Prognostic Implications of Preoperative Pneumonia to Patients Undergoing Hip Fracture Surgery or Arthroplasty

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Abstract

BACKGROUND: Preoperative pneumonia is one of the underlying comorbidities of patients undergoing hip fracture surgery or arthroplasty, which had been reported with an increased 30-day mortality. However, the influences that preoperative pneumonia or its different severity had to long term survival were hardly been reported.

METHODS: In this retrospective observational study, we reported outcomes of patients undergoing hip fracture surgery or arthroplasty with or without a diagnosis of preoperative pneumonia. We analyzed risk factors of 1-year mortality for patients with preoperative pneumonia and calculated the adjusted risk of 1-year mortality that stratified for pneumonia severity evaluated with CURB-65 score. Survival rates of patients free of pneumonia or with different pneumonia severity were also reported with COX regression.

RESULTS: The incidence of preoperative pneumonia was 7.86% in our cohort. Compared to patients without preoperative pneumonia, patients with this condition had longer hospital stay (15 vs. 12, p<0.001 and ICU length of stay (7 vs. 0, p<0.001), higher 30-day mortality (11.9% vs. 5%, p=0.002) and 1-year mortality (33.9% vs. 16.3%, p<0.001). BMI<18.5 kg/m², CURB-65 score ≥3 were risk factors of 1-year mortality in patients with preoperative pneumonia, while regional anesthesia was a protective factor for 1-year mortality. There was a linear trend of CURB-65 score to 1-year mortality after adjustment for BMI and anesthesia type (p for trend = 0.006). when CURB-65 score ≥3, patients had significant risk of 1-year mortality (OR: 3.85-7.87). COX regression reveals a higher risk of mortality over time in patients with preoperative pneumonia, as severity increases (CURB-65 score ≥3), the difference of risk to patients without preoperative pneumonia became significant.

CONCLUSION: In this single center retrospective study that consists of patients undergoing hip fracture surgery or arthroplasty, patients with preoperative pneumonia had worse prognoses than patients without this condition. BMI<18.5 kg/m², CURB-65 score ≥3 were risk factors of 1-year mortality in patients with preoperative pneumonia, while regional anesthesia was a protective factor for 1-year mortality. In patients with preoperative pneumonia, CURB-65 score ≥3 indicated higher risk of mortality over time.

Introduction

As the population ages, the incidence of hip fracture is expected to increase worldwide. The associated mortality and functional disability will contribute to a huge burden to society (1, 2). Various comorbidities have been reported to be related to increased 30-day and 1-year mortalities (3, 4) of hip fracture. Among them, pneumonia was one factor that frequently happens and may increase the mortality rate up to 4 times (4). Prevention and management of pre or post-operative pneumonia has been considered as a crucial method of improving patient prognosis in some society guidelines (5, 6).

However, the influence of preoperative pneumonia to the prognosis of patients who admitted for hip fracture surgery or arthroplasty has rarely been discussed. Preoperative pneumonia has a reported prevalence of 1.2-3.2%(7, 8), a recent study by Joseph et, al described preoperative pneumonia as a risk factor to a higher 30-day mortality after hip fracture surgery in geriatric patients, but its effects on long term survival were not discussed (8). In addition, previous studies had not evaluated the influence of the different severity of pneumonia to patient outcomes. The main purposes of this retrospective study are 1. Evaluate the prognoses of patients admitted for hip fracture or arthroplasty and diagnosed with or without preoperative pneumonia. 2. Find out risk factors of 1-year mortality in patients with preoperative pneumonia. 3. To analyze the influence of preoperative pneumonia and its severity to long term survival in these patients.

Methods
This non-interventional retrospective study was approved by the Research and Ethic committee of Peking University People’s Hospital (Approve Number: H18REA-013)

Patients

All data of patients who admitted to Peking University People’s Hospital between January, 2008 and September, 2018 from electronic medical record system were extracted and reviewed. Adult patients (> 18 years old) with the diagnosis of hip fracture and received hip fracture surgery or arthroplasty were included.

Data collection

The Baseline data were recorded at the time of admission, including (1) demographical characteristics: age, sex, body mass index (BMI). (2) evaluations of overall status of patients: American Society of Anesthesiologists physical status classification (ASA score)(9), activities of daily living (ADL) score(10). (3) comorbidities and other histories.

Data associated with surgical intervention and part of the outcomes were recorded at the time of discharge, including (1) surgical associated data: location of fracture (femoral neck, intertrochanteric, subtrochanteric or multiple locations), time interval(hours) between admission and surgery, surgery types (internal fixation or hemi/total-hip arthroplasty), anesthesia type (general or regional anesthesia). (2) outcomes: hospital stay, intensive care unit (ICU) length of stay.

30-day mortality, 1-year mortality, readmission rate within 1 year were evaluated at the time of our study initiated (calculated from the day of surgery), by following up through medical record system and phone calls.

Diagnosis and evaluation of preoperative pneumonia

Two experienced clinicians reviewed all included patients’ chest X-ray or chest CT (both were performed on admission) separately. According to society guidelines(11, 12), the criteria of pneumonia was as follow:

1. Symptoms and signs (cough, secretion of sputum, fever, rapid shallow breathing, etc.) of an acute lower respiratory tract infection;
2. Chest X-ray showing new shadowing that is not due to any other cause (such as pulmonary edema or infarction).

In case of disagreement between reviewers, data and image will be transferred to a senior pulmonology expert for the final decision of the diagnosis of pneumonia. Evaluation of the severity of pneumonia were performed simultaneously with CURB-65 score(13), ranging from 0 to 5, with 1 score for each of the following criteria:

1. Confusion;
2. urea >7 mmol/l;
3. respiratory rate ≥30/min;
4. low systolic (<90 mmHg) or diastolic (≤60 mm Hg) blood pressure;
5. age ≥65 years.

Statistical analysis

Collected data were recorded into a database which were subsequently analyzed with SPSS (Version 25, SPSS Inc, Chicago, IL, USA). Comparison of two groups of continuous variables was achieved with Mann-Whitney U test. Comparison of categorical variables was performed using χ² test or Fisher’s exact test as appropriate. Univariate and multivariate logistic models were used to investigate potential risk factors of 1-year mortality in the study cohort. Stratified analysis of odd ratios of 1-year mortality by CURB-65 scores was performed with logistic regression (adjusted for potential risk factors of 1-year mortality), meanwhile p value for trend was tested by using CURB-65 score as a continuous variable in logistic regression to test the linear trend between CURB-65 and 1-year mortality. A COX regression curve was constructed to analyze the survival rate of patients with or without preoperative pneumonia, also, to analyze the difference of survival rate of patients without preoperative pneumonia and different pneumonia severity (with CURB-65 score). All tests were two-sided and P
< 0.05 was considered as statistically significant.

**Results**

**Patients**

During the study period, the data of 1386 patients who met our inclusion criteria were successfully collected from medical record system. Among these patients, 109 were diagnosed with preoperative pneumonia by retrospective analysis of medical record and radiological images, which consists of 7.86% of all included patients. 1277 patients were free of preoperative pneumonia. The baseline characteristics of patients with or without preoperative pneumonia were depicted in Table 1. No significant difference between this two group exists except for ADL scores on admission, there were more patients with ADL scores lower than 45 for patients with preoperative pneumonia than in the other group (72.5% vs. 44.8%).
| Variable | No preoperative pneumonia n = 1277 | Preoperative pneumonia n = 109 | p  |
|----------|------------------------------------|-------------------------------|----|
| Age(y)   |                                    |                               |    |
| <70      | 363(28.4)                          | 28(25.7)                      | 0.482 |
| 70–84    | 568(44.5)                          | 55(50.6)                      |    |
| >84      | 346(27.1)                          | 26(23.7)                      |    |
| Sex      |                                    |                               |    |
| Female   | 829(64.9)                          | 75(68.8)                      | 0.413 |
| Male     | 448(35.1)                          | 34(31.2)                      |    |
| Admission BMI, kg/m² |                             |                               |    |
| <18.5    | 323(25.3)                          | 36(33.1)                      | 0.335 |
| 18.5–24.9| 611(47.8)                          | 48(44.0)                      |    |
| 25–29.9  | 320(25.1)                          | 24(21.9)                      |    |
| ≥ 30     | 23(1.8)                            | 1(0.9)                        |    |
| ASA physical status classification |                       |                               |    |
| 1        | 46(3.6)                            | 5(4.6)                        | 0.349 |
| 2        | 642(50.3)                          | 45(41.3)                      |    |
| 3        | 492(38.5)                          | 49(45.2)                      |    |
| ≥4       | 97(7.6)                            | 10(0.5)                       |    |
| ADL score |                                    |                               |    |
| 0–20     | 0(0.0)                             | 6(5.5)                        | <0.001 |
| 25–40    | 572(44.8)                          | 73(67.0)                      |    |
| 45–60    | 380(29.8)                          | 24(22.0)                      |    |
| 65–80    | 241(18.9)                          | 6(5.5)                        |    |
| 85–100   | 84(6.6)                            | 0(0.0)                        |    |
| Comorbidities and other histories |                       |                               |    |
| Congestive heart failure |                       |                               |    |
| Prior myocardial infarction |                       |                               |    |
| COPD     |                                    |                               |    |
| Anemia (hemoglobin <110 g/L) |                       |                               |    |
| Stroke   |                                    |                               |    |
| Dementia |                                    |                               |    |
| Diabetes |                                    |                               |    |
| Chronic Kidney Disease |                       |                               |    |
| Malignancy |                                    |                               |    |
| Smoking  |                                    |                               |    |
| Surgical characters |                       |                               |    |
| Fracture characteristics |                       |                               |    |
| Femoral neck fracture |                       |                               |    |
| Intertrochanteric fracture |                       |                               |    |
| Subtrochanteric fracture |                       |                               |    |
| Multiple Locations/other |                       |                               |    |
| Surgical delay(h) |                       |                               |    |
| ≤24      | 614(48.1)                          | 52(47.5)                      | 0.201 |
| >24 and ≤48 |                       |                               |    |
| >48      | 577(45.2)                          | 48(43.6)                      |    |
| Surgery type |                       |                               |    |
| Internal fixation |                       |                               |    |
| Hemiarthroplasty |                       |                               |    |
| Total hip arthroplasty |                       |                               |    |
| Anesthesia type |                       |                               |    |
| General  | 257(20.1)                          | 23(21.1)                      | 0.808 |
| Regional | 1020(79.9)                         | 86(78.9)                      |    |

Outcomes of patients with or without preoperative pneumonia

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Table 1
Baseline characteristics of enrolled patients

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a. Epidural, spinal anesthesia or peripheral neuro blockade; ADL: Activities of Daily Living; ASA, The American Society of Anesthesiologist BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease;
Outcomes of patients are reported in Table 2, patients with preoperative pneumonia were having longer hospital stay (15 vs. 12, p < 0.001) and ICU length of stay (7 vs. 0, p < 0.001) than patients free of preoperative pneumonia. Both 30-day mortality (11.9% vs. 5%, p = 0.002) and 1-year mortality (33.9% vs. 16.3%, p < 0.001) were higher in patients with preoperative pneumonia, while in comparison of the rate of 1-year readmission there were no difference (41.3% vs 37.1%, p = 0.379).

|                         | No preoperative pneumonia | Preoperative pneumonia | P     |
|-------------------------|---------------------------|------------------------|-------|
| Hospital stay(days)     | 12(7–16)                  | 15(11–19)              | < 0.001|
| ICU length of stay(days)| 0(0–3)                    | 7(2–12)                | < 0.001|
| 30-day mortality        | 64(5.0%)                  | 13(11.9%)              | 0.002 |
| 1-year mortality        | 208(16.3%)                | 37(33.9%)              | < 0.001|
| Readmission within 1 year| 474(37.1%)               | 45(41.3%)              | 0.379 |

Values are given as median (25th to 75th percentiles) or number (%). ICU: Intensive Care Unit.

Risk factors of 1-year mortality in patients with preoperative pneumonia

Analysis of risk factors for 1-year mortality with preoperative pneumonia was reported in Table 3. Based on previous studies, risk factors that may associated with 1-year mortality (including BMI, ADL score, CURB-65 score, surgical delay, anesthesia type, ASA score) were tested by univariate analysis. Only BMI, CURB-65 score, Anesthesia type had a p value lower than 0.1 and were tested by multivariate logistic regression model, as described in Table 4. After processing, the factors remained in the model including BMI (≤ 18.5 kg/m², OR 3.99, 95%CI 1.60–9.99, p = 0.003), CURB-65 score (≥ 3, OR 3.31, 95%CI 1.22–8.94, p = 0.018), Anesthesia type (Regional, 0.22, 95%CI 0.09–0.66, p = 0.006).

| Variable                  | Univariate analysis | Multivariate analysis |
|---------------------------|---------------------|-----------------------|
|                           | OR                  | 95% CI                | P       | OR                  | 95% CI                | P       |
| BMI (kg/m²)               |                     |                       |        |                     |                       |        |
| ≥18.5                     | 1                   | 4.594                 | 1.95–10.81 | < 0.001 | 3.99                 | 1.60–9.99            | 0.003 |
| <18.5                     |                     |                       |        |                     |                       |        |
| ADL score                 |                     |                       |        |                     |                       |        |
| ≥45                       | 1                   | 1.98                  | 0.67–5.87 | 0.219               |                       |                       |        |
| <45                       |                     |                       |        |                     |                       |        |
| CURB-65 score             |                     |                       |        |                     |                       |        |
| <3                        | 1                   | 12.50                 | 6.18–19.43 | < 0.001 | 3.31                 | 1.22–8.94            | 0.018 |
| ≥3                        |                     |                       |        |                     |                       |        |
| Surgical delay (h)        |                     |                       |        |                     |                       |        |
| ≤24                       | 1                   | 1.33                  | 0.39–4.5 | 0.650               |                       |                       |        |
| >24                       |                     |                       |        |                     |                       |        |
| Anesthesia type           |                     |                       |        |                     |                       |        |
| General                   | 1                   | 0.24                  | 0.10–0.59 | 0.002 | 0.22                 | 0.09–0.66            | 0.006 |
| Regional                  |                     |                       |        |                     |                       |        |
| ASA score                 |                     |                       |        |                     |                       |        |
| ≤3                        | 1                   | 0.80                  | 0.36–1.76 | 0.58          |                       |                       |        |
| >3                        |                     |                       |        |                     |                       |        |

ADL, Activities of Daily Living; ASA, The American Society of Anesthesiologists; BMI, Body Mass Index; CURB-65, Confusion, Uremia, Respiratory Rate, BP, Age ≥ 65 years;
Table 4
Adjusted OR of observed 1-year mortality stratified by CURB-65 scores

| CURB-65 score | Observed 1-year mortality (% of death/total) | OR (95% CI) | P | P for trend |
|---------------|---------------------------------------------|-------------|---|------------|
| 0             | 18.2 (2/11) (As reference)                  |             |   |            |
| 1             | 20.7 (6/29)                                 | 1.17 (0.20–6.94) | 0.860 | 0.006      |
| 2             | 28.6 (8/28)                                 | 1.80 (0.32–10.23) | 0.507 |            |
| 3             | 38.5 (6/13)                                 | 3.85 (1.08–25.30) | 0.047 |            |
| 4             | 41.2 (8/17)                                 | 4.00 (1.66–24.30) | 0.042 |            |
| 5             | 81.8 (7/11)                                 | 7.87 (2.10–38.12) | 0.039 |            |

OR analyzed by multivariate logistic regression with adjustments for BMI and Anesthesia type; CURB-65, Confusion, Uremia, Respiratory Rate, BP, Age ≥ 65 years; OR, Odd Ratio.

Distribution of preoperative pneumonia severity and its influences on 1-year mortality

Distribution of patients with preoperative pneumonia in different severity groups and the adjusted (for BMI, Anesthesia type) odd ratios (OR) of 1-year mortality with each CURB-65 score were depicted in Table 4. 1-year mortality of these patients ranged from 18.2–81.8%. The p value for trend of CURB-65 score to 1-year mortality after adjustment for BMI and anesthesia type was 0.006. When CURB-65 score ≥ 3, patients had significant risk of 1-year mortality. Patients with score 5 had the highest 1-year mortality of 81.8% (OR = 7.87, 95% CI 2.10–38.12).

Survival analysis of patients with preoperative pneumonia

Figure 1 depicted survival curve of patients free of preoperative pneumonia and patients with preoperative pneumonia. The analysis was performed with COX regression model, which adjusted for baseline difference between groups (ADL score) and possible risk factors of 1-year mortality (BMI, anesthesia type). The HR of 1-year mortality for patient with preoperative pneumonia and patients in the other group was 2.20 (95% CI 1.55–3.12, p < 0.001).

Analysis of survival condition of patients without preoperative pneumonia and patients with different pneumonia severity (evaluated with CURB-65 score) were also performed with COX regression, adjusting for aforementioned factors (depicted in Fig. 2). Only patients with CURB-65 score 3 (HR 3.12, 95% CI 1.39–7.03, p = 0.006), 4 (HR 3.41, 95% CI 1.69–6.92, p = 0.001) or 5 (HR 6.28, 95% CI 2.95–13.35, p < 0.001) had significant risk of mortality when compared with patients that were free of preoperative pneumonia.

Discussion

To our knowledge, this is the first study reported the long-term prognosis of preoperative pneumonia and the influence of the preoperative pneumonia had on outcomes in patients admitted for hip fracture surgery or arthroplasty.

Outcomes of patients

In this retrospective study, the incidence of preoperative pneumonia in this vary population was higher (7.86%) than the previous studies (1%-3.2%)(7, 8, 14, 15). One possible cause for this phenomenon was that we applied a case-by-case reviewing method for the diagnosis of preoperative pneumonia, which may achieve more positive diagnosis for cases with mild symptoms than using data extraction method in medical record or social health database system(8).

In our cohort, outcomes of patients with preoperative pneumonia were generally worse than that of the normal patients (Table 2). Similar to previous study(16), hospital stays were longer for patients with preoperative pneumonia.
pneumonia. In addition, we also observed a high ICU admission rate in these patients, which can be explained by high possibility of status aggravation after surgery of patients with preoperative pneumonia.

The overall 1-year mortality for hip fracture patients was 17.6%, which was close to previous studies(17, 18) (14%-22.8%) while patients with preoperative pneumonia had a 1-year mortality that significantly higher than that of patients without pneumonia (Table 2, 33.9% vs. 16.3%, p < 0.001). As depicted in Fig. 1, the survival rate of patients with preoperative pneumonia was decreasing over time and was significantly lower to those without the condition. The poor outcome of patients with preoperative pneumonia justified that it is necessary to evaluate potential risk factors for 1-year mortality in this group of patients.

**Risk factors of 1-year mortality in patients with preoperative pneumonia**

Through multivariate logistic regression, BMI < 18.5 kg/m² was identified as one of the risk factors. As reported in population based observational studies(19, 20), low BMI (< 20 or 22 kg/m² in this two study) was associated with high 30-day and 1-year mortality after surgery. A Meta-analysis by Nie et al. revealed that this kind of survival advantage in relatively “obese” patients also existed in patients of various populations that diagnosed with pneumonia. A possible explanation other researchers(21) proposed was that patients with lower BMI may have more comorbidities than other patients, which caused the high mortality rate. However, we did not find a difference of the distribution for most of the comorbidities across different BMI groups (see Appendix). A more specified study with larger sample size may provide better static power to show the difference.

Another factor we discovered in the model was the type of anesthesia in hip fracture surgery or arthroplasty. Patients under regional anesthesia (epidural, spinal or peripheral neural blockade) were having a low 1-year mortality rate. Patorno et al reported that regional anesthesia is associated with lower in hospital mortality for patients with hip fracture(22). While some studies failed to validate such an advantage(23, 24). According to a 2016 systemic review in Cochrane library(25) and another recent Meta-analysis(26), there were still no advantage of survival by regional anesthesia or more specifically peripheral neuro blockade. However, none of previous studies were focused on patients with preoperative pneumonia. The protective role of regional anesthesia in our study was possibly a result of avoiding further aggravation of pulmonary infection by avoiding intubation, deep sedation and mechanical ventilation.

CURB-65 score ≥ 3 was also indicated as a risk factor of 1-year mortality in patients with preoperative pneumonia. And in stratified analysis of odd ratios for 1-year mortality (Table 4), we found a linear correlation between CURB-65 score and 1-year mortality. However, compared to score 0, only when scores were higher than 3 that a significant increased risk of 1-year mortality existed. In COX regression (Fig. 2), the differences of survival rates were also not significant between patients with a CURB-65 score 0–2 and those free of pneumonia. Which indicating that patients with CURB-65 scores ≤ 2 may have similar long-term survival status to patients without pneumonia.

As a prediction tool for prognosis of patients with pneumonia, CURB-65 has been validated as a valuable scoring system for both 30-day and 1-year mortality in various populations(13, 27–29). Barlow et al reported that patients that were diagnosed with community acquired pneumonia and rated with low CURB-65 scores (i.e. 0-1) did not differ much in 30-day mortality, which was similar to our findings(30). Other studies have shown that a cut-off value of 3 in CURB-65 had the strongest prediction value of mortality in these patients(13, 31). Our findings indicate that in patients admitted for hip fracture surgery or arthroplasty, CURB-65 score ≥ 3 indicated significant increased risk of 1-year mortality in patients with preoperative pneumonia. Whether the integration of severity evaluation with CURB-65 score and different therapeutic strategies can improve outcomes yet to be tested in further studies.

This study must be interpreted in context of multiple limitations. First, the nature of retrospective and single center study had resulted in limited power of ruling out potential confounding factors of the prognosis of patients. Second, we were not able to include functional analysis for patients enrolled in this study for sufficient reply from patients in follow up period. Which have compromised the evaluation of influences that preoperative pneumonia had on patients. Lastly, we don’t have complete data to include detail therapies (including antibiotic treatment, airway management, ventilation support and other complementary therapies) into the analysis.
Some of these factors may affect the outcome of patients with preoperative pneumonia. These interventional factors need to be evaluated in more methodologically rigorous studies in the future.

**Conclusions**

In this single center retrospective study that consists of patients undergoing hip fracture surgery or arthroplasty, patients with preoperative pneumonia had worse prognoses than patients without this condition. BMI < 18.5 kg/m², CURB-65 score ≥ 3 were risk factors of 1-year mortality in patients with preoperative pneumonia, while regional anesthesia was a protective factor for 1-year mortality. In patients with preoperative pneumonia, CURB-65 score ≥ 3 indicated higher risk of mortality over time.

**Abbreviations**

ADL: Activities of Daily Living; ASA: American Society of Anesthesiologists; BMI: Body Mass Index; CURB-65: Confusion, Uremia, Respiratory Rate, BP, Age ≥ 65 years; HR: Hazard Ratio; OR: Odd Ratio;

**Declarations**

**Ethics approval and consent to participate**

The ethic committee of our institution waived the ethical review for this is a single case report.

**Consent for publication**

All authors have read and consented on the publication of this manuscript.

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

All authors report no conflicts of interest.

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**Authors' contributions**

SJ collected the clinical data and images and analyzed and interpreted the data, SJ wrote the manuscript in consultation with ZP, AY and JB. All authors read and approved the final manuscript.

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Figure 1

Survival curves of patients with or without preoperative pneumonia. Hazard Ratio: 2.20 (95% CI 1.55-3.12), p<0.001, adjusted for ADL score BMI and anesthesia type. ADL: Activities of Daily Living; BMI: Body Mass Index; HR: Hazard Ratio.
Figure 2

Survival curves of patients without preoperative pneumonia or different severity of preoperative pneumonia. Hazard ratio of mortality in patients with different CURB-65 scores to patients without preoperative pneumonia: CURB-65 0(HR 0.96, 95%CI 0.24-3.86, p=0.958), 1(HR 1.72, 95%CI 0.88-3.35, p=0.113), 2(HR 2.96, 95%CI 0.93-5.21, p=0.067), 3(HR 6.28, 95%CI 2.95-13.35, p<0.001), 4(HR 3.41, 95%CI 1.69-6.92, p=0.001), 5(HR 6.28, 95%CI 2.95-13.35, p<0.001). Adjusted for ADL score BMI and anesthesia type. ADL: Activities of Daily Living; BMI: Body Mass Index; CURB-65: Confusion, Uremia, Respiratory Rate, BP, Age ≥ 65 years; HR: Hazard Ratio.

Supplementary Files

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