3.1 Nutritional Prescription: Use of Indirect Calorimetry vs. Predictive Equations May 2015

There were no new randomized controlled trials since the 2013 update and hence there are no changes to the following summary of evidence.

2013 Recommendation: *There are insufficient data to make a recommendation on the use of indirect calorimetry vs. predictive equations for determining energy needs for nutrition or to guide when nutrition is to be supplemented in critically ill patients.*

2013 Discussion: It was noted that both the included studies examined the role of Indirect Calorimetry (IC) vs. Equations in unselected, heterogeneous patients. There are no randomized controlled trials of the use of IC in select patients (prolonged stay, obesity, for example). Given the differences in the methodological design of the 2 studies i.e. Singer (2011) used indirect calorimetry to guide supplementation of enteral nutrition with parenteral nutrition whereas Saffle (1990) compared the effectiveness of indirect calorimetry guided enteral nutrition to enteral nutrition guided by Curreri formula, the committee agreed not to combine the two studies in a meta-analysis. Similarly the assignment of values was also not thought to be meaningful because of the heterogeneous nature of the studies. There was no signal of benefit in clinical outcomes in either study and the committee noted the signal for harm associated with the use of indirect calorimetry in the Singer study (increase in length of stay, pneumonia and overall infections). The committee decided that there was insufficient evidence to put forward a recommendation.

2009 Recommendation: *There are insufficient data to make a recommendation on the use of indirect calorimetry vs. predictive equations for determining energy needs for enteral nutrition in critically ill patients*.

2009 Discussion: The committee noted the paucity of data and given the lack of treatment effect and the high costs associated with the use of indirect calorimetry (metabolic carts), despite no safety concerns, no recommendation was put forward.

Semi Quantitative Scoring

Values	Definition	2009 Score	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	0	1
Adequacy of control group	Extent to which the control group presented standard of care (large dissimilarities=1, minor dissimilarities=2, usual care=3)	3	1
Biological Plausibility	Consistent with understanding of mechanistic and previous clinical work (large inconsistencies=1, minimal consistencies=2, very consistent=3)	1	1
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
Low cost	Estimated cost of implementing the intervention listed--a higher score indicates a lower cost to implement the intervention in an average ICU	2	1
Feasible	Ease of implementing the intervention listed--a higher score indicates greater ease of implementing the intervention in an average ICU	0	1
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	3	2

3.1 Nutritional Prescription: Use of Indirect Calorimetry vs. Predictive Equations

Question: Does the use of indirect calorimetry vs. a predictive equation for determining energy needs (enteral nutrition) result in better outcomes critically ill adult patients?

Summary of evidence: There were two level 2 studies reviewed. Saffle 1990 compared the effectiveness of indirect calorimetry guided enteral nutrition to enteral nutrition guided by Curreri formula in burn patients, and Singer 2011 compared indirect calorimetry guided enteral nutrition supplemented with parenteral nutrition to enteral nutrition determined by a weight-based formula with attempts to give parenteral nutrition.

Mortality: The Saffle 1990 study found no differences in hospital mortality between the group that received indirect calorimetry guided enteral nutrition and the group that received enteral nutrition guided by Curreri formula (RR 1.33, 95% CI 0.24, 7.26, p=0.74*). On the other hand, the Singer 2011 study found a significant reduction in hospital mortality in patients that received indirect calorimetry guided enteral nutrition compared to patients that received enteral nutrition determined by a weight-based formula (RR 0.59, 95% CI 0.36, 0.97, p=0.04*). However, the use of indirect calorimetry guided enteral nutrition had no effect on either ICU or 60-day mortality.

Infections: Only the Singer study reported data on infections. Indirect calorimetry compared to weight-based predictive equation was associated with a trend towards an increase in ventilator associated pneumonia (RR 2.00, 95% CI 0.98, 4.06, p=0.06*), and was associated with a significant increase in overall infectious complications (RR 1.85, 95% CI 1.24, 2.76, p=0.002*).

LOS: Only the Singer study reported ICU length of stay, finding that the use of indirect calorimetry compared to predictive equations was associated with a significant increase in ICU length of stay (WMD 5.50, 95% CI 1.09, 9.91, p=0.01*). However, in both studies the use of indirect calorimetry had no effect on hospital LOS (Saffle: WMD 0.30, 95% CI -13.15, 13.75, p=0.97; Singer: WMD 2.00, 95% CI -7.33, 11.33, p=0.67*).

Ventilator days: Only the Singer study reported duration of ventilation and found that the use of indirect calorimetry compared to predictive equations was associated with a significant increase in the duration of ventilation (WMD 5.60, 95% CI 1.18, 10.02, p=0.01*).

Nutritional Outcomes: In the Saffle study, diarrhea, hyperglycemia, electrolyte imbalance did not differ between the two groups. Actual protein intake (grams/day) was significantly higher in the groups receiving enteral nutrition via indirect calorimetry in both the Saffle and Singer studies (respectively WMD 37.00, 95% CI 33.13, 40.87, p<0.00001*; and WMD 23, 95% CI 17.07, 28.93, p<0.00001*).

*p-values calculated using Review Manager

Conclusions:
1) The use of indirect calorimetry compared to predictive equations to meet enteral nutrition needs has no effect on mortality.
2) The use of indirect calorimetry compared to predictive equations as a guide to supplement EN with PN is associated with a significant reduction hospital mortality.
3) The use of indirect calorimetry compared to predictive equations as a guide to supplement EN with PN may be associated with a higher incidence of infections.
4) The use of indirect calorimetry compared to predictive equations as a guide to supplement EN with PN may be associated with a longer ICU length of stay, and duration of ventilation.,
5) The use of indirect calorimetry compared to predictive equations may result in improved nutritional intake.

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 indirect calorimetry vs. predictive equation in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)†		Infections # (%)	
				Indirect Calorimetry	Predictive Equation	Indirect Calorimetry	Predictive Equation
1) Saffle 1990	Burns 47 % TSBA N=49	C.Random: not sure ITT: yes Blinding: no (7)	EN via Indirect calorimetry (IC) vs. Curreri formula	3/26 (12)	2/23 (9)	NR	NR
2) Singer 2011*	Mechanically ventilated critically ill patients (Mixed medical, surgical, trauma) N=130	C.Random: Yes ITT: No Blinding: No (8)	EN via indirect calorimetry with measurements Q48H supplemented with PN and energy delivery adjusted accordingly vs. EN (using 25kcal/kg/day and not readjusted for 14 days). PN attempted to make up shortfall Non isocaloric/isonitrogenous	ICU 16/56 (29) Hospital 16/56 (29) 60-day 24/56 (58)	ICU 17/56 (30) Hospital 27/56 (48) 60-day 29/56 (48)	VAP 18/56 (32) Total 37/56 (66)	VAP 9/56 (16) Total 20/56 (36)

Table 1. Randomized studies evaluating indirect calorimetry vs. predictive equation in critically ill patients (continued)

Study	LOS days		Ventilator days		Cost		Other	
	Indirect Calorimetry	Predictive Equation	Indirect Calorimetry	Predictive Equation	Indirect Calorimetry	Predictive Equation	Indirect Calorimetry	Predictive Equation
1) Saffle 1990	Hospital 48.8 ± 22.9 (26)	Hospital 48.5 ± 24.9 (23)	NR	NR	NR	NR	Diarrhea 34.6 % Hyperglycemia 38.5 % Nausea 26.9 % Electrolyte imbalance 30.8 % Actual calories intake (kcals/day) 3530 ± 134 Actual protein intake (gms/day) 153 ± 7.1	 34.8 % 43.5 % 34.8 % 39.1 % 3490 ± 132 116 ± 6.7
2) Singer 2011	ICU 17.2 ± 14.6 (56) Hospital 33.8 ± 22.9 (56)	ICU 11.7 ± 8.4 (56) Hospital 31.8 ± 27.3 (56)	16.1 ± 14.7 (56)	10.5 ± 8.3 (56)	NR	NR	Energy (kcal/day) 2086 ± 460 Protein (gms/day) 76 ± 16	 1480 ± 356 53 ± 16

C.Random: concealed randomization
† presumed hospital mortality unless otherwise specified
ITT: intent to treat
NR: not reported

( ): mean ± standard deviation (number)

IC: indirect calorimetry