Should patients be fed to achieve full caloric goals rapidly? If so, does the route matter?

Dr Gordon S. Doig,
Associate Professor in Intensive Care,
Northern Clinical School Intensive Care Research Unit,
University of Sydney, Sydney, Australia
www.EvidenceBased.net
gdoig@med.usyd.edu.au

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Disclosures

Gordon S. Doig

Relevant financial relationships over past 5 years:

• Nestle Healthcare, Academic Research Grant, Consultant and Speaker’s Honoraria

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• Nutricia, Speakers Honoraria
Conclusions
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1. Should patients be fed to achieve full caloric goals rapidly?

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2. If so, does the route matter?

Yes. Early EN is cheaper than Early PN whilst Early PN is cheaper than not feeding at all!
Summary of this talk

- Understand Levels of Evidence.
- Investigate the concept of ‘caloric / energy debt’ in critical illness.
- Review the most recent clinical evidence on the topic.
- Investigate costs.
- Conclude, with succinct evidence-based recommendations.
Editorials, Expert Opinion

Systematic Reviews of RCTs
Randomized Controlled Trials
Cohort Studies
Case-Control Studies
Case Series, Case Reports
Editorials, Expert Opinion

Smaller treatment effects

Systematic Reviews of RCTs
Randomized Controlled Trials
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Finding the evidence:

Simple PubMed Search:

("intensive care" OR "intensive care units" OR "intensive therapy" OR "critically ill" OR "critical care")

AND

energy deficit

OR

energy debt
Results: 1 to 20 of 93

   - PMID: 25118838
   - **Similar articles**

2. **Optimal timing for introducing enteral nutrition in the neonatal intensive care unit.**
   - Liu J, Kong K, Tao Y, Cai W.
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3. **Fulfilling caloric demands according to indirect calorimetry may be beneficial for post cardiac arrest patients under therapeutic hypothermia.**
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- **Lactate in the intensive care unit: pyromaniac, sentinel or fireman?**

- **Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.**

- **Extruterine growth restriction: a continuing problem in the NICU.**

Summary  20 per page  Sort by Most Recent  Send to: 

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Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.

Villet S, Chiroleo RL, Bollmann MD, Revelly JP, Cayeux R N MC, Delarue J, Berger MM.

Abstract

BACKGROUND AND AIMS: Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. The study aimed at assessing the relationship between energy balance and outcome in critically ill patients.

METHODS: Prospective observational study conducted in consecutive patients staying > or = 5 days in the surgical ICU of a University hospital. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means +/- SD, linear regressions between energy balance and outcome variables.

RESULTS: Forty eight patients aged 57 +/- 16 years were investigated; complete data are available in 669 days. Mechanical ventilation lasted 11 +/- 8 days, ICU stay 15 +/- 9 was days, and 30-days mortality was 38%. Time to feeding was 3.1 +/- 2.2 days. Enteral nutrition was the most frequent route with 433 days. Mean daily energy delivery was 1090 +/-930 kcal. Combining enteral and parenteral nutrition achieved highest energy delivery. Cumulated energy balance was between -12,600 +/- 10,520 kcal, and correlated with complications (P < 0.001), already after 1 week.

CONCLUSION: Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.
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BACKGROUND AND AIDS: Critically ill patients are frequently hypermetabolic, energy catabolic, and at risk of underfeeding energy balance and outcome in critically ill patients.

METHODS: Prospective observational study in a surgical ICU of a University hospital. Daily energy intake and outcome were recorded. Energy balance was calculated by subtracting energy intake (expressed in kcal or g protein) from energy expenditure (calculated with metabolic cart or indirect calorimetry, expressed in kcal or g protein). Energy balance was expressed as kilocalories per kilogram per day (kcal/kg/d). Energy deficit was defined as negative energy balance and energy excess was defined as positive energy balance. Receiver operating characteristic (ROC) curve analysis was used to determine optimal cut-off values for energy intake and energy balance that were associated with mortality or complications. Univariate analysis was used to determine the correlation between energy balance and outcomes. Multivariate analysis was used to determine the independent correlation between energy balance and outcomes.

RESULTS: Forty-eight patients aged 18 to 80 years were included. Mechanical ventilation lasted 7.8 days. Time to feeding was 3.1+/-2.2 days. Baseline energy delivery was 1080+/-930 kcal/day. Cumulated energy balance was -1.520+/-1.53 kcal/kg. The correlations were also strong with the length of mechanical ventilation, the total number of complications, the infectious complications, the antibiotic days, and the length of ICU stay. Energy deficit was not correlated with mortality. Plasma proteins were not correlated to either of the above variables.

CONCLUSION: Energy intake and energy balance should be further tested. Delaying initiation of nutrition support should be compensated later on.

Figure 1 Progression of energy delivery compared to energy target over 4 weeks: the figure shows that energy delivery increases with time, reducing daily deficit.
Finding the evidence:

ICU stay. The correlations were also strong with the length of mechanical ventilation, the total number of complications, the infectious complications, the antibiotic days, and the length of ICU stay. Energy deficit was not correlated with mortality. Plasma proteins were not correlated to either of the above variables.

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- in the first week there were 148 unfed days out of a possible 336 fed patient-days.
Finding the evidence:

Should I be concerned about *earlier feeding* or the *amount of energy*?

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Amount of Energy

Should I be concerned about earlier feeding or the amount of energy?
Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial


Collaborators (210)

Abstract

CONTEXT: The amount of enteral nutrition patients with acute lung injury need is unknown.

OBJECTIVE: To determine if initial lower-volume trophic enteral feeding would increase ventilator-free days and decrease gastrointestinal intolerances compared with initial full enteral feeding.

DESIGN, SETTING, AND PARTICIPANTS: The EDEN study, a randomized, open-label, multicenter trial conducted from January 2, 2008, through April 12, 2011. Participants were 1000 adults within 48 hours of developing acute lung injury requiring mechanical ventilation whose physicians intended to start enteral nutrition at 44 hospitals in the National Heart, Lung, and Blood Institute ARDS Clinical Trials Network.

INTERVENTIONS: Participants were randomized to receive either trophic or full enteral feeding for the first 6 days. After day 6, the care of all patients who were still receiving mechanical ventilation was managed according to the full feeding protocol.

MAIN OUTCOME MEASURES: Ventilator-free days to study day 28.

RESULTS: Baseline characteristics were similar between the trophic-feeding (n = 508) and full-feeding (n = 492) groups. The full-feeding group received more enteral calories for the first 6 days, about 1300 kcal/d compared with 400 kcal/d (P < .001). Initial trophic feeding did not increase the number of ventilator-free days (14.9 [95% CI, 13.9 to 15.8] vs 15.0 [95% CI, 14.1 to 15.9]; difference, -0.1 [95% CI, -1.4 to 1.2]; P = .89) or reduce 60-day mortality (23.2% [95% CI, 19.6% to 26.9%] vs 22.2% [95% CI, 18.5% to 25.8%]; difference, 1.0% [95% CI, -4.1% to 6.3%]; P = .77) compared with full feeding. There were no differences in infectious complications between the groups. Despite receiving more prokinetic agents, the full-feeding group experienced more vomiting (2.2% vs 1.7% of patient feeding days; P = .05), elevated gastric residual volumes (4.9% vs 2.2% of feeding days; P < .001), and constipation (3.1% vs 2.1% of feeding days; P = .003). Mean plasma glucose values and average hourly insulin administration were both higher in the full-feeding group over the first 6 days.

CONCLUSION: In patients with acute lung injury, compared with full enteral feeding, a strategy of initial trophic enteral feeding for up to 6 days did not improve ventilator-free days, 60-day mortality, or infectious complications but was associated with less gastrointestinal intolerance.

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Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults.


Abstract

BACKGROUND: The appropriate caloric goal for critically ill adults is unclear. We evaluated the effect of restriction of nonprotein calories (permissive underfeeding), as compared with standard enteral feeding, on 90-day mortality among critically ill adults, with maintenance of the full recommended amount of protein in both groups.

METHODS: At seven centers, we randomly assigned 894 critically ill adults with a medical, surgical, or trauma admission category to permissive underfeeding (40 to 60% of calculated caloric requirements) or standard enteral feeding (70 to 100%) for up to 14 days while maintaining a similar protein intake in the two groups. The primary outcome was 90-day mortality.

RESULTS: Baseline characteristics were similar in the two groups: 96.8% of the patients were receiving mechanical ventilation. During the intervention period, the permissive-underfeeding group received fewer mean (±SD) calories than did the standard-feeding group (835±297 kcal per day vs. 1299±467 kcal per day, P<0.001; 46±14% vs. 71±22% of caloric requirements, P<0.001). Protein intake was similar in the two groups (57±24 g per day and 59±25 g per day, respectively; P=0.29). The 90-day mortality was similar: 121 of 445 patients (27.2%) in the permissive-underfeeding group and 127 of 440 patients (28.9%) in the standard-feeding group died (relative risk with permissive underfeeding, 0.94; 95% confidence interval [CI], 0.76 to 1.16; P=0.58). No serious adverse events were reported; there were no significant between-group differences with respect to feeding intolerance, diarrhea, infections acquired in the intensive care unit (ICU), or ICU or hospital length of stay.

CONCLUSIONS: Enteral feeding to deliver a moderate amount of nonprotein calories to critically ill adults was not associated with lower mortality than that associated with planned delivery of a full amount of nonprotein calories. (Funded by the King Abdullah International Medical Research Center; PermiT Current Controlled Trials number, ISRCTN68144908.)
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Enhanced feeding in very-low-birth-weight infants may cause electrolyte disturbances and septicemia—a randomized, controlled trial.


Abstract

**BACKGROUND & AIMS:** High supply of protein and energy has been introduced to very-low-birth-weight infants to improve growth and cognitive development. The aim of this study was to compare two different feeding strategies on postnatal growth and clinical outcome during neonatal hospitalization.

**METHODS:** Fifty very-low-birth-weight infants were randomized to either an enhanced or a standard feeding protocol within 24 h after birth. Chi-square and T-tests were applied.

**RESULTS:** First week protein, fat and energy supply was significantly higher in the intervention group compared to the control group (all $P < 0.001$). After inclusion of 50 patients we observed a higher occurrence of septicemia in the intervention group, 63% vs. 29% ($P = 0.02$), and no more patients were included. The infants in the intervention group demonstrated improved postnatal growth, but they also disclosed significant electrolyte deviations during the first week of life with hypophosphatemia, hypokalemia and hypercalcemia. First week phosphate nadir was lower in the infants experiencing septicemia (1.23 (0.50) mmol/L) as compared to the infants without (1.61 (0.61) mmol/L) ($P = 0.03$).

**CONCLUSION:** Our study implies that enhanced feeding may induce electrolyte imbalances in VLBW infants, and that deleterious side effects similar to those seen in refeeding syndrome may occur. ClinicalTrials.gov, number NCT01103219 and the EudraCT number is 2010-020464-38.

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METHODS: Fifty very-low-birth-weight infants were randomized to either an enhanced or a standard feeding protocol within 24 h after birth. Chi-square and T-tests were applied.

RESULTS: First week protein, fat and energy supply was significantly higher in the intervention group compared to the control group (all P < 0.001). After inclusion of 50 patients we observed a higher occurrence of septicemia in the intervention group, 63% vs. 29% (P = 0.02), and no more patients were included. The infants in the intervention group demonstrated improved postnatal growth, but they also disclosed significant electrolyte deviations during the first week of life with hypophosphatemia, hypokalemia and hypercalcemia. First week phosphate nadir was lower in the infants experiencing septicemia (1.23 (0.50) mmol/L) as compared to the infants without (1.61 (0.61) mmol/L) (P = 0.03).

CONCLUSION: Our study implies that enhanced feeding may induce electrolyte imbalances in VLBW infants, and that deleterious side effects similar to those seen in refeeding syndrome may occur. ClinicalTrials.gov, number NCT01103219 and the EudraCT number is 2010-020464-38.

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PMID: 23043722 [PubMed - indexed for MEDLINE]
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Refeeding hypophosphatemia: a potentially fatal danger in the intensive care unit.

Çoşkun R, Gündoğan K, Baldane S, Güven M, Sungur M

Abstract

AIM: To determine the overall and comparative incidence of refeeding hypophosphatemia (RH) between enteral and parenteral nutrition in general adult intensive care unit (ICU) patients.

MATERIALS AND METHODS: This study was performed as a retrospective analysis. A total of 117 patients who received enteral and parenteral nutrition were included in the study. Demographic characteristics, type of nutrition, daily energy intake, and serum phosphorus levels before and after the initiation of the nutrition were recorded for 7 days.

RESULTS: The mean age of the patients was 65.8 ± 16.7 years. RH was found in 61 patients (52.14%). There was no significant difference in RH with regard to nutrition type (P = 0.756). The duration of the ICU stay was longer in the patients with RH compared with the patients without RH [median: 12 (3-38) and 8.5 (3-41) days, respectively; P = 0.025]. The mortality rate was higher in patients with RH compared with patients without RH (P = 0.037).

CONCLUSION: The incidence of RH was quite high in our medical ICU. The mortality rate and the duration of ICU stay were higher in the patients with RH than those without RH.

PMID: 25558635 [PubMed - indexed for MEDLINE]
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Should I be concerned about *earlier feeding* or the *amount of energy*?
Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials.

Doig GS, Heiges PT, Simpson F, Sweetman EA, Davies AR

Abstract

PURPOSE: To determine whether the provision of early standard enteral nutrition (EN) confers treatment benefits to critically ill patients.

METHODS: Medline and EMBASE were searched. Hand citation review of retrieved guidelines and systematic reviews were undertaken, and academic and industry experts were contacted. Methodologically sound randomised controlled trials (RCTs) conducted in critically ill patient populations that compared the delivery of standard EN, provided within 24 h of intensive care unit (ICU) admission or injury, to standard care were included. The primary analysis was conducted on clinically meaningful patient-oriented outcomes. Secondary analyses considered vomiting/regurgitation, pneumonia, bacteraemia, sepsis and multiple organ dysfunction syndrome. Meta-analyses were conducted using the odds ratio (OR) metric and a fixed effects model. The impact of heterogeneity was assessed using the I² metric.

RESULTS: Six RCTs with 234 participants were analysed. The provision of early EN was associated with a significant reduction in mortality [OR = 0.34, 95% confidence interval (CI) 0.14-0.85] and pneumonia (OR = 0.31, 95% CI 0.12-0.78). There were no other significant differences in outcomes. A sensitivity analysis and a simulation exercise confirmed the presence of a mortality reduction.

CONCLUSION: Although the detection of a statistically significant reduction in mortality is promising, overall trial quality was low, trial size was small, and the findings may be restricted to the patient groups enrolled into included trials. The results of this meta-analysis should be confirmed by the conduct of a large multi-centre trial enrolling diverse critically ill patient groups.
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*There is no evidence from RCTs that demonstrates IF feeding is delayed, ‘catching up’ on caloric intake improves outcome.*
**Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients.**

Villet S¹, Chiolerio RL, Bollmann MD, Revelly JP, Cayeux R N MC, Delarue J, Berger MM.

**Abstract**

**BACKGROUND AND AIMS:** Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. The study aimed at assessing the relationship between energy balance and outcome in critically ill patients.

**METHODS:** Prospective observational study conducted in consecutive patients staying > or = 5 days in the surgical ICU of a University hospital. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means +/- SD, linear regressions between energy balance and outcome variables.

**RESULTS:** Forty eight patients aged 57 +/- 16 years were investigated; complete data are available in 669 days. Mechanical ventilation lasted 11 +/- 8 days, ICU stay 15 +/- 9 was days, and 30-days mortality was 38%. Time to feeding was 3.1 +/- 2.2 days. Enteral nutrition was the most frequent route with 433 days. Mean daily energy delivery was 1090 +/- 930 kcal. Combining enteral and parenteral nutrition achieved highest energy delivery. Cumulated energy balance was between -12,600 +/- 10,520 kcal, and correlated with complications (P < 0.001), already after 1 week.

**CONCLUSION:** Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.
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Conclusions

What should I do to minimise ‘early caloric debt’?
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*IF a patient is fed late, there is no evidence to suggest ‘rapid catching up’ improves outcome. It might cause harm!*
Loose ends

Does the route matter (EN vs. PN)?
Early EN vs Early PN


Trial of the route of early nutritional support in critically ill adults.

Abstract
BACKGROUND: Uncertainty exists about the most effective route for delivery of early nutritional support in critically ill adults. We hypothesized that delivery through the parenteral route is superior to that through the enteral route.

METHODS: We conducted a pragmatic, randomized trial involving adults with an unplanned admission to one of 33 English intensive care units. We randomly assigned patients who could be fed through either the parenteral or the enteral route to a delivery route, with nutritional support initiated within 36 hours after admission and continued for up to 5 days. The primary outcome was all-cause mortality at 30 days.

RESULTS: We enrolled 2400 patients; 2388 (99.5%) were included in the analysis (1191 in the parenteral group and 1197 in the enteral group). By 30 days, 393 of 1188 patients (33.1%) in the parenteral group and 409 of 1195 patients (34.2%) in the enteral group had died (relative risk in parenteral group, 0.97; 95% confidence interval, 0.86 to 1.08; P=0.57). There were significant reductions in the parenteral group, as compared with the enteral group, in rates of hypoglycemia (44 patients [3.7%] vs. 74 patients [6.2%]; P=0.006) and vomiting (100 patients [8.4%] vs. 194 patients [16.2%]; P<0.001). There were no significant differences between the parenteral group and the enteral group in the mean number of treated infectious complications (0.22 vs. 0.21; P=0.72), 90-day mortality (442 of 1184 patients [37.3%] vs. 464 of 1188 patients [39.1%], P=0.40), in rates of 14 other secondary outcomes, or in rates of adverse events. Caloric intake was similar in the two groups, with the target intake not achieved in most patients.

CONCLUSIONS: We found no significant difference in 30-day mortality associated with the route of delivery of early nutritional support in critically ill adults. (Supported by the United Kingdom National Institute for Health Research; CALORIES Current Controlled Trials number, ISRCTN17386141.)
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Collaborators (138)

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    - early PN saves your hospital $3,150 per patient (for every $1 spent, $5 are saved!!)


Conclusions

What should I do to minimise ‘caloric debt’?

- Meta-analysis based on 6 Level II RCTs demonstrates earlier feeding reduces mortality!
- Two major level I RCTs demonstrate that if feeding is started early, the amount of energy delivered over the first week of ICU care does not have an influence on outcome.
- A small RCT in VLBW infants and an observational study in adult critically ill patients suggest more than normal amounts of energy may induce refeeding syndrome.

You should do everything you can to prevent caloric debt by feeding early, at normal conservative rates.

IF a patient is fed late, there is no evidence to suggest ‘rapid catching up’ improves outcome. It might cause harm!