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Laryngeal Morbidity and Quality of Tracheal Intubation

A Randomized Controlled Trial

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Background: **Vocal cord sequelae and postoperative hoarseness during general anesthesia are a significant source of morbidity for patients and a source of liability for anesthesiologists. Several risk factors leading to laryngeal injury have been identified in the past. However, whether the quality of tracheal intubation affects their incidence or severity is still unclear.**

Methods: **Eighty patients were randomized in two groups (n = 40 for each) to receive a propofol–fentanyl induction regimen with or without atracurium. Intubation conditions were evaluated with the Copenhagen Score; postoperative hoarseness was assessed at 24, 48, and 72 h by a standardized interview; and vocal cords were examined by stroboscopy before and 24 and 72 h after surgery. If postoperative hoarseness or vocal cord sequelae persisted, follow-up examination was performed until complete restitution.**

Results: **Without atracurium, postoperative hoarseness occurred more often (16 *vs.* 6 patients; $P = 0.02$). The number of days with postoperative hoarseness was higher when atracurium was omitted (25 *vs.* 6 patients; $P < 0.001$). Similar findings were observed for vocal cord sequelae (incidence of vocal cord sequelae: 15 *vs.* 3 patients, respectively, $P = 0.002$; days with vocal cord sequelae: 50 *vs.* 5 patients, respectively, $P < 0.001$). Excellent intubating conditions were less frequently associated with postoperative hoarseness compared to good or poor conditions (11, 29, and 57% of patients, respectively; excellent *vs.* poor: $P = 0.008$). Similar findings were observed for vocal cord sequelae (11, 22, and 50% of patients, respectively; excellent *vs.* poor: $P = 0.02$).**

Conclusions: **The quality of tracheal intubation contributes to laryngeal morbidity, and excellent conditions are less frequently associated with postoperative hoarseness and vocal cord sequelae. Adding atracurium to a propofol–fentanyl induction regimen significantly improved the quality of tracheal intubation and decreased postoperative hoarseness and vocal cord sequelae.**

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INJURIES to the airway are well-recognized complications of anesthesia, and claims for airway injuries are frequent in the American Society of Anesthesiologists Closed Claims database.[1] According to this database, the most common site of injuries to the airway is the larynx, representing 33% of all airway injury claims. The most frequent types of laryngeal injury are vocal cord paralysis and hematoma or granuloma of the vocal cords. Moreover, hoarseness is a common postoperative complication with an incidence varying between 14.4 and 50%; it affects patient satisfaction and can affect a patient's activities even after leaving the hospital.[2–13] Indeed, prolonged or even permanent hoarseness may occur in 1% of patients.[11]

In the past, several risk factors for laryngeal injury and postoperative hoarseness (PH) have been identified, including endotracheal tube size, cuff design, and cuff pressure, as well as demographic factors such as sex or even the type of surgery.[3,8,12,14] However, whether the quality of tracheal intubation affects the incidence of laryngeal injury has not yet been systematically investigated. Kambic and Radsel[15] examined 1,000 patients postoperatively using the indirect mirror technique and reported 6.2% direct lesions. These were mainly hematoma or lacerations of the vocal cords. Similar results were reported by Peppard and Dickens[16] in a cohort of 475 patients. The authors of both studies speculated that poor muscle relaxation at the moment of intubation may have been causative for many of the observed laryngeal injuries, although this assumption still has not been proved by any randomized controlled trial. Therefore, the purpose of the current study was to test the following hypothesis: An induction technique including propofol, fentanyl, and a neuromuscular blocking agent (NMBA), *i.e.*, atracurium, results in a lower incidence of vocal cord sequelae (VCS) or PH compared to a propofol–fentanyl regimen without NMBA.

Materials and Methods

Patients

After obtaining approval from the Institutional Review Committee (University of the Saarland, Homburg/Saar, Germany) and written informed consent, we studied 80 adult patients aged 18–76 yr with American Society of Anesthesiologists physical status class I or II. All patients

Table 1. Scoring Conditions for Tracheal Intubation

Variable	Intubation Scores		
	Clinically Acceptable		Clinically Not Acceptable
	Excellent	Good	Poor
Laryngoscopy	—	—	—
Jaw relaxation	Relaxed	Not fully	Poor
Resistance to laryngoscope	None	Slight	Active
Vocal cords	—	—	—
Position	Abducted	Intermediate	Closed
Movement	None	Moving	Closing
Reaction to tube insertion or cuff inflation	—	—	—
Movement of limbs	None	Slight	Vigorous
Coughing	None	Slight	Sustained

Intubation conditions: excellent = all qualities are excellent; good = all qualities are excellent or good. Excellent and good intubation conditions are summarized as clinically acceptable intubation conditions.

underwent orotracheal intubation for elective surgery of the ear. Patients with obesity (defined as weight exceeding 20% of the normal weight); pregnant patients; patients suspected to have a difficult airway, *i.e.*, an abnormal airway anatomy (Mallampati score 3 or 4); and patients with a mouth opening of less than 3.5 cm or cervical spine disease were excluded, as were those with difficult intubation, *i.e.*, Cormack and Lehane score of 3 or greater. Patients with pathologic findings of the larynx revealed by the initial stroboscopic examination the day before surgery were also excluded. All patients were premedicated with 7.5 mg midazolam orally, 1 h before arrival in the operating room.

Induction and Maintenance of Anesthesia

Patients were randomized in two groups of 40 patients each, *via* random number draws, to receive either 0.5 mg/kg atracurium (atracurium group) or saline (saline group). The study drugs were administered in a double-blind fashion, and syringes were prepared (adjusted to a 5-ml volume) by an investigator who did not participate in the evaluation of intubating conditions, intubating score, and assessment of PH or VCS. After arrival of the patients in the operating room, monitoring, including electrocardiography, noninvasive arterial pressure monitoring, pulse oximetry, and capnography, was established, and baseline heart rate and mean arterial pressure were recorded (preinduction values). Induction regimen was standardized for both groups as follows: At time 0, 2–3 μg/kg fentanyl was injected; 3 min later, anesthesia was induced with 2.5–3 mg/kg propofol (injection over a period of 10 s). If necessary, additional doses of 30 mg propofol were titrated until loss of the eyelash reflex. Afterwards, the study drug (atracurium or saline) was injected over a 5-s period; exactly 3 min later, the patient's trachea was intubated by the same experienced anesthesiologist who was blinded to the group assignment. All drugs were administered in a rapidly running infusion of lactated Ringer's solution. After propofol administration and before tracheal intubation, *i.e.*, 3 min later, heart rate and mean arterial pressure were recorded as postinduction values. Two minutes after tracheal intubation, the postintubation values were noted. Anesthesia was maintained with 3–4% desflurane (end-tidal) in oxygen–air and bolus doses of fentanyl (1 μg/kg) as needed.

Assessment of Intubating Conditions and Intubating Scores

The intubating score was evaluated according to the consensus conference on Good Clinical Research Practice in Pharmacodynamic Studies of Neuromuscular Blocking Agents.[17] The intubating score was excellent if all variables were excellent, it was good if all variables were excellent or good, and it was poor if any variable was poor (table 1). In addition, the following parameters were also assessed by an independent observer after each intubation: glottic exposure as defined by Cormack and Lehane: grade 1 = complete visualization of the vocal cords, grade 2 = visualization of the inferior portion of the glottis, grade 3 = visualization of only the epiglottis, grade 4 = nonvisualized epiglottis; intubating time: time in seconds from the initial inserting of the laryngoscope until removing the blade from the patient's mouth after successful intubation; and the number of intubation attempts.

The following factors were standardized: tube size (men: ID = 8.5 mm; women: ID = 7.5 mm), type of tube, cuff inflation with 6–8 ml air leading to an intracuff pressure of less than 20 mmHg, and use of lignocaine gel. No intubation stylet or stomach tube was used.

Assessment of Postoperative Hoarseness

In the postanesthesia care unit and on postoperative days 1, 2, and 3, an investigator blinded to the group assignment of the patients and unaware whether patients had VCS asked the patients directly a specific question: Do you have any hoarseness at all since your operation? He recorded PH as follows[18]: 0 = none (no hoarseness), 1 = noticed by patient, 2 = obvious to

observer, 3 = aphonia. If PH persisted over postoperative day 3, a daily follow-up examination was performed until complete restitution.

Assessment of Postoperative Vocal Cord Sequelae

Vocal cord sequelae were examined by videolaryngostroboscopy by the same experienced ear, nose, and throat physician who was unaware of the patients' group assignments.[19] As part of the preoperative otolaryngeal evaluation, all patients underwent a stroboscopic examination of the vocal cords the day before surgery and were not included in the study if preexisting abnormalities of the larynx and vocal cords were revealed. VCS were recorded 24 h as well as 72 h after recovery from anesthesia. We concluded postoperative VCS if any of these two examinations revealed pathologic findings. If VCS persisted after 72 h, follow-up examination was performed twice a week until complete resolution. VCS were assessed as follows: location: unilateral (left or right vocal cord) or bilateral (both vocal cords); type of sequelae: thickening of the vocal folds (localized swelling at the vocal process of the arytenoid cartilage); edema (swollen mucosa at the vocal folds); erythema (redness of the mucosa with surrounding inflammatory swelling); hematoma (caused by bleeding into a vocal cord); granuloma of the vocal folds (granulation tissue remains as a chronic, localized, rounded tissue); arytenoid dislocation or luxation (displaced or luxated arytenoid with limited movement).

Statistical Analysis

Statistical analysis was performed using SigmaStat® for Windows 2.0 software (1995; Jandel Corporation, San Rafael, CA). The required number of patients was calculated in expectation of 45% VCS in the saline group and a 30% reduction of the absolute risk in the atracurium group. Type 1 error was set to 5%, and type 2 error was set to 20%. With this assumption, 72 patients were required. Numbers needed to harm (NNH) were calculateted.[20] A positive NNH indicated how many patients had to be exposed to the intervention (*i.e.*, omitting neuromuscular blockade) to produce one particular event (*i.e.*, VCS or PH) in one patient, who would not have had this event had he or she received neuromuscular blockade for induction of anesthesia. According to preset criteria, an NNH between 1 and 5 was considered a clinically relevant risk.[21] Data were expressed as mean (± SD) or median and range. Data on an ordinal scale were tested using the Mann–Whitney test and frequencies were tested using the Fisher exact test. To get insights into the contribution of the intubating scores to postoperative laryngeal morbidity, data from both study groups were pooled and analyzed with the Fisher exact test; the incidence of PH and VCS after excellent intubating scores was compared with the respective values after good and poor scores. $P < 0.05$ was considered statistically significant.

Table 2. Demographic Data and Duration of Surgery

	Atracurium (n = 37)	Saline (n = 36)	*P*
Age, yr	47.2 ± 13.2	47.7 ± 14.3	0.89
Weight, kg	77.7 ± 15.8	74.2 ± 14.9	0.36
Height, cm	171.3 ± 8.9	169.7 ± 9.6	0.48
Gender, male/female	19/18	16/20	0.72
Smoking	14	12	0.88
Reflux	4	3	1.00
Mallampati class 1/2	18/19	18/18	0.91
Duration of surgery (min)	70.5 (20–195)	65.0 (10–300)	0.57

Values are mean ± SD, numbers or median and range (duration of surgery).

Results

Eighty patients were enrolled in this study—40 patients in each group. Five patients were excluded from analysis because of a Cormack grade of 3 or greater (1 in the atracurium group and 4 in the saline group). Moreover, 1 patient in each group had an unexpected surgery of the pharynx and therefore had to be excluded. Thus, intubating conditions and incidence and severity of PH and VCS were investigated in the remaining 73 patients—37 in the atracurium group and 36 in the saline group. There were no significant differences among the two groups with respect to age, weight, height, sex distribution, history of smoking, reflux, and Mallampati class. Duration of surgery did not differ between the groups (table 2). The induction doses of fentanyl and propofol and the hemodynamic response to the intubation are shown in table 3.

In both groups, all patients could be intubated. Intubating time, number of attempts, and Cormack grades did not differ significantly between study groups. The

Table 3. Induction of Anesthesia and Hemodynamic Response to Tracheal Intubation

	Atracurium (n = 37)	Saline (n = 36)
Induction	—	—
Propofol, mg/kg	2.9 (1.8–4.8)	3.1 (2.1–6.3)
Fentanyl, μg/kg	2.4 (0.9–3.0)	2.3 (1.0–3.0)
Mean arterial pressure, mmHg	—	—
Preinduction	92 ± 13	88 ± 11
Postinduction	80 ± 12*	78 ± 11*
Postintubation	82 ± 14*	77 ± 13*
Heart rate, beats/min	—	—
Preinduction	77 ± 16	74 ± 13
Postinduction	71 ± 12	72 ± 14
Postintubation	72 ± 11	70 ± 14

Values are median and range or mean ± SD.

* $P < 0.05$ *versus* preinduction values.

Preinduction = before induction of anesthesia; Postinduction = 3 min after induction of anesthesia but before tracheal intubation; Postintubation = 2 min after tracheal intubation.

Table 4. Intubating Conditions and Intubating Scores

	Atracurium (n = 37)	Saline (n = 36)	*P*
Intubation conditions	—	—	—
Cormack grades	1 (1–2)	1 (1–2)	0.613
Time of intubation (s)	26 (10–106)	29 (7–90)	0.920
Attempts (n)	1 (1–3)	1 (1–3)	0.919
Intubation scores	—	—	—
Excellent	16	2	<0.001
Good	19	22	0.55
Poor	2	12	0.006
Clinically acceptable	35	24	0.006
Non-excellent	21	34	<0.001

Values are median and range (intubating conditions) or numbers.

rate of excellent intubating scores was significantly higher in the atracurium group compared with the saline group: 16 *versus* 2 patients, respectively; $P < 0.001$. The same was seen for the rate of clinically acceptable scores (excellent or good): 35 *versus* 24 patients, respectively; $P = 0.006$ (table 4).

Postoperative hoarseness occurred significantly more frequently in the saline group compared with the atracurium group: 16 patients (44%) *versus* 6 patients (16%); $P = 0.02$. The NNH to produce one patient with PH by omitting atracurium compared with giving this drug was 3.5 (confidence interval: 2.1–12.3). While in the atracurium group PH was limited to the postanesthesia care unit, PH persisted in five patients to the postoperative period in the saline group. In one patient, PH persisted for 96 h. Thus, the number of days with PH was significantly higher in the saline group compared with the atracurium group: 25 *versus* 6; $P = 0.003$ (table 5).

Vocal cord sequelae occurred significantly more frequently in the saline group compared with the atracurium group: 15 patients (42%) *versus* 3 patients (8%); $P = 0.002$ (table 5). The NNH to produce one patient with VCS by omitting atracurium compared with giving this drug was 2.9 (confidence interval: 1.9–6.6). The number of days with VCS was significantly higher in the saline group compared with the atracurium group: 50 *versus* 5; $P < 0.001$. In 13 patients, VCS was unilateral; most of them exhibited injury to the left vocal cord (9 *vs.* 4 patients). Hematomas were the most frequent laryngeal injury, occurring in 11 patients (table 6). Follow-up examination revealed that one patient had persistent bilateral hematoma and granuloma for 1 week, and another patient had bilateral hematoma and thickening of the vocal folds for 2 weeks (both patients from the saline group).

Table 6. Vocal Cord Sequelae: Stroboscopic Findings

	Atracurium (n = 37)	Saline (n = 36)	*P*
Unilateral	2	11	0.030
Left	1	8	0.047
Right	1	3	0.340
Bilateral	1	4	0.183
Morphology	—	—	—
Hematoma	1	10	0.008
Thickening of mucosa	3	6	0.31
Granuloma	0	2	0.24

Values are shown as numbers of patients (n).

There is a close correlation between the intubating score and PH: 2 of 18 patients with an excellent intubating score were hoarse (11%), 12 of 41 patients with good intubating scores were hoarse (29%), and 8 of 14 patients with poor intubating scores were hoarse (57%); excellent *versus* poor: $P = 0.008$; excellent *versus* nonexcellent (*i.e.*, good or poor conditions): $P = 0.08$; clinically acceptable (*i.e.*, excellent or good conditions) *versus* poor: $P = 0.02$. Similar findings were observed for VCS: 7 of 14 patients with poor intubating conditions had VCS (50%) compared with 9 of 41 patients with good scores (22%) and 2 of 18 patients with excellent intubating conditions (11%); excellent *versus* poor: $P = 0.02$; excellent *versus* nonexcellent (*i.e.*, good or poor conditions): $P = 0.2$; clinically acceptable (*i.e.*, excellent or good conditions) *versus* poor: $P = 0.03$. The intubation score subcomponents "vocal cords" and "reaction to tube insertion or cuff inflation" contributed to this result (figs. 1A and B and 2A and B).

Table 5. Incidence of Postoperative Hoarseness and Vocal Cord Sequelae

	Postoperative Hoarseness			Vocal Cord Sequelae		
	Atracurium (n = 37)	Saline (n = 36)	*P*	Atracurium (n = 37)	Saline (n = 36)	*P*
PACU	6	13	0.1	NA	NA	—
At 24 h	0	6	0.01	3	15	0.002
At 48 h	0	4	0.05	NA	NA	—
At 72 h	0	1	0.5	1	8	0.014
>72 h	0	1	0.5	0	2	0.25
Days*	6	25	<0.001	5	50	<0.001
Patients	6	16	0.02	3	15	0.002

Values are shown as numbers of patients (n).

* Days = number of days with PH or VCS. PH was first assessed in the PACU and thus, the day of surgery was takes as the first day with PH. VCS was first assessed at 24 h and thus, postoperative day 1 was taken as the first day with VCS. † Patients: number of patients with PH or VCS.

PACU = postanesthesia care unit; PH = postoperative hoarseness; VCS = vocal cord sequelae; NA = not assessed.

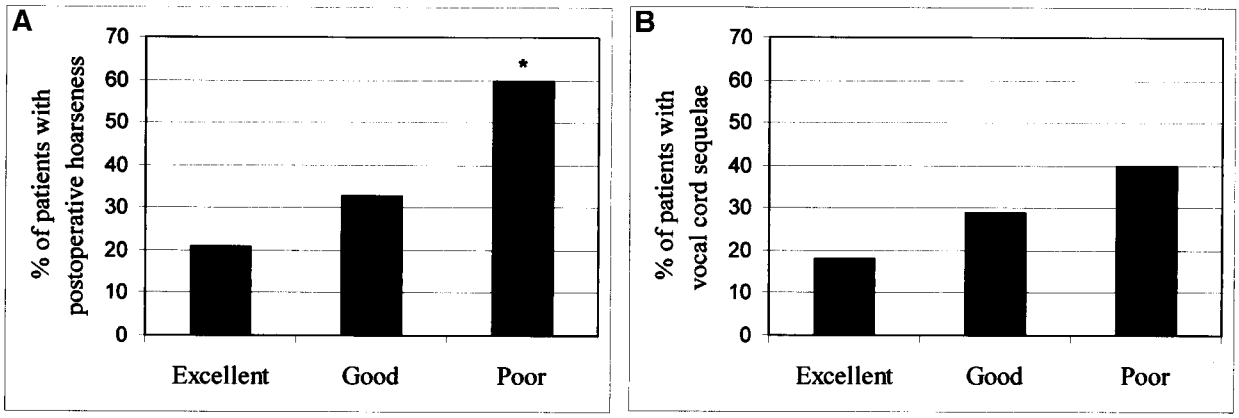

Fig. 1. (*A*) Relation between the intubation score subcomponent "vocal cords" and postoperative hoarseness (PH). Data from both study groups were pooled; the figure shows the percent of patients with excellent, good, and poor vocal cord conditions who had PH. *$P = 0.02$ compared to excellent conditions. (*B*) Relation between the intubation score subcomponent "vocal cords" and vocal cord sequelae (VCS). Data from both study groups were pooled; the figure shows the percent of patients with excellent, good, and poor vocal cord conditions who had VCS.

Discussion

The current study examined for the first time the influence of intubation conditions and induction technique on PH and VCS. The most important result of this study was that an induction technique including propofol and fentanyl but without atracurium was associated in 44% of patients with PH; VCS occurred in 42%. Adding atracurium significantly reduced this incidence to 16% and 8%, respectively (table 5). The NNH to produce one patient with VCS by omitting atracurium compared with giving this drug was 2.9. Moreover, excellent intubating scores were less frequently associated with either PH or VCS than good or poor scores (figs. 1 and 2).

Laryngeal damage, however, may not only occur during intubation, but may also be the result of some intraoperative factors. Increasing duration of surgery led to an increased incidence of PH, mainly because of mucosal damage caused by the endotracheal tube.[11] Moreover, movement of the tube in the trachea was found to be related with an increased incidence of hoarseness.[3] Thus, a baseline incidence of PH and VCS exists independently of the quality of tracheal intubation. This may explain why laryngeal damage could be observed in some patients despite optimal intubation conditions (figs. 1 and 2). In the current study, only patients undergoing ear, nose, and throat surgery were included. However, surgery of the larynx may lead to laryngeal damage independently of the intubation conditions, and surgery of the nose may postoperatively lead to temporary changes in the voice, thus influencing the evaluation of PH. Therefore, only patients undergoing surgery of the ear were enrolled, and the duration of surgery was similar between both groups. Moreover, demographic factors such as sex and technical factors such as size of the

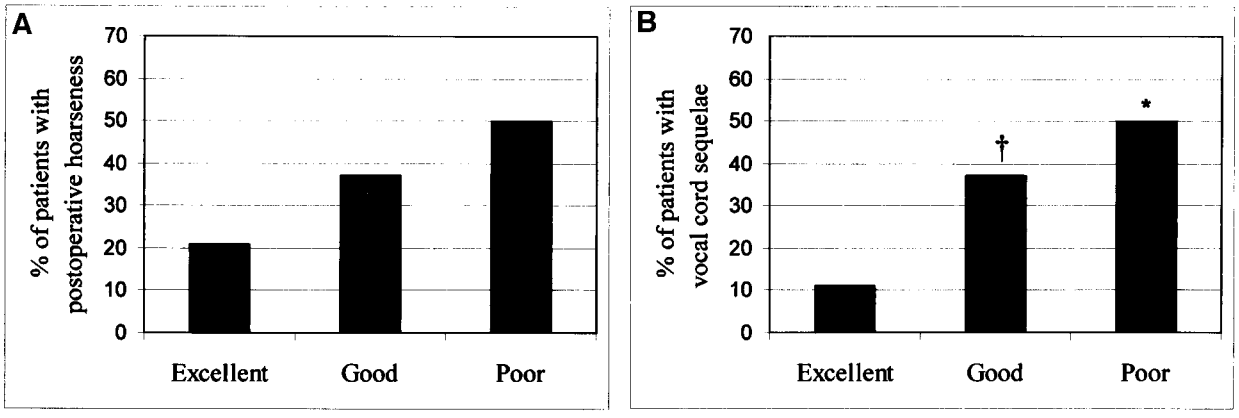

Fig. 2. (*A*) Relation between the intubation score subcomponent "reaction to tube insertion or cuff inflation" and postoperative hoarseness (PH). Data from both study groups were pooled; the figure shows the percent of patients with excellent, good, and poor conditions of the subcomponent with PH. (*B*) Relation between the intubation score subcomponent "reaction to tube insertion or cuff inflation" and vocal cord sequelae (VCS). Data from both study groups were pooled; the figure shows the percent of patients with excellent, good, and poor conditions of the subcomponent with VCS. *$P = 0.022$ compared to excellent conditions; †$P = 0.024$ compared to excellent conditions.

tube, cuff pressure, or gastric suction were standardized.[8,12,14] In addition, nicotine addiction and reflux, both suspected to be risk factors for hoarseness, were controlled[22] (table 2). Thus, the observed differences in PH and VCS in the current study should mainly reflect differences caused by tracheal intubation.

The observation that propofol causes greater suppression of laryngeal reflexes has renewed interest in the use of relaxant-free techniques of tracheal intubation. Intubation conditions attained using propofol alone, however, are far from ideal and have been considered adequate in only 38–60% of patients.[23–25] Addition of opioids improved intubation conditions; alfentanil, remifentanil, and fentanyl have been assessed in this context. Based on the recent findings of Andel *et al.*[26] as well as Ko *et al.*,[27] a propofol–fentanyl technique was used for the current study. Andel *et al.* determined the required propofol-dose in combination with fentanyl allowing reliably successful tracheal intubation without NMBA in all patients. According to their findings, a median propofol dose of 2.7 mg/kg is needed. Regarding the use of fentanyl in this context, Ko *et al.* reported that, in terms of blunting the hemodynamic response to laryngoscopy and tracheal intubation, it was more effective to administer the bolus dose of fentanyl 5 min before intubation than 1, 3, or 10 min before intubation. Thus, in the current study, 2–3 μg/kg fentanyl was given 5 min before intubation, and the median induction dose of propofol was 3.1 mg/kg in the saline group. As indicated by the hemodynamic response to laryngoscopy and tracheal intubation—both well-defined noxious stimuli for quantification of clinical depth of anesthesia[28]—intubation was performed at a deep plane of anesthesia in both groups (table 3). With this deep plane of anesthesia, all patients could be intubated even without atracurium (table 4). Without NMBA, however, VCS, mostly hematoma with unilateral localization of the left side, occurred in 15 of 36 patients, suggesting traumatic tracheal intubation as the underlying mechanism. Indeed, it has been proposed that the left vocal cord is more frequently injured because the laryngoscope is typically held in the left hand with the endotracheal tube being inserted from the right side.[29] Moreover, these 15 patients cumulated 50 days with VCS, compared to 5 days when atracurium was part of the induction regimen (tables 5 and 6 and figs. 3 and 4; Web Site Review). As a consequence of the observed sequelae of the vocal cords, a significantly higher proportion of patients had PH in the group with the relaxant-free induction regimen, and significantly more days with PH occurred in this group (table 5). Despite the sufficiently deep plane of anesthesia at the moment of tracheal intubation, the NNH to produce one patient with PH by omitting atracurium compared to giving this drug was 3.5. Thus, for 100 patients who were intubated with this technique, one may expect to cause PH in 29 patients. As revealed by the follow-up

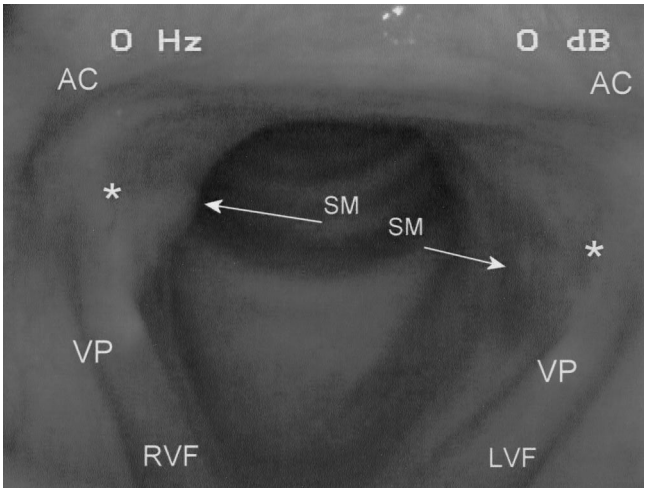

Fig. 3. Swollen mucosa (SM) and hematomas (*) at both arytenoid cartilages (AC) 24 h after intubation. VP = vocal process; LVF = left vocal fold; RVF = right vocal fold.

examination, two patients in the saline group had persistent hematoma and granuloma for 1 and 2 weeks, respectively. Jones *et al.*[11] reported PH in 54 of 167 patients after short-term intubation. All but five returned to normal within 7 days; however, these five patients were hoarse for 9, 10, 12, 54, and 99 days. Moreover, Kark *et al.*[30] comprised 100 women undergoing mastectomy as a control group for voice chances in patients undergoing thyroidectomy; 3% had persisted voice change for more than 6 months. Thus, PH can not be considered be a self-limiting minor problem, but the figures presented in the literature are alarming. Such a prolonged period of hoarseness would not only be catastrophic for the professional voice user such as a teacher, performer, or salesperson, but may be particularly harmful in the early postoperative period.

One may only speculate whether alfentanil or remifentanil instead of fentanyl would have improved the quality

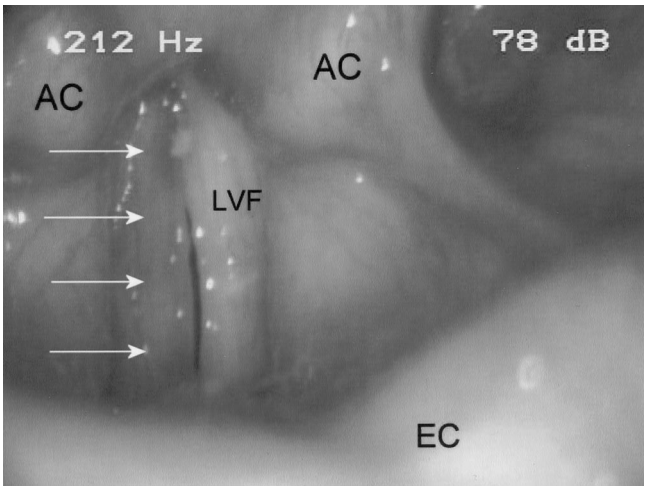

Fig. 4. Hematoma (arrow) at the right vocal fold 72 h after intubation. EC = epiglottis; AC = arytenoid cartilages; LVF = left vocal fold.

of tracheal intubation and led to a reduced incidence of PH or VCS. Scheller *et al.*[31] found the intubation conditions to be similar following propofol and alfentanil in doses of 50–60 μg/kg compared to thiopentone and suxamethonium. Another study, by Grange *et al.*,[32] comparing intubation conditions using propofol preceded by 20 μg/kg alfentanil showed that intubation could be performed in more than 90% of patients even with this dose of alfentanil. However, persistent coughing was noted in some patients in every group intubated without a relaxant in the study of Scheller *et al.*, and only half of the successful intubations in the study of Grange *et al.* were graded as excellent. Intubation without relaxants and using propofol with alfentanil has been reported by others as well but has been associated with coughing or movements of the limbs in a significant number of patients.[25,33–35] Similar results were reported for remifentanil.[36–40] Thus, without an NMBA, suboptimal conditions of the vocal cords or reaction to the intubation stimulus are regularly reported in all these studies, regardless of the dose of the opioid used. As demonstrated by the results of the current study, patients with overall good conditions had a three-times-higher incidence of PH compared with those with excellent conditions, and the subcomponents "vocal cords" and "reaction to intubation" may have led to this increased incidence. Eight of 39 patients (20%) with excellent vocal cord conditions had PH compared to 7 of 21 (33%) with good vocal cord conditions (fig. 1). Good vocal cord conditions, however, are characterized by an intermediate position of the vocal cords or moving vocal cords (table 1). Thus, if the intubation is performed in this situation, the risk of vocal cord injury is increased, and this may explain the higher incidence of PH. The same was observed for the subcomponent "reaction to intubation." Twenty-one percent of patients with excellent conditions of this subcomponent had PH compared with 37% of patients with good conditions of this variable (fig. 2). Even slight movements of the limbs or the diaphragm may lead to movements of the tube in the trachea, thus contributing to vocal cord injury and PH. This illustrates the significance to strive for excellent intubating conditions. Based on the above mentioned items, an NMBA-free induction regimen including propofol and alfentanil or remifentanil instead of fentanyl should also be associated with an elevated incidence of PH or VCS. To further examine this important issue, clinical trials realized in this context should assess not only intubation scores, but also laryngeal morbidity. Especially PH, as easy to assess and a clinically relevant outcome parameter, should regularly be considered. This information should contribute to better reflect the quality of tracheal intubation, thus allowing the clinician to balance the advantages of an induction technique against its risks for the patient's outcome.

Two more aspects should be considered in future research. First, onset properties of NMBAs are characterized by a large individual variability.[41] Timing of tracheal intubation by neuromuscular monitoring may allow determination of the best moment for intubation for each individual patient[42] and thus should decrease the incidence of laryngeal damage. Second, strategies for prevention and therapy of PH in patients at risk, such as professional voice users, must be developed.

This study demonstrated that the quality of tracheal intubation may affect the incidence of laryngeal morbidity. Adding atracurium to a propofol–fentanyl induction regimen significantly improved the quality of tracheal intubation and decreased PH and VCS. PH as a clinical relevant outcome parameter should regularly be assessed in studies investigating intubating conditions.

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