

**DETERMINING THE BEST PREDICTIVE
EQUATION FOR RESTING ENERGY
EXPENDITURE AMONG MECHANICALLY
VENTILATED CRITICALLY ILL PATIENTS IN A
MALAYSIAN TERTIARY HOSPITAL**

BY

KHAIRUL ANAM BIN MANSOR

A dissertation submitted in fulfilment of the requirement
for the degree of Master of Medicine (Anaesthesiology)

Kulliyyah of Medicine
International Islamic University Malaysia

NOVEMBER 2020

ABSTRACT

Introduction: Measurement of resting energy expenditure using indirect calorimetry in intensive care unit patient is the gold standard as recommended by guidelines. Unfortunately, technical difficulties and high cost prevent its widespread adoption by medical facilities. Predictive equations are largely used instead. We aim to validate commonly used predictive equation at different period of acute phase of critical illness.

Methods: Patients hospitalized from November 2019-August 2020 in a general ICU of Sultan Ahmad Shah Medical Center, a university affiliated, tertiary care hospital who had been ventilated with GE Carescape R860 to assess caloric targets were included. Measurement was done up to 3 times per day from day 1 of ICU admission to day 7 of ICU admission. Equation performance was assessed by comparing means, standard deviations, correlation, concordance and agreement, which was defined as a measurement within 90-110% of measured REE by indirect calorimetry. A total of 18 equations was evaluated.

Results: A total of 49 patients were recruited. Mean patient age was 63 years, 63.6% were male and 90.9% were Malay ethnic. Medical admission comprises of 69.7% of patients category. The mean of REE as measured by IC was 1176 ± 332 kcal during early acute phase and 1222 ± 321 kcal during late acute phase. There was no significant difference of REE during the two acute phases of critical illness. During acute phase, the Mifflin-St. Jeor have the highest accuracy (33.33%) but no agreement. In the late acute phase, WHO predictive equation shows the highest accuracy but poor agreement with IC. The Mifflin-St. Jeor equation demonstrates the second highest accuracy and moderate agreement with IC. None of the predictive equations have level of accuracy of more than 50% across both phases. Lack of sample size due to COVID-19 pandemic and technical issues affect the overall result of this study.

Conclusions: From this study, no predictive equation can be recommended during the early acute phase of critical illness. The Mifflin-St. Jeor can be recommended to be used in late acute phase of critically ill patients. This predictive equation include static variables of height, weight and age. Incorporation of dynamic variables such as maximum temperature, minute ventilation does not increase the accuracy of predictive equation such as Faisy and Ireton-Jones. Recommendations cannot be concluded due to lack of sample size.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion, it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Medicine(Anaesthesiology)

.....
Mohd Basri Bin Mat Nor
Supervisor

.....
Azrina Binti Md Ralib
Co-Supervisor

.....
Mohd Nizamuddin Bin Ismail
Co-Supervisor

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Medicine(Anaesthesiology)

.....
Nur Fariza Binti Ramly
Examiner

This dissertation was submitted to the Department of Anaesthesiology and is accepted as a partial fulfilment of the requirements for the degree of Master of Medicine(Anaesthesiology)

.....
Abdul Hadi Bin Mohamed
Head,
Department of Anaesthesiology

This dissertation was submitted to the Kulliyah of Medicine and is accepted as a partial fulfilment of the requirements for the degree of Master of Medicine(Anaesthesiology)

.....
Azmi Bin Md Nor
Dean, Kulliyah of Medicine

DECLARATION

I hereby declare that this thesis is the result of my own investigation, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other institutions.

Khairul Anam Bin Mansor

Signature.....

Date

INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA

**DECLARATION OF COPYRIGHT AND AFFIRMATION
OF FAIR USE OF UNPUBLISHED RESEARCH**

**DETERMINATING THE BEST PREDICTIVE EQUATION FOR RESTING
ENERGY EXPENDITURE AMONG MECHANICALLY VENTILATED
CRITICALLY ILL PATIENTS IN MALAYSIA TERTIARY HOSPITAL**

I declare that the copyright holder of this thesis/dissertation is International Islamic University Malaysia.

Copyright ©2020 by International Islamic University Malaysia. All rights reserved.

No part of this unpublished research may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise without prior written permission of the copyright holder except as provided below.

1. Any material contained in or derived from this unpublished research may be used by others in their writing with due acknowledgement.
2. IIUM or its library will have the right to make and transmit copies (print or electronic) for institutional and academic purposes.
3. The IIUM library will have the right to make, store in a retrieval system and supply copies of this unpublished research if requested by other universities and research libraries.

By signing this form, I acknowledged that I have read and understand the IIUM Intellectual Property Right and Commercialization policy.

Affirmed by Khairul Anam Bin Mansor

.....
Signature

.....
Date

ACKNOWLEDGEMENT

All glory is due to Allah, the Almighty, whose Grace and Mercies have been with me throughout the duration of my programme. Although, it has been tasking, His Mercies and Blessings on me ease the herculean task of completing this thesis.

I am most indebted to my supervisor, Prof. Dr. Mohd Basri Bin Mat Nor, whose enduring disposition, kindness, promptitude, thoroughness and friendship have facilitated the successful completion of my work. I put on record and appreciate his detailed comments, useful suggestions and inspiring queries which have considerably improved this thesis. His brilliant grasp of the aim and content of this work led to his insightful comments, suggestions and queries which helped me a great deal. Despite his commitments, he took time to listen and attend to me whenever requested. The moral support he extended to me is in no doubt a boost that helped in building and writing the draft of this research work.

I am also grateful to my co-supervisors, Asst. Prof. Dr. Mohd Nizamuddin Bin Ismail, whose support and cooperation contributed to the outcome of this work. I wish to express my personal gratitude to Dr. Muhammad Adil Bin Zainal Abidin from the Department of Community Medicine IIUM for guiding me through my analysis. To my brother in Islam, Dr. Saeed Samiullah, thank you for helping me throughout my journey in completing these thesis.

Above all, my deepest appreciation goes to my family, Mansor Bin Jaffar, Nor Azma Binti Ariffin, Khairul Asyraf Bin Mansor and especially to my dear compassionate wife Syifa Binti Zainal Azhar. Her understanding, patience, and encouragement made this book possible. Lastly, my gratitude goes to my beloved daughters, Marwa Binti Khairul Anam and Medina Binti Khairul Anam, for their prayers, understanding and endurance while away. Once again, we glorify Allah for His endless mercy on us one of which is enabling us to successfully round off the efforts of writing this dissertation. Alhamdulillah.

TABLE OF CONTENTS

Abstract	ii
Approval Page.....	iii
Declaration	iv
Acknowledgement	vi
Table of Contents	vii
List of Tables	ix
List of Figures	x
List of Abbreviations	Error! Bookmark not defined.

CHAPTER ONE: INTRODUCTION**ERROR! BOOKMARK NOT DEFINED.**

1.1 BACKGROUND OF THE STUDY	1
1.2 MALNUTRITION IN ICU.....	2
1.3 INDIRECT CALORIMETRY	2
1.4 PREDICTIVE EQUATION	2
1.5 STATEMENT OF THE PROBLEM.....	3
1.6 PURPOSE OF THE STUDY.....	4
1.7 RESEARCH OBJECTIVES	4
1.7.1 Specific objectives	4
1.8 RESEARCH QUESTIONS	5
1.9 THEORETICAL FRAMEWORK.....	5
1.10 SIGNIFICANCE OF THE STUDY	5
1.11 LIMITATIONS OF THE STUDY	6
1.12 DEFINITIONS OF TERMS	6
1.12.1 Critically ill	6
1.12.2 Resting energy expenditure.....	6
1.12.3 Indirect calorimetry	7
1.12.4 Predictive equations	7
1.13 CHAPTER SUMMARY	7

CHAPTER TWO: LITERATURE REVIEW.....**8**

2.1 INTRODUCTION	8
2.2 DIFFERENCES OF REE BETWEEN INDIVIDUAL	8
2.3 REE IN DIFFERENT PHASES OF ILLNESSES	9
2.4 REE IN ELDERLY	9
2.5 REE IN CRITICALLY ILL	10
2.6 REE IN PATIENTS WITH CHRONIC CONDITION	10
2.7 REE IN WOMEN	11
2.8 ACCURACY OF PREDICTIVE EQUATIONS.....	11
2.9 INDIRECT CALORIMETRY AS THE GOLD STANDARD.....	13
2.10 TECHNICAL CONCEPTS OF INDIRECT CALORIMETRY	14
2.11 PRACTICAL CONDITION TO USE INDIRECT CALORIMETR	15
2.11.1 Patients	15
2.11.2 Treatments.....	15
2.12 GUIDELINES AND RECOMMENDATIONS	16

2.13 CHAPTER SUMMARY	16
CHAPTER THREE: METHODOLOGY.....	18
3.1 INTRODUCTION	18
3.2 RESEARCH DESIGN.....	18
3.3 RECRUITMENT AND CONSENT.....	18
3.4 WITHDRAWAL OF PARTICIPANTS FROM STUDY	19
3.5 EXCLUSION CRITERIA	19
3.6 DATA COLLECTION	19
3.7 RESEARCH TOOLS	20
3.8 STUDY PROTOCOL.....	23
3.9 SAMPLE SIZE	27
3.10 INFORMED CONSENT AND INFORMATION SHEET	27
3.11 STATISTICAL ANALYSIS	28
3.12 CHAPTER SUMMARY	29
CHAPTER FOUR: RESULTS AND ANALYSIS	30
4.1 INTRODUCTION	30
4.2 BACKGROUND CHARACTERISTICS OF PATIENTS AT BASELINE	33
4.3 COMPARISON BETWEEN REE IC AND REE PREDICTIVE EQUATIONS	35
4.4 COMPARISON OF MEANS BETWEEN REE-IC AND REE PREDICTIVE EQUATIONS	40
4.5 CORRELATION ANALYSIS	43
4.6 CHAPTER SUMMARY	46
CHAPTER FIVE: DISCUSSIONS	47
5.1 INTRODUCTION	47
5.2 ACCURACY AND AGREEMENT.....	48
5.3 OVERESTIMATION AND UDERESTIMATION	49
5.4 STRENGTH	50
5.5 LIMITATIONS.....	50
5.6 CONCLUSION	50
REFERENCES.....	52
APPENDIX A: INFORMED CONSENT	56
APPENDIX B: CASE REPORT FORM	60
APPENDIX C: KULIYYAH RESEARCH COMMITTEE APPROVAL	65
APPENDIX D: IREC APPROVAL	66

LIST OF TABLES

Table 1.1 Studies Done on Predictive Equation Accuracy	12
Table 3.1 Predictive Equations Evaluated	23
Table 4.1 Demographic and Clinical Characteristics of Patients	33
Table 4.2 Proportions of Accuracy, Underestimation and Overestimation of The REE-PEs Compared with REE-IC During Early Acute Phase	35
Table 4.3 Proportions of Accuracy, Underestimation and Overestimation of The REE- PEs Compared with REE-IC During Late Acute Phase	37
Table 4.4 Comparison of Means Between REE-IC and REE PEs and Their p value	40
Table 4.5 Correlation Analysis by Intraclass Correlation Coefficient for REE-IC and REE-PEs.	43

LIST OF FIGURES

Figure 1.1 Diagram Describing Association Between REE and TEE	5
Figure 2.1 Degree of Under Prescription and Over Prescription of Energy Needs Among All Reviewed Predictive Equations	13
Figure 2.2 Schematic Diagram Showing The Connection of Calorimeter to A Mechanically Ventilated Patient	15
Figure 3.1 GE Carescape R860	21
Figure 3.2 Spirometry Module E-SCAIOV	21
Figure 3.3 Water Trap D-Fend	22
Figure 3.4 Spirometry Kit	22
Figure 3.5 Endotracheal Tube	22
Figure 4.1 CONSORT Flow Diagram for Patients Recruitment and Measurement	32

LIST OF ABBREVIATIONS

ICU	Intensive Care Unit
REE	Resting Energy Expenditure
TEE	Total Energy Expenditure
IC	Indirect Calorimetry
REE-IC	Resting Energy Expenditure Measured by Indirect Calorimetry
REE-PE	Resting Energy Expenditure Estimated by Predictive Equation
BW	Body Weight
IBW	Ideal Body Weight
AdjBW	Adjusted Body Weight
BMI	Body Mass Index
ht	Height
wt	Weight
APACHE II	Acute Physiology and Chronic Health Disease Classification System II
SOFA	Sequential Organ Failure Assessment
mNUTRIC	Modified Nutrition Risk in Critically Ill
Ve	Minute Ventilation
Tmax	Daily Maximal Temperature
MSJ	Mifflin-St. Jeor
PSU	Penn State University
HB	Harris-Benedict
IMNA	Institute of Medical of. National Academies

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Nutritional therapy is an important component of managing critically ill patients and have been accepted as part of standard care in intensive care unit (ICU). What was once known as nutritional support have been shown to positively impact patient's morbidity and mortality while being relatively inexpensive and available for doctors in different settings and level of healthcare. Efforts have been made to study nutrition as therapy, and from there we are beginning to understand its true potential in modern medicine. The full benefit however can only be achieved when the therapy is tailored to the individual, using individual resting energy expenditure to target caloric feeding (Waele & Honore, 2018). Achieving individual optimal target calorie and protein intake has been associated with reduction in mortality of critically ill patient and a ratio of 70% survival advantage (Waele & Honore, 2018). Nutritional therapy is indeed part of 'medication' for treatment.

Nutritional therapy can be prescribed by enteral or parenteral feeding. When prescribing enteral or parenteral feeding, measured or predicted resting energy expenditure (REE) is the parameter used to determine the amount of feeding. REE is the largest component of total energy expenditure (TEE) in hospitalized patient, more so in critically ill patient as most of them are bed bound, mechanically ventilated or sedated in ICU.

1.2 MALNUTRITION IN ICU

Malnutrition (include both under and overfeeding) is common in critically ill patients and have been associated with poor clinical outcome (Zusman et al., 2016). Reports of the rate of malnutrition differed according to geographical, patient population and assessment tools. An international, multicenter study involving 26 countries reports that majority of critically ill patients did not manage to get adequate intake of nutrition (define as >80% requirement). In Asia region, 82% was reported to received iatrogenic underfeeding in 2015, compared with 57% in Europe and South Africa (Heyland, Dhaliwal, Wang & Day, 2015). A study by Yip et al (Yip, Rai & Wong, 2014) regarding prevalence of underfeeding of critically ill patients in a Malaysian ICU shows 66% achieved 80% of caloric requirement within 3 days of ICU stay.

1.3 INDIRECT CALORIMETRY

Indirect calorimetry is the gold standard, the most precise way to determine resting energy expenditure in critically ill patient in ICU (Schlein & Coulter, 2014). It is suggested that to determine resting energy expenditure, indirect calorimetry is to be used when available (McClave et al., 2016). Despite this recommendation, its usage still limited worldwide and not routinely used. The complexity and the high cost of equipment have disrupted their adoption around the world in spite of its value for wide range of patients (Oshima et al., 2017).

1.4 PREDICTIVE EQUATION

Predictive metabolic rate equation is an alternative way to estimate resting energy expenditure in the absence of indirect calorimetry. Its accuracy however is varied from 30% up to 80%. Multiple guidelines have recommended the usage of predictive

equation to guide nutritional therapy in critically ill patients if indirect calorimetry not available (McClave et al., 2016).

1.5 STATEMENT OF THE PROBLEM

Nutritional therapy is highly dependent on accurate measurement of REE using indirect calorimetry or prediction of REE using equations, as underfeeding or overfeeding can lead to increase morbidity and mortality. Indirect calorimetry however is not widely available to be used by clinicians in Malaysian ICU.

Meanwhile, predictive equations have been shown to be limited by severity and phase of illness, interindividual variabilities of bodies composition, rate of metabolism, gender and age. Despite this limitation, degrees of accuracy up to 80% can still be obtained. This however is limited by studies done on western population. In Malaysia, previously study done to assess the accuracy of predictive equation. It is however among the healthy volunteer, and not representative of ICU patient which is critically ill.

1.6 PURPOSE OF THE STUDY

As the determination of accurate REE will influence the quality of nutritional therapy, multiple studies have been done to find out the best predictive equations for it. Ismail (Ismail et al., 1998) have conducted studies to determine best predictive equation using healthy volunteer among Malaysia. ICU patients however is a critically ill population with deranged physiology compared to healthy population. As nutritional therapy is used extensively in ICU, it is important to investigate the accuracy of predictive equations in critically ill population as they have deranged physiology compared to healthy population. Deranged physiology will lead to altered REE. This difference is affected by severity and acuteness of diseases, rate of metabolism and drugs. The purpose of these study is to explore the best predictive equation to be used in critically ill patients in ICU of Malaysian population.

1.7 RESEARCH OBJECTIVES

General objectives of this study are to assess the best predictive equation in critically ill patients against indirect calorimetry during early acute and late acute phase.

1.7.1 Specific objectives

To find out accuracy and correlations of predictive equations in comparison to indirect calorimetry in critically ill patients based on ASPEN definition (Singer et al., 2019) on

- a. Early acute phase, defined as day 1 to 2
- b. Late acute phase, defined as day 3 to 7

1.8 RESEARCH QUESTIONS

- a. Which predictive equations have the highest accuracy and agreement in critically ill patient?
- b. Does early acute and late acute phase of illness have different best predictive equation?

1.9 THEORETICAL FRAMEWORK

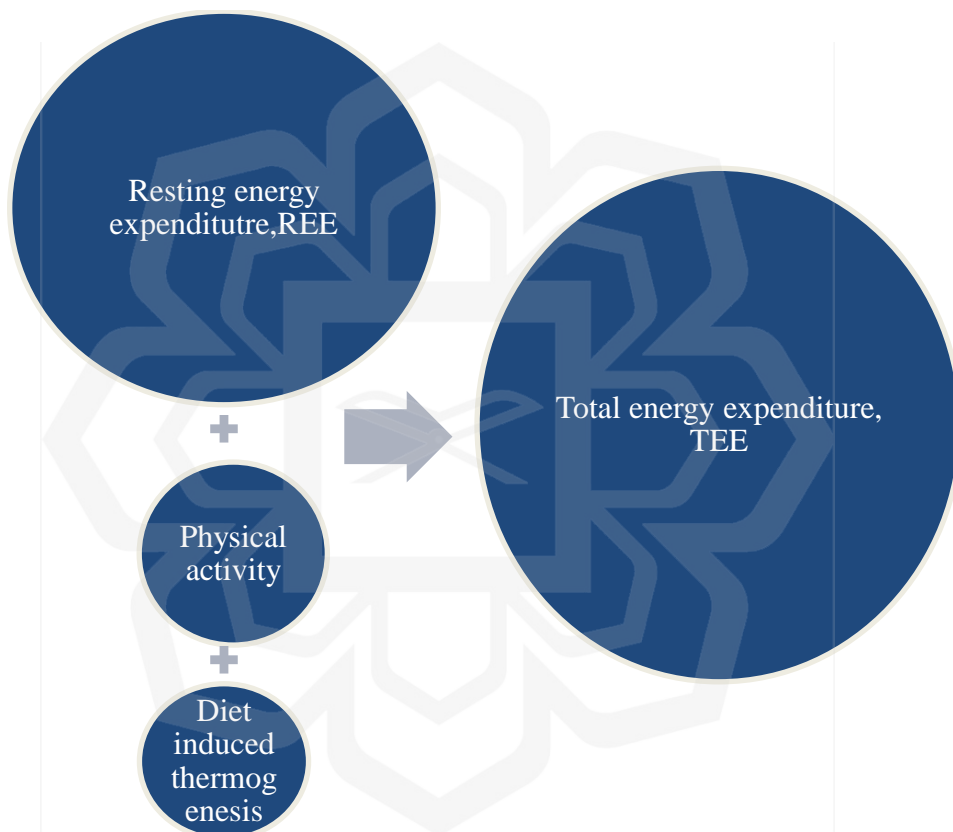


Figure 1.1 Diagram describing association between REE and TEE

1.10 SIGNIFICANCE OF THE STUDY

This study hopes to help guide the clinicians in Malaysian ICU in providing their patients with nutrition especially in settings where indirect calorimetry is not always available.

Despite indirect calorimetry is the gold standard for determination of energy requirement, it is not widely available for clinicians in Malaysian ICU. By using best predictive equations suited to the patient, we can aim for more accurate energy requirement. More accurate energy requirement determination will reduce patient mortality and morbidity rate, and length of stay in ICU by improving the effectiveness of nutritional therapy.

1.11 LIMITATIONS OF THE STUDY

The study sample was limited to patients admitted to intensive care unit of Sultan Ahmad Shah Medical Center. This study was confined to intubated patient, ventilated with GE Carescape R860 with indirect calorimetry module installed. The time scope of the study is between November 2019 till August 2020. The subject of the study comprised patients age more than 18, ventilated with GE Carescape R860 and BMI \leq 35. The population of patients was 49.

1.12 DEFINITIONS OF TERMS

1.12.1 Critically ill

Patients who are in severe respiratory, cardiovascular or neurological derangement, usually in combination, where the derangement is reflected in abnormal physiological observations.

1.12.2 Resting energy expenditure

Resting energy expenditure is body metabolism during a time period of steady resting conditions that are defined by a combination of assumptions of physiological

homeostasis and biological equilibrium. REE includes activities needed to sustain life, such as respiration, circulation, and body temperature.

1.12.3 Indirect calorimetry

A technique used to measure energy expenditure in critically ill patients which are mechanically ventilated, by measuring gaseous O² consumption and CO² production and using Weir's equation. Multiple conditions have to be fulfilled in order to ensure the energy measured is a resting energy expenditure.

1.12.4 Predictive equations

Equations developed to estimate individuals resting energy expenditure by using static variables and/or dynamic variables such as temperature, minute ventilations.

1.13 CHAPTER SUMMARY

This chapter provides the reader with an insight into nutritional therapy as part of management in ICU. This chapter also provides information on the purpose of the study, the research objectives, the research questions and also the significance of the study. Finally, this chapter outlines the theoretical framework of this study.

CHAPTER TWO

LITERATURE REVIEW

2.1 INTRODUCTION

Accurate estimation of energy expenditure is important for nutritional therapy. The most widely available and literally costless method is by using predictive equations. Hundreds of predictive equations have been developed. Generally, they can be divided into three groups. First group, formulas based on static variables (e.g. height, weight, gender) only e.g. Harris-Benedict, Fusco, Mifflin. Second group, formulas in which dynamic variables (e.g. body temperature, tidal and minute volume) was taken into account, reflecting their metabolism state e.g. Penn State, Swinamer, Faisy. Third group, formulas that adapt patient's pathology (e.g. burn, trauma) and type of patient (e.g. obesity). Examples of this include Ireton-Jones (Spapen et al., 2014).

2.2 DIFFERENCES OF REE BETWEEN INDIVIDUAL

Each individual has different percentage of visceral, muscle and fat tissues. As each tissue use different amount of energy, this leads to error in REE predicted. Different gender will have different composition of tissues types. Person with the same gender, height and weight as well will have variable composition of tissues (Wang, Heshka, Heymsfield, Shen & Gallagher, 2005). Increasing BMI is shown to reduce physician's accuracy in estimating requirement (De Waele & Honore, 2016). Even if bodies composition is known, genetic factor will play a role as different individual have different metabolism rate.

Trauma and disease will cause hypermetabolism. Trauma can increase EE up to twice the REE due to the hypermetabolism that occurs. Disease such as

hyperthyroidism will greatly increase REE. The metabolic response to stress include sequential changes in energy expenditure, stress hyperglycemia, changes in body composition, and psychological and behavioral problems (Preiser et al., 2015) . Taking these factors when predicting REE also cannot be simply done as we need to take into account their severity and time lapse. Hypermetabolism cause by trauma usually will peak between week 1 and 2 and begin to wean to about half.

All these factors influencing REE is not reflected by every predictive equation. And thus, reducing their accuracies. Individual optimization of nutritional therapy will be difficult(Oshima et al., 2016).

2.3 REE IN DIFFERENT PHASES OF ILLNESSES

Critical illness has different phases, usually described as ‘ebb’ and ‘flow’ phase. The ‘ebb’ phase includes hyperacute early phase of hemodynamic instability during which patient admitted to ICU. The ‘flow’ phase meanwhile follows the period after that with metabolic instability and catabolism and later period of anabolism. The acute phase can be divided into two periods: the early period, the ‘ebb’ phase and the late period, the ‘flow’ phase. ASPEN further divide the acute phase into early acute and late acute (Singer et al., 2019). The early acute phase is defined as day 1 to day 2 while the late acute phase is defined as day 3 to day 7.

2.4 REE IN ELDERLY

Aging cause physiological changes in the body. There will be decline at a rate of 1-2% per decade after the second decade of life for. Resting energy expenditure (Wang et al., 2005). This could be account due to decline in. Both the mass and cellular fraction of tissues and organs. The fat free mass particularly declines as people get older. The

changes occur despite body weight remain unchanged. The applicability and accuracy of commonly used REE equations among have been investigated before. For example, study done among octogenarian Swedish man found out that Mifflin-St. Jeor is the most accurate equation (Karlsson et al., 2017).

2.5 REE IN CRITICALLY ILL

A severely ill patients undergoes dynamic changes during its course of illness. The changes are the consequences of prolonged bed rest, atrophy of the metabolically active lean tissue, stress and effect of medications e.g. inotropes, sedatives, neuromuscular blocking agent (Finnerty, Mabvuure, Kozar & Herndon, 2013). Even therapies such as mechanical ventilation, renal replacement therapies and liver support therapies can modify the resting energy expenditure. Due to these dynamic changes throughout patient treatment in ICU, IC measurement is recommended to be repeated to define energy target.

2.6 REE IN PATIENTS WITH CHRONIC CONDITION

Chronic conditions and their treatments can alter lean body mass and the level of physical activity, both of this will in turn alter the resting energy expenditure (Oshima et al., 2016). Respiratory diseases like COPD and cystic fibrosis will increased respiratory effort and enhanced the level of activity. Metabolic diseases such as thyroid and adrenal gland can change the level of metabolism by altering the hormonal activity. Muscle diseases can reduce the REE by disuse or atrophy of the muscles. Presence of seizure can increase the muscle activity and hence the REE. Anorexia and malnutrition affect the REE by reducing the lean body mass.

In view of the broad chronic condition patients can present with in ICU, IC is recommended to confirm the REE for optimal nutrition therapy. The energy needs are challenging to be estimated with.

2.7 REE IN WOMEN

Women have different body composition compared to men. They have less muscle mass and more fat tissues percentage. This differences in body compartment can reduce the metabolic activity and so the REE. Women also are more predispose to obesity compared to men. Depending on the menstrual cycle also, the metabolic activity will differ (Mauvais-jarvis, 2015). Due to these reasons, the accuracy of predictive equation is affected by the gender of its subject.

2.8 ACCURACY OF PREDICTIVE EQUATIONS

All the factors influencing metabolic activity, necessitates the usage of IC for accurate measurement of REE. However, as explained before, IC is rarely routinely used in the medical institution around the world. Estimating the REE using predictive equation is an alternative for clinical practice. Unfortunately, multiple studies have shown these predictive equations to be variable in their reliability.

Table 1.1 Studies done on predictive equation accuracy

Authors	Population	Design	Result
Neelemaat et al., 2012	Malnourished older patient n = 194	Observational 23 predictive equations evaluated	Best equation have accuracy of 40% All equations under predict the measured REE
Weijs et al., 2018	Obese adult of US and Dutch n = 239	Retrospective analysis 27 predictive equations evaluated	Best equation have accuracy of 79%, only for US population
Campbell et al., 2005	Critically ill, underweight male n = 42	Retrospective analysis 4 predictive equations evaluated	Best equation have accuracy of 42%
Kross et al., 2012	Critically ill n = 927	Retrospective analysis 5 predictive equations evaluated	Best equation have accuracy of 31% Mostly underestimate
Lee et al., 2012	Healthy policemen n=28	Observational 12 predictive equations evaluated	Best equation have accuracy of 35.7%
Kruizenga et al., 2016	General hospital patient n=513	Observational 15 predictive equations evaluated	Best equation have accuracy of 49%
Zusman et al., 2018	Critically ill n = 1440	Retrospective analysis 8 predictive equations evaluated	Best equation have accuracy of 50%

Systematic literature review has been conducted to assess the accuracy of predictive equations for mechanically ventilated, critically ill patients. From 18 studies included out of 160 variation of predictive equations, 38% of equations underestimated and 12% equations overestimated energy expenditure by more than 10%. At an individual patient level, predictive equations underestimated and

overestimated energy expenditure in 13–90% and 0–88% of patients (Tatucu-babet, Hons, Ridley & Tierney, 2015).

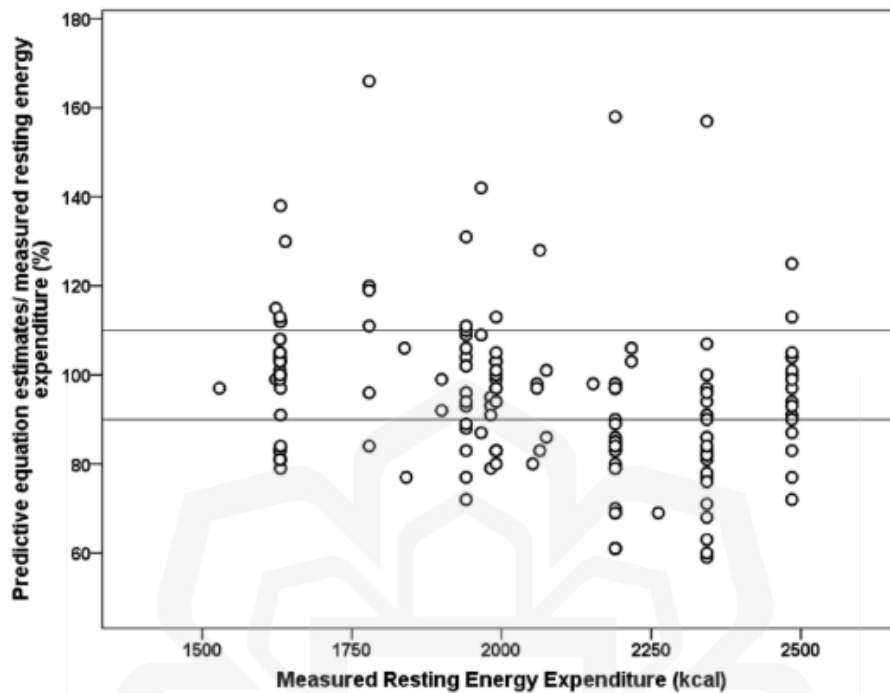


Figure 2.1 Degree of under prescription and over prescription of energy needs among all reviewed predictive equations

(N = 160) based on mean values of predicted and measured resting energy expenditure.

2.9 INDIRECT CALORIMETRY AS THE GOLD STANDARD

Indirect calorimetry (IC) remain the gold standard in measuring REE. With it, we are able to individualize the prescription of energy despite genetic variability, stages of trauma and composition of tissues(Schoeller, 2007). If adequate test stability can be achieved, IC measurements of only 15 minutes duration can successfully predict energy requirements with less than a 4% error in critically ill patients (McClave, Martindale & Kiraly, 2013).

Despite the IC is non-invasive, highly accurate to measure REE, due to cost factor and technical limitation, it is still not widely used in ICUs. Predictive equations