A RETROSPECTIVE STUDY OF RISK FACTORS FOR PROLONGED MECHANICAL VENTILATION AFTER CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA KUBANG KERIAN KELANTAN

DR. FIRMAN HARIRI

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE (GENERAL SURGERY)

UNIVERSITI SAINS MALAYSIA

MAY 2015

ACKNOWLEDGEMENTS

Immeasurable appreciation and deepest gratitude for the help and support are extended to the following persons who in one way or another have contributed in making this study possible:

- Dr Mohd Nor Gohar Rahman (Senior Lecturer and Consultant Urologist, Surgical Department HUSM) my dedicated supervisor, for all his guidance from the beginning of this research, until completion of this dissertation.

- Professor Dr Mohamad Ziyadi Haji Ghazali (Cardiothoracic Surgeon, Cardiothoracic Unit HUSM) my co supervisor, who has the attitude and the substance of genius. He continually and convincingly conveyed a spirit of adventure in regard to this research and excitement in regard to teaching. Without his guidance and persistent help this dissertation would not have been possible.

- Yang Berbahagia Dato' Dr. Anas Sjahroeddin Ressang Bin Haji Aminuddin (Cardiothoracic Surgeon, Cardiothoracic Unit Hospital Raja Perempuan II Zainab) who introduced and guided me through my cardiothoracic posting. His support, comments suggestions and initial provisions that benefited much in the completion of this study.

- All the lectures of Surgical Department HUSM, especially Dr Zaidi Zakaria (Head of Surgical Department) who have shared this wise wisdom, vase knowledge and unconditional support throughout this study.

- All the staffs in Medical Record Office HUSM, for the permission to grant access as part of my dissertation.

- Puan Siti Nur Farliza Zaharudin from Statistic Department, for her support, patience and guidance on statistical analysis.

- My colleagues and course mates, for their suggestions, concerns and cooperation throughout this study.

- My family, for their continous support and understanding, especially my parents, for all the sacrifices made.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ACS	Acute Coronary Syndrome
ASA	American Society of Anaesthesiologist
AXC	Aortic cross clamping
BA	Bronchial asthma
BMI	Body Mass Index
BSA	Body surface area
CABG	Coronary artery bypass graft
CI	Confidence interval
CICU	Coronary Intensive Care Unit
Cx	Complications
COPD	Chronic obstructive pulmonary disease
CPB	Cardiopulmonary bypass
CVD	Cardivascular disease
CVS	Cardiovascular system
dL	Decilitre
DM	Diabetes Mellitus
DOD	Date of discharge
DOV	Date of visit
FEV_1	Force Expiratory Volume in 1 second
FTE	Failure To Extubate

FiO_2	Fraction of inspired oxygen
Hb	Hemoglobin
HPE	Histopathological Examination
HPT	Hypertension
HUSM	Hospital Universiti Sains Malaysia
ICU	Intensive Care Unit
IHD	Ischaemic heart disease
IJN	Institute Jantung Negara
IMA	Internal mammary artery
IV	Intravenous
IABP	Intra aortic balloon pump
LOS	Length of stay
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
mg	Milligram
mL	Millilitres
mmHg	Millimetres of mercury
NYHA	New York Heart Association
OR	Odd ratio
OPCAB	Off- pump Coronary Artery Bypass
PaO_2	Partial arterial Oxygen
$PaCO_2$	Partial arterial Carbon Dioxide

PMV	Prolonged mechanical ventilation
SPSS	Statistical Package for Social Science
STS	Society of Thoracic Surgeons
WHO	World Health Organisation

LIST OF TABLES

LIST OF FIGURES

ABSTRAK

KAJIAN RETROSPEKTIF TERHADAP FAKTOR RISIKO BAGI PENGUDARAAN MEKANIKAL BERTERUSAN SELEPAS PEMBEDAHAN PINTASAN CANTUMAN ARTERI KORONARI (CABG) DI HOSPITAL UNIVERSITI SAINS MALAYSIA KUBANG KERIAN KELANTAN

PENGENALAN

Pengudaraan mekanikal berterusan selepas pembedahan CABG meningkatkan ruang udara dan trauma paru-paru sekaligus meningkatkan kos perubatan. Ianya telah dicatatkan bahawa antara kelebihan klinikal ekstubasi awal adalah mengurangkan kemungkinan kesan buruk tekanan pengudaraan positif dan mengurangkan ketidakselesaan yang dialami pesakit, potensi pengurangan jangkitan dan ambulasi awal. Ramai yang telah cuba mengesyorkan ekstubasi awal sebagai cara untuk mengurangkan penjagaan intensif dan kos hospital. Beberapa model telah dibangunkan dengan bertujuan untuk mengenalpasti pesakit yang berisiko untuk mengalami PMV. Sesetengah kajian telah dibuat bagi membandingkan model ramalan yang dibangunkan di ICU.

Objektif utama kajian ini adalah untuk mengenalpasti ciri-ciri pesakit dan angkubah operatif yang meramalkan PMV dalam kalangan pesakit yang menjalani pintasan cantuman arteri koronari (CABG). Rekod pesakit yang menjalani CABG dari Januari 2009 ke Disember 2013 akan diteliti secara retrospektif. Pesakit-pesakit ini akan

dibahagikan kepada kumpulan normal dan ventilasi mekanikal berterusan (PMV). Faktor-faktor punca yang memberi kesan terhadap jangka masa intubasi akan dimasukkan dalam analisis univariat dan seterusnya dijalankan ke atas model regresi logistik untuk menentukan faktor risiko yang dikaitkan dengan PMV.

Terdapat pelbagai kajian yang dijalankan dengan jayanya yang meramalkan risiko dan membina model risiko. Saya ingin mencuba untuk mengkaji ciri-ciri punca tersebut dan pembolehubah dalam unit kecil kardiotorasik di mana populasi pesakit adalah lebih homogenous dan dijalankan oleh seorang pakar bedah di Hospital Universiti Sains Malaysia dan membuat perbandingan faktor-faktor risiko yang telah dianggap sebelumnya.

KAEDAH

Ianya merupakan analisis kohort retrospektif pesakit dalam Unit Pembedahan Kardiotorasik di Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. Kesemua pesakit yang menjalani CABG elektif terpencil di antara Januari 2009 dan Disember 2013 dikesan. Senarai yang dijana komputer akan didapatkan daripada pejabat rekod perubatan. Kes-kes ini dikenalpasti menurut Kod-T Klasifikasi Antarabangsa Penyakit-Semakan Kesepuluh (ICD-10). Pesakit yang memenuhi kriteria kemasukan dan kriteria pengecualian diambil. Data ciri-ciri perioperatif terpilih akan dikumpul dengan meninjau rekod perubatan. Kata kunci yang digunakan apabila mengambil rekod adalah pintasan cantuman arteri koronari atau CABG. Analisis statistikal dilakukan dengan menggunakan perisian SPSS versi 22.0.

KEPUTUSAN

Terdapat 140 pesakit dianalisa, hanya dua puluh empat pesakit yang memerlukan pengudaraan mekanikal berterusan (PMV) lebih daripada 24 jam. Ini menjadikan kejadian kes sebanyak 17.1% . Pesakit lelaki menyumbang majoriti kumpulan PMV sebanyak 91.7%. Peratusan ini walaubagaimanapun tidak memberi gambaran sebenar taburan jantina kerana bilangan pesakit wanita hanyalah 19 orang dan 2 tergolong dalam kategori PMV. Analisis sebelum pembedahan menunjukkan kegagalan fungsi buah pinggang (20.8% berbanding 3.4%; p=0.05). NYHA kelas IV (37.5% berbanding 6.9%; p<0.01), MI terbaharu (58.3% berbanding 12.9%; p<0.01), LVEF <30% (16.7% berbanding 4.3%; p=0.037), sebelum pembedahan PaCO2 (35.0 berbanding 39.2; p=0.113), masa pintasan kardiopulmonari (136 minit berbanding 126 minit; p=0.175), transfusi darah semasa pembedahan (925 ml berbanding 831 ml; p=0.24), aritmia kardiak selepas pembedahan(37.5% berbanding 12.1%; p=0.004), kegagalan buah pinggang akut selepas pembedahan (33.3% berbanding 1.7%; p<0.001) dan pendarahan selepas pembedahan (58% berbanding 4.3%; p<0.001) adalah signifikan. Dalam analisis regresi logistik pelbagai, kajian menunjukkan kegagalan buah pinggang (OR=12.90;95% CI 1.33-124.99), NYHA kelas IV atas (OR=7.10;95% CI 1.33-37.93),MI terbaharu (OR=8.12;95% CI 1.81-36.38) dan pendarahan selepas pembedahan (OR 25.1;95% CI 4.73-132.76) didapati menjadi faktor risiko yang dikaitkan dengan PMV selepas pembedahan CABG. Kajian ini juga menunjukkan jangkamasa rawatan di hospital yang lebih lama di dalam kumpulan PMV. Untuk 1 hari tambahan di hospital,ianya meningkatkan risiko PMV sebanyak 1.18 kali (95% CI 1.05-1.31) apabila disesuaikan dengan lain-lain faktor.

KESIMPULAN

Pengudaraan mekanikal berpanjangaan selepas pembedahan CABG dikaitkan dengan kehadiran kegagalan fungsi buah pinggang, New York Heart Association (NYHA) gred IV, infarksi myocardium yang baru dan pendarahan selepas pembedahan. Pesakit-pesakit yang menggunakan pengudaraan berterusan memerlukan masa yang lebih panjang bagi rawatan dalam hospital.

ABSTRACT

A RETROSPECTIVE STUDY OF RISK FACTORS FOR PROLONGED MECHANICAL VENTILATION AFTER CORONARY ARTERY BYPASS GRAFTING (CABG) SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA KUBANG KERIAN KELANTAN

INTRODUCTION

Prolonged mechanical ventilation after CABG surgery increases airway and lung trauma ultimately increases hospitalization costs. It is well documented that the main clinical advantages of early extubation are reduced likelihood the adverse effects of positive pressure ventilation and minimized of associated patient discomfort, a potential decrease in infection and early ambulation. Many has attempted in promoting early extubation as a mean to reducing intensive care and hospitalization costs. A few models have been developed aim to identify patients at risks of PMV. Some studies attempted to compare those prediction models developed in the ICU.

The main objective of this study is to identify patient characteristics and operative variables that predict PMV in patients undergoing coronary artery bypass grafting (CABG). The record of patients who underwent CABG from January 2009 to December 2013 will be examined retrospectively. These patients will be divided into normal and prolonged mechanical ventilation (PMV) groups. Putative factors affecting the duration

of intubation will be included in univariate analysis and subsequently run into logistic regression model to determine the risk factors associated with PMV.

There were numerous studies that had successfully predicted the risks and established a risk models. We attempt to study those putative characteristics and variables in a relatively small cardiothoracic unit whereby patients population were more homogenous and operated by a single surgeon at Hospital Universiti Sains Malaysia (HUSM) and compare previously considered risk factors.

METHODOLOGY

It is a retrospective cohort analysis of patient's case notes in Cardiothoracic Surgery Unit of Hospital University Sains Malaysia, Kubang Kerian Kelantan. All patients who had undergone elective isolated CABG between January 2009 and December 2013 are traced. A computer generated list will be obtained from medical record office. The cases are identified according to T-codes of the international classification of disease-Tenth revision (ICD-10). Sampling frame is obtained and all patients fulfilling the inclusion and exclusion criteria were recruited. Selected perioperative characteristics data will be collected by reviewing traced medical records. Keywords used when retrieving records is coronary artery bypass grafting or CABG. Statistical analysis was done using SPSS software version 22.0.

RESULTS

There were 140 patients enrolled, only twenty four patients required prolonged mechanical ventilation (PMV) of more than 24 hours. This made the incidence of 17.1%. Male gender contributed to the majority of the PMV group 91.7%. This percentage however did not reflect the true gender distribution as the number of female population in the study was only 19 and only 2 fall into the PMV group. Perioperative univariate analysis showed that renal dysfunction (20.8% versus 3.4%; $p = 0.05$), NYHA class IV (37.5% versus 6.9%; $p < 0.01$), recent MI (58.3% versus 12.9%; $p < 0.01$), LVEF < 30% (16.7% versus 4.3%; $p = 0.037$), preoperative $PaCO_2$ (35.0 versus 39.2; $p = 0.113$), cardiopulmonary bypass time (136 minute versus 126 minute; $p = 0.175$), intraoperative blood transfusion (925 ml versus 831 ml; $p = 0.24$), post operative cardiac arrhythmias (37.5% versus 12.1%; $p = 0.004$), post operative acute renal failure (33.3% versus 1.7%; $p < 0.001$) and post operative hemorrhage (58% versus 4.3%; $p < 0.001$) were significant. In multiple logistic regression analysis, study demonstrates renal dysfunction (OR = 12.90; 95% CI 1.33-124.99), advance NYHA class IV (OR = 7.10; 95% CI 1.33-37.93), recent MI (OR = 8.12; 95% CI 1.81-36.38) and postoperative hemorrhage (OR = 25.1; 95% CI 4.73-132.76) were found to be independent risk factors associated with PMV after CABG surgery. The study also demonstrates significant higher length of hospital stay in PMV group. For 1 day additional hospital stay, it increases the risk of PMV by 1.18 times (95% CI 1.05-1.31) when adjusted to other factors.

CONCLUSION

Prolonged mechanical ventilation after CABG surgery is associated with the presence of existing renal dysfunction, NYHA class IV, recent myocardiac infarction and post operative hemorrhage. Those patients who require prolonged ventilation have significantly higher hospital stay.

CHAPTER 1

INTRODUCTION

1.1 Background Of The Study

It is well documented, the field of cardiac surgery unexpected prolonged mechanical ventilation (PMV) posed to a larger number of complications leading to significant postoperative morbidity and mortality. Undoubtedly, they present a significant financial burden. In a simplest term, the duration of mechanical ventilation may depend on various reasons; for examples certain characteristics, type of procedure and local protocols within individual cardiothoracic unit and the ICU. In some centres, patients are extubated early while others may significantly later. Attempts for early extubation may yield medical and financial benefits however may as well exposed the patients to the risk of hypothermia, bleeding and cardiorespiratory instability(Royse *et al.,* 1999; Reis *et al.,* 2002; Kogan *et al.,* 2008). Therefore the time of postoperative ventilation after cardiac surgery depends on many factors, extubation criteria may vary between departments and dependent on the technique of anaesthesia.

Coronary artery bypass grafting (CABG) is defined as "open-heart surgery in which a section of a blood vessel is grafted from the aorta to the coronary artery to bypass the blocked section of the coronary artery in attempt to improve the blood supply to the heart." Adam Hammer established the pathophysiology of coronary artery disease in 1876. He postulated that angina (imbalance of coronary perfusion supply and demand) was due to the interruption of coronary blood flow and that myocardial infarction occurred after the occlusion of at least one coronary artery.

It has been six decades since the introduction of CABG in humans. The idea of coronary artery bypass grafting surgery dated back to 1910 when Dr. Carrel made his first attempt to suture a carotid artery graft to the left coronary system in an experimental canine. The animal did not survive; but the principle of directly grafting into the coronary artery branches was demonstrated. In tandem, in early 1940s, a Canadian surgeon named Gordon Murray introduced anticoagulant heparin into the field of vascular surgery. Simultaneously cardiac surgery had developed slowly in just handful of operations: closure of patent ductus, coartation repair as examples. It become tremendously apparent to those interested in the field that a heart lung machine was necessary in order to deal with larger and intense cardiac operation. Hence, in the late 1950s, the first heart lung machine invented(Stoney, 2009).

Despite the introduction of heart lung machine, the initial attempts at cardiopulmonary bypass during those years were disastrous with an appalling mortality rate. These were due to multiple contributing factors. They encountered that the main problem with the heart lung machine was to develop an artificial oxygenator. Many had developed their own device based on limited laboratory experience. Secondly, each attempted surgeon was self-taught in a hard way and by trial and error. Goetz using the sutureless technique in 1960 performed the first CABG using the internal mammary artery (IMA) in humans. Four years later in 1964, V. Kolessov performed the first sutured bypass grafting using the IMA. From 1962 to 1967, series of CABG using autogenous saphenous vein grafts were performed successfully by D. Sabiston in 1962, H. Garrett in 1964, D. Kahn in 1966, and R. Favaloro in 1967(Endo, 2000). In 1973, Benetti, Calafiore and Subramaniam successfully completed coronary anastomoses on a beating heart(Siddiqui *et al.*, 2012; Diodato and Chedrawy, 2014). In 1975, Trapp and

Ankeney presented their landmark reports of CABG performed without heart lung machine which also known as off pump CABG(Ankeny, 1975).

Despite the achievement, the mortality and morbidity were still intolerably high. Post CABG complications were numerous mainly due to respiratory failure, coagulopathy and bleeding. There were no institutional review boards until 1974 and therefore the decision to try on a new experimental operational steps or device was left to the conscience of the surgeon. Recent great advances in anaesthesia, myocardial protection and surgical techniques over the decades have led to fast track CABG, in which patients have been extubated within as early as 4 hours and discharged within 3 to 5 days of operation(Cheng *et al.*, 1996). Significant improvement in every aspect of perioperative areas has taken placed in order to improve on mortality and morbidity.

In CABG, those previous cardiac surgeons believe that due to the magnitude of the surgery, the concern on the cardiovascular system and the ability of lungs after operation had led them to place the system "on hold" until cardiac stability was evident (Cheng *et al.*, 1996; Cislaghi *et al.*, 2009). Hence, a number of conclusion and practice established to maintain intubation and ventilation to a minimum period of 24 hour followed by tracheostomy and continued ventilatory support. Some centers even advocated immediate tracheostomy during surgery in belief prolonged ventilation as part of recovery. However, for the past two decades, the field of cardiac surgery has changed drastically. Surgeons and physicians have more understanding of the physiology and co-exist improvement in cardiac surgery and cardiac anesthesias have led to a more realistic approach.

Undoubtedly, the care of CABG patients is always associated with substantial utilization of healthcare resources (Lee JH, 1996 Oct; Konstantakos and Lee, 2000). Current economic constraints lead to significant efforts to shorten the length of hospitalization and to reduce cost. In current practice, there is a growing trend towards early extubation. Evidence has suggested that early extubation after CABG is safe and consequently reduce the length of Intensive Cardiac Unit (ICU) and hospital stay and costs without compromising patient's clinical outcomes.

Conversely, PMV after CABG is unusual. The incidence of PMV patients however, varies depending on the definition of prolonged ventilation period used. They were reported at the range between 2% to 69%(Suematsu *et al.*, 2000; Murthy *et al.*, 2007; Reddy *et al.*, 2007; Cislaghi *et al.*, 2009; Ji *et al.*, 2010; Saleh *et al.*, 2012; Siddiqui *et al.*, 2012; Gumus *et al.*, 2015). PMV results in worse physiologic outcomes as results of atelectasis and intrapulmonary shunting. It delays ciliary function and mucous transport causing inspissation of secretion, hence promoting bacterial colonization eventually leading to infections(Cohen *et al.*, 2000; C., 2004). When these occur they are always associated with significant morbidity and mortality, prolonged ICU and hospital stay and eventually escalating resource utilization and health care cost (Lee JH, 1996 Oct; Cohen *et al.*, 2000; Doering *et al.*, 2000; Saleh *et al.*, 2012).

Many studies have attempted to identify preoperative and operative predictors for prolonged ventilation after CABG. Risk stratification may be an important tool for perioperative management of CABG preparation. Patients with high risks of PMV can be identified and be prepared in according manner. There were studies that attempted to

develop a prediction model or compare so that it can be used in day to day practice(Suematsu *et al.*, 2000; Reddy *et al.*, 2007; Knapik *et al.*, 2011).

1.2 Justification Of The Study

The history of the cardiothoracic surgery services in Malaysia dated back to the 60's when the first service was provided by the Lady Templer Hospital in Kuala Lumpur. The first open heart surgery was performed at the University Hospital, Kuala Lumpur in 1975, subsequently by Hospital Kuala Lumpur in 1982. In 1992, National Heart Institute was established.

According to World Health Organisation (WHO) data published in 2011, coronary heart disease death in Malaysia reached 22,701 or 21.18% of total death. Unfortunately, in Malaysia, due to lack of systematic data collection, it is difficult to estimate the actual number and outcome of CABG or any cardiac procedure in the country. There is no study available so far examining the risk factors for PMV after CABG in Malaysia (OVID, Pub Med, and Science Direct). The western figures are often used as reference values and this may not be precisely accurate to reflect the Malaysian population(Anas *et al.*, 2008).

The Cardiothoracic Unit in HUSM established in early 2001 and its first CABG was performed later in November. It was the first CTS centre on the East Coast of West Malaysia. Professor Dr Mohamad Ziyadi Ghazali, the sole cardiac surgeon in the unit has headed tirelessly since its commencing. From its opening until December 2013, approximately 600 cases of open CABG were performed. The success stories sparked a new era of such surgery for local patients from the East Coast. HUSM had a Memorandum of Understanding with the IJN regarding technicality and expertise

training. In spite of the success, there was no adequate systematic review of the numbers or type of cardiac surgeries done. The local data as well as the national data is lacking due to various reasons, hence to compare or review is extremely impossible. For these pertaining reasons, I feel it is beneficial if local data are retrieved, studied and published. I attempt to identify the demographic data and perioperative risk factors following CABG and compare with the international data. The parameters of each characteristics be analysed and later may be used as a predictive tool in near future.

CHAPTER 2

LITERATURE REVIEW

2.1 The Incidence Of PMV After CABG

Previous studies have reviewed on independent risk factors for prolonged mechanical ventilation following CABG. PMV does occasional occur with a reported incidence between 5% and 69%. This wide variability is due to discrepant definitions of PMV. According to The Society of Thoracic Surgeons guidelines endorsed in 12th June 2011, the definition of prolonged intubation is patients aged 18 years and older undergoing isolated CABG who require intubation for more than 24 hours. The numerator time frame is in the setting of hospitalization for such surgery, which includes the entire postoperative period up to the discharge, even if over 30 days(Members *et al.*, 2011). Regardless its strict definition, the criteria of extubation varies between hospital cardiothoracic departments. The time of postoperative ventilation after cardiac surgery depends on many factors, such hospital resource, work force, types of operation, local protocols within individual cardiothoracic unit and the type of anaesthesia used(Habib *et al.*, 1996; Yende and Wunderink, 2002). There has been massive development in the field of cardiac surgery technicality over the last decades. Recent advances in anesthesia and myocardial protection has led to fast tract CABG as early as 6 hours following surgery (Sato *et al.*, 2009).

Among the latest study incidence documented was 5.6% (Gumus *et al.*, 2015). It was done in highly specialised Bagcilar Research and Training Hospital, Istanbul

Turkey. The authors prospectively analyzed the collected data of 830 on- and off-pump coronary bypass patients from December 1, 2010 to February 18, 2014. (Siddiqui *et al.*, 2012) conducted retrospective analysis of 1617 CABG patients at the largest cardiac centre in Pakistan, CPE Institute of Cardiology, Multan from March 2009 to May 2011. The authors included elective CABG either isolated CABG or complex CABG. All operations were conducted by at least 3 consultant surgeons. The incidence of PMV was 4.76%. Both of the studies above, the PMV was defined at more than 24 hour. Meanwhile, a similar retrospective analysis of 167 patients who underwent either emergency or elective or redo on pump CABG between 1994 and 1998 at Department of Cardiothoracic Surgery, Tokyo Japan documented a staggering incidence of 44% PMV. Despite of similar PMV definition of 24 hour, their population cohort included a wide range of heterogeneity and high risk groups. Other authors(Saleh *et al.*, 2012) retrospectively analyzed a series of 11016 consecutive patients who underwent elective primary isolated CABG at Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, UK between April 1997 and September 2010. Their definition of PMV was more than 72 hour. By narrowing the homogeneity of the population cohort and prolonged definition, their incidence of PMV was only 1.96%.

There was a study that put the elapsed time between CABG and extubation of more than 8 hours was defined as late extubation(Ji *et al.*, 2010). The authors studied 416 patients undergoing elective isolated on- and off pump CABG between June 2005 and June 2008 at the Tongji Hospital, China. The incidence of late extubation or PMV after CABG was 69.23%. The figure was expected to be high due to their definition of PMV.

2.2 Definition Of Prolonged Mechanical Ventilation

There are various way of putting the term of prolonged mechanical ventilation. Whilst many used PMV itself, some authors opted for different term such as late extubation; delayed extubation; prolonged intubation; failure to wean; failure to extubate. Regardless the term used, their purpose still posed a similar objective. A question occurs to me as a researcher. One should ask the reason STS committee endorsed an elapse of more than 24 hour as a defining period of prolonged mechanical ventilation (PMV).

A prospective observational cohort study was conducted at Methodist Healthcare University Hospital between the period of June 1999 and October 2000 to evaluate the causes of failure extubation following CABG surgery(Yende and Wunderink, 2002). The authors studied 400 patients undergoing CABG surgery who were then extubated by a standardized respiratory protocol. They classified patients who failed extubation into three groups; one at 8 hour; and at 24 hour and at 48 hour, each were labelled as failure to extubate (FTE); prolonged mechanical ventilation (PMV) > 24 hour and prolonged mechanical ventilation (PMV) > 48 hour respectively. They gathered 41.75%, 6.75% and 5.25% of patients respectively, could not be extubated at FTE at hours, PMV > 24 hours and PMV > 48 hours. Those who were in the FTE at 8 hours, they concluded depressed level of consciousness was the most common reason. Prolonged sedation as a result of anesthetic agents was thought to be the major cause. The second cause was thought to be due to the hypoxaemia, followed by excessive bleeding. At PMV > 24 hours, the authors noted that depressed level of consciousness was no longer a significant reason for extubation failure. Instead, hypoxaemia was the

sole principle reason for the PMV. This finding was similar to those who remained intubated after 48 hours (PMV > 48 hours). The authors overall duration of mechanical ventilation following CABG surgery was comparable to previous studies in particular, the incidence of PMV > 24 hours was similar to the STS committee database dated in 2002 (6.75% versus 5.5%).

2.3 Risk Factors For Prolonged Mechanical Ventilation (PMV) After CABG Surgery

The heterogeneity of patient populations studied may have limited the success of previously suggested risk prediction models. As an attempt to verify the validity of previously identified predictors in a more homogenous group of patients, the aim of this study is to identify the incidence and risks of PMV after elective isolated on pump CABG. Elective isolated on pump means patients was electively planned for a single procedure; that is sole CABG surgery. In order to further reduce the heterogeneity of the population group, the operation was performed by a single surgeon and the decision to extubate was solely based by his judgments and clinical expertise. The surgical procedure was standardized with on- pump CABG only. Each procedure did not undergo fast tract anesthesia.

The Department of Cardiothoracic Surgeon, in Tel Aviv University Israel has done a retrospective study on 1112 patients undergoing on- pump CABG from January 1, 1994 to December 31, 1996 to evaluate the morbid results of PMV which the authors defined as more than 48 hours after CABG(Cohen *et al.*, 2000). All operations were

conducted by their resident consultant surgeons and procedure included elective or emergency cases. Over those 30 months, 66 out of 1112 (5.93%) required prolonged intubation. This group was match with other 66 patients who did not require prolonged intubation. They analyzed 14 preoperative characteristics and 8 operative characteristics. The authors attempted to answer questions pertaining to the subset of patients. They revealed 3 independent risks factors that predisposed them to prolonged intubation. The risks were patient with: 1) Reduced FEV1/BSA of less than 1; 2) Renal failure and; 3) Positive fluid balance of more than 3 liter at 24 hour post operative. The authors also concluded that prolonged intubation results in significant acute and midterm morbidity and mortality. Patients had longer ICU and hospital stays. In this group, nearly half had infections such as mediastinitis. As in other study they suffered several limitations such as they did not assess the ejection fraction in those patients known to have poor ventricular function (1984; O'Connor *et al.*, 1992). It is known that ventricular function is a significant determinant for the prolonged intubation. Secondly, their study group mainly composed of older group age as compared to the matched group. As such, it was difficult to determine the cause of prolonged intubation by preoperative morbidity.

At the same time, there was other retrospective study taken placed at Department of Cardiothoracic Surgery, University of Tokyo Japan. It is a specialized cardiothoracic centre with list numbers of cardiothoracic surgeons. The study was done to elucidate patient characteristics and operative variables that predict delayed extubation in 167 patients undergoing on pump CABG from January 1994 to December 1998(Suematsu *et al.*, 2000). These numbers included emergency and elective CABG as well as re do CABG cases. They analyzed a total of 56 characteristics consist of 26 preoperative, 14

intraoperative and 16 post operative characteristics. The authors defined the Delayed Extubation as mechanical intubation needed of more than 24 hours. Their reported incidence of Delayed Extubation in patient undergoing CABG was 44%. Multivariate analysis revealed 6 independent risks factors that predisposed patients to delayed extubation of more than 24 hours. Those risks were; 1) Age of more than 60 years old; 2) Duration of surgery involving period of cardiopulmonary bypass time (CPB) of more than 250 minutes and period of cross clamping (AXC) of more than 100 minutes; 3) Perioperative heart failure; 4) Glucose level of more than 10 mg/dl during CPB; 5) Postoperative transfusion and; 6) PaO2/FiO2 ratio of less than 300. Those in delayed extubation group has longer ICU stay but do not did not display statistically significant. The incidence was comparatively higher than Cohen *et all* study may be due to the choice of PMV definition. In addition to this, they recorded larger older group of 70 years of age in relatively small sample and analyzed more characteristics including the glucose level during operative time. It has shown in studies that CPB to have an adverse effects in diabetic patients(Seki *et al.*, 1993).

Another study was conducted in 1994 at Department of Cardiothoracic Surgery and Anesthesiology, St. Vincent Medical Centre, Toledo, Ohio(Habib *et al.*, 1996). The authors retrospectively analyzed and elucidated a total number of 48 variables and characteristics in determining the period of ventilator support in 507 patients following on- pump CABG surgery. Operations were either elective or emergency CABG or re do cases and performed by multicentre cardiothoracic unit involving 5 consultant surgeons. The definition of PMV was taken at those prolonged intubation in excess of 24 hour. The authors reported incidence was less than 3% (15/507). The results yielded 18 variables linked to late extubation by univariate analysis were correlated. After

multivariate analysis, there were 5 independent predictors of PMV. These were: 1) Age of more than 65 year old; 2) NYHA class IV; 3) Positive fluid balance normalized to body surface area; 4) Use of postoperative intraaortic balloon pump (IABP); 5) percentage of blood transfusion to body surface area (BSA). They also concluded those in PMV group were significantly has longer ICU and hospital stay. The study had low incidence of 3% as compared to 44% by (Suematsu *et al.*, 2000) despite having the same definition. I believe the differing results between these two study were mostly a consequenc of analyses used. Suematsu *et al* studied a total of 56 characteristics in 167 patients whilst the current one studied a total of 48 characteristics in 507 patients.

One group of authors attempted to identify intraoperative and postoperative risks factors that predispose respiratory impairment following CABG surgery. It was taken place at Department of Cardiothoracic Surgery, The Heart Institute, Albany Medical College, New York. They analyzed a total of 8802 consecutive patients who underwent primary CABG with or without concomitant cardiac operation performed by multiple cardiac surgeons from January 1993 to December 2000(Canver and Chanda S, 2003). They analyzed a massive 56 variables of which 38; 10; and 8 profiling the preoperative, intraoperative and postoperative respectively. The author defined respiratory failure as the need for postoperative mechanical ventilation more than 72 hours. They reported an incidence of 5.6%. The value was expected to be low due to the definition of PMV of 72 hours. The authors identified 39 statistically significant preoperative risk factors, only 6 were significant by multivariate analysis. They questioned many previous studies which analyzed the preoperative characteristics that predict postoperative survival, which its reliability of their predictive value remains controversial(Shroyer *et al.*, 1999). They concluded the possibility of an individual with adequate pulmonary function

before CABG may develop respiratory failure postoperatively due to other organ dysfunction. Their multivariate analysis for independent risk factors of respiratory failure revealed 10 variables. There were; 1) Postoperative septic endocarditis; 2) postoperative gastrointestinal bleeding; 3) postoperative renal failure; 4) postoperative new stroke; 5) postoperative deep sterna wound infection; 6) rebleeding requiring reoperartion; 7) preoperative insertion intraaortic balloon pump IABP; 8) congestive cardiac failure at current admission; 9) chronic obstructive pulmonary disease; 10) CPB time in 30 minute increment. The study major limitation was that it included a large set of variables into a single multivariate analysis which was difficult and overwhelming. In addition to this, although the author analyzed the morbidity, study did not specify on duration of hospital stay. It was presumed that prolonged intubation led longer ICU stay hence hospital stay.

In separate study by Sato *et al*, at Division of Cardiovascular Surgery and Anesthesiology, Nagasaki, Konsekai Hospital, Japan, a group of surgeons evaluated the status of early tracheal extubation after on- pump CABG surgery(Sato *et al.*, 2009). Their aimed was to established factors for successfully early extubation. They retrospectively reviewed a total of 485 patients undergoing on- pump CABG either elective or emergency setting. All patients were subjected to early extubation protocol. In the same study, authors indirectly analyzed pooled of population that categorized into prolonged mechanical ventilation of more than 24 hours. Their variables were analyzed. The study reported that those in PMV group was 7 patients (1.4%). These patients developed heart failure and respiratory failure. The authors concluded these following factors to be the predictors to PMV: 1) Presence of unstable angina; 2) Ejection fraction of less than 50%; 3) pre-existing COPD; 4) acute renal failure; 5) preoperative stroke;

6) reoperation for bleeding; 7) preoperative MI. Although the study mainly aimed to establish risk factors and feasibility of early extubation, but the *Sato et al* successfully demonstrated the risk factors for PMV following CABG were compatible to PMV study in their reference namely by (Legare *et al.*, 2001).

Legare *et al* retrospectively evaluated 1805 consecutive patients undergoing isolated on- pump CABG on both either elective or emergency setting at Dalhousie University, Halifax, Nova Scotia, Canada between January 1997 and March 1999 (Legare *et al.*, 2001). They attempted to identify the predictors of prolonged ventilation in a large group of CABG patients. The CABG surgeries were conducted by seven cardiothoracic surgeons. Each procedure underwent standardized anesthetic protocol. The authors attempted to reduce the heterogeneity of the study population by evaluating preoperative predictors. Inclusion criteria based on these 10 preoperative variables: age, gender, ejection fraction, renal function, diabetes, angina status, NYHA class, number of disease vessels, urgency of procedure, re-operation and presence of COPD. The analyzed via predictive model to allow estimation of the preoperative risk of PMV with 95% confidence interval. Prolonged mechanical ventilation was defined as the need for intubation following CABG of more than 24 hour. The results showed PMV incidence of 8.6% (150/1805). The independent risk factors for PMV were: 1) Unstable angina; 2) EF less than 50; 3) presence of COPD; 4) preoperative renal failure (creatinine of more than 177 mmol/L); 5) female gender; 6) age of more than 70. Their findings also exhibited those in the PMV group had longer ICU and hospital stay. Their incidence of PMV was considerably low (8.6%) in ratio to the number of patients studied. This could be due to only one segment of perioperative variables analyzed. They addressed intraoperative complications such as the used of IABP and cardiopulmonary bypass

(CPB) time greater than 120 minutes. It has been shown on several studies that these two variables posed a significant impact on postoperative morbidity (Habib *et al.*, 1996; Canver and Chanda S, 2003; Ji *et al.*, 2010). Yet the author opted to exclude in order to calculate the predictive model.

Meanwhile at the Department of Thoracic Cardiovascular Surgery, Tongji Hospital of Tongji University, Shanghai, China, a groups of authors led by one main researcher Qiang Ji, conducted 2 simultaneous retrospective studies to evaluate the independent risk factors for ventilator dependency following isolated CABG surgery. Both of elective or emergent surgeries were included. All patients underwent fast tract anesthesia. One group concerned on controversial reports on independent risk factors for ventilator dependency after on- pump CABG and in this group the authors defined the time elapsed between CABG surgery and extubation of more than 48 hours as Post Operative Dependency (PVD) (Ji *et al.*, 2012). They retrospectively analyzed a sum of 37 perioperative variables from a total of 588 consecutive patients between January 2003 and December 2008. The incidence of PVD was 13.8% (81/588). The independent risk factors for PVD following CABG surgery were: 1) Preoperative congestive heart failure; 2) Preoperative hypoalbuminemia; 3) Preoperative arterial oxygen partial pressure PaO2 of less than 70 mmHg; 4) Postoperative anemia. They also exhibited PVD was significantly correlated with prolonged ICU and hospital stay.

The latter group meanwhile was astonished that the proportion of their early to late extubation at Tongji Hospital was lower than in the literatures. This had prompted them to evaluate the risk factors for late extubation following isolated on- pump and off- pump CABG surgery (Ji *et al.*, 2010). They retrospectively analyzed a massive

number of 45 perioperative characteristics of 416 consecutive patients who underwent isolated on- pump CABG surgery between June 2005 and June 2008. The definition of Late Extubation after CABG surgery was more than 8 hours. The incidence documented was 69.23% (288/416) expectedly higher compared to the former group due to the definition of mechanical ventilation. They identified 5 independent risk factors contributing for late extubation of > 8 hours following CABG surgery. The risks were: 1) Age of more than 65; 2) Preoperative arterial partial oxygen PaO2 of 70 mmHg; 3) Duration of CPB more than 110 minutes; 4) Perioperative IABP requirement; 5) Postoperative anemia. Contrary to the former study, patients in late extubation group had significant longer ICU stay but did not have significant effect on the hospital stay. The findings from these two studies, in spite of the same demographic group and same cardiac unit setting there were only 2 compatible risks factors; the preoperative PaO2 and postoperative anemia. One can generally conclude that the risk factors of prolonged mechanical ventilation following CABG surgery may differ from each study depending on the operative protocol as well as the definition itself.

The Society of Thoracic Surgeons (STS) National Cardiac Surgery Database had compiled a staggering number of more than 300,000 patient data from 1990 through 1994. These huge numbers of patients who underwent isolated CABG were analyzed and extrapolated to develop a risk model of operative morbidity and mortality. Despite of some controversial variables, the risk models for isolated CABG modestly served as reasonable predictors over those decades(Shroyer *et al.,* 1999). Since the inception, the demographic population has changed drastically. Cardiac anesthesia has improved. The surgeons, perfusionists and anesthetists have become technically superior. Their knowledge inside the concept of inflammatory response to cardiopulmonary bypass are

tremendous hence obviating problem in aggressive manner. In order to adapt to the fast changing environment, the STS risk models for CABG surgery have undergone periodic revisions. In 2008, the new STS risk model for CABG has been published(Shahian *et al.*, 2009). It is reportedly performing excellent.

In tandem, the Department of Cardiac Surgery, CPE Institute of Cardiology, Multan, Pakistan, one of the largest cardiac institute in the country conducted a study to re-evaluate the risk factors of PMV (Siddiqui *et al.*, 2012). The authors attempted to identify the risks factors for prolonged mechanical ventilation following on- pump CABG surgery. Inclusion criteria included elective or emergency setting and isolated or combined procedures (such as valve replacement, coronary endarterectomies). The operations were conducted by three resident consultant surgeons. All studied population were subjected to fast track extubation protocol. From March 2009 to May 2011, they pooled total number 1617 patients scrutinizing 65 perioperative variables. The PMV was defined as the elapsed time of more than 24 hour following CABG surgery to extubation. The incidence was at 4.76% (77/1617). The authors concluded 10 independent risk factors for PMV: 1) Preoperative renal failure; 2) pre-existing COPD; 3) Ejection Fraction (EF) of less than 30%; 5) Emergency operation; 6) Preoperative critical state including liver failure or heart failure; 7) Prolonged cardiopulmonary bypass (CPB) time of more than 120 minutes; 8) Prolonged aortic cross clamp time of more than 80 minute; 9) Complex surgical procedures and; 10) Preoperative myocardial infarction(Siddiqui *et al.*, 2012). Their incidence for PMV was remarkably low for a large numbers of patients with numerous analyzed variables. This could be attributed to fast tract extubation protocol which include substitution of long acting narcotics with short acting alternative. Furthermore, all cases conducted in highly specialized center by

highly experienced surgeons. The authors had demonstrated that previous risk factors such as old age (Suematsu *et al.*, 2000; Legare *et al.*, 2001), advanced NYHA class IV (Habib *et al.*, 1996), the used of IABP (Habib *et al.*, 1996; Legare *et al.*, 2001; Canver and Chanda S, 2003) and redo surgery (Habib *et al.*, 1996; Legare *et al.*, 2001; Canver and Chanda S, 2003) were no longer to have a significant odds ratio for PMV.

Recent study which is published in February 2015 by Gumus *et al* attempted to evaluate the risk factors for PMV after CABG surgery patients. It was conducted by the Department of Cardiovascular Surgery, Bagcilar Research and Training Hospital, Instanbul, Turkey (Gumus *et al.*, 2015). The authors retrospectively scrutinized 72 perioperative characteristic from a total of 830 on- and off- pump CABG surgery patients. Subject patients included those categorized as elective or emergency and isolated or combined operations. All subjects did not use fast tract protocol and operated by 4 cardiothoracic consultant surgeons. They defined PMV as requirement of mechanical ventilation following CABG surgery of more than 24 hours. The results show 46 patients (5.6%) required PMV following CABG surgery. Multivariate regression analysis, authors showed independent risk factors for PMV were: 1) NYHA class IV; 2) chronic renal dysfunction and: 3) CPB above 83 minutes. They also demonstrated PMV led to longer ICU and hospital stay. Similar to the data of Siddiq and colleagues, the incidence of PMV was at par ranging between 3-5% despite of the population sample comprised of a heterogenous group who had concomitant procedures as well as involving the emergency surgeries.

2.4 On Pump CABG Surgery Versus Off Pump CABG Surgery

Off- pump coronary artery bypass (OPCAB) has gained its popularity in the mid-20th century. Cardiac surgeons believe OPCAB has the potential to lessen the morbidities associated with CPB, aortic cross clamping, hypothermic cardioplegic arrest and systemic dilution. Many had reviewed its benefits and limitations and comparing it against the conventional on- pump CABG.

Reston *et al.* conducted randomized and nonrandomized controlled studies on OPCAB and analyzed the short term and midterm outcomes. They concluded that OPCAB significantly reduced the hospital stay by lowering the operative morbidity and mortality associated with OPCAB and conventional CABG (Sellke *et al.*, 2005). Similar study by Yacoub *et al*. retrospectively analyzed 286 OPCAB patients and 1112 on-pump CABG patients between 1996 and 2001. They concluded that OPCAB significantly reduced the perioperative occurrence of myocardial infarction, reduced ICU stay and reduced mortality (Al-Ruzzeh *et al.*, 2003).

Nevertheless, there is conflicting evidence from published trials comparing the outcomes between OPCAB and conventional CABG surgeries. Some published trials were unable to demonstrate any advantage in terms of patient morbidity. Van Dijk attempted to establish the cardiac outcome and the quality of life between 281 patients who were randomly assigned in their multicenter setting. The cardiac outcome was determined by survival free stroke, MI and re do surgery. The authors showed similar percentage of survival free from MI between OPCAB (93%) versus on- pump CABG (94.2%). There was no difference in terms of stroke postoperatively. The short term mortality was similar in both groups (Van Dijk *et al.*, 2002). Similar study by Legare *et al.* in 1999. The authors analyzed 300 patients who were randomized to undergo

OPCAB and conventional on- pump CABG. They concluded the was no significant difference between OPCAB and on- pump CABG in term of mortality, number of transfusion, perioperative myocardial infarction, stroke. The authors failed to establish any advantage over each other in terms of morbidity (Légaré *et al.*, 2004).

2.5 Elective Versus Emergency Coronary Artery Bypass Graft Surgery

Many authors believe that emergency CABG exposes patients to greater risk and therefore have a major impact on the rates of morbidity and mortality as compared to the elective CABG. Such morbidity includes prolonged ventilation, re do surgery, postoperative MI that eventually led to prolonged ICU and hospital stay.

Kurki and colleagues at Department of Anesthesiology, Helsinki University Central Hospital, Finland studied the association between preoperative risk factors and postoperative outcomes in emergency and elective coronary artery bypass graft (CABG) patients. They retrospectively analyzed database from 4,001 emergency CABG and 7,489 elective CABG patients. Preoperatively, 47.1% of patients in the emergency group had angina and 34.1% had MI whilst the elective group had 33.9% and 15.2% respectively. The mortality rate was 4.7% in the emergency group and 2.6% in the elective group. The emergency group had lengthy hospital stay 17.5 +/- 15.8 days (median 14 days) whilst the elective group had 12.9 +/- 15.1 days (median 9 days). The authors concluded that patients undergoing emergency CABG had greater postoperative morbidity and mortality, longer hospital stay, than patients undergoing elective surgery (Kurki *et al.*, 2003).

Crossman and colleague critically reviewed the published information on the timing of coronary artery bypass graft surgery following acute myocardial infarction. They extracted a Medline search of the literature published between 1984 and October 2000. As results, 11 retrospective and prospective studies were analyzed. The studies suggests that timing of bypass surgery after infarction is not an independent predictor of outcome, however respective patients must be adequately optimised preoperatively. Resuscitation and stabilization reduce the risk of ischemic perfusion injury perioperatively. The timing suggested can be safely after 48 hours of infarction event. Further delaying coronary bypass surgery for an arbitrary period of time following acute MI is unwarranted. The authors stressed that the mortality risk of infarction related was greater than delaying the surgery (Crossman *et al.*, 2002).

We can conclude that the previous studies were conducted in a specialized referral center with multi surgeons performing a relatively large number of operations per year, and therefore the results may not be completely generalizable to other centre with a lower volume of CABG cases such as in the HUSM. Furthermore, majority of studies include emergency CABG, CABG with concomitant procedures, redo CABG cases or off- pump CABG, in which my review shown these extrapolate variables have influenced on morbidity. All of these factors reduced homogeneity of the study population.

CHAPTER 3

OBJECTIVES

3.1 General Objectives

The aim of this study is to identify the risk factors for prolonged mechanical ventilation (PMV) after elective isolated on pump coronary artery bypass grafting (CABG) surgery in HUSM Kubang Kerian, Kelantan.

3.2 Specific Objectives

3.2.1 To determine the incidence rate of PMV following CABG surgery.

3.2.2 To identify the preoperative, intraoperative and postoperative risks variables responsible for PMV in patients undergoing CABG surgery over given period of time.

3.2.3 To determine the independent risk factors that contributes for PMV following CABG surgery.

3.2.4 To demonstrate that those in the PMV group expose patients to longer hospital stays.