
Total score (Severity of disease + Impaired nutritional status + Age) :			

2. GLIM diagnosis of malnutrition: ☐No malnutrition ☐Malnutrition ☐Severe malnutrition

☐Phenotypic criteria	☐Involuntary weight loss	Malnutrition	Severe malnutrition
		☐> 5% within the past 6 months, ☐> 10% beyond 6 months.	☐> 10% within the past 6 months, ☐> 20% beyond 6 months.
	☐Body mass index < 18.5 kg/m^2 with impaired general condition		
☐Etiologic criteria	☐Reduced food intake or assimilation	☐≤ 50% of energy requirements for more than 1 week, ☐any reduction of energy requirements for more than 2 weeks, ☐any chronic gastrointestinal symptoms that adversely impacts food assimilation or absorption. Such as: ☐dysphagia ☐nausea or vomit ☐diarrhea ☐constipation ☐abdominal pain ☐others ☐Related disease. Such as: ☐short bowel syndrome ☐pancreatic insufficiency ☐bariatric surgery ☐esophageal strictures ☐gastroparesis ☐bowel obstruction ☐steatorrhea ☐stomas with high flow ☐others	
	☐Inflammatory	☐Acute disease or injury. Such as: ☐severe infection ☐burns ☐trauma ☐closed brain injury ☐Chronic disease-relate. Such as: ☐Malignant tumor, location: _____ ☐COPD ☐heart failure ☐CKD ☐chronic liver disease ☐rheumatoid arthritis ☐Significant elevated inflammatory marker	

Figure 6. Worksheet for nutritional assessment

Nutritional Care

Date: _____ In plan: ☐Yes, ☐No

1. Weight____cm, Height____kg, BMI_____kg/m^2.
2. NRS 2002 score____, GLIM diagnosis: ☐malnutrition ☐severe malnutrition.
3. Relevant diseases: _____。
4. Laboratory indices: _____。
5. Nutrition goals: Energy_____kcal/kg/d, Protein_____g/kg/d。
6. Current nutritional Supplies: _____。

Nutritional care forms and orders	Nutritional Supplies
☐Diets:	
☐ONS:	
☐EN(tube feeding):	
☐PN:	

7. Intravenous transfusion of other nutritional drugs: ☐No, ☐Yes: _____。
8. Intravenous transfusion of human albumin: ☐No, ☐Yes: _____。
9. Oral or tube feeding of other nutritional drugs or dietary supplements: ☐No, ☐Yes: _____。
10. Complications related to parenteral or enteral nutrition: ☐No, ☐Yes: _____。
11. Other considerations: ☐No, ☐Yes: _____。
12. Interventions from pharmacists: ☐No, ☐Yes: _____。
13. Feedbacks from physicians: ☐Accepted, ☐Partial accepted, ☐Not accepted, details: _____。
14. Patient education: ☐No, ☐Yes, details: _____。
15. Next scheduled nutritional care date: _____。

Figure 7. Worksheet for nutritional care

3.6. Follow-up

Clinical pharmacists should follow up patients with nutritional risks and diagnosed malnutrition through pharmacy clinics. Follow-up visits should focus on nutritional care and patient education (see Figure 7 for the worksheet).

Home enteral nutrition (HEN)[31] and home parenteral nutrition (HPN)[32] have become increasingly important with advances in nutrition support concepts and technology. However, there is currently no standardized model of home nutrition practice in China. Most patients who need home nutrition involve multiple drug uses. Clinical pharmacists can look into surgical pharmacy practice models for home nutrition in the future.

4. Conclusion

This consensus focuses on the overall practice of nutrition support in surgical pharmacy. It must be emphasized that many implementation details still need to be further refined. New clinical research and practical experience in the future will help to improve and update this consensus.

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