

7.2 Early vs. Delayed Supplemental Parenteral Nutrition

There were no new randomized controlled trials since the 2015 update but functional status outcomes have been added to the summary of evidence.

Question: Does the use of early vs delayed supplemental parenteral nutrition result in better outcomes in the critically ill adult patient?

Summary of evidence: There was 1 level 1 study reviewed that compared early initiation of parenteral nutrition (day 3) with late initiation (day 8 if insufficient enteral intake by day 7) in adults in the (ICU) to supplement insufficient enteral nutrition. This trial is confounded by the fact that patients in the early group received high dose insulin to achieve tight glycemic control along with IV dextrose until day 3 when PN started. There is evidence that the groups separated early (by day 3-4, see Table 2 of primary publication) before the PN started so some of the harm may be due to IV glucose/insulin, not the PN.

Mortality: Early supplemental PN vs late had no effect on ICU mortality (RR 1.04, 95% CI 0.83, 1.30, $p=0.72$), hospital mortality (RR 1.04, 95% CI 0.88, 1.23, $p=0.61$), or 90-day mortality (RR 1.00, 95% CI 0.85, 1.18, $p=0.99$).

Infections: Early supplemental PN vs late was associated with a significant increase in all infectious complications (RR 1.15, 95% CI 1.04, 1.27, $p=0.008$). The early PN group had a significantly higher incidence of sepsis (RR 1.23, 95% CI 1.00, 1.53, $p=0.05$) compared to the late PN group.

LOS & ventilator days: Early supplemental PN vs late was associated with significantly longer lengths of stay in ICU ($p=0.02$), significantly longer LOS in hospital ($p=0.004$) and significantly longer time spent on mechanical ventilation ($p=0.02$) compared to late initiation of supplemental PN.

Costs: Early vs late supplemental PN resulted in significantly higher total health care costs per patient ($p=0.04$).

Functional Status: Early vs late supplemental PN had no difference on 6 minute walk distance or activities of daily living at hospital discharge ($p=0.57$ and 0.31 , respectively).

Compared to late initiation of PN (day 8) in patients receiving EN:

- 1) Early supplemental PN has no effect on mortality in critically ill patients.
- 2) Early supplemental PN may be associated with an increase in infectious complications in critically ill patients.
- 3) Early supplemental PN may be associated with a longer ICU and hospital length of stay in critically ill patients.
- 4) Early supplemental PN may be associated with an increase in duration of ventilation in critically ill patients.
- 5) Early supplemental PN may be associated with higher total health care costs per patient.

6) Early supplemental PN has no effect on functional status outcomes in critically ill patients.

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 early vs delayed supplemental PN in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)‡	
				EN + PN	EN	EN + PN	EN
1) Casaer 2011	Critically ill from 7 ICUs Admitted with a nutrition risk ≥3 based on Nutrition Risk Screening (NRS) N=4640	C.Random: Yes ITT: Yes Blinding: No (11)	EN + early PN (20% IV glucose; kcal target day 1=400kcal, day 2=800 kcal, Day 3 initiate PN with goal of 100% caloric goal with EN+PN: caloric needs based on IBW, PN d/c if kcal via EN ≥80% requirements, restarted if EN ≤50%) vs EN + late PN (Late initiation: 5% glucose IV equal to PN group to match hydration) If EN sufficient >7 days, PN added on day 8 to reach kcal requirements) Non-isocaloric/isonitrogenous	ICU 146/2312 (6) RR 1.04, 95% CI 0.83, 1.30 p=0.72 Hospital 251/2312 (11) RR 1.04, 95% CI 0.88, 1.23 p=0.61 90-day 255/2312 (11) RR 1.00, 95% CI 0.85, 1.18 p=0.99	ICU 141/2328 (6) Hospital 242/2328 (10) 90-day 257/2328 (11)	Total 605/2312 (26) RR 1.15, 95% CI 1.04, 1.27 p=0.008	Total 531/2328 (23)

Study	LOS days		Ventilator days		Cost		Physical Function	
	EN + PN	EN	EN + PN	EN	EN + PN	EN	EN + PN	EN
1) Casaer 2011	ICU 4 (2-9) p=0.02 Hospital 16 (9-29) p=0.004	ICU 3 (2-7) Hospital 14 (9-27)	2 (1-5) p=0.02	2 (1-5)	Mean total incremental health care cost, Euros (IQR) 17973 (8749-18677) 16863 (8793-17774) P=0.04		6 Minute Walk Test Distance at hospital discharge, metres (IQR) 283 (205-336), n=603 277 (210-345), n=624 P=0.57 Independent in all activities of daily living at hospital discharge, no. (%) 752/996 (75.5) 779/1060 (73.5) P=0.31	

ITT: intent to treat

ICU: intensive care unit

† presumed hospital mortality unless otherwise specified

C. Random: concealed randomization

RR: relative risk; CI: confidence interval

EN: enteral nutrition

LOS: length of stay

‡ refers to the # of patients with infections unless specified

PN: parenteral nutrition

NR: not reported