General Surgery RPAC

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PERIOPERATIVE NUTRITIONAL SUPPORT (PNS)

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SYNOPSIS OF PRESENTATION

1) Introduction
   - Studley's 1936 paper
   - Prevalence of hospital malnutrition
   - Indices of malnutrition

2) The Potential Need for Perioperative Nutritional Support
   - Metabolic and nutritional effects of surgery
   - Algorithm for decisions about perioperative nutritional support
   - Patient classification for perioperative nutritional support
   - Considerations in enteral nutritional support
   - Considerations in total parenteral nutritional support

3) Specific Nutritional Requirements in PNS
   - Total energy requirements
   - Carbohydrate/fat/protein balance
   - Essential amino acids and omega fatty acids
   - Glutamine
   - Arginine
   - Branched chain and aromatic amino acids
   - Electrolytes and micronutrients

4) Surgical States Possibly Requiring Nutritional Support
   - GI and related (liver, pancreas, etc.) surgical procedures
   - Otolaryngological surgical procedures
   - Urological surgical procedures
   - Fistula
   - Laparotomy
   - Orthopedic surgery and amputation
   - Transplantation

5) Recent Studies and Surveys of PNS
   - Enteral: Braga et al. (2002)
   - Parenteral: VA study (1991)
     Heyland et al. (2001)

6) Conclusions and Summary

PERIOPERATIVE NUTRITIONAL SUPPORT (PNS)

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FREQUENCY OF MALNUTRITION RELATED TO DISEASE SITE

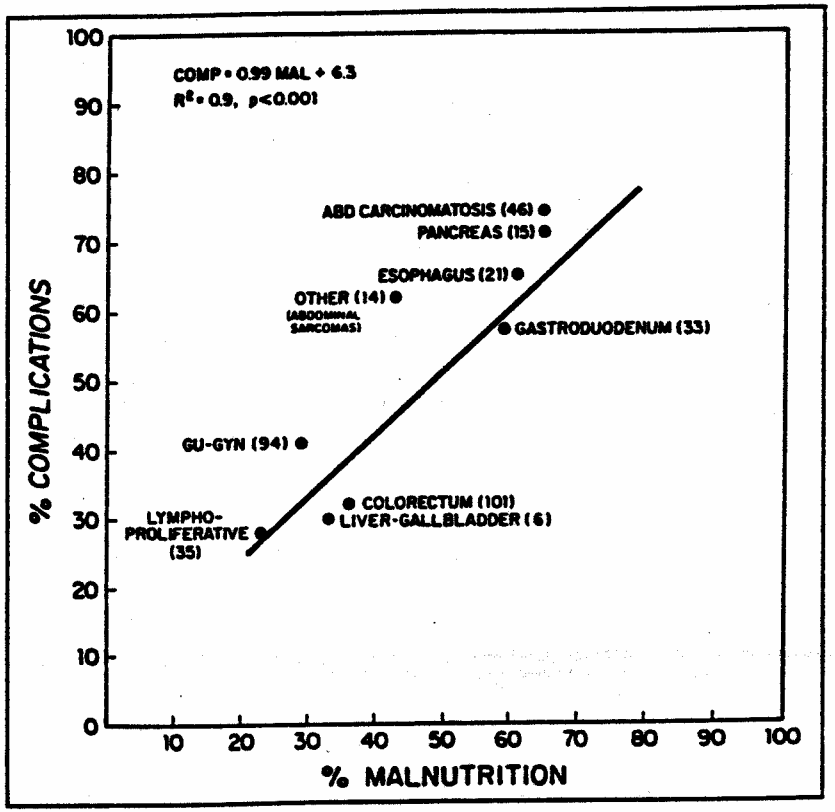


Figure 1. Frequency of malnutrition as related to disease site. Note the linear correlation between the incidence of malnutrition and complications that occurred in different disease sites. Numbers in parentheses refer to number of patients. Reproduced with permission from Meguid MM, Meguid V. Preoperative identification of the surgical cancer patient in need of postoperative supportive total parenteral nutrition. Cancer 1985; 55: 258–62.

SERUM PROTEINS USED IN NUTRITIONAL ASSESSMENT

Serum protein	Approximate molecular mass, Da	Biosynthetic site	Normal value $\bar{X} \pm$ SD or (range)*	Half-life, days	Function
Albumin	66,000	Hepatocyte	45 (35–50)	14–20	Maintain plasma oncotic pressure; carrier for small molecules
Transferrin	77,000	Hepatocyte	2.3 (2.0–3.2)	8–9	Binds Fe^{2+} in plasma and transports to bone
Transthyretin (Prealbumin)	61,000	Hepatocyte	0.30 (0.2–0.5)	2–3	Binds T_3 and to a lesser extent T_4. Carrier for retinol-binding protein
Retinol-binding protein (RBP)	21,000	Hepatocyte	0.0372 ± 0.0073‡	0.5	Transports vitamin A in plasma; binds noncovalently to prealbumin

* Units are g/L. Normal range varies between centers; check local values.
† All of the listed proteins are influenced by hydration and the presence of hepatocellular dysfunction.
‡ Normal values are age- and sex-dependent. Table value is for pooled subjects.
SOURCE: Heymsfield and Williams.

EFFECTS OF HYPOPROTEINEMIA

- **Delayed gastric emptying**
- **Prolonged ileus**
- **Elevated wound dehiscence**
- **Delayed bone callus formation**
- **Increased risk of infection**

ASSESSMENT OF PROTEIN-ENERGY MALNUTRITION

Method of assessment	Moderate PEM	Severe PEM
Weight loss, %	15–25	>25
Fat depletion*	<16 ± 6	<12 ± 5
Albumin, g/L	25–30	<25
Transferrin, g/L	1–2.0	<1
Total lymphocyte count, 10^6/L	0.8–1.2	<0.8
Delayed hypersensitivity index†	1	0

* Fat depletion assessed from triceps skin fold in millimeters.

† Delayed hypersensitivity index quantitates the centimeters of induration with common antigens such as *Candida*, trichophytin, or mumps: 0 = <0.5, 1 = 0.5, 2 = 1.0.

EVALUATION OF WEIGHT CHANGE

Time	Significant Weight Loss	Severe Weight Loss
1 week	1–2%	>2%
1 month	5%	>5%
3 months	7.5%	>7.5%
6 months	10%	>10%

Values charted are for percent weight change: Percent Weight Change = (Usual weight − Actual weight)/(Usual weight) × 100.

PROGNOSTIC INDICES FOR HOSPITALIZED PATIENTS

Index	Incorporated parameters	Correlates with	Reference
Likelihood of malnutrition	Serum folate, serum vitamin C, serum albumin, lymphocyte count, hematocrit, triceps skinfold, arm muscle circumference, weight	Duration of hospitalization	Am J Clin Nutr 32:418, 1979
Prognostic nutritional index	Serum albumin, serum transferrin, delayed hypersensitivity, triceps skinfold	Incidence of postoperative complications and mortality	Cancer 47:2375, 1981
Instant nutritional index	Serum albumin, lymphocyte count	Incidence of postoperative infection	J Parent Ent Nutr 12:195, 1988
Hospital prognostic index	Serum albumin, delayed hypersensitivity, presence of sepsis or cancer	Hospital mortality	Am J Clin Nutr 34:2013, 1981

PROGNOSTIC NUTRITIONAL INDEX (PNI)

PNI = 158% - 16.6(Alb) - 0.78(TSF) – 0.2(TFN) – 5.8(DH)

Where: Alb = albumin (g/dL)
TSF = triceps skinfold thickness (mm)
TFN = transferrin (mg/dL
DH = delayed cutaneous hypersensitivity:
<5 mm induration = 2;
1-5 mm induration = 1;
anergy = 0

PNI designations:

>50% : High risk
40-49%: Intermediate risk
<40%: Low risk

ENERGY EXPENDITURE IN ILLNESS

Daily energy data for a 70 kg 46-year old male with rheumatoid arthritis of mild severity causing limited physical activity.

Resting energy expenditure	**1800 kcal**
Activity-related expenditure	**400 kcal**
Illness-related expenditure	**180 kcal**
Diet-induced thermogenesis	**238 kcal**
Total	**2618 kcal**

NUTRITIONAL NEEDS FOR WOUND HEALING

Substance	Role in wound healing	Supplementation
Amino acids	Protein building blocks	Standard enteral or parenteral nutrition 40 kcal maximum including 2 gm/kg protein maximum
Lipids	Membrane assembly; assists immune responses	Same as above
Carbohydrates	Prevents gluconeogenesis from protein stores	Same as above
Vitamin A	Assists epithelialization; membrane labilizer	10-25,000 IU/day acutely
Vitamin C	Necessary for collagen maturation and wound strength	500 mg 2-3 times/day
Trace elements (iron, copper, zinc, magnesium)	Role controversial; may contribute to overall healing	Zinc sulfite 220 mg 3 times/day

PROTEIN NEED IN DISEASE STATES

Clinical condition	Protein requirements (g/kg IBW/day)
Healthy, nonstressed	0.8
Bone marrow transplant	1.4–1.5
Liver disease without encephalopathy	1.0–1.5
Liver disease with encephalopathy	0.5–0.75 (advance as tolerated)
Renal failure without dialysis	0.6–1.0
Renal failure with dialysis	1.0–1.3
Pregnancy	1.3–1.5
Simplified estimates:	
Mild metabolic stress (elective hospitalization)	1.0–1.1
Moderate metabolic stress (complicated postoperative care, infection)	1.2–1.4
Severe metabolic stress (major trauma, pancreatitis, sepsis)	1.5–2.5

IBW = ideal body weight.
Source: Adapted from *Barnes Hospital Nutrition Support Handbook*. St. Louis, 1992. P 19.

ALGORITHMS FOR ENERGY AND PROTEIN REQUIREMENTS

BMR (men) = (66.47 + 13.75W + 5.04H - 6.76A) x (activity factor) x (injury factor)

BMR (women) = (655.10 + 9.56W + 1.85H - 4.68A) x (activity factor) x (injury factor)

Where W = weight in kg, H = height in cm, A = age in years.

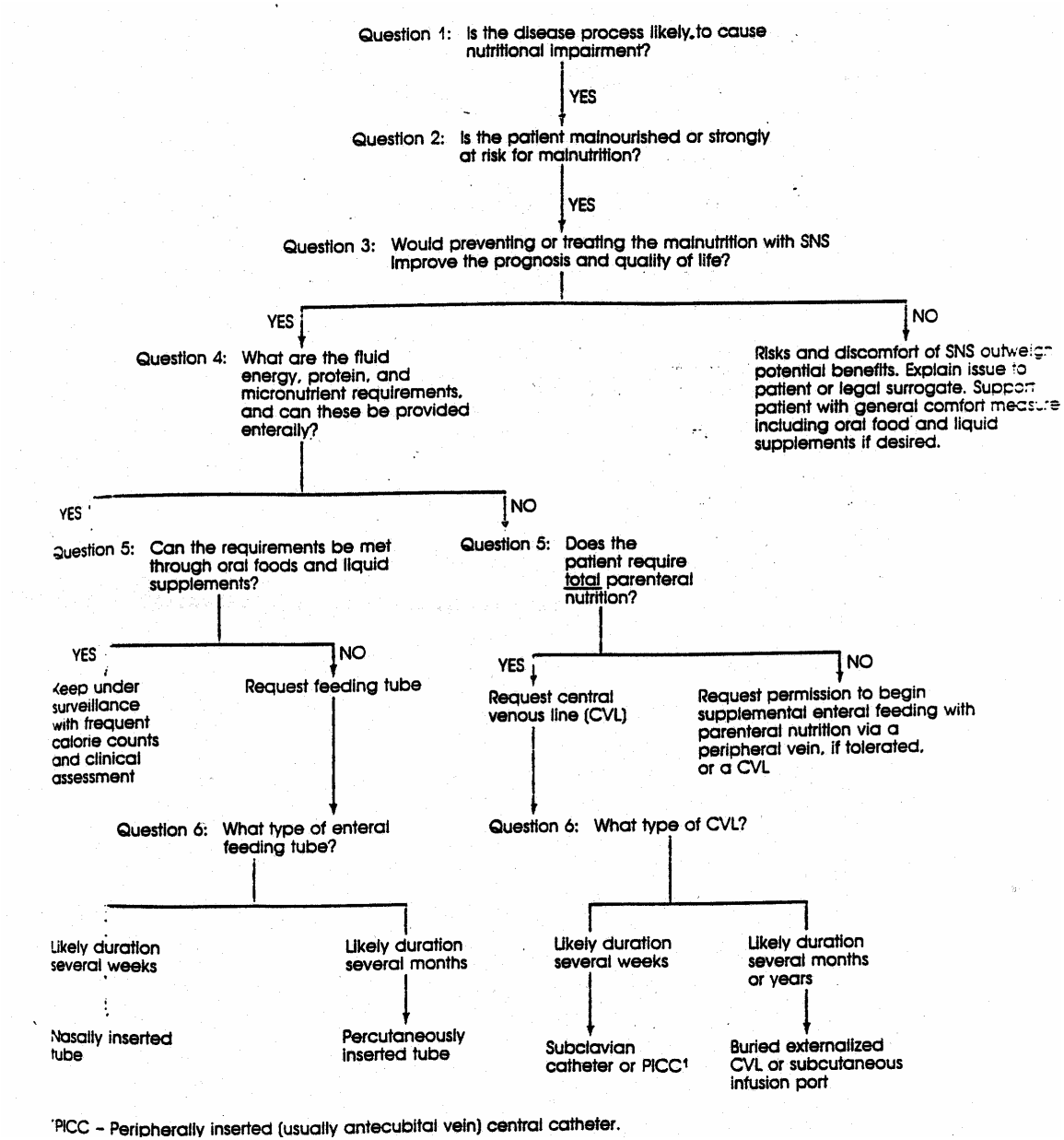
Activity Factor	**Use**
a) Confined to bed	1.2
b) Out of bed	1.3

Injury Factor	**Use**
a) Minor Operation	1.20
b) Skeletal Trauma	1.35
c) Major Sepsis	1.60
d) Severe Thermal Burn	2.10

Protein

Normal man	0.5 - 1.0 gm Pro/kg
Moderate Stress	1.0 - 1.5 gm Pro/kg
Severe Stress	1.5 - 2.0 gm Pro/kg

AN ALGORITHM FOR NUTRITIONAL SUPPORT



[1]PICC – Peripherally inserted (usually antecubital vein) central catheter.

PATIENT CLASSIFICATION FOR PNS CONSIDERATION

Group 1: High Risk, PNS needed
malnourished, carcinoma of GI tract, liver, pancreas or gall bladder

Group 2: Low Risk, PNS not needed
nourished and <40, primary carcinoma

Group 3: Intermediate risk, PNS considered
nourished and >40; malnourished at any age; UG, OB/GYN, colorectal malignancies, Post-op IONIP >7-10 d

PNS FOR PATIENTS NOT MALNOURISHED PREOPERATIVELY

Prolonged IONIP expected post-operatively

- **Biliary pancreatitis**
- **Enterocutaneous fistula**
- **Crohn's disease**
- **Non-functional GI tract**

ENTERAL FEEDING

Table 4 Indications for enteral feeding*

In gastrointestinal disease
Short bowel syndrome
Malabsorption syndrome
Gastrointestinal fistulae
Granulomatous disease of the gastrointestinal tract
In severe catabolic states, particularly burns
In malnourished patients with acute illness or before surgery
In anorexia, especially in the elderly
In those having treatment for cancer

* Where it is not possible to use the gastrointestinal tract these are also indications for parenteral feeding.

Table 7 Some complications of enteral nutrition

Mechanical
Tube insertion: Misplacement and oesophageal problems (inflammation, erosions, stricture)
Regurgitation and aspiration
Gastrointestinal
Diarrhoea and vomiting
Abdominal pain and distention
Metabolic
Hyperglycaemia
Low circulating levels of K, P, and Zn
Low red cell folate
Hypoprothrombinaemia
Deficiency of essential fatty acids

The mechanical problems of tube insertion are particularly prominent if a wide inflexible tube is used, and diarrhoea is most troublesome with hypertonic elemental feeds. For these reasons whole protein solutions given through narrow bore tubes are to be preferred.

Complications associated with total parenteral nutrition (TPN)

First 48 h	First 2 weeks	3 months onward
MECHANICAL		
Complications from catheter insertion: Cephalad displacement Pneumothorax Hemothorax Detachment of line at catheter hub with blood loss or air embolism	Catheter coming out of vein, more common if Silastic Detachment of line at catheter hub with blood loss or air embolism	Detachment of line at catheter hub with blood loss or air embolism Fractures or tears in catheter
METABOLIC		
Fluid overload Hyperglycemia Hypophosphatemia Hypokalemia	Cardiopulmonary failure Hyperosmolar nonketotic hyperglycemic coma Acid-base imbalance Electrolyte imbalance	Essentially fatty acid deficiency Zinc, copper, chromium, selenium, molybdenum, deficiency Iron deficiency Vitamin deficiencies Refeeding edema TPN metabolic bone disease TPN liver disease
INFECTIOUS		
	Catheter-induced sepsis	Catheter-induced sepsis Tunnel infections

TUBE FEEDING AND TPN FORMULATIONS

Composition	Tube feeding[1]	TPN[2]
Energy (kJ/L)	4200	4200
Energy distribution		
(% amino acids)	18	18
(% fat)	6	6
(% carbohydrate, dextrose)	76	76
Nonprotein energy:nitrogen	115:1	112:1
Total glutamine (g/L)	10.00	10.58
Total nitrogen (g/L)	7.13	7.32

[1] Vivonex Plus (Sandoz, Minneapolis), an elemental formula with amino acids, soybean oil, maltodextrin, modified cornstarch, and standard multivitamins and minerals.

[2] 6.5% Ren Amin (Baxter, Glendale, CA), L-glutamine (Ajinomoto, Teaneck, NJ), 20% Liposyn III (Abbott, Abbott Park, IL), 70% dextrose (Abbott), and standard multivitamins and minerals (Astra, Westboro, MA).

Nutritional goals: 107 kJ(26 kcal)/kg/d; 1.5 g protein/kg/d; 0.3 g Gln/kg/d

ENTERAL DIETS

	Per 100 ml	
	Enriched	Control
Total proteins (g)	5.6	5.6
Free L-arginine	1.25	—
L-serine	—	0.93
L-glycine	—	0.77
L-alanine	—	0.51
L-proline	—	0.45
RNA (g)	0.12	—
Total lipids (g)	2.8	2.8
n-3-fatty acids (%)	10.5	—
n-6-fatty acids (%)	8.3	24.1
Carbohydrates (g)	13.4	13.4
Total energy (kcal)	101	101
Osmolarity (mosm/L)	293	486

Nutritional goal: 25 kcal/kg/d and 0.25 g N/kg/d

GLUTAMINE ROLES

1) A protein amino acid

2) Used in N transport from peripheral tissues to liver

3) Precursor for purine and pyrimidine (i.e. nucleic acid) biosynthesis

4) Sparing effect on gluconeogenesis

5) Principal energy metabolite of enterocytes (50% of total energy)

6) Enhances neutrophil and macrophage phagocytotic function

Gln is the most abundant amino acid in the body and in the circulatory system

ARGININE ROLES

1) A protein amino acid

2) Used in N detoxification (urea cycle)

3) Precursor for NO (about 1% of body Arg use)

4) Enhancer of T-cell mediated immune function

5) Maintains IL-6 release during trauma

Arg is probably an essential amino acid in very young children, but only conditionally essential in adults

PHYSIOLOGICAL ROLES OF NITRIC OXIDE (NO)

- **Vasodilation**
- **Stimulation of macrophage bactericide**
- **Increased glucose uptake by cells**
- **Neuronal signaling**

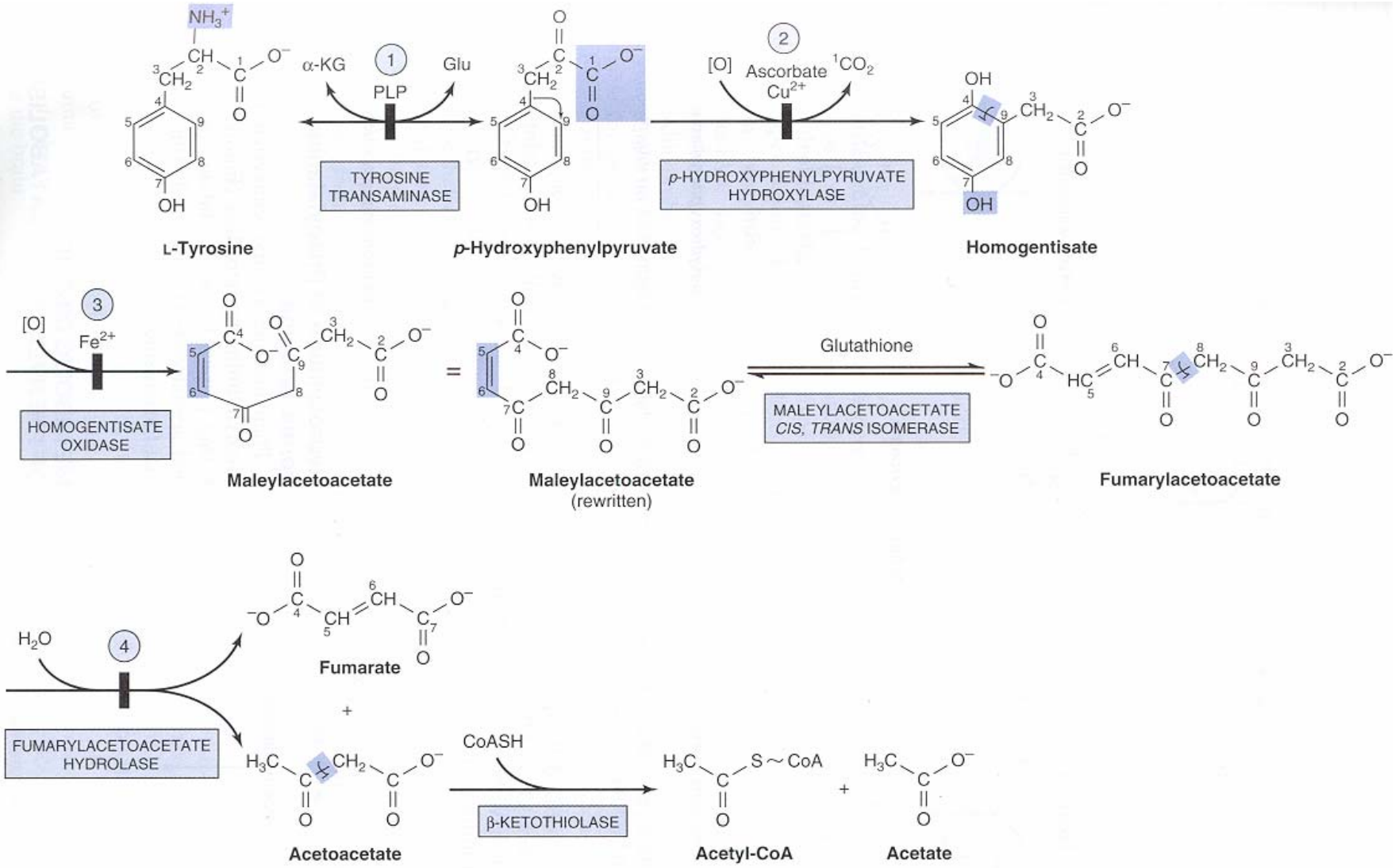
Some of these effects are related to the activation of guanylate cyclase by NO, which increases intracellular cGMP levels.

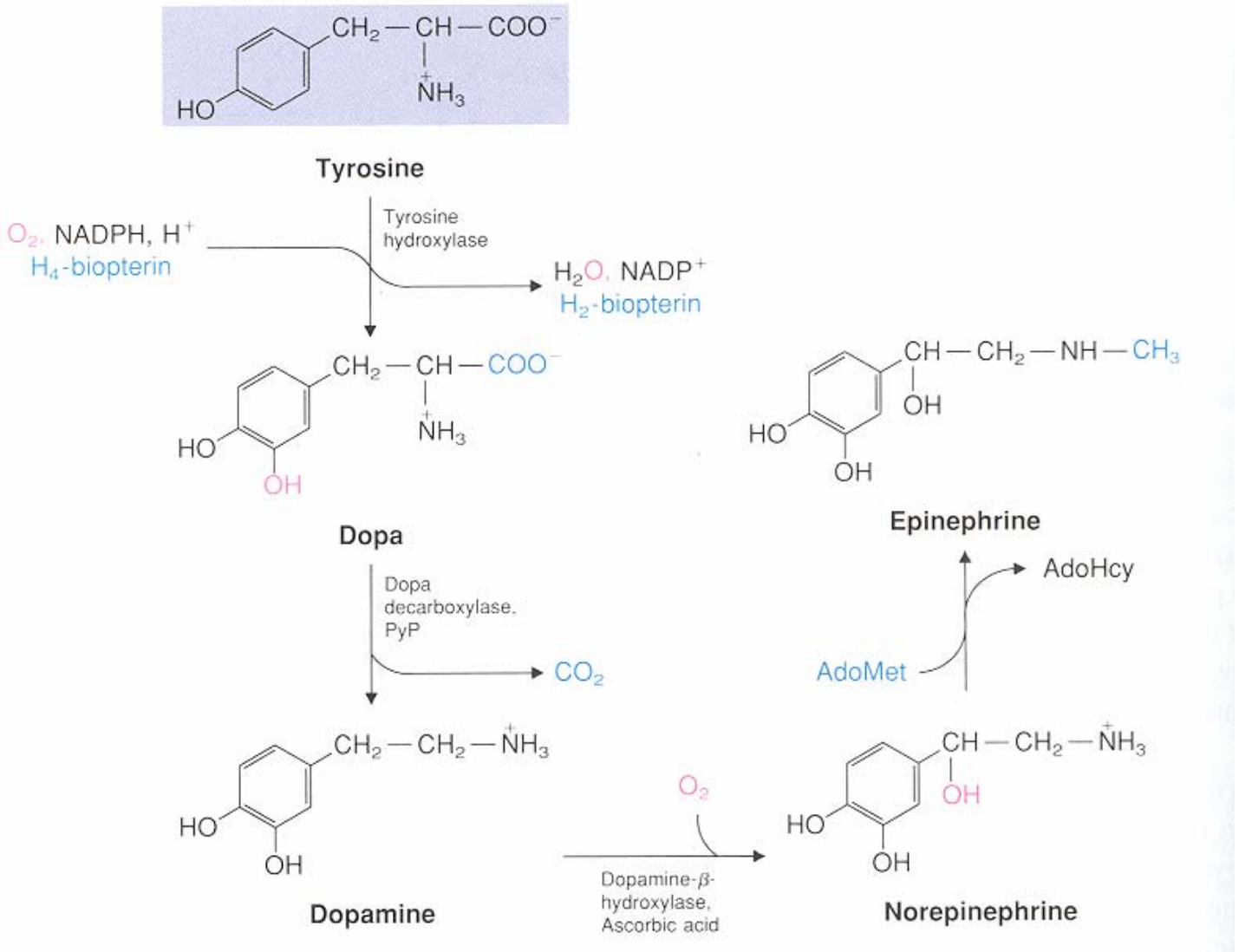
THE ROLES OF BRANCHED CHAIN AMINO ACIDS (BCAAs)

1. **Preferred substrates in muscle oxidative metabolism of amino acids.**

2. **Compete with aromatic amino acids (AAAs) for transport across the blood-brain barrier.**

BCAAs: Val, Ile, Leu
AAAs: Phe, Tyr, Trp


L-Tyrosine
α-KG
1
Glu
PLP
TYROSINE TRANSAMINASE
p-Hydroxyphenylpyruvate
[O]
2
Ascorbate
Cu2+
1CO2
p-HYDROXYPHENYLPYRUVATE HYDROXYLASE
Homogentisate
[O]
3
Fe2+
HOMOGENTISATE OXIDASE
Maleylacetoacetate
=
Maleylacetoacetate
(rewritten)
Glutathione
MALEYLACETOACETATE CIS, TRANS ISOMERASE
Fumarylacetoacetate
H2O
4
FUMARYLACETOACETATE HYDROLASE
Fumarate
+
Acetoacetate
CoASH
β-KETOTHIOLASE
Acetyl-CoA
+
Acetate


Tyrosine
Tyrosine hydroxylase
O2, NADPH, H+
H4-biopterin
H2O, NADP+
H2-biopterin
Dopa
Dopa decarboxylase, PyP
CO2
Dopamine
Epinephrine
AdoMet
AdoHcy
O2
Dopamine-β-hydroxylase, Ascorbic acid
Norepinephrine

ELECTROLYTE, TRACE ELEMENT AND VITAMIN CONTENTS IN A TNP DIET

Na, mmol/d	80–120
K, mmol/d	100–120
Mg, mequiv/d	15
Ca, mequiv/d	10–15
P, mmol/d	15
Fe mg/d	1 (men and postmenopausal women) 2 (premenopausal women)
Cu, mg/d	1 2.5 (when infusing amino acids) +12 mg./l. of small intestinal fluid loss +17 mg./l. of stool loss 0.3 0.5 (with diarrhea) None with abnormal liver function
Cr, microg/d	10–20
Se, microg/d	120
I, mg/d	120
Mn, mg/d	0.2–0.3
Vitamins	
A, IU/d	2,500
D, IU/d	400
E, IU/d	50 (α-tocopherol)
K, mg/wk	10
Thiamine, mg/d	5
Riboflavin, mg/d	5
Niacin, mg/d	50
Pantothenate, mg/d	15
Pyridoxine, mg/d	5
Folate. Mg/d	5
B12, microg/d	12
C, mg/d	300–500
Biotin, mg/d	60

GI CARCINOMA

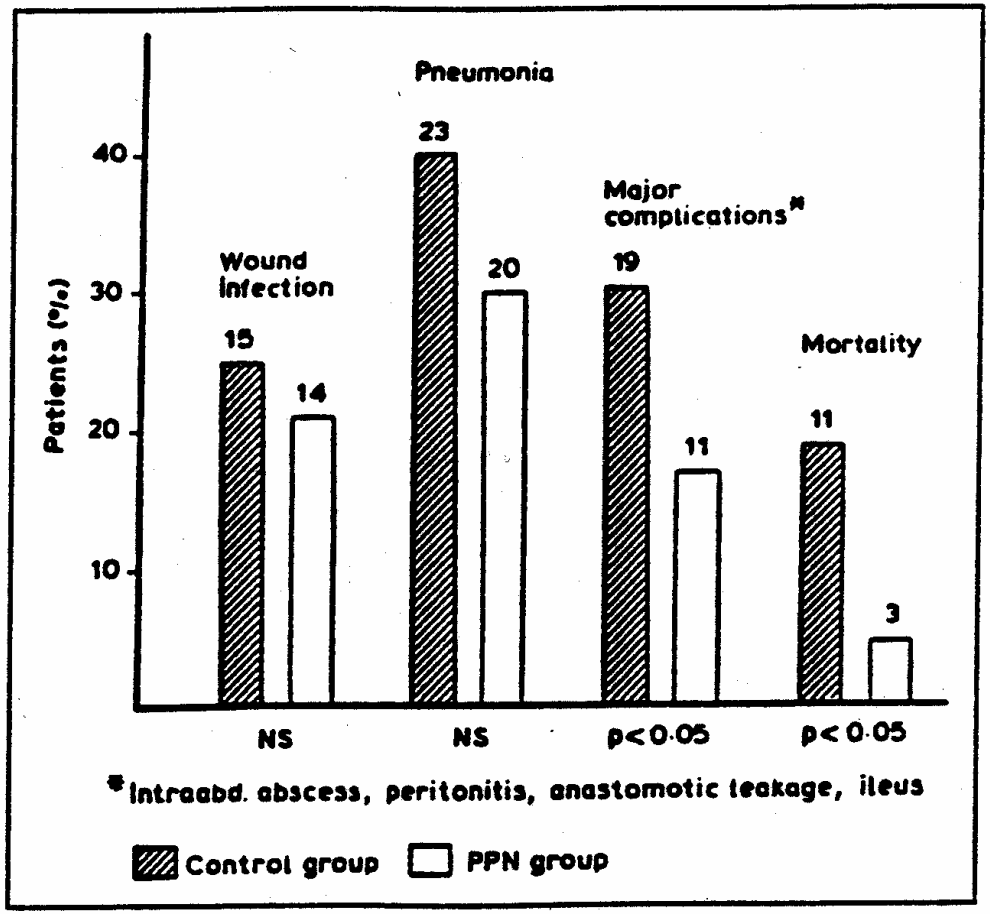


Figure 2. Instances of major postoperative complications in patients who received preoperative parenteral nutrition as compared with control subjects. Numbers on top of columns refer to number of cases.

Muller et al., Lancet 1982, 1, 68-71.

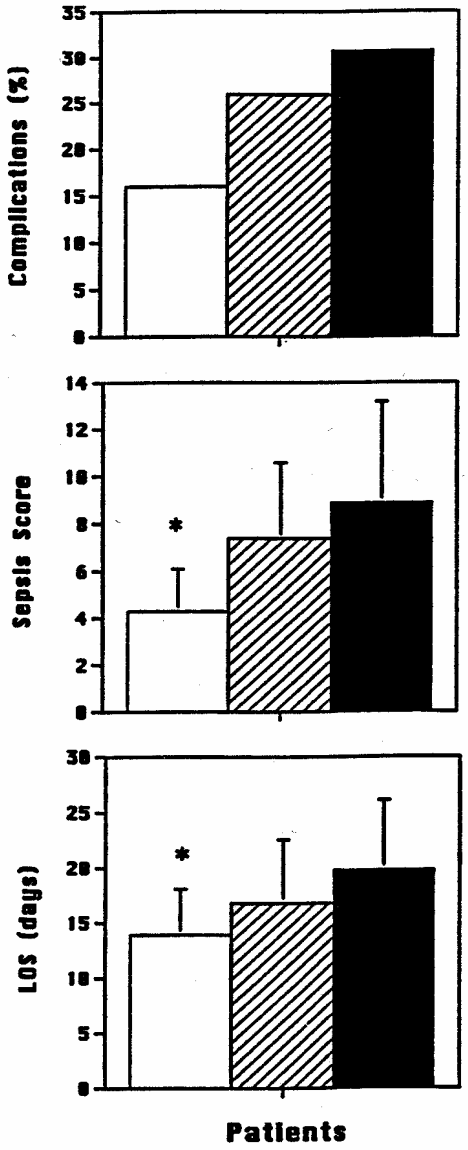


Figure 2. Clinical outcome of malnourished patients (n = 78). Values are expressed as mean ± SD. *LOS*, length of stay. *$p < .05$ vs. total parenteral nutrition. *Open bars*, enriched enteral nutrition group; *hatched bars*, control group; *solid bars*, total parenteral nutrition group.

TPN AND ENTERAL NUTRITION IN GASTRECTOMY AND PANCREATODUODENECTOMY

Braga et al., (1998), Crit. Care. Med. 26, 24-30

SPECIAL PNS ISSUES IN TRANSPLANTATION

- **Kidney**
  Low purines, low protein, high omega-3s

- **Liver**
  High protein, BCAA supplementation

- **Heart**
  Low lipid, high carbohydrate, possible insulin therapy to keep blood glucose <250 mg/dL

Nutritional Approach in Malnourished Surgical Patients

A Prospective Randomized Study

Marco Braga, MD; Luca Gianotti, MD, ScD; Luca Nespoli, MD; Giovanni Radaelli, PhD; Valerio Di Carlo, MD

Archives of Surgery, 137, 174-180 (2002)

A randomized clinical trial of pre- and perioperative immunonutrient-enhanced enteral nutrition of 150 malnourished patients who had major surgery for GI malignancies.

DIETARY FORMULATIONS IN BRAGA et al. STUDY

Component	Standard diet	Supplemented diet
Protein, g/L	56	56
Arginine, g/L	0	12.5
Lipids, g/L	28	28
omega-6 FAs, g/L	24.1	8.3
omega-3 FAs, g/L	0	10.5
Carbs, g/L	134	134
Total energy, kcal/L	1010	1010

OUTCOMES OF THE STUDY OF BRAGA et al.

Variable	Control Group (n = 50)	Preoperative Group (n = 50)	Perioperative Group (n = 50)
Patients with major complications, No.	12	9	6
Patients with infectious complications, No.	12	8	5
Patients with noninfectious complications, No.	11	10	6
Patients with complications, total No.	21	14	9*
Length of hospital stay, mean (SD), d	15.3 (4.1)	13.2 (3.5)†	12.0 (3.8)‡

Death	2	1	0
Anastomotic leak	5	3	3
Reason for transfer to intensive care unit			
Respiratory tract failure	2	1	1
Circulatory insufficiency	0	1	0
Multiple organ dysfunction syndrome	0	0	1
Reason for relaparotomy			
Abdominal abscess	1	1	0
Bleeding	1	0	1
Intestinal obstruction	0	1	0
Percutaneous drainage of an abdominal abscess	0	1	1

MINOR

	C	PRE	PERI
Infectious			
Respiratory tract	6	3	3
Wound	4	2	2
Urinary tract	2	2	1
Bacteremia	2	1	0
Noninfectious			
Pleural effusion/atelectasis	3	2	2
Delayed gastric emptying*	2	3	1
Pancreatic fistula	1	2	1
Systemic inflammatory response syndrome	2	2	1
Bleeding	2	0	0
Deep vein thrombosis	1	0	0
Arrythmia	1	2	1
Renal dysfunction	0	1	0

SUMMARY STATEMENTS OF BRAGA et al.

Complications occurred in 24/50 patients in the control group, 14/50 in the preoperative group and 9/50 in the perioperative group.

Post-operative length of stay was significantly shorter in the preoperative (13.2 d) and perioperative (12.0 d) groups compared to the control group (15.3 d).

Perioperative immunonutrition seems to be the best support for malnourished cancer patients.

POST-SURGICAL COMPLICATIONS AND TPN EFFICACY

VA TPN study (1991), NEJM, 325, 525-532.

	Degree of Malnutrition*		
	Borderline	Mild	Severe
Major infectious complications			
Subjective Global Assessment			
TPN group (%)	12.2	15.2	12.9
Control group (%)	4.0	6.6	10.5
P value (TPN vs. control)	0.15	0.05	1.00
Relative risk	3.05	2.30	1.23
95% Confidence interval	0.80–11.67	0.99–5.32	0.25–6.06
Nutrition Risk Index			
TPN group (%)	12.5	14.4	15.8
Control group (%)	9.1	3.7	21.4
P value	0.75	0.004	1.00
Relative risk	1.38	3.86	0.74
95% Confidence interval	0.45–4.22	1.48–10.08	0.17–3.12
Major noninfectious complications			
Subjective Global Assessment			
TPN group (%)	14.3	16.1	22.6
Control group (%)	16.0	22.6	42.1
P value	1.00	0.23	0.21
Relative risk	0.89	0.71	0.54
95% Confidence interval	0.38–2.11	0.41–1.23	0.23–1.24
Nutrition Risk Index			
TPN group (%)	12.5	20.0	5.3
Control group (%)	23.6	19.4	42.9
P value	0.20	1.00	0.03
Relative risk	0.53	1.03	0.12
95% Confidence interval	0.22–1.28	0.63–1.69	0.02–0.91

1991 VA STUDY ON PERIOPERATIVE TPN IN SURGICAL PATIENTS

CONCLUSION:

The use of preoperative TPN in major abdominal or thoracic surgery should be limited to patients who are severely malnourished unless there are other specific indications.

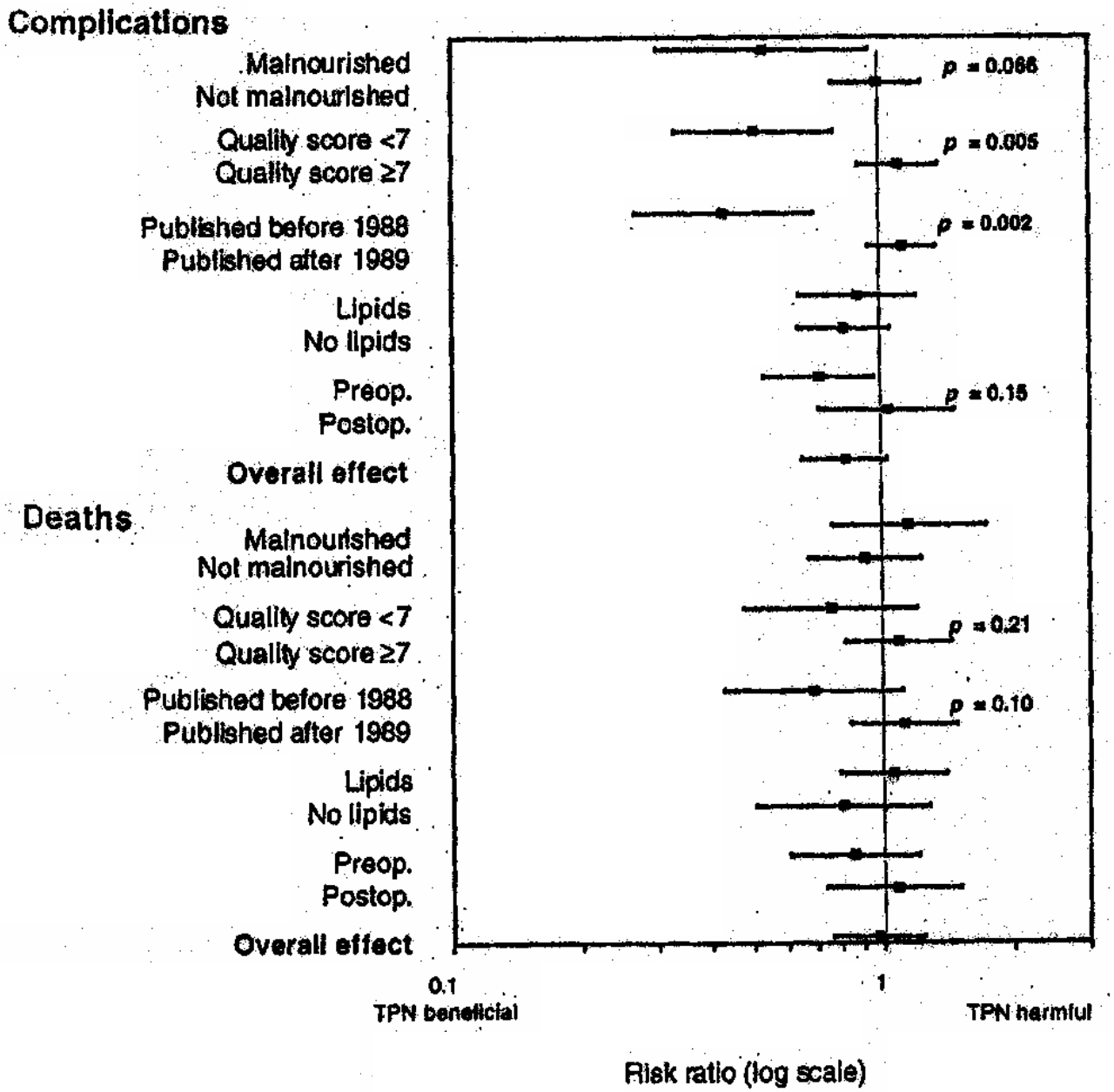
Total parenteral nutrition in the surgical patient: a meta-analysis

Daren K. Heyland, MD, MSc;* Max Montalvo, MD;† Shaun MacDonald, MD;* Laurie Keefe, RD;‡ Xiang Yao Su; John W. Drover, MD‡

Can. J. Surg. 44, 102-111 (2001)

An analysis of 27 previous randomized trials (involving 2907 patients) comparing TPN to standard care in terms of mortality and post-operative complications. Most of the surgeries were performed on the GI tract.

TNP IN SURGERY (HEYLAND et al., 2001)



SUMMARY STATEMENT OF HEYLAND et al.

TPN had no effect on mortality.

Only malnourished patients showed a decrease in complications with TPN.

Preoperative TPN preoperatively may cause a decrease in complications, but this effect was seen only in pre-1988 studies and in those of poor methodological quality.

Lipid supplementation in TPN had no effect on mortality or complications.

Overall, in surgical patients, there seemed to be no advantage to perioperative TPN.

SOME KEY REFERENCES ON PERIOPERATIVE NUTRITIONAL SUPPORT

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