Cost Effectiveness of Immediate Tracheostomy versus Early Tracheostomy in Decompressive Craniectomy Patients: A Retrospective Study

DR. HEZRY BIN ABU HASAN

Dissertation Submitted In Partial Fulfillment Of The Requirements For The Degree of Master Of Surgery (Neurosurgery)

UNIVERSITY SAINS MALAYSIA

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Last but not least, to my parents, who are always a constant source of inspiration, motivation, and the reason I dedicate this work to.

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LIST OF ABBREVIATIONS

ED	Emergency Department
EDH	Extradural Hemorrhage
ET	Early Tracheostomy
DRG	Diagnosis Related Group
DRS	Disability Rating Scale
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
HDU	High Dependency Unit
HQE	Hospital Queen Elizabeth
ICU	Intensive Care Unit
IT	Immediate Tracheostomy
IVH	Intraventricular Hemorrhage
IVI	Intravenous Infusion
LOS	Length of Stay
MY-DRG	Malaysian Diagnosis Related Group
NOG	No Organism Cultured
OT	Operation theatre
RM	Ringgit Malaysia
SAH	Subarachnoid Hemorrhage
SDH	Subdural Hemorrhage
SPSS	Statistical Package for the Social Sciences (SPSS): Statistical analysis software
TBI	Traumatic Brain Injury
USD	United States Dollar
VAP	Ventilator-Acquired Pneumonia
WTP	Willingness-to-Pay

ABSTRAK: BAHASA MALAYSIA

Cost Effectiveness of Immediate Tracheostomy versus Early Tracheostomy in Decompressive Craniectomy Patients: A Retrospective Study

Dr. Hezry bin Abu Hasan [1], Dr. Sofan bin Zenian [1], Dr. Regunath Kandasamy [2], Prof. Dato' Dr. Syed Mohamed Aljunid Syed Junid [3, 4].

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Latar Belakang: Pesakit yang mengalami kecederaan otak sering mengalami masalah tekanan intrakranial (dalaman tengkorak) yang terlampau tinggi dan tidak terkawal. Ini membuatkan mereka terpaksa melalui pembedahan 'supratentorial decompressive craniectomy'untuk menurunkan dan mengawal tekanan intrakranial untuk mengelakkan kecederaan otak daripada berpanjangan. Walaubagaimanapun, akibat daripada kesan otak yang tercedera, golongan pesakit ini sering kali memerlukan bantuan mesin pernafasan untuk memastikan saluran pernafasan

mereka terjaga dan pemberian rawatan efektif untuk menurunkan tekanan intrakranial dapat dilakukan. Malangnya, proses pemulihan fungsi otak sering berlangsung secara perlahan dan ramai pesakit yang mengalami kecederaan otak memerlukan pembedah 'tracheostomy' untuk membantu proses pernafasan pada jangka masa yang panjang. Pernafasan secara berpanjangan melalui mesin pernafasan memerlukan kelengkapan yang lebih tinggi seperti penjagaan rapi di Unit Rawatan Rapi (ICU) dan kegunaan mesin pernafasan. Beban hospital yang makin meningkat akibat daripada hasil tanggungan rawatan para pesakit ini mendorong pihak kami untuk menginovasikan strategi pelaksanaan 'tracheostomy' dengan melakukan 'tracheostomy' sekaligus dengan pembedahan otak mereka (Immediate Tracheostomy) bagi para pesakit yang dijangkakan akan memerlukan bantuan pernafasan untuk tempoh yang lama. Dengan membandingkan kesan klinikal dan kos harga rawatan pesakit kecederaan otak, kami cuba menjawab persoalan 'Se-awal bilakah patut strategi tracheostomy ini dilaksanakan?'.

Kaedah dan Metodologi: Kajian secara retrospektif dilaksanakan melibatkan para pesakit yang memerlukan 'supratentorial decompressive craniectomy' dan 'tracheostomy' yang dilakukan dalam tempoh masa 7 hari selepas pembedahan otak mereka, dari tempoh Januari 2013 hingga ke Disember 2019 di Hospital Queen Elizabeth. Para pesakit yang menerima tracheostomy sekaligus dengan pembedahan otak digolongkan dalam kumpulan Immediate Tracheostomy (IT), manakala mereka yang menerima tracheostomy dalam tempoh masa 7 hari selepas pembedahan otak digolongkan dalam kumpulan Early Tracheostomy (ET). Data kuantitatif yang mempunyai taburan secara normal diuji menggunakan independent T-test, manakala data yang mempunyai taburan secara bukan normal diuji dengan ujian Mann-Whitney U. Data kualitatif diuji dengan

ujian Chi-square. Kos rawatan setiap pesakit dianggarkan berdasarkan maklumat dari pangkalan data kos rawatan pesakit Malaysia (Casemix System MY-DRG).

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Hasil Keputusan: Dari 411 pesakit, sebanyak 63 pesakit disertakan dalam kajian ini. 21 pesakit (33.3%) digolongkan dalam kumpulan Immediate Tracheostomy (IT), manakala 42 pesakit (66.7%) digolongkan dalam kumpulan Early Tracheostomy (ET). Pesakit dalam kumpulan Immediate Tracheostomy (IT) menunjukkan skor GCS yang lebih rendah (Median (IQR): 6 (3) lawan 9 (4), $p = 0.011$), tempoh penggunaan mesin pernfasan yang lebih pendek (Median (IQR): 72 jam (48) lawan 120 jam (72), $p = < 0.001$), pengurangan tempoh penggunaan ubat penenang (Median (IQR): 48 jam (24) lawan 72 jam (54), $p = < 0.001$), dan tempoh penjagaan di ICU yang lebih singkat (Median (IQR): 72 jam (48) lawan 144 jam (96), $p = < 0.001$). Pengurangan kos rawatan dengan Immediate Tracheostomy (IT) strategi dianggarkan sebanyak RM 18,463.14 – RM 39,223 untuk setiap pesakit. Diagnosis kecederaan otak tahap teruk (Severe TBI), skor GCS ≤ 6 sewaktu tiba di hospital, dan bukti pendarahan dalam ventrikel otak (IVH) pada CT brain dikenalpasti sebagai petanda para pesakit yang akan menerima manfaat dari pelaksanaan strategi Immediate Tracheostomy (IT).

Kesimpulan: Strategi Immediate Tracheostomy (IT) terbukti mampu mengurangkan kos rawatan dan meningkatkan keberkesanan penggunaan katil ICU. Beberapa petanda pesakit yang akan menerima manfaat dari pelaksanaan strategi Immediate Tracheostomy (IT) turut dikenalpasti. Dengan terbuktinya kebolehannya, strategi Immediate Tracheostomy (IT) perlu diambil kira dalam pelaksanakan rawatan pesakit kecederaan otak.

Kata Kunci: Immediate Tracheostomy, Early Tracheostomy, Decompressive Craniectomy, Mechanical Ventilation, Length of Stay, Casemix, MY-DRG, Traumatic Brain Injury.

ABSTRACT: ENGLISH

Cost Effectiveness of Immediate Tracheostomy versus Early Tracheostomy in Decompressive Craniectomy Patients: A Retrospective Study

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Background: Traumatic Brain Injury (TBI) patients often present with refractory intracranial hypertension, necessitating a supratentorial decompressive craniectomy to relieve malignant intracranial pressure and prevent further neurological insult. However, due to the poor neurological condition of these patients, many are electively intubated and put on mechanical ventilation to protect the airway and facilitate cerebral protective measures. Unfortunately, as a result of poor and prolonged neurological recovery, many patients have to be put on

tracheostomy in view of prolonged intubation. Prolonged mechanical ventilation also inefficiently utilizes the already limited mechanical ventilators and Intensive Care Unit (ICU) beds. In an attempt to maximize our limited hospital resources, we innovate a new method of tracheostomy timing strategy by performing the tracheostomy in the same setting as the supratentorial decompressive craniectomy (Immediate Tracheostomy) in patients who are anticipated to require prolonged mechanical ventilation. We attempt to answer 'How early should Early Tracheostomy be done?' by comparing the clinical and cost-saving benefit of the Immediate Tracheostomy strategy.

Methods: A retrospective study on patients requiring a supratentorial decompressive craniectomy and tracheostomy done within 7 days of the cranial surgery from January 2013 to December 2019 in Hospital Queen Elizabeth was done. Patients receiving a tracheostomy in the same setting of their supratentorial decompressive craniectomy were assigned to the Immediate Tracheostomy (IT) group, whereas those who received a tracheostomy within 7 days of their cranial surgery was assigned to the Early Tracheostomy (ET) group. Normally distributed quantitative data was analyzed using the independent T-test, while non-normally distributed data was analyzed using the Mann-Whitney U-test. Qualitative variables were analyzed with a Chi-square test. Cost of treatment of each patient was obtained based on Malaysian costing database provided by Casemix System MY-DRG. Of 411 patients reviewed, a total of 63 patients were included in the study. 21 patients (33.3%) were allocated to the Immediate Tracheostomy (IT) group and 42 patients (66.7%) in the other.

Results: Patients in the Immediate Tracheostomy (IT) group had significantly lower total GCS scores (Median (IQR): 6 (3) versus 9 (4), $p = 0.011$), reduced duration of mechanical ventilation (Median (IQR): 72 hours (48) versus 120 hours (72), $p = < 0.001$) and sedation (Median (IQR): 48 hours (24) versus 72 hours (54), $p = < 0.001$), and shorter ICU length of stay (Median (IQR): 72 hours (48) versus 144 hours (96), $p = < 0.001$). Cost reduction with the Immediate Tracheostomy (IT) strategy was estimated to be RM 18,463.14 – RM 39,223 per patient. The diagnosis of severe TBI, total GCS score ≤ 6 on presentation, and the presence of Intraventricular Hemorrhage (IVH) on CT brain imaging were identified as possible indicators for patients who will benefit from the Immediate Tracheostomy (IT) strategy.

Conclusion: The Immediate Tracheostomy strategy has shown evidence of increasing ICU bed turnover and reducing the cost of treatment. Patients presenting with a total GCS of ≤ 6 and presence of IVH on CT Brain were seen to benefit from Immediate Tracheostomy. With the clinical and treatment cost benefits seen, the Immediate Tracheostomy (IT) strategy should be considered a viable option for the management of Traumatic Brain Injury patients undergoing supratentorial decompressive craniectomy.

Keywords: Immediate Tracheostomy, Early Tracheostomy, Decompressive Craniectomy, Mechanical Ventilation, Length of Stay, Casemix, MY-DRG, Traumatic Brain Injury.

1. INTRODUCTION

1.1 BACKGROUND AND SIGNIFICANCE

Intracranial hypertension is a Neurosurgical emergency in which urgent and effective management is needed in order to prevent cerebral herniation and the resulting neurological decline, morbidity and mortality.

Based on the Monro-Kellie doctrine [11], which describes the relationship of the intracranial components (blood, brain, and cerebrospinal fluid) and the resulting intracranial pressure, in a fixed and limited space which is the intracranial cavity, an increase of one of the intracranial components will result in the compensatory reduction of the other intracranial components, which occurs to ensure the intracranial pressure is maintained. A continued and increasing imbalance of these intracranial components will result in a decompensation and cerebral herniation [11].

The etiologies of these kinds of intracranial hypertension are various and spans from traumatic cerebral bleeds (extradural and subdural hemorrhage, cerebral contusions), spontaneous vascular events (malignant middle cerebral artery (MCA) infarcts, hypertensive intracranial bleeds, ruptured cerebral aneurysms), space occupying lesions (cerebral abscess and tumours), to accumulation of cerebrospinal fluid in hydrocephalus.

Pioneered by Kocher [9], and modernized by Harvey Cushing [12], the supratentorial decompressive craniectomy requires the removal of a large frontotemporoparietal calvarial bone flap followed by

a wide opening of the dura, in an attempt to increase the potential volume of the intracranial compartment as a means for rapidly reducing intracranial hypertension [8,9,12].

Often, due to the severity of their cerebral insult from the intracranial hypertension, these post-craniectomy patients are often in a poor neurological state whom are either already in a comatose state, or induced into a comatose state for continued management of their refractory intracranial hypertension via cerebral resuscitation. These patients require constant nursing care for their hygiene, feeding, and are dependent on mechanical ventilation for their respiration [14]. Immobilized and bed bound, they are also susceptible to other associated complications of mechanical ventilation such as Ventilator-Acquired Pneumonia (VAP), endotracheal tube obstruction or dislodgement, and prolonged Intensive Care Unit (ICU) / High Dependency Unit (HDU) stay [3,5,13].

Ventilator-Acquired Pneumonia (VAP) is a particular concern and is responsible for an estimated 25% of all ICU infections [7], and 50% of all hospital-acquired pneumonias [5]. Recent studies show the incidence of VAP to be 1 to 9 cases per 1000 ventilator days [3], and mortality rates of patients with VAP are estimated to be 9-13% [5], and up to 40% of Neurosurgical patients end up developing VAP [13,14]. These figures reveals the extent of VAP risk towards Neurosurgical patients and the associated increase in morbidity and mortality risk needs an effective management strategy for VAP prevention.

Tracheostomy is a procedure of creating a surgical airway in patients whom already are, or are anticipated to be on prolonged intubation by exteriorizing the trachea to the skin [15], often by the insertion of a tracheostomy tube. Benefits of tracheostomy are many; Herritt et al. [1] and Hyde et

al. [2] in their respective works have listed the benefits which includes the prevention of tracheal scarring by the endotracheal tube, reduced risk of self-extubation, improved comfort and reduced sedation requirement, improved airway dynamics by diminishing work of breathing by the patient, as well as improved oral hygiene and care. The incidence of VAP has also been showed to be reduced with tracheostomy [2,4]. On the other hand, tracheostomy complications such as tracheostomy tube obstruction and dislodgement (1%), subcutaneous emphysema (<11%), bleeding (7-11%), pneumothorax (<4%), stoma site infection (Up to 63%) tracheal stenosis (11-63%) and tracheal malacia (<8%) are known to occur [16], and their risks should be considered.

Though tracheostomy has been proven to be an effective strategy in the prevention of VAP, the timing of tracheostomy in critically ill patients is a subject of discussion, with a lack of consensus of the definitions for early and late tracheostomy [3,17]. Definition for 'Early Tracheostomy' varies from author to author, with tracheostomy done from as early as the 4th day of intubation (Herritt et al.) [1], 5th day (Hyde et al.) [2], and as late as the 10th day of intubation (Catalino et al.) [3]. A mid-range figure of tracheostomy done before the 7th day of intubation is defined by Siddiqui et al. and Kim TH et al. as 'Early Tracheostomy', and 'Late Tracheostomy' as tracheostomy done after the 7th day of intubation [4,26].

The benefits of early versus late tracheostomy has been reported by multiple authors such as Hyde et al. [2], Catalino et al. [3], Siddiqui et al. [4] and Arabi et al [17]. Early tracheostomy was noted to reduced duration of mechanical ventilation and length of ICU and hospital stay [2,3,4,17]. Though Catalino et al. has found no reduction in the incidence of VAP and mortality rates [3], Siddiqui et al. and Hyde et al. found Early Tracheostomy to be beneficial in reducing VAP incidence [2,4]. Noting that the

risk for VAP is greatest during the first 5 days of intubation, with the mean duration between intubation and development of VAP being 3.3 days [5, 18], and the variability in the timing of Early Tracheostomy, a question arises of how early should Early Tracheostomy be done to bring the most benefit to our patients?

Apart from the clinical benefits of early tracheostomy, in view of recent increases in the cost of medical care and the limitation of monetary and physical resources of our healthcare system, the cost effectiveness of early versus late tracheostomy needs to be analyzed. ICU care is associated with a significant portion of hospital expenditure, with a per day cost of $2,500 to $4,300 (United States Dollars, USD), and amounts to 13.2% of hospital expenditure in the United States [1]. $108 billion USD were spent for ICU care in 2010, which is a doubling of the $56 billion USD spent in 2000 [1] in the United States as a result of longer ICU LOS, new medications and technologies employed, and increasing labor costs. ICU care also utilizes a disproportionate share of resources for a more limited number of people, as a study of ICU patients in Florida (United States) revealed that 40-60% of their total hospital cost was utilized for their ICU care, despite their ICU LOS amounting to only 20% of their total hospital LOS [29].

On the home front, a study by Aung et al. of the cost and length of stay for ICU patients in Malaysia supports the fact that ICU care is a major source of hospital expenditure. The mean ICU LOS was 5.7 days, and the cost of ICU care ranges between $427-1,324 USD per day depending on the type of ICU unit, with a mean cost of $5,473 USD per ICU stay [30]. This amounted to a sizeable 47.2% of their total hospital cost being spent for ICU care [30].

With these costs in mind, we postulate that ICU LOS is an important determinant and study outcome in the cost analysis of tracheostomy timing, as we endeavor to see for any possible reduction in ICU LOS and costs with Immediate Tracheostomy. Increasingly, the cost effectiveness of our treatment decisions in an environment of limited resources such as in Sabah, and Malaysia as a whole, is gaining importance.

Liu et al. has done a cost-effectiveness analysis of early versus late tracheostomy by obtaining data from multiple meta-analysis and local healthcare cost database, and using the obtained the daily cost of ICU multiplied by the average ICU LOS to obtain the total ICU cost, combined with the tracheostomy cost, cost of treatment of tracheostomy complications and the cost of treatment of pneumonia, to obtain a weighted mean cost for patients undergoing early and late tracheostomy [19].

Liu et al. has found that the cost of a late tracheostomy strategy costs $ 45,943.81 USD, whereas an early tracheostomy strategy cost a lower value of $ 31,979.12 USD [19]. They have postulated that a late tracheostomy strategy will also reduce the number of inappropriate tracheostomies, as some of these patients may be successfully extubated if given more time. However, the possible cost savings of avoiding a tracheostomy may be counteracted by longer ICU LOS and days of mechanical ventilation. In view of this, they have identified the Willingness-to-Pay (WTP) value for avoidance of one tracheostomy to be $ 80,000 USD [19], where the WTP value is the amount a consumer or healthcare provider is willing to pay for a particular treatment in order to obtain its benefit [20], which in this case is to avoid undergoing a possibly unnecessary tracheostomy. To conclude, the early tracheostomy strategy is more beneficial in reducing costs[19]. Unfortunately,

there is a lack of data for similar cost-effectiveness studies for tracheostomy timing in Malaysia, and we endeavor to provide these in our study.

With regards to the clinical practice in our center, in view of the relatively limited resources of Hospital Queen Elizabeth, and the anticipated prolonged intubation of certain Neurosurgical patients with poor prognosis, a concurrent tracheostomy is performed after undergoing an emergency supratentorial decompressive craniectomy in the same setting by the Neurosurgical team, which for the purpose of this study we have define this to be an 'Immediate Tracheostomy'. Based on the evidence from the previously referenced studies, an immediate tracheostomy was done in an attempt to shorten mechanical ventilation time, shorten ICU LOS, improve the oral toileting and hygiene, and to prevent an additional OT visit to perform the tracheostomy at a later time. These efforts are done in order to increase turnover of ICU beds and ventilators, and reduce the overutilization of the OT.

The decision to subject the patients to immediate tracheostomy after an emergency supratentorial decompressive craniectomy is undertaken by the Neurosurgeons of the Neurosurgical team of Hospital Queen Elizabeth based on knowledge of the clinical benefits of the previously quoted studies. Though Catalino et al. and Siddiqui et al. has outlined several predictors of patients who may benefit from an early tracheostomy (i.e. GCS <8, unequal pupils on presentation, rapid neurological deterioration on presentation and presence of hydrocephalus) [3,4], there are no established criteria at the moment for determining patients that will benefit from concurrent / immediate tracheostomy after a supratentorial decompressive craniectomy, and we endeavor to establish a criterion for these group of patients by observing their clinical outcomes via the

Glasgow Outcome Scale (GOS), Disability Rating Scale (DRS) and 30-day mortality rates with their clinical data on presentation.

In summary, the purpose of this study is to determine the cost-effectiveness of Immediate Tracheostomy (IT) versus Early Tracheostomy (ET) in patients who had underwent an emergency supratentorial decompressive craniectomies, by determining the average cost difference between the two study groups. Calculation of the cost of treatment in each group will be determined by the cost of utilization of hospital resources, dictated by the average hospital LOS and the VAP incidence and its treatment in each of the study groups. A possible criterion for patients that will benefit from Immediate Tracheostomy will also be established.

1.2 OBJECTIVES

To determine the clinical benefits in terms of duration of mechanical ventilation, ICU length of stay, incidence of VAP and cost effectiveness of Immediate versus Early Tracheostomy in patients who had underwent emergency supratentorial decompressive craniectomies, in Hospital Queen Elizabeth from 1st January 2013 to 31st December 2019.

Specific objectives include:

1. To determine the average cost difference between emergency supratentorial decompressive craniectomy patients who had underwent Immediate (IT) versus Early Tracheostomy (ET).

2. To determine the average ICU length of stay (LOS) between emergency supratentorial decompressive craniectomy patients who had underwent Immediate (IT) and Early Tracheostomy (ET).
3. To determine the incidence of Ventilator-Acquired Pneumonia (VAP) between Immediate (IT) and Early Tracheostomy (ET).
4. Investigate a possible criterion for patients that will benefit from Immediate Tracheostomy (IT) on presentation.

2. METHODOLOGY

This is a cross-sectional study that was conducted in Hospital Queen Elizabeth in Kota Kinabalu, Sabah. The study involves the use of retrospective data of patients undergoing emergency supratentorial decompressive craniectomy with tracheostomy done within 7 days post-craniectomy, during the period 1st January 2013 to 31st December 2019.

Hospital Queen Elizabeth is a government hospital providing tertiary-level of care and is the main referral center in Malaysia's second largest state, Sabah. The hospital provides 775 general beds with 16 ICU beds, 28 Medical HDU beds, and 4 Neurosurgical HDU beds, and accommodates referrals from 21 district hospitals, 106 health clinics (Klinik Kesihatan) and the flying doctor air service [35]. Catering to a population of 3.91 million people across a large state of 73,864 square km in size, Sabah unfortunately is also the poorest state in Malaysia with the lowest Human Development Index (HDI) of 0.704 [36]. Poor infrastructure and underdevelopment in the second-largest state in terms of land size and population, Hospital Queen Elizabeth faces unique challenges to its logistical and resource management. This is especially true with regards to the limited ICU / HDU beds, in whom patient turnover and efficiency has to be maximized. Neurosurgical patients requiring critical care and mechanical ventilator support are admitted into the Neurosurgical HDU, under the care of 2 doctors and 4 nurses. Mechanically ventilated patients are co-managed with the peripheral Anesthesia team, headed by an Anesthetist. In the event of shortage of Neurosurgical HDU beds, patients are admitted into the ICU and Medical HDU, co-managed by the peripheral Neurosurgical team.

2.1 STUDY PROCESS

1. **Patient Identification & Selection:**

- Potential patients were identified from the Neurosurgery Operation Theatre (OT) Registry. In view of a change from physical patient registry (logbook) to digital patient registry in 2018, multiple sources were used to identify potential patients: Neurosurgery OT Registry Logbook (Cases from January 2013 – December 2017), Neurosurgery OT Notes Google Drive (January 2018 onwards), and Neurosurgery OT Desktop Database (January 2018 onwards)
- Potential patients were then selected based on the inclusion criteria.

2. **Medical Records Tracing**:

- Medical records of the selected patients were then obtained from the Record Unit of Hospital Queen Elizabeth.
- In the event of an incomplete or missing medical record, the medical records were also checked in other potential locations such as the Neurosurgical ward and Neurosurgery outpatient clinic. If the medical records were still not located, a final check with the different specialist clinics (Otorhinolaryngology (ENT), Oral & Maxillofacial Surgery (OMFS), Plastic & Reconstructive Surgery etc.) was done as patients medical records may be dispatched there for an outpatient appointment.
- Failing all these measures, the medical records were deemed missing or incomplete and patient is withdrawn from the study.

3. **Medical Record Analysis & Patient Grouping**:

- Medical records of the selected patients obtained were then analyzed to ensure the patients had met the inclusion and exclusion criteria. Patients were withdrawn if exclusion criteria were met or if their medical records were deemed missing or incomplete for data extraction.
- The patients were then divided into 2 groups:
    - Immediate Tracheostomy (IT)
        - Supratentorial decompressive craniectomy and tracheostomy were done in the same setting.
        - I.e. After completion of the craniectomy, tracheostomy was then done for the patient before the patient is discharged from the operation theatre.
    - Early Tracheostomy (ET)
        - Tracheostomy was done within 7 days of post-craniectomy.

4. Data Collection:

- Data was extracted from the medical records for the following parameters:

- Length of Stay (LOS): Number of days in:
    - HDU/ICU
    - Neurosurgery ward
- Duration of mechanical ventilation (days)
- Duration of sedation (days)
- Incidence of Ventilator-Acquired Pneumonia (VAP):
    - Type of antibiotics used
    - Duration of antibiotics administered (days)

- Incidence of tracheostomy-related complications:
    - Intra-operative
    - Post-operative
    - The need of re-operation / re-tracheostomy
- Patient condition on arrival & on discharge:
    - GCS & pupils on arrival
    - GOS, DRS, & 30-day mortality on discharge

- Data was collected with the use of a data collection form, where patient's identity is not collected and done anonymously to protect patient's privacy.

5. **Data Processing & Conclusion**:

- The collected data were processed & statistical analysis conducted using SPSS software and under the guidance of a statistician.
- Study findings were analyzed and correlated to bring the study to a conclusion.

Study Methodology & Process

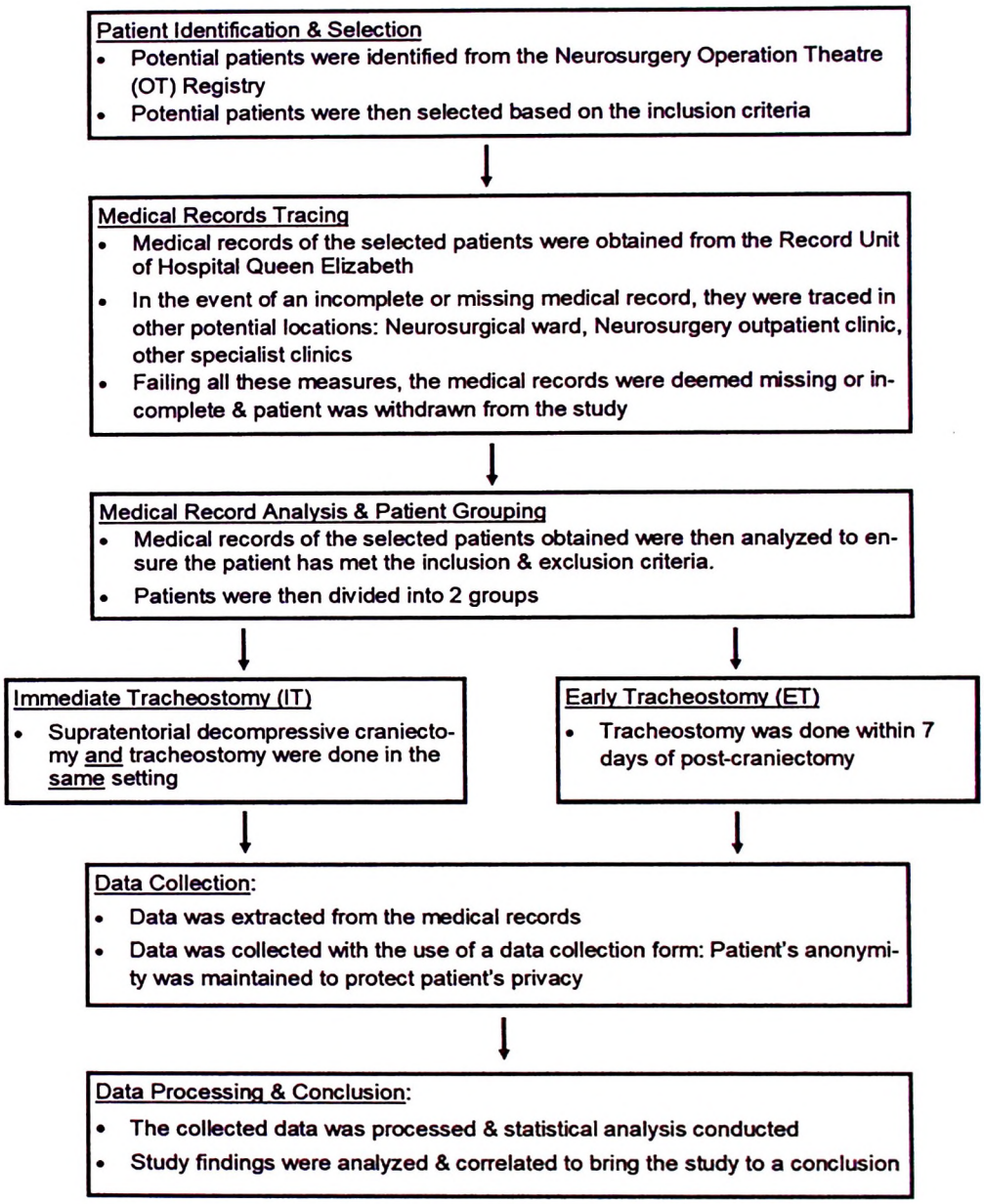

Figure 1: Flowchart of the study Methodology & process.

2.2 STUDY DESIGN

This is a retrospective cross-sectional study design. The study aims to determine the cost effectiveness for the different timing of tracheostomy performed in patients whom had underwent an emergency supratentorial decompressive craniectomy in Hospital Queen Elizabeth.

2.2.1 PATIENT GROUPS

There are 2 patient groups being studied and the ratio for both these groups are aimed to be equal in number (1:1):

1. Immediate Tracheostomy (IT):
    - Tracheostomy and craniectomy done in the same setting.
    - I.e. After completion of the craniectomy, tracheostomy is then done for the patient before the patient is discharged from the operation theatre.
2. Early Tracheostomy (ET): Tracheostomy done within 7 days post-craniectomy

2.2.2 OUTCOMES AND VARIABLES MEASURED

The determination of outcomes in this study is divided into two parts; the first part being the measurement of the clinical outcomes, and the second part being the calculation of costs based on the clinical outcomes, to arrive at the cost difference between the two study groups for the purpose of cost effectiveness analysis.

Comparing between the IT and ET groups, several variables will be analyzed to determine whether Immediate Tracheostomy (IT) will be a more cost-effective option when managing these group of patients.

The following variables will be analyzed in this study:

- Length of Stay (LOS):
  - The number of days patient was admitted to:
    - HDU/ICU
    - Neurosurgery ward
  - The length of one day is taken as a period of admission from the 1st hour and up to 24th hour. I.e.:
    - 14 hours of admission in the HDU/ICU is equivalent to 1 day.
    - 26 hours of admission in the Neurosurgery ward is equivalent to 2 days.
  - Longer hospital LOS incur higher costs per day and reduces available beds for other patients.

- Duration of mechanical ventilation (days):
  - The number of days patient was on ventilator support for respiration.
  - Patient will be gradually weaned-off of ventilator support (ventilator liberation) once their neurological and respiratory function recovers to an acceptable level, and allowed to breathe independently (aided by supplemental oxygen).

- Longer ventilation periods incur higher costs per day with the utilization of the ventilator and its disposables, as well reducing the ventilator availability for other patients.

- Duration of sedation (days):
  - The number of days patient was on intravenous sedation infusion.
  - Patients are often put on intravenous sedation in order to facilitate effective ventilator support of the patient's respiration.
  - Sedation will be tapered-down once function recovers to aid in weaning-off of ventilator support.
  - Longer sedation periods incur higher costs as more sedative medications and nursing care is needed for the comatose patients.
  - In Hospital Queen Elizabeth, patients are sedated using intravenous infusion of Midazolam and Fentanyl at a rate of 3ml/hour.

- Incidence of Ventilator-Acquired Pneumonia (VAP):
  - VAP is defined as pneumonia in patients intubated for more than 48 hours, with clinical and radiological imaging findings supportive of pneumonia and a positive microbial culture [5,6]:
  - Incidence of VAP is associated with higher mortality and poorer clinical outcomes [5], and thus the prevention and reduction in the incidence of VAP may be associated with preventing higher cost of treatment [7].
  - Type of antibiotics used for treatment of VAP:

- Different antibiotics used are associated with different costs and needs to be considered for calculation of cost effectiveness.
- Resistant organisms & severe VAP-related sepsis requires more potent and advanced antibiotics, thereby increasing costs.

- Duration of antibiotics administered (days):
  - The number of days patients was on antibiotic therapy for the treatment of VAP
  - Longer antibiotic therapies may increase treatment cost as more antibiotics are utilized.

- Incidence of tracheostomy-related complications:
  - The number and type of complications are noted during Intra-operative and Post-operative period. The need of re-operation / re-tracheostomy is also noted.
  - Higher complication rates may incur higher costs in the rectification of these complications, and the timing of tracheostomy is observed to be associated with possibility of reduced complication rates

- Patient condition on arrival & on discharge:
  - Glasgow Coma Scale (GCS) & pupils on arrival to the Emergency Department
  - Glasgow Outcome Scale (GOS) on discharge and 6 months post-discharge
  - Disability Rating Scale (DRS) on discharge
  - 30-day mortality post-discharge

- These factors are analyzed for any correlation in the outcomes and mortality of the two study groups to aid in determining possible criteria for patients that may benefit from Immediate Tracheostomy (IT).

The primary outcome measured is the mean value for the number of days of ICU LOS. Other secondary outcomes include the incidence of VAP, mean duration of mechanical ventilation, mean duration of sedation, mean Neurosurgery ward LOS, and tracheostomy complication rates. Determining the cost-effectiveness of immediate versus early tracheostomy is the endpoint.

2.2.3 CALCULATION OF TREATMENT COSTS AND COST EFFECTIVENESS

A study by Aung et al. of the cost and length of stay for ICU patients in Malaysia supports the fact that ICU care is a major source of hospital expenditure. The mean ICU LOS was 5.7 days, and the cost of ICU care ranges between $427-1,324 USD per day depending on the type of ICU unit, with a mean cost of $5,473 USD per ICU stay [30]. This amounted to a sizeable 47.2% of their total hospital cost being spent for ICU care [30].

With these costs in mind, we postulate that ICU LOS is an important determinant and study outcome in the cost analysis of tracheostomy timing, as we endeavor to see for any possible reduction in ICU LOS and costs with Immediate Tracheostomy.

For the purpose of cost estimation for this study, the cost of treatment for every individual patient involved in the study was derived using the Casemix System MY-DRG software (MY-DRG Code Assist version 2.4) (Casemix Solutions Sdn. Bhd., Kuala Lumpur, Malaysia). Developed in 1976

by Bob Fetter and John Thompson from Yale University, the Casemix System is a patient classification system that classifies patients with similar clinical characteristics into one single homogenous costing group [31]. The Diagnosis Related Group (DRG) was the first grouping system developed under the Casemix System and was used as a mean of relating the type of patients a hospital treats to the cost incurred by the hospital [31]. Based on the DRG, patients with similar diagnosis are grouped together as they were noted to have similar treatment costs. The Casemix DRG system has been adopted by various countries such as the United Kingdom (Healthcare Resources Groups, HRG), Australia (Australia Refined Diagnostic Group, AR-DRG) and Germany (G-DRG) [31]. By incorporating local costing data of their respective countries into the Casemix DRG system, a more accurate costing data was able to be derived which is tailored to their own countries. The Casemix System has been used in multiple international costing studies involving countries such as the Netherlands, United States, United Kingdom, Australia, Canada and Malaysia [30-34], thereby proving the effectiveness of the Casemix System in estimating the cost of treatment [31].

The Malaysia DRG (MY-DRG) was created based on Malaysian costing data. Pioneered in 1996 involving 12 public hospitals and 3 university teaching hospitals, MY-DRG was derived from the UNU-CBG (United Nations University Case Base Groups) by Universiti Kebangsaan Malaysia (UKM). Based on the Casemix System and MY-DRG, the MY-DRG Code Assist software calculates the treatment costs incurred based on the disease diagnosed and treated during the patient's presentation, as well as the treatment procedures and medications received during the admission such as mechanical ventilation and its duration, antibiotic therapy, and surgical intervention such as tracheostomy, re-tracheostomy for complications arising from the initial

tracheostomy, and decompressive craniectomy. Other costs such as the administrative overhead, staff salary, ICU cost and operation theatre costs has been incorporated into the treatment cost calculation by the MY-DRG Code Assist software.

With the treatment cost for every patient in this study obtained, the cost of treatment for the two patient groups can then be statistically analyzed to determine the presence of a significant cost difference and the cost effectiveness of Immediate Tracheostomy (IT) versus Early Tracheostomy (ET) for patients undergoing emergency supratentorial decompressive craniectomy. For the purpose of comparison of costs, values stated in USD is taken at the exchange rate of 1 USD = RM 4.14 (As of exchange rates seen in May 2021). Calculation examples using the MY-DRG Code Assist software can be found in the Appendix

Figure 2: Screenshot of the welcome screen of the MY-DRG Code Assist software.

2.2.4 TRACHEOSTOMY TIMING & OTHER OPERATIONAL DEFINITIONS

The timing for tracheostomy of critically ill patients were variable, with the definition of 'Early Tracheostomy' also varying from author to author, as early as the 4th day of intubation (Herritt et al.) [1], 5th day (Hyde et al.) [2], and as late as the 10th day of intubation (Catalino et al.) [3].

For this study, a mid-range figure of tracheostomy performed on the 7th day of intubation and below is defined as 'Early Tracheostomy', as was similarly defined by Siddiqui et al. [4] in his paper.

'Immediate Tracheostomy' was defined as tracheostomy done concurrently or in the same setting as the emergency supratentorial decompressive craniectomy. I.e. After completion of the craniectomy, tracheostomy is then done for the patient before the patient is discharged from the operation theatre.

Emergency supratentorial decompressive craniectomy was defined as the emergency removal of a large frontotemporoparietal calvarial bone flap followed by a wide opening of the dura, in an attempt to increase the potential volume of the intracranial compartment as a means of rapidly reducing intracranial hypertension [8,9]. Causes for the intracranial hypertension needs to be managed effectively and rapidly to prevent cerebral herniation and can be due to various etiologies such as post-traumatic intracranial bleeding and spontaneous hypertensive intracranial hemorrhage and malignant cerebral infarcts.

All tracheostomies were performed via an open method by either the Neurosurgical or Otorhinolaryngology (ENT) teams, using a low-pressure cuffed tracheostomy tube under aseptic technique in the Operation Theatre (OT).

The neurological outcome was evaluated using the Glasgow Outcome Score (GOS); commonly used to describe outcomes of head injury patients.

Neurological outcome was assessed as follows:

1: Death

2: Persistent vegetative state with inability to interact with the environment

3: Severe disability with inability to live independently, but with the ability to follow commands

4: Moderate disability with the ability to live independently, but with the inability to return to work or school

5: Mild or no disability with the ability to return to work or school.

A favorable outcome is deemed for scores 3 to 5, and an unfavorable outcome is deemed for scores 1 to 2 [10].

Another metric of assessment of neurological outcome is the Disability Rating Scale (DRS), which is used to assess the impairment and disability of the patients during their recovery. Patients are assessed on 4 categories such as awareness and response, self-care ability, independence, and psychosocial adaptability. Points are assigned based on the patient's ability in each category, and the total score is calculated on a scale of 0 (no impairment) to 29 (extreme vegetative state) to

determine their level of disability. A breakdown of the DRS scoring and disability categories are detailed in the Appendix.

2.3 STUDY POPULATION

All adult patients (aged 12 years and above) undergoing emergency supratentorial decompressive craniectomy with tracheostomy done within 7 days post-craniectomy in Hospital Queen Elizabeth from 1st January 2013 to 31st December 2019.

2.4 INCLUSION CRITERIA

- Age: 12 years old & above (Adults)
- Emergency supratentorial decompressive craniectomy who also underwent:
    - Immediate tracheostomy: Within same setting as cranial surgery
    - Early tracheostomy: Within one week (7 days) of cranial surgery

2.5 EXCLUSION CRITERIA

- Age less than 12 years old (Pediatric)
- Patients with brain tumour, abscess, aneurysm or vascular malformations
- Patients who were extubated successfully post-decompressive craniectomy without tracheostomy and later required re-intubation & tracheostomy
- Patients who had been ventilated for more than 3 days prior to surgery
- Coexisting life-threatening thoracic trauma (Severely compromised respiratory function)

2.6 WITHDRAWAL CRITERIA

Patients found to have met the exclusion criteria and/or not satisfied the inclusion criteria were withdrawn from the study.

Medical records of the selected patients if deemed to be missing or if found to be incomplete and unsuitable for the purpose of data extraction, the patients were also withdrawn from the study.

Withdrawn patients will not be replaced, and the study will proceed with the other remaining data. Withdrawn patients were also not placed on any follow-up with regards to this study as there were no intervention, no adverse events anticipated, and their treatment has already been completed.

2.7 SAMPLE SIZE

Incorporation of an economic evaluation into a clinical study may prove to be a challenge in terms of determining the sample size required, as the sample size needs to be adequate to provide sufficient power to both the clinical and economic endpoints [21,22,25]. However, a power calculation may prove useful in guiding the sample size estimation, based on the sample size calculated for the clinical effect [21,22,24,25].

For the sample size needed to determine the clinical endpoints, the calculation of the sample size is based on two studies that compares the outcome of tracheostomy timing for patients whom had underwent decompressive craniectomy surgery, with Kim et al. studying patients with traumatic brain injury, and Catalino et al. studying patients with spontaneous etiologies (Ischemic and hemorrhagic stroke).