







# Initial assessment in emergency departments by chief complaint and respiratory rate

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## Abstract

**Background:** Understanding heterogeneity of the respiratory rate (RR) as a risk stratification marker across chief complaints is important to reduce misinterpretation of the risk posed by outcome events and to build accurate risk stratification tools. This study was conducted to investigate the associations between RR and clinical outcomes according to the five most frequent chief complaints in an emergency department (ED): fever, shortness of breath, altered mental status, chest pain, and abdominal pain.

**Methods:** This retrospective cohort study examined ED data of all adult patients who visited the ED of a tertiary medical center during April 2018–September 2019. The primary exposure was RR at the ED visit. Outcome measures were hospitalization and mechanical ventilation use. We used restrictive cubic spline and logistic regression models to assess the association of interest.

**Results:** Of 16 956 eligible ED patients, 4926 (29%) required hospitalization; 448 (3%) required mechanical ventilation. Overall, U-shaped associations were found between RR and the risk of hospitalization (eg, using RR = 16 as the reference, the odds ratio [OR] of RR = 32, 6.57 [95% CI 5.87–7.37]) and between RR and the risk of mechanical ventilation. This U-shaped association was driven by patients' association with altered mental status (eg, OR of RR = 12, 2.63 [95% CI 1.25–5.53]). For patients who have fever or shortness of breath, the risk of hospitalization increased monotonously with increased RR.

**Conclusions:** U-shaped associations of RR with the risk of overall clinical outcomes were found. These associations varied across chief complaints.

## KEYWORDS

chief complaint, emergency department, hospitalization, mechanical ventilation, respiratory rate

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## 1 | INTRODUCTION

Respiratory rate (RR), an important vital sign, is observed routinely in primary care settings and at emergency departments (EDs). Abnormal RR indicates patient severity and severe underlying conditions, including cardiovascular and respiratory diseases.<sup>1,2</sup> Although RR has likely been neglected in busy settings despite its clinical importance,<sup>3,4</sup> current practice can include measurement of RR with the emergence of innovative devices (eg, wearable devices<sup>5</sup>) and an e-triage system.<sup>6</sup>

Physicians are unable to assess RR apart from patient chief complaints because the prognostic value of RR might differ across underlying medical conditions.<sup>3</sup> This difficulty is represented by chief complaints as patient-reported symptoms.<sup>2</sup> Therefore, the estimated risk of clinical outcomes (eg, hospitalization) based on RR is expected to differ across chief complaints. For example, the estimated risk of hospitalization based on an RR of 30/min is expected to be different between patients with headache (suggesting hyperventilation) and those with fever (suggesting sepsis).<sup>7</sup> It remains unclear whether the associations of RR with clinical outcomes differ across chief complaints. Understanding the actual heterogeneity in the importance of RR as a risk stratification marker across chief complaints is important to reduce the misinterpretation of estimated risk of outcomes and to build accurate risk stratification tools.

To address knowledge gaps in the literature, we investigated the association of RR with clinical outcomes (ie, hospitalization and mechanical ventilation use) according to the five most frequent chief complaints in the ED: fever, shortness of breath, altered mental status, chest pain, and abdominal pain.

## 2 | METHODS

### 2.1 | Study design and setting

This retrospective cohort study used data from the ED of Hitachi General Hospital accumulated from April 1, 2018, through September 31, 2019. Hitachi General Hospital, a tertiary care center with approximately 20 000 annual ED visits, serves an area with approximately 3 million residents. The ED of Hitachi General Hospital is staffed by emergency attending physicians. It has affiliations with transitional and emergency medicine residency training programs. Hitachi General Hospital has 18 intensive care units and 6 cardiac care units. The medical charts were structured using the Next Stage ER system (TXP Medical Co., Ltd.).<sup>8</sup> Using it, physicians can input data such as vital signs, chief complaints,<sup>9</sup> past medical history, physical assessments, and clinical diagnoses using prespecified forms. Consequently, reliably structured data are obtainable more efficiently than by retrospective extraction of structured information by the application of natural language processing techniques to unstructured electronic medical records.<sup>8</sup> This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Hitachi General Hospital.

The requirements for informed consent were waived because of the retrospective characteristics of the study.

### 2.2 | Study population

After including all adults (aged  $\geq 18$  years) who visited the ED for medical reasons, we used the *International Classification Codes, Tenth Revision (ICD-10)*, to exclude patients with trauma, cardiac arrest, postcardiac arrest syndrome at the time of arrival, and patients who visited the ED for other nonmedical reasons.<sup>10</sup> Specifically, we excluded patients with ICD-10 codes of I46 (cardiac arrest) or S00-U85 (Table S1 provides details) in the primary diagnostic field.

### 2.3 | Data collection

We extracted information related to patient demographics (age and gender), chief complaints, past medical history according to the Charlson Comorbidity Index,<sup>11</sup> vital signs, use of mechanical ventilation, and patient disposition (eg, hospitalization and in-hospital death). Chief complaints were entered by nurses or physicians using the prespecified list of chief complaints and free full texts. The chief complaints were recorded in both forms: (a) original text and (b) standardized data using 223 chief complaint categories based on the Japan Acuity and Triage Scale (JTAS), which was developed based on the Canadian Triage and Acuity Scale.<sup>12</sup> Past medical history was translated into ICD-10 codes. Then, the Charlson Comorbidity Index was calculated.<sup>13</sup>

### 2.4 | Exposure

The primary exposure was RR counted by a nurse or physician. At Hitachi General Hospital, RR is measured by counting breaths for 15 seconds and then multiplying that number by four in most cases. In some cases, RR was measured using a chest wall movement sensor, or using the standard method of recording counts during a minute.

### 2.5 | Outcome measures

Primary outcomes were hospitalization and mechanical ventilation use. The decision for admission was made based on the physician's discretion. The use of mechanical ventilation was defined using the procedure code of tracheal intubation, mechanical ventilation, and noninvasive positive pressure ventilation referred from earlier reports of the literature.<sup>14</sup>

### 2.6 | Statistical analysis

The dataset was cleaned. Missing values were imputed because there were readily apparent outliers (respiratory rate  $<3$ /min

or  $>60/\text{min}$ )<sup>15</sup> and *missingness* in the dataset because of the retrospective design. We treated the readily apparent outliers as missing (24 records in RR). Missing data occurred with 35.3% of the RR among patients who visited the ED for medical reasons (Table S2). We conducted imputations using the random forest method to address the missing data.<sup>16</sup> for main analysis and multiple imputation chained equations for sensitivity analysis. Random forest imputation is a nonparametric algorithm that can accommodate nonlinearities and interactions. It requires no particular parametric model to be specified.<sup>17</sup> We used the following variables for multiple imputations: patient characteristics, vital signs, comorbidities, and outcomes. Correlation of the log-transformed proportion of patients for each RR was found between preimputation and postimputation data, as presented in Figure S1. For data shown in the plot, the correlation efficiency was 0.94. The Frobenius norm of the correlation matrix of the features included in the imputation model was 29751.97.

Next, we depicted the associations of the RR with clinical outcomes using a locally weighted scatterplot smoother (Lowess) curve because the association of interest might have a nonlinear association. Lowess is a method for estimating local regression surfaces to remove noise from raw data and to clarify graphical presentations.<sup>18</sup> We then fitted restrictive cubic spline regression models to calculate the odds ratios (OR) for outcomes to ascertain the association of interest.<sup>19</sup> Whereas logistic regression using an independent variable as a categorical variable is the conventional method to address the nonlinear relation, this transformation induces a loss of power, has ineffective fitting, and engenders poor modeling of the relation. The restrictive cubic spline regression model is useful for exploring nonlinear associations and for representing nonlinear relations for continuous variables.<sup>20</sup> The observed range of the variable is divided by breakpoints, called knots.<sup>20</sup> Within each knot is a cubic polynomial.<sup>21</sup> These polynomials are constrained to fit together smoothly at each knot.

We also depicted the associations of RR with clinical outcomes according to the five most frequent chief complaints in the current dataset: fever, shortness of breath, altered mental status, chest pain, and abdominal pain. In cases where a patient had multiple chief complaints, we used the primary chief complaint according to the physician's discretion at the initial assessment. Restricted cubic spline regression models were fitted to calculate the odds ratios for the risk of hospitalization.

To verify the robustness of our inference, we first employed a logistic regression model using RR as a categorical variable and a missing indicator (ie, create a category of missing). Second, because approximately two-thirds of the patients were missing in RR, we compared the observed characteristics and outcomes between patients with RR and those without to assess the generalizability of our findings in patients with no record of RR. Two-sided *P*-values  $<.05$  were inferred as significant. Statistical analyses were performed using software (Stata ver. 15.0 SE; StataCorp LP).

## 3 | RESULTS

### 3.1 | Patient characteristics

From April 2018 through September 2019, there were 29 669 ED visits. Of these, we excluded 8078 children, 2125 for unknown age, 2178 visits for nonmedical reasons, and 332 visits for cardiac arrest on arrival. The remaining 16 956 visits were eligible for inclusion in the primary analysis. Table 1 displays summary statistics of the study population. The median age was 69 years, and 54% of the patients were male; 38% had been transported to the hospital by emergency medical services. Approximately 23% of patients had a Charlson Comorbidity Index  $\geq 1$  such as cerebrovascular disease, chronic pulmonary disease, or congestive heart failure.

At the initial assessment, according to the JTAS criteria, 24% were emergent, 19% were urgent, 18% were less urgent, and 6% were nonurgent. The median values of the respective vital signs at the initial assessment were the following: 139 mm Hg of systolic blood pressure (interquartile range [IQR], 121-160 mm Hg), 81 mm Hg of diastolic blood pressure (IQR, 69-93 mm Hg), 86 per minute of pulse rate (IQR, 74-100 per min), 20 per minute of RR (IQR, 18-24 per min), 97% of oxygen saturation (IQR, 96%-98%), and 36.7°C of body temperature (IQR, 36.3-37.2°C). The distribution of RR is shown in Figure S2. The most frequent chief complaint was abdominal pain (7.6%), followed by fever (7.5%), shortness of breath (5.2%), altered mental status (3.7%), and chest pain (3.6%). Overall, 4926 (29%) required hospitalization; 448 (2.6%) required mechanical ventilation.

### 3.2 | Associations between the respiratory rate and clinical outcomes

In the graphical assessment with the Lowess curve (Figure 1), a U-shaped association was found between RR and the risk of hospitalization. In the spline regression model using a RR of 16 as the reference, the risk of hospitalization was significantly higher with a higher RR but not with a lower RR (eg, using RR of 16 as the reference, the OR of RR = 12 was 0.96 [95% CI, 0.79-1.18] and the OR of RR  $\geq 32$  was 6.57 [95% CI, 5.87-7.37]) (Table 2). The numbers of patients in the respective categories of RR are shown in Table S3.

Subgroup analysis by chief complaint showed that the associations of RR with the risk of hospitalization varied across chief complaints (Figure 2 and Table 2). In patients with fever, shortness of breath, or abdominal pain, the risk of hospitalization increased monotonously with an increase in RR (using RR of 16 as the reference, the OR of RR of  $\geq 32$  was 5.52 [95% CI, 3.48-8.74] in fever, 7.62 [95% CI, 4.67-12.43] in shortness of breath, and 3.06 [95% CI, 1.83-5.12] in abdominal pain). A U-shaped association was found in patients with altered mental status (eg, using a RR of 16 as the reference, the OR of RR = 12 was 2.63 [95% CI, 1.25-5.53] and RR  $\geq 32$  was 9.55 [95% CI, 3.54-25.67]), whereas the relation was moderate in patients with chest pain.

Similar associations were found in the analyses using mechanical ventilation use as an outcome (Figure 1 and Table 2), whereas a significant

**TABLE 1** Patient characteristics in the overall study population (n = 16 956)

Variables	n = 16 956
Age, year, median (IQR)	69 (50, 80)
Male gender	9170 (54.1%)
Route	
Emergency medical service	6351 (37.5%)
Walk-in	10 432 (61.5%)
Rapid response system	164 (1.0%)
Others	2 (<1%)
Charlson Comorbidity Index	
Low (0)	13 065 (77.0%)
Medium (1-2)	2868 (16.9%)
High (3-4)	760 (4.5%)
Very high (≥5)	263 (1.6%)
Japan Triage Acuity Scale (JTAS)	
1: Blue (resuscitation)	1018 (6.0%)
2: Red (emergent)	4080 (24.1%)
3: Yellow (urgent)	3132 (18.5%)
4: Green (less urgent)	3052 (18.0%)
5: White (nonurgent)	993 (5.9%)
Chief complaint	
Fever	1264 (7.5%)
Shortness of breath	879 (5.2%)
Altered mental status	632 (3.7%)
Chest pain	612 (3.6%)
Abdominal pain	1282 (7.6%)
Vital signs	
Systolic blood pressure, mm Hg, median (IQR)	139 (121, 160)
Diastolic blood pressure, mm Hg, median (IQR)	81 (69, 93)
Pulse rate, /min, median (IQR)	86 (74, 100)
Respiratory rate, /min, median (IQR)	20 (18, 24)
Oxygen saturation, %, median (IQR)	97 (96, 98)
Body temperature, °C, median (IQR)	36.7 (36.3, 37.2)
Outcomes	
Hospitalization	4926 (29.0%)
Mechanical ventilation	448 (2.6%)
Death	478 (2.8%)

Abbreviation: IQR, interquartile range.

U-shaped association was found overall for patients with limited statistical power (using a RR of 16 as the reference, the OR of a RR = 12 was 2.69 [95% CI, 1.24-5.85]; the RR ≥ 32 was 33.85 [95% CI, 22.98-49.86]).

### 3.3 | Sensitivity analyses

A similar association was observed when using a logistic regression model and a missing indicator. For example, the OR of RR < 12 was

3.35 (95% CI 1.41-7.91) for hospitalization outcomes (Table S4); the OR of RR < 12 was 17.55 (95% CI 3.90-79.08) for mechanical ventilation use. We conducted additional analyses using cutoff values of NEWS and APACHE II score, with results as presented in Table S5. Similarly, to the main analysis, both higher and lower categories were found to be associated with a higher risk of hospitalization. From the subgroup analysis limited to walk-in patients, similar associations were observed (Table S6). There were 478 deaths (2.8%). As shown in Table S7, higher RR was associated with higher in-hospital mortality in the case-complete analysis. We also applied multiple imputation chained equations and analyzed data to ascertain similar associations to those found through the primary analysis (Table S8).

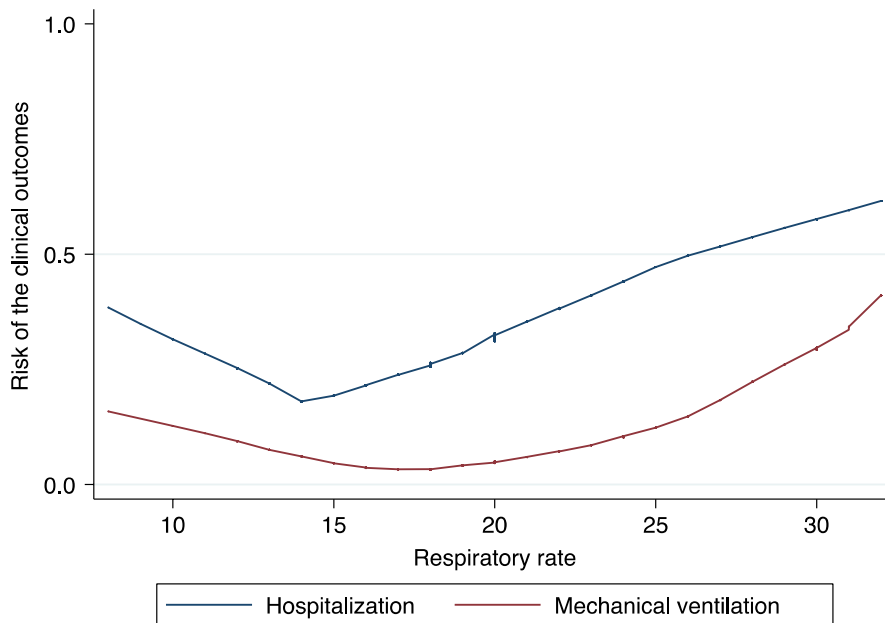
### 3.4 | Comparison of imputed data with case-complete data

When comparing the characteristics and outcomes between patients with a record of RR and those without, patients with a record of RR had a more severe condition than those without (Table S9). Moreover, patients without a record of RR were more likely to be walk-in patients, have lower urgency, and have a lower risk of hospitalization or mechanical ventilation use, although no significant difference was found in vital signs.

## 4 | DISCUSSION

For this analysis of 16 956 patients who presented to the ED for medical reasons, U-shaped associations of RR were found with the risk of hospitalization and mechanical ventilation use. In addition, the risk of clinical outcomes varied across chief complaints. Specifically, a U-shaped association was found in patients with altered mental status. The increased risk of clinical outcomes with higher RR was prominent in patients with shortness of breath, but the relation was moderate in patients with chest pain. This report is the first of a comprehensive study conducted to demonstrate nonlinear associations of RR with clinical outcomes, with subgrouping by chief complaint. These fundamental, visualized associations represent an important basis for the initial assessment and the development of risk stratification tools using RR.

The best discriminator among vital signs for identifying high-risk patients in the ED is RR.<sup>22</sup> Indeed, an earlier case-control study (n = 320) demonstrated that RR has a linear relation with the requirement for admission to the ED.<sup>23</sup> Despite the attracting discrimination ability of RR, earlier studies of initial assessments were likely to disregard the importance of chief complaints<sup>23</sup> and to collapse RR into categorical variables under the assumption of a linear relation between RR and clinical outcomes.<sup>24</sup> Furthermore, the importance of chief complaints for initial assessment is well known, but their use for clinical research has been discouraged because of the difficulty in extracting chief complaints from the free full-text area and limited availability for standardized data.



**FIGURE 1** Association between respiratory rates and the risk of clinical outcomes among overall emergency department visits. Associations are shown between the RR and clinical outcomes using a locally weighted scatterplot smoother (Lowess) curve. RR, respiratory rate

**TABLE 2** Association between respiratory rate and the risk of hospitalization using cubic spline models (n = 16 956)

Outcomes	Respiratory rate (per minute)					
	12	16	20	24	28	32
Hospitalization						
Overall	0.96 (0.79-1.17)	Ref.	1.85 (1.66-2.07)	4.54 (4.13-4.99)	6.11 (5.54-6.75)	6.57 (5.87-7.37)
Grouped by selected chief complaint						
Fever	0.95 (0.33-2.69)	Ref.	0.79 (0.49-1.27)	3.35 (2.21-5.09)	5.42 (3.51-8.38)	5.52 (3.48-8.74)
Shortness of breath	1.18 (0.66-2.11)	Ref.	1.14 (0.75-1.74)	3.55 (2.26-5.58)	6.13 (3.96-9.48)	7.62 (4.67-12.43)
Altered mental status	2.63 (1.25-5.53)	Ref.	1.23 (0.76-1.99)	2.27 (1.45-3.56)	4.05 (2.40-6.85)	9.55 (3.54-25.76)
Chest pain	1.4 (0.61-3.22)	Ref.	2.19 (1.35-3.57)	2.62 (1.67-4.10)	2.23 (1.37-3.65)	2.15 (1.25-3.72)
Abdominal pain	0.98 (0.49-1.93)	Ref.	1.94 (1.44-2.61)	2.99 (2.11-4.22)	3.03 (2.06-4.46)	3.06 (1.83-5.12)
Mechanical ventilation	2.69 (1.24-5.85)	Ref.	0.7 (0.39-1.25)	12.03 (8.03-18.03)	30.33 (20.64-44.57)	33.85 (22.98-49.86)

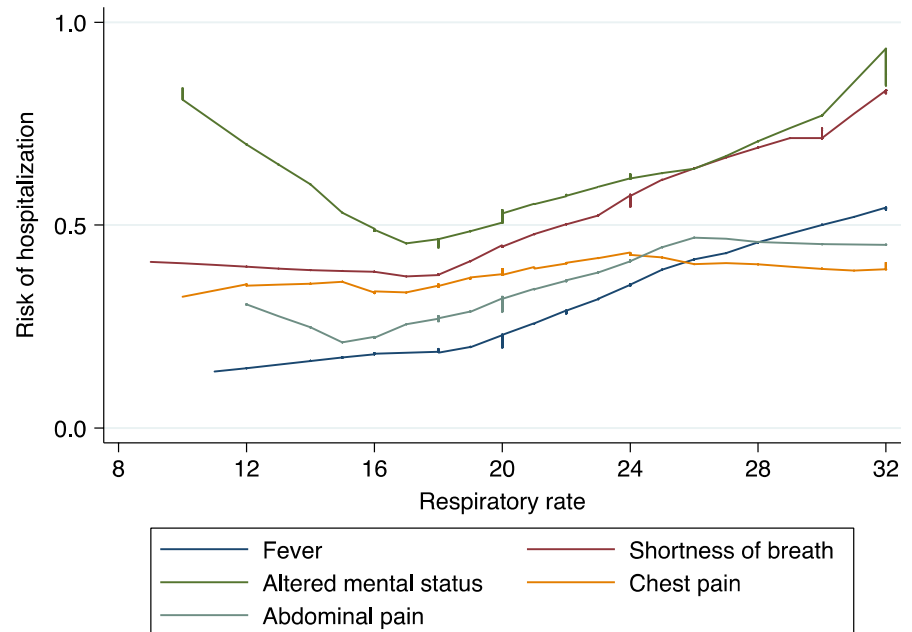
Abbreviation: Ref., reference.

Because current information technology and informatics present solutions to these barriers, future studies of the initial assessment using chief complaints, vital signs, and present illness should be accelerated with the emergence of machine-learning approaches.<sup>6</sup> In this context, our study can provide fundamentally important information to assess patient conditions and to develop more complex models for differentiating critical conditions from non-life-threatening conditions.

The heterogeneity observed in the association of RR with clinical outcomes is clinically plausible. The U-shaped association in patients

with altered mental status is explained by factors that depress the respiratory drive and the respiratory response to hypoxia and hypercarbia, such as severe stroke, metabolic and endocrine diseases (eg, hypothyroidism), and drug overdoses. The apparent, linearly increased risk of clinical outcomes in patients with shortness of breath is intuitive. When patients complain of dyspnea, their breathing is often rapid and shallow because alveolar ventilation (a product of RR and tidal volume) is driven by the arterial partial pressure of oxygen (PaO<sub>2</sub>) and the arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>).<sup>25</sup> In addition, the resulting increase in dead space is reported to be a

**FIGURE 2** Association between respiratory rates and the risk of hospitalization by chief complaint. Associations are shown between the RR and clinical outcomes by performing subgroup analysis by chief complaint using a locally weighted scatterplot smoother (Lowess) curve. RR, respiratory rate



response to increased ventilation.<sup>26</sup> Consequently, deterioration can be detected early by measuring the RR.

This analysis of 16 956 patients who presented to the ED for medical reasons revealed U-shaped associations of RR with the risk of hospitalization and mechanical ventilation use. The observed heterogeneity in the association of RR with clinical outcomes across chief complaints suggests the importance of assessing RR with chief complaints. These findings are expected to enhance the development of an accurate risk stratification tool for the initial assessment.

#### 4.1 | Potential limitations

Our study has several potential limitations. First, our data include missing data, which might represent a potential source of bias. However, this issue was minimized in our analyses using random forest imputation for missing data in continuous variables, a technique for the imputation of missing data. We observed similar findings in case-complete analysis. The results demonstrate an association between RR and clinical outcome among patients with measured RR, suggesting that such knowledge can be useful for patients regarded by medical personnel as more urgently in need of care and for decisions to measure RR in EDs. Second, our analysis did not include detailed information such as medication history, prehospital treatments (eg, oxygen flow rates), and "do not intubate" status. However, in a clinical setting, collecting all information at the time of initial assessment is impractical. Therefore, our findings are expected to be in line with the clinical setting. Third, although we used the primary chief complaint for subgroup analysis, chief complaints were not mutually exclusive. Consequently, the associations in each chief complaint might be confounded by the coexisting chief complaints. Fourth, the counting methods of RR varied among practitioners.

Nevertheless, measuring RR during one minute for every patient in a busy ED setting is impractical.<sup>27,28</sup> Finally, this was a single-center study conducted in Japan, which limits the generalizability of the results. For instance, the thresholds for hospitalization at other hospitals might differ. However, the threshold of mechanical ventilation probably does not vary.

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#### CONFLICT OF INTEREST

Dr Soeno, Dr Hara, Mr Fujimori, Dr Hashimoto, Dr Shirakawa, and Dr Goto are the contracted researchers of TXP Medical Co. Ltd. and have received personal fees from TXP Medical Co. Ltd. outside the submitted work. Dr Goto is the Chief Scientific Officer, TXP Medical Co. Ltd. Dr Sonoo is the Chief Executive Officer, TXP Medical Co. Ltd.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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