

8.0 Parenteral Nutrition vs. Standard care

There were no new randomized controlled trials since the 2015, but changes to included articles and outcomes have been made to this summary of evidence.

Question: Compared to standard care (IV fluids, oral diet, etc. but not EN), does parenteral nutrition (PN) result in improved clinical outcomes in critically ill patients with an intact GI tract?

Summary of Evidence: There are three level 2 studies included in this topic. Two studies compared PN with lipids vs IVF (Sax 1987, Xian-Li 2005) and 1 study compared early PN with lipids vs standard care in which the physician chose the nutrition plan (Doig 2013). Three articles (Abel 1976, Reilly 1990 and Sandstrom 1993) were previously included in this topic for our CPGs, but have been excluded from this review since they were in elective surgery patients.

Mortality: When the 3 studies were aggregated, compared to IVF/standard care, PN had no effect on mortality (RR 0.72, 0.37, 1.43, $p=0.35$; figure 1).

Infections: Two studies (Sax 1987, Doig 2013) reported the number of patients with infectious complications and parenteral nutrition was not associated with an increase in infectious complications (RR 1.20, 95% CI 0.45, 3.21, $p=0.72$, $I^2=32\%$; figure 2).

LOS: Based on 2 studies (Sax 1987, Xian-Li 2005) that reported hospital length of stay, the use of parenteral nutrition had no effect (weighted mean difference, WMD -2.55, 95% CI -17.73, 12.64, $p=0.74$; figure 3).

Ventilator Days: Doig et al reported fewer days of invasive ventilation in the patients receiving PN vs standard care: mean (95% CI) days per 10 patients x ICU days: 7.26 (7.09-7.44) vs 7.73 (7.55-7.92), $p=0.01$.

Quality of Life and Physical Function: Doig et al conducted 3 questionnaires at study day 60 to assess quality of life and physical function. The use of parenteral nutrition resulted in significantly higher quality of life scores (RAND-36 general health status, $p=0.01$) but had no effect on physical function scores (ECOG performance status, $p=0.70$, and RAND-36 physical functions, $p=0.33$). The day-60 quality of life score was also statistically higher in the PN Group, but this was not clinically meaningful ($p=0.01$).

Conclusions:

Compared to standard of care,

- 1) Parenteral nutrition has no effect on mortality in critically ill patients.
- 2) Parenteral nutrition has no effect on infectious complications in critically ill patients.

- 3) Parenteral nutrition has no effect on hospital stay.
- 4) Parenteral nutrition may be associated with decreased time on the ventilator.
- 5) Parenteral nutrition is associated with improved quality of life following critical illness but has no effect on physical function.

Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.

Level 2 study: if any one of the above characteristics are unfulfilled.

Table 1. Randomized studies evaluating parenteral nutrition vs. standard care in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				PN	Control	PN	Control
1) Sax 1987	Acute pancreatitis N=54	C.Random: not sure ITT: yes Blinding: no (8)	PN with lipids after admission vs IV fluids	1/29 (3)	1/26 (4)	Total 4/29 (14) Infected catheters per group 28/29	Total 1/26 (4) Infected catheters per group 13/26
2) Xian-Li 2005*	Severe acute pancreatitis N=69	C.Random: yes ITT: yes Blinding: no	PN with lipids vs IV fluids	3/21 (14)	10/23 (44)	Infectious complications** 21	Infectious complications** 11
3) Doig 2013	Multicenter mixed ICUs N=1372	C.Random: yes ITT: yes Blinding: no (12)	PN 3-in-1 bag (Kabiven G19%) goal to reach target on day 3 as per protocol vs Standard care (attending clinician selected the route, starting rate, metabolic targets, and composition of nutrition to be provided)	ICU 81/678 (11.89) Hospital 140/678 (20.6) Day 60 146/678 (21.5)	ICU 100/680 (14.66) Hospital 151/680 (22.1) Day 60 155/680 (22.8)	Any major infection 74/678 (10.9) P=0.80 Catheter 31/678 (4.55) p>0.99 Bloodstream 39/678 (5.73) P=0.47 Airway/lung 101/678 (14.83) P=0.12 Pneumonia 43/678 (6.31) P=0.91	Any major infection 78/680 (10.9) Catheter 32/680 (4.55) Bloodstream 33/680 (5.73) Airway/lung 123/680 (14.83) Pneumonia 45/680 (6.31)

Table 1. Randomized studies evaluating parenteral nutrition vs. standard care in critically ill patients (continued)

Study	LOS days		Ventilator days		Cost		Other	
	PN	Control	PN	Control	PN	Control	PN	Control
1) Sax 1987	Hospital 15 ± 4	Hospital 10 ± 3	NR	NR	NR	NR		
2) Xian-Li 2005*	Hospital 28.6 ± 6.9	Hospital 39.1 ± 10.6	NR	NR	NR	NR	ARDS 2/21	5/23
3) Doig 2013	ICU 8.6 (8.2-9)	ICU 9.3 (8.9-9.7)	7.26 (7.09 - 7.44)	7.73 (7.55 - 7.92)	NR	NR	Muscle wasting increase in SGA score 0.27	0.43 (p=0.01)

	Hospital 25.4 (24.4-26.6)	Hospital 24.7 (23.7-25.8)					Fat Loss increase in SGA score 0.31 0.44 (p=0.04) Renal failure, mean, days per 10 pt x ICU days 1.65 (1.51-1.81) 1.66 (1.51-1.82) P=0.98 Pulmonary failure, mean, days per 10 pt x ICU days 8.54 (8.37-8.71) 8.51 (8.34-8.69) P=0.88
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* Only data comparing the groups receiving standard PN and IV fluids reported here.

** Not included in meta-analysis as not reported as number of patients with infections.

C.Random: concealed randomization

‡ refers to the # of patients with infections unless specified

ITT: intent to treat

† hospital mortality unless otherwise specified

NR: not reported

± () : mean ± Standard deviation (number)

PN: parenteral nutrition

ICU: intensive care unit

SGA: subjective global assessment

NS: not significant

Table 2. Quality of Life (QOL) and Physical Function Outcomes

Study	QOL		Physical Function	
	PN	Control	PN	Control
3) Doig 2013	RAND-36 general health status (n) at study day 60 49.8 ± 27.6 (525) 45.5 ± 26.8 (516) P=0.01 ECOG performance status (n) at study day 60 1.51 ± 1.1 (525) 1.53 ± 1.1 (516) P=0.70 RAND-36 physical functions (n) at study day 60 42.5 ± 30.8 (524) 40.7 ± 29.6 (513) P=0.33		NR	

Figure 1. Mortality

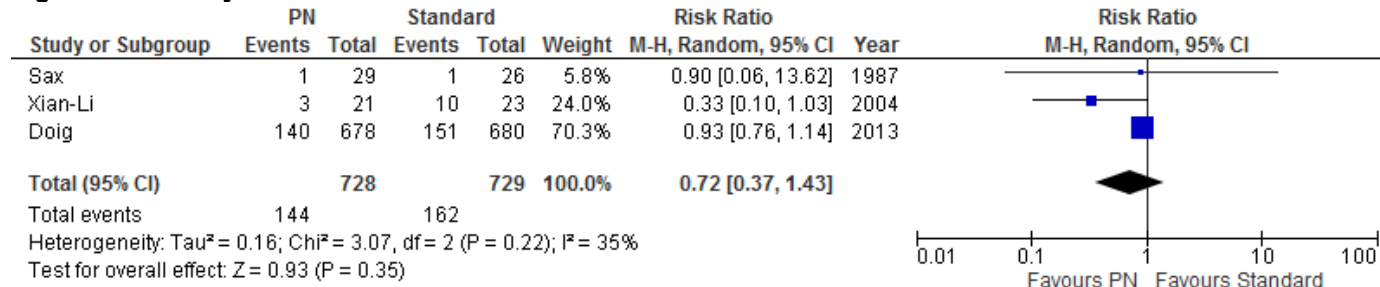


Figure 2. Infections

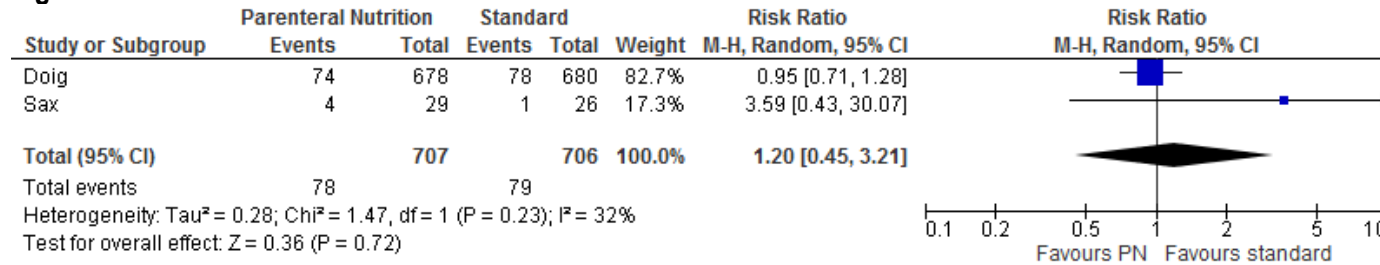
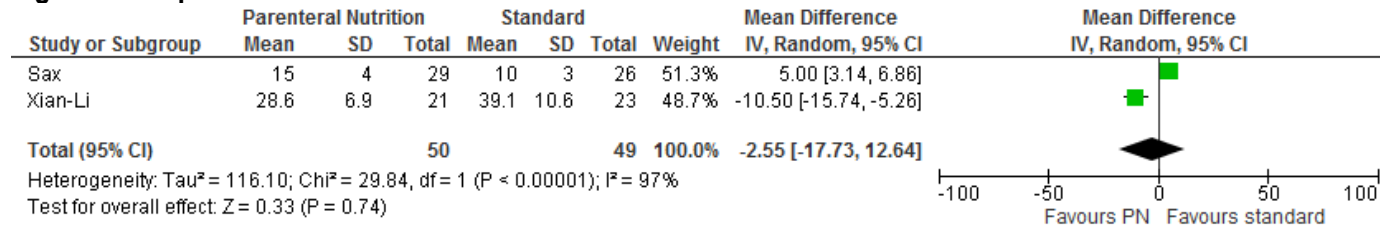


Figure 3. Hospital LOS



References

Included Articles

1. Abel RM, Fischer JE, Buckley MJ, Barnett GO, Austen WG. Malnutrition in cardiac surgical patients. Results of a prospective, randomized evaluation of early postoperative parenteral nutrition. *Arch Surg.* 1976 Jan;111(1):45-50.
2. Sax HC, Warner BW, Talamini MA, Hamilton FN, Bell RH Jr, Fischer JE, Bower RH. Early total parenteral nutrition in acute pancreatitis: lack of beneficial effects. *Am J Surg.* 1987 Jan;153(1):117-24.
3. Reilly J, Mehta R, Teperman L, Cemaj S, Tzakis A, Yanaga K, Ritter P, Rezak A, Makowka L. Nutritional support after liver transplantation: a randomized prospective study. *JPEN J Parenter Enteral Nutr.* 1990 Jul-Aug;14(4):386-91.
4. Sandström R, Drott C, Hyltander A, Arfvidsson B, Scherstén T, Wickström I, Lundholm K. The effect of postoperative intravenous feeding (TPN) on outcome following major surgery evaluated in a randomized study. *Ann Surg.* 1993 Feb;217(2):185-95.
5. Xian-Li He et al. Effect of total parenteral nutrition (TPN) with and without glutamine dipeptide supplementation on outcome in severe acute pancreatitis (SAP). *Clinical Nutrition Supplements* 2004(1):43.
6. Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, Davies AR, O'Leary M, Solano T, Peake S; for the Early PN Investigators of the ANZICS Clinical Trials Group. Early Parenteral Nutrition in Critically Ill Patients With Short-term Relative Contraindications to Early Enteral Nutrition A Randomized Controlled Trial. *JAMA.* 2013;309(20):2130-2138.

Excluded Articles

#	Reason excluded	Citation
1	Cancer pts	Heim ME, Leweling H, Edler L, Queiber W. Adjuvant parenteral nutrition in patients with colorectal cancer receiving polychemotherapy: a randomized clinical trial. <i>TumorDiagnostik & Therapie.</i> 1985 6:129-133
2	Cancer pts	Cardona D, Del Moral V, Salvador R, Andreu MA, Trias R, Bonal J. Early postoperative total parenteral nutrition in gastric cancer: a cost-effectiveness study. <i>J Clin Nutr Gastroenterol.</i> 1986 1:267-270
3	Not ICU pts	Perioperative total parenteral nutrition in surgical patients. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. <i>N Engl J Med.</i> 1991 Aug 22;325(8):525-32. PubMed PMID: 1906987
4	Surgery pts	Buzby GP. Overview of randomized clinical trials of total parenteral nutrition for malnourished surgical patients. <i>World J Surg.</i> 1993 Mar-Apr;17(2):173-7.
5	Cancer pts	Gil MJ, Franch G, Guirao X, Oliva A, Herms R, Salas E, Girvent M, Sitges-Serra A. Response of severely malnourished patients to preoperative parenteral nutrition: a randomized clinical trial of water and sodium restriction. <i>Nutrition.</i> 1997 Jan;13(1):26-31.
6	Systematic review	Heyland DK, MacDonald S, Keefe L, Drover JW. Total parenteral nutrition in the critically ill patient: a meta-analysis. <i>JAMA.</i> 1998 16;280(23):2013-9.
7	Surgery pts	Hu SS, Fontaine F, Kelly B, Bradford DS. Nutritional depletion in staged spinal reconstructive surgery. The effect of total parenteral nutrition. <i>Spine.</i> 1998 Jun 15;23(12):1401-5.
8	Elective surgery pts	Bozzetti F, Gavazzi C, Miceli R, Rossi N, Mariani L, Cozzaglio L, Bonfanti G, Piacenza S. Perioperative total parenteral nutrition in malnourished, gastrointestinal cancer patients: a randomized, clinical trial. <i>JPEN J Parenter Enteral Nutr.</i> 2000 Jan-Feb;24(1):7-14.
9	Systematic review	Heyland DK. Parenteral nutrition in the critically-ill patient: more harm than good? <i>Proc Nutr Soc.</i> 2000 Aug;59(3):457-66.
10	Meta Analysis	Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: a meta-analysis. <i>Am J Clin Nutr.</i> 2001

		Oct;74(4):534-42.
11	Not all ICU patients, not PN vs standard	Koretz RL, Lipman TO, Klein S; American Gastroenterological Association. AGA technical review on parenteral nutrition. <i>Gastroenterology</i> . 2001 Oct;121(4):970-1001.
12	Not all studies of ICU pts	Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. <i>Crit Care Med</i> . 2005 Jan;33(1):213-20; discussion 260-1.
13	Not all studies of ICU pts	Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. <i>Intensive Care Med</i> . 2005 Jan;31(1):12-23. Epub 2004 Dec 9.
14	No clinical outcomes	Meersseman P, Boonen E, Peeters B, Vander Perre S, Wouters PJ, Langouche L, Van den Berghe G. Effect of Early Parenteral Nutrition on the HPA Axis and on Treatment With Corticosteroids in Intensive Care Patients. <i>J Clin Endocrinol Metab</i> . 2015 Jul;100(7):2613-20. doi: 10.1210/jc.2015-1846. Epub 2015 May 5. PubMed PMID: 25942482.