Nasal breathing is superior to oral breathing when performing and undergoing transnasal endoscopy: a randomized trial

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submitted 12.1.2022
accepted after revision 13.7.2022
published online 14.7.2022

Bibliography
Endoscopy
DOI 10.1055/a-1900-6004

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**ABSTRACT**

**Background** Transnasal endoscopy presents a technical difficulty when inserting the flexible endoscope. It is unclear whether a particular breathing method is useful for transnasal endoscopy. Therefore, we conducted a prospective randomized controlled trial to compare endoscopic operability and patient tolerance between patients assigned to nasal breathing or oral breathing groups.

**Methods** 198 eligible patients were randomly assigned to undergo transnasal endoscopy with nasal breathing or with oral breathing. Endoscopists and patients answered questionnaires on the endoscopic operability and patient tolerance using a 100-mm visual analog scale ranging from 0 (non-existent) to 100 (most difficult/unbearable). The visibility of the upper-middle pharynx was recorded.

**Results** Patient characteristics did not differ significantly between the groups. Nasal breathing showed a higher rate of good visibility of the upper-middle pharynx than oral breathing (91.9% vs. 27.6%; P<0.001). Nasal breathing showed lower mean [SD] scores than oral breathing in terms of overall technical difficulty (21.0 [11.4] vs. 35.4 [15.0]; P<0.001). Regarding patient tolerance, nasal breathing showed lower scores than oral breathing for overall discomfort (22.1 [18.8] vs. 30.5 [20.9]; P=0.004) and other symptoms, including nasal and throat pain, choking, suffocating, gagging, belching, and bloating (all P<0.05). The pharyngeal bleeding rate was lower in the nasal breathing group than in the oral breathing group (0% vs. 9.2%; P=0.002).

**Conclusions** Nasal breathing is superior to oral breathing for those performing and undergoing transnasal endoscopy. Nasal breathing led to good visibility of the upper-middle pharynx, improved endoscopic operability, and better patient tolerance, and was safer owing to decreased pharyngeal bleeding.

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**Introduction**

Transnasal endoscopy is currently essential for the screening of upper gastrointestinal (UGI) disease in general practice and in health examinations. The recent development of ultrathin endoscopes has made the image quality comparable with that of high definition oral endoscopes [1]. Previous reports have shown good tolerance and acceptance for transnasal endoscopy compared with conventional endoscopy [2, 3]. Furthermore, transnasal endoscopy provided advantages in terms of pharyngeal observation, cost-effectiveness, and having less impact on cardiovascular function [4–6]. However, it is controversial whether the selection of transnasal or peroral route is preferable in terms of the physicians’ operability and patients’ tolerance when using an ultrathin endoscope [7–10]. In addition, the clinical use of transnasal endoscopy is limited in Asia, Latin America, and some European countries [11]. This is because transnasal endoscopy carries a technical difficulty when the endoscope is being inserted owing to the flexibility of the ultra-thin endoscope, resulting in lower acceptance by healthcare physicians [11–13]. Therefore, further technical advancements in transnasal endoscopy are required to enable its routine implementation [13].

Previous studies have shown that the success of transnasal intubation depends on the nasal pretreatment, nasal meatus selection, scope diameter, and the endoscopist’s skill [2, 14, 15]. So far, there have been no reports on the relationship between breathing method and transnasal endoscopy. In nasal breathing, the soft palate moves downward to the root of the tongue; in oral breathing, it moves upward to the posterior wall of the pharynx [16]. These positional changes of the soft palate in nasal and oral breathing seem to influence endoscopic operability and patient tolerance. We herein report the first prospective randomized controlled trial to compare endoscopic operability and patient tolerance between patients allocated to either the nasal or oral breathing group.

**Methods**

**Patients**

This study was a prospective randomized controlled trial performed at Asahikawa Medical University (AMU) Hospital, En-garu-Kosei General Hospital, and Harada Hospital. We recruited patients who were scheduled to undergo transnasal endoscopy at one of the three institutions from June 2021 to December 2021. The inclusion criteria were as follows: (i) aged 20 or over; (ii) willing to undergo transnasal endoscopy; and (iii) agreed to give written informed consent. The exclusion criteria were as follows: (i) failed insertion of an endoscope through the nasal cavity; (ii) needing to undergo sedation-assisted endoscopy; (iii) therapeutic intervention being scheduled; (iv) history of UGI surgery; and (v) refusal to provide written informed consent.

The study protocol was approved by the ethics committee of each institution. All patients provided written informed consent for this study.

**Randomization and masking**

Randomization was conducted centrally using the Mujinwari software cloud service for random assignment. Following the determination of their eligibility, patients were randomly assigned to one of the two groups – nasal breathing or oral breathing – in a 1:1 ratio, using a computer-generated permuted block method with variable blocks of four. The number of patient enrolments at each institution was determined in proportion to the number of transnasal endoscopies performed during the previous year.
Once a patient had been enrolled, a nurse used the randomization sequence to assign the breathing method. The nurse then explained the breathing method to the patient in the preparation room. After the patient had been prepared for transnasal endoscopy and the breathing method had been explained, the patient entered the examination room and underwent transnasal endoscopy. Transnasal endoscopies were performed by endoscopists to whom the patient’s assignment was masked.

Preparation and endoscopic procedures

In the preparation room, a nurse administered rhinenchysis with 0.05% naphazoline nitrate as per the standard of care and inserted a 16-Fr stick with 2% lidocaine hydrochloride viscous and 8% lidocaine spray for topical nasopharyngeal anesthesia. The endoscope was chosen from the GIF-XP290N, GIF-XP260NS (Olympus Medical Systems, Tokyo, Japan), and EG-L580NW7 (Fujifilm Corporation, Tokyo, Japan) at each institution. The GIF-XP290N, GIF-XP260NS, and EG-L580NW7 have a 5.4-mm, 5.4-mm, and 5.8-mm outer diameter, 2.2-mm, 2.0-mm, and 2.4-mm forceps channel, and 140°, 120°, and 140° visual field angle, respectively.

All patients that participated in this study were in a conscious state without receiving sedation. All of the transnasal endoscopies were performed by fourteen well-trained endoscopists who had experience of performing more than 500 transnasal endoscopies. During the examination, the times from insertion of the endoscope to arrival at the cervical esophagus and at the descending part of the duodenum, and to removal of the endoscope were recorded. The heart rate and percutaneous oxygen saturation ($\text{SpO}_2$) level of the patients were continuously monitored and recorded at rest before the examination, when the endoscope reached the descending part of the duodenum, and at removal of the endoscope. Complications such as nasal bleeding, pharyngeal bleeding, and hypoxemia were also recorded.

Evaluation of endoscopic operability and patient tolerance

In the preliminary endoscopic examination, we examined the visibility and patency from the epipharynx to the oropharynx when the patient breathed through the nose or mouth (Video 1). The schema of the positional relationship between the soft palate, posterior wall of the pharynx, and endoscope in each breathing method is displayed in Video 1a, b. In nasal breathing, the soft palate moves downward to the tongue root, resulting in good visibility of the upper-middle pharynx. During oral breathing, the soft palate moves downward to the tongue root, resulting in good visibility of the upper-middle pharynx. The primary outcomes were the endoscopic operability and patient tolerance, which were measured using a 100-mm VAS. Endoscopic operability was assessed based on the handling difficulty and technical difficulties faced while inserting the endoscope into the nasal cavity, upper-middle pharynx, piriform recess, and duodenum. Patient tolerance was evaluated on the basis of the responses given by the patients in their questionnaires with regard to pain, discomfort, choking, suffocation, gagging, belching, and bloating. Secondary outcomes were the visibility and patency of the upper-middle pharynx and the complications with each breathing method.

Outcomes

The primary outcomes were the endoscopic operability and patient tolerance, which were measured using a 100-mm VAS. Endoscopic operability was assessed based on the handling difficulty and technical difficulties faced while inserting the endoscope into the nasal cavity, upper-middle pharynx, piriform recess, and duodenum. Patient tolerance was evaluated on the basis of the responses given by the patients in their questionnaires with regard to pain, discomfort, choking, suffocation, gagging, belching, and bloating. Secondary outcomes were the visibility and patency of the upper-middle pharynx and the complications with each breathing method.
Sample size

In previous reports that had assessed the effect of transnasal endoscopy using a 100-mm VAS, enhancement of more than about 10 points demonstrated significant differences [8, 19]. Based on these reports and our preliminary examination, we hypothesized that the endoscopic operability and patient tolerance in the nasal breathing group would improve by an average of 10 points on the 100-mm VAS with an expected SD of 25. A sample size of 99 subjects per group was calculated as being required to detect differences at a 5% significance level (two-sided) with a power of 80%.

Statistical analyses

Statistical analyses were performed using the R Project for Statistical Computing version 4.0.5 software program. Student’s t test was used to compare continuous variables, and Fisher’s exact probability test was used to compare nominal scale data. We used Spearman’s rank correlation coefficient in multivariate correlation analysis and subsequent hierarchical clustering. A linear discriminant analysis (LDA) was performed using the “MASS” package for R. P values of <0.05 were considered to indicate statistical significance.

Results

Study population and baseline characteristics

A total of 217 patients who visited our hospitals to undergo transnasal endoscopy were assessed for eligibility (Fig. 1). Of these patients, 19 were excluded from this study: 12 for refusal to participate in the study; two because of a history of transnasal endoscope insertion failure; three because of a scheduled therapeutic intervention under sedation; and two owing to a history of UGI surgery. The indications for transnasal endoscopy were medical examinations in 158 patients, bowel symptom investigation in 14 patients, and follow-up endoscopy in 26 patients.

A total of 198 patients were randomly assigned to one of the two groups: nasal or oral breathing. Following randomization, five patients assigned to the nasal breathing group performed oral breathing during transnasal endoscopy; two patients allocated to the oral breathing group performed nasal breathing during transnasal endoscopy. The breathing methods that the patients performed were confirmed by their answers to the questionnaire. In addition, one patient assigned to the oral breathing group was excluded from the study because the endoscope could not be passed through the nasal cavity and the
transnasal endoscopy was terminated. Therefore, 99 patients in the nasal breathing group and 98 patients in the oral breathing group were analyzed for the intention-to-treat (ITT) analysis. Subsequently, 94 patients in the nasal breathing group and 96 patients in the oral breathing group were analyzed in the per-protocol analysis.

The characteristics of the patients in the two groups are shown in Table 1. There were no significant differences in the patient characteristics, including examination facility, age, sex, height, body weight, body mass index (BMI), antithrombotic agent use, number of previous esophagastroduodenoscopies (EGDs), and indication for endoscopy, between the two groups.

**Clinical and endoscopic data of the patients**

The clinical and endoscopic data of the patients are presented in Table 2. There were no significant differences in terms of the endoscope used, duration of endoscopy, number of biopsies, detection rate of pharyngeal lesions, nasal bleeding, hypoxemia, or heart rate. Pharyngeal bleeding was seen in 0/99 patients (0%) in the nasal breathing group and 9/98 patients (9.2%) of the oral breathing group, this being significantly higher in the oral breathing group. The posterior wall of the pharynx, which the transnasal endoscope contacted while passing through the pharynx, was the source of all of this bleeding (Fig. 2s). Once pharyngeal bleeding had been observed, hemostasis was achieved, and no patients required intervention in this study.

The mean (SD) SpO2 at rest was statistically higher in the nasal breathing group (98.3 % [1.3 %]) than in the oral breathing group (97.9 % [2.0 %]) in the nasal breathing group and 98.2 % (1.9 %) in oral breathing group, which was not significantly different. As the endoscope was passed through the stomach, hypoxemia (SpO2<90%) was seen in 4/98 patients (4.1%) in the oral breathing group, although these levels were returned to normal by telling the patients not to hold their breath. The SpO2 at the time of removal of the endoscope did not show a signifi-
cant difference between the nasal breathing (98.0% [1.7%]) and oral breathing groups (98.0% [2.0%]).

**Visibility of the upper-middle pharynx, endoscopists’ operability scores, and patients’ tolerance scores**

The types of visibility and patency of the upper-middle pharynx are shown in Table 3. The rate of good visibility (type 1) was significantly higher in the nasal breathing group than in the oral breathing group (91.9% vs. 27.6%, respectively; P<0.001). With regard to poor visibility, nasal breathing resulted in 7.1% type 2 (7/99) and 1.0% type 3 (1/99), while oral breathing resulted in 40.8% type 2 (40/98) and 31.6% type 3 (31/98).

The endoscopists’ operability scores measured by VAS (0, non-existent, to 100, most difficult) are also shown in Table 3. Nasal breathing showed lower mean (SD) scores in terms of overall technical difficulty of handling the endoscope, nasal breathing showed significantly lower scores than oral breathing (21.0 [11.4] vs. 35.4 [15.0]; P<0.001). Patients’ tolerance scores measured by VAS (0, non-existent, to 100, unbearable) and patients’ answers for overall tolerance are shown in Table 3. Nasal breathing showed lower mean (SD) scores in terms of overall discomfort compared with oral breathing (22.1 [18.8] vs. 30.5 [20.9]; P=0.004). The scores associated with pain and discomfort in the nose were significantly improved by nasal breathing (both P<0.05). The scores for throat discomfort did not show a significant difference in the ITT analysis, while in the per-protocol analysis the scores were significantly lower in the nasal breathing group than in the oral breathing group (P=0.02). Nasal breathing also improved the scores for choking, suffocation, gagging, belching, and bloating.

In addition, regarding overall tolerance including pain and discomfort, the rate of answering “better than expected” was...
69/99 (69.7 %) in the nasal breathing group and 46/98 (46.9 %) in the oral breathing group, this being significantly higher for nasal breathing. Therefore, the patients’ tolerance scores for nasal breathing were significantly lower than those for oral breathing ($P<0.001$).

### Multivariate correlation analysis

In multivariate correlation analysis, we investigated the correlation between five factors of endoscopic operability and 11 factors of patient tolerance that were measured using the 100-mm VASs. The correlation coefficients were computed from a data set of 197 patients for all pairs among the 16 factors (Fig. 3s, part a). By applying hierarchical clustering based on the correlation matrix, the 16 factors could be classified into two groups of high correlation of five factors of endoscopic operability and 11 factors of patient tolerance (Fig. 4s).

We then introduced two new factors: a sum of the five VASs for endoscopic operability and a sum of the 11 VASs for patient tolerance. With respect to these new factors describing total VAS scores, VASope for endoscopists and VAStol for patients, we performed an LDA to compare between the two breathing methods. The associated discriminant function (Fig. 3s, part b) is:

$$3.0709 - 0.0138 \text{VAS}_{\text{ope}} - 0.0037 \text{VAS}_{\text{stol}} = 0$$

as indicated by the dotted line which separates the (VASope, VAStol) plane of the scatter plot into two regions.

### Table 3: Visibility and patency of the upper-middle pharynx, endoscopists’ operability scores and patients’ tolerance scores measured by visual analog scales.

<table>
<thead>
<tr>
<th></th>
<th>Intention-to-treat analysis</th>
<th>Per-protocol analysis</th>
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<tbody>
<tr>
<td></td>
<td>Nasal breathing</td>
<td>Oral breathing</td>
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<tr>
<td>Upper-middle pharynx visibility and patency, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Type 1</td>
<td>91 (91.9)</td>
<td>27 (27.6)</td>
</tr>
<tr>
<td>• Type 2</td>
<td>7 (7.1)</td>
<td>40 (40.8)</td>
</tr>
<tr>
<td>• Type 3</td>
<td>1 (1.0)</td>
<td>31 (31.6)</td>
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<tr>
<td>Endoscopists’ operability score, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Nasal cavity</td>
<td>36.3 (15.4)</td>
<td>37.6 (14.6)</td>
</tr>
<tr>
<td>• Upper-middle pharynx</td>
<td>18.1 (11.8)</td>
<td>36.8 (18.6)</td>
</tr>
<tr>
<td>• Piriorm recess</td>
<td>23.3 (12.3)</td>
<td>32.1 (12.7)</td>
</tr>
<tr>
<td>• Descending part of the duodenum</td>
<td>35.9 (11.4)</td>
<td>37.0 (10.3)</td>
</tr>
<tr>
<td>• Overall</td>
<td>21.0 (11.4)</td>
<td>35.4 (15.0)</td>
</tr>
<tr>
<td>Patient tolerance score, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Nasal pain</td>
<td>24.2 (19.2)</td>
<td>32.6 (21.3)</td>
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<tr>
<td>• Throat pain</td>
<td>25.1 (21.2)</td>
<td>32.7 (21.1)</td>
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<tr>
<td>• Overall abdominal pain</td>
<td>10.1 (14.3)</td>
<td>15.2 (17.4)</td>
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<tr>
<td>• Nasal discomfort</td>
<td>24.7 (18.1)</td>
<td>34.9 (23.2)</td>
</tr>
<tr>
<td>• Throat discomfort</td>
<td>31.0 (22.9)</td>
<td>37.3 (23.0)</td>
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<tr>
<td>• Overall discomfort</td>
<td>22.1 (18.8)</td>
<td>30.5 (20.9)</td>
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<tr>
<td>• Choking</td>
<td>14.4 (18.9)</td>
<td>25.9 (24.6)</td>
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<tr>
<td>• Suffocating</td>
<td>11.8 (15.1)</td>
<td>20.5 (19.5)</td>
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<tr>
<td>• Gagging</td>
<td>8.6 (13.9)</td>
<td>22.1 (25.5)</td>
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<tr>
<td>• Belching</td>
<td>9.6 (12.5)</td>
<td>22.0 (24.9)</td>
</tr>
<tr>
<td>• Bloating</td>
<td>14.2 (16.1)</td>
<td>20.4 (20.9)</td>
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<tr>
<td>Overall tolerance, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Better than expected</td>
<td>69 (69.7)</td>
<td>46 (46.9)</td>
</tr>
<tr>
<td>• As expected</td>
<td>26 (26.3)</td>
<td>49 (50.0)</td>
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<tr>
<td>• Worse than expected</td>
<td>4 (4.0)</td>
<td>3 (3.1)</td>
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</tbody>
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Testing the discriminant function line for 99 data points for nasal breathing (98 data points for oral breathing), 74 points were correctly classified into the group with nasal breathing (66 points into the group with oral breathing). The accuracy rate was 140/197. The values of Wilks’ $\lambda$ and its significance probability for the LDA were $\lambda = 0.806$ and $P<0.001$, respectively. The result of the LDA suggested that nasal breathing showed lower scores of endoscopic operability and patient tolerance than oral breathing.

Discussion

We believe this is the first prospective randomized controlled trial to compare the endoscopic operability and patient tolerance between nasal and oral breathing during transnasal endoscopy. Our primary outcomes were the endoscopic operability and patient tolerance, which were measured using 100-mm VASs. In the overall scores of endoscopic operability, nasal breathing showed better scores than oral breathing (21.0 [11.4] vs. 35.4 [15.0]; $P<0.001$). With regard to patient tolerance, the scores for nasal breathing were significantly ($P<0.05$) better than those for oral breathing. Additionally, regarding the overall tolerance, including pain and discomfort, the rate of answering “better than expected” was significantly higher in nasal breathing group (69.7% vs. 46.9% in the oral breathing group; $P<0.001$). In terms of the complications with each breathing method, the occurrence rate of pharyngeal bleeding was 9.2% for oral breathing and 0% for nasal breathing, this being significantly higher in the oral breathing group ($P=0.002$). Therefore, nasal breathing in transnasal endoscopy improved the endoscopic operability and patient tolerance, and showed better safety by decreasing the occurrence rate of pharyngeal bleeding. These findings suggest that nasal breathing can be expected to resolve the technical difficulty encountered when inserting flexible endoscopes and the low rates of acceptability among physicians, subsequently making the procedure more popular worldwide.

The soft palate has a role in partitioning the oronasal airflow when breathing [16]. During nasal breathing, the soft palate moves downward to the root of the tongue, and airflow passes to the nose [16, 20], so that good visibility of the upper-middle pharynx is maintained when inserting the endoscope (Fig. 1a). Our study showed that the rate of type 1 visibility and patency was 91.9% for nasal breathing. This good visibility and patency make it easier for endoscopists to insert the endoscope into the upper-middle pharynx and piriform recess. During oral breathing, the soft palate stays in an intermediate position between the tongue and posterior pharyngeal wall and rises to close the upper pharynx as the ventilatory air volume increases (Fig. 1b) [16,21,22]. Our data show that there was poor visibility of the upper-middle pharynx in 72.4% of the oral breathing group, consisting of type 2 in 40.8% and type 3 in 31.6%. This poor visibility of the upper-middle pharynx led to difficulty in inserting the endoscope in the upper-middle pharynx and piriform recess. We hypothesized that the difference in patency between type 2 and type 3 was determined by the ventilatory air volume of oral breathing: a low tidal volume produced type 2 and a high tidal volume produced type 3.

In transnasal endoscopy, nasal pain is the most frequent symptom during insertion [6, 14]. Our results revealed that nasal breathing resulted in less nasal pain and discomfort than oral breathing. When performing intubation into the upper-middle pharynx, the endoscope is prone to trigger nasal pain by pushing against the upper wall of the nasal meatus [23]. Nasal breathing enabled there to be no resistance to passage of the endoscope through the upper-middle pharynx and this may cause less pressure on the nasal meatus, resulting in less pain and discomfort.

With regard to the gag reflex, transnasal endoscopy reportedly causes less gagging, choking, and retching than transoral endoscopy because intubation via the nasal route can avoid the endoscope touching the root of the tongue [9, 12]; however, the gag reflex is also triggered when the endoscope touches the posterior wall of the pharynx [18, 24]. Nasal breathing might offer less chance of the endoscope being wedged between the soft palate and the posterior wall of the pharynx (Fig. 1a,b), thereby causing less gagging, choking, retching, and pharyngeal bleeding than oral breathing.

The result of the LDA for endoscopic operability and patient tolerance supports the suggestion that nasal breathing is superior to oral breathing in transnasal endoscopy. Furthermore, there is a tendency that when endoscopists find technical difficulties, patients also feel pain and discomfort, and experience symptoms during transnasal endoscopy.

The mean (SD) SpO2 level at rest was statistically higher in the nasal breathing group (98.3% [1.3%]) than that in the oral breathing group (97.9% [1.9%]). Patients assigned to the nasal breathing group may experience anxiety as a result of breathing through the nose while one nostril is occupied by the endoscope. This stress may cause a slight increase in the breathing rate. Indeed, the SpO2 with nasal breathing decreased slightly from 98.3% (1.3%) at rest to 97.9% (2.0%) when the endoscope reached the descending part of the duodenum. However, this SpO2 decrease was slight and hypoxemia was not seen in patients in the nasal breathing group. In contrast, hypoxemia was seen in 4.1% of patients in the oral breathing group when the endoscope was passed through the stomach. This hypoxemia was caused by breath-holding and may have resulted from suffering during the transnasal endoscopy in the oral breathing group.

The present study had some limitations. First, different models of endoscopes were used at the institutions involved in this study; however, the proportion of each endoscope did not show a significant difference between the two groups. Second, this study included small numbers of patients under the age of 30 and over the age of 80. Transnasal endoscopy may be more stimulating for younger patients and less stimulating for elderly patients, although nasal breathing still has the potential to show superiority in such populations. Third, the mouth and nose of the patients were not covered by anything such as a mask, which would have been required to completely conceal the patients’ assignment from the endoscopists. In this study, it was important that the respiratory status could be assessed by nurses, with oxygen administered or suction performed ra-
Nasal breathing resulted in good visibility of the upper-middle gate for those performing and undergoing transnasal endoscopy. This resulted in poor patient tolerance. Therefore, if patients breathe through their nose as much as possible, some patients may prefer to breathe through their nose while undergoing transnasal endoscopy. A prospective trial comparing unsedated ultrathin versus standard esophagastroduodenoscopy (EGD) versus peroral small-caliber EGD versus conventional EGD. Endoscopy 2003; 35: 641–646

In conclusion, nasal breathing is superior to oral breathing and showed better safety by decreasing pharyngeal bleeding.

Competing interests

The authors declare that they have no conflict of interest.

Funding

Japan Gastroenterological Endoscopy Society, Hokkaido chapter

Clinical trial

Trial Registration: UMIN Japan | Registration number (trial ID): UMIN000044451 | Type of study: Prospective, Randomized, Multi-Center Study

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