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RESPIRATION AND THE AIRWAY

Avoidance of neuromuscular blocking agents may increase the risk of difficult tracheal intubation: a cohort study of 103 812 consecutive adult patients recorded in the Danish Anaesthesia Database

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Background. Previous studies indicate that avoiding neuromuscular blocking agents (NMBAs) may be a risk factor for difficult tracheal intubation (DTI). We investigated whether avoiding NMBA was associated with DTI.

Methods. A cohort of 103 812 consecutive patients planned for tracheal intubation by direct laryngoscopy was retrieved from the Danish Anaesthesia Database. We used an intubation score based upon the number of attempts, change from direct laryngoscopy to a more advanced technique, or intubation by a different operator. We retrieved data on age, sex, ASA physical status classification, priority of surgery, time of surgery, previous DTI, modified Mallampati score, BMI, and the use of NMBA. Using logistic regression, we assessed whether avoiding NMBA was associated with DTI.

Results. The frequency of DTI was 5.1 [95% confidence interval (CI): 5.0–5.3]%. In a univariate analysis, avoiding NMBA was associated with DTI, odds ratio (OR) 1.52 (95% CI: 1.43–1.61)%, $P<0.0001$. Using multivariate analysis, avoiding NMBA was associated with DTI, OR 1.48 (95% CI: 1.39–1.58), $P<0.0001$. Among patients intubated using NMBA, a multivariate analysis identified patients anaesthetized with only non-depolarizing NMBA to be more at risk for DTI than those anaesthetized with depolarizing NMBA alone.

Conclusions. Avoiding NMBA may increase the risk of DTI. However, confounding by indication may be a problem in this observational study and systematic reviews with meta-analysis or more randomized clinical trials are needed.

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Difficult airway management including difficult tracheal intubation (DTI) may be a major cause of severe perioperative morbidity and mortality related to anaesthesia.[1–4] Predicting DTI enables the anaesthesiologist to take precautions to reduce the risks associated with tracheal intubation.[5] Several studies have focused on one or more factors related to the patient which may identify those at risk of difficult intubation.[6 7] In addition to patient factors, successful airway management is determined by the anaesthetist's technical skills, non-technical skills, the facilities available, and the local environment.[8 9] The results of previous randomized trials, although small and with surrogate outcome measures, indicate that avoiding neuromuscular blocking agents (NMBAs) may be associated with

increased risk of difficult intubation and more postoperative discomfort to the patients.[10–18]

An evaluation of the use of neuromuscular blocking drugs during anaesthesia of patients recorded in the Danish Anaesthesia Database from January 2005 to December 2007 demonstrated a decrease in the use of these drugs for general anaesthesia including intubation. In light of this change of practice, the aim of this study was to evaluate whether avoiding the use of neuromuscular blocking drugs for general anaesthesia including intubation by direct laryngoscopy is a risk factor for difficult intubation and failed tracheal intubation (FTI). Also, the use of non-depolarizing drugs was compared with depolarizing drugs as a risk factor for difficult intubation.

Methods

Fourteen Danish anaesthesia departments in 2005 and 25 in 2006–7 prospectively and consecutively reported data on patients undergoing anaesthesia and surgery to the Danish Anaesthesia Database version 2. The Danish Anaesthesia Database contains specific quantitative anaesthetic and surgical indicators describing the perioperative period. This information is recorded immediately after each operation by the anaesthesiologist. The departments (Appendix I) are connected online, via the Internet, to a central server.

The Danish National Board of Health and The Danish Data Protection Agency approved the registration in the Danish Anaesthesia Database of all patients undergoing anaesthesia. The steering committee of the Danish Anaesthesia Database approved this study and provided access to the data.

We retrieved 148 546 records of patients undergoing general or combined anaesthesia with tracheal intubation from January 1, 2005, to December 31, 2007 (Fig. 1). We excluded patients aged <15 yr, those already intubated, and those primarily undergoing rigid and flexible fibreoptic intubation. We included 103 812 patients, who were intubated 126 433 times in this study. About 15 512 patients were anaesthetized and undergoing intubation by direct laryngoscopy on more than one occasion, for these patients only the last record was included. Thus, the final cohort includes 103 812 patients each represented by only one session of attempted tracheal intubation by direct laryngoscopy. Of these patients, 84 had missing records of an intubation score (Table 1). About 12 850 patients had missing records for one or more covariates, whereas 90 962 patients had complete records without any missing data. All types of surgery are represented in the Danish Anaesthesia Database except for cardiothoracic surgery.

There is no national recommendation for the evaluation and handling of the airway in patients undergoing tracheal intubation in Denmark. Therefore, participating anaesthetic departments may differ in their recommendations for airway management.

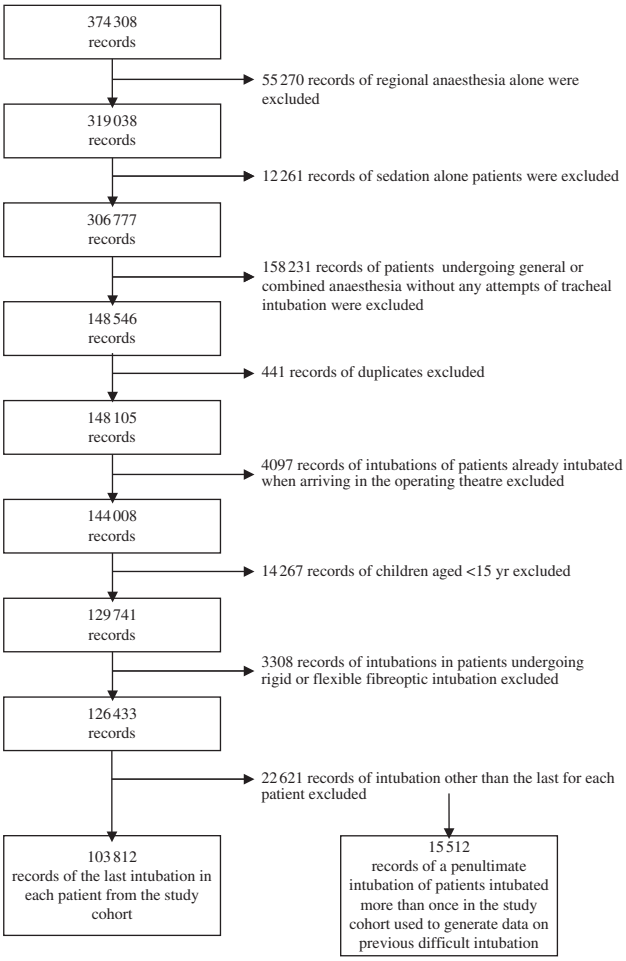

Fig 1 Selection of the study cohort. About 374 308 records of patients undergoing anaesthesia were identified in the Danish Anaesthesia Database. Excluding records of anaesthesia other than patients undergoing general or combined anaesthesia who were primarily undergoing tracheal intubation, the cohort included 148 546 records. Recorded intubations were excluded as explained in the figure. The subgroup of 15 512 records representing the penultimate intubations of patients intubated more than once was merged to the corresponding last intubation for the specific patient, and thereby information for the covariate PDI was created. Thus, 88 265 patients were only tracheal intubated once, 15 512 patients were intubated two or more times, while information was missing for 35.

Intubation score and covariates recorded in the Danish Anaesthesia Database

International consensus defining a DTI does not exist. Often, difficult laryngoscopy is used as a surrogate for difficult intubation,[19] whereas others suggest a specific definition of DTI.[5 20] We devised an intubation score based on fields in the Danish Anaesthesia Database (DTI score, Table 1) and recorded this score for all patients in whom tracheal intubation by direct laryngoscopy was attempted

Table 1 The Danish Anaesthesia Database tracheal intubation score. DTI was defined as an intubation score >1. Consequently, the definition of DTI includes FTI

All patients in whom the primary airway management plan was tracheal intubation by direct laryngoscopy were scored as follows	
Score=1	Intubated by direct laryngoscopy by the first anaesthetist and in two attempts maximally
Score=2	Intubated by direct laryngoscopy by the first anaesthetist but with more than two attempts or intubated by a supervising anaesthetist after one or more failed attempts at intubation
Score=3	Intubated by a method other than direct laryngoscopy
Score=4	Intubation failed after multiple attempts, no tracheal tube was inserted

and was the primary strategy planned for airway management.

The following data were obtained from the database: DTI score, age, sex, BMI, classification of ASA physical status, modified Mallampati score,[21] history of previous difficult intubation (PDI), priority of surgery, time of surgery, and the use of NMBA.

Each patient in the Danish Anaesthesia Database is recorded with a unique identifying number from the centralized civil register. This unique identifier contains information regarding the patient's sex and date of birth and enables exclusion of duplicate anaesthesia reports and identification of patients anaesthetized and recorded more than once during the period of observation. Patients anaesthetized more than once and with a previous record of at least one DTI in Danish Anaesthesia Database based on the intubation score (Table 1) were categorized as 'PDI'. The remaining patients were categorized as 'No or unknown PDI'.

Priority of surgery was defined as non-scheduled, if a patient was anaesthetized without being planned for surgery the previous day. Otherwise, surgery was categorized as scheduled. Time of surgery was categorized as 'Daytime' if start of surgery was between 08:00 and 16:00 or as 'Shift' if start of surgery was between 16:00 and 08:00. Height and weight were recorded in the Danish Anaesthesia Database based on preoperative measurements at the surgical wards or as reported by the patients. If records of height or weight were omitted, they were categorized as missing values. Height and weight ranges of 125–230 cm and 30–250 kg, respectively, were accepted as valid entries for the purpose of this analysis. BMI was calculated as weight/height^2 (kg m^{-2}). A warning appears during registration, if the calculated BMI exceeds 35 or is below 17, to emphasize that the weight and height entries should be reconsidered. If the Mallampati score was recorded as unknown, it was categorized as a missing value. For the analyses, the Mallampati score was dichotomized by combining class I with II and class III with IV. The use of NMBA was classified as 'depolarizing drugs with or without non-depolarizing drugs', 'non-depolarizing drugs only', or 'none'. If NMBA were used, it was not possible to distinguish between NMBA used exclusively for intubation, to facilitate surgery, or both. We also conducted analyses using a covariate combining the two classes describing the use of NMBA into one common class. The use of NMBA was dichotomized as the 'use of NMBA' and 'avoidance of NMBA'. For our assessments, we therefore used variables describing the use of NMBA in either two or three categories. There are no records of actual anaesthetic drugs used for the anaesthesia. It is not recorded in the Danish Anaesthesia Database whether neuromuscular monitoring is used for quantifying the degree of NMBA. It is not possible to acquire detailed information of airway management from the Danish Anaesthesia Database such as the type of laryngoscope blade or other types of equipment used for intubation.

Statistical analysis

We performed univariate regression analyses to evaluate the possible associations between DTI and the predefined covariates. A subsequent multivariate logistic regression analysis was performed including all significant covariates from the univariate analyses. Backward stepwise regression was performed to identify a final model. In logistic regression, it is assumed that the effect of a covariate is independent of the other covariates on the outcome measure. We tested if there were any first-order interactions between the use of NMBA and all the other covariates on the occurrence of DTI.

All regression analyses are presented with the significant covariates listed with their odds ratios (ORs) and corresponding 95% confidence interval (CI). A model control was performed with the Hosmer and Lemeshow goodness-of-fit test. In the model, it is assumed that continuous covariates have a linear association with DTI. This assumption of linearity was tested for age by testing whether replacing Age with (Age×Age) resulted in any model improvement.

We evaluated whether the 'avoidance of NMBA' increased the risk of FTI. Uni- and multivariate analyses were performed based upon the cohort selected as previously described. The Danish Anaesthesia Database does not offer a description of the type of NMBA used in patients with failed intubation, if a planned general anaesthetic is changed into a regional anaesthetic or monitored anaesthesia care (sedation).

The prevalence and pattern of missing data among all covariates were examined. We used the statistical method of multiple imputations for handling missing data. We imputed 10 data sets and pooled the estimates as described by Rubin[22] and Schafer and colleagues.[23 24] If there were any noticeable differences between the pooled estimates of

Table 2 The use of neuromuscular blocking agents over the 3 yr of the study for patients undergoing tracheal intubation. Each figure is: number of patients (percentage of column total). NMBA, neuromuscular blocking agent. The table illustrates complete cases. Data were missing in 84 patients

Year	2005	2006	2007	Total
No use of NMBA	3115 (17.5)	9159 (25.8)	15 917 (31.6)	28 191 (27.2)
Non-depolarizing NMBA	9266 (52.0)	15 769 (44.4)	18 342 (36.4)	43 377 (41.8)
Depolarizing ± non-depolarizing NMBA	5453 (30.6)	10 551 (29.7)	16 156 (32.0)	32 160 (31.0)
Total	17 834	35 479	50 443	103 728

the multiple imputation and the original estimates, both results are presented. In all analyses, $P<0.05$ was regarded as statistically significant. SPSS v15.0 and AMOS v7.0 were used for the analyses. NORM v2.03 by Schafer was used for pooling of estimates from the statistical analyses of each imputed data set.

This study has been presented according to the STROBE statement on the reporting of an observational cohort study.[25]

Results

The frequency of patients undergoing tracheal intubation without the use of NMBA increased over the 3 yr of observation from 17.5% in 2005 to 25.8% in 2006 and to 31.6% in 2007 (Table 2). The incidence of 'no use of NMBA' may have been influenced by the large increase of patients from different hospitals included over the years of observation. The incidence of 'no use of NMBA' in the original 14 hospitals over the 3 yr increased from 17.5% in 2005 to 24.8% in 2007. The overall frequency (95% CI) of DTI was 5.1 (5.0–5.3)%. The frequencies of DTI in 2005, 2006, and 2007 were 5.8%, 4.9% and 5.1%, respectively. Failed intubation occurred in 277 patients with an overall frequency of 0.27 (0.24–0.30)%. The characteristics of all patients are displayed in Table 3.

The univariate analysis of the dichotomized covariate of the use/avoidance of NMBA demonstrated an OR for DTI of 1.52 (1.43–1.61, $P<0.0001$) with 'avoidance of NMBA'. In the univariate analyses, the covariates: sex, priority of surgery, time of surgery, ASA classification, BMI, Mallampati score, PDI, and age were all statistically significantly associated with difficult intubation ($P<0.0001$). These covariates were included in the subsequent multivariate analyses.

A multivariate analysis of the 90 962 patients without any missing data, including all the statistically significant covariates from the univariate analyses, identified all covariates except the ASA classification and time for surgery to be independent risk factors of DTI (Table 4). The multivariate analysis of the dichotomized covariate of the avoidance of NMBA/use demonstrated an OR for DTI 1.48 (1.39–1.58, $P<0.0001$) with 'avoidance of NMBA'.

Exploring the model for interactions identified a statistically significant interaction of NMBA with surgical priority ($P<0.0001$). This means that the association between DTI and the use of NMBA is dependent on surgical priority and vice versa. Therefore, we introduced a new covariate combining the use/avoidance of NMBA and levels of surgical priority and repeated the multivariate analysis with this covariate having four levels. Among the patients undergoing non-scheduled surgery, the OR of difficult intubation was 3.10 (2.69–3.57, $P<0.0001$) for those anaesthetized without the use of NMBA. In those undergoing scheduled surgery, the OR of difficult intubation was 1.26 (1.18–1.35, $P<0.0001$) for those anaesthetized without the use of NMBA. These analyses show that regardless of surgical priority, the risk of DTI was highest in patients anesthetized and intubated without using NMBA, and the impact of avoiding the use of NMBA on the risk of DTI was highest for non-scheduled patients.

The dichotomized covariate avoidance of NMBA (as opposed to the use of NMBA) was statistically significantly associated with FTI. In a multivariate analysis, the OR of FTI was 1.72 (1.21–2.43, $P<0.0001$) for 'avoidance of NMBA'. The model in this case included adjustments for BMI as a continuous covariate; Mallampati score; sex male; PDI; and age were also significantly associated with FTI in this multivariate analysis.

We repeated our analysis with the use of NMBA stratified into three classes as 'depolarizing drugs with or without non-depolarizing drugs', 'non-depolarizing drugs only', or 'none'. Univariate analysis with 'depolarizing drug with or without non-depolarizing drug' as the reference group demonstrated an OR for DTI of 1.80 (1.68–1.94, $P<0.0001$) for the avoidance of NMBA and of 1.33 (1.24–1.43, $P<0.0001$) for 'non-depolarizing drug only'. Multivariate analysis demonstrated an OR for DTI of 1.74 (1.59–1.90, $P<0.0001$) with avoidance of NMBA and of 1.26 (1.16–1.37, $P<0.0001$) for 'non-depolarizing drug only'.

Performing multiple imputations for handling missing values did not exhibit noticeable differences between our original estimates and the pooled imputed estimates. As an example, because of missing data concerning the use of NMBA, the original assessment did not include 109 patients for whom a general anaesthesia was converted into a regional anaesthesia or sedation because of an FTI. We included these patients in a new assessment by using multiple imputations. The OR for FTI for 'avoidance of NMBA' was 1.85 (1.37–2.51) after multiple imputations and 1.72 (1.21–2.43) in our complete case analysis, respectively.

Table 3 Characteristics of the patients. The table shows the number of patients. The figures in parentheses are the column percentage within each categorical covariate. For continuous covariates, the figures in parentheses show the range. NMBA, neuromuscular blocking agent; ASA, American Society of Anesthesiologists physical status classification

	Use of NMBA			**Total**	**Missing of total**
	No NMBA	**Non-depolarizing**	**Depolarizing ± non-depolarizing**		
All patients	28 201	43 394	32 189		84 (0.1%)
Categorical covariates					
Difficult intubation					84 (0.1%)
Yes	1899 (6.7)	2192 (5.1)	1239 (3.9)	5330	
No	26 292 (93.3)	41 185 (94.9)	30 921 (96.1)	98 398	
Sex					84 (0.1%)
Male	12 388 (43.9)	18 676 (43.1)	13 429 (41.8)	44 493	
Female	15 803 (56.1)	24 701 (56.9)	18 731 (58.2)	59 235	
Priority of surgery					88 (0.1%)
Scheduled	23 897 (84.8)	37 089 (85.5)	12 048 (37.5)	73 034	
Non-scheduled	4292 (15.2)	6286 (14.5)	20 112 (62.5)	30 690	
Time of surgery					106 (0.1%)
Daytime	26 110 (92.7)	40 369 (93.1)	19 653 (61.1)	86 132	
Shift	2064 (7.3)	3004 (6.9)	12 506 (38.9)	17 574	
ASA classification					1770 (1.7%)
I	14 879 (53.9)	15 357 (35.8)	10 582 (33.5)	40 818	
II	9883 (35.8)	19 075 (44.5)	12 931 (40.9)	41 889	
III	2570 (9.3)	7537 (17.6)	6772 (21.4)	16 879	
IV	232 (0.8)	809 (1.9)	1222 (3.9)	2263	
V	25 (0.1)	71 (0.2)	97 (0.3)	193	
BMI					1747 (1.7%)
<35	26 818 (96.3)	41 106 (96.0)	28.146 (89.7)	96 070	
≥35	1043 (3.7)	1735 (4.0)	3224 (10.3)	6007	
Mallampati score					11 741 (11.3%)
I and II	22 635 (93.0)	37 083 (93.7)	25 433 (90.2)	85 151	
III and IV	1696 (7.0)	2495 (6.3)	2749 (9.8)	6940	
Previous difficult intubation					84 (0.1%)
Yes	243 (0.9)	351 (0.8)	312 (1.0)	906	
Unknown	24 690 (87.6)	37 265 (85.9)	26 279 (81.7)	88 234	
No	3258 (11.6)	5761 (13.3)	5569 (17.3)	14 588	
Continuous covariates					
	Means				
Age (yr)	48 (15–104)	56 (15–104)	53 (15–106)	0 (0%)	
Weight (kg)	75 (30–213)	74 (30–195)	77 (30–225)	857 (0.8)	
Height (cm)	172 (125–218)	171 (130–211)	171 (125–218)	1640 (1.6)	

Table 4 Multivariate model for DTI. References comparators were: 'Use of NMBA'; Surgical priority: non-scheduled; 'no or unknown PDI'; Sex: female; Mallampati class I or II; BMI <35

Covariates	**Odds ratio**	**95% CI**	***P*-value**
Avoidance of NMBA	1.48	1.39–1.58	<0.0001
Surgical priority: scheduled	1.46	1.36–1.57	<0.0001
Sex: male	1.34	1.26–1.42	<0.0001
BMI ≥35	1.31	1.16–1.46	<0.0001
Mallampati class III and IV	3.72	3.44–4.01	<0.0001
PDI	3.94	3.27–4.75	<0.0001
Age (yr)	1.01	1.01–1.01	<0.0001

Discussion

We found a frequency of 5.1% of DTI confirming the estimate in a previous meta-analysis.[7] The frequency of patients intubated without the use of NMBA increased considerably over the 3 yr of observation whereas the frequency of DTI was relatively constant during the same period. In both our univariate and multivariate analyses of this large Danish Anaesthesia Database cohort, avoiding NMBA was associated with DTI with an OR of 1.5. We identified a statistical interaction between the covariates such that the impact of avoiding NMBA on DTI differed with surgical priority. Regardless of surgical priority, the risk of DTI was highest in patients anaesthetized and intubated without the use of NMBA. Among patients intubated using NMBA, a multivariate analysis identified that patients anaesthetized with only non-depolarizing NMBA to be more at risk for DTI than those anaesthetized with depolarizing NMBA alone. Meta-analyses indicate that succinylcholine offers better conditions for tracheal intubation than rocuronium when evaluating both excellent and clinically acceptable conditions of tracheal intubation.[26 27] Our results may support the position that the use of a depolarizing neuromuscular blocking drug is associated with fewer difficult intubations than that of a non-depolarizing NMBA. However, the

Danish Anaesthesia Database does not contain data on whether patients were intubated using a rapid sequence induction or not. Including more covariates, especially records of rapid sequence induction, in our investigation may have changed the result, and ultimately remove 'non-depolarizing NMBA' as an independent risk factor for difficult intubation. Finally, avoiding NMBA was identified as a significant risk factor for failed intubation with an OR of 1.7.

In our multivariate analysis, we found that a Mallampati score III and IV was associated with DTI with an OR of 3.7, which is slightly lower than reported by Shiga and colleagues.[7] PDI was associated with difficult intubation with an OR of 3.9. Both male sex and a BMI of $\geq$35 were identified as risk factors of DTI with an OR of 1.3 in each case.[28]

Confounding by indication[29] is recognized to introduce bias in non-randomized studies evaluating interventions.[30] In this case, the clinical choice of tracheal intubation with or without the use of NMBA depends on multiple factors related to the patient, to the surgery, and to other aspects of the clinical situation. The choice to use or avoiding neuromuscular blocking drugs may be based on reasons not recorded in the Danish Anaesthesia Database. Therefore, patients in whom NMBA are avoided, tracheal intubation may be fundamentally different from those in whom such drugs are used. This may be the reason for the patients anaesthetized without the use of these drugs were more likely to be difficult to intubate. The airway management of a patient with an anticipated difficult intubation is likely to differ from that of a patient with unanticipated difficult intubation. If a difficult intubation is anticipated, this may influence the decision to use or avoid NMBAs. Likewise, a more experienced physician may be allocated for the task, or the patient may be undergoing a fibreoptic intubation, with a rigid or flexible scope, making the patient ineligible for our analysis. Thus, despite the fact that our study clearly exhibits a robust statistical association between avoiding NMBA and DTI, it does not prove unequivocally that avoiding NMBAs is a cause of difficult intubation.

Several studies indicate[13 16 31–33] numerous possible disadvantages associated with avoiding neuromuscular blocking drugs. However, our results illustrate a dramatic change in clinical behaviour among Danish anaesthesiologists with the avoidance of NMBAs during anaesthesia having almost doubled between 2005 and 2008.

The Danish Anaesthesia Database does not contain any information on the actual anaesthetic drugs. However, based on our experiences, we believe that total i.v. anaesthesia with propofol and remifentanil makes up the majority of the anaesthesia without any use of neuromuscular blockers. Several studies have evaluated the optimal doses of drugs used for different regimens for tracheal intubation without the use of relaxants.[14 34–36] As there are no records of anaesthetic drugs and dosing, it is impossible to assess the influence of these drugs on intubating conditions. Hence, we cannot exclude that a suboptimal administration of the adjuvant hypnotics and analgesics contributes to our result.

Despite the evidence that avoiding neuromuscular blocking drugs is associated with difficult intubation, the overall frequency of difficult intubation did not increase over the study period, whereas avoidance of neuromuscular blockers increased considerably. There may be more explanations for this, as time-related factors, observed and unobserved, may have changed over the years of observation. First, the overall characteristics of the populations recorded in the Danish Anaesthesia Database may have changed within each of the participating departments. Secondly, the overall characteristics of the populations recorded in the Danish Anaesthesia Database may have changed after 2005 due to substantial differences in the populations of the 11 new participating departments. Finally, during this period, the anaesthesiologists and the departments may have learned to manage tracheal intubation without using neuromuscular blockers, so reducing the incidence of difficult or failed intubation.

There is no international consensus definition of a 'difficult intubation'. An intubation score simply based upon the number of attempts shows that multiple attempts at tracheal intubation may be associated with morbidity.[37] The intubation difficulty scale[20] in contrast gives a detailed description of the circumstances of the tracheal intubation. An intubation score, which includes all possible factors of importance for a successful intubation, may not be feasible. Therefore, most intubation scores are compromises. The intubation score in the Danish Anaesthesia Database is based upon: the number of attempts, intubation by a different operator, or change from direct laryngoscopy to a more advanced technique.

The present study is based upon a large cohort of prospectively and consecutively collected data representing everyday experience from clinical practice. The interface to register the airway-evaluation, -plan, and -management was the same for all the registration sites as was the validation and the online user manual for the Danish Anaesthesia Database. This confers a high external validity. The large number of patients enabled us to detect or reject weak associations with adequate statistical power and strengthened the precision of the estimates. However, we cannot ensure that controlled and uniform conditions were met and applied in all the patient encounters due to a heterogeneous population of patients and reporters and a lack of national recommendations for airway management. This may reduce the internal validity of this study.

It is a limitation of our study that there were no records of the degree of relaxation measured by nerve stimulation during intubation and there were no records of actual anaesthetic drugs used for the anaesthesia. It is also a limitation of the study that when NMBAs were used, it was impossible to distinguish whether this was for intubation or to facilitate surgery. This is of greater concern for the records dealing with the sole use of non-depolarizing agents. It seems reasonable that when a depolarizing agent was used, this was exclusively for intubation. Difficult

intubation in patients who received a non-depolarizing NMBA to facilitate surgery may explain why the use of non-depolarizing agents was associated with more at risk of difficult intubation than the use of a depolarizing with or without additional non-depolarizing agents.

There were numerous missing records of the use of neuromuscular blocking drugs in the patients recorded as failed intubation. Therefore, the validity of our results regarding failed intubation may be limited. It is a limitation of the study that records of the educational level or years of experience of the anaesthetists performing the intubations are not available. Those with the least experience may have more episodes of difficult intubation. Finally, the number of risk factors for difficult intubation examined in our study is limited. Additional risk factors for difficult intubation may change the importance of neuromuscular blocking drugs as an independent risk factor for difficult intubation.

The present study adds to previous studies dealing with the risk of difficult intubation and offers a description of the risk of difficult intubation in daily anaesthetic practice. In our large Danish cohort, avoiding neuromuscular blocking drugs was demonstrated to be a risk factor for difficult and failed intubation independent of other risk factors recorded in the Danish Anaesthesia Database. Confounding by indication is a major problem in observational studies to describe the effect of interventions. Randomized clinical trials comparing the avoidance and use of neuromuscular blocking drugs for intubation and examining patient-centred outcomes would be of value.

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Appendix I: Contributing departments

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Department of Anaesthesiology, Horsens Hospital, Horsens.
Department of Anaesthesiology, Vejle Hospital, Vejle.
Department of Anaesthesiology, Kolding Hospital, Kolding.
Department of Anaesthesiology, Brædstrup Hospital, Brædstrup.
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