The morbidity due to tachycardia seems to be relatively higher in critically ill patients than in other patients, but the relationship between tachycardia and mortality has not been well studied. In contrast, the association between arrhythmia (mostly consisting of atrial fibrillation [Af]) and postoperative [1], critically ill [2-4], and septic patients [5-15] has been investigated in many studies. Tachycardia is commonly seen in intensive care unit (ICU) settings, e.g., intensive surgical, neurological, and medical settings. There have been few investigations regarding whether a higher heart rate (HR) or a prolonged higher HR actually affects patient outcomes. We conducted the present study to evaluate the association between tachycardia and mortality in critically ill patients. We stratified the patients (n = 476) by heart rate (HR) as LowHR, MediumHR, and HighHR groups. We also stratified them by their durations of HR > 100 (prolonged HR; tachycardia): MildT, ModerateT, and SevereT groups. We determined the six groups’ mortality. The ICU mortality rates of the LowHR, MediumHR, and HighHR groups were 1.0%, 1.5%, and 7.9%, respectively; significantly higher in the HighHR vs. LowHR group. The in-hospital mortality rates of these groups were 1%, 4.5%, and 14.6%, respectively; significantly higher in the HighHR vs. LowHR group. The ICU mortality rates of the MildT, ModerateT, and SevereT groups were 0.9%, 5.6%, and 57.1%, respectively. The mortality of the HRT = 0 (i.e., all HR ≤ 100) patients was 0%. The in-hospital mortality rates of the MildT, ModerateT, and SevereT groups were 1.8%, 16.7%, and 85.7%, respectively; that of the HRT = 0 patients was 0.5%. Both higher HR and prolonged tachycardia were associated with poor outcomes.

Key words: tachycardia, mortality, ICU, in-hospital

Tachycardia is common in intensive care units (ICUs). It is unknown whether tachycardia or prolonged tachycardia affects patient outcomes. We investigated the association between tachycardia and mortality in critically ill patients. This retrospective cohort study’s primary outcome was patient mortality in the ICU and the hospital. We stratified the patients (n = 476) by heart rate (HR) as LowHR, MediumHR, and HighHR groups. We also stratified them by their durations of HR > 100 (prolonged HR; tachycardia): MildT, ModerateT, and SevereT groups. We determined the six groups’ mortality. The ICU mortality rates of the LowHR, MediumHR, and HighHR groups were 1.0%, 1.5%, and 7.9%, respectively; significantly higher in the HighHR vs. LowHR group. The in-hospital mortality rates of these groups were 1%, 4.5%, and 14.6%, respectively; significantly higher in the HighHR vs. LowHR group. The ICU mortality rates of the MildT, ModerateT, and SevereT groups were 0.9%, 5.6%, and 57.1%, respectively. The mortality of the HRT = 0 (i.e., all HR ≤ 100) patients was 0%. The in-hospital mortality rates of the MildT, ModerateT, and SevereT groups were 1.8%, 16.7%, and 85.7%, respectively; that of the HRT = 0 patients was 0.5%. Both higher HR and prolonged tachycardia were associated with poor outcomes.

Key words: tachycardia, mortality, ICU, in-hospital

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Patients and Methods

Study design. This study was approved by the Institutional Review Board (IRB) of Okayama University Hospital. The requirement of written informed consent was waived by the IRB due to the retrospective cohort design of the study. This manuscript adheres to the applicable STROBE guidelines. The primary outcome was patient mortality in the ICU and in the hospital. After the IRB’s approval was obtained, we reviewed the records of patients in the ICU and in the hospital from September 1, 2014 to August 31, 2015, and the patients’ HR values were extracted from automatically recorded vital signs.

A total of 1,863 patients were admitted to Okayama University Hospital’s ICU during this period of time. Of these patients, we excluded the cases of the patients who were admitted to the ICU more than twice, or were discharged from the ICU within 48 h of their admission to the ICU, or were under 17 years old (Fig. 1). The remaining 476 patients were eligible and enrolled.

We first stratified the patients into three groups based only on their HR values: LowHR (100 ≤ HR < 110), MediumHR (110 ≤ HR < 120) and HighHR (HR ≥ 120). All patients’ HR values were recorded automatically in the ICU every 60 sec. For this stratification, when we describe a patient as having had an HR value ≥ 100, the HR was > 100 continuously for > 10 min in that patient. When HR values that were in-between each group’s thresholds were observed for > 10 min, the enrolled group was determined. For example, when a patient’s HR values were 105, 106, 108, etc. for >10 min, the patient was assigned to the 100 ≤ HR < 110 (LowHR) group.

We then created another three patient groups based on the duration of higher HR (tachycardia), according to our hypothesis that a prolonged higher HR is more life-threatening. The duration of higher HR was measured using the patients’ HR records, and when the HR value was over 100, it would have been counted as (HR-100). The concept of prolonged tachycardia is expressed by the following formula: (HR-100)×the time duration (min) during which the HR was >100. Since the result of this calculation is HR×time, we named this value the “HRT.” As a result, we created the formula HRT = (HR-100)×the time duration (min) during which the patient’s HR was >100. This expresses a variable equal to the areas under the curve (AUC) over 100 beats per min.

Using this formula and the patients’ data, we stratified the 476 patients into the MildT (1 ≤ HRT < 50400), ModerateT (50400 ≤ HRT < 151200), and SevereT (HRT ≥ 151200) tachycardia groups. The label ‘1 ≤ HRT < 50400’ indicates that the HR value 105 was recorded in the patient for 1 week: (105-100)×60×24×7.

The statistical analyses were performed with JMP Pro® ver. 12.2.0 (Tokyo), and differences were considered significant when the p-values were <0.05. The p-values for mortality were calculated with Fisher’s exact test. The p-values for the Kaplan-Meier curves were calculated by log rank test.

Results

The mean age of all patients was 58.4±0.9 years (Table 1). Of the 476 patients, 200 (42%) were female. The severity of illness was validated with the acute physiology and chronic health evaluation II (APACHE II) score, and the average score was 16.6±0.3 (Table 1). β-blockers were administered to 117 (24.6%) patients, and sinus rhythm was preserved in 391 (82.1%) patients (Table 1).

The characteristics of the patients in the LowHR, MediumHR, and HighHR groups (stratification by HR only) are summarized in Table 1. The ICU mortality rates of the LowHR, MediumHR, and HighHR groups were 1.0%, 1.5%, and 7.9%, respectively; the mortality of the HR <100 group was 0%. The ICU mortality
was significantly higher in the HighHR group compared to the LowHR group (Fig. 2A). The in-hospital mortality rates of the LowHR, MediumHR, and HighHR groups were 1.0%, 4.5%, and 14.6%, respectively; that of the HR < 100 group was 0.5%. In-hospital mortality was significantly higher in the HighHR group compared to the LowHR group (Fig. 2A, B).

The odds ratios (ORs) of MediumHR and HighHR against LowHR were calculated. In terms of ICU mortality, the ORs of MediumHR and HighHR were 1.5 (95%CI: 0.1-37.2) and 7.3 (95%CI: 1.2-138.0, p < 0.05), respectively. With respect to in-hospital mortality, the ORs of MediumHR and HighHR were 4.5 (95%CI: 0.6-91.7) and 13.7 (95%CI: 2.5-256.6, p < 0.01), respectively (Table 2).

We next analyzed the three groups stratified by the duration of HR > 100: MildT, ModerateT, and SevereT. The groups’ patient characteristics are shown in Table 3.

### Table 1 Stratification of patients by HR

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (n = 476)</th>
<th>HR &lt; 100 (n = 222)</th>
<th>100 ≤ HR &lt; 1110 (n = 98)</th>
<th>110 ≤ HR &lt; 120 (n = 67)</th>
<th>120 ≤ HR (n = 89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.4 ± 0.9</td>
<td>59.8 ± 1.2</td>
<td>60.9 ± 1.9</td>
<td>55.4 ± 2.3</td>
<td>54.6 ± 2.0</td>
</tr>
<tr>
<td>The number of Female (%)</td>
<td>200</td>
<td>92</td>
<td>53</td>
<td>23</td>
<td>32</td>
</tr>
<tr>
<td>APACHE II Score</td>
<td>16.6 ± 0.3</td>
<td>15.7 ± 0.4</td>
<td>16.3 ± 0.7</td>
<td>16.9 ± 0.8</td>
<td>18.8 ± 0.7</td>
</tr>
<tr>
<td>Use of β-blockers (%)</td>
<td>117</td>
<td>45</td>
<td>23</td>
<td>17</td>
<td>41</td>
</tr>
<tr>
<td>Sinus rhythm (%)</td>
<td>391</td>
<td>195</td>
<td>81</td>
<td>55</td>
<td>60</td>
</tr>
<tr>
<td>Int. Med. (%)</td>
<td>38 (8.0)</td>
<td>13 (5.9)</td>
<td>4 (4.1)</td>
<td>4 (10.5)</td>
<td>17 (14.4)</td>
</tr>
<tr>
<td>GI Surg.</td>
<td>138 (29.0)</td>
<td>61 (27.5)</td>
<td>30 (30.6)</td>
<td>10 (26.3)</td>
<td>37 (31.4)</td>
</tr>
<tr>
<td>Lung Surg.</td>
<td>26 (5.5)</td>
<td>6 (2.7)</td>
<td>4 (4.1)</td>
<td>4 (10.5)</td>
<td>12 (10.2)</td>
</tr>
<tr>
<td>Esop h. Surg.</td>
<td>13 (2.7)</td>
<td>7 (3.2)</td>
<td>2 (2.0)</td>
<td>2 (5.3)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Cardiac surg.</td>
<td>54 (11.3)</td>
<td>23 (10.4)</td>
<td>18 (18.4)</td>
<td>2 (5.3)</td>
<td>11 (9.3)</td>
</tr>
<tr>
<td>Neuro Surg.</td>
<td>40 (8.4)</td>
<td>24 (10.8)</td>
<td>7 (7.1)</td>
<td>1 (2.6)</td>
<td>8 (6.8)</td>
</tr>
<tr>
<td>Others</td>
<td>167 (35.1)</td>
<td>88 (39.6)</td>
<td>33 (33.7)</td>
<td>15 (39.5)</td>
<td>31 (26.3)</td>
</tr>
</tbody>
</table>

(†: < 0.05, *: < 0.01)

**Fig. 2 A.** The mortality in the ICU and in the hospital. The patients were stratified by HR alone as LowHR (100 ≤ HR < 110), MediumHR (110 ≤ HR < 120), and HighHR (HR ≥ 120). Both the ICU and in-hospital mortality rates were significantly higher in the HighHR group compared to the LowHR group. †p < 0.05, *p < 0.01 by Fisher’s exact test; B. The Kaplan-Meier curves of the LowHR, MediumHR, and HighHR groups. These results confirmed those illustrated in panel A. †p < 0.05, *p < 0.01 by log rank test.
The usage of β-blockers was significantly higher in the ModerateT and SevereT groups compared to the MildT group. For the MildT, ModerateT, and SevereT groups, the ICU mortality rates were 0.9%, 5.6%, and 57.1%, respectively, while that of the HRT = 0 group was 0%, since HR ≤ 100 means HRT = 0. The ICU mortality was significantly higher in the SevereT group than in the MildT group (p < 0.01) (Fig. 2A). The in-hospital mortality rates of the MildT, ModerateT, and SevereT groups were 1.8%, 16.7%, and 85.7%, respectively; that of the HRT = 0 group was 0.5%. In-hospital mortality was significantly higher in the ModerateT and SevereT groups compared to the MildT group (p < 0.05 and p < 0.01, respectively) (Fig. 3A, B).

We calculated the ORs of ModerateT and SevereT against MildT. In terms of ICU mortality, the ORs of ModerateT and SevereT were 3.3 (95%CI: 0.2-24.0) and 75.0 (95%CI: 12.9-514.9, p < 0.01), respectively. For in-hospital mortality, the ORs of ModerateT and SevereT were 5.5 (95%CI: 1.1-21.5, p < 0.05) and 165.8 (95%CI: 24.6-3333.7, p < 0.01), respectively (Table 4).

**Discussion**

Our retrospective analyses revealed three major findings. First, higher HR was associated with poor patient outcomes and tachyarrhythmia. Second, prolonged tachycardia and higher HR were also profoundly associated with poor patient outcomes. Finally, patients with HR < 100 had substantially lower mortal-
ity.

Regarding the first finding that higher HR alone contributed to poor patient outcomes, our results suggest that both the ICU mortality and the in-hospital mortality of patients with HR ≥ 120 (the HighHR group) were significantly higher than those of the patients with 100 ≤ HR < 110 (the LowHR group) (Fig. 2A, B). With this patient stratification, the modality of arrhythmia, which is predominantly Af, was significantly higher compared to the LowHR patients with HR < 100, the LowHR group, or the MediumHR group (Table 1). This suggests that higher HR has a significant association not only with Af or other arrhythmias but also with significantly increased mortality. Although the association between arrhythmia and mortality was unclear in the present study, there were no cardiac deaths, such as those due to ventricular fibrillation.

Our second major finding was that prolonged tachycardia with higher HR contributed to higher mortality of patients in the ICU and hospital. Interestingly, even though mortality was highest in the SevereT group, the number of patients with arrhythmia in this group was not significantly higher than the other groups. This result suggests that prolonged tachycardia with higher HR contributes independently to increased mortality.

Finally, the most surprising finding was that critically ill patients with HR < 100 had 100% survival in the ICU, and their hospital survival rate was still > 99%. Overall, 12.2% of the 222 patients with HR < 100 had arrhythmias, which suggests that even if a patient has an arrhythmia, maintaining his or her HR at < 100 may be beneficial.

To the best of our knowledge, the association between tachycardia and mortality has been investigated very rarely [16], but the relationship between Af and mortality has been investigated several times [4-12, #151] and was confirmed in the present study.

Fig. 3 A, The mortality in the ICU and in the hospital. The patients were stratified by (HR-100) × duration of time (min) when HR is > 100: MildT (1 ≤ HRT < 50400), ModerateT (50400 ≤ HRT < 151200), and SevereT (HRT ≥ 151200). In terms of both the ICU and in-hospital mortality, the mortality rates of the SevereT group were significantly higher than those of the MildT group. †p < 0.05, *p < 0.01 by Fisher’s exact test; B, The Kaplan-Meier curve of the MildT, ModerateT, and SevereT groups. The survival rates of ModerateT and SevereT groups were significantly higher than those of the MildT group, confirming the results shown in panel A. †p < 0.05, *p < 0.01 by log rank test.

Table 4 Odds Ratio of group SevereT and ModerateT to MildT

<table>
<thead>
<tr>
<th>Group</th>
<th>OR</th>
<th>95%CI</th>
<th>p value</th>
<th>OR</th>
<th>95%CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MildT</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ModerateT</td>
<td>3.3</td>
<td>0.2-24.0</td>
<td>0.35</td>
<td>5.5</td>
<td>1.1-21.5</td>
<td>&lt;0.05†</td>
</tr>
<tr>
<td>SevereT</td>
<td>75.0</td>
<td>12.9-514.9</td>
<td>&lt;0.01*</td>
<td>165.8</td>
<td>24.6-3333.7</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

(†: <0.05, *: <0.01)
15-17]. Several studies have shown an association between AF and sepsis or septic shock [5-9, 11-17]. Annane concluded that supraventricular arrhythmias did not significantly impact the hospital survival of critically ill patients [3], while other researchers suggested that supraventricular arrhythmia, especially new-onset AF, had quite a large impact on the survival of patients with sepsis [5, 7-9, 11, 12]. Our hospital's ICU has a mixed-function design, and it functions relatively more like a surgical ICU, but the present HighHR group still had significantly more patients with arrhythmias and had higher mortality rates. Theerawit noted that critically ill patients with HR >130 had a higher mortality than patients with HR ≤130 [6]; our present findings might reflect that result.

Although there have been few reports of the association between HR and patient outcomes, a few research groups have investigated the effect of the β1-receptor blocker esmolol in patients with septic shock [13, 15]. They concluded that esmolol could achieve HR reduction to the target level without adverse events [15] and without changing cardiac output, whereas norepinephrine requirements were reduced [13]. There is only one report of an investigation of the relationships of HR and new-onset atrial fibrillation in patients with septic shock: a prospective observational study. Crit Care (2010) 14: R108.

References


