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ORIGINAL RESEARCH

Associated Factors of In-hospital Mortality among Intubated Older Adults in Emergency Department; a Cross-sectional Study

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Abstract: **Introduction:** A decision-making guideline on when to intubate an older person based on predictors of intubation outcome would be extremely beneficial. This study aimed to identify the associated factors that could predict the outcomes of endotracheal intubation among older adults in the Emergency Department (ED). **Methods:** In this retrospective cross-sectional study, patients aged ≥65 years intubated at the ED of University of Malaya Medical Centre, Kuala Lumpur, Malaysia, from 2015 to 2019 were studied. The association between age, gender, place of inhabitation, Identification of Seniors at Risk (ISAR) score for frailty, Charlson Comorbidity Index (CCI), Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, indication for intubation, and diagnosis on admission with in-hospital mortality (primary outcome) and duration of ventilation, and length of stay (secondary outcomes) were evaluated using univariate analysis and Cox's regression survival analysis. **Results:** 889 cases aged 65 years and above were studied (61.5% male). The rate of in-hospital mortality was 71.4%. There was a significant association between age ($p < 0.001$), nursing home residency ($p = 0.008$), CCI≥ 5 ($p = 0.001$), APACHE-II ($p < 0.001$), pre-intubation Glasgow Coma Scale (GCS) ($p < 0.001$), cardiac arrest as indication of intubation ($p < 0.001$), diagnosis on admission ($p < 0.001$), length of stay ($p < 0.001$), and length of ventilation ($p = 0.003$) and in-hospital mortality. Age ≥ 85 years (HR= 1.270; 95%CI=1.074 to 1.502) and 75 to 84 years (HR=1.642; 95%CI=1.167 to 2.076), cardiac arrest as indication of intubation (HR: 1.882; 95% CI: 1.554 – 2.279), and APACHE-II scores 25 – 34 (HR: 1.423; 95% CI: 1.171 - 1.730) and ≥ 35 (HR: 1.789; 95%CI: 1.418 - 2.256) were amongst the independent predictive factors of in-hospital mortality. **Conclusion:** Nearly three out of four individuals aged ≥65 years intubated at the ED died during the same admission. Older age, cardiac arrest as indication of intubation, and APACHE-II score were independent predictors of in-hospital mortality.

Keywords: Aged; intubation; emergency service, hospital; Respiration, Artificial

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1. Introduction

Population ageing is occurring faster in low- to middle-income countries than high-income countries (1). In 2020, the number of older adults aged 65 years and above has increased to 7.0% of the total Malaysian population, compared to 6.7% in 2019. By 2030, older adults are expected to make up more than 15% of the Malaysian population (2). This demographic shift has been attributed to improved nutrition and sanitation, increasing life expectancy, and declining fertility rates (3).

Advancements in medical science have led to improved critical care and surgical management. While critical care management regularly involves ventilatory support, such life-sustaining treatment in some individuals, particularly those in the older age group, may not necessarily lead to survival benefits (4).

The decision whether to perform endotracheal intubation and artificial ventilation among older adults presenting with respiratory compromise in the emergency department (ED) is highly challenging. A retrospective cohort study by Ouchi et al. suggested that one in three older adults intubated in the emergency department died in hospital (5). A study by Foerch et al. mentioned that a quarter of intubated older stroke patients survived with good neurological outcome and

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reasonable quality of life (6). In a cross-sectional stratified random national survey, Steinhouser et al. stated that more than 70% of older adults would choose quality of life above longevity (7). Despite this, the intubation rate for critically ill older adults has increased by 30% from 2001 to 2011 and further doubled by 2020 (8).

A decision-making guideline on when to intubate an older person based on predictors of intubation outcome would be extremely beneficial. Therefore, this study aimed to evaluate the in-hospital mortality rate and its associated factors among older adults who received endotracheal intubation and ventilation at the ED.

2. Methods

2.1. Study design and setting

This retrospective cross-sectional study was conducted on patients aged ≥65 years intubated at the ED of University of Malaya Medical Centre (UMMC), Kuala Lumpur, Malaysia, from 2015 to 2019. The association between age, gender, place of inhabitation, Identification of Seniors at Risk (ISAR) score for frailty, Charlson Comorbidity Index (CCI), Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score, indication for intubation, and diagnosis on admission with in-hospital mortality, duration of ventilation, and length of stay were evaluated. The UMMC is a large teaching hospital with a total of 1100 beds. It receives 1.1 million visits annually with a 70-75% bed occupancy rate. The ED itself receives 25,000 older patients a year. Ethical approval was obtained from the University of Malaya Medical Center Medical Research Ethics Committee (MREC ID No: 2020224-8310). The researchers adhered to the confidentiality of patients' profiles and ethical considerations in biomedical research.

2.2. Participants

All patients aged 65 years and above attending the ED who received endotracheal intubation were identified from the hospital electronic medical records (EMR) using the ICD-10 procedural code for "Insertion of Endotracheal Airway into Trachea, via Natural or Artificial Opening" and included in the study. Those intubated outside the hospital, before arrival to hospital, and in the hospital ward were excluded. The list obtained was cross-checked with the Medical Records Department.

2.3. Data gathering

Data was extracted from the EMR system using a standardized data collection document. Information on age (9), gender, place of inhabitation (home, nursing home or others) (10), the Identification of Seniors at Risk (ISAR) score for frailty (11), the Charlson Comorbidity Index (CCI) on admission (12), the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score (13, 14), the Glasgow Coma Scale (GCS) before intubation (15), indications for intubation, and diagnosis on admission (16-18), was retrieved. The ISAR is a six-item tool, which quantifies frailty using commonly measured variables in the ED (19). The responses are dichotomized as "yes" or "no", and for each "yes" answer one point is allocated. Those with a score ≥2 out of 6 were considered "at risk" of adverse outcomes. The Charlson Comorbidity Index (CCI) estimates the risk of death and is calculated by adding up weighed scores assigned to its 19 items, which are then summed up to a total score that ranges from 0–33. A total score of ≥5 was considered to show high risk of death (20). The APACHE-II score assigns scores of 0-4 to 11 physiological measurements, including temperature, blood pressure, heart rate, respiratory rate, arterial pH, arterial oxygen saturation, serum sodium, serum potassium, serum creatinine, hematocrit, and white cell count, in addition to 0-6 to age and 2 or 5 for chronic health points (21). The GCS score is added to the sum of scores to obtain a maximal total score of 71. A total APACHE-II score of ≥ 35 indicates a mortality risk of 80%.

2.4. Outcomes

The primary outcome was in-hospital mortality, and the secondary outcomes were the duration of ventilation, and length of hospital stay. The date of death was obtained through the hospital EMR.

2.5. Statistical analysis

Data analysis was carried out with the Statistical Package for Social Sciences software (SPSS, Chicago, IL, USA) version 22.0. The univariate association between each potential predictor and the primary outcome was analyzed using the chi-square test. The Cox's proportional hazards regression was used to develop a predictor model for time to hospital death. Hazard ratios (HR) and 95% confidence intervals (CI) were reported. Variables with a p-value < 0.05 in the univariate analyses and variables of clinical significance were selected for inclusion.

3. Results

3.1. Baseline characteristics of participants

Eight hundred and eighty-nine individuals aged 65 years and above were intubated at the studied ED from 2015 to 2019 (7.5% ≥ 85 years and 61.5% male). Baseline characteristics of studied cases are summarized in table 1. 8% were nursing home residents. 424 (52 %) patients had a CCI of ≥ 5, while 660 (74%) patients had an ISAR score of ≥ 2, and 203 (23%) cases had an APACHE-II score of ≥ 35. A total of 316 (36%) patients had a pre-intubation GCS of 3. Of the 889 included individuals, 220 (25%) underwent crash intubation for cardiac arrest.

Table 1: Baseline characteristics of intubated elder adults in emergency department (ED)

Variable	Value (%)
Age (years)	
65 – 74	505 (56.8)
75 – 84	317 (35.7)
≥ 85	67 (7.5)
Gender	
Male	547 (61.5)
Female	342 (38.5)
Origin before ED visit	
Nursing home	68 (7.6)
Others	821 (92.4)
Charlson Comorbidity Index (CCI)	
< 5	465 (52.3)
≥ 5	424 (47.7)
Identification of Seniors at Risk (ISAR)	
< 2	229 (25.8)
≥ 2	660 (74.2)
APACHE-II Score	
10 – 24	336 (37.8)
25 – 34	350 (39.4)
≥ 35	203 (22.8)
Pre-intubation Glasgow coma scale (GCS)	
15	204 (22.9)
4 – 14	369 (41.5)
3	316 (35.5)
Indication of intubation	
Cardiac arrest	220 (24.7)
Other	669 (75.3)
Admission diagnosis	
Cardiac arrest	220 (24.7)
Sepsis/septic shock	142 (16.0)
ACS/heart failure	79 (8.9)
Pneumonia	89 (10.0)
Cerebrovascular accident	88 (9.9)
Traumatic Brain Injury	51 (5.7)
Others	220 (24.7)

APACHE-II: Acute Physiology and Chronic Health Evaluation -II; ACS: acute coronary syndrome.

3.2. Univariate analysis

Of all intubated older adults, 635 (71.4%) died in the hospital. Table 2 summarizes the univariate analysis of factors associated with in-hospital mortality. There were a significant association between age ($p < 0.001$), nursing home residency ($p = 0.008$), CCI≥ 5 ($p = 0.001$), APACHE-II score ($p < 0.001$), pre-intubation GCS ($p < 0.001$), cardiac arrest as indication of intubation ($p < 0.001$), diagnosis on admission ($p < 0.001$), length of stay ($p < 0.001$), and length of ventilation ($p = 0.003$) and in-hospital mortality of intubated older adults in emergency department.

3.3. Predictors of in-hospital mortality

Age ≥ 85 years (HR= 1.270; 95%CI=1.074 to 1.502) and 75 to 84 years (HR=1.642; 95%CI=1.167 to 2.076), cardiac arrest as indication of intubation (HR: 1.882; 95% CI: 1.554 – 2.279), and APACHE-II scores 25 – 34 (HR: 1.423; 95% CI: 1.171 - 1.730) and ≥ 35 (HR: 1.789; 95%CI: 1.418 - 2.256) were amongst the independent predictive factors of in-hospital mortality among intubated older adults in emergency department.

4. Discussion

The management of the critically ill older adults, especially in the intensive care unit is resource heavy with a corresponding increase in healthcare cost burden (22, 23). Hence, early decision making on the risk-benefit of intubation and ventilation of critically ill older persons in the emergency department is paramount.

In this study, nearly three out of four individuals aged 65 years and over intubated in the ED died in hospital. If only those aged 85 years and above were considered, the inpatient mortality rate was 90%. This proportion was far higher than that reported by a similar study conducted in a developed country, which reported a mortality rate of 33% (5). While this discrepancy could be accounted for by better prehospital and critical care (24), an alternative explanation could also be the far higher caseloads handled in the ED in developing countries with patients presenting at a later stage of illness (25). This is also supported in a study in China and Iran during the COVID-19 pandemic, in which critically ill older persons had a significantly higher mortality rate than those younger(26, 27). Another possible explanation was the lack of validated criteria or risk scoring on the selection of patients who might benefit from critical care as supported by a study in India (28). However, our study supported the poorer outcome of older persons aged more than 85 years old as reported by Bertrain Guidet et al. (29).

Providing care for older patients does not mean subjecting them to aggressive treatments, such as intubation, which may lead to avoidable suffering to the patients and their families, and unnecessarily burdening the healthcare system (30). Previously published data have reported high mortality following adult out-of-hospital or in-hospital cardiac arrest (18, 31), but little is known about the effect of most interventions during cardiac arrest, including drugs and the use of advanced airway management. In a study involving adult patients with in-hospital cardiac arrest, the initiation of tracheal intubation within the first 15 minutes of resuscitation, compared with no intubation, was associated with decreased survival to hospital discharge (18). Within this study, older adults who underwent emergency crash intubation during a cardiac arrest event had a higher inpatient mortality, highlighting the potential futility of intubation in the majority of

Table 2: Comparing the characteristics of patients between survived and non-survived cases who were intubated in emergency department

Predictors	In-hospital mortality		p-value
	Yes (n = 635)	No (n = 254)	
Age (year)			
65 – 74	328 (65.0)	117 (35.0)	< 0.001
75 – 84	247 (77.9)	70 (22.1)	
≥ 85	60 (89.6)	7 (10.4)	
Gender			
Male	379 (69.3)	168 (30.7)	0.074
Nursing home			
Yes	58 (85.3)	10 (14.7)	0.008
CCI ≥ 5			
Yes	326 (76.9)	98 (23.1)	0.001
ISAR ≥ 2			
Yes	477 (72.3)	183 (27.7)	0.344
APACHE-II			
10 – 24	193 (57.4)	143 (42.6)	
25 – 34	260 (74.3)	90 (25.7)	< 0.001
≥ 35	182 (89.7)	21 (10.3)	
Pre-intubation GCS			
15	121 (59.3)	83 (40.7)	
4 – 14	249 (67.5)	120 (32.5)	< 0.001
3	265 (83.9)	51 (16.1)	
Indication of intubation			
Cardiac arrest	200 (90.9)	20 (9.1)	< 0.001
Admission diagnosis			
Cardiac arrest	200 (90.9)	20 (9.1)	
Sepsis, septic shock	116 (81.7)	26 (18.3)	
ACS/heart failure	55 (69.6)	24 (30.4)	< 0.001
Pneumonia	60 (67.4)	29 (32.6)	
Stroke/ICH	67 (76.1)	21 (23.9)	
Traumatic Brain Injury	37 (72.5)	14 (27.5)	
Others	100 (45.5)	120 (54.5)	
Duration of ventilation (week)			
< 1	438 (75.1)	145 (24.9)	
1-2	159 (63.6)	91 (36.4)	0.003
>4	38 (67.9)	18 (32.1)	
Length of hospital stay (week)			
< 1	435 (96.5)	16 (3.5)	
1-4	154 (48.7)	162 (51.3)	< 0.001
> 4	46 (37.7)	76 (62.3)	

Data are presented as number (%). CCI: Charlson Comorbidity Index; ISAR: Identification of Seniors at Risk; APACHE-II: Acute Physiology and Chronic Health Evaluation-II; GCS: Glasgow coma scale; ACS: acute coronary syndrome; ICH: intracranial hemorrhage.

older adults who suffer cardiac arrest in the hospital. However, this does not necessarily advocate blanket avoidance of artificial ventilation in all older adults with cardiac arrest in hospital, and further research is required to ensure that the minority who will survive to discharge are not deprived of life saving treatment and are accurately identified.

The APACHE-II score has long been established as an accurate measure of mortality among critically ill individuals (13, 14, 32). However, it has yet to be evaluated as a measure for survival following intubation in older patients. Within this study, the APACHE-II emerged as an independent predictor of in-hospital mortality. Although presence of comorbidities was associated with inpatient mortality within the univariate analysis, it did not emerge within the final predictor model. Multiple studies have identified poorer outcomes in critically ill older adults with more underlying comorbidities (12, 20, 33). This has led to the common practice among health care workers, using comorbidities to facilitate end-of-life decisions for critically ill older adults. Our findings imply that the influence of comorbidity on inpatient mortality

Table 3: Independent predictors of in-hospital mortality among intubated older adults in emergency department based on Cox's Regression Survival Analysis

Predictors	B	Hazard Ratio (95% CI)
Age (Years)		
65 – 74 (reference)		
75 – 84	0.239	1.270 (1.074 - 1.502)
≥ 85	0.496	1.642 (1.167 - 2.076)
Indication of intubation		
Cardiac arrest	0.632	1.882 (1.554 – 2.279)
APACHE-II score		
10 – 24		
25 – 34	0.353	1.423 (1.171 - 1.730)
≥ 35	0.582	1.789 (1.418 - 2.256)

CI: confidence interval; APACHE-II: Acute Physiology and Chronic Health Evaluation-II.

is accounted for by severity of illness, and the latter should be considered as the determinant of likelihood of survival to discharge rather than the former in the context of older adults who are intubated. Numerous frailty assessment tools have been developed based on adverse outcomes, which included mortality and hospitalization. A previous study found that critically ill frail patients have higher in-hospital mortality than non-frail patients, and the frail survivors were also more likely to become functionally dependent (34). The Identification of Senior at Risk (ISAR) tool has been developed as an identifier of those at high risk of adverse health outcomes after an Emergency Department visit. However, within this study, when applied within the context of intubation, frailty identified with the ISAR did not predict survival to discharge. Our finding, therefore, suggests that once an older individual is intubated, the likelihood of survival is determined by severity of illness rather than frailty status before admission, but age alone still plays a significant role in influencing outcomes of artificial ventilation. This does imply that frailty measured using the ISAR tool does not predict intubation outcomes and is not an appropriate tool to aid decisions against intubation in older adults (35). This does not conform with other studies advocating the use of frailty scores as a modality of estimating outcome (29). A possible explanation is that ISAR has a poor to fair predictive validity in prediction of outcome and should not be use alone for identifying older persons at risk of adverse outcome in the emergency department (36). Decisions to withhold life-sustaining treatment such as endotracheal intubation are often challenging for medical professionals, with various cultural and religious views potentially influencing such decisions (37). Appropriate training for healthcare professionals on medical ethics and communication skills may help reduce the burden of delivery of life-prolonging treatment that is likely to be futile, and this could be additionally facilitated with guidelines and decision aids.

5. Limitation

This study is limited by its retrospective design, with potential inaccuracies associated with retrospective data collection such as misinterpretation of records in the EMR. It was not possible to verify the accuracy of the predictor scores recorded within the EMR. Nevertheless, the issue of high in-patient mortality rates in those intubated in the ED within our setting has been clearly highlighted, with important ethical and resource implications. Future studies should investigate the reasons underlying this high mortality rate, as well as develop accurate predictor tools to aid decision making. In addition, evaluation of the role of ethics and communication training, guidelines, and decision aids should also be considered in this regard.

6. Conclusion

Age ≥ 75, cardiac arrest as indication for intubation, and APACHE-II scores ≥ 25 were independent predictive factors of in-hospital mortality following intubation of older adults in the ED. Frailty and comorbidities evaluated with the ISAR tool and CCI, respectively, were not predictors of in-hospital mortality, challenging the existing practice of using pre-hospitalization frailty status and comorbidity burden to guide decision for or against intubation.

7. Declarations

7.1. Acknowledgments

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7.2. Authors' contributions

Mohd Idzwan and Tan Maw Pin designed the protocol on methodology, ethical approval, writing, review and editing the manuscript. Mohd Idzwan also supervised the comple-

tion of the manuscript. Nor Hadila was involved in research literature review, gaining ethical approval, sample collection, data analysis, writing and editing the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

7.3. Funding and supports

This was an unfunded study.

7.4. Conflict of interest

None declared.

7.5. Availability of data

The datasets generated and analyzed during the current study are available from Mohd Idzwan bin Zakaria.

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