Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

J Cardiothorac Vasc Anesth. Author manuscript; available in PMC 2019 June 01.

Published in final edited form as:

J Cardiothorac Vasc Anesth. 2018 June ; 32(3): 1256–1263. doi:10.1053/j.jvca.2017.12.038.

Impact of Intubation Time on Survival following Coronary Artery Bypass Grafting: Insights from the Surgical Treatment for Ischemic Heart Failure (STICH) trial

Nadia Bouabdallaoui, MD[1], **Susanna R. Stevens**[2], **Torsten Doenst, MD**[3], **Krzysztof Wrobel, MD**[4], **Denis Bouchard, MD, PhD**[1], **Marek A. Deja, MD**[5], **Robert E. Michler, MD**[6], **Yeow Leng Chua, MD**[7], **Renato A. K. Kalil, MD, PhD**[8], **Craig H. Selzman, MD**[9], **Richard C. Daly, MD**[10], **Benjamin Sun, MD**[11], **Ljubomir T. Djokovic, MD**[12], **George Sopko, MD**[13], **Eric J. Velazquez, MD**[2], **Jean L. Rouleau, MD**[1], **Kerry L. Lee, Ph.D.**[2], **Hussein R. Al-Khalidi, Ph.D.**[2], and **STICH Trial Investigators**

[1]Departments of Medicine (NB, JLR) and Surgery (DB), Montreal Heart Institute, University of Montreal, Montreal, Canada [2]Duke Clinical Research Institute (SS), Departments of Biostatistics and Bioinformatics (KLL, HRA) and Medicine (EJV), Duke University School of Medicine, Durham, North Carolina [3]Department of Cardiothoracic Surgery, Jena University Hospital, Friedrich-Schiller-University Jena, Jena, Germany [4]Department of Cardiac Surgery, Medicover Hospital, Warsaw, Poland [5]Department of Cardiac Surgery, Medical University of Silesia, Katowice, Poland [6]Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center, Albert Einstein College of Medicine, New York, New York [7]National Heart Centre, Singapore [8]Postgraduate Program, Instituto de Cardiologia/FUC and UFCSPA, Porto Alegre, Brazil [9]Department of Surgery, University of Utah, Salt Lake City, Utah [10]Department of Cardiovascular Surgery, Mayo Clinic, Rochester, Minnesota [11]The Minneapolis Heart Institute, Minneapolis, Minnesota [12]Dedinje Cardiovascular Institute, Belgrade, Serbia [13]Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

Abstract

Objective—We aimed to assess determinants of intubation time and evaluate its impact on 30-day and 1-year postoperative survival in STICH patients.

Design, Setting, Participants and Interventions—A multivariable Cox proportional hazards model was used among the 1446 surgical patients from the STICH trial that survived 36 hours after operation, in order to identify peri-operative factors associated with 30-day and 1-year

Corresponding Author: Nadia Bouabdallaoui, MD, Montreal Heart Institute, 5000 Belanger Street, Montréal, Québec (H1T 1C8), Canada, Phone : +1 (514) 376-3330, Fax: +1 (514) 593-2575, nadia.bouabdallaoui@gmail.com.

Conflict of interest statement

Dr. Velazquez disclosed relationships with NHLBI, Alnylam Pharmaceuticals, Amgen, Expert Exchange, Merck, Novartis, and Pfizer. There are no other conflicts to disclose.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

postoperative mortality. A multivariable logistic regression model was used to determine risk factors associated with intubation time.

Measurements and Main Results—At 36 hours post operation, 1298 (out of 1446) were extubated and 148 (10.2%) still intubated. Median postoperative intubation time was 11.4 hours. Among patients surviving 36 hours, a multivariable model was developed to predict 30-day (c-index=0.88) and 1-year (c-index=0.78) mortality. Intubation time was the strongest independent predictor of 30-day (HR 5.50) and 1-year mortality (HR 3.69). Predictors of intubation time > 36 hours included mitral valve procedure, NYHA class, left ventricular systolic volume index, creatinine, previous CABG, and age. Results were similar in patients surviving 24 hours post-operation, where intubation time was also the strongest predictor of 30 day (HR 4.18, C-index 0.87) and 1 year (HR 2.81, C-index 0.78) mortality.

Conclusions—Intubation time is the strongest predictor of 30-day and 1-year mortality among patients with ischemic heart failure undergoing CABG. Combining intubation time with other mortality risk factors may allow the identification of patients at the highest risk for whom the development of specific strategies may improve outcomes.

Keywords

Coronary artery bypass grafting; intubation; coronary artery disease; heart failure

Introduction

The Surgical Treatment for Ischemic Heart Failure (STICH) trial demonstrates that in patients with left ventricular ejection fraction (LVEF) ≤ 35% and coronary artery disease (CAD) amenable to coronary artery bypass grafting (CABG), CABG prolongs survival, and that adding surgical ventricular restoration (SVR) to CABG in patients with predominant anterior akinesis did not improve outcomes (1–4).

The overwhelming majority of STICH patients survived to 24–36 hours after operation, a time when the outcome of patients becomes better defined and adjustments to the course of the patient are ongoing (5, 6). Intubation time, which likely reflects the convergence of multiple pre-, intra- and postoperative parameters, has proven to be strongly associated with a poor prognosis in patients undergoing cardiac surgery. Combining intubation time with other independent risk factors for a poor outcome in early post-operation survivors could identify patients at highest risk and lead to proactive therapeutic interventions that could improve outcome.

The aims of the present analysis were to: (1) assess the determinants of 30-day and 1-year postoperative mortality when including intubation time; and (2) evaluate the pre- and intra-operative determinants of death or still intubated by 24 and 36 hours after operation.

Materials and methods

Patient Population

The overall objective of the Surgical Treatment for Ischemic Heart Failure trial (STICH trial) was to assess the role of surgical revascularization in patients with severe left

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

ventricular (LV) dysfunction, ischemic heart failure (HF), and coronary artery disease (CAD) amenable to coronary artery bypass grafting (CABG) (1–4). Between July 2002, and May 2007, 2136 eligible patients were enrolled in the STICH trial. Of these, 1534 patients were randomly assigned to surgery along with medical therapy; 1460 did receive surgery and were allocated as follows: CABG (n=965), CABG + SVR, (n=495). Among the 1460 surgical patients, 5 (0.3%) died in the operating room (OR), and 9 (0.6%) in the intensive care unit (ICU) within the first 36 postoperative hours (Figure 1). Only 1 patient died in the ICU between 24 and 36 hours. Risk-factors associated with 30-day and 1-year postoperative mortality were assessed in the 1446 STICH patients who received surgery and were still alive at 24 and 36-hours following discharge from the OR (Figure 1).

Data collection

In the STICH trial pre-, intra- and post-operative data were prospectively acquired using structured data forms with standardized definitions of common operative and postoperative conduct. Follow-up was performed at the time of hospital discharge or at 30 days following surgery if the patient remained hospitalized for ≥ 30 days, and at 4-month intervals for the first year of follow-up, and thereafter at 6-month intervals over the entire follow-up period (1–4).

Intubation Time

Intubation time was defined in patients discharged from the OR as the time from ICU arrival to the time of extubation. Prolonged intubation time was considered when intubation time was > 24 or 36 hours. Decisions for both extubation and reintubation were made by the surgical/medical staff at each site on an individual case-by-case basis. Cause of death was determined by an independent clinical endpoint committee (7). Deaths that occurred prior to 30 days after operation were generally deemed to be the result of the surgery.

Ethical considerations

As detailed elsewhere, the Duke University Medical Center Institutional Review Board and the institutional review board or ethics committee for each participating center approved the study protocol (4). All patients provided written informed consent.

Statistical analyses

A post-hoc analysis of the STICH database was performed for the present sub analysis. Among the 1460 patients receiving surgery, logistic regression with backward elimination was used to determine patient characteristics associated with death or still intubated at 24 and 36 hours after operation, the variable “intubation time” being analyzed either as categorical according to different time windows (intubation time > 24 hours; intubation time > 36 hours), or as continuous. A multivariable Cox proportional hazards model with backward elimination was used to determine factors associated with 30-day and one-year mortality in 24 and 36 hours survivors. These models were adjusted for baseline clinical variables (Age, hypertension, diabetes, hyperlipidemia, NYHA class, CCS angina class, blood pressure, Duke CAD index, MR, MV procedure, non-elective procedures, OR time, history of AF/ flutter, history of stroke, number of medications at initial evaluation), as well

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

as LVESVI, hemoglobin, and creatinine (Tables 2, 3, S-1 and S-2). Model discrimination was evaluated with Harrell's c-index and its 95% confidence interval. Patient characteristics were summarized as number (percentage) for categorical variables and as median (25th, 75th percentile) for continuous variables. Nominal variables were compared with chi-square or Fisher's exact tests as appropriate and continuous or ordinal variables were compared with Wilcoxon rank-sum tests. P values of < 0.05 were considered statistically significant. All analyses were performed with SAS version 9.2 (SAS Institute, Inc, Cary, NC).

Results

Pre- and Intraoperative Characteristics of patients surviving 36 hours postoperation (Table 1, Figure 1)

Patients alive and still intubated at 36 hours were significantly older (63.6 *vs.* 60.8 years; p=0.0019), had more severe peripheral vascular disease (p=0.0026), and higher creatinine levels (p=0.0035). They had a more severe presentation (mitral regurgitation (p=0.0008), prior CABG (p=0.0007), higher NYHA class (p<0.0001)), significantly lower LVEF (25.8% *vs.* 28.0%; p=0.0020) and a significantly higher LV end-systolic volume Index (LVESVI) (87.3 *vs.* 77.3 ml/m^2; p=0.0003). They also had significantly more surgical procedures including SVR (p=0.0105) and mitral valve procedures (p<0.0001), significantly prolonged cardiopulmonary bypass (CBP) time (p<0.0001) and operating room (OR) time (p<0.0001).

Outcomes according to intubation time

Postoperative mortality significantly increased with the duration of mechanical ventilation with a slight leveling off at 36 hours (Figures 2 and 3).

In patients extubated within 36 hours

Among the 1460 surgical patients, 1446 were discharged alive from the OR and survived the first 36 hours following surgery, while 14 (1.0%) died prior to 36 hours. Of the 1446 patients that survived 36 hours after operation, 1386 were still alive at 30-days (36-hours to 30-day mortality of 4.15%), and 1265 were still alive at 1-year following surgery (30-day to 1-year mortality of 8.7 %). Of these 1446, 1298 (89.8%) patients were successfully extubated within the first 36 postoperative hours, while 148 (10.2%) were still intubated. Median postoperative intubation time was 11.4 hours (6.8–18.3 hours). Of the 1298 extubated patients, 34 (2.6%) died prior to 30 days and by one year, another 89 (6.4% of 30-day survivors) had died and 1173 (90.4 %) were still alive. Two patients were lost to follow-up.

In patients extubated after 36 hours

Of the 148 patients alive and still intubated at 36 hours, 121 (81.8%) were alive and extubated at 30 days, 10 (6.8%) were alive but still intubated at 30 days, and 17 (11.5%) had died by 30 days. Between 30-days and one year, another 39 of these patients died (30% of 30-day survivors) such that 62.2% survived 1-year post-operation.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

In patients reintubated

Of patients still alive, and extubated at 36 hours, re-intubation occurred in 33 (2.5%) patients, of which 9 (27.3%) had died by 30 days, and 17 (51.5%) had died by 1 year. Of the 14 patients extubated then re-intubated, 6 had died by 30 days, and another 2 by 1 year. Of the patients still intubated 30 days after operation, 5 of the10 patients had died by 1 year.

Determinants of 30-day Mortality (Table 2)

A multivariable Cox proportional hazards model for 30-day mortality (N=1446, c-index=0.88 [95% CI 0.84, 0.92]) showed that intubation time >36 hours was the strongest predictor of 30-day postoperative mortality (HR 5.50; 95% CI 3.09–9.77, p<0.0001). The strength of this model for 30-day mortality supports an independent role for being still intubated at 36 hours. Other strong predictors of 30-day mortality included LVESVI, prolonged OR time, preoperative creatinine levels, mitral regurgitation, mitral valve operative procedure (protective), CCS angina class, and age. LVEF was not independently associated with 30-day mortality.

Determinants of 1-year Mortality (Table 3)

A multivariable Cox proportional hazards model (c-index=0.78 [95% CI 0.75, 0.81]) showed that intubation time >36 hours was again the strongest predictor of 1-year postoperative mortality in patients surviving 36 hours after operation (HR 3.69; 95% CI: 2.60–5.26, p<0.0001). Again, the strength of this model for 1-year mortality supports an independent role for being still intubated at 36 hours. Other predictors of 1-year mortality included LVESVI, creatinine, age, preoperative atrial fibrillation or flutter, history of stroke, mitral valve surgery (protective), mitral regurgitation, OR time, and diabetes.

Determinants of death or still Intubated at 36 hours (Table 4)

The number of patients alive and still intubated decreased markedly by 24 hours after operation (Figure 1). Mortality increased progressively with intubation time (Figures 2 and 3). A multivariable logistic regression model (N=1460, c-index=0.75 [95% CI 0.71, 0.79]) showed that the strongest determinants of death or still intubated at 36 hours included mitral valve surgery, NYHA class, LVESVI, creatinine, previous CABG, lower diastolic blood pressure and age.

Causes of death at 1-year

At 1-year, among patients with intubation time > 36 hours, 101 had died from a cardiovascular cause (33 as a result of the surgery, 33 of sudden death, 21 of pump failure, 5 of stroke and 9 of other cardiovascular causes); 16 from a non-cardiovascular cause; and 6 from unknown causes. Among patients alive and still intubated at 36 hours after operation, at 1 year, 48 had died of cardiovascular causes (29 as a result of the surgery, 8 of sudden death, 8 of pump failure, 1 of a myocardial infarction, and 2 of a stroke); 7 of non-cardiovascular causes; and 1 of unknown cause.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

24 hours survivors

Among patients surviving 24 hours, results were similar. A multivariable model was developed to predict 30-day (c-index=0.87 [95% CI 0.84, 0.91]) and 1-year (c-index=0.78 [95% CI 0.74, 0.81]) mortality (Supplement Tables S-1 and S-2). Intubation time was also the strongest independent risk factor predicting both 30-day (HR= 4.18 [95% CI 2.39, 7.28] and 1-year (HR=2.81 [95% CI 2.01–3.93], both p<0.0001) mortality. The strongest predictors of mortality or still intubated at 24 hours were mitral valve procedure, LVESVI, creatinine, previous CABG, SVR, and NYHA class (Supplement Table S-3).

Discussion

These analyses suggest that in patients with a LVEF ≤ 35% undergoing CABG, intubation time > 24 or 36 hours is the strongest predictor of 30-day and 1-year postoperative mortality in patients surviving the first 24 or 36 hours post operation. Other important determinants of both 30-day and 1-year mortality include LVESVI, creatinine, age, OR time, mitral regurgitation, and mitral valve surgery (protective). Preoperative and intraoperative determinants of death or still intubated at 36 hours after operation included many of the same variables, including LVESVI, creatinine, and age, but also variables such as mitral valve procedure, SVR and previous CABG. The characterization of risk factors for intubation time > 24 or 36 hours allows for the identification of patients at highest risk, in whom the development of preventative and/or therapeutic strategies may help guide surgical decisions and enhance postoperative management. In the postoperative setting, in patients with intubation times > 24 or 36 hours, results of the present analyses also identifies other independent risk factors for survival and thus patients in which more aggressive post-operative management may be warranted.

Determinants of 30-day Mortality

Early extubation after cardiac surgery has become the rule (8–10), so when intubation time is prolonged, it heralds a complicated postoperative course, and has a significant impact on postoperative mortality, morbidity, and cost-effectiveness (10–12). In STICH, most patients were extubated by 36 hours (89.8%), and the risk associated with intubation time increased progressively, the increase being greatest after 12 hours of intubation. In this analysis, we report a 10% incidence of intubation time >36 hours in a relatively high-risk population, results which compare favourably with other reports (8–12) that reflects proper postoperative care provided to STICH patients.

In addition to being still intubated at 24 or 36 hours, we demonstrate that prolonged operating room (OR) time was also a powerful predictor of poor outcome. In a previous publication, Wrobel *et al.* displayed consistent results, as prolonged cardiopulmonary bypass time was associated with 30-day mortality (13). Both prolonged OR time and intubation time are considered the result of the integration of multiple variables, including patient's preoperative condition, the complexity of surgical procedure, and intraoperative complications. Other determinants of 30-day mortality were also similar to those reported by Wrobel *et al*, including LVESVI, creatinine, mitral regurgitation, mitral valve surgery (protective) and age being risk factors (13).

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Determinants of 1-year Mortality

Intubation time > 36 hours was also the most powerful predictor of 1-year mortality among survivors to 24 and 36 hours. Previous studies evaluating the impact of intubation time included patients with a wide range of LV function (8–12). These studies did not assess the independent predictive value of intubation time as reported in the present analysis. Thus, this is the first study reporting the prognostic significance of intubation time in addition to other known risk factors after CABG on survival in patients with poor LV function. Other less important predictors of 1-year postoperative mortality included many of the same as those at 30 days, such as LVESVI, creatinine, age, mitral valve procedure, atrial fibrillation, mitral regurgitation and OR time.

Determinants of Mortality or still Intubated hours Post-Operation

Risk factors for intubation time > 36 hours reported in STICH patients, such as creatinine, LV function, NYHA class and age have also been reported by others (14–22). However, this is the first study to report that LVESVI is more important than LVEF as a risk factor for intubation time > 36 hours and that mitral valve surgery increases the risk of prolonged intubation time, but provides favourable long-term outcome, suggesting that although mitral valve surgery prolongs operative time and delays extubation, it improves hemodynamics and long-term outcomes, and thus is overall beneficial for the patient.

It would appear that being still intubated at 24 hours is more sensitive to factors such as SVR than being still intubated at 36 hours, but as expected previous CABG was associated with both intubation time > 24 and 36 hours.

Re-intubation and Mortality

Re-intubation also carried a poor prognosis, whether occurring in patients extubated at 36 hours (9 of 33 [27.3%] patients died within 30 days) or patients still intubated at 36 hours (6 of 14 [42.9%] patients died within 30 days). One-year mortality of patients extubated by 30 days and re-intubated was also very elevated with 25 of 47 patients (53%) dying. As with intubation, reintubation likely reflects a complex postoperative course (23).

Causes of Death at 1 year

Mortality associated with the operative procedure (generally defined as within 30 days of surgery) was more frequent in patients still intubated at 36 hours (19.6%) than in extubated patients (2.5%). Later mortality from pump failure (5.4% vs 1.6%) and from sudden death (5.4% vs 2.5%) were also more common in patients still intubated at 36 hours as compared with extubated patients. Noticeably, literature data are scarce in this setting, and, as far as we know, this is the first time that intubation time, as a multifactorial parameter, is linked to 1-year mortality in this specific population.

Clinical Implications

Understanding which factors lead to early operative mortality or prolonged intubation time in this high risk population may have important clinical implications as it may allow for the implementation of targeted preventative and adaptive strategies such as “prophylactic”

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

respiratory or circulatory support, off-pump revascularization or reducing the number of procedures in order to limit OR time. In patients still intubated 24–36 hours post operation, the presence of risk factors for mortality independent of intubation time may help identify patients in which an early aggressive post-operative approach to cardiorespiratory support could improve outcome. The additional information provided in these analyses may also help interactions with families when discussing postoperative prognosis.

Limitations

This is a post-hoc analysis of a randomized trial that was not designed for the specific purpose of the present sub-analysis. In this analysis, patients differed significantly from that of those included in previous trials, limiting the ability of extrapolating the results of this cohort to the general population of post-operative patients. However, we demonstrate a low (10%) and consistent incidence of intubation time > 36 hours in a relatively high-risk population, which is reassuring regarding the accuracy of our results regarding this specific high-risk population. The cause of death for patients dying within 30 days of operation was generally defined by the STICH clinical endpoints committee as being the result of the operative procedure, thus the exact mode of death during that early postoperative period is not available. The indication of both extubation and reintubation was not standardized. Finally, a number of variables known to be important predictors of intubation time or post-operative acute respiratory syndromes, such as baseline respiratory status and known chronic obstructive pulmonary disease, as well as clinical severity scores were not documented in STICH.

Conclusion

Prolonged intubation time either defined as either > 24 or > 36 hours after CABG in patients with ischemic HF is a strong independent risk factor for 30-day and one-year mortality among patients surviving 24 and 36 hours after operation. Identification of risk factors for intubation time may have important clinical implications as it allows for the identification of patients and targets for the development of pre-operative, intra-operative and post-operative preventative and adaptive strategies to enhance the care of STICH-like patients, and more precise information regarding outcomes for interactions with patient families.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

We thank Seanna Horan and Vanessa Moore for their valuable input, preparation and editing of this manuscript.

Funding statement

This work was supported by grants U01HL69015, U01HL69013, and RO1HL105853 from the National Institutes of Health/National Heart, Lung, and Blood Institute. This work is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or National Heart, Lung, and Blood Institute.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

References

1. Velazquez EJ, Lee KL, Jones RH, et al. STICHES Investigators. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. N Engl J Med. 2016;374(16):1511–20. [PubMed: 27040723]
2. Velazquez EJ, Lee KL, Deja MA, et al. STICH Investigators. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med. 2011;364(17):1607–16. [PubMed: 21463150]
3. Jones RH, Velazquez EJ, Michler RE, et al. STICH Hypothesis 2 Investigators. Coronary bypass surgery with or without surgical ventricular reconstruction. N Engl J Med. 2009;360(17):1705–17. [PubMed: 19329820]
4. Velazquez EJ, Lee KL, O'Connor CM, et al. STICH Investigators. The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg. 2007;134(6):1540–7. [PubMed: 18023680]
5. Stephens RS, Whitman GJ.Postoperative Critical Care of the Adult Cardiac Surgical Patient. Part I: Routine Postoperative Care.Crit Care Med 2015;43(7):1477–97. [PubMed: 25962078]
6. Zhu F, Lee A, Chee YE.Fast-track cardiac care for adult cardiac surgical patients. Cochrane Database Syst Rev. 2012;10:CD003587. [PubMed: 23076899]
7. Carson P, Wertheimer J, Miller A, et al. The STICH trial (Surgical Treatment for Ischemic Heart Failure): mode-of-death results. JACC Heart Fail 2013;1:400–408. [PubMed: 24621972]
8. Cheng DC, Karski J, Peniston C, et al. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomized controlled trial. J Thorac Cardiovasc Surg 1996;112:755–764. [PubMed: 8800165]
9. Silbert BS, Santamaria JD, O'Brien JL, et al. Early extubation following coronary artery bypass surgery: a prospective randomized controlled trial. The Fast Track Cardiac Care Team. Chest 1998;113:1481–1488. [PubMed: 9631781]
10. Wong WT, Lai VK, Chee YE, et al. Fast-track cardiac care for adult cardiac surgical patients. Cochrane Database Syst Rev. 2016;9:CD003587. [PubMed: 27616189]
11. Reis J, Mota JC, Ponce P, et al. Early extubation does not increase complication rates after coronary artery bypass graft surgery with cardiopulmonary bypass. Eur J Cardiothorac Surg 2002;21:1026–1030. [PubMed: 12048081]
12. Pappalardo F, Franco A, Landoni G, et al. Long-term outcome and quality of life of patients requiring prolonged mechanical ventilation after cardiac surgery. Eur J Cardiothorac Surg 2004;25:548–552. [PubMed: 15037270]
13. Wrobel K, Stevens SR, Jones RH, et al. Influence of Baseline Characteristics, Operative Conduct, and Postoperative Course on 30-Day Outcomes of Coronary Artery Bypass Grafting Among Patients With Left Ventricular Dysfunction: Results From the Surgical Treatment for Ischemic Heart Failure (STICH) Trial. Circulation 2015;132:720–730. [PubMed: 26304663]
14. Wise ES, Stonko DP, Glaser ZA, Garcia KL, Huang JJ, Kim JS, Kallos JA, Starnes JR, Fleming JW, Hocking KM, Brophy CM, Eagle SS. Prediction of Prolonged Ventilation after Coronary Artery Bypass Grafting: Data from an Artificial Neural Network. Heart Surg Forum. 2017;20(1):E007–E014. [PubMed: 28263144]
15. Combes A, Costa MA, Trouillet JL, et al. Morbidity, mortality, and quality-of-life outcomes of patients requiring >or=14 days of mechanical ventilation. Crit Care Med 2003;31:1373–1381. [PubMed: 12771605]
16. Walthall H, Ray S. Do intraoperative variables have an effect on the timing of tracheal extubation after coronary artery bypass graft surgery? Heart Lung 2002;31:432–439. [PubMed: 12434144]
17. Kogan A, Ghosh P, Preisman S, et al. Risk factors for failed "fast-tracking" after cardiac surgery in patients older than 70 years. J Cardiothorac Vasc Anesth 2008; 22:530–535. [PubMed: 18662626]
18. Dunning J, Au J, Kalkat M, et al. A validated rule for predicting patients who require prolonged ventilation post cardiac surgery. Eur J Cardiothorac Surg 2003;24:270–276. [PubMed: 12895619]
19. Yende S, Wunderink R. Causes of prolonged mechanical ventilation after coronary artery bypass surgery. Chest 2002;122:245–252. [PubMed: 12114366]

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

20. Suematsu Y, Sato H, Ohtsuka T, et al. Predictive risk factors for delayed extubation in patients undergoing coronary artery bypass grafting. Heart Vessels 2000; 15:214–220. [PubMed: 11560357]
21. Rajakaruna C, Rogers CA, Angelini GD, et al. Risk factors for and economic implications of prolonged ventilation after cardiac surgery. J Thorac Cardiovasc Surg 2005;130(5):1270–1277. [PubMed: 16256778]
22. Gumus F, Polat A, Yektas A, et al. Prolonged mechanical ventilation after CABG: risk factor analysis. J Cardiothorac Vasc Anesth. 2015;29(1):52–8 [PubMed: 25620139]
23. Beverly A, Brovman EY, Malapero RJ, et al. Unplanned Reintubation Following Cardiac Surgery: Incidence, Timing, Risk Factors, and Outcomes. J Cardiothorac Vasc Anesth. 2016;30(6):1523–1529. [PubMed: 27595531]

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

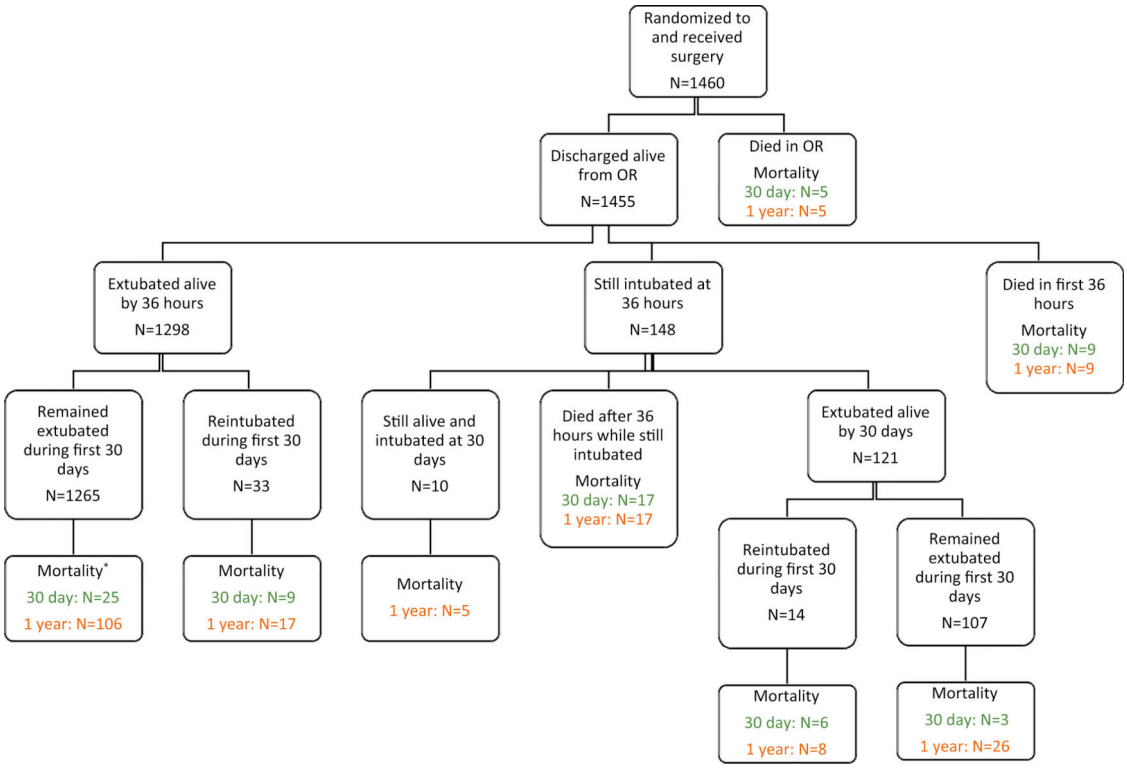

Figure 1:
Consort diagram indicating patient outcomes over first postoperative year.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

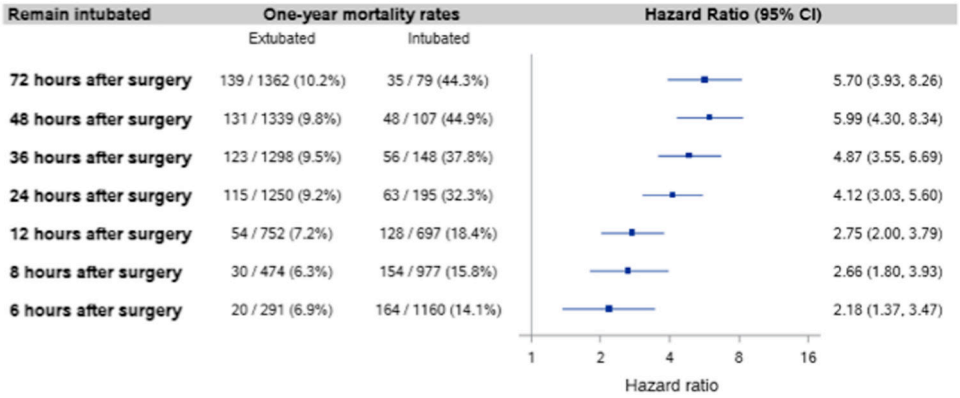

Figure 2:

Impact of several intubation time cut-off on 1-year mortality in STICH surgical patients.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

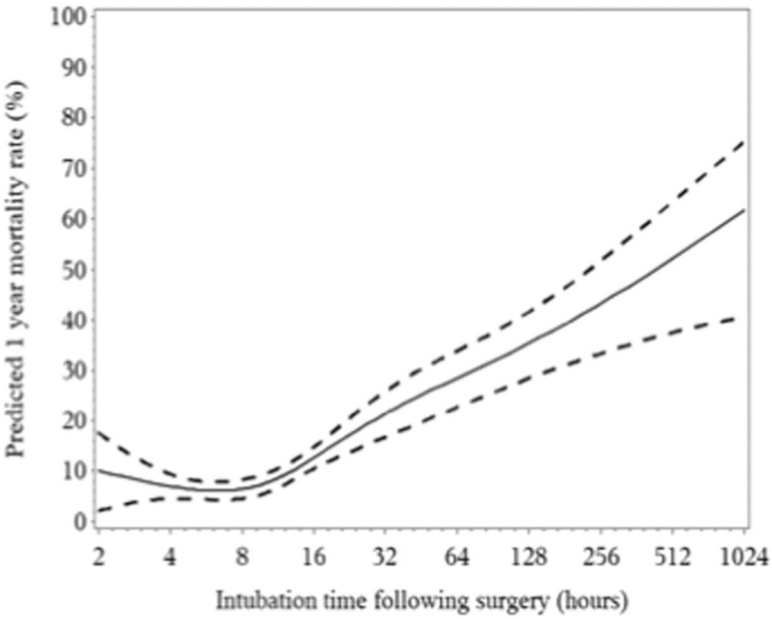

Figure 3:

Continuous relationship between intubation time and 1-year mortality in STICH surgical patients.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1.

Baseline characteristics based on intubation status at 36 hours post-operation

Variable	Overall (N=1446)	Still intubated at 36h (N=148)	Alive and extubated at 36h (N=1298)	p*
Age	61.1 (54.0 – 68.2)	63.6 (57.0 – 71.8)	60.8 (53.7 – 68.0)	0.0019
Female	198 (13.7)	24 (16.2)	174 (13.4)	0.3459
Diabetes	527 (36.4)	64 (43.2)	463 (35.7)	0.0697
Peripheral vascular disease	212 (14.7)	34 (23.0)	178 (13.7)	0.0026
Chronic renal insufficiency	117 (8.1)	28 (18.9)	89 (6.9)	<0.0001
Stroke	95 (6.6)	12 (8.1)	83 (6.4)	0.4253
Previous CABG	37 (2.6)	11 (7.4)	26 (2.0)	0.0007
Current CCS angina class				0.2759
None	420 (29.0)	56 (37.8)	364 (28.0)	
I	143 (9.9)	12 (8.1)	131 (10.1)	
II	383 (26.5)	27 (18.2)	356 (27.4)	
III	416 (28.8)	42 (28.4)	374 (28.8)	
IV	84 (5.8)	11 (7.4)	73 (5.6)	
NYHA class				<0.0001
I	66 (4.6)	2 (1.4)	64 (4.9)	
II	463 (32.0)	29 (19.6)	434 (33.4)	
III	667 (46.1)	71 (48.0)	596 (45.9)	
IV	250 (17.3)	46 (31.1)	204 (15.7)	
Mitral regurgitation				0.0008
None or trace	524 (36.2)	43 (29.1)	481 (37.1)	
Mild (≤2+)	681 (47.1)	63 (42.6)	618 (47.6)	
Moderate (3+)	195 (13.5)	30 (20.3)	165 (12.7)	
Severe (4+)	46 (3.2)	12 (8.1)	34 (2.6)	
Duke CAD Index (0–100)	65 (39 – 77)	65 (52 – 91)	65 (39 – 77)	0.0194
Creatinine (mg/dL)	1.09 (0.93 – 1.26)	1.15 (0.95 – 1.40)	1.09 (0.92 – 1.24)	0.0035
LVESVI	78.0 (59.9 – 99.0)	87.3 (68.8 – 108.4)	77.3 (59.0 – 97.3)	0.0003
EF	28 23 – 34)	26 22 – 31)	28 23 – 34)	0.0020
Type of surgery done†				<0.0001
CABG with CPB	668 (46.2)	49 (33.1)	619 (47.7)	
CABG without CPB	158 (10.9)	5 (3.4)	153 (11.8)	
CABG+MVR	131 (9.1)	30 (20.3)	101 (7.8)	
CABG+SVR	390 (27.0)	42 (28.4)	348 (26.8)	
CABG+MVR+SVR	99 (6.8)	22 (14.9)	77 (5.9)	
CPB surgery ± other procedures	1288 (89.1)	143 (96.6)	1145 (88.2)	0.0019
Mitral valve procedure	230 (15.9)	52 (35.1)	178 (13.7)	<0.0001
SVR procedure	489 (33.8)	64 (43.2)	425 (32.7)	0.0105
Surgery was not elective	178 (12.3)	29 (19.6)	149 (11.5)	0.0044
Bypass pump time, minutes	99 (67 – 133)	139 (90.5 – 186)	96 (64 – 126)	<0.0001

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variable	Overall (N=1446)	Still intubated at 36h (N=148)	Alive and extubated at 36h (N=1298)	p*
Operating room time, hours	5.00 (4.08 – 6.17)	6.10 (4.96 – 7.79)	4.92 (4.00 – 6.00)	<0.0001
Total intubation time, hours	16.0 (11.5 – 23.2)	80.3 (52.8 – 170)	14.8 (11.0 – 20.8)	<0.0001
CCU/ICU time, hours	64.9 (40.3 – 114.8)	168 (117 – 336)	48.8 (38.0 – 93.5)	<0.0001
Hours from OR discharge to extubation	11.4 (6.8 – 18.3)	76.6 (47.1 – 166.5)	10.3 (6.4 – 16.0)	<0.0001

[†]The 5 surgical procedure combinations are mutually exclusive and totals for each procedure with and without others follow.

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Determinants of 30-day mortality in 36-hour post-operation survivors: Multivariable Cox proportional hazards model N=1446, c-index=0.88 (95% CI 0.84, 0.92).

	HR (95% CI)	**p-value**
Still intubated at 36 hours	5.50 (3.09, 9.77)	<0.0001
LVESVI, HR for 10 unit increase above 70	1.17 (1.09, 1.27)	<0.0001
Mitral valve procedure	0.18 (0.07, 0.45)	0.0003
Operating room time, HR for each hour increase above 6 hours	1.34 (1.13, 1.59)	0.0009
Duke CAD Index, HR for 10 unit increase		0.0011
0–53	2.10 (1.29, 3.42)	
>53	0.68 (0.55, 0.85)	
Creatinine, HR for 0.1 mg/dL increase		0.0011
≤1.0	0.71 (0.53, 0.95)	
1.0–1.4	1.45 (1.19, 1.76)	
Hypertension	2.60 (1.37, 4.93)	0.0036
Mitral regurgitation, HR for 1 category increase over none or trace, ≤2+, 3+, or 4+	1.80 (1.21, 2.68)	0.0040
CCS Angina Class, HR for 1 category increase over 0/1, 2, 3, or 4	1.34 (1.04, 1.72)	0.0240
SBP HR for 10 mmHg increase	0.84 (0.72, 0.98)	0.0302
Age HR for 10-year increase	1.36 (1.01, 1.81)	0.0395

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Determinants of one-year mortality in 36-h post-operation survivors: Multivariable Cox proportional hazards model N=1446, c-index=0.78 (95% CI 0.75– 0.81)

Variable	HR (95% CI)	p
Still intubated at 36 hours	3.69 (2.60, 5.26)	<0.0001
LVESVI, HR for 10 unit increase above 70	1.10 (1.05, 1.15)	<0.0001
Creatinine, HR for 0.1 mg/dL increase between 1.0 and 1.4	1.18 (1.08, 1.30)	0.0003
Age, HR for 10 year increase	1.32 (1.12, 1.57)	0.0012
Mitral valve procedure	0.46 (0.28, 0.74)	0.0013
Atrial flutter or fibrillation	1.75 (1.22, 2.51)	0.0024
Stroke	1.92 (1.22, 3.01)	0.0049
Mitral regurgitation, HR for 1 category increase over none or trace, ≤2+, 3+, 4+	1.37 (1.10, 1.70)	0.0053
Operating room time, HR for 1 hour increase above 6 hours	1.19 (1.05, 1.34)	0.0059
NYHA class, HR for 1 category increase	1.31 (1.06, 1.62)	0.0143
Diabetes	1.45 (1.07, 1.97)	0.0154
Duke CAD index, HR for 10 unit increase		0.0172
0 – 53	1.45 (1.12, 1.88)	
> 53	0.88 (0.78, 1.00)	
Non-elective procedure	0.59 (0.37, 0.94)	0.0250

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4.

Pre- and intra-operative determinants of death or still intubated at 36h N=1460, c-index=0.75 (95% CI 0.71, 0.79).

Variable	OR (95% CI)	p-value
Mitral valve procedure	2.69 (1.83, 3.96)	<0.0001
NYHA class, OR for 1 category increase	1.62 (1.26, 2.08)	0.0002
LVESVI, OR for 10 unit increase		0.0004
≤ 115	1.18 (1.09, 1.29)	
≥ 115	0.84 (0.71, 0.98)	
Creatinine, OR for 0.1 mg/dL increase between 1.1 and 1.4	1.23 (1.07, 1.41)	0.0030
Previous CABG	3.05 (1.42, 6.57)	0.0044
Age, OR for 10-year increase	1.23 (1.01, 1.48)	0.0349

IPR2023-01064
Murray & Poole v. MHI
M&P Ex. 1071