Usefulness of Acoustic Monitoring of Respiratory Rate in Patients Undergoing Endoscopic Submucosal Dissection

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Aim. The study assessed the usefulness of a recently developed method for respiratory rate (RR) monitoring in patients undergoing endoscopic submucosal dissection (ESD) under deep sedation. Methods. Study subjects comprised 182 consecutive patients with esophageal cancer or gastric cancer undergoing ESD. The usefulness of acoustic RR monitoring was assessed by retrospectively reviewing the patients’ records for age, gender, height, weight, past history, serum creatinine, RR before ESD, and total dose of sedative. Results. Respiratory suppression was present in 37.9% (69/182) patients. Continuous monitoring of RR led to detection of respiratory suppression in all these patients. RR alone was decreased in 24 patients, whereas both RR and blood oxygen saturation were decreased in 45 patients. Univariate analysis showed female gender, height, weight, and RR before treatment to be significantly associated with respiratory suppression. Multivariate analysis showed RR before treatment to be the only significant independent predictor [odds ratio (OR) 0.83, 95% confidence interval (CI) 0.73–0.95, and \( P = 0.006 \)] of respiratory suppression. Conclusion. In this study, the difference in RR before treatment between patients with and without respiratory suppression was subtle. Therefore, we suggest that acoustic RR monitoring should be considered in patients undergoing ESD under sedation to prevent serious respiratory complications.

1. Introduction

Gastric cancer remains one of the most common causes of cancer death in the world [1]. The technique of endoscopic submucosal dissection (ESD) was initially developed in Japan. This technique is increasingly used around the world as it results in increased en bloc and complete resection rates and reduced local recurrence rate [2, 3]. Since this technique requires relatively long procedure time and involves complicated maneuvers, appropriate sedation to reduce patient’s discomfort, anxiety, and pain is vital to achieve safe and effective ESD. However, sedation might lead to many serious unexpected events, such as apnea, hypotension, bradycardia, and cardiac arrest. Notably, these cardiorespiratory-related complications are a leading cause of morbidity and mortality during endoscopic procedures. Continuous venous access should be maintained to administer antagonists or resuscitated medications until sedated patients recover completely. Additionally, continuous monitoring of patient under sedation is essential for avoiding serious complications and ensuring safe endoscopic treatment. Standard monitoring of the patient undergoing endoscopic treatment includes pulse rate, arterial oxygen saturation, blood pressure, level of consciousness based on patient’s ability to respond to
This study conducted between September 2012 and March 2014 at Tokai University Hospital comprised of 182 consecutive patients with esophageal cancer or gastric cancer undergoing ESD. Continuous acoustic RR monitoring was done in all these patients. Initially, patients received 1-2 mg midazolam and 35 mg pethidine hydrochloride for induction of venous anesthesia. Additional midazolam (1-2 mg) was repeatedly administered to maintain the depth of sedation.

2. Methods

This study involved retrospective analysis of prospectively collected data on 182 consecutive patients including 24 patients...
with esophageal cancer and 158 patients with early gastric cancer. The incidence of respiratory suppression was 37.9% (69/182). RR alone was decreased in 24 patients, whereas both RR and blood oxygen saturation were decreased in 45 patients. There was no patient with decreased blood oxygen saturation alone. The incidence of circulatory suppression was 25.8%. Although some patients developed transient cardiorespiratory suppression, no severe complications attributable to sedation were reported during ESD. Therefore, resuscitation maneuvers or resuscitation drugs were not used in any patients with respiratory suppression. Similarly, no serious complications related to the ESD procedure were noted.

As shown in Table 1, univariate analysis revealed that there were no significant differences in age, past history, serum creatinine, dose of sedative, procedure time, incidence of circulatory suppression, and type of ESD between the patients with and without respiratory suppression. Notably, univariate analysis showed that female gender, height, weight, and RR before treatment were significantly associated with respiratory suppression. To rule out confounding factors, a logistic regression analysis was performed (Table 2). The RR before treatment was the only independent risk factor for respiratory suppression during ESD under deep sedation.

### 4. Discussion

Although recent studies have reported that acoustic RR monitoring is well tolerated and has sensitivity and specificity similar to those of capnometry in patients after general anesthesia, there is little information about the usefulness of this monitoring technique in patients undergoing gastrointestinal endoscopic treatment under conscious sedation [5, 8]. To the best of our knowledge, this is the first study to evaluate the usefulness of acoustic RR monitoring in patients undergoing ESD. In fact, we used it to measure the incidence of respiratory suppression in patients undergoing ESD and to assess the risk factors for respiratory suppression in these patients. Previous studies have shown that the incidence of respiratory suppression in patients undergoing gastrointestinal endoscopic treatment under conscious sedation ranges from 10 to 70%, depending on the definition of respiratory suppression, patient population, type of endoscopy, and type of sedatives [9, 10]. Markedly, in these studies, pulse oximetry was used as a surrogate measure of ventilation. However, it seems obvious that the physiological range (93%–98%) measured by pulse oximetry would not ensure adequate measurement of respiratory ventilation. Furthermore, this monitor lags far behind to detect respiratory suppression especially in patients receiving supplemental oxygen [4]. An important criterion in monitoring respiratory function during endoscopic treatment is the ability to find out those respiratory suppressed patients who remain undetected by pulse oximetry. Consequently, some recent studies recommend monitoring the patients undergoing gastrointestinal endoscopy under sedation for respiratory suppression using capnometry, since it has been increasingly acknowledged as a superior method for detecting early respiratory suppression during therapeutic upper endoscopy [9]. However, it is technically difficult to measure RR using capnometry in patients receiving nasal oxygen, as both these procedures usually require nasal cannulas or face masks. Furthermore, patients undergoing ESD could be breathing through the open mouth contributing to the unreliability of the measured RR. Additionally, since carbon dioxide insufflation is being increasingly used in ESD to reduce abdominal pain and discomfort caused by bowel hyperextension, it may be quite difficult to accurately monitor RR by measuring end tidal carbon dioxide using capnometry. Therefore, an accurate and reliable method of monitoring the RR in patients undergoing ESD is an urgent need.

In this study, we used acoustic RR monitoring continuously in patients undergoing ESD. Based on our definition of respiratory suppression, approximately 40% of the study subjects developed at least one episode of respiratory suppression. A decrease in both RR and blood oxygen saturation occurred approximately in two-thirds of the patients who developed respiratory suppression, whereas

#### Table 1: A comparison of patients who developed respiratory suppression during endoscopic submucosal dissection [RS(+) ] and those who did not [RS(−)].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RS(−)</th>
<th>RS(+)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>86/27</td>
<td>42/27</td>
<td>0.03</td>
</tr>
<tr>
<td>Age (y, mean ± SD)</td>
<td>69.9 ± 7.6</td>
<td>71.3 ± 9.1</td>
<td>0.20</td>
</tr>
<tr>
<td>Height (cm, mean ± SD)</td>
<td>162.6 ± 7.6</td>
<td>159.2 ± 8.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weight (kg, mean ± SD)</td>
<td>60.2 ± 9.4</td>
<td>56.4 ± 11.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Past history (−/+ )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>50/63</td>
<td>38/31</td>
<td>0.16</td>
</tr>
<tr>
<td>Lung</td>
<td>101/22</td>
<td>60/9</td>
<td>0.50</td>
</tr>
<tr>
<td>Liver</td>
<td>108/5</td>
<td>68/1</td>
<td>0.51</td>
</tr>
<tr>
<td>Cr (mg/dL)</td>
<td>1.04 ± 1.0</td>
<td>1.20 ± 1.6</td>
<td>0.60</td>
</tr>
<tr>
<td>RR before treatment (mean ± SD)</td>
<td>175.2 ± 2.6</td>
<td>165.2 ± 2.5</td>
<td>0.01</td>
</tr>
<tr>
<td>BP &lt; 90 mmHg (−/+ )</td>
<td>86/27</td>
<td>49/20</td>
<td>0.45</td>
</tr>
<tr>
<td>Dose of sedative (mg)</td>
<td>6.5 ± 4.5</td>
<td>6.2 ± 3.4</td>
<td>0.69</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>105.5 ± 78.1</td>
<td>106.6 ± 50.0</td>
<td>0.15</td>
</tr>
<tr>
<td>ESD (esophagus/stomach)</td>
<td>15/98</td>
<td>9/60</td>
<td>0.86</td>
</tr>
</tbody>
</table>

RS: respiratory suppression, RR: respiratory rate, Cr: serum creatinine, and BP: blood pressure.

#### Table 2: Multivariate logistic regression analysis of possible risk factors for respiratory suppression in patients undergoing endoscopic submucosal dissection.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>1.14</td>
<td>0.44–2.95</td>
<td>0.79</td>
</tr>
<tr>
<td>Height</td>
<td>0.96</td>
<td>0.90–1.02</td>
<td>0.16</td>
</tr>
<tr>
<td>Weight</td>
<td>0.98</td>
<td>0.94–1.02</td>
<td>0.38</td>
</tr>
<tr>
<td>RR before treatment</td>
<td>0.83</td>
<td>0.73–0.95</td>
<td>0.006</td>
</tr>
</tbody>
</table>

RR: respiratory rate, CI: confidence interval.
no patient with respiratory suppression had a decrease in blood oxygen saturation alone. Detailed analysis revealed that a decrease in RR alone occurred in 35% of the patients who developed respiratory suppression. In the absence of acoustic RR monitoring, respiratory suppression could not have been detected in these patients by measuring the blood oxygen saturation alone and, consequently, some of these patients might have progressed to clinical situations similar to apnea. Resuscitation maneuvers or resuscitation drugs were not used for any patients with respiratory suppression in this study. However, monitoring RR during ESD might be of great importance for avoiding overdose of sedative especially in patients with decrease in RR. Taken together, these data corroborate the indispensability of acoustic RR monitoring in patients undergoing ESD. Furthermore, this monitoring technique is easier to use and less expensive than capnography.

Published literature has revealed that longer duration of procedures [11], body weight [12–14], hypertension, diabetes, heart diseases, procedures that combine esophagogastroduodenoscopy and colonoscopy, and increasing age [15, 16] are risk factors for respiratory suppression in patients undergoing gastrointestinal endoscopy under sedation. However, these risk factors would depend on many other variables such as study design, patient population, type of endoscopy, and type of sedatives, to name a few. In this study, univariate analysis revealed that female gender, low height and weight, and low RR before treatment were significantly associated with respiratory suppression. Multivariate analysis revealed that RR before treatment was the only significant independent predictor of respiratory suppression during ESD under deep sedation. Notably, in our study, the difference in RR between patients with and without respiratory suppression was subtle. This underscores the practical difficulty in beforehand predicting the patients who would subsequently develop respiratory suppression during ESD. When the patients in whom respiratory suppression was detected solely by acoustic RR monitoring were compared with those who did not develop respiratory suppression, the difference in RR before treatment between the two groups of patients was more than two per minute (17.5 ± 2.6 versus 15.1 ± 2.3, \( P = 0.00002 \)). This suggests that acoustic RR monitoring might be useful in predicting respiratory suppression. To summarize, as all patients who developed respiratory suppression were detected by acoustic RR monitoring in our study, it seems critical to continuously monitor RR during ESD using the technique to avoid serious respiratory complications.

Our study has some limitations. Firstly, the study was conducted retrospectively in a single institution with a relatively small sample size. Since very few studies are available on the usefulness of acoustic RR monitoring during endoscopic treatment, further well-designed, prospective studies employing large sample size are necessary to verify our findings. Likewise, trials focused on pathological mechanisms underlying respiratory suppression should be undertaken. The second limitation relates to the controversy that surrounds the diagnostic and clinical relevance of respiratory suppression. Developing a standardized definition of respiratory suppression might be essential in order to investigate the effects of sedatives and to delve into the issue of safe and reliable monitoring. Thirdly, acoustic RR monitoring cannot effectively detect signals when the patient is snoring or coughing during endoscopy.

5. Conclusions

This is the first study to identify RR before treatment as an independent predictor of respiratory suppression during ESD. Furthermore, our results indicate that acoustic RR monitoring may be more useful than monitoring blood oxygen saturation in patients undergoing upper gastrointestinal ESDs under sedation and may facilitate early detection of respiratory suppression in these patients.

Abbreviations

RR: Respiratory rate
ESD: Endoscopic submucosal dissection
OR: Odds ratio
SD: Standard deviation
CI: Confidence interval
Cr: Serum creatinine
BP: Blood pressure.

Ethical Approval

Ethics committee of Tokai University approved the study protocol.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contribution

Takayoshi Suzuki designed the research; Takayoshi Suzuki and Shingo Tsuda analyzed the data; Takayoshi Suzuki, Masashi Matsushima, Shingo Tsuda, Hirohiko Nakae, Jin Imai, Kana Sawamoto, Maiko Kijima, Yoko Tsukune, Tetsufumi Uchida, Muneki Igarashi, Jun Koike, Toshiyasu Suzuki, and Tetsuya Mine performed the research; Takayoshi Suzuki wrote the paper.

References


