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COMPARATIVE ANALYSIS OF EARLY AND LATE TRACHEOSTOMY AMONG PATIENTS WITH ACUTE HEART FAILURE EXACERBATION, TRENDS, CLINICAL AND ECONOMIC OUTCOME ASSESSMENT, FROM 2005 TO 2014 NATIONWIDE

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Heart failure is one of the leading causes of high morbidity and mortality. Acute exacerbation of heart failure may result in acute respiratory failure, which requires mechanical ventilator support. Despite supportive management, patients can fail extubation of the endotracheal tube and need a tracheostomy to continue mechanical ventilator support. However, optimal timing of tracheostomy has been controversial. Systemic study to assess the clinical and economic outcome of early tracheostomy among patients with acute heart failure exacerbation is lacking. The purpose of the study was to assess the national trend of tracheostomy among those who are admitted for acute respiratory failure with acute congestive heart failure exacerbation and to compare clinical and economic outcomes between the two groups (early and late tracheostomy) using national discharge data between from 2005 to 2014. We also conducted an economic evaluation comparing early and late tracheostomy among them using average cost and incremental costs with an outcome of length of stay. Among those who are admitted with acute heart failure exacerbation, 0.30% patients underwent the tracheostomy, and among them, 9.69% received early tracheostomy. There was no trend in the percentage of early tracheostomy. The length of stay in the hospital has decreased over time in late tracheostomy group, but it was stable in early tracheostomy group. Median total hospital length of stay (19 days) and total hospital cost ($52,158.23) in early tracheostomy group were significantly lower than late tracheostomy group (25 days and $68,037.40). Patients with coronary artery disease, pneumonia, and liver disease are less likely to receive early tracheostomy (OR 0.79, 0.63 and 0.64 respectively). After propensity score matching, it showed that the two groups did not show a significant difference in in-hospital mortality (OR 0.91, *p*-value 0.676), or decannulation rate (OR 2.01, *p*-value 0.571). However, early tracheostomy was associated with higher likelihood of having a complication from tracheostomy with OR 2.08 (*p*-value 0.044) but was also associated with lower total hospital length of stay with coefficient factor -6.50 (*p*-value 0.000) from the linear regression model. From the economic evaluation, the early tracheostomy dominates the late tracheostomy with the outcome of total hospital length of stay and post-procedural length of stay with lower cost and higher effectiveness. The incremental cost-effectiveness ratio (ICER) is negative, meaning it costs $3,492.65 for each additional day in the hospital for late tracheostomy compared to early tracheostomy. ICER with the outcome of post-procedural length of stay was again negative, showing $2,032.67 per extra day in the hospital after the procedure among late tracheostomy group. Early tracheostomy among patients with acute heart failure exacerbation had no significant difference in mortality but had significant economic benefit with lower cost and less total hospital length of stay.

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BACKGROUND

Heart failure is one of the leading causes of high morbidity and mortality. Based on the data from National Health and Nutrition Examination Survey (NHANES) 2009 to 2012, it was estimated that total 5.7 million Americans older than 20 years of age had heart failure. That number is anticipated to increase 46% from 2012 to 2030, which can result in more than 8 million people older than 18 years of age with heart failure.[1] One in nine deaths has heart failure on the death certificates, according to the National Center for Health Statistics in 2013.[2] Acute exacerbation of heart failure may result in acute respiratory failure, which requires mechanical ventilator support. Despite supportive management, patients can fail extubation of the endotracheal tube and need a tracheostomy to continue mechanical ventilator support.

Tracheostomy usually is done to minimize the mechanical trauma to the larynx or trachea, facilitate the weaning process, or protect the airway for a long time. Predictors of tracheostomy have been mostly reported among trauma or surgical patients, but it has not been studied among patients with acute respiratory failure from acute heart failure exacerbation. Also, there has not been a systemic study to assess the optimal timing of tracheostomy among them. Studies have shown that early tracheostomy reduces the hospital stay without clinical outcome difference.

Literature Review

- Background

Heart failure is one of the leading causes of high morbidity and mortality. Based on the data from National Health and Nutrition Examination Survey (NHANES) 2009 to 2012, it was estimated that total 5.7 million Americans older than 20 years of age had heart failure. That number is anticipated to increase 46% from 2012 to 2030, which can result in more than 8 million people older than 18 years of age with heart failure. [1] One in nine deaths has heart failure on the death certificates, according to the National Center for Health Statistics in 2013. [2] Data from Framingham Heart Study indicated that its incidence reached 10 per 1000 population after the age of 65. [3] Even though overall mortality from cardiovascular disease has declined, heart failure is the only major cardiovascular disease whose prevalence and incidence is still increasing with poor long term-prognosis. [4-6] Approximately half of the people who were diagnosed with heart failure die within 5 years. [7]

- The burden of heart failure

Considering the development and implementation of life-prolonging interventions along with the growing elderly population, the number of individuals with heart failure will be significantly increased, which will also increase the cost of heart failure. [7,8] In 2012, the estimate of heart failure related direct cost was $20.9 billion, and the indirect cost was $9.80 billion. [4,7] By 2030, it is anticipated that the total cost will increase to $69.7 billion which will equal $244 for every United States adult. Costs of heart failure are mainly driven by hospitalization, home nursing, hospice care, medical devices including cardiac resynchronization, ventricular assist device, and transplantation. [8] A study using 10-year data from the National Medical Expenditure Panel Survey (2002-2011) showed that individuals with heart failure had 4 times higher yearly expenditure ($23,854) compared to those without heart failure ($5,511). Heart failure-related costs increased by $5,836 (28% relative increase), from $21,316 in 2002 to $27,152 in 2010. The single largest driving component of this increase was inpatient costs ($11,318).[8]

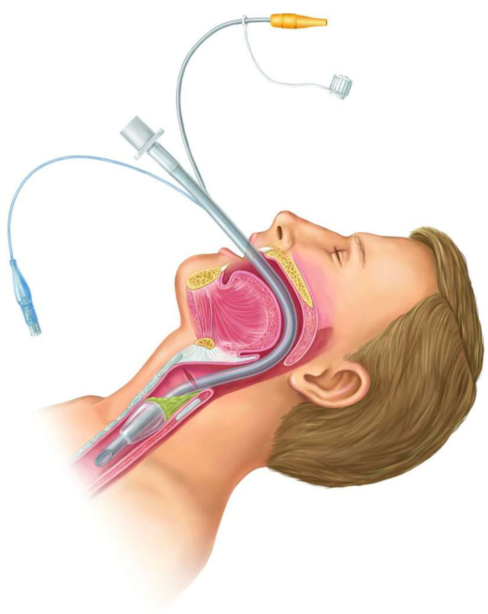
- Acute respiratory failure due to acute congestive heart failure exacerbation

Acute congestive heart failure is a common but potentially fatal condition, caused by congestive heart failure and may result in acute respiratory failure. It is characterized by acute dyspnea caused by acute fluid accumulation in the lungs. Most of the times, it is caused by a rapid increase in hydrostatic pressure in the pulmonary capillaries due to elevated cardiac filling pressure. This condition is also called cardiogenic pulmonary edema.[9] In treating patients with acute congestive heart failure exacerbation, routine oxygen supplementation is not indicated, but if the patient demonstrates hypoxemia (SpO2 <90%), oxygen supplementation should be initiated.[10] If the patient still shows respiratory distress, the patient will need assisted ventilation. First line treatment is a trial of noninvasive ventilation. However, if noninvasive ventilation is contraindicated or patient fails to improve with noninvasive ventilation within 1-2 hours, the patient should be intubated for conventional mechanical ventilation.

- Mechanical ventilation for treatment of respiratory failure

A mechanical ventilator is a machine, which assists or replaces the patient's spontaneous breathing using positive pressure. Mechanical ventilation for respiratory failure due to congestive heart failure exacerbation is usually initiated to reverse life-threatening hypoxemia (low oxygen level in blood), to provide sufficient oxygen delivery to vital organs, to maintain alveolar stability, and to decrease the work of breath to prevent respiratory muscle fatigue. [11,12] For the patient to receive mechanical ventilation, the patient should have a special form of a device, which allows the patient's airway to be directly connected to the mechanical ventilator. Usually, this special airway is achieved through the procedure "endotracheal intubation" in an emergent situation. Endotracheal intubation is a procedure to place a plastic tube in the patient's trachea, which can be connected to the mechanical ventilator to make a circuit for mechanical ventilation. [13] (Figure 1) The tube may be made of rubber or plastic and usually has a balloon cuff to keep the tube in place and closed system with the ventilator.

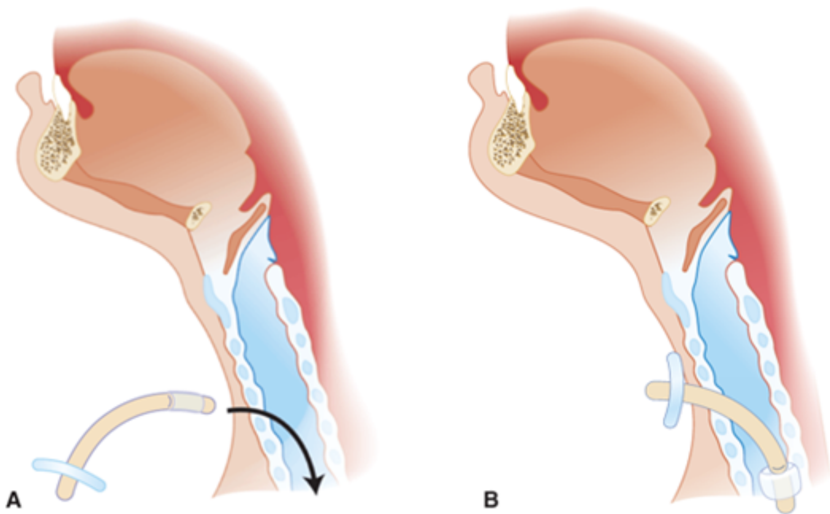
Figure 1. Endotracheal intubation



- The role of tracheostomy

Despite ongoing treatment for congestive heart failure, not all the patients can be weaned off the ventilator. In such cases, the health care providers should consider tracheostomy. [11,14] (Figure 2) Tracheostomy is a procedure to make an external artificial opening to the trachea. It could be done as a traditional surgical procedure in an operating room, or it also could be done at the bedside using percutaneous method. [15-19] Tracheostomy is considered to be beneficial among the patients who need prolonged mechanical ventilation, as it is thought to be more comfortable for the patients, requires less sedation, and provides more stable airway compared to an endotracheal tube. [11] However, tracheostomy does carry several complications, such as bleeding, cardiopulmonary arrest, hypoxia, structural damage, pneumothorax, pneumomediastinum, infection, tracheal stenosis, granulation and erosion of the innominate artery. [11] Hence, the optimal time for tracheostomy with the goal of getting extubated, and also to prevent complications from prolonged intubation and to secure more stable airway, has been controversial. [15,20] However, tracheostomy is typically done between 10^{th} and 14^{th} days of intubation. [15,21] Also, there is no clear definition when is “early” tracheostomy or “late” tracheostomy. Moreover, there is also no clear evidence supporting the optimal timing of tracheostomy. [22-24] However, some studies have shown a benefit of early tracheostomy with shorter hospital stays, shorter length of stay in the intensive care unit, and shorter duration of mechanical ventilation. However, benefit in overall mortality is still controversial. [25-28] Furthermore, most of the studies comparing early and late tracheostomy are done among trauma patients or excluded certain underlying respiratory conditions. A specific study investigating the optimal timing for patients with respiratory failure due to congestive heart failure acute exacerbation is lacking.

Figure 2. Tracheostomy [14]



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- Comparison early and late tracheostomy

Several studies are comparing early and late tracheostomy to assess various outcomes, but those studies have shown inconsistent outcomes, or their outcomes do not provide strong evidence due to heterogeneity of the study populations and outcome variables. [15,21-24,26,29-41] Most of the studies focus on trauma patients or were conducted at surgical care unit, [21-26,29,35,36,38-40,42] and several studies have included critically ill medical patients. [33,34,37,40,41] Furthermore, those studies included patients with various reasons for intubation. [15,30,31,34,40]

Most recently, Andriolo et al. published a systematic review comparing early and late tracheostomy in critically ill patients. [15] However, they reported mortality result from individual studies rather than reporting the result from the review, because of the inconsistency and the possibility of substantial statistical heterogeneity among the studies. Rumbak et al. conducted a prospective randomized trial comparing early and late tracheostomy among patients in a medical intensive care unit, and reported a significant mortality benefit (31.7% vs. 61,7%) and less pneumonia (5% vs. 25%), for the early cohort. [37] Young et al. also conducted a randomized control clinical trial comparing early and late tracheostomy, but there was no significant difference in mortality (30.8% vs. 31.5%). [33] From another randomized controlled trial, Zheng et al. also reported no significant difference in mortality between the two groups. [32] Studies have also used various clinical outcome variables. For example, Terragni et al. used outcome as prevention of ventilator-associated pneumonia and found out that early tracheostomy did not result in significant improvement in preventing ventilator-associated pneumonia. [34] Young et al. also included several outcomes in the systematic review, other than 30-day mortality, such as two-year mortality, medical intensive care unit length of stay and tracheostomy-related complications. [33] Several studies are comparing the duration of mechanical ventilation, and most of them reported a shorter duration of mechanical ventilation among early tracheostomy groups, but with mixed statistical significance. [32-34,37]

Public Health Significance

Considering the significant economic burden of acute heart failure exacerbation and subsequent respiratory failure requiring intubation, an optimal strategy to manage those patients should be investigated. Liu et al. reported cost-effectiveness of early versus late tracheostomy with the outcome of tracheostomy prevented and it showed that early tracheostomy could be more cost-effective with a willingness to pay threshold of $80,000 per tracheostomy avoided.[30] Other studies have shown that early tracheostomy may provide less mortality and fewer healthcare resources utilization. However, most of the studies included heterogeneous clinical conditions in their outcome assessment. Furthermore, to the best of our knowledge, studies comparing early and late tracheostomy for patients with acute respiratory failure due to congestive heart failure are lacking. The result of the study will provide evidence to assist both clinicians and hospital administrator in determining the most efficient care strategy for managing patients with respiratory failure from acute heart failure exacerbation requiring ventilator assistance.

Hypothesis, Research Question, Specific Aims or Objectives

The purpose of the study is to assess the national trend of tracheostomy among those who are admitted for acute respiratory failure with acute congestive heart failure exacerbation and to compare clinical and economic outcomes between the two groups (early and late tracheostomy) using propensity score matching. Lastly, we will conduct an economic evaluation comparing early and late tracheostomy among them using average and incremental costs with an outcome of length of stay.

- Objectives
    - Aim 1. To identify the national trend of tracheostomy among those who developed respiratory failure with acute congestive heart failure exacerbation.
        - Trend of tracheostomy use– early (<7 days) vs. late (≥7 days)
        - Identify the predictors of tracheostomy – early vs. late

- Aim 2: Compare the two groups (early vs. late) in outcomes – in-hospital mortality, total hospital length of stay and total hospital cost.
- Aim 3: Economic evaluation of early and late tracheostomy among those who developed respiratory failure with acute congestive heart failure exacerbation- average and incremental costs with outcome of total hospital length of stay, and post-procedural length of stay.

METHODS

Conceptual Model

We used the conceptual model for health service research, introduced by Begley et al. (Table 1).[43] This conceptual model provides frameworks and methods for assessing health services and system with the three objectives: effectiveness, efficiency, and equity. Effectiveness evaluates the intended and desired outcomes by the health services, such as mortality or life expectancy, but is not limited to health outcome but also includes the impact of health outcomes such as quality of life or well-being. The second objective, efficiency, is to monitor and assess both production efficiency and allocative efficiency of a certain health care service. It evaluates the health care service whether it maximized the performance with the minimum cost with an optimal combination of investments. Equity focuses on distributional fairness in the delivery of the health service. Eventually, those three objectives provide the criteria for evaluating the health services overall performances. This study's each goal fits each perspective of health service research as below. (Table 2)

Table 1. Definitions of Effectiveness, Efficiency, and Equity Criteria

Criteria	Level of analysis	
	Clinical	Population
Effectiveness	Clinical effectiveness: Improving the health of individual patients through the delivery of healthcare services	Population effectiveness: Improving the health of populations through medical or nonmedical services
Efficiency	Production efficiency: Combining inputs to produce services at the lowest cost	Production efficiency: combining inputs to produce services at the lowest cost Allocative efficiency: Combining health services and other health-related investments to produce maximum health given available resources
Equity	Procedural equity: Maximizing the fairness in the distribution of services across individuals Substantive equity: Minimizing the disparities in the distribution of health across individuals	Procedural equity: Maximizing the fairness in the distribution of services across groups Substantive equity: Minimizing the disparities in the distribution of health across groups

Table 2. Conceptual model for each aim in this study

Criteria	Level of analysis	
	Clinical	Aim
Effectiveness	Clinical effectiveness: Improving the health of individual patients through the delivery of healthcare services	Aim 2. Compare the two groups (early vs. late) in outcomes – in-hospital mortality, length of stay, and total hospital cost
Efficiency	Production efficiency: Combining inputs to produce services at the lowest cost	Aim 3. Economic evaluation of early and late tracheostomy among those who developed respiratory failure with acute congestive heart failure exacerbation- average and incremental costs with outcome of total hospital length of stay, and post-procedural length of stay.
Equity	Procedural equity: Maximizing the fairness in the distribution of services across individuals Substantive equity: Minimizing the disparities in the distribution of health across individuals	Aim 1. C. Predictors of early and late tracheostomy will be evaluated by multivariate logistic regression.

Usually, these three perspectives are assessed in clinical and population level (Table 1). At the clinical level, the analysis focuses on personal health care resources, such as technology, expertise, equipment, and facilities. Outcomes are usually measured at a personal level. At the population level, the analysis focuses on the improvement of population health. In this study, we will focus on clinical analysis since the analysis will be done at an individual level.

REFERENCES

1. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the united states: A policy statement from the American heart association. *Circ Heart Fail*. 2013;6(3):606-619.

2. National Center for Health Statistics. Mortality multiple cause micro-data files, 2013: Public-use data file and documentation: NHLBI tabulations. http://www.cdc.gov.utsph.idm.oclc.org/nchs/data_access/Vitalstatsonline.htm#Mortality_Multiple. Accessed 05/19, 2015.

3. Lloyd-Jones DM, Larson MG, Leip EP, et al. Lifetime risk for developing congestive heart failure: The Framingham heart study. *Circulation*. 2002;106(24):3068-3072.

4. Cook C, Cole G, Asaria P, Jabbour R, Francis DP. The annual global economic burden of heart failure. *Int J Cardiol*. 2014;171(3):368-376.

5. Gibbs LM, Addington-Hall J, Gibbs JS. Dying from heart failure: Lessons from palliative care. many patients would benefit from palliative care at the end of their lives. *BMJ*. 1998;317(7164):961-962.

6. Croft JB, Giles WH, Pollard RA, Keenan NL, Casper ML, Anda RF. Heart failure survival among older adults in the united states: A poor prognosis for an emerging epidemic in the Medicare population. *Arch Intern Med*. 1999;159(5):505-510.

7. Writing Group Members, Mozaffarian D, Benjamin EJ, et al. Heart disease and stroke statistics-2016 update: A report from the American heart association. *Circulation*. 2016;133(4):e38-360.

8. Echouffo-Tcheugui JB, Bishu KG, Fonarow GC, Egede LE. Trends in health care expenditure among US adults with heart failure: The medical expenditure panel survey 2002-2011. *Am Heart J*. 2017;186:63-72.

9. Ware LB, Matthay MA. Clinical practice. acute pulmonary edema. *N Engl J Med*. 2005;353(26):2788-2796.

10. Park JH, Balmain S, Berry C, Morton JJ, McMurray JJ. Potentially detrimental cardiovascular effects of oxygen in patients with chronic left ventricular systolic dysfunction. *Heart*. 2010;96(7):533-538.

11. Celli BR. Mechanical ventilatory support. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's principles of internal medicine, 19e.* New York, NY: McGraw-Hill Education; 2015. accessmedicine.mhmedical.com/content.aspx?aid=1120808698. Accessed 2017/11/08.

12. Marini JJ. Chapter 29. mechanical ventilation in the acute respiratory distress syndrome. In: Tobin MJ, ed. *Principles and practice of mechanical ventilation, 3e.* New York, NY: The McGraw-Hill Companies; 2013. accessmedicine.mhmedical.com/content.aspx?aid=57070342. Accessed 2017/11/09.

13. Mosby's Medical Dictionary, 8th edition. Endotracheal intubation. https://medical-dictionary.thefreedictionary.com/endotracheal+intubation. Updated 2017. Accessed 11/9, 2017.

14. Gaillard JP. Complications of airway devices. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, eds. *Tintinalli's emergency medicine: A comprehensive study guide, 8e.*

New York, NY: McGraw-Hill Education; 2016.

accessmedicine.mhmedical.com/content.aspx?aid=1121515597. Accessed 2017/11/09.

15. Andriolo BN, Andriolo RB, Saconato H, Atallah AN, Valente O. Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev*. 2015;1:CD007271.

16. Friedman Y. Percutaneous versus surgical tracheostomy: The continuing saga. *Crit Care Med*. 2006;34(8):2250-2251.

17. Gullo A, Sorbello M, Frova G. Percutaneous versus surgical tracheostomy: An unfinished symphony. *Crit Care Med*. 2007;35(2):682-683.

18. Pappas S, Maragoudakis P, Vlastarakos P, et al. Surgical versus percutaneous tracheostomy: An evidence-based approach. *Eur Arch Otorhinolaryngol*. 2011;268(3):323-330.

19. Schultz MJ, Veelo DP, Dongelmans DA. Percutaneous tracheostomies are preferable to surgical tracheostomies. *Crit Care Med*. 2007;35(2):676-7; author reply 677.

20. Heffner JE. Tracheotomy application and timing. *Clin Chest Med*. 2003;24(3):389-398.

21. Armstrong PA, McCarthy MC, Peoples JB. Reduced use of resources by early tracheostomy in ventilator-dependent patients with blunt trauma. *Surgery*. 1998;124(4):763-6; discussion 766-7.

22. Barquist ES, Amortegui J, Hallal A, et al. Tracheostomy in ventilator-dependent trauma patients: A prospective, randomized intention-to-treat study. *J Trauma*. 2006;60(1):91-97.

23. Dunham CM, Ransom KJ. Assessment of early tracheostomy in trauma patients: A systematic review and meta-analysis. *Am Surg*. 2006;72(3):276-281.

24. Lesnik I, Rappaport W, Fulginiti J, Witzke D. The role of early tracheostomy in blunt, multiple organ trauma. *Am Surg*. 1992;58(6):346-349.

25. Arabi Y, Haddad S, Shirawi N, Al Shimemeri A. Early tracheostomy in intensive care trauma patients improves resource utilization: A cohort study and literature review. *Crit Care*. 2004;8(5):R347-52.

26. Rodriguez JL, Steinberg SM, Luchetti FA, Gibbons KJ, Taheri PA, Flint LM. Early tracheostomy for primary airway management in the surgical critical care setting. *Surgery*. 1990;108(4):655-659.

27. Clec'h C, Alberti C, Vincent F, et al. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical ventilation: A propensity analysis. *Crit Care Med*. 2007;35(1):132-138.

28. Freeman BD. Tracheostomy update: When and how. *Crit Care Clin*. 2017;33(2):311-322.

29. Dunham CM, LaMonica C. Prolonged tracheal intubation in the trauma patient. *J Trauma*. 1984;24(2):120-124.

30. Liu CC, Rudmik L. A cost-effectiveness analysis of early vs late tracheostomy. *JAMA Otolaryngol Head Neck Surg*. 2016;142(10):981-987.

31. Liu X, Wang H, Xing Y, He Y, Zhang Z, Wang T. The effect of early and late tracheotomy on outcomes in patients: A systematic review and cumulative meta-analysis. *Otolaryngology--Head and Neck Surgery*. 2014;151(6):916-922.

32. Zheng Y, Sui F, Chen XK, et al. Early versus late percutaneous dilational tracheostomy in critically ill patients anticipated requiring prolonged mechanical ventilation. *Chin Med J (Engl)*. 2012;125(11):1925-1930.

33. Young D, Harrison DA, Cuthbertson BH, Rowan K, TracMan Collaborators. Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: The TracMan randomized trial. *JAMA*. 2013;309(20):2121-2129.

34. Terragni PP, Antonelli M, Fumagalli R, et al. Early vs late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients: A randomized controlled trial. *JAMA*. 2010;303(15):1483-1489.

35. Sugerman HJ, Wolfe L, Pasquale MD, et al. Multicenter, randomized, prospective trial of early tracheostomy. *J Trauma*. 1997;43(5):741-747.

36. Saffle JR, Morris SE, Edelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehabil*. 2002;23(6):431-438.

37. Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med*. 2004;32(8):1689-1694.

38. Koch T, Hecker B, Hecker A, et al. Early tracheostomy decreases ventilation time but has no impact on mortality of intensive care patients: A randomized study. *Langenbecks Arch Surg*. 2012;397(6):1001-1008.

39. Bosel J, Schiller P, Hook Y, et al. Stroke-related early tracheostomy versus prolonged orotracheal intubation in neurocritical care trial (SETPOINT): A randomized pilot trial. *Stroke*. 2013;44(1):21-28.

40. Brook AD, Sherman G, Malen J, Kollef MH. Early versus late tracheostomy in patients who require prolonged mechanical ventilation. *American Journal of Critical Care*. 2000;9(5):352.

41. Aissaoui Y, Azendour H, Balkhi H, Haimeur C, Kamili Drissi N, Atmani M. Timing of tracheostomy and outcome of patients requiring mechanical ventilation. *Ann Fr Anesth Reanim*. 2007;26(6):496-501.

42. Hosseinian L, Chiang Y, Itagaki S, Polanco A, Rhee A, Chikwe J. Earlier versus later tracheostomy in patients with respiratory failure after cardiac surgery in the united states. *J Cardiothorac Vasc Anesth*. 2014;28(3):488-492.

43. Begley, Charles E., Lairson, David R., Morgan, Robert O., Rowan, Paul J., Balkrishnan, Rajesh. Introduction to health service research and policy analysis. In: Michael R. Meacham, ed. *Evaluating the healthcare systems effectiveness, efficiency, and equity.* 4th ed. Chicago, Illinois: Health Administration Press; 2013:6.

JOURNAL ARTICLE I

Title of Journal: National Trend of Tracheostomy Among Patients with Acute Heart Failure Exacerbation from 2005 to 2014.

Name of Journal Proposed for Submission: CHEST Journal

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ABSTRACT

Background

Acute exacerbation of heart failure may result in acute respiratory failure, requiring endotracheal intubation. For those who fail extubation, tracheostomy is indicated. However, the optimal timing of tracheostomy among patients with acute heart failure exacerbation has not been determined, despite multiple studies assessing the utility of early tracheostomy. Furthermore, there is no study evaluating the benefit of early tracheostomy among patients who are admitted with acute heart failure exacerbation.

Methods

We conducted a retrospective cohort study using National Inpatient Sample data from 2005 to 2014 to assess the trend of utilization and outcome of early tracheostomy among patients with acute heart failure exacerbation.

Results

Among those who are admitted with acute heart failure exacerbation, 0.30% patients underwent the tracheostomy, and among them, 9.69% received early tracheostomy. There was no significant trend in the percentage of early tracheostomy. The length of stay in the hospital has decreased over time in late tracheostomy group, but it was stable in early tracheostomy group. Median total hospital length of stay (19 days) and total hospital cost ($52,158.23) in early tracheostomy group were significantly lower than late tracheostomy group (25 days and $68,037.40).

Conclusion

Early tracheostomy has been used in 9.69% of the patients who underwent tracheostomy with heart failure acute exacerbation in the United States from 2005 to 2014 without any trend in utilization. Early tracheostomy is associated with lower hospital length of stay and costs.

INTRODUCTION

Heart failure is one of the leading causes of high morbidity and mortality. Based on the data from National Health and Nutrition Examination Survey (NHANES) 2009 to 2012, it was estimated that total 5.7 million Americans older than 20 years of age had heart failure. That number is anticipated to increase 46% from 2012 to 2030, which can result in more than 8 million people older than 18 years of age with heart failure. [1] Acute heart failure exacerbation is a common but potentially fatal condition which may result in acute respiratory failure. Once developed, the patient will need assisted ventilation. First line treatment is a trial of noninvasive ventilation. However, if noninvasive ventilation is contraindicated or patient fails to improve with noninvasive ventilation within 1-2 hours, the patient should be intubated for mechanical ventilation. Despite ongoing treatment, not all the patients can be weaned off the ventilator. In such cases, tracheostomy is indicated. [11,14] Tracheostomy is considered to be beneficial among the patients who need prolonged mechanical ventilation, as it is thought to be more comfortable for the patients, requires less sedation, and provides more stable airway compared to an endotracheal tube. [11] However, tracheostomy carries several complications, such as bleeding, cardiopulmonary arrest, hypoxia, structural damage, pneumothorax, pneumomediastinum, infection, tracheal stenosis, granulation and erosion of the innominate artery. [11] Hence, the optimal time for tracheostomy with the goal of getting extubated, and also to prevent complications from prolonged intubation and to secure more stable airway, has been studied. [15,20] Some studies have shown a benefit of early tracheostomy with shorter length of stay in the intensive care unit and shorter duration of mechanical ventilation. However, benefit in overall mortality is still controversial. [25-28] Furthermore, most of the studies comparing early and late tracheostomy are done among trauma patients or excluded certain underlying respiratory conditions. A specific study investigating the utilization of early tracheostomy for patients with respiratory failure due to congestive heart failure acute exacerbation is lacking. The purpose of the study is to assess the national trend in utilization of early tracheostomy among those who are admitted for acute respiratory failure with acute congestive heart failure exacerbation and assess its outcomes.

METHODS

Study subjects

We conducted a retrospective cohort study using publically accessible national survey data, National Inpatient Sample (NIS) from 2005 to 2014. NIS is the largest all-payer inpatient care database in the United States, which is developed by the Healthcare Cost and Utilization Project (HCUP) [44] NIS is designed to be representative of all non-federal acute care inpatient admissions in the United States. It contains both patient and hospital information. NIS can approximate a 20 percent stratified sample of discharges nationwide. From the NIS dataset, patients who are older than 17 were included for the current study. Then, patients who were admitted with acute heart failure were selected using the International Classification of Diseases Ninth Revision, Clinical Modification (ICD-9-CM) code. NIS data provides total 30 ICD-9-CM codes. If any of the codes for "acute" heart failure, 428.21 (acute systolic health failure), 428.23 (acute on chronic systolic heart failure), 428.31 (acute diastolic heart failure), 428.33 (acute on chronic diastolic heart failure), 428.41 (acute combined systolic and diastolic heart failure) and 428.43 (acute on chronic combined systolic and diastolic heart failure) was listed in the first five diagnosis codes, that visit was considered as heart failure acute exacerbation related admission. We used the first five diagnosis codes out of thirty diagnosis codes, since the diagnosis codes already had "acute" components in the diagnosis, and tried to minimize the chances of missing samples. Then, patients who underwent intubation were selected using ICD-9-CM codes, 96.04 (Insertion of the endotracheal tube) and 96.05 (other intubation of respiratory tract). Also, if the patient had any of the code for "tracheostomy," 31.1 (temporary tracheostomy), 31.2 (permanent tracheostomy), 31.21 (mediastinal tracheostomy) or 31.29 (other permanent tracheostomy) among the 15 procedural codes, then the case was selected. Early tracheostomy was defined if the tracheostomy was performed in less than 7 days after intubation. Those who underwent "major therapeutic surgery" based on the classification from HCUP were excluded,[45]

Statistical Analysis

First, the nationally representative estimated number of tracheostomy was evaluated using discharge weight (variable DISCWT), provided by AHRQ[46-48]. By using this weight, NIS allows the researchers to obtain the national estimate for the variable interested. Then, age-adjusted percentages of each procedure were also plotted over time. A Cochran-Armitage test was used to assess the trend of the percentage of tracheostomy and early tracheostomy. Trends of the days between the intubation and the tracheostomy, total length of stay in the hospital and total hospital cost over time were also assessed using linear regression test. All the costs were calculated from the total hospital charges using an adjustment factor from the provided by AHRQ.[49] Then, the costs were again adjusted to 2014 currency using consumer price index.

Then, the days between the intubation and the tracheostomy, total hospital costs, and total hospital length of stay were compared between the two groups (early and late tracheostomy) using a propensity score matching. Propensity score matching is a statistical method allowing an observational study to estimate the effect of an intervention by controlling the covariates in a way analogous to a randomized trial. [50,51] In this study, we used nearest neighbor 1:1 matching method using the propensity score of being assigned to early tracheostomy to identify a matched pair. Co-variables to be used to calculate the propensity score are age, sex, race, payers, location of the hospital (urban vs. rural) and comorbidities (coronary arterial disease, hypertension, cerebrovascular disease, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, cancer, liver disease, pneumonia). Comorbidities were selected from a literature using NIS dataset assessing a cardiologic procedure and additional significant systemic disorders. [52] and they were identified using relevant ICD-9 CM diagnosis code and Clinical Classification Software (CCS) category provided by HCUP from the 30 diagnosis codes, which were documented at the time of discharge. [45]

After matching, Mann-Whitney U test was used to compare the outcomes. Since the cost and length of stay were not normally distributed, median with the quartiles was reported.

All analyses were conducted using STATA 14 (College Station, TX). A p-value less than 0.05 was considered as statistical significance for all tests.

Sample size calculation

Various methods for sample size calculation for trend analysis exist. Hyndman and Kostenko, and they recommended a minimum 6 observations for yearly trend analysis, but

Hanke recommended minimum 20 to 60 observations for trend analysis. [53,54] We will use a sample size of 60 for trend analysis.

RESULTS

From 2005 to 2014, NIS data included total 77,394,755 patients. Among them, total 64,827,613 patients were more than 17 years old. First, we selected patients who had diagnostic codes for acute heart failure exacerbation from the first five diagnostic codes (1,623,013 left). Among them, 214,265 patients underwent major therapeutic surgery during the hospitalization, and they were excluded. The 52 cases were excluded due to negative values for length of stay and cost. Total 1,408,696 patients were included in the final analysis. Figure 1 shows the flow chart selecting the final subjects.

Trend and percentage of tracheostomy among acute heart failure exacerbation

Among 1,408,696 eligible patients, 3,698 patients underwent tracheostomy. This is approximately 0.30% of the total patients who were admitted with acute heart failure exacerbation after adjusted with age. Table 1 shows the observed counts, estimated counts of tracheostomy and the percentage of tracheostomy from the estimated counts among patients with acute heart failure exacerbation.

Age distribution tables for each year from the United States Census were used for calculation of age-adjusted percentage. [55] The age-adjusted percentage of tracheostomy among acute heart failure exacerbation patients using the national estimate counts were 0.35% in 2005, 0.18% in 2006, 0.30% in 2007, 0.26% in 2008, 0.26% in 2009, 0.33% in 2010, 0.33% in

2011, 0.36% in 2012, 0.30% in 2013, and 0.29% in 2014. (Figure 2) The percentage of tracheostomy over time from the estimated population was stable over time (*p*-value 0.9268).

Figure 1. Selection of cohort for the final analysis

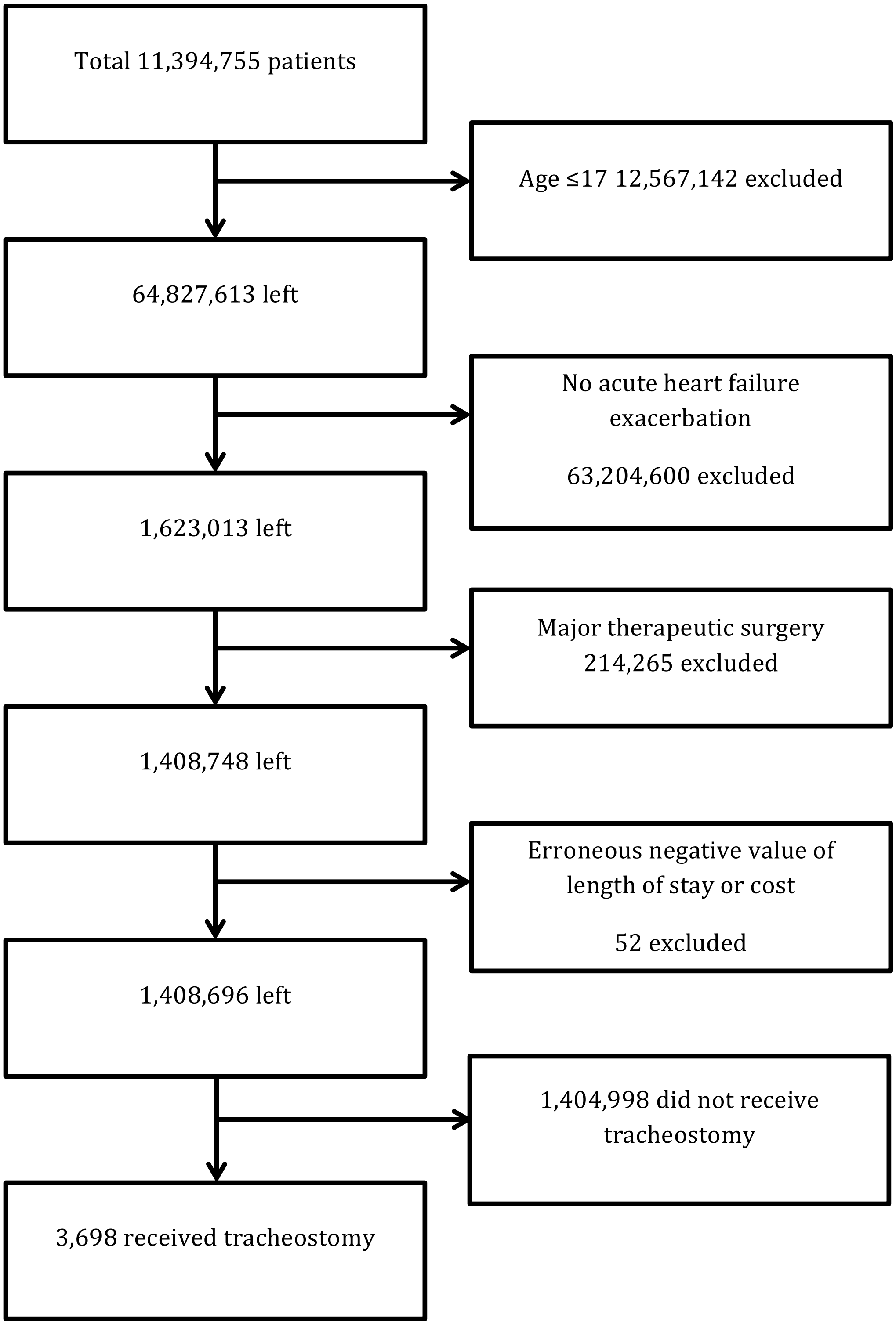
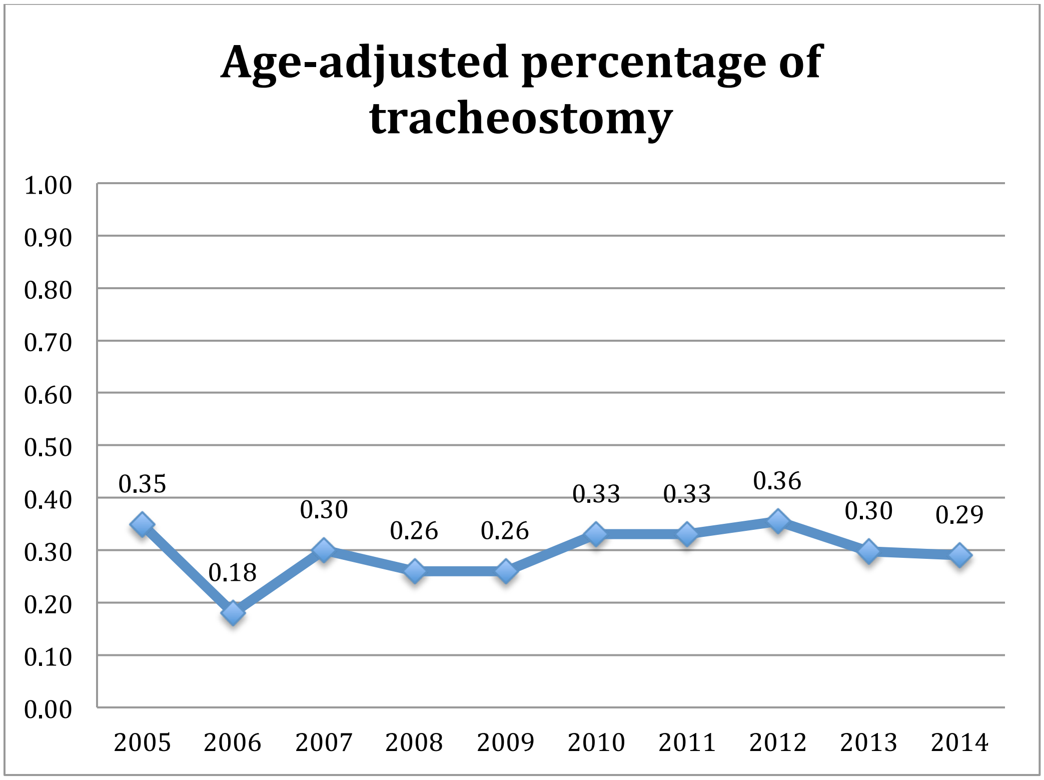


Table 1. Age-adjusted percentage of tracheostomy among patients with acute heart failure exacerbation

Year	Total		Tracheostomy			
	Observed counts	Weighted counts	Observed counts (N)	Weighted counts (N)	Crude percentage (%)	Age adjusted percentage (%)
2005	13,742	66,713	42	206	0.31	0.35
2006	13,095	64,675	32	158	0.24	0.18
2007	25,505	127,682	46	230	0.18	0.30
2008	110,281	544,485	229	1,129	0.21	0.26
2009	157.590	799,454	376	1,915	0.24	0.26
2010	183,254	917,482	530	2,665	0.29	0.33
2011	221,170	1,063,300	653	3,157	0.30	0.33
2012	208,637	1,043,185	593	2,965	0.28	0.36
2013	226,906	1,134,530	571	2,855	0.25	0.30
2014	248,516	1,242,681	626	3,130	0.25	0.29
Total	1,408,696	7,004,087	3,698	18,410	0.26	0.30

Figure 2. Age-adjusted percentage of tracheostomy among patients who are admitted for acute heart failure exacerbation (%)



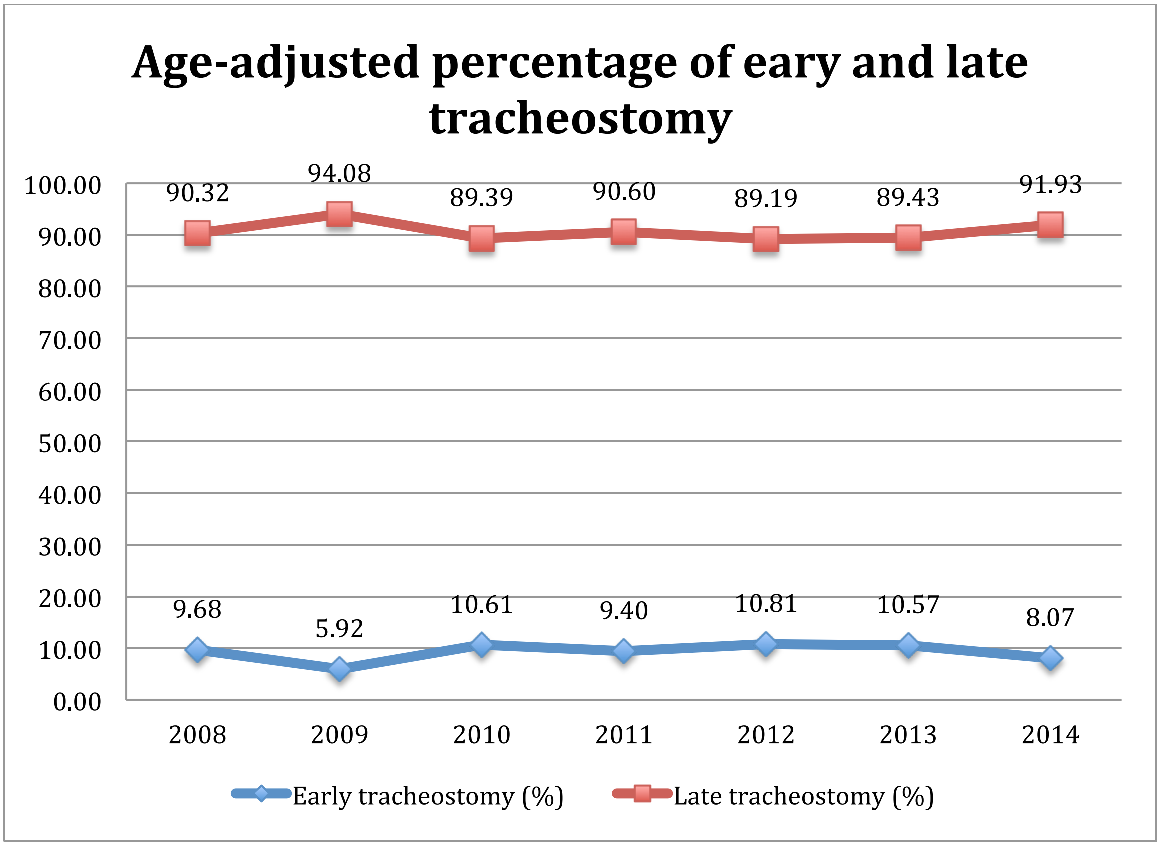
Trend and percentage of early tracheostomy among patients who received a tracheostomy

Among those who underwent the tracheostomy, overall 9.69% received early tracheostomy (tracheostomy < 7 days after intubation). The age-adjusted percentage of early tracheostomy among those who received tracheostomy during the admission with acute heart failure exacerbation was 22.13% in 2005, 3.21% in 2006, 6.47% in 2007, 9.68% in 2008, 5.92% in 2009,10.61% in 2010, 9.40% in 2011, 10.81% in 2012, 10.57% in 2013 and 8.07% in 2014 (Table 2 and Figure 3). Due to the low sample size in the year of 2005, 2006 and 2007, they were not included in trend analysis. From 2008 to 2014, there was no specific trend in the percentage of early tracheostomy (p-value 0.7660).

Table 2. Age-adjusted percentage of early tracheostomy among patients who underwent tracheostomy during the admission with acute heart failure exacerbation

Year	Total		Early tracheostomy			
	Observed counts	Weighted counts	Observed counts (N)	Weighted counts (N)	Crude Percentage (%)	Age-adjusted percentage (%)
2008	229	1,129	28	137	12.17	9.68
2009	376	1,915	35	175	9.15	5.92
2010	530	2,665	73	365	13.7	10.61
2011	653	3,157	77	371	11.75	9.40
2012	593	2,965	78	390	13.15	10.81
2013	571	2,855	86	430	15.06	10.57
2014	626	3,130	76	380	12.14	8.07
Total	3,698	18,410	464	2,301	12.5	9.69

Figure 3. Age-adjusted percentage of early tracheostomy among patients who underwent tracheostomy during the admission with acute heart failure exacerbation



Trend of tracheostomy day, total hospital length of stay and total hospital cost

The median length of days between intubation and tracheostomy (tracheostomy day) was 13 in late tracheostomy group, and it had a trend to decrease over time (p-value 0.025 with coefficient factor -0.29). The median tracheostomy day was 4 in early tracheostomy group, and there was no specific trend in tracheostomy day (*p*-value 0.855 and coefficient factor -0.04). The median total hospital length of stay in late tracheostomy group was 25, and it showed a trend to decrease over time (*p*-value 0.042 with coefficient factor 0.89). The median length of stay in the hospital for early tracheostomy was 19, and it has decreased over time (*p*-value 0.019 with coefficient factor -1.107). Trend analysis for early tracheostomy group included years from 2008 to 2014 due to the low sample size in the years from 2005 to 2007. (Table 3, Figure 4 and Figure 5)

Table 3. Trend of tracheostomy day and total hospital length of stay between the two groups

	Tracheostomy day		Total hospital length of stay	
	Late tracheostomy	Early tracheostomy	Late tracheostomy	Early tracheostomy
2005	16	3	32	18
2006	16	5	36	36
2007	13	0	23	15
2008	13	3	26	24
2009	13	4	28	22
2010	13	5	26	22
2011	13	5	24	18
2012	13	3	26	18
2013	13	3	23	16
2014	13	4	25	19
Total	13	4	25	19
p-value for trend	0.025	0.855*	0.042	0.019*
Coefficient factor	-0.29	-0.04	-0.89	-1.107

* Trend analysis in early tracheostomy group includes data from the year 2008 to 2014

Figure 4. Tracheostomy day for each group

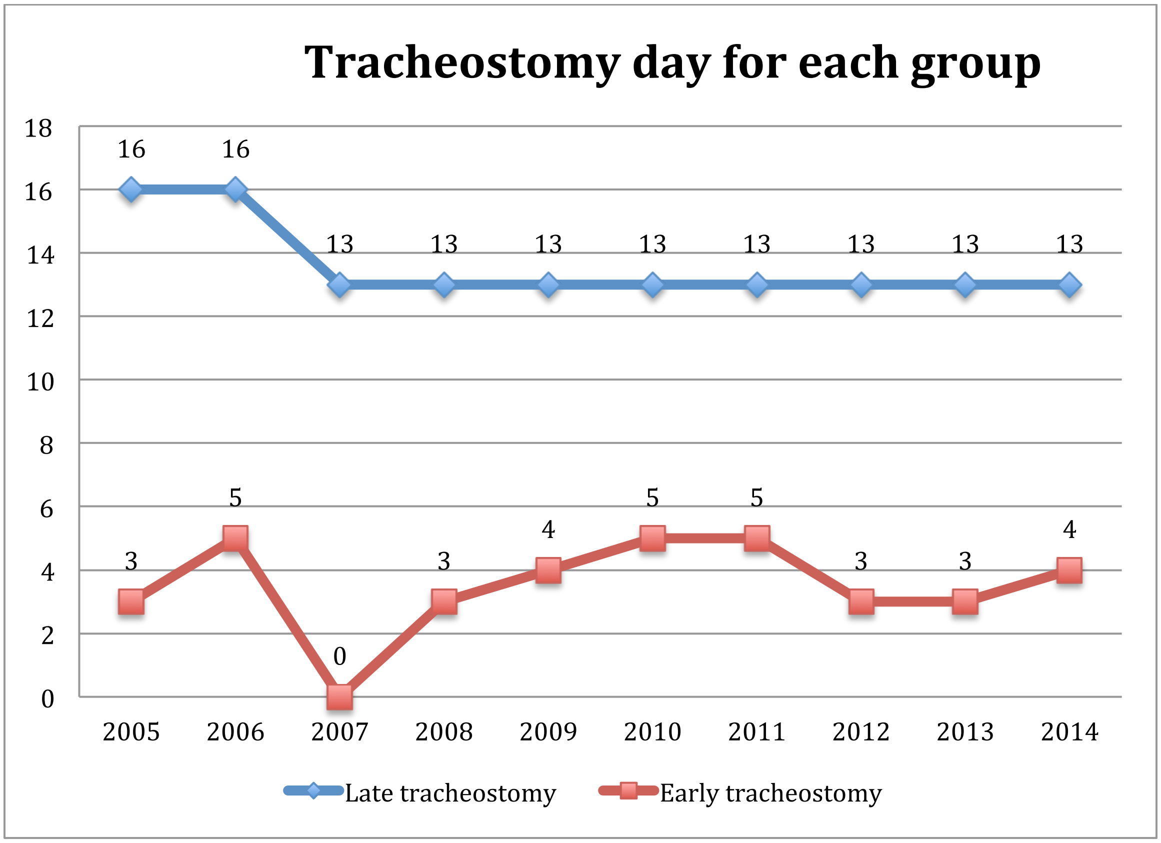
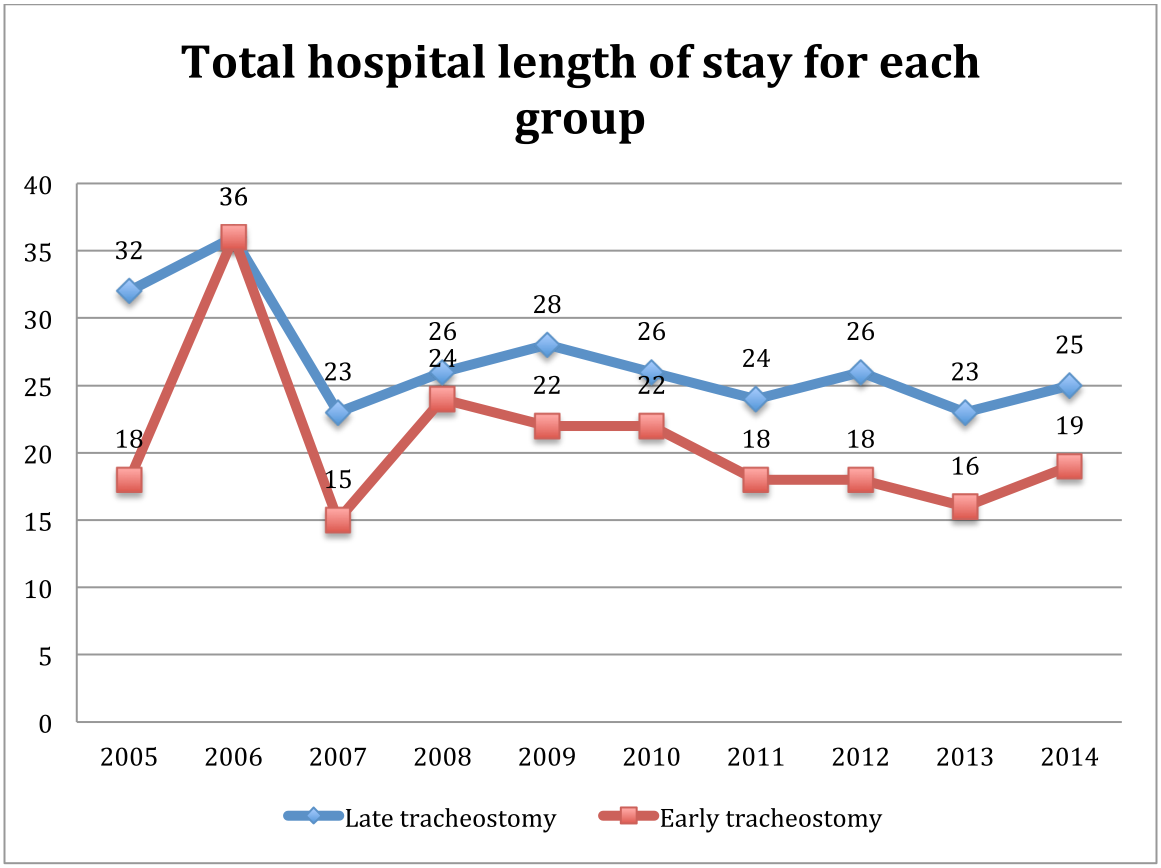


Figure 5. Total hospital length of stay for each group



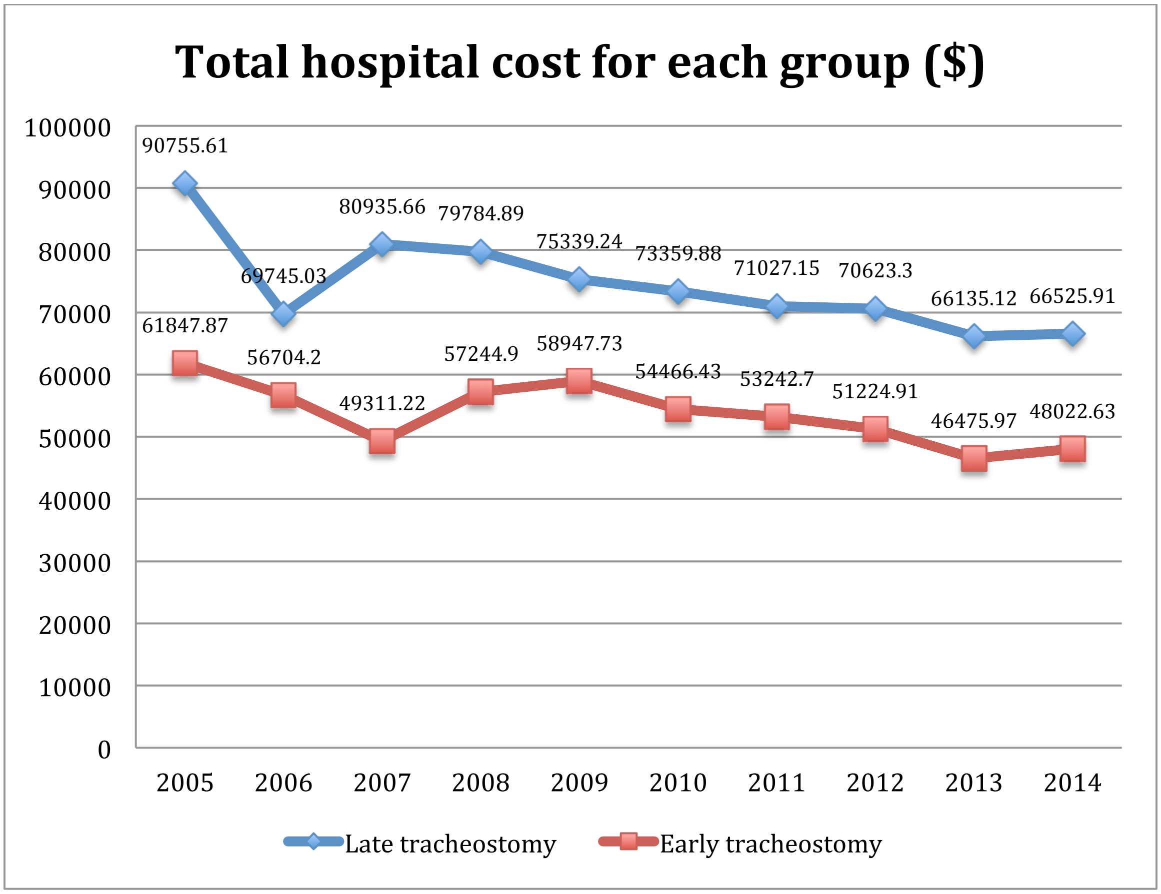
The median hospital cost was $71,181.13 in late tracheostomy group, and the median hospital cost over time significantly decreased from 2005 to 2014 with *p*-value 0.008 and coefficient factor from linear regression model -1,958.49. The median hospital cost in early tracheostomy group was $51,573.30, and it also showed a trend to decrease over time *p*-value 0.002 with coefficient factor -1,994.71). (Table 4 and Figure 6)

Table 4. Trend of total hospital cost in two groups

	Late tracheostomy ($)	Early tracheostomy ($)
2005	90,755.61	61,847.87
2006	69,745.03	56,704.20
2007	80,935.66	49,311.22
2008	79,784.89	57,244.90
2009	75,339.24	58,947.73
2010	73,359.88	54,466.42
2011	71,027.15	53,242.70
2012	70,623.30	51,224.91
2013	66,135.12	46,475.97
2014	66,525.91	48,022.63
Total	71,181.13	51,573.30
p-value for trend	0.008	0.002
Coefficient factor	-1,958.49	-1,994.71

* Trend analysis in early tracheostomy group include data from year 2008 to 2014

Figure 6. Total hospital cost for each group



Comparison of tracheostomy day, total hospital length of stay and total hospital cost between the two groups.

After propensity score matching, the matched cohort had 329 cases in each group. Table 5 shows the characteristics of covariates before and after matching.

Table 5. Characteristics of covariates before and after matching

	Before match			After match		
	Early tracheostomy N=464	Late tracheostomy N=3,234	*p*-value	Early tracheostomy N=329	Late tracheostomy N=329	*p*-value
Age (year)	66.25	66.88	0.342	66.20	66.772	0.537
Sex (%)	52.37	52.94	0.819	52.24	51.53	0.837
Non-white (%)	42.96	40.31	0.296	43.29	48.00	0.169
Non-public insurance (%)	31.47	31.17	0.897	30.82	33.18	0.463
Urban hospital (%)	84.84	84.24	0.744	85.41	84.24	0.744
Coronary artery disease (%)	37.50	41.47	0.104	36.94	34.35	0.431
Hypertension (%)	62.50	57.85	0.058	63.29	60.47	0.397
Cerebrovascular disease (%)	11.42	8.94	0.084	11.06	11.77	0.747
Diabetes mellitus (%)	43.89	39.21	0.130	43.29	43.29	>0.99
Peripheral arterial disease (%)	4.31	5.69	0.224	4.05	4.56	0.605
Chronic obstructive pulmonary disease (%)	40.52	38.06	0.310	40.47	45.65	0.128
Cancer (%)	12.72	9.83	0.055	12.94	10.82	0.341
Chronic kidney disease (%)	32.76	33.09	0.889	32.94	32.94	>0.99
Liver disease (%)	7.76	10,48	0.069	7.294	6.118	0.494
Pneumonia (%)	5.95	75.51	<0.001	66.59	69.65	0.339

The comparison of the outcomes between the early tracheostomy group and late tracheostomy group from the matched pair is shown at table 6. The median tracheostomy day was significantly longer in late tracheostomy group (12 days), compared to early tracheostomy group (4 days) with *p*-value <0.001. Median total hospital cost was significantly higher in late tracheostomy group ($68,037.4) than in early tracheostomy group ($52,168.23) with *p*-value <0.001. Median total length of stay in the hospital was significantly longer in late tracheostomy group (25 days) than in early tracheostomy group (19 days) with *p*-value <0.001.

Table 6. Comparison of tracheostomy day, total hospital length of stay, and total hospital cost from the matched pair

	Late tracheostomy	Early tracheostomy	*p*-value
Median tracheostomy day (days, quartiles)	12 (9~16)	4 (1~5)	<0.001
Median total hospital cost ($, quartiles)	68,037.4 (46,949.75~104,730.5)	52,158.23 (36,656.73~75,114.96)	<0.001
Median length of stay (days, quartiles)	25 (18~36)	19 (13~28)	<0.001

DISCUSSION

The decision when to place a tracheostomy is not a simple procedure, and it is affected by various factors, including the patient's condition, the patient's preference, the surgeon's preference or the hospital policy. In addition, there is no consensus or guideline for the optimal timing of tracheostomy. Nevertheless, a large body of literatures showed various benefits of early tracheostomy in a different clinical setting and in different patient groups.

However, there is no study assessing the utility of early tracheostomy among patients with acute heart failure exacerbation. Current study tried to evaluate the national trends in tracheostomy and early tracheostomy among those who are admitted to the hospital with acute congestive heart failure exacerbation. We also compared clinical and economic outcomes between early tracheostomy group and late tracheostomy group.

The overall utilization of tracheostomy and early tracheostomy among the study population has been stable over time from 2005 to 2014 from our study. There are a couple of studies that evaluated the trend of tracheostomy in different study populations, but there is no study evaluating the trend of early tracheostomy. Mehta et al. conducted a similar study to assess the trend in tracheostomy for mechanically ventilated patients using NIS dataset from 1993 to 2012. [56] They reported that the utilization of tracheostomy had risen significantly over time from 1993 to 2008 and then declined afterward. Chatterjee et al. also reported the trend in tracheostomy after stroke using NIS dataset, and concluded that tracheostomy use has increased from 1994 to 2013. However, their results cannot be directly compared to ours since the study population and the time period are different. [57]

Further in-depth analysis to assess the trends in other parameters of utilization of tracheostomy showed that, in late tracheostomy group, the length of days between the intubation and tracheostomy (tracheostomy day) decreased from 16 days (in 2005 and 2006) to 13 days in 2014. However, after 2007, there is no specific trend, and the tracheostomy day had been 13 until 2014. (Table 3) The median length of stay in the hospital in both group decreased over time (from 32 days to 25 days in late tracheostomy group and from 24 days to 19 days in early tracheostomy group).

Interestingly, the total hospital cost continued to decrease over time in both late and early tracheostomy group. Considering the stable length of stay in both groups, this finding suggests that the cost per day in the hospital has declined over time. It is noteworthy that other literatures suggest the economic burden of heart failure would increase over time. [1,58] However this result should be interpreted in the context that our study population was people who underwent tracheostomy. We conducted a subanalysis trending total hospital cost for acute heart failure exacerbation regardless tracheostomy status, and it showed that the hospital cost increased overtime with *p*-value 0.003 and coefficient factor 63.48. A possible explanation could be more efficient care after tracheostomy or decreasing cost of the procedure over time. However, given the limited information from the dataset, we could not verify such a hypothesis.

We also compared the days between the intubation and the tracheostomy, total hospital cost and total length of stay in the hospital between the two groups using propensity score matching. We used propensity score matching to reduce the selection bias. After matching, the outcomes were compared, and it did show a significant association of early tracheostomy with lower total hospital cost and total length of stay in the hospital.

The current study holds several limitations. First, this study is a retrospective study using discharge data. Even though the data is a nationally representative dataset and we used a propensity score matching to minimize the confounding effect of other variables, selection bias cannot be completely eliminated. Choice of timing for tracheostomy might be affected by the clinician's preference, the patient's decision, hospital policy or other co-existing clinical conditions that were not captured in this study. Furthermore, the comorbidities were identified from the discharge diagnosis code, and it is possible that the comorbidities had not existed at the time of the decision of tracheostomy.

Second, we used first five diagnosis codes, rather than only the first diagnosis, among 30 diagnosis codes to identify the patients with acute heart failure exacerbation, to minimize the chances to miss any case. Additionally, the etiology of respiratory failure requiring intubation could be documented in second or third place of the diagnosis list. However, it is also possible that the patient might have several clinical conditions to be admitted with respiratory failure requiring intubation, such as chronic obstructive pulmonary disease or pneumonia, which will make our study group heterogeneous. Furthermore, NIS does not provide information regarding the severity of heart failure, which could impact the decision of early and late tracheostomy.

Last, the sample size was fairly small for analysis. We used weight to get a national estimate, but still, the sample size for the year of 2005, 2006 and 2007 was not enough for trend analysis. Even though we had enough sample size for other years, the fact that they were estimated numbers, rather than actual observations is still carries a limitation for this study.

CONCLUSION

From 2005 to 2014, the percentage of early tracheostomy among those who underwent tracheostomy with acute heart failure exacerbation had been stable. The length of stay in the hospital among those who underwent early tracheostomy had been stable over time, but the total hospital cost had been decreased. Early tracheostomy group showed a shorter length of stay in the hospital (19 days) and less total hospital cost ($52,158.23) compared to late tracheostomy group (25 days and $68,037.4).

REFERENCES

1. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the united states: A policy statement from the American heart association. *Circ Heart Fail*. 2013;6(3):606-619.

2. Celli BR. Mechanical ventilatory support. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's principles of internal medicine, 19e.* New York, NY: McGraw-Hill Education; 2015. accessmedicine.mhmedical.com/content.aspx?aid=1120808698. Accessed 2017/11/08.

3. Gaillard JP. Complications of airway devices. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, eds. *Tintinalli's emergency medicine: A comprehensive study guide, 8e.* New York, NY: McGraw-Hill Education; 2016. accessmedicine.mhmedical.com/content.aspx?aid=1121515597. Accessed 2017/11/09.

4. Andriolo BN, Andriolo RB, Saconato H, Atallah AN, Valente O. Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev*. 2015;1:CD007271.

5. Heffner JE. Tracheotomy application and timing. *Clin Chest Med*. 2003;24(3):389-398.

6. Arabi Y, Haddad S, Shirawi N, Al Shimemeri A. Early tracheostomy in intensive care trauma patients improves resource utilization: A cohort study and literature review. *Crit Care*. 2004;8(5):R347-52.

7. Rodriguez JL, Steinberg SM, Luchetti FA, Gibbons KJ, Taheri PA, Flint LM. Early tracheostomy for primary airway management in the surgical critical care setting. *Surgery*. 1990;108(4):655-659.

8. Clec'h C, Alberti C, Vincent F, et al. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical ventilation: A propensity analysis. *Crit Care Med*. 2007;35(1):132-138.

9. Freeman BD. Tracheostomy update: When and how. *Crit Care Clin*. 2017;33(2):311-322.

10. Healthcare Cost and Utilization Project (HCUP). Overview of the national (nationwide) inpatient sample (NIS). https://www.hcup-us.ahrq.gov/nisoverview.jsp. Updated 2018. Accessed 2/21, 2018.

11. Healthcare Cost and Utilization Project (HCUP). Clinical classifications software (CCS) for ICD-9-CM. https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Updated 2017. Accessed 2/23, 2018.

12. Method series report 2015-09. healthcare cost and utilization project (HCUP). https://www.hcup-us.ahrq.gov/reports/methods/2015_09.jsp. Updated 2016.

13. Schulman AR, Abougergi MS, Thompson CC. Assessment of the July effect in post-endoscopic retrograde cholangiopancreatography pancreatitis: Nationwide inpatient sample. *World journal of gastrointestinal endoscopy*. 2017;9(7):296.

14. Patel N, Kalra R, Doshi R, et al. Hospitalization rates, prevalence of cardiovascular manifestations, and outcomes associated with sarcoidosis in the united states. *J Am Heart Assoc*. 2018;7(2):10.1161/JAHA.117.007844.

15. Agency for Healthcare Research and Quality Healthcare Research and Quality. HCUPnet: Healthcare cost and utilization project. https://hcupnet.ahrq.gov/#setup. Accessed 2/22, 2018.

16. Rubin DB. Using propensity scores to help design observational studies: Application to the tobacco litigation. *Health Serv Outcomes Res*. 2001;2(3-4):169-188.

17. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55.

18. Dhoble A, Bhise V, Nevah MI, et al. Outcomes and readmissions after transcatheter and surgical aortic valve replacement in patients with cirrhosis: A propensity matched analysis. *Catheter Cardiovasc Interv*. 2018;91(1):90-96.

19. Hyndman RJ, Kostenko AV. Minimum sample size requirements for seasonal forecasting models. *Foresight*. 2007;6(Spring):12-15.

20. Hanke J, Wichern D. *Business forecasting.* 9th ed. Pearson; 2008.

21. United States census bureau - age and sex. https://www.census.gov/topics/population/age-and-sex/data/tables.html.

22. Mehta AB, Syeda SN, Bajpayee L, Cooke CR, Walkey AJ, Wiener RS. Trends in tracheostomy for mechanically ventilated patients in the united states, 1993–2012. *American journal of respiratory and critical care medicine*. 2015;192(4):446-454.

23. Chatterjee A, Chen M, Gialdini G, et al. Trends in tracheostomy after stroke: Analysis of the 1994 to 2013 national inpatient sample. *The Neurohospitalist*. 2018:1941874418764815.

24. Tran DT, Ohinmaa A, Thanh NX, et al. The current and future financial burden of hospital admissions for heart failure in Canada: A cost analysis. *CMAJ Open*. 2016;4(3):E365-E370.

JOURNAL ARTICLE II

Title of Journal: Predictors of Early Tracheostomy Among Patients with Acute Heart Failure Exacerbation and its clinical outcomes, from 2005 to 2014

Name of Journal Proposed for Submission: JACC: Heart Failure

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ABSTRACT

Background

Acute exacerbation of heart failure may result in acute respiratory failure, requiring endotracheal intubation. For those who fail extubation, tracheostomy is indicated. The utility of early tracheostomy has been studied, but not specifically for patients with acute heart failure exacerbation.

Methods

We conducted a retrospective cohort study using National Inpatient Sample data from 2005 to 2014 to assess the predictors of early tracheostomy (<7 days after intubation) and compare various outcomes between early and late tracheostomy group among patients with acute heart failure exacerbation.

Results

The result from multivariate logistic regression adjusting covariables (age, sex, insurance, hospital location, race, comorbidities) it showed that patients with coronary artery disease, pneumonia, and liver disease are less likely to receive early tracheostomy (OR 0.79, 0.63 and 0.64 respectively). The matched pair was compared after propensity score matching, and it showed that the two groups did not show a significant difference in in-hospital mortality (OR 0.91, *p*-value 0.676), or decannulation rate (OR 2.01, *p*-value 0.571). However, early tracheostomy was associated with higher likelihood of having a complication from tracheostomy with OR 2.08 (*p*-value 0.044) but was also associated with lower total hospital length of stay with coefficient factor -6.50 (*p*-value 0.000) from linear regression model.

Conclusion

Patients with coronary artery disease, liver disease, and pneumonia were associated lower likelihood to receive early tracheostomy (<7 days after intubation) rather than late tracheostomy among patients who were admitted to the hospital with acute heart failure exacerbation. There were no other demographic factors that were associated with early tracheostomy. When the two groups were compared using propensity score matching, they did not differ from each other in in-hospital mortality, but clearly showed that early tracheostomy was associated with lower total hospital length of stay.

INTRODUCTION

Heart failure is one of the leading causes of high morbidity and mortality. Based on the data from National Health and Nutrition Examination Survey (NHANES) 2009 to 2012, it was estimated that total 5.7 million Americans older than 20 years of age had heart failure. That number is anticipated to increase 46% from 2012 to 2030, which can result in more than 8 million people older than 18 years of age with heart failure. [1] One in nine deaths has heart failure on the death certificates, according to the National Center for Health Statistics in 2013. [2] Acute exacerbation of heart failure may result in acute respiratory failure, which requires mechanical ventilator support. Despite supportive management, patients can fail extubation of the endotracheal tube and need a tracheostomy to continue mechanical ventilator support.

Tracheostomy usually is done to minimize the mechanical trauma to the larynx or trachea, facilitate the weaning process, or protect the airway for a long time. Predictors of tracheostomy have been mostly reported in trauma or surgical patients, but it has not been studied among patients with acute respiratory failure from acute heart failure exacerbation. Also, there has not been a study to compare the outcomes of early tracheostomy in patients with acute heart failure exacerbation. The purpose of this study is to identify predictors of early tracheostomy (<7 days after intubation) and compare the clinical and economic outcomes between the two groups (early tracheostomy and late tracheostomy) among patients who were intubated from acute heart failure exacerbation nationwide from 2005 to 2014.

METHODS

Study subjects

We conducted a retrospective cohort study using publically accessible national survey data, National Inpatient Sample (NIS) from 2005 to 2014. NIS is the largest all-payer inpatient care database in the United States, which is developed by the Healthcare Cost and Utilization Project (HCUP)[44] NIS is designed to be representative of all non-federal acute care inpatient admissions in the United States, and it can approximate a 20 percent stratified sample of discharges nationwide. From the NIS dataset, patients who are older than 17 were included for the current study. Then, patients who were admitted with acute heart failure were selected using ICD-9-CM code. NIS data provides total 30 ICD-9-CM codes. If any of the codes for "acute" heart failure, 428.21 (acute systolic health failure), 428.23 (acute on chronic systolic heart failure), 428.31 (acute diastolic heart failure), 428.33 (acute on chronic diastolic heart failure), 428.41 (acute combined systolic and diastolic heart failure) and 428.43 (acute on chronic combined systolic and diastolic heart failure) was listed for the first five diagnosis codes, that visit was considered as heart failure acute exacerbation related admission. We used the first five diagnosis codes out of thirty diagnosis codes, since the diagnosis codes already had "acute" components in the diagnosis, and tried to minimize the chances of missing samples. Then, patients who underwent intubation were selected using ICD-9-CM codes, 96.04 (Insertion of the endotracheal tube) and 96.05 (other intubation of respiratory tract). Also, if the patient had any of the code for "tracheostomy," 31.1 (temporary tracheostomy), 31.2 (permanent tracheostomy), 31.21 (mediastinal tracheostomy) or 31.29 (other permanent tracheostomy), then the case was selected. Early tracheostomy was defined if the tracheostomy was performed within 7 days after intubation date. Those who underwent major therapeutic surgery based on the classification from HCUP were excluded, using ICD9-CM codes.[45]

Statistical Analysis

Predictors of early and late tracheostomy were evaluated by multivariate logistic regression. Co-variables to be used for multivariate logistic regressions are age, sex, race, payers, location of the hospital (urban vs. rural) and comorbidities (coronary arterial disease, hypertension, cerebrovascular disease, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, cancer, liver disease, pneumonia). Comorbidities were selected from the literature using NIS dataset assessing a cardiologic procedure and additional significant systemic disorders.[52] Comorbidities were identified using relevant ICD-9 CM diagnosis code and Clinical Classification Software (CCS) category provided by HCUP from the 30 diagnosis codes, which were documented at the time of discharge.[45] Survey (svy) commands were used to account for the stratified sampling design of the NIS.[47,59]

Then, in order to assess various clinical outcomes of early tracheostomy, total hospital length of stay, hospital mortality, complication, and decannulation rate were compared between the two groups (early tracheostomy group and late tracheostomy group) using a propensity score matching. Propensity score matching is a statistical method allowing an observational study to estimate the effect of an intervention by controlling the covariates in a way analogous to a randomized trial.[50,51] Then a matched pair with similar propensity scores is identified, and the researchers compare the effect of the intervention using the selected pair. In this study, we used nearest neighbor 1:1 matching method using the propensity score of being assigned to early tracheostomy to identify a matched pair. Co-variables to be used to calculate the propensity score are age, sex, race, payers, location of the hospital (urban vs rural) and comorbidities (coronary arterial disease, hypertension, cerebrovascular disease, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, cancer, liver disease, pneumonia), which were used for previous multivariate logistic regression. After propensity score matching, logistic and linear regression analysis was used to compare the mortality, complications, decannulation and total hospital length of stay.

RESULT

Predictors of early tracheostomy among patients with acute heart failure exacerbation

We estimated the odds ratio (OR) of getting early tracheostomy with various co-variables (Table 1).

Among various co-variables, coronary artery disease, pneumonia, and liver disease had a significant association with the early tracheostomy, meaning patients with coronary artery disease, pneumonia, and liver disease are less likely to receive early tracheostomy (OR 0.79, 0.63 and 0.64 respectively). Otherwise, there were no significant

Table 1. Odds ratio of demographic and clinical characteristics for early tracheostomy

		Odds ratio	95% CI	*p*-value
Age		1.00	0.99, 1.00	0.583
Sex	Female	0.93	0.75, 1.15	0.522
Insurance	Private	Reference		0.824
	Medicare/Medicaid	0.86	0.63, 1.19	
	Self pay	1.03	0.56, 1.91	
	Other	0.91	0.43, 1.90	
Hospital location	Urban	1.05	0.12, 1.42	0.735
Race	White	Reference		0.644
	Black	1.10	0.86, 1.40	
	Hispanic	1.03	0.69, 1.53	
	Asian	0.85	0.32, 2.22	
	Native American	2.52	0.80, 7.89	
	Other	1.18	0.67, 2.06	
Comorbidities	Coronary arterial disease	0.79	0.63, 0.98	0.034
	Hypertension	1.17	0.92, 1.47	0.200
	Cerebrovascular disease	1.28	0.91, 1.77	0.165
	Diabetes mellitus	1.12	0.91, 1.39	0.291
	Peripheral arterial disease	0.71	0.43, 1.17	0.174
	Chronic obstructive pulmonary disease	1.12	0.91, 1.39	0.281
	Cancer	1.36	0.99, 1.88	0.059
	Chronic kidney disease	0.87	0.69, 1.09	0.230
	Liver disease	0.64	0.44, 0.95	0.026
	Pneumonia	0.63	0.51, 0.79	<0.001

demographic differences in getting early tracheostomy among patients who are admitted with acute heart failure exacerbation.

Early tracheostomy and its clinical outcomes

After propensity score matching, a matched cohort was used for analysis to assess the association between the early tracheostomy and various clinical outcomes, total hospital length of stay, in-hospital mortality, complication, and decannulation. Table 2 shows the characteristics of covariates before and after matching and table 3 shows the comparison of the outcomes between the two groups. Early tracheostomy was not significantly associated with in-hospital mortality (OR 0.91, *p*-value 0.676), or decannulation (OR 2.01, *p*-value 0.571). However, early tracheostomy was associated with a higher likelihood of having a complication from tracheostomy with OR 2.08 (*p*-value 0.044). Early tracheostomy was also associated with less total hospital length of stay with coefficient factor -6.50 (*p*-value 0.000) from linear regression model.

Table 2. Characteristics of covariates before and after matching

	Before Match			Matched pair		
	Early tracheostomy N=464	Late tracheostomy N=3,234	*p*-value	Early tracheostomy N=329	Late tracheostomy N=329	*p*-value
Age (year)	66.25	66.88	0.342	66.20	66.772	0.537
Sex (%)	52.37	52.94	0.819	52.24	51.53	0.837
Non-white (%)	42.96	40.31	0.296	43.29	48.00	0.169
Non-public insurance (%)	31.47	31.17	0.897	30.82	33.18	0.463
Urban hospital (%)	84.84	84.24	0.744	85.41	84.24	0.744
Coronary artery disease (%)	37.50	41.47	0.104	36.94	34.35	0.431
Hypertension (%)	62.50	57.85	0.058	63.29	60.47	0.397
Cerebrovascular disease (%)	11.42	8.94	0.084	11.06	11.77	0.747
Diabetes mellitus (%)	43.89	39.21	0.130	43.29	43.29	>0.99
Peripheral arterial disease (%)	4.31	5.69	0.224	4.05	4.56	0.605
Chronic obstructive pulmonary disease (%)	40.52	38.06	0.310	40.47	45.65	0.128
Cancer (%)	12.72	9.83	0.055	12.94	10.82	0.341
Chronic kidney disease (%)	32.76	33.09	0.889	32.94	32.94	>0.99
Liver disease (%)	7.76	10,48	0.069	7.294	6.118	0.494
Pneumonia (%)	5.95	75.51	<0.001	66.59	69.65	0.339

Table 3. Result from regression models for clinical outcomes of early tracheostomy using the matched cohort.

	Odds Ratio	*p*-value
In-hospital mortality	0.91	0.676
Complication from tracheostomy	2.08	0.044
Decannulation	2.00	0.571
	Coefficient factor	
Total hospital length of stay	-6.5	<0.001

DISCUSSION

The current study assessed the predictors of early tracheostomy among patients who were admitted with acute heart failure exacerbation. The results showed that coronary arterial disease, liver disease, and pneumonia are related to lower odds ratio of getting the early tracheostomy with odds ratio of 0.79, 0.64 and 0.63, respectively. However, there is no other demographic factor that is significantly associated with early tracheostomy. There are few studies that assessed the predictors of early tracheostomy, and they do not correlate with current studies' result. A retrospective study by Brook et al. reported that male gender had a high likelihood of getting the early tracheostomy. [40] Another retrospective study by Shaw reported that women, black race, Hispanics, and patients with Medicaid were less likely to receive the early tracheostomy. [60] The current study did not show any gender or racial differences in getting an early tracheostomy. However, the studies referred above included heterogeneous groups, but the current study only included patients with acute heart failure exacerbations, which may explain the different results from the other studies. Among the comorbidities, liver disease and pneumonia could be the complications of prolonged illness or shock, which could have served as a reason for late tracheostomy at the later stage of hospitalization course, explaining less likelihood to get an early tracheostomy. Coronary arterial disease is one of the major comorbidities related to heart failure, and its presence might have delayed the decision of tracheostomy since it could prompt the physician to pursue additional curative intervention for coronary arterial disease during that hospitalization.

Another objective of the current study was to compare clinical outcomes between the two groups. There was no difference in in-hospital mortality and decannulation rate between the two groups. However, a complication from the tracheostomy was more common in early tracheostomy group (OR 2.08 with *p*-value 0.044). Total hospital length of stay was significantly different, and the early tracheostomy group had 6.5 shorter days than the late tracheostomy group. (*p*-value <0.001). The mortality benefit from early tracheostomy has been controversial based on multiple studies. However, a recent systemic review and meta-analysis by Liu et al. reported that early tracheostomy has lower short-term mortality.[31] The current study did show less mortality in early tracheostomy group, but it was not statistically significant. Complication from the tracheostomy was higher in early tracheostomy group in our study. It is not consistent with the result from other studies. Young et al. reported a lower complication rate in early tracheostomy group (5.5% in early tracheostomy group and 7.8%

in late tracheostomy group), without statistical significance. Further studies are warranted to compare the complication rates between the two groups since the results are not consistent between the two studies. Early tracheostomy clearly showed a shorter total length of stay in the hospital, shortening the length of stay by 6.5 days. Most of the previous studies comparing early and late tracheostomy have mainly focused on the cost and length of stay in the ICU, not the total hospital stay. [37,61] Rumbak et al. showed that early tracheostomy could reduce the ICU stay up to 11.40 days. [37] Our study did not look into the ICU stay because of the limitation of the information from the original dataset. However, it did confirm that the early tracheostomy reduces the length of stay in the hospital.

The current study has several limitations. First, this study used a discharge dataset and conducted a retrospective cohort study. Although potential confounders were adjusted through propensity score matching and multivariate logistic regression, selection bias cannot be completely eliminated. Choice of timing for tracheostomy can be affected by multiple factors including the clinician's preference, the patient's decision, hospital policy or other co-existing clinical conditions, which we were not able to obtain from the dataset. However, the result of propensity score matching actually showed that the two groups did not much differ each other even before the matching.

Second, we identified acute heart failure exacerbation cases using the first five diagnosis codes from total 30 diagnosis codes, rather than only the first diagnosis, We used this method because the etiology of respiratory failure requiring intubation could be placed in second or third place of the diagnosis list, and we wanted to maximize our sample size without missing a case. However, it is also possible that there might be another clinical condition, which required intubation, such as chronic obstructive pulmonary disease, pneumonia, trauma or surgical conditions. If it is the case, then our study group might be somewhat heterogeneous. However, we tried to adjust such conditions through multivariate regression and propensity score matching. We also excluded patients who underwent therapeutic surgery to avoid this problem.

Lastly, we did not have information regarding the severity of heart failure. The severity of heart failure affects the clinical courses and prognosis, which plays a significant role in the decision of tracheostomy. However, we do not have such information, so we could not stratify the patients according to the severity of the primary disease.

CONCLUSION

Despite several limitations, the current study has several strengths. It used a nationally representative data to evaluate the predictors of early tracheostomy in patients with a specific condition, acute heart failure exacerbation. Patients with coronary artery disease, liver disease, and pneumonia were associated lower likelihood to receive early tracheostomy (<7 days after intubation) rather than late tracheostomy among patients who were admitted to the hospital with acute heart failure exacerbation. There were no other demographic factors that were associated with early tracheostomy. When the two groups were compared using propensity score matching, they did not differ from each other in in-hospital mortality, but clearly showed that early tracheostomy was associated with lower total hospital length of stay.

REFERENCES

1. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the united states: A policy statement from the American heart association. *Circ Heart Fail*. 2013;6(3):606-619.

2. National Center for Health Statistics. Mortality multiple cause micro-data files, 2013: Public-use data file and documentation: NHLBI tabulations. http://www.cdc.gov.utsph.idm.oclc.org/nchs/data_access/Vitalstatsonline.htm#Mortality_Multiple. Accessed 05/19, 2015.

3. Healthcare Cost and Utilization Project (HCUP). Overview of the national (nationwide) inpatient sample (NIS). https://www.hcup-us.ahrq.gov/nisoverview.jsp. Updated 2018. Accessed 2/21, 2018.

4. Healthcare Cost and Utilization Project (HCUP). Clinical classifications software (CCS) for ICD-9-CM. https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Updated 2017. Accessed 2/23, 2018.

5. Dhoble A, Bhise V, Nevah MI, et al. Outcomes and readmissions after transcatheter and surgical aortic valve replacement in patients with cirrhosis: A propensity matched analysis. *Catheter Cardiovasc Interv*. 2018;91(1):90-96.

6. Schulman AR, Abougergi MS, Thompson CC. Assessment of the July effect in post-endoscopic retrograde cholangiopancreatography pancreatitis: Nationwide inpatient sample. *World journal of gastrointestinal endoscopy*. 2017;9(7):296.

7. Final report on calculating national inpatient sample (NIS) variances for data years 2012 and later. 2015. HCUP methods series report # 2015-09 . https://www.hcup-us.ahrq.gov/reports/methods/2015_09.jsp. Updated 2015.

8. Rubin DB. Using propensity scores to help design observational studies: Application to the tobacco litigation. *Health Serv Outcomes Res*. 2001;2(3-4):169-188.

9. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55.

10. Brook AD, Sherman G, Malen J, Kollef MH. Early versus late tracheostomy in patients who require prolonged mechanical ventilation. *American Journal of Critical Care*. 2000;9(5):352.

11. Shaw JJ, Santry HP. Who gets early tracheostomy?: Evidence of unequal treatment at 185 academic medical centers. *Chest*. 2015;148(5):1242-1250.

12. Liu X, Wang H, Xing Y, He Y, Zhang Z, Wang T. The effect of early and late tracheotomy on outcomes in patients: A systematic review and cumulative meta-analysis. *Otolaryngology--Head and Neck Surgery*. 2014;151(6):916-922.

13. Herritt B, Chaudhuri D, Thavorn K, Kubelik D, Kyeremanteng K. Early vs. late tracheostomy in intensive care settings: Impact on ICU and hospital costs. *J Crit Care*. 2018;44:285-288.

14. Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med*. 2004;32(8):1689-1694.

JOURNAL ARTICLE III

Title of Journal: Economic Evaluation of Early and Late Tracheostomy Among Patients with Acute Heart Failure Exacerbation

Name of Journal Proposed for Submission: JAMA Cardiology

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ABSTRACT

Background

The optimal time of tracheostomy among patients with acute heart failure exacerbation has been controversial. Several studies have proposed economic benefit from the early tracheostomy, but no research has focused only on those with acute heart failure exacerbation. The purpose of this study was an economic evaluation of early and late tracheostomy among those who developed respiratory failure with acute congestive heart failure exacerbation using average and incremental costs with the outcome of total hospital length of stay and post-procedure length of stay.

Methods

We conducted an economic evaluation of early tracheostomy for the outcome of total hospital length of stay and post-procedural length of stay among patients who are admitted with acute heart failure exacerbation. We used mortality, costs, length of stay, and post-procedural length of stay from an observational study using National Inpatient Sample data from 2005 to 2014.

Results

The early tracheostomy dominates the late tracheostomy with the outcome of total hospital length of stay and post-procedural length of stay with lower cost and higher effectiveness. The incremental cost-effectiveness ratio is actually negative, that is, it costs $3,492.65 dollars for each additional day in the hospital for late tracheostomy versus early tracheostomy. Furthermore, the average cost per effectiveness is higher in late tracheostomy group

($2,743.43) than in the early group ($2,420.82). The average post-procedural cost per effectiveness was $2,440.17 in late tracheostomy group and $2,591.03 in the early group. However, the incremental cost-effectiveness ratio is again negative, at $2,032.67 dollars per extra day in the hospital after the procedure.

Conclusions

The current study showed that early tracheostomy is more cost-effective with the outcome of total hospital length of stay and post-procedural length of stay than late tracheostomy among patients with acute heart failure exacerbation.

INTRODUCTION

Heart failure is one of the leading causes of high morbidity and mortality. Based on the data from National Health and Nutrition Examination Survey (NHANES) 2009 to 2012, it was estimated that total 5.7 million Americans older than 20 years of age had heart failure. That number is anticipated to increase by 46% from 2012 to 2030, which can result in more than 8 million people older than 18 years of age with heart failure.[1] Considering the development and implementation of life-prolonging interventions along with the growing elderly population, the number of individuals with heart failure will be significantly increased, which will also increase the cost of heart failure.[7,8] Hence, the economic burden for society is an issue. A study using 10-year data from the National Medical Expenditure Panel Survey (2002-2011) showed that individuals with heart failure had 4 times higher yearly expenditure ($23,854) compared to those without heart failure ($5,511) and the single largest driving component of this increase was inpatient costs ($11,318).[8] Acute heart failure exacerbation is one of the leading causes of hospitalization among patients with heart failure. It is also potentially fatal, which may result in acute respiratory failure requiring intubation and admission to the intensive care unit and mechanical ventilator care. Despite ongoing treatment for congestive heart failure, not all the patients can be weaned off the ventilator. In such cases, the health care providers should consider tracheostomy.[11,14] Tracheostomy is considered to be beneficial to be more comfortable for the patients, requires less sedation, and provides more stable airway compared to an endotracheal tube, but it still carries several complications including bleeding, hypoxia, structural damage or cardiopulmonary arrest.[11] Hence, the optimal time for tracheostomy with the goal of getting extubated, and also to prevent complications from prolonged intubation and to secure more stable airway, has been controversial.[15,20] Considering the significant economic burden of acute heart failure exacerbation and subsequent respiratory failure requiring intubation, a strategy to determine the optimal timing of tracheostomy should be investigated. Liu et al. reported cost-effectiveness of early versus late tracheostomy with the outcome of tracheostomy prevented and it showed that early tracheostomy could be more cost-effective with a willingness to pay threshold of $80,000 per tracheostomy avoided.[30] Other studies have shown that early tracheostomy may provide less mortality and fewer healthcare resources utilization. However, most of the studies included heterogeneous clinical conditions in their outcome assessment. Furthermore, to the best of our knowledge, studies comparing early and late tracheostomy for patients with acute respiratory failure due to congestive heart failure are lacking.

The purpose of this study was an economic evaluation of early and late tracheostomy among those who developed respiratory failure with acute congestive heart failure exacerbation using average and incremental costs with the outcome of total hospital length of stay and post-procedure length of stay. The result of the study will provide evidence to assist both clinicians and hospital administrator in determining the most efficient care strategy for managing patients with respiratory failure from acute heart failure exacerbation requiring ventilator assistance.

METHODS

We used a publically accessible national survey data, National Inpatient Sample (NIS) from 2005 to 2014 to obtain cost and effectiveness data for economic evaluation. NIS is the largest all-payer inpatient care database in the United States, which is developed by the Healthcare

Cost and Utilization Project (HCUP) [44] It allows the researchers to assess national estimates of clinical and resource-use information such as diagnosis, procedures, morbidity codes, patient's demographic characteristics, hospital characteristics, expected payment source, total charges, length of stay, and severity and comorbidity measures from hospital inpatient stays in the United States. It is drawn from all states participating in HCUP and represents more than 97 percent of the U.S. population.

Effectiveness was defined total hospital length of stay and post-procedure length of stay. Both average and incremental cost-effectiveness ratios (ICER) were used for the economic evaluation. With the effectiveness of hospital length of stay, ICER was calculated by dividing incremental total hospital cost by incremental length of stay. With the effectiveness of post-procedural length of stay, ICER was obtained using incremental post-procedural hospital cost and incremental post-procedural length of stay.

The number of early and late tracheostomies, mortality for each intervention, the costs and the length of stay in the hospital came from the current dataset for the base case analysis (Table 1). The mortality was obtained from a comparative analysis using propensity score matching. From the NIS database from 2004 to 2015, patients who were admitted with the diagnosis of acute heart failure exacerbation were selected using ICD-9-CM codes. Patients who were younger than 18 years old and who received therapeutic surgery were excluded from the study. Then a matched pair, early tracheostomy group versus late tracheostomy group, was obtained using propensity score matching adjusting covariates including age, sex, race, payers, location of the hospital (urban vs rural) and comorbidities (coronary arterial disease, hypertension, cerebrovascular disease, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, cancer, liver disease, pneumonia). We used nearest neighbor 1:1 matching method. Early tracheostomy was defined if the patient received tracheostomy within 7 days. Then, the mortality rate from each group was obtained from the matched pair.

Other probabilities for the economic evaluation came from a literature review. The mean costs and length of stay for each node were obtained using discharge weight (variable DISCWT), provided by AHRQ.[46-48] Total hospital cost was provided by the dataset, but the post-procedural cost was calculated by multiplying the post-procedural length of stay by daily cost, and the daily cost was calculated by dividing the total hospital cost by the total length of stay.

If one intervention shows higher effectiveness and lower cost, that intervention could be said to dominate another one.[62] For example, if one intervention requires less total cost, but resulted in a shorter stay in the hospital, then we would state that that intervention dominates another one. The time horizon was during the admission, and discounting was not applied because of short time horizon. This study was conducted from the U.S. health care all-payers perspective. All costs were adjusted to 2014 U.S dollars using consumer price index.

Table 1. Model parameters for probabilities

Variables	Value	Distribution	Source	Range
Probabilities				
Intra-operation mortality	0.004	β	Halum et al. [63]	(0~1)
Early tracheostomy, a complication related to tracheostomy	0.054	β	Young et al. [33]	(0~1)
Late tracheostomy, a complication related to tracheostomy	0.075	β	Young et al. [33]	(0~1)
Early tracheostomy, decannulation	0.51	β	Koch et al. [38]	(0~1)
Late tracheostomy, decannulation	0.33	β	Koch et al. [38]	(0~1)
Early tracheostomy, mortality	0.14	β	Present study	(0-1)
Late tracheostomy, mortality	0.15	β	Present study	(0-1)
Variables	Value	Distribution	Source	Range
Costs				
Early tracheostomy, cost for each node ($)		γ	Present study	±25%
Late tracheostomy, cost for each node ($)		γ	Present study	±25%
Effects				
Total hospital length of stay for each node (days)		NA	Present study	NA
Post-procedural length of stay days for each node (days)		NA	Present study	NA

Sensitivity analysis was conducted on probabilities and costs, using probabilistic sensitivity analysis. The minimum value and maximum values were estimated 25% lower and 25%

more than the mean value, respectively. There were several nodes where the dataset did not have any case, so values (cost and effectiveness) of those nodes were substituted from the neighboring branches. Those nodes were intra-operation mortality in early tracheostomy (EarlyNosurvive), those with complication from the tracheostomy, and decannulated but died in the hospital in early tracheostomy group (EarlySurviveCompDecanDeath), those with complication from the tracheostomy, decannulated and discharged from the hospital alive in early tracheostomy group EarlySurviveCompLive), those without complication from the tracheostomy, and decannulated but died in the hospital in early tracheostomy group (EarlySurviveNocompDecDeath), and those with complication from the tracheostomy, and decannulated but died in the hospital in late tracheostomy group (LateSurviveCompDecanDeath). The range of the probabilities was 0 to 1. A Tornado diagram was utilized to determine the factors that had the most impact on the choice of tracheostomy. Probabilistic sensitivity analysis was conducted using the distribution assigned to the probabilities and costs, using a willingness to pay threshold, and the cost-effectiveness acceptability curve was plotted. Stata/IC 14.2 was used to estimate the cost and effectiveness from the NIS database, and TreeAge Pro program was used to construct the decision tree model and calculate both ratios.

RESULT

Economic evaluation with the outcome of total hospital length of stay

Figure 1 shows the decision tree from the economic evaluation with the outcome of the total hospital length of stay between the early tracheostomy and late tracheostomy. The first economic evaluation was conducted with the outcome of the total hospital length of stay. The result showed that early tracheostomy dominates late tracheostomy with lower total hospital cost and shorter total hospital length of stay (Table 2 and Figure 2). The incremental cost-effectiveness ratio is actually negative, that is, it costs $3,492.65 dollars for each additional day in the hospital for late tracheostomy versus early tracheostomy. Furthermore, the average cost per effectiveness is higher in late tracheostomy group ($2,743.43) than in the early group ($2,420.82).

Figure 1. Decision tree for the economic evaluation with the outcome of total hospital length of stay

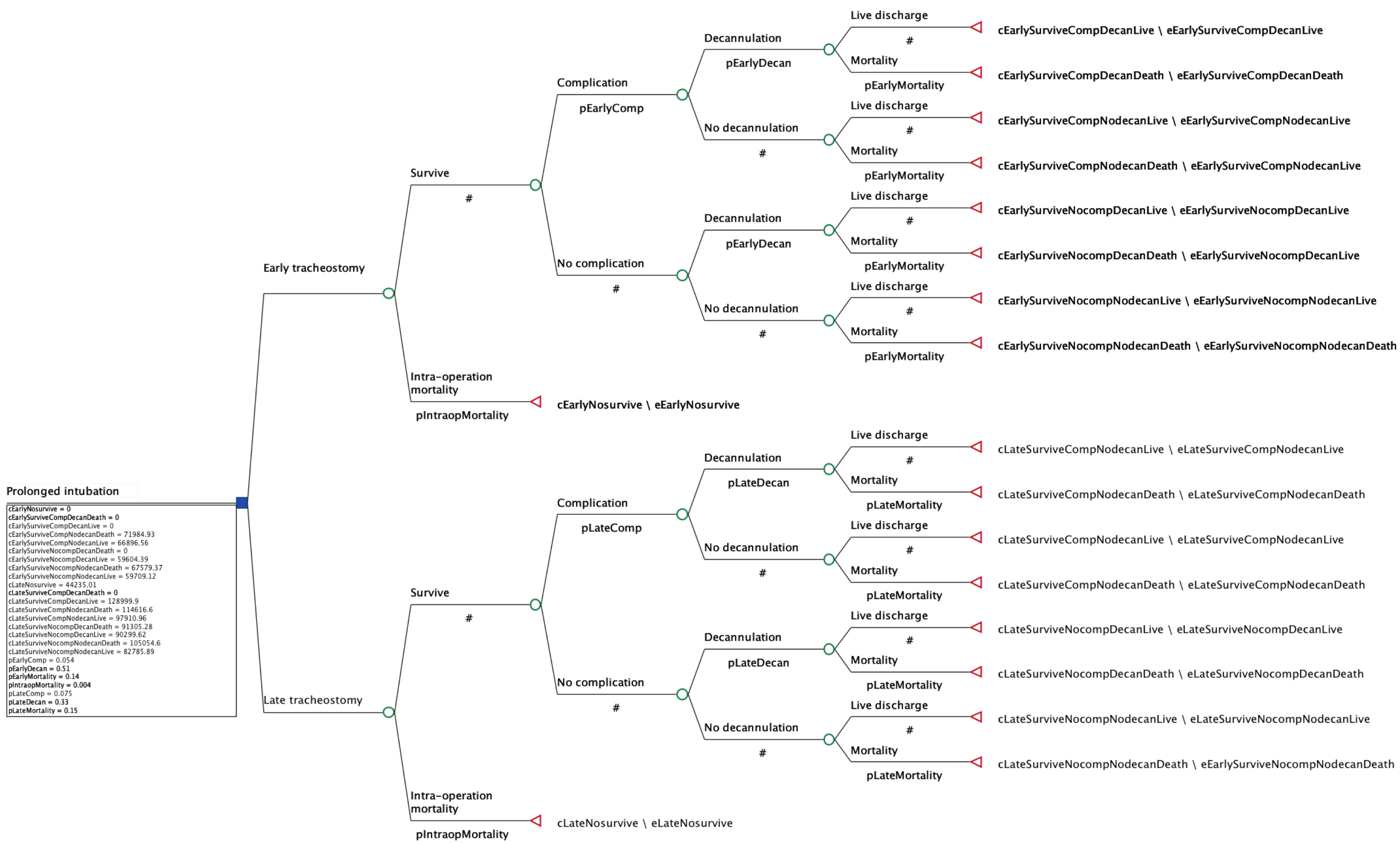


Figure 2. Cost-effectiveness analysis graph with outcome total hospital length of stay

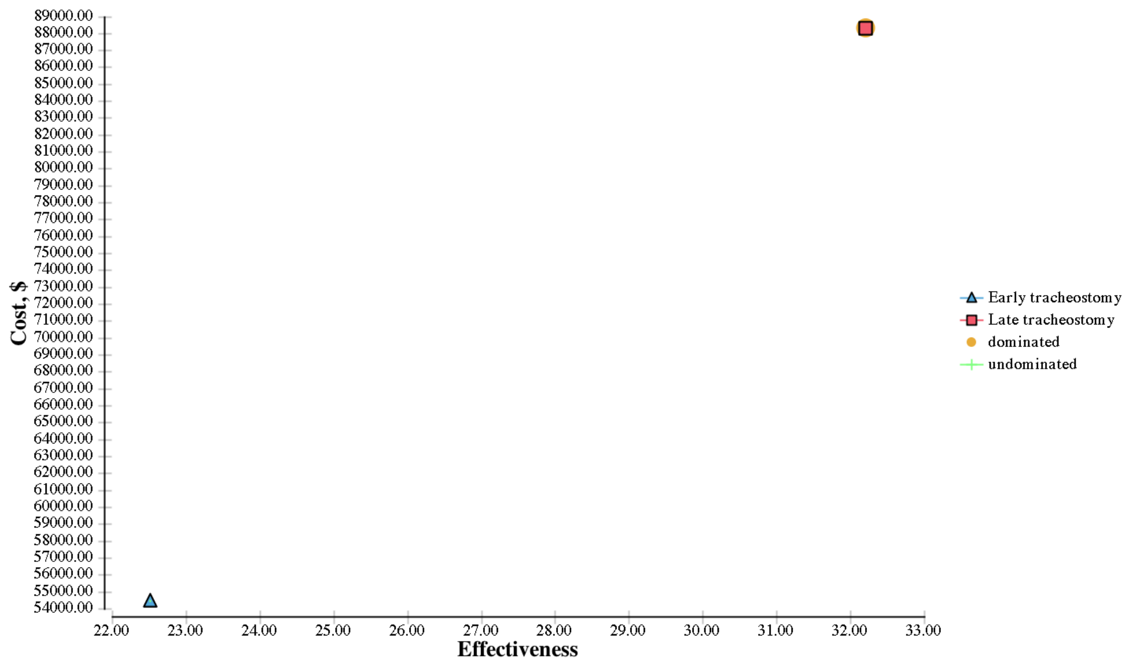


Table 2. Cost-effectiveness analysis using outcome total hospital length of stay

Strategy	Cost	Incr Cost	Eff	Incr Eff	Incr C/E	Average C/E
Early tracheostomy	54,489.20		22.51			2,420.82
Late tracheostomy	88,340.84	33,851.64	32.20	-9.69	-3,492.65	2,743.43

*Incr : Incremental, Eff: Effectiveness, C: Cost, E: Effectiveness

For sensitivity analysis, we performed a tornado diagram and probabilistic sensitivity analysis. Figure 3 shows the decision tree for the sensitivity analysis. We assumed that all the probabilities have beta distribution and costs have gamma distribution. For range, if the confidence interval is known from the literature, we used them, but if not, we used high as 1 and low as 0 for probability, and ±25% of the average cost.

From the tornado gram, the probability of tracheostomy-related complication in early tracheostomy group had the highest impact on ICER resulting in a range from -3,195.03 to 4,976.14 (Figure 4). Then, we sampled 1000 observations and formulated a cost-effectiveness acceptability curve. Even after the sensitivity analysis, early tracheostomy still dominates for the effectiveness of less total length of stay in the hospital, and cost-effectiveness acceptability curves do not cross over (Figure 5).

Figure 3. Decision tree for the sensitivity analysis with the outcome of total hospital length of stay

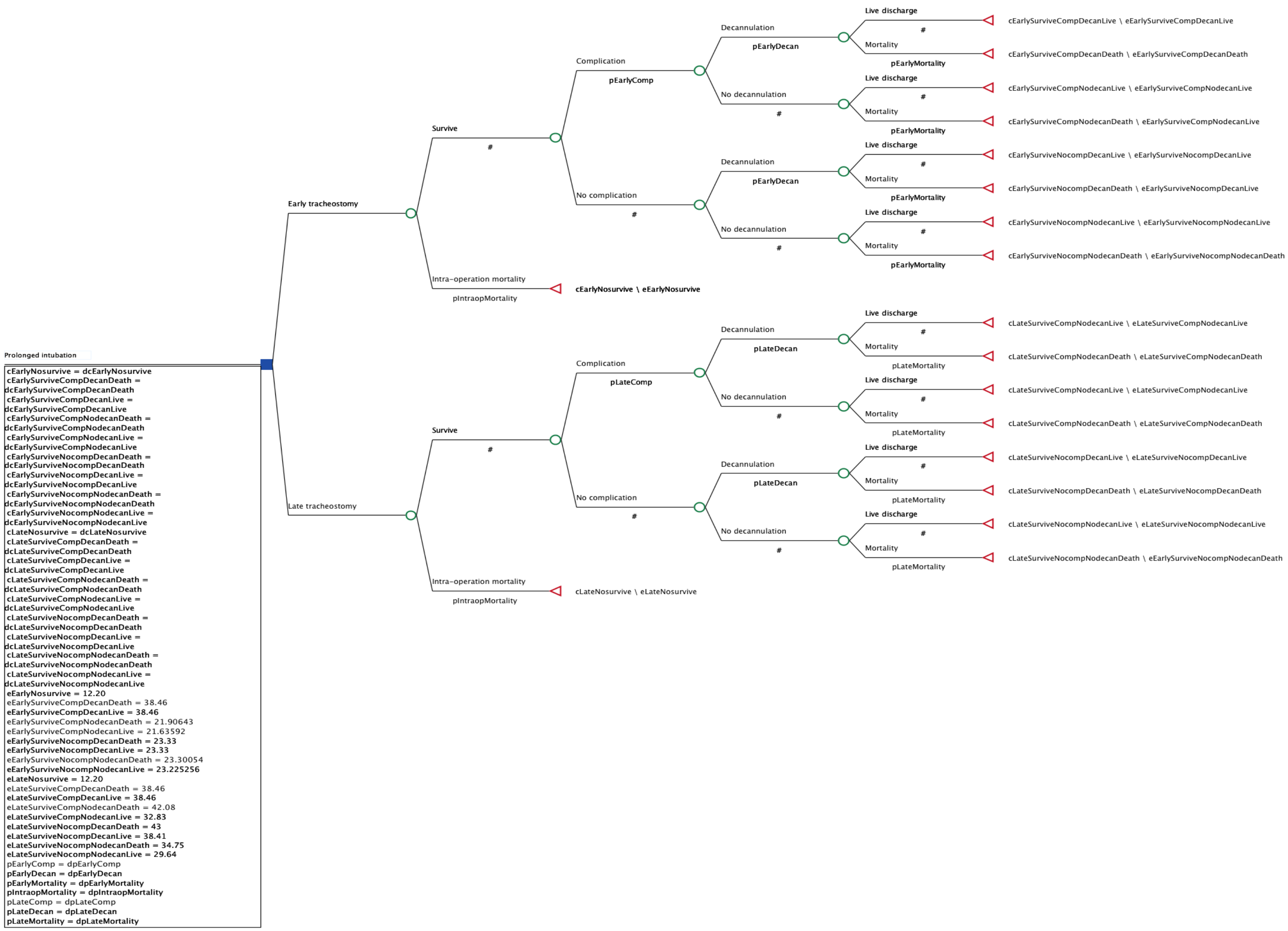


Figure 4. Tornado diagram of ICER using outcome total hospital length of stay

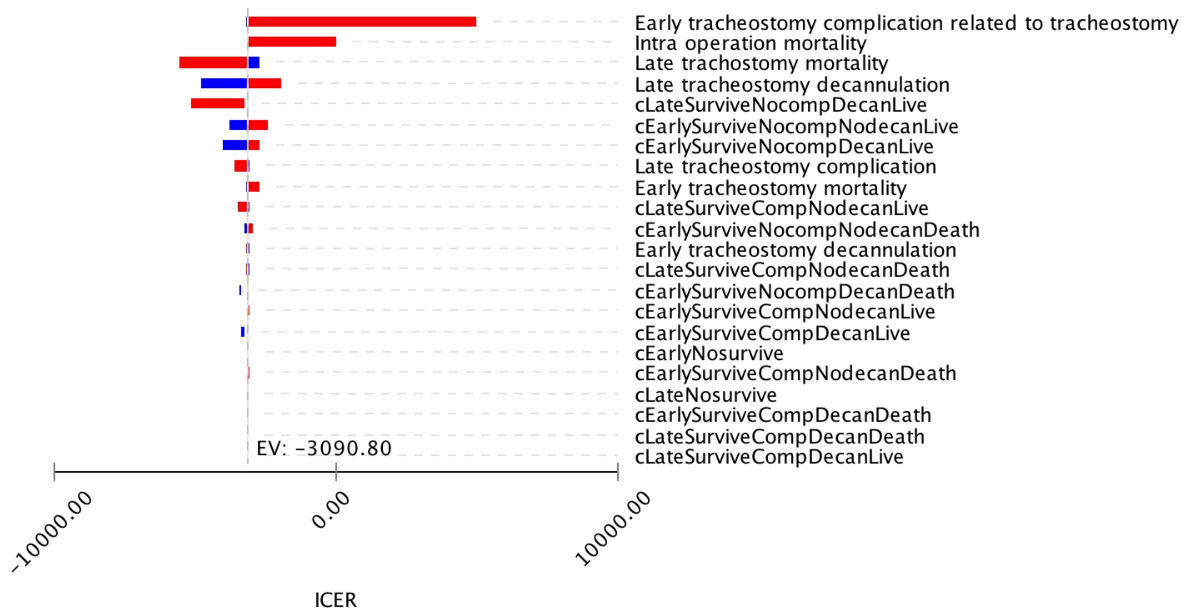
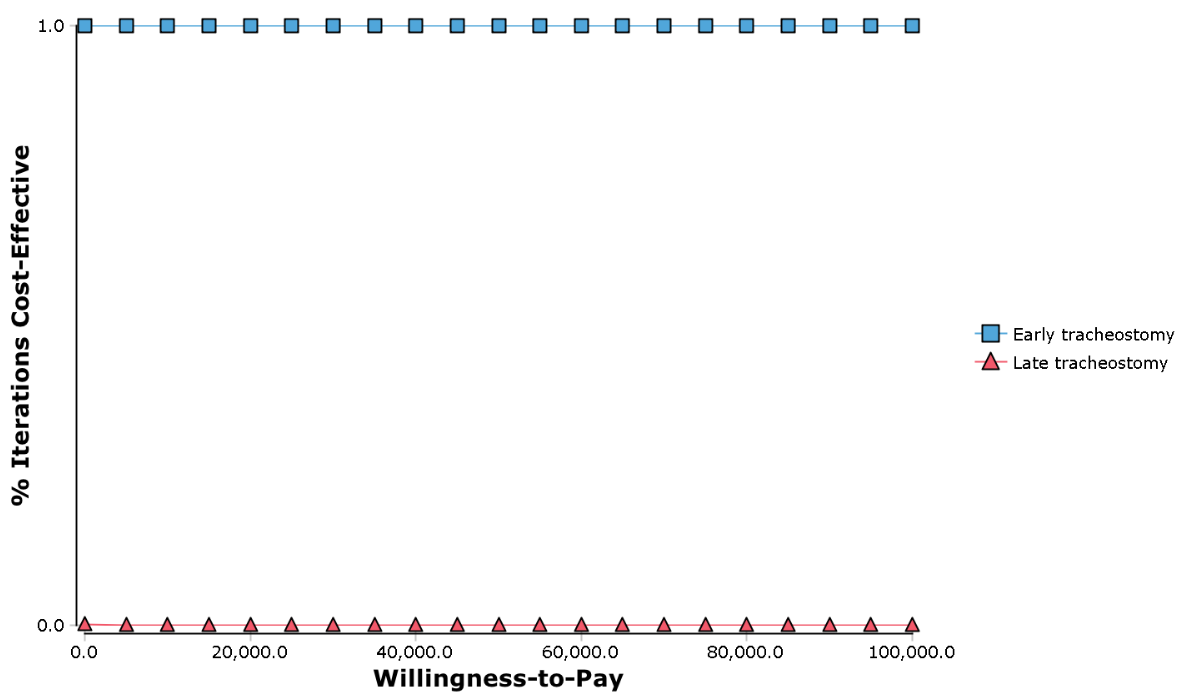


Figure 5. Cost-effectiveness acceptability curve with outcome total hospital length of stay



Economic evaluation with the outcome of post-procedural hospital length of stay

The second economic evaluation was conducted with the outcome of the post-procedural length of stay, meaning the length of stay after tracheostomy. Figure 6 shows the decision tree with the outcome of post-procedural length of stay. The result showed that early tracheostomy again dominates late tracheostomy with lower post-procedural hospital cost and shorter post procedural hospital length of stay (Table 3 and Figure 7). The average cost per effectiveness was $2,440.17 in late tracheostomy group and $2,591.03 in the early group. However, the incremental cost-effectiveness ratio is again negative, at $2,032.67 dollars per extra day in the hospital after the procedure.

Table 3. Cost-effectiveness analysis using outcome post-procedural length of stay

Strategy	**Cost**	**Incr Cost**	**Eff**	**Incr Eff**	**Incr C/E**	**C/E**
Early tracheostomy	46,366.49	0	17.89	0	0	2,591.03
Late tracheostomy	59,832.38	13,465.89	24.52	-6.62	-2,032.67	2,440.17

*Incr : Incremental, Eff: Effectiveness, C: Cost, E: Effectiveness

Again, for sensitivity analysis, we performed a tornado diagram and probabilistic sensitivity analysis. We assumed that all the probabilities have beta distribution and costs have gamma distribution. For range, if the confidence interval is known from the literature, we used them, but if not, we used high as 1 and low as 0 for probability, and ±25% of the average cost. From the tornado gram, the probability of complication after tracheostomy among patients who underwent late tracheostomy had the highest impact on ICER resulting in a range from -7,075.09 to -1,561.15 (Figure 9). Then, we sampled 1000 observations and formulated a cost-effectiveness acceptability curve. Even after the sensitivity analysis, again, early tracheostomy still dominates for the effectiveness of less post-procedural length of stay in the hospital, and cost-effectiveness acceptability curves do not cross over (Figure 10).

Figure 6. Decision tree with the outcome of post-procedural length of stay

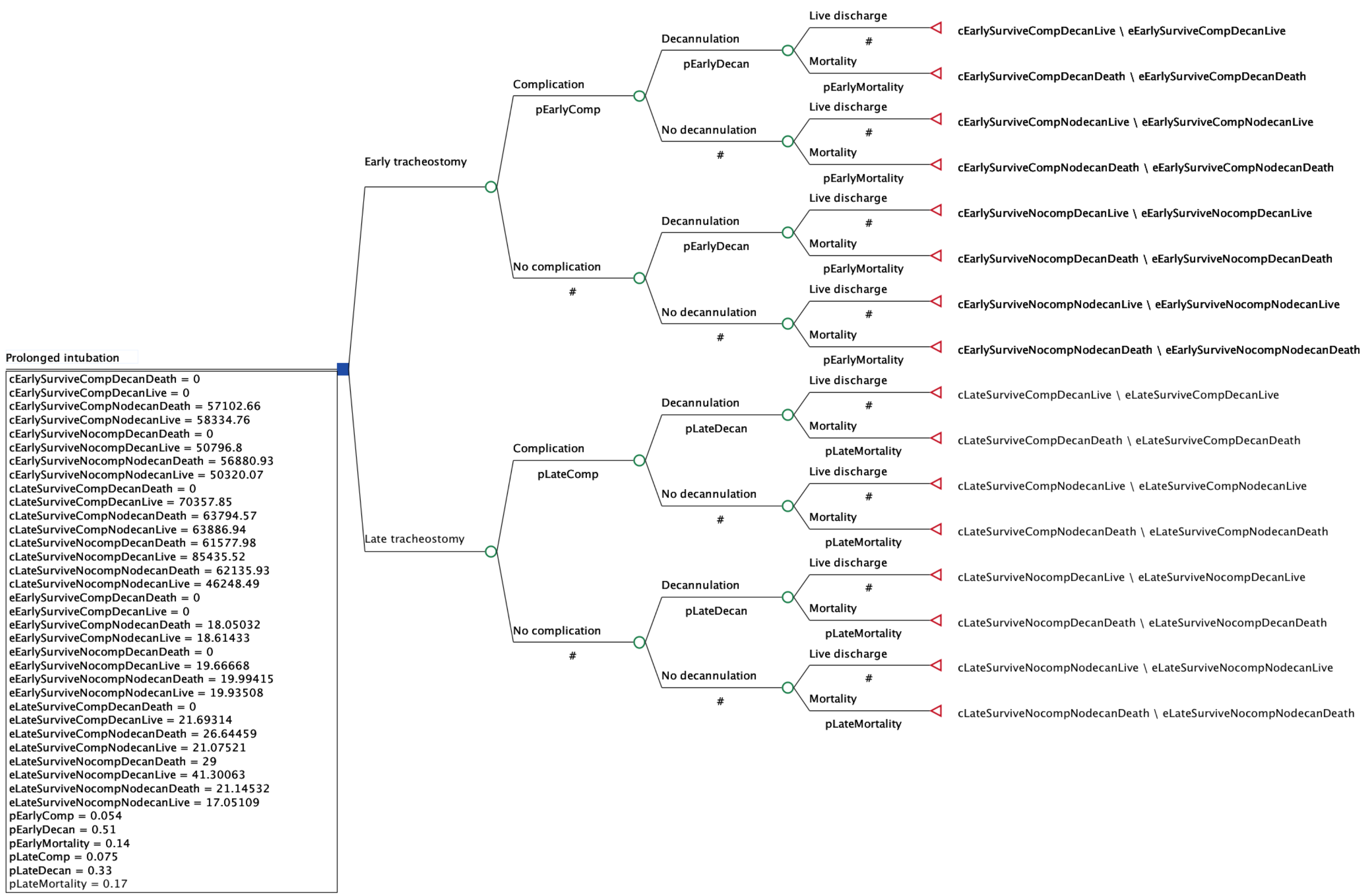


Figure 7. Cost-effectiveness analysis graph with outcome post-procedural length of stay

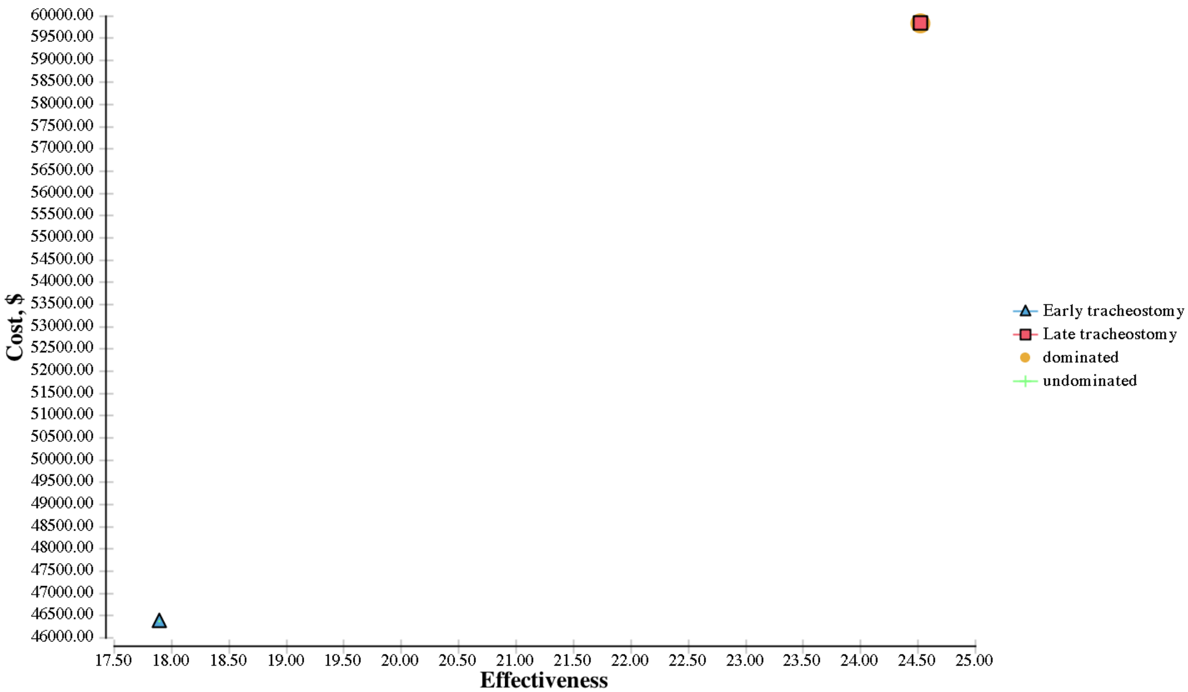


Figure 8. Decision tree for sensitivity analysis with outcome of post-procedural length of stay

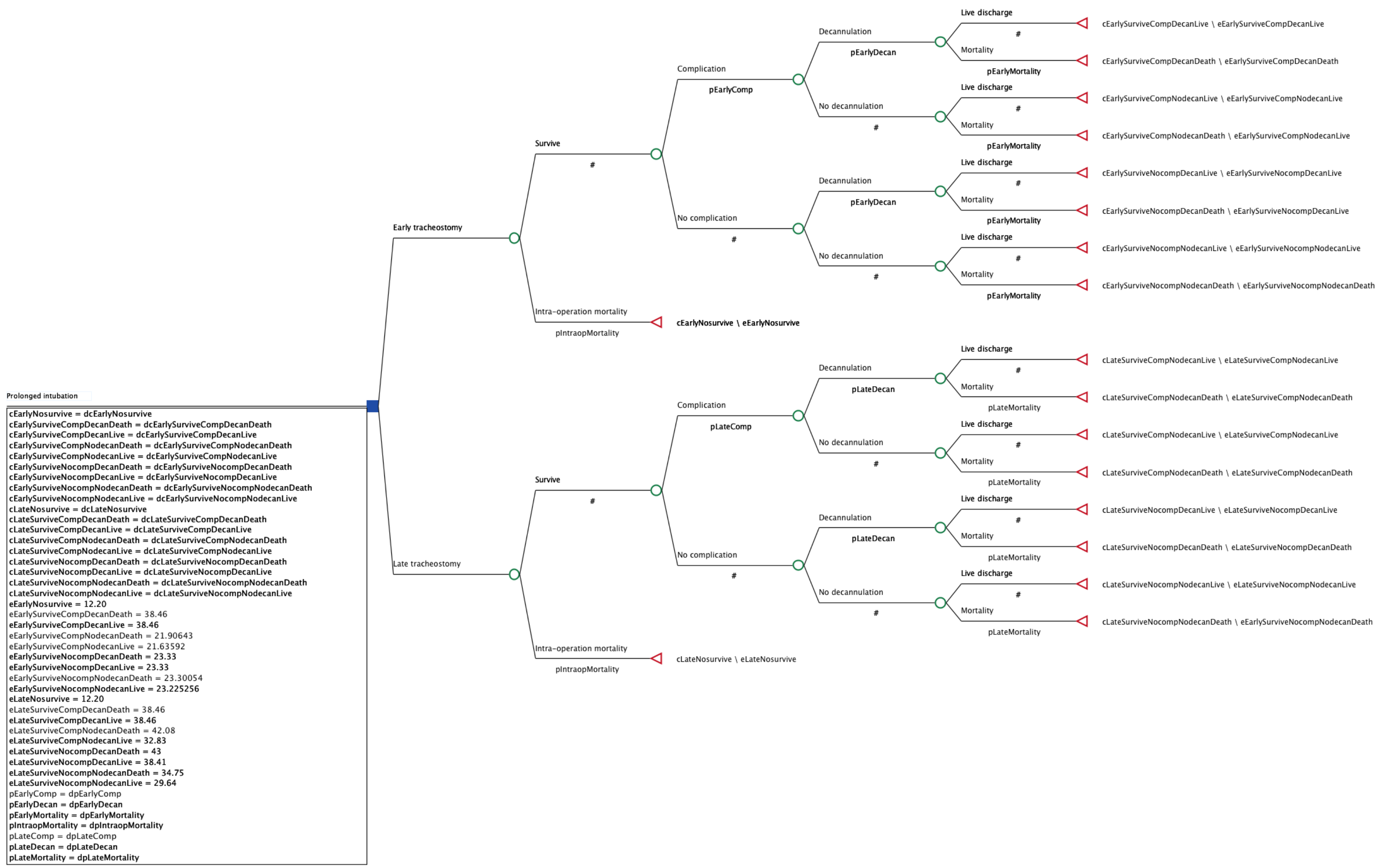


Figure 9. Tornado diagram of ICER using outcome post-procedural length of stay

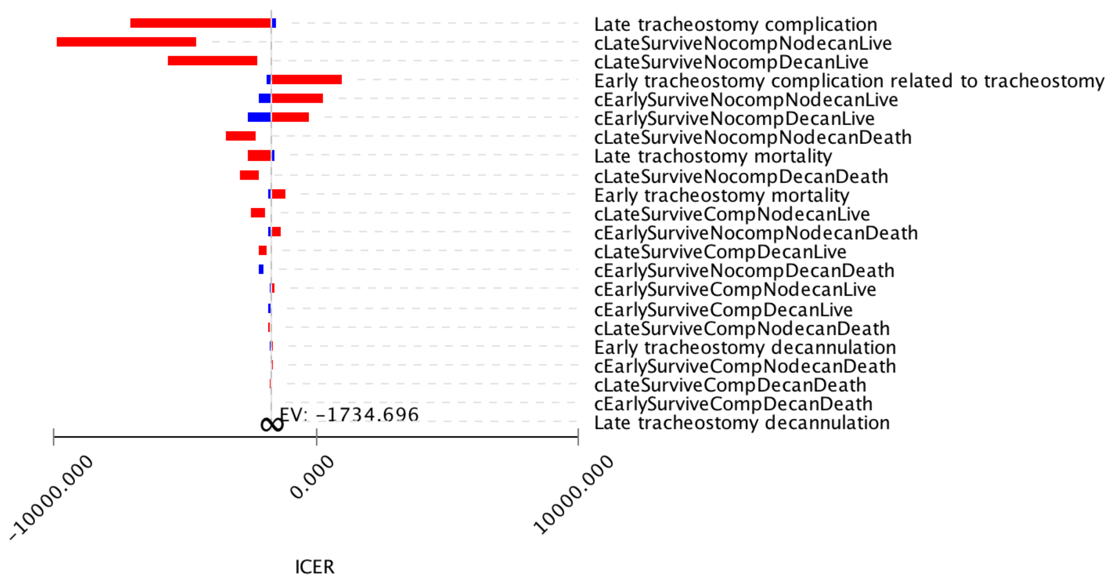
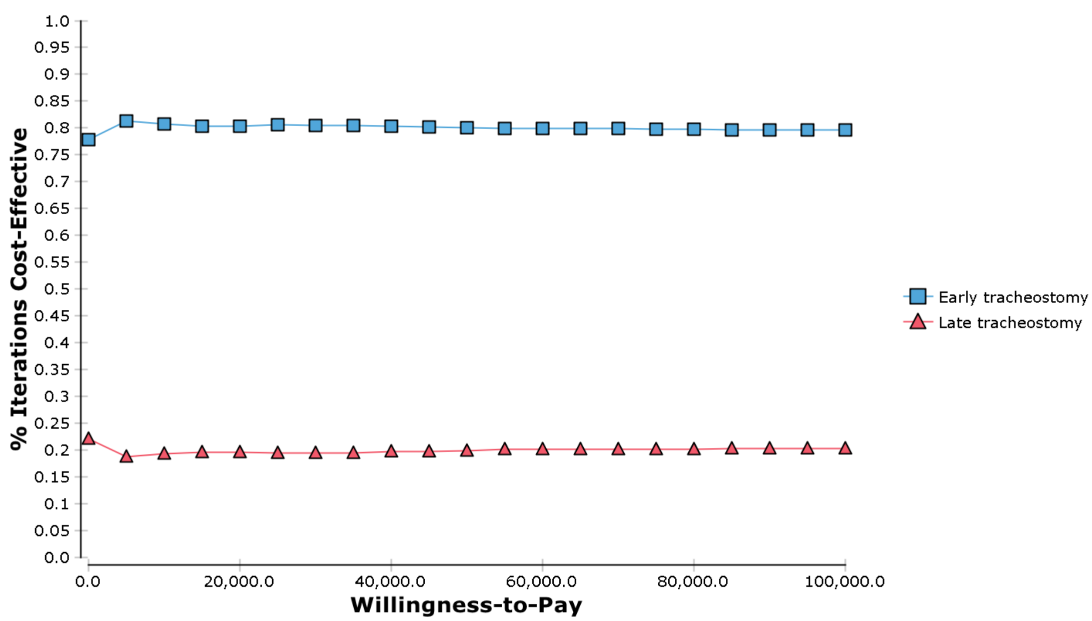


Figure 10. Cost-effectiveness acceptability curve using the outcome post procedural length of stay



DISCUSSION

The current study evaluated the cost-effectiveness of early tracheostomy using the outcome of total hospital length of stay, and post-procedural length of stay. For both outcomes, early tracheostomy dominated late tracheostomy. It had a lower cost with less hospital length of stay. Even after sensitivity analysis, early tracheostomy remains to dominate late tracheostomy with a willingness to pay up to $100,000.

We particularly chose the length of stay as the outcome of the economic evaluation since previous studies have shown very controversial results for mortality differences between early and late tracheostomy, but somewhat consistent results for less health care utilization in early tracheostomy group. Furthermore, from our own analysis of NIS dataset, mortality rates from the two interventions were incorporated into the decision tree as probabilities and reflected the final economic analysis.

To the best of our knowledge, there has been only one economic evaluation study assessing early tracheostomy. Liu et al. reported cost-effectiveness of early versus late tracheostomy with the outcome of tracheostomy prevented and it showed that early tracheostomy could be more cost-effective with a willingness to pay threshold of $80,000 per tracheostomy avoided. [30] However, this study focused on the cost-effectiveness per tracheostomy avoided, not health care utilization such as length of stay. Several other studies have reported less health care resources utilization among early tracheostomy group with various medical or surgical conditions, proposing less intensive care unit stay or shorter ventilation dependent days. [25,27] However, the current study is the first study to perform cost-effectiveness analysis using outcomes of hospital length of stay among patients who are admitted with acute heart failure exacerbation. Furthermore, the cost and effectiveness information came from real patients data, rather than literature review or expert opinion, and it makes the result of evaluation more credible.

However, the current study holds several limitations. First, even though the mortality, cost, and effectiveness were derived from real patients' data, the result is still from a retrospective cohort study, not a randomized controlled study. The information still could be confounded by selection bias. However, we tried to reduce its effect by sensitivity analysis. When performing sensitivity analysis, for the probability we used the widest range possible, from 0 to 1, and still, the result showed that early tracheostomy dominates the late tracheostomy.

Second, based on the decision tree, each node should have its own cost and effectiveness from the database, but some nodes did not have any sample from the database since the sample size was small. In such cases, we used the cost and effectiveness from the neighboring nodes for sensitivity analysis. Hence, the tree does not reflect the real clinical situation, but we tried to overcome it through sensitivity analysis.

Last, for the economic analysis with the outcome of post-procedural length of stay, we used the estimated cost that was calculated by the daily cost ((Total hospital cost/total length of stay) * post-procedural length of stay). It may not reflect the actual cost after the procedure, since the patient care after the procedure may be significantly different. However, due to the limitation of the dataset and information availability, we tried to use the best alternative.

CONCLUSION

The current study showed that early tracheostomy is more cost-effective with the outcome of total hospital length of stay and post-procedural length of stay than late tracheostomy among patients with acute heart failure exacerbation.

APPENDIX

APPENDIX A. Variable values for cost effectiveness analysis with outcome of total hospital length of stay

Name	Root Definition
cEarlyNosurvive	0
cEarlySurviveCompDecanDeath	0
cEarlySurviveCompDecanLive	0
cEarlySurviveCompNodecanDeath	71,984.93
cEarlySurviveCompNodecanLive	66,896.56
cEarlySurviveNocompDecanDeath	0
cEarlySurviveNocompDecanLive	59,604.39
cEarlySurviveNocompNodecanDeath	67,579.37
cEarlySurviveNocompNodecanLive	59,709.12
cLateNosurvive	44,235.01
cLateSurviveCompDecanDeath	0
cLateSurviveCompDecanLive	128,999.90
cLateSurviveCompNodecanDeath	114,616.60
cLateSurviveCompNodecanLive	97,910.96
cLateSurviveNocompDecanDeath	91,305.28
cLateSurviveNocompDecanLive	90,299.62
cLateSurviveNocompNodecanDeath	105,054.60
cLateSurviveNocompNodecanLive	82,785.89
eEarlyNosurvive	0
eEarlySurviveCompDecanDeath	0
eEarlySurviveCompDecanLive	0
eEarlySurviveCompNodecanDeath	21.91
eEarlySurviveCompNodecanLive	21.64
eEarlySurviveNocompDecanDeath	0
eEarlySurviveNocompDecanLive	23.33
eEarlySurviveNocompNodecanDeath	23.30
eEarlySurviveNocompNodecanLive	23.23
eLateNosurvive	12.20
eLateSurviveCompDecanDeath	0
eLateSurviveCompDecanLive	38.46
eLateSurviveCompNodecanDeath	42.08
eLateSurviveCompNodecanLive	32.83
eLateSurviveNocompDecanDeath	43
eLateSurviveNocompDecanLive	38.41
eLateSurviveNocompNodecanDeath	34.75
eLateSurviveNocompNodecanLive	29.64

APPENDIX B. Variable values for PSA with outcome of total hospital length of stay

Name	Root Definition
cEarlyNosurvive	44,235.01
cEarlySurviveCompDecanDeath	128,999.90
cEarlySurviveCompDecanLive	128,999.90
cEarlySurviveCompNodecanDeath	71,984.93
cEarlySurviveCompNodecanLive	66,896.56
cEarlySurviveNocompDecanDeath	59,604.39
cEarlySurviveNocompDecanLive	59,604.39
cEarlySurviveNocompNodecanDeath	67,579.37
cEarlySurviveNocompNodecanLive	59,709.12
cLateNosurvive	44,235.01
cLateSurviveCompDecanDeath	128,999.90
cLateSurviveCompDecanLive	128,999.90
cLateSurviveCompNodecanDeath	114,616.60
cLateSurviveCompNodecanLive	97,910.96
cLateSurviveNocompDecanDeath	91,305.28
cLateSurviveNocompDecanLive	90,299.62
cLateSurviveNocompNodecanDeath	105,054.60
cLateSurviveNocompNodecanLive	82,785.89
eEarlyNosurvive	12.20
eEarlySurviveCompDecanDeath	38.46
eEarlySurviveCompDecanLive	38.46
eEarlySurviveCompNodecanDeath	21.91
eEarlySurviveCompNodecanLive	21.64
eEarlySurviveNocompDecanDeath	23.33
eEarlySurviveNocompDecanLive	23.33
eEarlySurviveNocompNodecanDeath	23.30
eEarlySurviveNocompNodecanLive	23.23
eLateNosurvive	12.20
eLateSurviveCompDecanDeath	38.46
eLateSurviveCompDecanLive	38.46
eLateSurviveCompNodecanDeath	42.08
eLateSurviveCompNodecanLive	32.83
eLateSurviveNocompDecanDeath	43.00
eLateSurviveNocompDecanLive	38.41
eLateSurviveNocompNodecanDeath	34.75
eLateSurviveNocompNodecanLive	29.64

APPENDIX C. Variable values for cost effectiveness analysis with outcome of post procedural length of stay

Name	Root Definition
cEarlySurviveCompDecanDeath	0
cEarlySurviveCompDecanLive	0
cEarlySurviveCompNodecanDeath	57,102.66
cEarlySurviveCompNodecanLive	58,334.76
cEarlySurviveNocompDecanDeath	0
cEarlySurviveNocompDecanLive	50,796.8
cEarlySurviveNocompNodecanDeath	56,880.93
cEarlySurviveNocompNodecanLive	50,320.07
cLateSurviveCompDecanDeath	0
cLateSurviveCompDecanLive	70,357.85
cLateSurviveCompNodecanDeath	63,794.57
cLateSurviveCompNodecanLive	63,886.94
cLateSurviveNocompDecanDeath	61,577.98
cLateSurviveNocompDecanLive	85,435.52
cLateSurviveNocompNodecanDeath	62,135.93
cLateSurviveNocompNodecanLive	46,248.49
eEarlySurviveCompDecanDeath	0
eEarlySurviveCompDecanLive	0
eEarlySurviveCompNodecanDeath	18.05
eEarlySurviveCompNodecanLive	18.61
eEarlySurviveNocompDecanDeath	0
eEarlySurviveNocompDecanLive	19.67
eEarlySurviveNocompNodecanDeath	19.99
eEarlySurviveNocompNodecanLive	19.94
eLateNosurvive	0
eLateSurviveCompDecanDeath	0
eLateSurviveCompDecanLive	21.69
eLateSurviveCompNodecanDeath	26.64
eLateSurviveCompNodecanLive	21.08
eLateSurviveNocompDecanDeath	29
eLateSurviveNocompDecanLive	41.30
eLateSurviveNocompNodecanDeath	21.15
eLateSurviveNocompNodecanLive	17.05

APPENDIX D. Variable values for PSA with outcome of post-procedural length of stay

Name	Root Definition
cEarlySurviveCompDecanDeath	70,357.85
cEarlySurviveCompDecanLive	70,357.85
cEarlySurviveCompNodecanDeath	57,102.66
cEarlySurviveCompNodecanLive	58,334.76
cEarlySurviveNocompDecanDeath	50,796.80
cEarlySurviveNocompDecanLive	50,796.80
cEarlySurviveNocompNodecanDeath	56,880.93
cEarlySurviveNocompNodecanLive	50,320.07
cLateSurviveCompDecanDeath	70,357.85
cLateSurviveCompDecanLive	70,357.85
cLateSurviveCompNodecanDeath	63,794.57
cLateSurviveCompNodecanLive	63,886.94
cLateSurviveNocompDecanDeath	61,577.98
cLateSurviveNocompDecanLive	85,435.52
cLateSurviveNocompNodecanDeath	62,135.93
cLateSurviveNocompNodecanLive	46,248.49
eEarlySurviveCompDecanDeath	21.69
eEarlySurviveCompDecanLive	21.69
eEarlySurviveCompNodecanDeath	18.05
eEarlySurviveCompNodecanLive	18.61
eEarlySurviveNocompDecanDeath	19.67
eEarlySurviveNocompDecanLive	19.67
eEarlySurviveNocompNodecanDeath	19.99
eEarlySurviveNocompNodecanLive	19.94
eLateSurviveCompDecanDeath	21.69
eLateSurviveCompDecanLive	21.69
eLateSurviveCompNodecanDeath	26.64
eLateSurviveCompNodecanLive	21.08
eLateSurviveNocompDecanDeath	29
eLateSurviveNocompDecanLive	41.30
eLateSurviveNocompNodecanDeath	21.15
eLateSurviveNocompNodecanLive	17.05

REFERENCES

1. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the united states: A policy statement from the american heart association. *Circ Heart Fail*. 2013;6(3):606-619.

2. Echouffo-Tcheugui JB, Bishu KG, Fonarow GC, Egede LE. Trends in health care expenditure among US adults with heart failure: The medical expenditure panel survey 2002-2011. *Am Heart J*. 2017;186:63-72.

3. Writing Group Members, Mozaffarian D, Benjamin EJ, et al. Heart disease and stroke statistics-2016 update: A report from the american heart association. *Circulation*. 2016;133(4):e38-360.

4. Celli BR. Mechanical ventilatory support. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's principles of internal medicine, 19e.* New York, NY: McGraw-Hill Education; 2015. accessmedicine.mhmedical.com/content.aspx?aid=1120808698. Accessed 2017/11/08.

5. Gaillard JP. Complications of airway devices. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, eds. *Tintinalli's emergency medicine: A comprehensive study guide, 8e.* New York, NY: McGraw-Hill Education; 2016. accessmedicine.mhmedical.com/content.aspx?aid=1121515597. Accessed 2017/11/09.

6. Andriolo BN, Andriolo RB, Saconato H, Atallah AN, Valente O. Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev*. 2015;1:CD007271.

7. Heffner JE. Tracheotomy application and timing. *Clin Chest Med*. 2003;24(3):389-398.

8. Liu CC, Rudmik L. A cost-effectiveness analysis of early vs late tracheostomy. *JAMA Otolaryngol Head Neck Surg*. 2016;142(10):981-987.

9. Healthcare Cost and Utilization Project (HCUP). Overview of the nationa (nationwide) inpatient sample (NIS). https://www.hcup-us.ahrq.gov/nisoverview.jsp. Updated 2018. Accessed 2/21, 2018.

10. Patel N, Kalra R, Doshi R, et al. Hospitalization rates, prevalence of cardiovascular manifestations, and outcomes associated with sarcoidosis in the united states. *J Am Heart Assoc*. 2018;7(2):10.1161/JAHA.117.007844.

11. Schulman AR, Abougergi MS, Thompson CC. Assessment of the july effect in post-endoscopic retrograde cholangiopancreatography pancreatitis: Nationwide inpatient sample. *World journal of gastrointestinal endoscopy*. 2017;9(7):296.

12. Method series report 2015-09. healthcare cost and utilization project (HCUP). https://www.hcup-us.ahrq.gov/reports/methods/2015_09.jsp. Updated 2016.

13. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. . 2005.

14. Halum SL, Ting JY, Plowman EK, et al. A multi-institutional analysis of tracheotomy complications. *Laryngoscope*. 2012;122(1):38-45.

15. Young D, Harrison DA, Cuthbertson BH, Rowan K, TracMan Collaborators. Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: The TracMan randomized trial. *JAMA*. 2013;309(20):2121-2129.

16. Koch T, Hecker B, Hecker A, et al. Early tracheostomy decreases ventilation time but has no impact on mortality of intensive care patients: A randomized study. *Langenbecks Arch Surg*. 2012;397(6):1001-1008.

17. Arabi Y, Haddad S, Shirawi N, Al Shimemeri A. Early tracheostomy in intensive care trauma patients improves resource utilization: A cohort study and literature review. *Crit Care*. 2004;8(5):R347-52.

18. Clec'h C, Alberti C, Vincent F, et al. Tracheostomy does not improve the outcome of patients requiring prolonged mechanical ventilation: A propensity analysis. *Crit Care Med*. 2007;35(1):132-138.