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## Indirect calorimetry versus usual care: a retrospective cohort study.

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## ABSTRACT

**INTRODUCTION:** This is a study evaluating the effect of Indirect calorimetry on the length of stay. The study comprises of the comparison between the use of indirect calorimetry versus usual care in critically ill mechanically ventilated patients with respect to the length of stay in the intensive care unit, and duration of time on ventilator. Patients were divided on basis of their nutrition risk to study the effect of Indirect calorimetry on the length of stay.

**MATERIAL AND METHODS:** This was a retrospective cohort study of 166 mechanical ventilated patients in S .L Raheja Hospital. Data was collected from 83 patients who were mechanically ventilated between January 2019 and November 2019 on whom indirect calorimetry was used to measure energy requirements. This cohort was compared to 83 patients between January 2018 and November 2018 where the energy requirements were calculated with the use of predictive equations. Both groups were matched for age, sex, comorbidities, APACHE score and use of vasopressors.

**RESULTS:** Significant difference in the sicker group of patients was seen in the Length of stay in the intensive care unit. ( $9.23 \pm 8.14$  vs.  $11.52 \pm 5.65$ ,  $p = 0.0034$ ) Patients at risk for malnutrition demonstrated reduced length of time on ventilation as compared to those not at risk. ( $10.2 \pm 11.01$  vs.  $13 \pm 5.87$ ;  $p = 0.0042$ ).

**CONCLUSIONS:** The use of indirect calorimetry may be associated with a lower length of ICU stay among ventilated patients in a reasonably sick group of mixed surgical patients.

**KEY WORDS:** Indirect calorimetry, critical care, mechanical ventilation, energy requirements, APACHE.

## INTRODUCTION

Underfeeding and overfeeding the I.C.U patient can increase the length of stay, nosocomial infections etc. and may contribute to morbidity and mortality [1]. The carbon-dioxide production and oxygen consumption can be measured and used to calculate energy expenditure [2,3]. This is the principle behind the indirect calorimeter (I.C). Very few centers in the world use this monitoring on a regular basis citing expenditure, lack of training, calibration etc [4]. However I.C is the gold standard in clinical settings [5,6]. The alternative to the I.C is to use predictive equations to calculate calorie requirements [7].

However literature in this regards is limited to few observational studies where I.C was compared to predictive equations. There are no studies of the use of indirect calorimetry from India and Nepal. The study comprises of the comparison between the use of indirect calorimetry versus usual care in critically ill mechanically ventilated patients with respect to the length of stay in the intensive care unit, and duration of time on ventilator. The purpose of the study was to evaluate the effect of Indirect calorimetry on the length of stay.

## MATERIAL AND METHODS

This was a retrospective cohort study of 166 patients admitted to the mixed medical and surgical intensive care unit of a tertiary care center in Mumbai, India. Indirect calorimetry was introduced in our unit in December 2018 for regular use before which the energy requirements were calculated on the basis of simple predictive equation of 25 kcal/kg/day [8]. Patients were divided on basis of their nutrition risk.

83 mechanically ventilated patients (group A) between January 2019 and November 2019 on whom indirect calorimeter was used to measure calorie requirements were compared to 83 matched historical controls (group B) where calorie requirements were based on simple predictive equations. Indirect calorimetry to estimate the total energy expenditure per day was done by using the E-sCOVX module in Carescape R860 ventilator from GE Healthcare. The entire study was done by extracting data from hospital information systems and from chart reviews where applicable. The demographics of the patients are shown as per table 1. All patients were managed as per standard routine protocols of usual ICU management. Indirect calorimetry taken once every 48 hours and nutrition was provided as per the value measured. Proteins for all patients were provided at 1.5 g/kg body weight. Patients with contraindications for indirect calorimetry namely with high oxygen requirements more than 60 %, peep more than 12, and patients with intercostal drainage were excluded from the study. These patients were further subclassified into three groups based on APACHE II (acute physiology and chronic health evaluation) scores 0-15, 15-23 and more than 23 to study them separately as per their severity as shown in table 2. These Further patients who were diagnosed with and without sepsis or septic shock were studied separately. Those at risk for malnutrition classified by either one of the Nutrition risk screening tool 2002 or the NUTRIC score were further studied. The outcome studies for all the groups were the length of intensive care unit stay(LOS-ICU) and the duration of mechanical ventilation in days(LOS on ventilator).

Software-SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for statistics. Mann Whitney U test and Chi score test were used appropriately and  $p < 0.05$  was considered to be statistically significant.

## RESULTS

Results are summarized in tables 3 to 7. Those patients whose APACHE II scores were between 15 to 23 had reduced length of ICU stay ( $9.23 \pm 8.14$  vs  $11.52 \pm 5.65$  with  $p$  value = 0.0034) and this result was statistically significant. The results in the rest of the APACHE II score groups (i.e less than 15 and more than 23) did not reach statistical significance as shown in table 3. Also there was no relation to duration of mechanical ventilation (table 3).

**Table 1.** Patient demographics.

Parameters	Group A (83)	Group B(83)
age	54 $\pm$ 12	55 $\pm$ 14
<b>Apache score</b>		
0-15	19	19
15-23	44	44
Above 23	20	23
At risk for malnutrition	40	47
<b>Reason for admission</b>		
Sepsis	48	49
Diagnosis other than sepsis	35	37
COPD	12	10
Stroke	8	12
IHD	15	15
<b>Comorbidities</b>		
Diabetes mellitus	48	46
Hypertension	44	42
COPD	12	10
IHD	15	15

**Table 2.** Distribution as per APACHE scores.

APACHE Score	With Indirect Calorimetry	Without Indirect Calorimetry	p-value*
5-14	19	19	
15-23	44	44	0.925
Over 24	20	23	

\*Calculated using chi-square test.  $P < 0.05$  considered statistically significant

**Table 3.** Comparisons of length of stay in ICU and duration on ventilator with respect to the APACHE scores.

APACHE Score	With Indirect Calorimetry		Without Indirect Calorimetry		p-value*
	Mean ± SD	Range	Mean ± SD	Range	
<b>LOS on ventilator</b>					
5-14	4.79 ± 2.90	1 – 12	5.32 ± 3.92	2 – 16	0.968
15-23	5.11 ± 3.55	2 – 20	5.36 ± 3.54	1 – 16	0.689
Over 24	3.95 ± 2.14	2 – 10	5.0 ± 2.61	2 – 11	0.159
<b>LOS in ICU</b>					
5-14	9.21 ± 4.86	2 – 18	9.47 ± 4.61	5 – 18	0.944
15-23	9.23 ± 8.14	2 – 50	11.52 ± 5.65	3 – 26	<b>0.003</b>
Over 24	8.25 ± 5.98	2 – 20	8.91 ± 4.47	3 – 18	0.368

\*Calculated using the Mann Whitney U test.  $P < 0.05$  considered statistically significant

**Table 5.** Patients with diagnosis of sepsis and septic shock.

APACHE Score	With Indirect Calorimetry		Without Indirect Calorimetry		p-value*
	Mean ± SD	Range	Mean ± SD	Range	
<b>LOS on ventilator</b>					
5-14	12.0 ± 5.61	5 – 18	10.62 ± 4.99	5 – 18	0.803
15-23	10.45 ± 9.27	2 – 50	11.70 ± 5.97	4 – 26	0.090
Over 24	7.25 ± 5.71	2 – 20	8.69 ± 4.39	3 – 18	0.246
<b>LOS in ICU</b>					
5-14	6.40 ± 3.97	3 – 12	6.0 ± 4.49	2 – 16	0.697
15-23	5.71 ± 3.85	2 – 20	5.10 ± 3.21	1 – 14	0.646
Over 24	4.08 ± 2.5	2 – 10	4.63 ± 2.36	2 – 11	0.401

\*Calculated using the Mann Whitney U test.  $P < 0.05$  considered statistically significant

**Table 5.** Patients without diagnosis of sepsis and septic shock.

APACHE Score	With Indirect Calorimetry		Without Indirect Calorimetry		p-value*
	Mean ± SD	Range	Mean ± SD	Range	
<b>LOS on ventilator</b>					
5-14	8.21 ± 4.35	2 – 15	7.0 ± 2.45	5 – 11	0.652
15-23	6.31 ± 3.07	3 – 13	11.38 ± 5.49	3 – 20	<b>0.003</b>
Over 24	9.75 ± 6.45	2 – 20	9.43 ± 4.96	5 – 18	0.905
<b>LOS in ICU</b>					
5-14	4.21 ± 2.33	1 – 9	3.83 ± 1.72	2 – 6	0.803
15-23	3.69 ± 2.25	2 – 10	5.58 ± 3.84	2 – 16	0.162
Over 24	3.75 ± 1.58	2 – 6	5.86 ± 3.13	2 – 10	0.223

\*Calculated using the Mann Whitney U test.  $P < 0.05$  considered statistically significant

**Table 6.** Patients at risk for malnutrition.

APACHE Score	With Indirect Calorimetry		Without Indirect Calorimetry		p-value*
	Mean ± SD	Range	Mean ± SD	Range	
<b>LOS on ventilator</b>					
5-14	8.17 ± 5.12	2 – 17	8.86 ± 4.95	5 – 18	0.944
15-23	10.20 ± 11.01	3 – 50	13.08 ± 5.87	5 – 26	<b>0.004</b>
Over 24	8.79 ± 6.3	2 – 20	9.27 ± 4.54	3 – 18	0.542
<b>LOS in ICU</b>					
5-14	4.0 ± 2.19	1 – 7	4.86 ± 3.98	2 – 12	0.944
15-23	4.95 ± 3.36	2 – 12	6.60 ± 3.71	2 – 16	0.074
Over 24	3.79 ± 1.63	2 – 6	4.73 ± 2.40	2 – 10	0.337

\*Calculated using the Mann Whitney U test.  $P < 0.05$  considered statistically significant

**Table 7.** Patients not at risk for malnutrition.

APACHE Score	With Indirect Calorimetry		Without Indirect Calorimetry		p-value*
	Mean ± SD	Range	Mean ± SD	Range	
<b>LOS on ventilator</b>					
5-14	5.15 ± 3.18	1 – 12	5.58 ± 4.03	2 – 16	0.826
15-23	5.25 ± 3.77	2 – 20	3.74 ± 2.58	1 – 11	0.080
Over 24	4.33 ± 3.20	2 – 10	5.50 ± 3.07	2 – 11	0.368
<b>LOS in ICU</b>					
5-14	9.69 ± 4.87	2 – 18	9.83 ± 4.59	5 – 18	0.976
15-23	8.42 ± 4.70	2 – 22	9.47 ± 4.75	3 – 20	0.430
Over 24	7.0 ± 5.48	2 – 16	8.25 ± 4.56	4 – 18	0.478

\*Calculated using the Mann Whitney U test.  $P < 0.05$  considered statistically significant

Statistically significant results were also seen in the subgroup of patients who did not have sepsis and septic shock (6.31 +/- 3.07 vs 11.38 +/- 5.49 with p value= 0.0031) as shown in table 5. No such findings were seen in those patients who had sepsis and septic shock as seen in table 4. The same category of patients with APACHE II scores between 15 and 23 who were at risk for malnutrition were also noted to have a reduced length of ICU stay and this reached statistical significance (10.2 +/- 11.01 vs 13.08 +/- 5.87 with p value =0.0042) as shown in table 6. No such results were seen in the group who were not at risk for malnutrition as seen in table 7.

## DISCUSSION

Predictive equations are used worldwide in calculation of energy requirements as they are readily available, easy to perform and do not require trained personnel or equipment. However these equations are only population based estimates with subjectivity in the application of stress factors with a direct relationship to the body weight which thus are known to give wrong estimates in underweight and overweight patients [7].

Indirect calorimetry has not been extensively used in world citing reasons like need for calibration, training required, expenditure etc [9,10]. Even though indirect calorimetry is considered the gold standard the evidence to conclusively prove the effectiveness has been really sparse and not been robust. In face there is no evidence that indirect calorimetry directly has any impact on duration of mechanical ventilation and length of stay in the ICU [11].

This study showed that in a certain category of patients, especially those that are reasonably sick (APACHE II between 15 and 23) may benefit with the use of indirect calorimeter in reducing the number of days in the ICU which would thus mean immense cost savings. In the authors institute and in many institutes around the world the majority of patients admitted to the ICU are between APACHE II scores between 15 and 23 and thus the study results are of immense value. However it is not apparent as to why this relationship did not exist in the severest of the patients (i.e. APACHE II scores > 23) where the non operative mortality is upto 51% [12]. However since indirect calorimetry directly measures the resting energy expenditure and helps in personalizing our nutrition charting the potential role of this modality cannot be overlooked especially so because the alternative method which involves predictive equations are known to result in underfeeding and overfeeding which can lead to adverse outcomes [13,14].

Our study is not without few limitations. The retrospective nature of the study, small sample size and the fact that this was a study done in a single center may be some of the limitations of the study. Nevertheless this may add to the body of evidence emphasizing the importance of personalizing critical care nutrition via indirect calorimetry.

## CONCLUSIONS

This study shows that the use of calorimetry can help shorten the duration of stay by a significant number of days in a group of reasonably sick mechanically ventilated patients. This gives impetus to conduct larger more conclusive studies to prove the effectiveness of this form of measurement of energy expenditure. Prospective multicenter, large randomized controlled trials are awaited in this regards.

## SUPPLEMENTARY INFORMATION

**Funding:** No fund was received related to this study.

**Institutional Review Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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