Age and comorbidity as risk factors for vocal cord paralysis associated with tracheal intubation

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Background. Vocal cord paralysis after tracheal intubation may be attributed to ageing and comorbidity. However, the relationship between patient characteristics and the risk of vocal cord paralysis is unknown.

Methods. We prospectively analysed data representing 31,241 consecutive surgery patients who underwent tracheal intubation to determine whether duration of intubation, age, sex, and cardiovascular, cerebrovascular, and metabolic diseases were risk factors for vocal cord paralysis associated with intubation. Patients with vocal cord paralysis from any other causes were excluded.

Results. Twenty-four (0.077%) suffered vocal cord paralysis (left, 16 patients; right, 8 patients). The risk was increased when intubation lasted 3–6 h (odds ratio, 2.0; 95% confidence interval, 1.1–5.6; \(P = 0.002\)) or 6 h or more (odds ratio, 14.5; 95% confidence interval, 5.2–40.9; \(P < 0.0001\)). The risk was increased in patients aged 50–69 (odds ratio, 3.6; 95% confidence interval, 1.2–11.1; \(P = 0.02\)) and 70 yr or above (odds ratio, 3.9; 95% confidence interval, 1.2–12.8; \(P = 0.02\)). The risk was increased with diabetes mellitus (odds ratio, 2.5; 95% confidence interval, 1.1–7.3; \(P = 0.03\)) and hypertension (odds ratio, 2.1; 95% confidence interval, 1.1–6.0; \(P = 0.03\)).

Conclusions. The risk of vocal cord paralysis was increased three-fold in patients aged 50 or above, two-fold in patients intubated 3–6 h, 15-fold in patients intubated 6 h or more, and two-fold in patients with a history of diabetes mellitus or hypertension. Our results are informative for informed consent, patient counselling, and intubation decision-making.


Keywords: anaesthesia, general; complications, diabetes mellitus; complications, hypertension; complications, intubation tracheal; larynx, vocal cord paralysis

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Vocal cord paralysis is one of the most serious complications associated with tracheal intubation, resulting in severe vocal disability and aspiration.\(^1\)–\(^5\) There are numerous claims for airway injury in the American Society of Anaesthesiologists Closed Claims database. The most common site of such injury is the larynx, representing 33% of all airway injuries claimed.\(^5\) The most common types of laryngeal injury are vocal cord paralysis, haematoma, and granuloma of the vocal cords.\(^5\)\(^\text{6}\) Moreover, hoarseness is a common postoperative complaint varying in incidence between 14.4% and 50%, affecting patient satisfaction and postoperative activities even after leaving the hospital.\(^7\)–\(^9\) Indeed, prolonged or even permanent hoarseness occurs in approximately 1% of patients.\(^8\) Vocal cord paralysis not only affects the patient’s satisfaction, but it also become a risk factor for aspiration pneumonia, which in turn increases postoperative morbidity and mortality.\(^10\)

Previous studies have identified several factors affecting laryngeal injury and postoperative hoarseness, including size of the tracheal tube, cuff pressure, and quality and duration of tracheal intubation.\(^7\)\(^\text{11}\)–\(^\text{13}\) Despite advances in
intubation techniques and devices, patients remain in danger of vocal cord paralysis and subsequent vocal cord dysfunction. Because of an increase in the elderly population and pre-existing morbidities in surgical patients, patient factors may increase the incidence of postoperative vocal cord paralysis. However, the relationship between patient characteristics and the risk of vocal cord paralysis is unclear.

The aim of this large observational cohort study was to test a hypothesis that the duration of intubation, tracheal tube size, patient age, sex, type of surgery, and pre-existing cardiac, cerebral, vascular, or metabolic disease are risk factors for vocal cord paralysis associated with tracheal intubation.

**Methods**

**Study participants**

The study protocol was approved by the institutional review board of Hamamatsu Medical Center and Sei-rei Mikatabara General Hospital, Hamamatsu, Japan. We consecutively enrolled patients who underwent elective surgery between January 1, 1991 and December 31, 2003. Informed consent was obtained from all patients. Patients undergoing brain surgery, thyroid surgery, carotid endarterectomy, panendoscopy, laryngeal or pharyngeal surgery, anterior cervical surgery, thoracic surgery, or cardiac surgery were excluded. Patients who had vocal cord paralysis before surgery and patients who required fiberoptic intubation or postoperative tracheal intubation for respiratory support were excluded.

The study group comprised 31,241 surgical patients who had required tracheal intubation. Anaesthesia and tracheal intubation were achieved with the use of a Macintosh laryngoscope and a stylet (limited to the tracheal tube) by board-certified anaesthetists. Anaesthesia was achieved by standard methods, and details were left to the discretion of the attending board-certified anaesthetist. In adults, general anaesthesia was induced with thiopental 4–5 mg kg⁻¹ or propofol 1.5–2.0 mg kg⁻¹, fentanyl 2–3 μg kg⁻¹, and vecuronium bromide 1.0–2 mg kg⁻¹. General anaesthesia was maintained with sevoflurane in oxygen and nitrous oxide. In infants and children, general anaesthesia was induced with thiopental 4–5 mg kg⁻¹ or sevoflurane in oxygen–nitrous oxide delivered via mask, fentanyl 1–2 μg kg⁻¹, and vecuronium bromide 1.0–2 mg kg⁻¹. General anaesthesia was maintained with sevoflurane in oxygen and nitrous oxide.

For patients less than 20 yr of age, the size of the tracheal tube was determined according to the patient’s age, and was adjusted to the size of the trachea measured on a routinely obtained chest X-ray film. For females aged 20 or older, a tracheal tube of internal diameter 7.0 or 7.5 mm was used, and for males aged 20 or older, a tracheal tube 7.5 or 8.0 mm in internal diameter was used. Once the tracheal tube was seen to pass through the vocal cords, the position was checked by looking for equal chest movement, bilateral axillary auscultation, and expired carbon dioxide. The tracheal tube was fixed in the right angle of the patient’s mouth. The cuff was inflated with 4–8 ml air until no leak was present and a cuff pressure of <20 mm Hg. As nitrous oxide can increase the pressure in air filled spaces over time, the cuff pressure was intermittently measured by a pressure monitor kit (Cuff Pressure Gauge™, Smith Medical Japan, Tokyo) and was adjusted to be <20 mm Hg (this is our usual practice) during tracheal intubation. Lidocaine gel (2%) was used as the lubricant in all cases. Tracheal intubation was performed after complete muscle relaxation approximately 3 min after administering vecuronium bromide. After surgery, patients’ trachea were extubated at the discretion of the anaesthetist in charge of the patient. Extubation criteria included: full reversal of neuromuscular block by administration of atropin 0.02 mg kg⁻¹ and neostigmine 0.04 mg kg⁻¹, spontaneous ventilation and the ability to follow verbal commands, eye opening or hand grip, and adequate oropharyngeal suction. All patients included in the present study were extubated immediately after surgery.

**Diagnosis of vocal cord analysis and following-up**

All patients underwent postoperative assessment for possible vocal cord paralysis by a board-certified anaesthetist on the day of surgery or the first postoperative day. Subsequently, the physician in charge assessed all patients for postoperative symptoms in the ward and clinic. All patients with notable or persistent dysphonia within postoperative 30 days were evaluated by the hospital’s otolaryngology service. Vocal cord paralysis associated with tracheal intubation was defined as immobility of the vocal cords when other causes of immobility had been ruled out. Assessment and diagnosis of vocal cord paralysis by board-certified oto-rhino-laryngologists included postoperative interviews and flexible fibrescopy.

**Pre-existing morbidities**

All study patients underwent preoperative assessment for pre-existing morbidities. Pre-existing morbidities included hypertension (defined as systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or both), diabetes mellitus [defined as a blood glucose level of at least 126 mg (6.93 mmol litre⁻¹) after an overnight fast, a glycosylated haemoglobin value of at least 6.5%, or both], hyperlipidaemia [serum total cholesterol level of at least 220 mg dl⁻¹ (5.72 mmol litre⁻¹), LDL-cholesterol level of at least 140 mg dl⁻¹ (2.8 mmol litre⁻¹)], and hyperuricaemia [serum uric acid level of at least 7.0 mg dl⁻¹ (0.42 mmol litre⁻¹)]. Pre-existing morbidities also included cardiovascular disease diagnosed by a board-certified cardiologist. This included atrial fibrillation.
fibrillation confirmed by electrocardiography, stable angina (symptoms of frequent chest pain, dyspnea on exertion, or nuclear imaging abnormalities), unstable angina (increased frequency, intensity, or duration of chest pain, or decreased response to nitrates in the previous 2 months), myocardial infarction (diagnosed on the basis of symptoms meeting the World Health Organization criteria, abnormal levels of cardiac enzymes, or diagnostic electrocardiographic criteria), valvular disease (diagnosed on the basis of symptoms, echocardiographic findings, cardiac catheterization findings, or angiographic findings), and pulmonary hypertension (diagnosed via cardiac catheterization, mean pulmonary arterial pressure ≥25 mm Hg, echocardiographic or angiographic findings). Pre-existing morbidities also included cerebrovascular disease diagnosed by a board-certified neurologist. This included ischaemic stroke (based on new neurologic deficits that persisted for more than 24 h, computed tomography scans or magnetic resonance images). The computerized medical database file of each patient was obtained at the time of enrollment and secured in the Division of Medical Records and Information of our institutions.

Statistical analysis

Incidences and risks of vocal cord paralysis were calculated. The characteristics of the patients who were associated or not with vocal cord paralysis after tracheal intubation were compared by one-way analysis of variance followed by Bonferroni multiple comparison test. Potential associations of the duration of tracheal intubation, size of the tracheal tube, patient age, sex, history of cardiac, and cerebral, vascular, or metabolic disease with the occurrence of vocal cord paralysis after the tracheal tube were analysed by the chi-square test and Fisher’s exact test for trend. To estimate odds ratios and 95% confidence intervals by multivariate logistic regression analysis, the duration of intubation, size of the tracheal tube, patient’s age, sex, and history of cardiac, cerebral vascular, or metabolic disease were treated as independent categorical variables. Vocal cord paralysis after tracheal intubation was treated as the dependent categorical variable. All independent variables that were significant (two-tailed nominal P-value of less than 0.1) in univariate analyses were entered into a multivariate logistic analysis by the proportional odds model. Stepwise logistic regression was performed, and variables that were significant (two-tailed nominal P-value of less than 0.05) were retained.

Results

Study participants

Characteristics of patients are summarized in Table 1. The age distribution and duration of intubation of these patients are shown in Figures 1A and 2A, respectively. The types of surgery were general (42.0%), orthopaedic (22.2%), nasal/otologic (11.9%), abdominal and peripheral vascular (7.5%), obstetric/gynaecologic (6.2%), urologic (4.0%), plastic (2.6%), ophthalmic (1.9%), and dental (1.7%).

Incidences of vocal cord paralysis

The incidence of vocal cord paralysis in patients who underwent tracheal intubation is summarized in Table 1. The age-specific incidence is shown in Figure 1n, and the intubation duration-specific incidence is shown in Figure 2n. A total of 24 patients (0.077%) suffered vocal cord paralysis due to tracheal intubation, and all such complications occurred within 30 days after surgery. There was no incidence of difficult tracheal intubation in any of these patients. Incidences were significantly increased in patients aged 50 or above, patients intubated for 3 h or more, and patients with a history of hypertension or diabetes mellitus (all P-values of <0.05). Of the 24 patients who suffered vocal cord paralysis, eight (0.026%) suffered right vocal cord paralysis and 16 (0.051%) suffered left vocal cord paralysis (left vs right, P<0.01). The occurrences of vocal cord paralysis in type of surgery were as follows: in three patients (0.081%) after otological surgery, 14 patients (0.107%) after general surgery, one patient (0.052%) after gynaecologic surgery, three patients (0.043%) after orthopaedic surgery, and three patients (0.238%) after urological surgery.

Postoperative diagnosis of vocal cord paralysis

In all 24 patients, dysphonia was notable with the earliest postoperative examination on the day of surgery or the first postoperative day. There were certain periods from the notice of dysphonia to the diagnosis of vocal cord paralysis. The median period between surgery and the date of diagnosis of vocal cord paralysis was 14 days, with a range of 1–30 days (males: 13 days, range: 1–25 days; females: 14 days, range: 1–30 days). Nine of the 24 patients (37.5%) with vocal cord paralysis were diagnosed within 7 days after surgery, 14 (58.3%) were diagnosed within 14 days, and 17 (70.8%) were diagnosed within 21 days. All of those 24 patients were treated with mecobalamin (vitamin B12) for treatment and mobility of the paralysed vocal cords was observed in all of these patients after 68 (17) days (41–97 days, approximately within 2–3 months).

Risk factors for vocal cord paralysis

The results of multivariate logistic regression analysis of the risk factors for vocal cord paralysis in patients who underwent tracheal intubation are summarized in Table 2. The risk and incidence of vocal cord paralysis increased with age (for every year: multivariate odds ratio, 1.030; 95% confidence interval, 1.006–1.052; P=0.013) and was three times higher (P=0.02) for patients aged 50–69 and
for patients older than 70 yr than for patients in other age categories. The risk and incidence of vocal cord paralysis increased with the duration of intubation (for every hour: multivariate odds ratio, 1.4; 95% confidence interval, 1.3–1.6; \( P = 0.0001 \)); the risk doubled for a duration of more than 3 h but less than 6 h (\( P = 0.002 \)), seven times for a duration of more than 6 h but less than 9 h (\( P = 0.001 \)), and nearly 30 times for a duration of 9 h or more (\( P < 0.0001 \)).

The risk doubled in patients with diabetes mellitus (\( P = 0.03 \)) and hypertension (\( P = 0.03 \)).

### Discussion

Data obtained from this large observational study of consecutively surgery patients offer physicians important, clinically relevant information about the relation of patient’s age, history of diabetes mellitus, and hypertension, and duration of tracheal intubation to the incidence, and risk of vocal cord paralysis. This study basically supports the theory that vocal cord paralysis after intubation is likely to be due to nerve damage caused by microcirculatory compromise affecting laryngeal nerves. Age, diabetes mellitus, hypertension, and prolonged intubation would all potentially increase the risk of vocal cord paralysis. The left vocal cord was shown to be two times more vulnerable to vocal cord paralysis than the right vocal cord. This may be due to rightward insertion and fixation of the tracheal tube in the right angle of mouth. The critical period to accomplish diagnosis of vocal cord paralysis is during postoperative week 2 or 3; 50–70% of all cases in our study were diagnosed within this period. The mobility of the paralyzed vocal cords was observed in all of these patients after approximately 2–3 months.

Placement of the tracheal tube is thought to immobilize the vocal cords and muscles and paralyse the peripheral nerves.\(^6\)\(^{17–19}\) A relation between prolonged intubation and an increased risk of vocal cord immobility and injury was clear in previous studies.\(^18\)\(^\text{19}\) The causal relationship between prolonged intubation and vocal cord paralysis remains unclear. There are several possible mechanisms for this. The tracheal tube may cause acute inflammation in the larynx, that is, erythema, ulceration, and granuloma formation, and these pathologic changes may induce vocal cord immobility. The pressurized tracheal tube cuff could potentially compress the recurrent nerve and its peripheral branches in the larynx, causing degeneration and subsequent nerve paralysis. Insufficient microcirculatory supply to the recurrent nerve and its peripheral branches in
the larynx due to the cuff pressure may cause ischaemic neuronal degeneration and subsequent recurrent nerve paralysis and vocal cord immobility. The incidence of vocal cord paralysis increased with age. Multivariate analysis showed the risk of vocal cord paralysis to be increased three-fold in patients aged 50 or above.

Hypertension is associated with atherosclerotic changes in the arterial vasculature of the larynx. Microcirculatory insufficiency in the laryngeal nerve may be caused by mechanical compression by the cuff of the tracheal tube. The recurrent nerve and its peripheral branches, vocal cord muscles, and laryngeal tissues may be more vulnerable to mechanical damage and pressure from the tracheal tube cuff in patients with diabetes mellitus and hypertension than in other patients.

We also found a clear relationship between ageing and an increased risk of vocal cord paralysis. However, the underlying mechanism is again not well understood. Tissues in the laryngeal system that have degenerated with age may be more vulnerable to acute inflammation and microcirculatory insufficiency due to cuff pressure and mechanical damage by the tracheal tube. Age as the risk factor of vocal cord paralysis may be related to the
In conclusion, the risk of vocal cord paralysis was found to be increased three-fold in patients aged older than 50 yr, two-fold in patients intubated 3–6 h, 15-fold in patients intubated 6 h or more, and two-fold in patients with a history of diabetes mellitus or hypertension. Our results are informative for informed consent, patient counselling, and intubation decision-making.

### Table 2 Multivariate logistic regression analysis of risk factors for vocal cord paralysis in patients who underwent tracheal intubation (n=31 241)

<table>
<thead>
<tr>
<th>Age</th>
<th>Odds ratio (95% confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 yr</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>50–69 yr</td>
<td>3.6 (1.2–11.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>≥70 yr</td>
<td>3.9 (1.2–12.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.8 (0.8–4.1)</td>
<td>0.19</td>
</tr>
<tr>
<td>Intubation duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 h</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3–6 h</td>
<td>2.0 (1.1–5.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>6–9 h</td>
<td>7.6 (2.3–25.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt;9 h</td>
<td>29.8 (8.2–108.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Internal diameter of tracheal tube</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men (≥20 yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.5 mm</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>8.0 mm</td>
<td>1.2 (0.5–3.2)</td>
<td>0.68</td>
</tr>
<tr>
<td>Women (≥20 yr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0 mm</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>7.5 mm</td>
<td>2.3 (0.6–9.8)</td>
<td>0.23</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5 (1.1–7.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.1 (1.1–6.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>1.6 (0.4–6.4)</td>
<td>0.08</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>1.5 (0.4–6.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.3 (0.2–4.7)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

In all 24 patients in our study who suffered vocal cord paralysis due to tracheal intubation, dysphonia was noted on the day of surgery or the first postoperative day. However, there was a certain delay from symptom onset to establishment of a diagnosis of vocal cord paralysis. We cannot explain this delay with certainty, but it is possible that dysphonia observed in the early postoperative period progressed to vocal cord paralysis in the later period.

Previous reports have shown an association between the size of the tracheal tube and a risk of postoperative laryngeal morbidity. We use 7.5 or 8.0 mm tube for males aged 20 or above and 7.0 or 7.5 mm tube for females in this age category. In the present study, a 0.5 mm difference in tracheal tube size did not pose a significant risk of vocal cord paralysis in either males or females. Similarly, previous reports have indicated that vocal cord paralysis occurs more on the left side than on the right. This was also observed in our study. This might be due to the fact that the tracheal tube is usually introduced from the right side by the right hand whereas the laryngoscope is held in the left hand and fixed in the right angle of the patient’s mouth. Thus, the tracheal tube is in contact with the left vocal cord.

There are some study limitations that should be mentioned.

First, because our investigation focused on patients in whom postoperative vocal cord paralysis diagnosed after the onset of dysphonia, we did not examine how many patients suffered transient or asymptomatic vocal cord dysfunction without paralysis. We also did not identify the patients who had potential pre-existing vocal cord pathology, such as smokers or those with gastro-oesophageal reflux disease. They would be at risk of postoperative vocal cord morbidities. It is likely that our study underestimated patients with postoperative vocal cord morbidities, and thus the relationship between pre-existing vocal cord pathology and the risk of postoperative vocal cord dysfunction was unclear. Secondly, we did not systematically assess the quality and difficulty of tracheal intubation as a risk factor for various postoperative laryngeal morbidities. Therefore, the relationship between the quality and difficulty of tracheal intubation and postoperative vocal cord dysfunction was unclear. Thirdly, we did not analyse the relationship between the incidence of postoperative vocal cord paralysis and any intraoperative critical ischaemic events, such as prolonged hypotension or anaemia due to significant blood loss. These events may worsen the laryngeal nerve damage caused by microcirculatory compromise.

Vocal cord paralysis and tracheal intubation

There is an increased risk of vocal cord paralysis that is associated with an increased age. We did not experience postoperative vocal cord paralysis in patients under 20 yr old. We considered that the laryngeal system in younger patients might be less vulnerable than in elderly patients. Eighty-eight percent of the patients under 20 yr old underwent surgery that lasted for less than 3 h. The shorter duration of surgery might be another reason for a lack of patients with vocal cord paralysis in young patients.

Difficult tracheal intubation occurs in approximately 5% of surgical patients, and sub-optimal quality of intubation contributes to postoperative hoarseness and laryngeal morbidity. Having reviewed the anaesthetic records, all of the patients who developed vocal cord paralysis were intubated at the first attempt under general anaesthesia and complete muscle relaxation; none were recorded as a difficult intubation. Vocal cord paralysis observed in our study was therefore not likely to have been caused by trauma on intubation.

It is still unclear how to reduce the incidence of vocal cord paralysis associated with tracheal intubation because the occurrence is relatively rare and few studies have been conducted pertaining to risk reduction. Surgeries for which laryngeal mask airway can be used are limited, and this type of airway itself poses some risk of vocal cord paralysis. Nevertheless, large surveys support the safety of laryngeal mask airway in both adults and paediatric surgery patients. It is likely therefore that the use of a laryngeal mask airway would reduce mechanical damage to the laryngeal system and thus vocal cord morbidity, especially in higher-risk patients.
Acknowledgements

M.K. designed the study and wrote the paper. M.K., K.S., T.I., and T.T. collected the data and performed the statistical analysis. M.K. and S.S. provided critical insight into the interpretation of the results. M.K. had full access to all the data in the study and takes responsibility for integrity of the data and accuracy of the data analysis.

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