Original Article

Sepsis is a Predictor of In-hospital Mortality in Critically Ill Patients Receiving Airway Rescue by Difficult Airway Response Team

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Objective: This retrospective study aimed at investigating whether airway rescue by the difficult airway response team (DART) would increase in-hospital mortality in the intensive care unit (ICU) setting.

Methods: All adult ICU patients receiving airway rescue by the DART were reviewed and divided into survival and mortality groups. Patient characteristics, comorbidities, indications for intubation, and airway maintenance technique were compared.

Results: Of the totally 56 patients (survival group, n = 35; mortality group, n = 21) in the current study, the most common indications for tracheal intubation in ICU patients were respiratory distress (64.3%) and consciousness change (17.9%). Compared with the survival group, the prevalence of comorbidities such as a history of coronary artery disease (38.1% vs. 5.7%, p = 0.004), sepsis (52.4% vs. 5.7%, $p < 0.001$), renal disease (61.9% vs. 20%, p = 0.002), and electrolyte imbalance (33.3% vs. 5.7%, p = 0.01) was higher in the mortality group. By contrast, those who expired had a lower incidence of trauma (4.8% vs. 31.4%, p = 0.021). There was no significant difference in the prevalence of indications, the frequency of fiberoptic intubation, and time for airway management between the two groups. Multivariant logistic regression analysis identified sepsis as a predictor of in-hospital mortality in ICU patients receiving airway rescue by DART.

Conclusions: Our findings showed that sepsis was a predictor of in-hospital mortality in ICU patients receiving airway rescue by DART. Besides, airway rescue by DART was safe and effective in a critical care setting.

Key words: difficult airway response team, tracheal intubation, intensive care unit, rapid response team

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Introduction

Tracheal intubation (TI) is a life-saving procedure in critically ill patients suffering from respiratory failure, shock, or cardiopulmonary arrest. Although deterioration of physiological condition of patients in the intensive care unit (ICU) can often be timely identified, the incidences of difficult TI as well as intubation-related complications and cardiac arrest remain high in this patient population.[1-3] The incidence of difficult TI ranged from 8% to 12%,[1-3] and that of cardiac arrest immediately after TI varied between 2% – 3% in the ICU setting.[1,2] To improve patient safety, several studies had attempted to identify the predictors of intubation-related complications.[2,3] Although the predictors of immediate and severe life-threatening complications following emergent TI (e.g., multiple intubation attempts) were well characterized,[2,3] predictors of in-hospital mortality in these patients receiving airway rescue remained unknown.

A number of studies have shown improved outcomes through the activation of rapid response teams (RRT) for distressed hospitalized patients.[4-6] A previous study also demonstrated a reduced frequency of in-hospital code blue following the implementation of an emergency airway response team for airway stabilization.[7] Considering the increased difficulty of TI in the non-operating room (OR) setting,[3] a difficult airway response team (DART) that comprises anesthesiologists and nurse anesthetists was implemented at our hospital.[8] Because patients in the ICU may have undergone multiple TI attempts before the activation of DART, we hypothesized that the risk factors for in-hospital mortality in this population requiring airway rescue by DART would be distinct from those previously reported such as age,[9] new-onset atrial fibrillation,[10] loss of functional independence, severe and moderate cognitive impairment, and low body mass index.[11] Identification of these predictors may allow clinicians to implement appropriate strategies to reduce in-hospital mortality rate. Our study also aimed at investigating the safety of DART activation for critically ill patients who needed airway rescue in the ICU setting and identifying significant predictors of mortality in this special population.

Methods

Patient population

From January 1, 2014 to December 31, 2016, all call events for DART in the ICU at a tertiary referral center were retrospectively reviewed. The call events were identified from the hospital electronic databank. All ICU patients aged 18 and older requiring DART activation were considered eligible. All patients fulfilled the criteria for being admitted to the ICU at our institute. Exclusion criteria included: (1) incomplete data, (2) pregnancy, (3) tracheal intubation not performed (observation only), (4) documented "not for resuscitation" order, (5) requirement for TI because of accidental self-extubation, (6) tracheostomy in situ. All patient data were de-identified and anonymized prior to analysis. Patients recruited were divided into two groups: (1) those alive at the time of discharge from hospital with stable vital signs. (i.e., survival group); and (2) those succumbed during hospitalization (i.e., mortality group). The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the institute (IRB number: EMRP-106-028). Informed written consent was waived because of the retrospective nature of the study.

Characteristics of difficult airway response team

The characteristics of DART at our hospital were previously described.[8] In brief, The DART comprises an anesthesia resident

with a minimum of two years of anesthesia training, an anesthesia nurse, and an attending anesthesiologist. The DART provides airway rescue services 24 hours per day and 7 days per week. The DART is dispatched to the location of the patient in need of airway rescue via a "stat" alert. Although the attending anesthesiologist may elect to participate in TI, the anesthesia resident acts as a first responder for airway management. According to policies at our institution, airway rescue is initially attempted in patients with cardiopulmonary distress without the use of neuromuscular blocking agents (e.g., succinylcholine), while the use of sedatives (e.g., midazolam) or neuromuscular blockers is reserved for those unable to cooperate with the intubation procedure at the discretion of the DART. Three unsuccessful intubation attempts mandates summoning an otolaryngologist to the scene to establish a surgical airway. A chest radiograph is routinely taken after intubation to assess the distance between the tip of the tracheal tube and the carina.

At our institute, there are still no established criteria or standards guiding the use of airway devices or medications for airway rescue outside OR. Therefore, the choice of airway devices was at the discretion of the DART. Advanced airway equipment, including McCoy laryngoscope (Truphatek International Ltd, Netanya, Israel),[12] fiberoptic bronchoscopes (Olympus LF-GP; Olympus Optical Co, Ltd, Japan), ProSeal™ laryngeal mask airway (Laryngeal Mask Company, San Diego, CA, USA), Trachway intubating stylet (Trachway; Biotronic Instrument Enterprise, Tai Chung, Taiwan, China),[13,14] Flexi-Slip stylet (Willy Rüsch AG, Kernen, Germany), Eschmann intubation stylet (tracheal tube introducer; SIMS Portex, Hythe, UK), and a Portex Cricothyrotomy Kit (PCK; Smith Medical International Ltd, Hythe, Kent, UK), are available at the bedside in a tackle box carried by the DART.

Indications for DART activation

When ICU patients require TI because of physiological deterioration or airway protection, residents or attending intensivists in charge perform TI. If the airway is found to be more complicated than expected (e.g., history of head and neck tumor, limited cervical spine range of motion, or limited oral opening) or if it cannot be successfully established after two intubation attempts with the Macintosh laryngoscopes, then the DART is activated. Despite these common indications for DART activation, the activation of DART is still at the discretion of the attending intensivist in charge.

Definition of comorbidities

Comorbidities were defined as any occurrence of a specific diagnosis code from 30 days before DART activation through 30 days after DART activation. The diagnostic criteria for sepsis included the presence (probable or documented) of infection together with systemic manifestations of infection (e.g., fever > 38.3 °C or altered mental status, or WBC count > 12,000 μL^{-1}).[15]

Data collection and statistical analysis

Data on patient characteristics, anthropometric parameters, comorbidities (e.g., diabetes mellitus, hypertension), indications for airway management (e.g., altered mental status or respiratory distress), airway devices (e.g., fiberscope), and time of intervention were retrospectively collected. All data were entered into a database using Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Quantitative variables were expressed as mean values and standard deviations (SD), and qualitative variables were expressed as percentages (%). Continuous variables between the two groups were compared using the two-tailed Student's t test, whilst categorical variables were compared using the Chi-square or Fisher's exact test. Data were analyzed using SPSS (version 20, SPSS Inc, Chicago, IL, USA) and a p value of < 0.05 was considered statistically

Table 1. Characteristics and comorbidities in survival group and mortality group.

Variables	Survival group (n = 35)	Mortality group (n = 21)	*p*
Age (yrs)	58.0 ± 18.0	64.2 ± 16.6	0.203
Sex/male	25 (71.4%)	18 (85.7%)	0.33
Height (cm)	165 ± 10.1	163.5 ± 6.8	0.545
Weight (kg)	65.8 ± 15.3	71.8 ± 16.5	0.175
BMI (kg/m^2)	24 ± 5.2	25.9 ± 8.6	0.307
Underlying disease			
CAD	2 (5.7%)	8 (38.1%)	0.004*
Heart failure	3 (8.6%)	5 (23.8%)	0.136
AMI	2 (5.7%)	1 (4.8%)	1
Sepsis†	2 (5.7%)	11 (52.4%)	< 0.001*
Arrhythmias	5 (14.3%)	3 (14.3%)	1
Hypertension	13 (37.1%)	8 (38.1%)	0.943
DM	11(31.4%)	5 (23.8%)	0.541
Lung disease	17 (48.6%)	8 (38.1%)	0.445
Renal disease	7 (20%)	13 (61.9%)	0.002*
Liver disease	6 (17.1%)	6 (28.6%)	0.334
Neurologic disease	19 (54.3%)	9 (42.9%)	0.408
Electrolyte imbalance	2 (5.7%)	7 (33.3%)	0.01*
ENT cancer	4 (11.4%)	0 (0%)	0.286
Other cancer	2 (5.7%)	1 (4.8%)	1
Trauma	11 (31.4%)	1 (4.8%)	0.021*
GI bleeding	0 (0%)	2 (9.5%)	0.136

BMI: body-mass index, CAD: coronary artery disease, AMI: acute myocardial infarction, DM: diabetes mellitus, ENT cancer: Ear, nose and throat cancer, GI: gastrointestinal, †The diagnostic criteria for sepsis included the presence (probable or documented) of infection together with systemic manifestations of infection (e.g., fever > 38.3 °C), *$p < 0.05$.

significant.

Results

Frequency of DART activation and patient grouping

In the 36-month study period, there were 56 call events for the DART in the ICU with an average of 1.56 calls per month (Fig 1). Of the 56 patients, 62.5% of patients were alive at discharge (n = 35; survival group) and 37.5% patients expired during hospitalization (n = 21; mortality group).

Demographics of recruited subjects and underlying diseases

The baseline characteristics and comorbidities of the two groups are summarized in Table 1. There was no significant difference in age, gender prevalence, and body mass index between the two groups. Compared with patients in the survival group, the prevalence of comorbidities including history of coronary artery disease (38.1% vs. 5.7%, $p = 0.004$), sepsis (52.4% vs. 5.7%, $p < 0.001$), renal disease (61.9% vs. 20%, $p = 0.002$), and electrolyte imbalance (33.3% vs. 5.7%, $p = 0.01$) was higher in the mortality group. By contrast, the incidence of trauma was lower in those who succumbed than that in the survivors (4.8% vs. 31.4%, respectively, $p = 0.021$) (Table 1).

Indications for tracheal intubation, advanced airway techniques, and time of intubation

The overall indications for TI are shown in Figure 2. Respiratory distress was the most common indication (64.3%), followed by change of consciousness (17.9%) (Fig. 2). After dividing the patients into survival and mortality groups, their indications for TI, fiberoptic intubation, and time of intervention (i.e., daytime

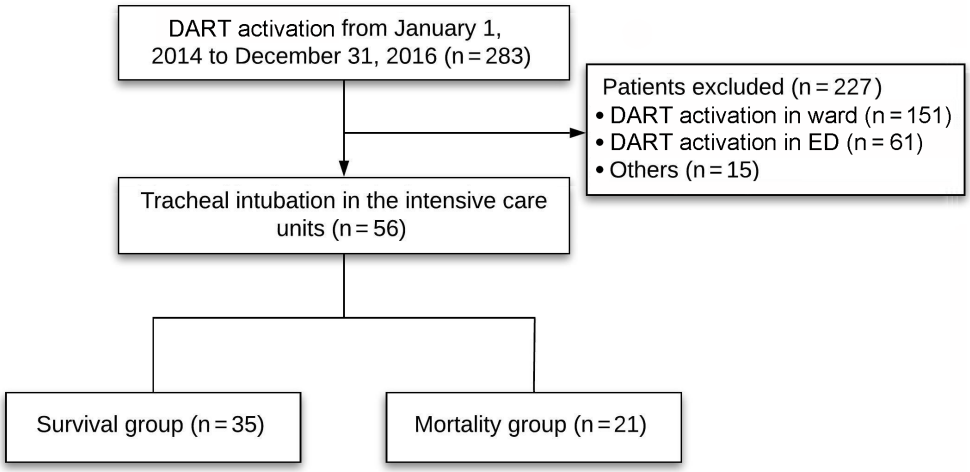

Fig. 1 Flowchart of recruitment process in the retrospective study. DART: difficult airway response team, ETI: emergent tracheal intubation; ICU: intensive care unit; ED: emergency department.

vs. nighttime) are shown in Table 2. The most frequent indication for TI in both survival and mortality groups was respiratory distress (60% vs. 71.4%, respectively, p = 0.388), followed by change of consciousness (20% vs. 14.3%, respectively, p = 0.727). There was also no significant difference in the prevalence of indications, the frequency of fiberoptic intubation, and time for airway management between the two groups (Table 2).

Airway rescue-related complications and predictor of mortality

All airway rescues were successfully performed by the DART without resort to surgical airway. There were no intubation-related complications including esophageal intubation, pneumothorax, cardiac arrest, subcutaneous emphysema, hypoxia, or hypotension in all patients during the airway rescue procedure. Predictors of in-hospital mortality following airway rescue using multivariant logistic regression analysis are shown in Table 3. Only the presence of sepsis was a significant predictor of in-hospital mortality in ICU patients receiving airway rescue by DART (odd ratio, 12.84; 95% confidence interval, 1.97-83.88; p = 0.0077).

Discussion

There is no currently available guideline on the activation of DART in the critical care setting. The present study is the first to evaluate whether activation of the DART in the critically ill population with airway management problems would increase airway-related complications and mortality. Our results showed that sepsis was the only significant predictor of mortality, suggesting that airway rescue by

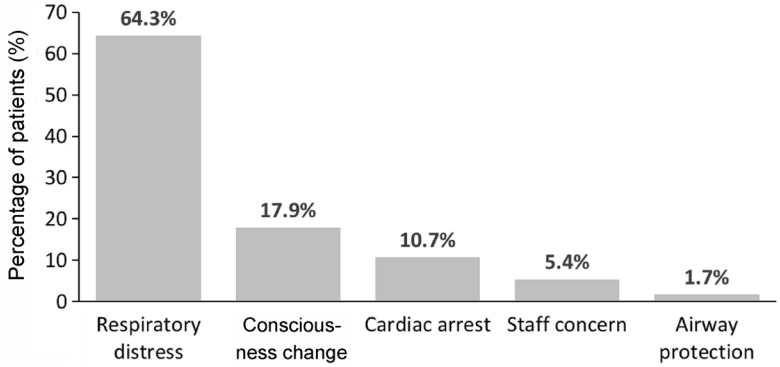

Fig. 2 The indications for tracheal intubation for patients (n = 56) in intensive care units.

Table 2. Indications for emergent airway management, advanced airway techniques, and time of intubation.

	Survival group (n = 35)	Mortality group (n = 21)	*p* value
Indications			
Conscious change	7 (20%)	3 (14.3%)	0.727
Respiratory distress	21 (60%)	15 (71.4%)	0.388
Staff concern	3 (8.6%)	0 (0%)	0.284
Airway obstruction	1 (2.9%)	0 (0%)	1
Cardiac arrest	3 (8.6%)	3 (14.3%)	0.352
Fiberoptic intubation	8 (22.9%)	2 (9.5%)	0.29
Daytime intubation	12 (34.3%)	4 (19%)	0.222

DART was effective without notable negative impact on mortality in this setting. Our finding may also provide a treatment guideline for intensivists when caring for this special patient population. Not only did the finding encourage the activation of RRT in the ICU for difficult airway management but it also underscored the importance of sepsis control.

A previous study reported that delay in RRT activation in wards was more likely if the incident happened between midnight and 08:00 a.m. compared with other time in a day.[16] Previous studies have demonstrated that delays in RRT activation or RRT activation at nighttime for patients in wards,[16,17] which are attributable to repaired recognition of deterioration of patient's condition,[18] are independently associated with elevated risks of mortality and morbidity.[18] Therefore, the findings of those studies highlighted the importance of early RRT activation in the non-critical care setting.[16-18] In contrast, monitoring of clinical deterioration for patients in the ICU is unlikely to be delayed. As shown in our results, although patients in the survival group had a higher frequency of DART activation between 8:00 and 16:00 compared to that in the mortality group, the difference was not significant (34.3% vs. 19%, $p = 0.222$). In this way, our results supported that DART activation due to delayed recognition of deterioration of patient's condition is unlikely in the ICU setting. In our study, the in-hospital morality was 37.5% in ICU patients. In contrast, our previous study has shown that the in-hospital mortality was high in ward patients requiring airway rescue (i.e., 55.6%).[8] Real-time monitoring and ready availability of advanced life support skills and personnel may at least partly contribute to the lower mortality in the former compared to that of the latter.

Table 3. Multivariate logistic regression analysis of factors associated with in-hospital mortality (n = 56).

Variable	Odds ratio	95% CI	*P* value
CAD	5.40	0.67 - 43.45	0.1131
Sepsis†	12.84	1.97 - 83.88	0.0077*
Renal disease	1.61	0.29 - 8.99	0.5873
Electrolyte imbalance	5.18	0.63 - 42.31	0.1250

CAD: coronary artery disease; CI: confidence interval; †The diagnostic criteria for sepsis included the presence (probable or documented) of infection together with systemic manifestations of infection (e.g., fever >38.3 °C); *$p < 0.05$.

Although the consensus for DART activation included multiple intubation attempts and anticipated difficult airway in daily practice at our institute, DART activation was still at the discretion of the intensivist in charge. Several previous studies had assessed the predictors of immediate intubation-related complications in ICU patients. For example, a study demonstrated that three or more intubation attempts and difficult laryngoscopic view (i.e., grade III or IV view) were associated with increased risk of airway complication in nonoperative intubation.[1] Additionally, another study showed that acute respiratory failure and shock as indications for TI were predictors of post-intubation complications.[2] Besides, a large-scale study in the ICU setting reported that intubation-

related cardiac arrest was an independent risk factor for 28-day mortality.[19] Taken together, the findings of previous studies all indicated a negative impact of intubation-related complications on patient outcomes in a critical care setting.[1,2,19] Unlike in ward where emergent airway management is unexpected and relatively inexperienced physicians are in charge, the ICU is well-prepared for critical airway management both in equipment and personnel. In comparison with the former where DART may be activated at an early stage as soon as the need for emergent airway management is realized, it is rational to assume that DART is activated only after multiple futile attempts in airway establishment by experienced intensivists. On top of the already critical condition of the patients in the ICU, multiple intubations would further increase their risk of mortality.[1,2] The 100% success rate of airway rescue by DART as well as the lack of intubation-related complications and mortalities further underscored the safety and effectiveness of this approach in a critical care setting.

Although previous studies have reported predictors of mortality in the ICU patient population including age,[9] new-onset atrial fibrillation,[10] loss of functional independence, severe and moderate cognitive impairment, and low body mass index,[11] the current study identified sepsis as the only significant predictor of mortality despite the apparently higher incidences of comorbidities in the mortality group (i.e., history of coronary artery disease, sepsis, renal disease, and electrolyte imbalance). Our study is the first to demonstrate that sepsis was a predictor of in-hospital mortality in ICU patients following DART activation. The identification of sepsis as a contributor to mortality in this patient population may warrant the implementation of a special treatment protocol. For instance, the criteria for DART activation in septic patients may be widened for allocation of experienced first responders for airway management. Regarding medical treatment, prompt and adequate antibiotic treatment is crucial to successful outcomes for patients admitted to the ICU for sepsis.[20-22] Although early empirical antibiotic treatment of patients suspected of having sepsis is a standard practice, previous studies reported that about 9% – 23% of patients with sepsis syndrome were not treated with adequate or appropriate antibiotics.[21,22] In one study,[22] the mortality rate increased significantly from 33% to 43% in patients receiving inadequate antibiotic treatment. Other strategies for sepsis control include the incorporation of multidisciplinary care teams[23] and implementation of sepsis intervention bundle[24] which had been demonstrated to reduce the mortality rate of critically ill patients. This multifaceted approach to airway management based on the results of this study and those of previous investigations may be of potential in improving the management of septic patients requiring airway rescue.

In our study, the most common indication for TI was respiratory distress (i.e., 64.3%), underscoring the high risk of hypoxemia during TI in our patients. In critically ill adults, hypoxemia has been found to contribute to intubation-related cardiac arrest[19,25] that would increase the odds of hospital mortality by 14 folds.[26] To minimize the risk, bag-mask ventilation prior to TI in ICU patients may be a feasible option as it has been demonstrated to increase oxygenation after TI without increasing the risk of pulmonary aspiration.[27]

There were several limitations in this study. First, the low frequency of DART activation limited the number of patients in our study. Second, because information on peri-intubation hemodynamic changes, hypoxemia, and the number of failed laryngoscopic intubation attempts was not routinely documented in the medical record, the present retrospective review failed to provide relevant data for comparison between the two groups. Third, data in the present study from a single institute with a DART may not be extrapolated to other

hospitals without similar functional teams. Fourth, although all patients fulfilled the criteria for ICU admission, severity of their diseases (e.g., APACHE and SOFA scores) was not analyzed. Therefore, the impact of disease severity on the outcomes of the present study could not be assessed. Finally, although other advanced airway equipment, including the McCoy laryngoscope and Trachway intubating stylet, are available in the OR, their use outside the OR is rare. Therefore, the impact of this airway equipment on patient outcomes was not evaluated.

Conclusion

The results of the present study demonstrate sepsis was a predictor of in-hospital mortality in ICU patients receiving airway rescue by DART. Besides, airway rescue by DART was safe and effective in a critical care setting.

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