# 4.2c Composition of Enteral Nutrition: High Protein vs. Low Protein March 2013

*Recommendation 2013: There are insufficient data to make a recommendation regarding the use of high protein diets or escalating doses of protein in critically ill patients.*

*Discussion 2013:* The committee noted the addition of one new study (Scheinkestel et al 2003) in continuous renal replacement therapy (CRRT) patients of an escalating dose of protein over a short duration which had no treatment effect with respect to mortality. The lack of an effect of a higher vs. lower protein formula on clinical outcomes in head injured patients from an older study was also noted (Clifton 1985). Despite the signals from observational studies showing improved outcomes with higher protein intakes in critically ill patients (1, 2) and no safety concerns, there is limited data from randomized trials that prevents making strong conclusions about the dose of protein in critically ill patients (3). Given this, the committee decided against making a recommendation.

1. Allingstrup MJ et al. Provision of protein and energy in relation to measured requirements in intensive care patients. Clin Nutr. 2012 Aug;31(4):462-8.
2. Heyland D et al. Enhanced Protein-Energy Provision via the Enteral Route Feeding Protocol in Critically Ill Patients (The PEP uP Protocol): Results of a cluster randomized trial. Critical Care Medicine 2013 (in press).
3. Hoffer LJ, Bistrian BR. Appropriate protein provision in critical illness: a systematic and narrative review. Am J Clin Nutr. 2012 Sep;96(3):591-600.

Recommendation 2009: *There are insufficient data to make a recommendation regarding the use of high protein diets for head injured patients and other critically ill patients.*

Discussion 2009: The committee noted the lack of treatment effect with respect to both mortality and infectious complications from 1 small study in head injured patients. Given this and the concerns regarding cost, the committee decided against a recommendation. The committee agreed that given the choice of a lower protein control formula, this study should not be added to the High Fat/Low CHO section (4.2 (a)).

# Semi Quantitative Scoring

| Values | Definition | 2009 Score 0, 1, 2, 3 | 2013 Score 0, 1, 2, 3 |
|---|---|---|---|
| Effect size | Magnitude of the absolute risk reduction attributable to the intervention listed--a higher score indicates a larger effect size | 0 | 0 |
| Confidence interval | 95% confidence interval around the point estimate of the absolute risk reduction, or the pooled estimate (if more than one trial)--a higher score indicates a smaller confidence interval | 1 | 1 |
| Validity | Refers to internal validity of the study (or studies) as measured by the presence of concealed randomization, blinded outcome adjudication, an intention to treat analysis, and an explicit definition of outcomes--a higher score indicates presence of more of these features in the trials appraised | 2 | 2 |
| Homogeneity or Reproducibility | Similar direction of findings among trials--a higher score indicates greater similarity of direction of findings among trials | 1 | 1 |
| Adequacy of control group | Extent to which the control group represented standard of care (large dissimilarities = 1, minor dissimilarities=2, usual care=3) | 3 | 3 |
| Biological plausibility | Consistent with understanding of mechanistic and previous clinical work (large inconsistencies =1, minimal inconsistencies =2, very consistent =3) | 2 | 2 |
| Generalizability | Likelihood of trial findings being replicated in other settings (low likelihood i.e. single centre =1, moderate likelihood i.e. multicentre with limited patient population or practice setting =2, high likelihood i.e. multicentre, heterogeneous patients, diverse practice settings =3. | 1 | 1 |
| Cost | Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU | 2 | 2 |
| Feasible | Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU | 2 | 2 |
| Safety | Estimated probability of avoiding any significant harm that may be associated with the intervention listed--a higher score indicates a lower probability of harm | 2 | 3 |

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Question: Compared to a lower enteral protein intake does a higher protein intake enteral formula result in better outcomes in the critically ill adult patient?

Summary of evidence: There were 2 level 2 studies that compared the effect of a higher protein regimen to a lower protein regimen. Clifton (1985) compared the high-protein formula Traumacal to the lower protein formula Magnacal in head injured patients. Scheinkestel et al (2003) compared a higher escalating protein feeding schedule (starting at 1.5 gm/kg/day to 2.5 gm/kg/day over 6 days) to a constant level of protein (1.5 gm/kg/day) in patients on with renal failure on continuous renal replacement therapy (CRRT) in a 4:1 trial.

Mortality: A meta-analyses could not be done on as one study reported on 3 month mortality (Clifton 1985) while the other study reported on ICU mortality Scheinkestel (2003). There were no statistically significant differences in mortality between the groups in either study (Clifton 1985 RR 1.00, 95 % CI 0.07-13.9; Scheinkestel et al 2003 RR 0.56, 95 % CI 0.22-1.46).

Infections: In the study that reported on infections (Clifton, 1985), there were more bacterial infections in the group receiving the higher protein formula but this was not statistically significant (Relative Risk 1.50, 95 % confidence Intervals 0.32, 7.1)

LOS and Ventilator days Not reported.

Other: In the study by Clifton (1985), nitrogen balance was higher in the higher protein group but this was not statistically significant. Nitrogen balance became positive in patients in the escalating protein group compared to the control group over time (p =0.0001) in the Scheinkestel (2003). study.

Conclusions:

1) An escalating protein feeding schedule (1.5 to 2.5 gm/kg/day) vs 2 gm/kg/day has no effect on mortality in critically ill patients on CRRT.
2) A higher protein formula has no effect on mortality and infectious complications in head injured 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 Higher Protein vs. Low Protein Enteral Formula in Critically ill Patients

| Study | Population | Methods (score) | Intervention | Mortality # (%) | | RR (CI)** | Infections # (%) | | RR (CI)** |
|---|---|---|---|---|---|---|---|---|---|
| 1) Clifton 1985 | Head injured patients<br>Comatose for 24 hrs<br>N=20 | C.Random: not sure<br>ITT: yes<br>Blinding: no<br>(8) | 22% pro, 38 % CHO, 41 % fat, 1.5 Kcal/ml (Traumacal vs. 14 % pro, 50 % CHO, 36 % fat, 2.0 Kcal/ml (Magnacal)<br><br>Isocaloric,<br>29 gm Nitrogen vs.17.6 gms Nitrogen | High protein<br>1/10 (10) | Low protein<br>1/10 (10) | 1.00<br>(0.07-13.9) | High protein<br>3/10 (30) | Low protein<br>2/10 (20) | 1.50<br>(0.32, 7.1) |
| 2) Scheinkestel 2003 | Critically ill ventilated pts on 6 days CRRT for renal failure<br>N=50 | C.Random: yes<br>ITT: yes<br>Blinding: no<br>(9) | 1.5 g/kg/d protein x2 days, 2.0 g/kg/d protein x2 days and 2.5 g/kg/d protein x2 days while receiving CRRT<br><br>vs 2.0 g/kg/d protein x6 days while receiving CRRT | High protein<br>ICU: 9/40 (23) | Low protein<br>ICU: 4/10 (40) | 0.56<br>(0.22-1.46) | NA | NA | NA |

C.Random: concealed randomization
ITT: intent to treat
NR: Not reported

± : mean ± standard deviation
** RR= relative risk, CI= Confidence intervals