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A Retrospective Assessment of the Influence of Nasotracheal Intubation
Versus Conventional Airway Management in Critically Ill Patients on
Sedation and Outcome (NaTra-R-Study).

Dissertation

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1. Introduction

Endotracheal intubation is a technique which allows securing of the airway and mechanical ventilation. There are two main routes of intubation: orotracheal and nasotracheal intubation, as well as surgically securing the airway, which is also known as tracheostomy.

1.1. Historical Background

Successful endotracheal intubation was first documented during the early nineteenth century. The Frenchman Bouchut (Bouchut, 1858) is thought to have been the first physician to seriously consider endotracheal intubation a viable option to tracheostomy, even though at the time his idea was not well received among his colleagues. The Scottish surgeon Macewen popularized orotracheal intubation and managed the induction of general anesthesia for the first time in humans (Macewen, 1880, Luckhaupt and Brusis, 1986).

In the early twentieth century, Kuhn pioneered nasotracheal intubation (Luckhaupt and Brusis, 1986, Kuhn, 1902, Thierbach, 2001), which did not reap success until World War I, when physicians realized that nasotracheal intubation in soldiers with severe facial injuries was a feasible option. The physicians were, inter alia, Magill and Rowbotham, who continued to develop intubation techniques and advance refined instruments during the first World War (Magill, 1923, Rowbotham and Magill, 1921, Condon and Gilchrist, 1986, Thomas, 1978, Baskett, 2003, Nosker and Swan, 2007). They also established the official term 'blind nasal intubation' (Szmuk et al., 2008, Magill, 1975). The Macintosh laryngoscope, which is still used these days, was invented by Macintosh in the mid twentieth century, in order to facilitate orotracheal intubation (Macintosh, 1943).

Nowadays orotracheal intubation is preferred to nasotracheal intubation. Towards the end of last century several prospective studies were published showing that nasotracheally intubated patients develop hospital acquired sinusitis more frequently than patients intubated orotracheally (Salord et al., 1990, Aeberli et al., 1988, Michelson et al., 1991). Holzapfel et al. ascertained that patients intubated nasotracheally run a higher risk of developing nosocomial pneumonia and septicemia (Holzapfel et al., 1993).

Non-infectious complications such as epistaxis and sinusitis are also associated with nasal tube placement (Hariri et al., 2018) and therefore might have contributed to the increasing popularity of orotracheal intubation over nasotracheal intubation.

1.2. Significance

In intensive care medicine endotracheal intubation and mechanical ventilation are frequently required. A secure airway must be guaranteed for surgery and diagnostics taking place under general anesthesia, and in situations, in which patients are unable to ventilate and/or oxygenate sufficiently by themselves, such as when experiencing respiratory distress or failure (Grensemann et al., 2019), or when the airway needs protection from impending aspiration (Kabrhel et al., 2007). A further indication for endotracheal intubation is the suffering from underlying conditions, such as pneumonia, chronic obstructive pulmonary disease, sepsis, myocardial infarction, and trauma (Mort, 2004, Knapp and Popp, 2017). Mechanical ventilation can be achieved through either oral or nasal tube placement, however nowadays nasotracheal intubation has mostly been replaced by orotracheal intubation (Hariri et al., 2018), but is still performed in certain circumstances such as during oral surgery (Prasanna and Bhat, 2014, Chauhan and Acharya, 2016). Orotracheal intubation is the most common method of intubation and usually requires preoxygenation and administering of narcotics and muscle relaxants (Grensemann et al., 2019, Holzapfel et al., 1993).

Towards the end of the last century orotracheal intubation became increasingly popular which led to nasotracheal intubation being replaced by orotracheal intubation due to various reasons including fewer occurrences of epistaxis and sinusitis (Holdgaard et al., 1993, Stauffer et al., 1981). In their paper 'Nasotracheal intubation in ICU: an unfairly forgotten procedure' Hariri et al discuss the advantages of nasotracheal intubation in an intensive care setting (Hariri et al., 2018). The medical, medicinal, and hygienic standards and possibilities of today's medicine have greatly evolved since orotracheal intubation became the preferred route of intubation, therefore calling for a reconsideration of nasotracheal intubation and a re-evaluation of its risks opposed to those of orotracheal intubation.

1.3. Anatomy

1.3.1. Nasal anatomy

The nasal skeleton is made up of the bony nasal pyramid and the nasal cartilage. The nose opens into two nares which lead into the left and right nasal cavity divided by the nasal septum. The paired superior, middle, and inferior nasal conchae protrude into the internal nose creating four airway passages. The left and right nasal cavities meet at the choana and open into the nasopharynx. The nasopharyngeal region then continues into the oropharynx, laryngopharynx with the vocal cords and the epiglottis, and finally into the trachea which connects to the lungs (Fritsch and Kuehnel, 2015).

During nasotracheal intubation the tube can either be placed through the airway passage below the inferior turbinate or between the inferior and middle turbinate (Prasanna and Bhat, 2014).

1.3.2. Oral anatomy

The oral cavity is comprised anteriorly of the lips, laterally of the cheeks, superiorly of hard and soft palate, which separate the oral from the nasal cavity, and inferiorly by the muscular floor of the mouth. The oral cavity leads directly into the oropharynx, then into the laryngopharynx and eventually connects to the trachea (Fritsch and Kuehnel, 2015).

1.4. Technique

Endotracheal intubation is the placement of a breathing tube into the trachea and is usually performed with the help of a laryngoscope. Direct visualization of the vocal cords is known as direct laryngoscopy whereas visualization of the cords by means of a video or mirror is referred to as indirect laryngoscopy (Grensemann et al., 2019). Both methods can be used during endotracheal intubation. The laryngoscope enables visualization of the larynx with the vocal cords and prevents esophageal tube placement. Laryngoscopes can be utilized during orotracheal as well as nasotracheal intubation.

Orotracheal intubation is usually preceded by sedation, administering of muscle relaxants, and preoxygenation as to avoid triggering of the gag reflex with subsequent vomiting and potential gastric aspiration as well as to prevent desaturation and hypoxia

during the process. Following the preparations, the laryngoscope is inserted into the mouth allowing visualization of the epiglottis and the vocal cords. Then the breathing tube can be advanced through the mouth into the pharynx and then larynx and finally into the trachea through the vocal cords ensuring gas exchange (Kabrhel et al., 2007, Grensemann et al., 2019).

Laryngoscopic nasotracheal intubation may follow the same preparatory measures as orotracheal intubation, in other words sedation, administering of muscle relaxants, and preoxygenation. However, this method of endotracheal intubation can also be performed on an awake patient and therefore does not necessarily require sedation and muscle relaxant application as it is often sufficient to use a topical anesthetic (Prasanna and Bhat, 2014, Gaskill, 1967, Hariri et al., 2018). The tube is lubricated and then inserted into the nares and advanced most commonly through the inferior turbinate into the trachea whilst the healthcare professional is able to see all relevant anatomical structures by the means of a laryngoscope or a flexible bronchoscope (Atanelov and Rebstock, 2020, Prasanna and Bhat, 2014, Chauhan and Acharya, 2016).

As the name suggests blind nasal intubation does not require a visualization aid. This method can be utilized in patients who are awake or those with a difficult airway where visualization is barely possible or not possible at all (Yoo et al., 2015). The nasopharynx is anaesthetized and the lubricated breathing tube is advanced through the nares into the larynx and finally into the trachea (Chauhan and Acharya, 2016).

Nowadays blind nasal intubation is not performed routinely as flexible fiberscopes are usually available, allowing the demonstration of anatomical structures such as the vocal cords when intubating. The advantage of blind nasal intubation is that this procedure can be performed very quickly, without any special preparation, it does not require any instruments that can increase the risk of causing traumatic injuries to the upper airways (Chauhan and Acharya, 2016, Gaskill, 1967) and it seems to induce hemodynamic changes less frequently than when intubating with a laryngoscope (King et al., 1951).

1.5. Alternatives

The most common alternative to endotracheal intubation in situations of prolonged mechanical ventilation in the intensive care unit is tracheostomy (Durbin, 2010, Grensemann et al., 2019). There are different techniques of tracheostoma implantation, namely percutaneous dilatational and open surgical tracheostomy (Cheung and Napolitano, 2014, Grensemann et al., 2019). Percutaneous dilatational tracheostomy methods are Ciaglia I (Ciaglia et al., 1985), and II (Ciaglia, 1999), Frova (Frova and Quintel, 2002), and Griggs (Griggs et al., 1990). The main method used in German ICUs is Ciaglia II (Baumann et al., 2010).

Before open surgical tracheostomy local anesthetics, vasoconstrictors, and neuromuscular blockers, inter alia are administered. A transverse incision is made into the skin of the neck between the second and fifth tracheal ring under sterile conditions. The surgical field is carefully dissected to expose the trachea, into which the tracheostoma is inserted through a small incision. The dissected edges of the tracheal wall are sutured to the skin (Durbin, 2010, Muscat et al., 2017).

As with the open surgical tracheostomy medication is administered and sterile conditions are ensured in preparation for the percutaneous dilatational tracheostomy. A bronchoscope might be used to allow for visualization during the process but is not essential. An ultrasound of the neck is a less invasive method resulting in fewer complications (Grensemann et al., 2017). A small incision in the neck is made, which is then bluntly dilated until a tracheostoma can be inserted. Depending on the technique different steps in securing the artificial airway via percutaneous dilatational tracheostomy can be observed (Hazard et al., 1991, Durbin, 2010, Cheung and Napolitano, 2014, Baumann et al., 2010).

Advantages of tracheostomy compared to endotracheal intubation are the improved respiratory mechanics, facilitated tracheobronchial toilet, tracheal suctioning and oral hygiene, higher patient comfort during mechanical ventilation, and earlier oral food intake amongst other things (Hazard et al., 1991, Blot and Melot, 2005, De Leyn et al., 2007).

Disadvantageous is the fact that a tracheostomy is an operation bearing all risks of surgical intervention such as hemorrhage, infection, impaired wound healing,

damage to surrounding anatomical structures, inter alia. Furthermore, with tracheostomy pneumothorax or pneumomediastinum, tracheal stenosis, subcutaneous emphysema, hypoxemia, and fistula formation between the trachea and the esophagus or the brachiocephalic artery can occur (Smith, 1966, Hazard et al., 1991, Epstein, 2005, De Leyn et al., 2007, Stauffer et al., 1981). Lethal outcomes are seldom but also pose a risk (Simon et al., 2013).

Other complications associated with mechanical ventilation and intubation, such as perforation or dislocation of the breathing tube, reddening and swelling of the trachea and larynx, mucosal irritation, and lesions, as well as bleeding, and air trapping can also occur (Bontempo and Manning, 2019, Murray et al., 2022).

Emergency airway management can be achieved through the usage of a face mask or a laryngeal mask, although neither one of these methods allows definite securing of the airway (Walls and Murphy, 2008).

Cricothyroidotomy also known as coniotomy can be implemented for emergency airway management if all other options fail. As with tracheostomy the skin barrier is penetrated in order to place a breathing tube in the trachea, although the coniotomy is performed more cranially than the tracheostomy, just below the laryngeal prominence (Thurnher, 2020).

1.6. Pros and Cons

Nasotracheal intubation can be performed in a sitting position. This is advantageous for patients with certain conditions, such as heart failure, which prevent them from lying on their back. Furthermore, a tube which is placed nasally is supported by the connective tissue, muscular, and cartilaginous anatomical structures of the nose whereas the orotracheal tube can dislocate more easily due to the lack of structural support. A disadvantage of nasotracheal intubation is the need for narrow tubes which can complicate pulmonary hygiene as they are easily obstructed (Atanelov and Rebstock, 2020).

Orotracheal intubation is associated with fewer episodes of sinusitis (Salord et al., 1990), which is predominantly linked with nasotracheal intubation, although a more recent study by van Zanten et al. suggests, that hospital-acquired sinusitis might be a common cause for fever of unknown origin in orotracheally intubated patients (van

Zanten et al., 2005). Orotracheal intubation is said to be performed faster and more easily than nasotracheal intubation (Holzapfel, 2003). Due to the discomfort caused by the tube patients can be more prone to self-extubating and therefore, in order to prevent this from occurring, may require sedation or hand restraints (Kabrhel et al., 2007). Moreover, oral hygiene can be complicated by the tube (Atanelov and Rebstock, 2020).

1.7. Complications

Both methods of intubation can lead to complications. Endotracheal intubation is a tricky procedure. When performed by someone lacking experience or practice this can increase the risk for complications (Griesdale et al., 2008).

In orotracheally intubated patients, common complications are side effects of sedative and muscle relaxant agents (Wadbrook, 2000), ventilator-associated pneumonia (Grensemann et al., 2019, Kabrhel et al., 2007) or tracheal tube biting (Holzapfel et al., 1993).

Furthermore, complications during the process of intubating can occur. These can be hemodynamic changes due to manipulation caused by the tube and laryngoscope, as well as injury of the mucosa, teeth, larynx, or trachea (King et al., 1951, Jaber et al., 2006, Kabrhel et al., 2007).

In nasotracheally intubated patients, complications such as nosocomial sinusitis and epistaxis as well as complete or partial obstruction of the tracheal tube can be observed (Hariri et al., 2018, Salord et al., 1990). Perforation of the pharynx can ensue in nasotracheal intubation (Tintinalli and Claffey, 1981). Nasotracheal intubation can also lead to hemodynamic changes, specifically to a hypertensive response (Singh and Smith, 2003, Smith and Grewal, 1991).

The most severe complication in both nasotracheal as well as orotracheal intubation is the accidental intubation of the esophagus rather than the trachea which results in hypoxemia and can cause respiratory arrest and in the worst case can lead to a lethal outcome (Kabrhel et al., 2007, White-Dzuro et al., 2022).

1.8. Aims

The objective of this study was to retrospectively examine the influence of nasotracheal versus orotracheal intubation in critically ill patients.

The hypothesis is that patients intubated nasotracheally require less sedative medication and are therefore more awake and alert and show higher rates of spontaneous breathing compared to those with conventional airway management.

The areas of focus were the patients' outcome, their level of sedation, whether they developed ventilator-associated pneumonia or nosocomial sinusitis whilst intubated, and whether complications regarding intubation and mechanical ventilation occurred. This study aims to support the general clinical experience that patients intubated nasotracheally usually show a higher rate of spontaneous breathing while requiring less sedative medication and vasopressors.

Furthermore, this study was compiled to generate hypotheses for further prospective studies.

2. Methods

2.1. Ethics

The study was conducted in accordance with the Declaration of Helsinki. As all data was obtained retrospectively and anonymized, no review board approval and no informed consent was required.

2.2. Study design

The study was conducted retrospectively and is a single-center, exploratory cohort-study.

2.3. Data acquisition

The data was obtained from the patient data management system (Intensive Care Manager V10 and ICMiq V1.3, both Drägerwerk AG, Lübeck, Germany and Soarian Clinicals 4.01 SP08, Cerner Health Services, Idstein, Germany) in the Department of Intensive Care Medicine at the University Medical Centre Hamburg-Eppendorf. The data was anonymized and managed with Microsoft Excel 365 and Visual Basic V7.1 (both Microsoft Inc., Redmond, WA, USA).

2.4. Inclusion and exclusion criteria

The study was carried out at the Department of Intensive Care at the University Medical Center Hamburg-Eppendorf. In total there are twelve intensive care units (surgical, conservative, and interdisciplinary) which yield one hundred and forty ICU beds.

Patients included in this study were those, who were hospitalized in the intensive care units of the Medical Center Hamburg-Eppendorf during the timeframe from the 1st of January 2018 to the 31st of December 2020, and who were intubated for at least forty-eight hours. All adult patient files with recorded intubation episodes of a minimum of forty-eight hours were extracted from the electronic databank and assigned to either the orotracheal (OTI), or the nasotracheal (NTI) group according to the route of intubation.

Patients were assessed during the first ten days after intubation, or if they were

extubated before reaching day ten until that point in time. Patients who were intubated for surgery or other procedures, as well as those who were intubated nasotracheally due to a difficult airway were excluded from this study. Patients who were intubated repeatedly were assessed, but merely the last instance of intubation was included in the analysis of time and outcome variables.

2.5. Variables

2.5.1. Descriptive data

The demographic parameters age, sex, height, weight, and BMI were extracted from the electronic database, as well as the length of intensive care stay, and the length of intubation.

Moreover, patients' score on the Glasgow Coma Scale (GCS) (Teasdale and Jennett, 1974) at admission to hospital was obtained to determine patients' state of consciousness and coma. We used the ICU scores Simplified Acute Physiology Score II (SAPS II) (Le Gall et al., 1993) to estimate the mortality risk, as well as the Acute Physiology and Chronic Health Evaluation Score (APACHE II) (Knaus et al., 1985) as a measure of the severity of patients' illness and risk of mortality, which were both determined on the first day. The Sepsis-related or Sequential Organ Failure Assessment Score (SOFA) (Vincent et al., 1996) was ascertained initially at admission and daily throughout a ten day period to determine patients' organ function or failure and their general status during their ICU stay. The Richmond Agitation and Sedation Scale (RASS) (Sessler et al., 2001) for day one to ten, as well as a time weighted average for each day was measured in order to assess the level of sedation during mechanical ventilation.

2.5.2. Calculated parameters

Calculations for the time weighted average daily RASS, for the fraction of time with RASS 0 and -1, and the rate of spontaneous breathing for ten days or until extubation if this occurred earlier were performed with custom written code in Visual Basic for Applications (V7.1, Microsoft Corp., Redmond, WA, USA).

2.5.3. Primary outcome measure

Our primary endpoint was to determine the fraction of time with spent with RASS 0 or -1 on the first day after intubation to the end of day three.

2.5.4. Secondary outcome measures

Secondary endpoints were the fraction of time with a RASS score of +1, -2, -3, -4, -5 on the first day after intubation to the end of day ten or until extubation if this occurred earlier. We extracted the rate of successful extubations and if extubation failed, the rate of tracheostomies performed. Successful extubation was defined as discharged alive from the ICU without the need for tracheostomy. Extubation failed if the patient received a tracheostomy, had to be re-intubated shortly after extubation, or deceased while still on the ventilator. The rate of spontaneous breathing for day one to day ten was also compiled. We organized the patients' main diagnosis for admission, underlying conditions, and the reason requiring intubation into the following categories: peritonitis, abdominal surgery, cardiac etiology, decreased vigilance due to neurological etiology, community acquired pneumonia, orthopedics, cardiopulmonary resuscitation, intoxication, liver cirrhosis, immunosuppression, oncology, and other. The patients were further categorized according to the outcome of their ICU stay, with the possible options being no transfer, transfer to a normal ward, transfer to an intermediate care unit, transfer to another hospital, discharged to home from hospital, or death. In order to determine how a patient's stay in the intensive care unit came to an end, the last instance of intubation was studied. We checked the patients' documentation for episodes of ventilator-associated pneumonia, clinical signs of sinusitis, and for complications regarding intubation and mechanical ventilation which might have arisen.

Complications which occurred during intubation and mechanical intubation were accidental esophageal intubation, contact bleeding, epistaxis, perforation, dislocation, or biting of the breathing tube, chewing or coughing against the tube with negative effects on mechanical ventilation, apnea possibly requiring cardiopulmonary resuscitation, ventilation which was not lung protective, respiratory acidosis, pain, erythema and/or swelling of the trachea, ulceration or necrosis on the trachea, mucosal irritation or erosion, swelling of the larynx, newly formed dys- or atelectasis, pneumothorax, leakage of the cuff, obstruction of the breathing tube, retention of secretion (ischemia), retention of carbon dioxide despite measures taken, failure to oxygenate after intubation, repeated oxygen desaturation, bronchospasm, air trapping, self-extubation, missing phonation post extubationem, inspiratory stridor or expiratory wheezing after extubation, and vocal cord paresis.

The ICU Mobility Scale (Hodgson et al., 2014) was implemented to assess how often and to what extent physiotherapy sessions took place during the first ten days of intubation or until extubation if this occurred at an earlier point in time. In order to examine the extent of physiotherapy a patient received over the course of the period of observation the ICU Mobility Scale was implemented. The numbers zero to ten and their corresponding range of movement during physiotherapy are outlined in figure one.

ICU Mobility Scale.

Classification	Definition
0 Nothing (lying in bed)	Passively rolled or passively exercised by staff, but not actively moving
1 Sitting in bed, exercises in bed	Any activity in bed, including rolling, bridging, active exercises, cycle ergometry and active assisted exercises; not moving out of bed or over the edge of the bed
2 Passively moved to chair (no standing)	Hoist, passive lift or slide transfer to the chair, with no standing or sitting on the edge of the bed
3 Sitting over edge of bed	May be assisted by staff, but involves actively sitting over the side of the bed with some trunk control
4 Standing	Weight bearing through the feet in the standing position, with or without assistance. This may include use of a standing lifter device or tilt table
5 Transferring bed to chair	Able to step or shuffle through standing to the chair. This involves actively transferring weight from one leg to another to move to the chair. If the patient has been stood with the assistance of a medical device, they must step to the chair (not included if the patient is wheeled in a standing lifter device)
6 Marching on spot (at bedside)	Able to walk on the spot by lifting alternate feet (must be able to step at least 4 times, twice on each foot), with or without assistance
7 Walking with assistance of 2 or more people	Walking away from the bed/chair by at least 5 m (5 yards) assisted by 2 or more people
8 Walking with assistance of 1 person	Walking away from the bed/chair by at least 5 m (5 yards) assisted by 1 person
9 Walking independently with a gait aid	Walking away from the bed/chair by at least 5 m (5 yards) with a gait aid, but no assistance from another person. In a wheelchair bound person, this activity level includes wheeling the chair independently 5 m (5 yards) away from the bed/chair
10 Walking independently without a gait aid	Walking away from the bed/chair by at least 5 m (5 yards) without a gait aid or assistance from another person

Figure 1. ICU Mobility Scale. (Hodgson et al., 2014, 21)

Furthermore, we analyzed the dose of vasopressor therapy, namely Noradrenaline, and the dose of sedative drugs, specifically Propofol, Sufentanil, and Midazolam administered throughout the first ten days of mechanical ventilation or until extubation if this occurred before day ten.

Table one gives an overview of all parameters examined.

Table 1. Overview of parameters.

One-time only assessment	Daily assessment
Extubation	RASS -5 to -2 and +1
Tracheostomy	Average RASS
Diagnosis	Fraction of time with RASS 0 or -1
Outcome	Rate of spontaneous ventilation
Ventilator-associated pneumonia (VAP)	Dose of vasopressor therapy
Sinusitis	Dose of sedative drugs
Complications	ICU Mobility Scale
Length of ICU stay	
Length of intubation	

2.6. Data management and statistical analysis

The data was compiled in an excel table (Microsoft Excel for Mac, Version 16.55, 2021) and was anonymized to ensure data privacy protection.

The program used for statistical evaluation and analysis was Statistical Package for the Social Sciences (SPSS) (version 27, IBM Inc., Armonk, NY, USA). Univariate analysis was carried out using standard statistical tests, including t-tests, cross tabs, and chi-square tests. T-tests were performed on demographic parameters, specifically age, height, weight, and body mass index (BMI), as well as on the length of ICU stay, length of intubation, and on the ICU scores, including SOFA on day one, SAPS II, APACHE II, and GCS as to highlight the significant differences between the orotracheal and nasotracheal group. In addition, crosstabs were used to compare the two groups regarding ventilator-associated pneumonia, sinusitis, categories of diagnosis leading to admission and intubation, and failure to extubate after surgery or after diagnostic measures, therefore requiring continued mechanical ventilation.

A multivariable analysis was achieved using different regression models with appropriate filters so that a distinction between the different episodes of intubation could be made. A multinomial logistic regression was used to analyze the polytomous variables 'outcome', and 'possibility of extubation'. The dichotomous variable 'failure to extubate after surgery/diagnostic measures' was examined using a binominal logistic regression.

For the logistic regression analyses, parameters with a p-value of <0.1 were tested as covariates. The sensitivity analyses included only patients with one instance of intubation, as well as patients' diagnoses.

For those variables that were appraised daily a generalized linear mixed model in the long format (variables to cases) was implemented. These variables include the sequential organ failure assessment (SOFA) score, doses of medication, namely of Propofol, Sufentanil, Midazolam, and Noradrenaline, the rate of spontaneous breathing, the score on the Richmond Agitation Sedation Scale (RASS), and the ICU Mobility Scale.

3. Results

3.1. Descriptive Data

In total, 1209 patients met our inclusion criteria. The gender distribution was as follows: four hundred and sixteen females and seven hundred and ninety-three males, the percentage of males was similar within the two groups with 63% in the OTI group versus 67% in the NTI group ($p = 0.634$). The age span of all patients included lay between 16 and 98 years old.

Overall, 1627 instances of endotracheal intubation were included in the study. Of those, 1298 were episodes of orotracheal intubation and 329 were nasotracheal intubation episodes.

Significant differences between the orotracheally intubated group and nasotracheally intubated group were determined for length of intubation, age, and initial SOFA-score. Patients in the OTI group were intubated for 6.9 days on average while NTI patients were intubated for 5.8 days ($p < 0.001$). The mean age in the OTI group was significantly younger being 63 ± 15 , NTI patients were 66 ± 13 years old ($p = 0.004$). The initial SOFA-score at admission was 11 ± 3 in the OTI group and 10 ± 3 in the NTI group ($p < 0.001$). In regard to the length of the ICU stay, weight, height, BMI, APACHE II-score, SAPS II-score, and GCS-score there was no significant difference between the OTI and NTI group. The length of the ICU stay was twenty-six days for both groups, the standard deviation in the OTI group was ± 26 days, and in the NTI group ± 29 days ($p = 0.704$). Patients in the OTI group weighed 78.8 ± 18.6 kg on average, while the mean weight for NTI patients was 79.5 ± 21.5 kg ($p = 0.615$). The mean height of patients was 173 ± 10 cm in both groups ($p = 0.461$). The BMI of orotracheally intubated patients was 26.4 ± 6.8 kg/m² on average versus 27.2 ± 12.5 kg/m² for nasotracheally intubated patients ($p = 0.236$). The ICU mortality prediction score SAPS II was 55 ± 18 in the orotracheally intubated group and 54 ± 18 in the nasotracheally intubated group ($p = 0.350$). The APACHE II-score was 31 ± 7 in the OTI group and 31 ± 8 in the NTI group ($p = 0.111$). Patients' mean GCS-score at admission was 10 ± 5 in the OTI group and 9 ± 6 in the NTI group ($p = 0.059$), therefore NTI patients had a slightly more impaired consciousness than OTI patients. The initial sepsis-related organ failure assessment, SOFA-score, at admission was significantly higher in the OTI group compared to the NTI group, putting patients in

the OTI group at higher risk of organ dysfunction or failure and an increased mortality risk (Vincent et al., 1998).

All parameters are summarized in table 2.

Table 2. Patients' descriptive parameters and outcome.

Parameter	Orotracheal intubation (n = 988)	Nasotracheal intubation (n = 221)	p-value
Length of ICU stay [d]	26 ± 26	26 ± 29	0.704
Length of intubation [d]	6.9 ± 4.7	5.8 ± 3.8	<0.001
Age [years]	63 ± 15	66 ± 13	0.004
Weight [kg]	78.8 ± 18.6	79.5 ± 21.5	0.615
Height [cm]	173 ± 10	173 ± 10	0.461
BMI [kg/m ²]	26.4 ± 6.8	27.2 ± 12.5	0.236
APACHE II	31 ± 7	31 ± 8	0.111
SAPS II	55 ± 18	54 ± 18	0.350
Initial SOFA	11 ± 3	10 ± 3	<0.001
GCS	10 ± 5	9 ± 6	0.059

The SOFA-score, which in addition to being ascertained at admission, was assessed daily, and showed significant differences for the two groups on day one, two, three, six, seven, eight, nine, and ten, with the OTI group having higher scores on the scale than then NTI group as can be seen in table 3 and in figure 2.

Table 3. SOFA-scores for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1 (admission)	10.9 (10.7, 11.1)	10.0 (9.6, 10.5)	<0.001
Day 2	10.5 (10.3, 10.8)	9.8 (9.3, 10.2)	0.002
Day 3	10.0 (9.8, 10.2)	9.3 (8.9, 9.8)	0.006
Day 4	9.4 (9.2, 9.6)	9.0 (8.6, 9.5)	0.139
Day 5	9.0 (8.8, 9.2)	8.6 (8.2, 9.1)	0.123
Day 6	8.6 (8.4, 8.8)	8.0 (7.6, 8.5)	0.026
Day 7	8.3 (8.1, 8.5)	7.8 (7.3, 8.2)	0.032
Day 8	7.9 (7.7, 8.1)	7.3 (6.8, 7.7)	0.008
Day 9	7.6 (7.4, 7.9)	7.1 (6.6, 7.5)	0.019
Day 10	7.4 (7.2, 7.7)	6.8 (6.3, 7.2)	0.011

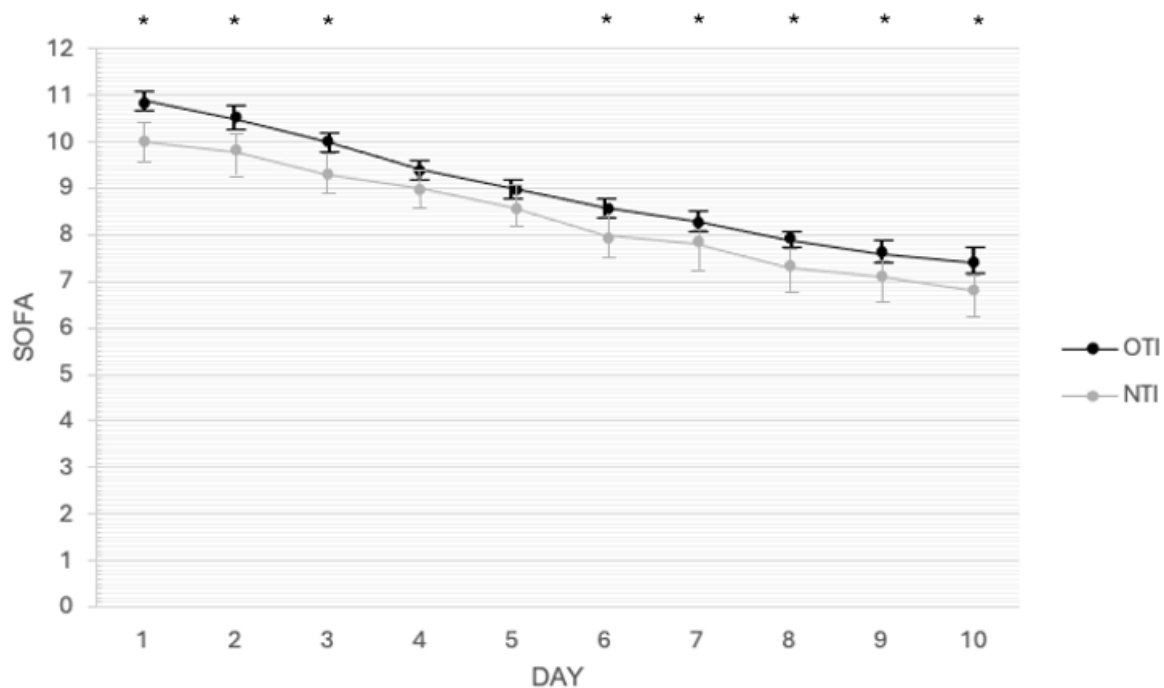


Figure 2. SOFA-scores day 1-10. Error bars represent 95% confidence interval.

To allow an overview of the main diagnoses leading to admission and subsequently to endotracheal intubation categories were formed based on the most commonly occurring diagnoses. These were peritonitis, abdominal surgery, cardiac etiology, decreased vigilance due to neurological etiology, community acquired pneumonia, orthopedics, cardiopulmonary resuscitation, intoxication, liver cirrhosis, immunosuppression, oncology, and other. Each patient's main diagnosis was added to the category with the best fit.

Table 4. Patients' main diagnosis.

Category	Orotracheal intubation (n = 988)	Nasotracheal intubation (n = 221)
Peritonitis	117 (11.8%)	20 (9.0%)
Abdominal surgery	84 (8.5%)	17 (7.7%)
Cardiac genesis	128 (13.0%)	23 (10.4%)
Neurological genesis	135 (13.7%)	43 (19.5%)
Community-acquired pneumonia	84 (8.5%)	11 (5.0%)
Trauma surgery/ orthopedics	25 (2.5%)	4 (1.8%)
CPR	2 (0.2%)	0
Liver cirrhosis	78 (7.9%)	14 (6.3%)
Immunosuppression	143 (14.5%)	27 (12.2%)
Oncology	62 (6.3%)	20 (9.0%)
Intoxication	9 (0.9%)	2 (0.9%)
Other	116 (11.7%)	39 (17.6%)

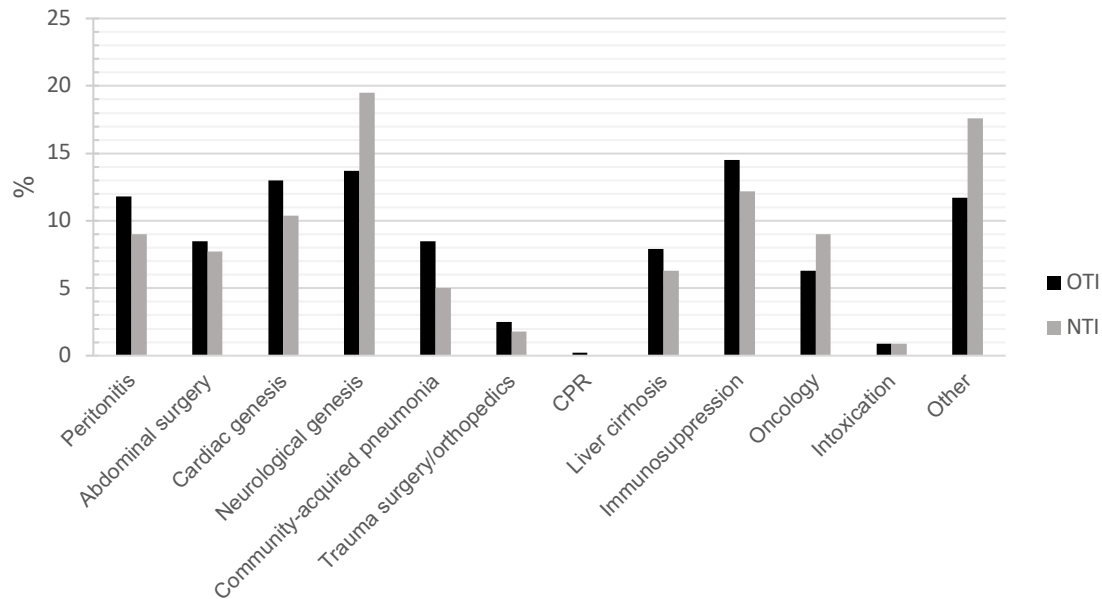


Figure 3. Main diagnoses.

3.2. Primary Endpoint

The primary endpoint of the NaTra-Study was to evaluate the depth of sedation by determining the fraction of time spent in a RASS range of 0 and -1 for the time from day one to the end of the third day of observation. In addition to examining the time spent with a score of 0 or -1 on the Richmond Agitation Sedation Scale for the first three days of observation, a RASS of 0 or -1 was determined for the whole observation period of ten days. On average, patients in the OTI group spent 4.0 ± 6.1 hours per day with a RASS of 0 or -1 and patients in the NTI 9.4 ± 8.4 hours per day ($p < 0.001$). Patients in the NTI group showed a statistically significant higher fraction of time spent with RASS 0 or -1 for each day of observation as can be seen in table 5 and figure 4.

Table 5. RASS 0, -1 for day 1-10 in h/d. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n= 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1	2.4 (2.0, 2.9)	7.8 (6.9, 8.7)	<0.001
Day 2	4.2 (3.7, 4.7)	9.6 (8.7, 10.6)	<0.001
Day 3	5.8 (5.3, 6.2)	10.8 (9.9, 11.8)	<0.001
Day 4	7.1 (6.6, 7.7)	11.8 (10.8, 12.9)	<0.001
Day 5	8.0 (7.4, 8.5)	12.1 (10.9, 13.3)	<0.001
Day 6	8.9 (8.3, 9.6)	13.0 (11.6, 14.4)	<0.001
Day 7	8.6 (7.9, 9.3)	13.5 (11.9, 15.1)	<0.001
Day 8	8.9 (8.1, 10.5)	12.4 (10.5, 14.2)	0.001
Day 9	8.6 (7.8, 9.5)	11.6 (9.5, 13.7)	0.009
Day 10	8.7 (7.7, 9.6)	13.0 (10.7, 15.3)	0.001

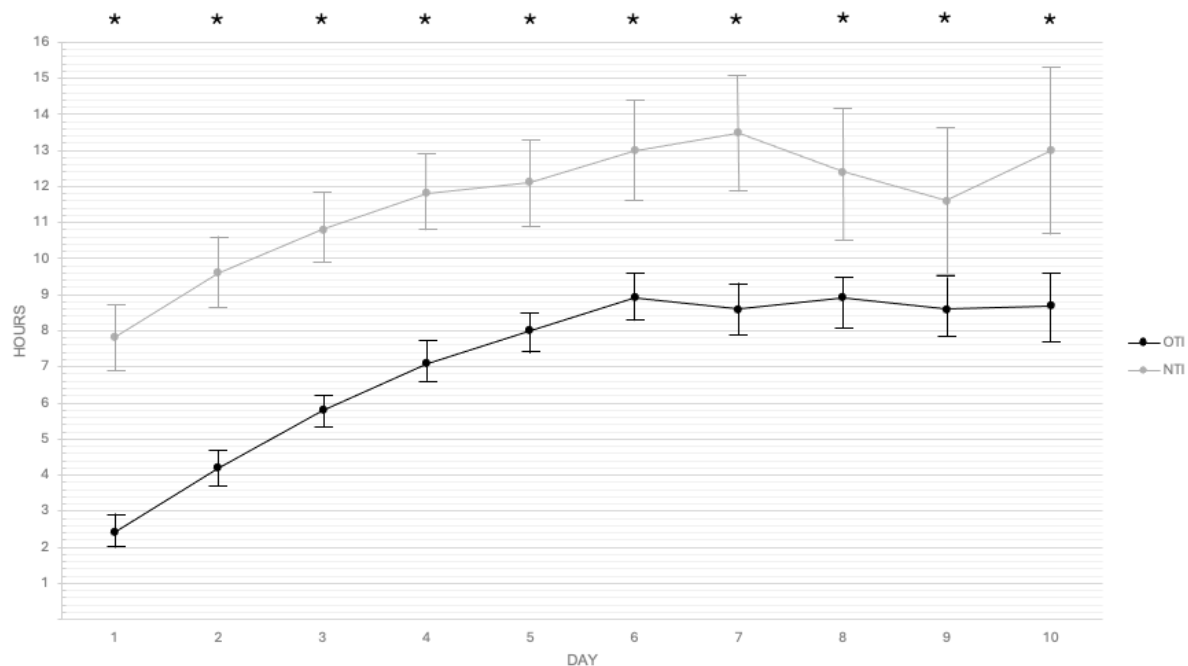


Figure 4. RASS 0, -1 in h/d for days 1-10. Error bars represent 95% confidence interval.

3.3. Secondary Endpoints

3.3.1. Fraction of time with RASS +1, -2, -3, -4, -5

The fraction of time with a score of +1, -2, -3, -4 and -5 on the Richmond Agitation Sedation Scale during the entire time of observation was a secondary endpoint. These scores on the RASS-scale are concomitant with sedation and reduced vigilance and respectively, reflect a state of being restless, lightly sedated, moderately sedated, deeply sedated, and unarousable. The OTI group spent more time with RASS scores of +1, -2, -3, -4 and -5 on all ten days of observation than the NTI group as seen in table 6 and figure 5.

Table 6. Time spent with RASS of +1, -2, -3, -4 and -5 in h/d for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n= 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1	21.3 (20.8, 21.8)	15.7 (14.7, 16.6)	<0.001
Day 2	19.6 (19.1, 20.0)	13.8 (12.9, 14.8)	<0.001
Day 3	17.8 (17.3, 18.3)	12.4 (11.4, 13.4)	<0.001
Day 4	16.4 (15.9, 16.9)	11.4 (10.3, 12.5)	<0.001
Day 5	15.6 (15.0, 16.2)	10.9 (9.7, 12.1)	<0.001
Day 6	14.5 (13.9, 15.2)	10.6 (9.2, 12.0)	<0.001
Day 7	14.8 (14.1, 15.5)	9.8 (8.2, 11.4)	<0.001
Day 8	14.5 (13.8, 15.3)	11.2 (9.3, 13.1)	0.001
Day 9	14.7 (13.8, 15.6)	11.6 (9.5, 13.7)	0.008
Day 10	14.4 (13.4, 15.4)	10.3 (8.0, 12.7)	0.002

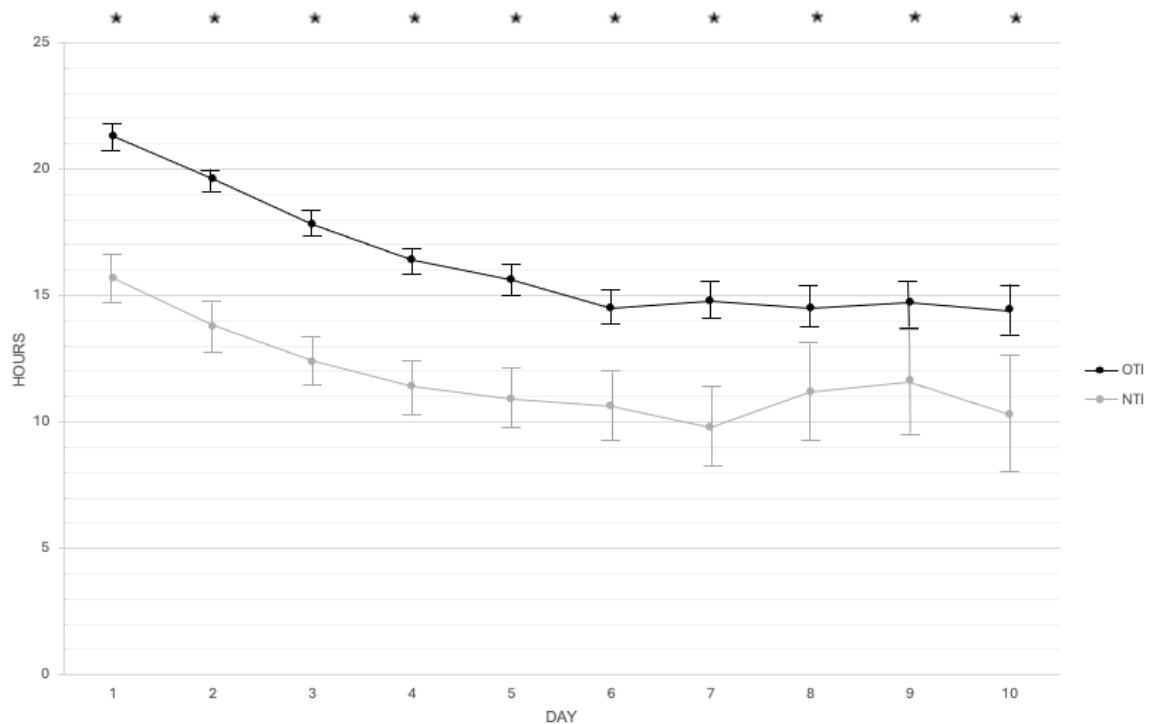


Figure 5. Time spent with RASS of +1, -2, -3, -4, -5 in h/d for day 1-10. Error bars represent 95% confidence interval.

3.3.2. Average RASS

The average scores on the Richmond Agitation Sedation Scale for day one to day ten are reported in table 7. The difference in the depth of sedation was statistically significant throughout the entire period of observation. The nasotracheally intubated group of patients showed higher values on the Richmond Agitation Sedation Scale on every day over the course of the ten-day observation period. In the NTI group the mean score on the Richmond Agitation Sedation Scale reached a plateau on day four, in the group of orotracheally intubated patients this occurred on day five.

Table 7. Average scores on the Richmond Agitation Sedation Scale. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1	-3.0 (-3.1, -2.9)	-2.0 (-2.2, -1.9)	<0.001
Day 2	-2.6 (-2.7, -2.5)	-1.8 (-1.9, -1.6)	<0.001
Day 3	-2.3 (-2.4, -2.2)	-1.6 (-1.7, -1.4)	<0.001
Day 4	-2.1 (-2.2, -2.0)	-1.3 (-1.5, -1.2)	<0.001
Day 5	-1.9 (-2.0, -1.8)	-1.4 (-1.5, -1.2)	<0.001
Day 6	-1.9 (-2.0, -1.8)	-1.3 (-1.5, -1.1)	<0.001
Day 7	-1.9 (-2.0, -1.8)	-1.3 (-1.6, -1.1)	<0.001
Day 8	-1.9 (-2.0, -1.8)	-1.4 (-1.7, -1.1)	0.003
Day 9	-1.9 (-2.0, -1.7)	-1.4 (-1.8, -1.1)	0.013
Day 10	-1.8 (-1.9, -1.6)	-1.3 (-1.7, -0.9)	0.016

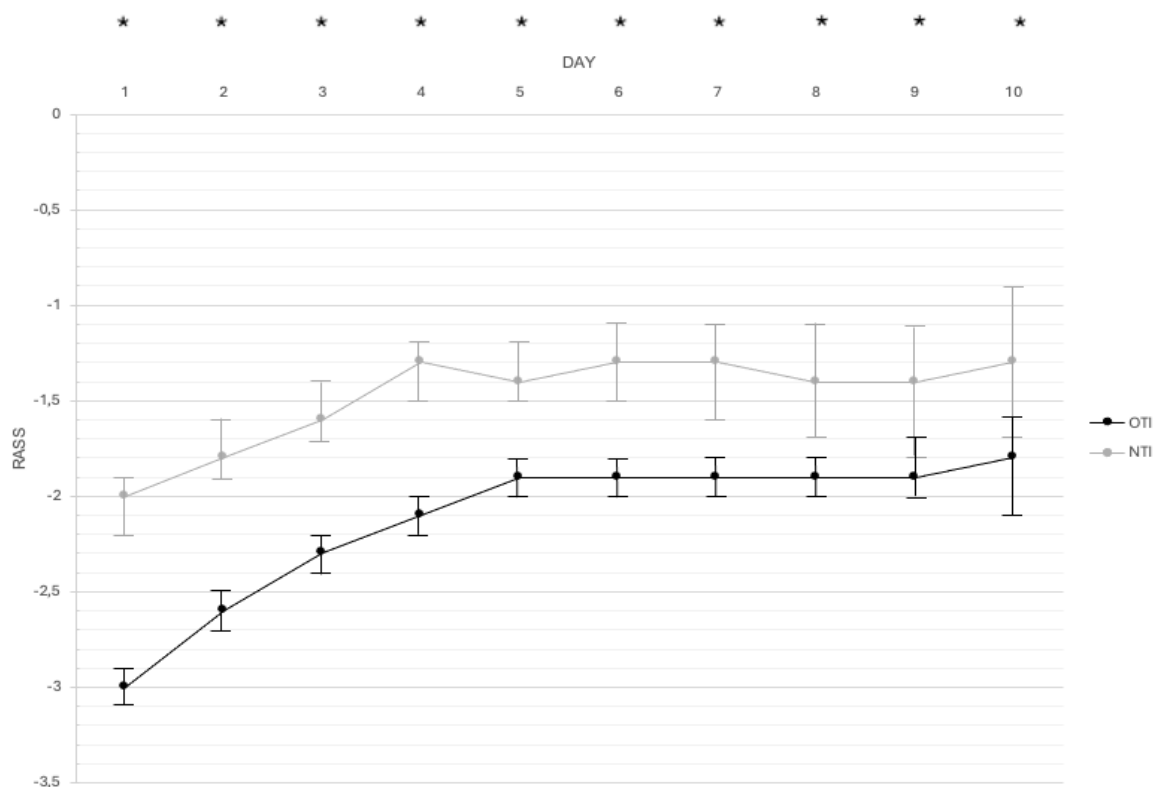


Figure 6. Average RASS scores for day 1-10. Error bars represent 95% confidence interval.

3.3.3. Duration of spontaneous breathing

The rate of spontaneous ventilation throughout the fixed ten days of observation was distinguished for both groups. The mean duration of spontaneous ventilation was 6.9 ± 5.9 hours per day in the OTI group and 10.2 ± 6.9 in the NTI group ($p < 0.001$).

Table 8 shows the differences between the groups. Nasotracheally intubated patients spent more time breathing spontaneously throughout the entire period of observation. Statistically significant differences occurred on days one to seven, and day ten.

Table 8. Duration of spontaneous ventilation in h/d for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1	3.8 (3.4, 4.3)	7.7 (6.9, 8.6)	<0.001
Day 2	5.7 (5.3, 6.1)	9.6 (8.7, 10.4)	<0.001
Day 3	7.1 (6.7, 7.5)	10.1 (10.0, 11.8)	<0.001
Day 4	8.2 (7.7, 8.6)	11.5 (10.5, 12.4)	<0.001
Day 5	9.1 (8.6, 9.6)	11.8 (10.7, 12.9)	<0.001
Day 6	9.4 (8.8, 10.0)	12.4 (11.1, 13.6)	<0.001
Day 7	9.6 (9.0, 10.2)	12.0 (10.7, 13.4)	0.002
Day 8	9.8 (9.1, 10.5)	11.4 (9.8, 13.0)	0.068
Day 9	9.5 (8.8, 10.3)	11.0 (9.3, 12.9)	0.118
Day 10	9.9 (9.1, 10.8)	12.3 (10.3, 14.4)	0.030

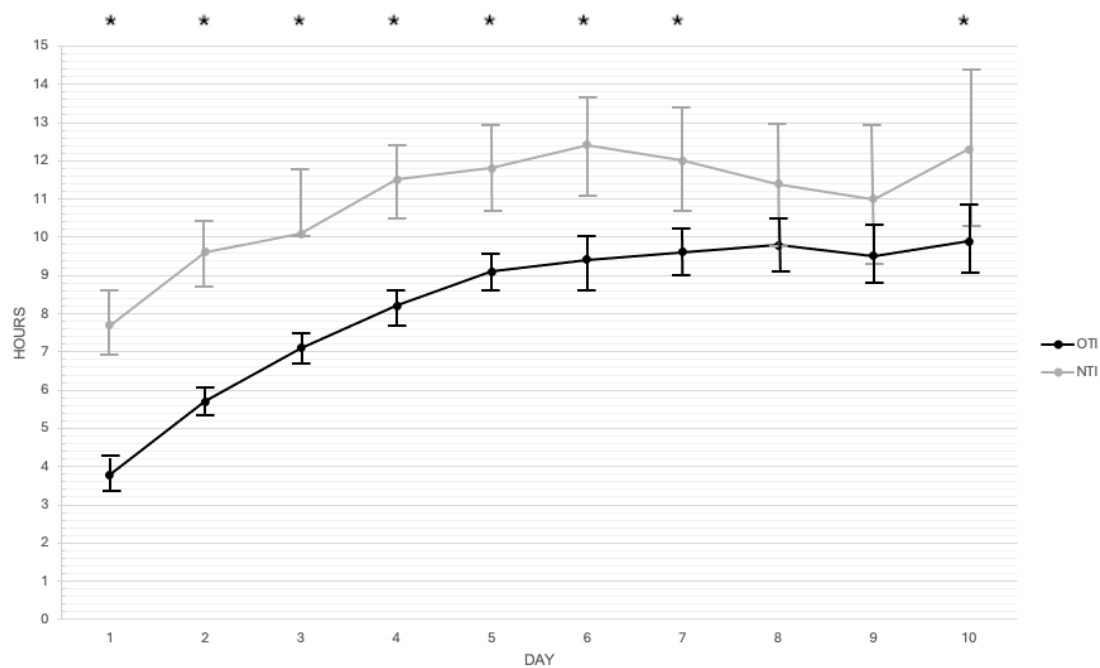


Figure 7. Duration of spontaneous ventilation in h/d for day 1-10. Error bars represent 95% confidence interval.

3.3.4. Dose of vasopressor therapy

The results of this study show that patients in the group of nasotracheal intubation received lesser amounts of the vasopressor Noradrenaline over the course of observation. There is no point in time during the ten-day observation period in which orotracheally intubated patients received average lower doses of Noradrenaline compared to nasotracheally intubated patients. The difference in doses of the vasopressor Noradrenaline administered between the two groups was statistically significant for the first three days. The doses for each day are listed in table 9.

Table 9. Dose of Noradrenaline in $\mu\text{g/kg/min}$ for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	Difference	p-value
Day 1	0.254 (0.236, 0.272)	0.150 (0.114, 0.186)	0.104	<0.001
Day 2	0.195 (0.176, 0.213)	0.127 (0.090, 0.163)	0.068	0.001
Day 3	0.172 (0.153, 0.191)	0.095 (0.056, 0.133)	0.077	<0.001
Day 4	0.132 (0.111, 0.153)	0.086 (0.043, 0.128)	0.046	0.056
Day 5	0.127 (0.104, 0.150)	0.086 (0.037, 0.135)	0.041	0.141
Day 6	0.125 (0.099, 0.150)	0.078 (0.020, 0.136)	0.047	0.150
Day 7	0.117 (0.089, 0.145)	0.086 (0.021, 0.151)	0.031	0.397
Day 8	0.123 (0.092, 0.154)	0.081 (0.005, 0.158)	0.042	0.319
Day 9	0.131 (0.096, 0.165)	0.095 (0.010, 0.180)	0.036	0.442
Day 10	0.137 (0.098, 0.175)	0.072 (0.00, 0.165)	0.065	0.210

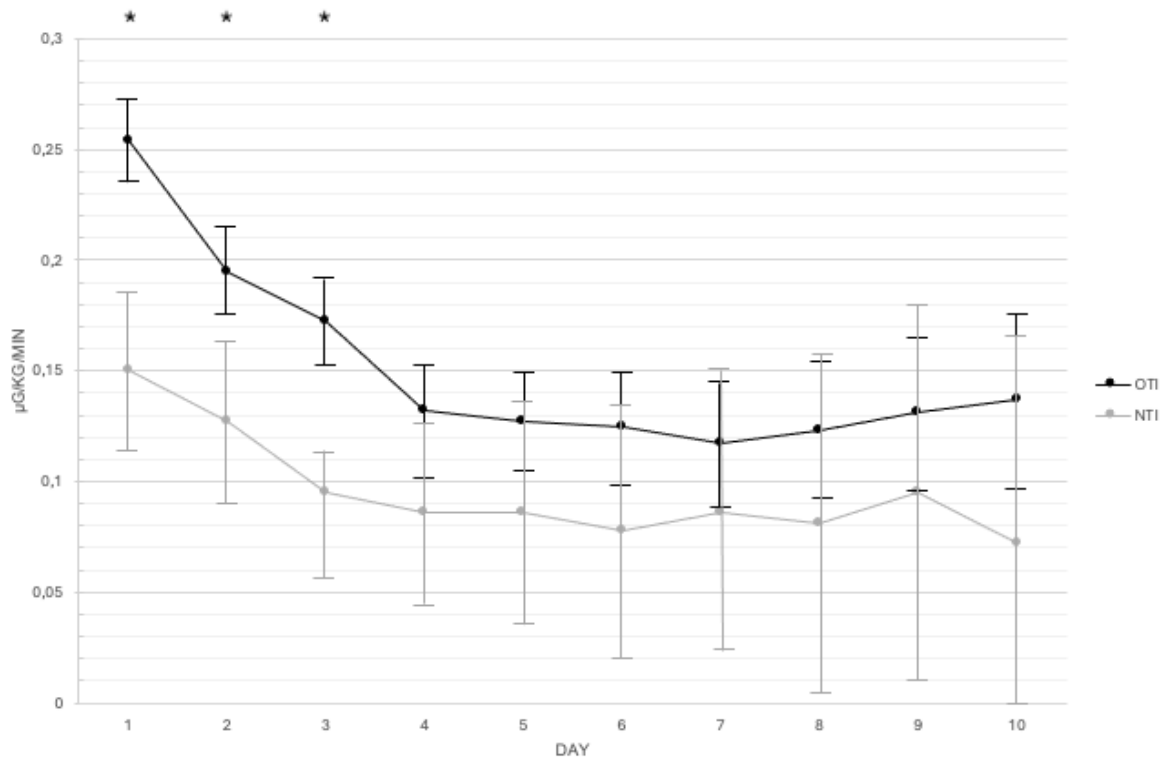


Figure 8. Dose of Noradrenaline in $\mu\text{g/kg/min}$ for day 1-10. Error bars represent 95% confidence interval.

The mean dose of Noradrenaline administered throughout the observational period was $0.171 \pm 0.214 \mu\text{g/kg/min}$ in the orotracheal intubated group and $0.105 \pm 0.197 \mu\text{g/kg/min}$ in the nasotracheal intubation group ($p = 0.002$).

3.3.5. Dose of sedative drugs

In this study, the difference in doses of sedative drugs required during the treatment of patients in both groups was examined over the fixed ten-day observation period. The sedatives which were analyzed were Propofol, Sufentanil, and Midazolam. Patients in the nasotracheally intubated group received less sedative medication than those in the orotracheally intubated group on every day of the ten-day observation period.

The mean doses for Propofol given during the ten-day period were $1768 \pm 1473 \text{ mg/d}$ in the orotracheal intubation group and $1077 \pm 1355 \text{ mg/d}$ in the nasotracheal intubation group ($p = 0.014$). On average, orotracheally intubated patients received $693 \pm 639 \mu\text{g/d}$ of Sufentanil, while the mean dose was $395 \pm 547 \mu\text{g/d}$ in the nasotracheal intubation group ($p < 0.001$). In the orotracheal intubation group an average dose of $6.5 \pm 23.8 \text{ mg/d}$ of Midazolam was administered, while the mean dose in the nasotracheal intubation group was $3.6 \pm 20.6 \text{ mg/d}$ ($p < 0.001$).

For Propofol the difference in doses was statistically significant during the first five days and on day seven as shown in table 10 and figure 9.

Table 10. Dose of Propofol in mg/d for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	Difference	p-value
Day 1	3034 (2928, 3140)	1740 (1530, 1950)	1294	<0.001
Day 2	2163 (2057, 2269)	1204 (993, 1414)	959	<0.001
Day 3	1548 (1439, 1657)	927 (719, 1145)	621	<0.001
Day 4	1162 (1045, 1278)	842 (607, 1077)	320	0.017
Day 5	950 (822, 1078)	646 (380, 912)	304	0.044
Day 6	880 (739, 1020)	642 (332, 953)	238	0.172
Day 7	817 (662, 971)	281 (0, 635)	536	0.007
Day 8	730 (559, 901)	368 (0, 780)	362	0.112
Day 9	735 (544, 925)	371 (0, 837)	364	0.157
Day 10	636 (423, 849)	514 (0, 1031)	122	0.669

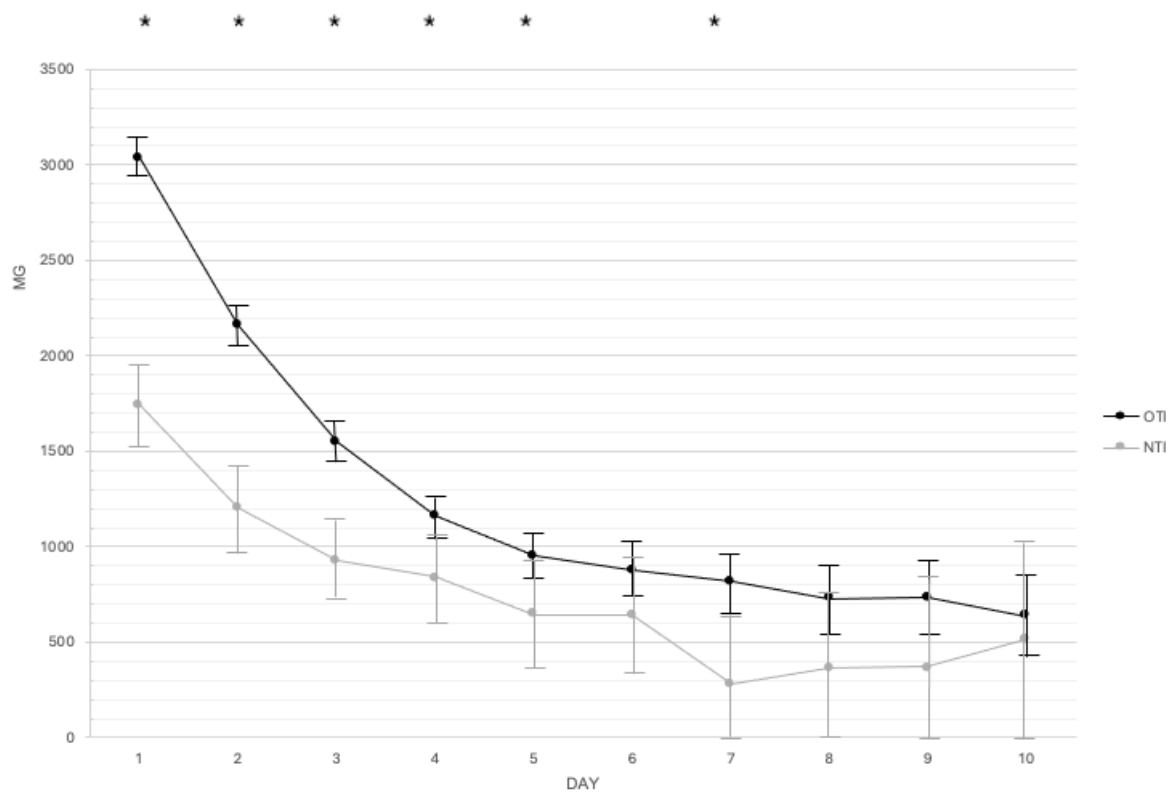


Figure 9. Dose of Propofol in mg/d for day 1-10. Error bars represent 95% confidence interval.

The difference in dosage of Sufentanil between the orotracheally intubated group and the nasotracheally intubated group was statistically significant on all ten days as seen in table 11 and figure 10. The orotracheally intubated group of patients received significantly higher doses of the sedative drug.

Table 11. Dose of Sufentanil in $\mu\text{g/d}$ for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	Difference	p-value
Day 1	905 (864, 946)	521 (439, 603)	384	<0.001
Day 2	782 (741, 834)	444 (362, 526)	338	<0.001
Day 3	663 (621, 705)	358 (274, 442)	305	<0.001
Day 4	581 (536, 625)	316 (227, 404)	265	<0.001
Day 5	519 (471, 566)	315 (217, 412)	204	<0.001
Day 6	509 (458, 561)	315 (205, 426)	194	0.002
Day 7	482 (426, 537)	254 (130, 379)	228	0.001
Day 8	421 (360, 482)	255 (112, 399)	166	0.037
Day 9	465 (397, 532)	267 (106, 429)	198	0.027
Day 10	457 (383, 532)	222 (43, 402)	235	0.018

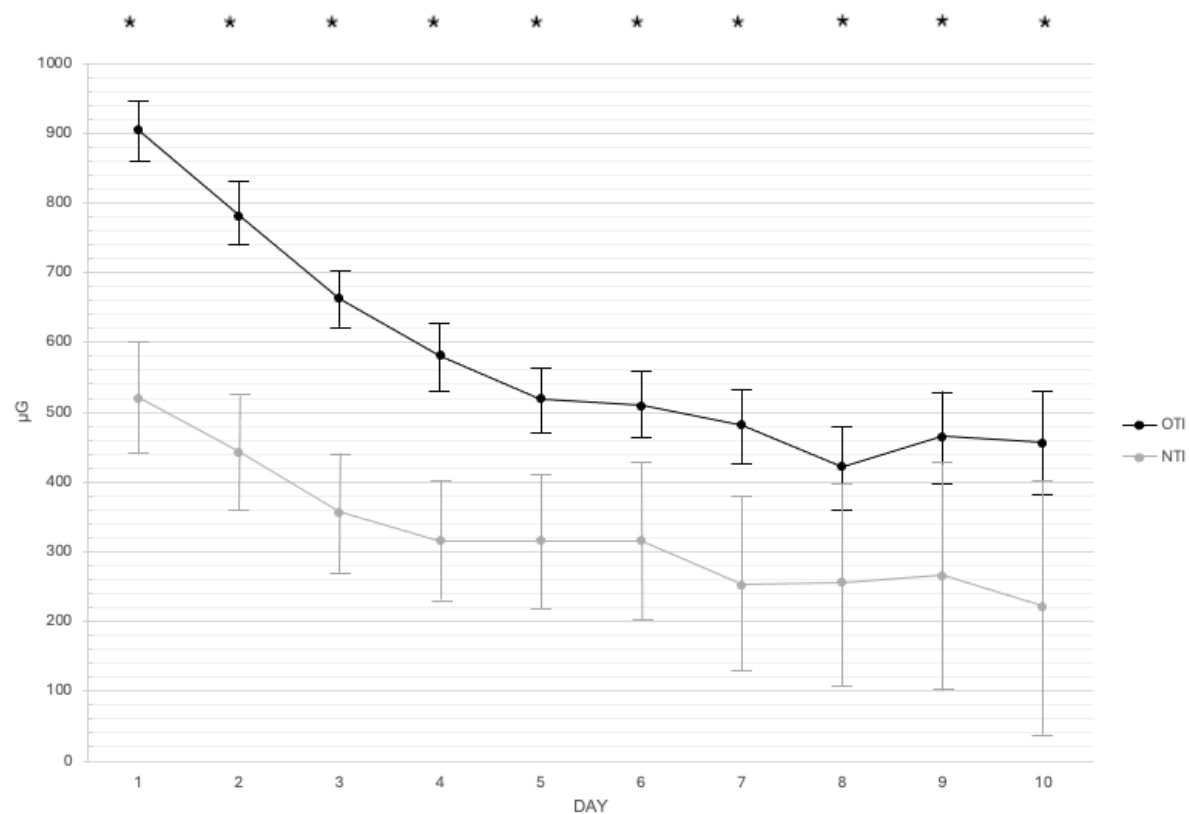


Figure 10. Dose of Sufentanil in $\mu\text{g/d}$ for day 1-10. Error bars represent 95% confidence interval.

There was no statistically significant difference regarding the dose of Midazolam, although the NTI group did receive constantly less of the sedative throughout the ten-day period compared to the OTI group as can be seen in table 12 and figure 11.

Table 12. Dose of Midazolam in mg/d for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)	Difference	p-value
Day 1	7.0 (5.2, 8.8)	4.7 (1.0, 8.3)	2.3	0.266
Day 2	7.7 (5.8, 9.5)	4.0 (0.3, 7.6)	3.7	0.074
Day 3	6.7 (4.8, 8.6)	3.4 (0.0, 7.1)	3.3	0.121
Day 4	6.3 (4.3, 8.3)	4.1 (0.1, 8.1)	2.2	0.343
Day 5	5.9 (3.8, 8.1)	3.2 (0.0, 7.7)	2.8	0.277
Day 6	6.0 (3.6, 8.3)	4.1 (0.0, 9.3)	1.9	0.518
Day 7	6.7 (4.1, 9.3)	4.1 (0.0, 9.9)	2.6	0.418
Day 8	6.5 (3.6, 9.3)	2.7 (0.0, 9.5)	3.8	0.314
Day 9	6.6 (3.4, 9.8)	2.7 (0.0, 10.4)	3.9	0.357
Day 10	7.3 (3.7, 10.8)	2.7 (0.0, 11.2)	4.6	0.330

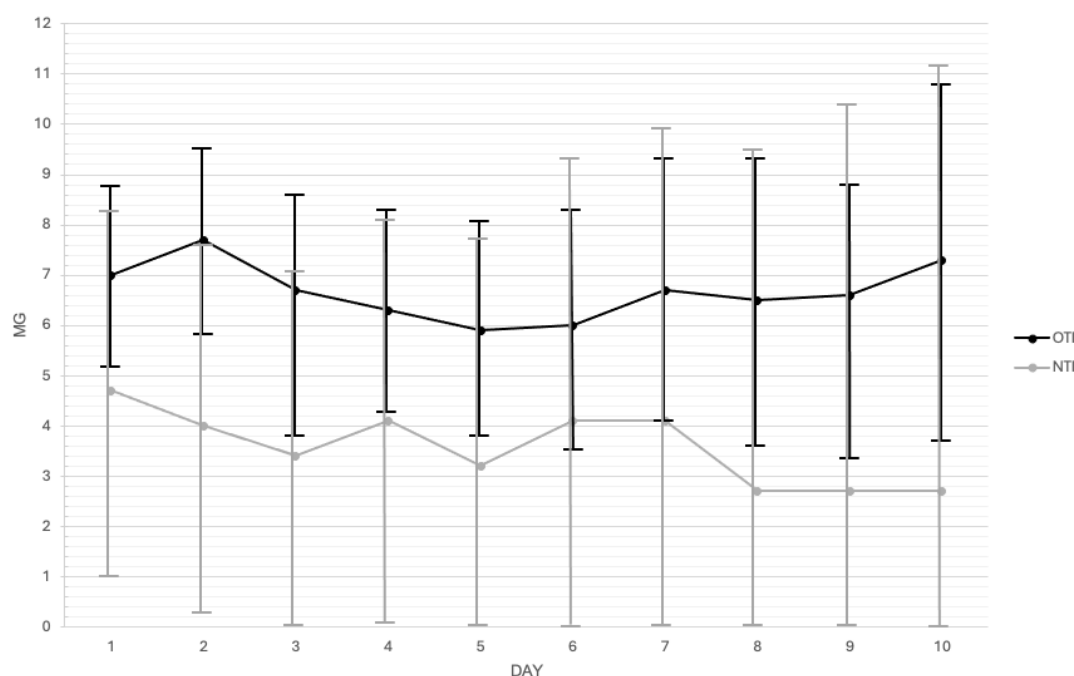


Figure 11. Dose of Midazolam in mg/d for day 1-10. Error bars represent 95% confidence interval.

3.3.6. Rate of successful extubation

In the orotracheally intubated group of patients 56.5% or seven hundred and twenty-five patients were extubated successfully and in the nasotracheal group it was 65.5% or two hundred and thirteen patients. Failed extubation occurred in five hundred and fifty-eight cases in the OTI group and in one hundred and twelve NTI patients.

Table 13. Rate of extubation.

Extubation	Orotracheal intubation (n = 1283)	Nasotracheal intubation (n = 325)
Yes	725 (56.5%)	213 (65.5%)
No	558 (43.5%)	112 (34.5%)

In the multinomial logistic regression, significant dependent variables for a successful extubation were length of mechanical ventilation ($p < 0.001$), length of ICU stay ($p < 0.001$), GCS at admission ($p < 0.001$), SOFA-score at admission ($p < 0.001$), and APACHE II-score ($p < 0.001$).

3.3.7. Rate of tracheostomy

The rate of tracheostomy was determined during the last episode in alive patients. In the orotracheally intubated group of patients 40.9% or two hundred thirty-two patients received a tracheostomy. The nasotracheally intubated group of patients showed a higher rate of tracheostomy at 47.5%, which were seventy-five patients ($p = 0.141$) as reported in table 14. In the multivariable analysis, the length of mechanical ventilation ($p < 0.001$), the length of ICU-stay ($p < 0.001$), the GCS at admission ($p < 0.001$), the APACHE II-score ($p = 0.001$), and the initial SOFA-score ($p < 0.001$) showed a significant impact on the tracheostomy rate, making them dependent variables.

Table 14. Rate of tracheostomy during last episode in alive patients.

Tracheostomy	Orotracheal intubation (n = 567)	Nasotracheal intubation (n = 158)
Yes	232 (40.9%)	75 (47.5%)
No	335 (59.1%)	83 (52.5%)

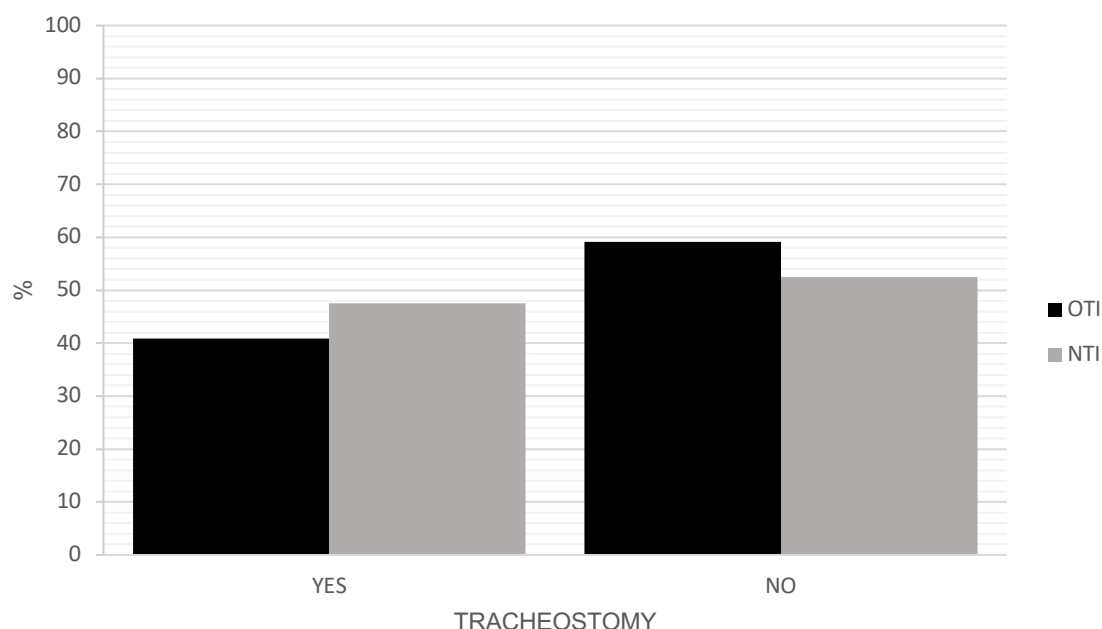


Figure 12. Rate of tracheostomy during last episode in alive patients.

3.3.8. Outcome

As shown in table 15, the category 'death' was the one with the most OTI patients with 43% of the patient collective. The category with the most NTI patients was 'transfer to another hospital or rehabilitation center' closely followed by the category 'death'.

Table 15. Outcome. ($p < 0.001$).

Outcome possibilities	Orotracheal intubation (n = 988)	Nasotracheal intubation (n = 221)
ICM	45 (4.6%)	28 (12.7%)
General ward	304 (30.8%)	61 (27.6%)
Hospital / rehabilitation center	206 (20.9%)	67 (30.3%)
Discharged home	8 (0.8%)	1 (0.5%)
Death	425 (43%)	64 (29%)

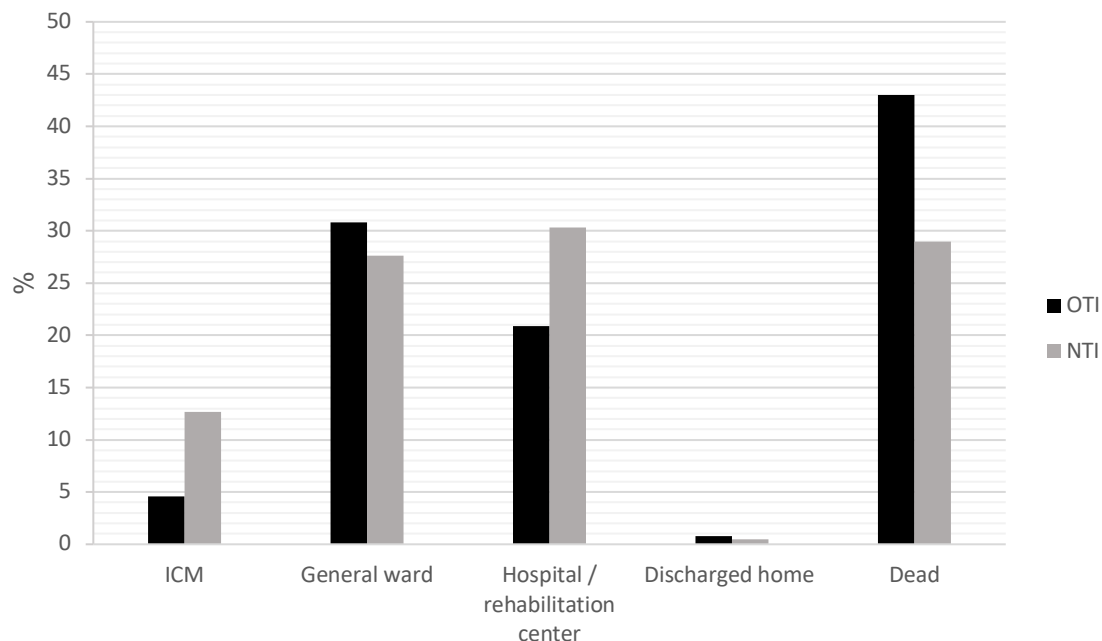


Figure 13. Outcome.

3.3.9. Incidence of ventilator acquired pneumonia

In total, there were three hundred and twelve recorded incidences of ventilator-associated pneumonia. Of these cases, two hundred and forty-seven occurred in the orotracheally intubated group and sixty-five in the nasotracheally intubated group. There was no statistically significant difference between the two groups ($p = 0.728$).

Table 16. Incidence of ventilator-associated pneumonia (VAP).

VAP	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)
Yes	247 (19.1%)	65 (19.9%)
No	1051 (80.9%)	349 (80.1%)

3.3.10. Incidence of sinusitis

Overall, four clinically apparent cases of sinusitis were diagnosed, three within the orotracheally intubated group, and one in the nasotracheal group ($p = 0.807$).

3.3.11. Complications of intubation and mechanical ventilation

Complications of intubation and mechanical ventilation were accidental esophageal intubation, contact bleeding, epistaxis during nasotracheal intubation, perforation of the airways, and dislocation of the tube. Furthermore, biting of the breathing tube, chewing on the tube or other situations leading to impaired mechanical ventilation, such as increased abdominal pressure during coughing, apnea possibly requiring cardiopulmonary resuscitation, and the inability to ensure lung-protective ventilation were complications that occurred in some patients included in this study. Respiratory acidosis, pain, erythema and/or swelling of the trachea, mucosal irritation, erosion, ulceration or necrosis on the trachea, swelling of the larynx, newly formed dys- or atelectasis, pneumothorax, leakage of the cuff, obstruction of the breathing tube, retention of secretion, retention of carbon dioxide despite measures taken, failure to oxygenate after intubation, repeated oxygen desaturation, bronchospasm, air trapping, self-extubation, missing phonation after being extubated, inspiratory stridor or expiratory wheezing after extubation, and vocal cord paresis were also complications which can arise due to intubation and mechanical ventilation. Complications occurred in two hundred and eighty of the orotracheally intubated patients and in ninety of the nasotracheally intubated patients ($p = 0.010$).

Table 17. Incidence of complications.

Complications	Orotracheal intubation (n = 1298)	Nasotracheal intubation (n = 329)
Yes	280 (21.6%)	90 (27.5%)
No	1018 (78.4%)	239 (72.5%)

3.3.12. Possibility and extent of physiotherapy

Overall, 4345 sessions of physiotherapy took place during the ten-day timeframe. Of these, 3513 (46.6%) were in the orotracheally intubated group, and 832 (48.9%) in the nasotracheally intubated group ($p = 0.094$). These numbers indicate that regardless of which group patients belonged to the frequency of physiotherapy sessions was nearly the same with no physiotherapy recorded in over 50% of the instances (53.4% in the OTI group versus 51.1% in the NTI group).

During the ten-day period nasotracheally intubated patients showed a significantly

higher range of movement which is reflected in the higher mean values on the ICU Mobility Scale as seen in table 18 and in figure 14.

Table 18. Average scores on the ICU Mobility Scale for day 1-10. 95% confidence interval given in brackets.

Timepoint	Orotracheal intubation (n= 1298)	Nasotracheal intubation (n = 329)	p-value
Day 1	0.4 (0.3, 0.5)	1.0 (0.8, 1.3)	<0.001
Day 2	0.5 (0.4, 0.6)	1.2 (1.1, 1.4)	<0.001
Day 3	0.6 (0.5, 0.7)	1.2 (1.0, 1.3)	<0.001
Day 4	0.6 (0.5, 0.7)	1.6 (1.5, 1.8)	<0.001
Day 5	0.7 (0.6, 0.8)	1.5 (1.3, 1.8)	<0.001
Day 6	0.7 (0.5, 0.8)	1.3 (1.0, 1.6)	<0.001
Day 7	0.7 (0.6, 0.8)	1.4 (1.1, 1.7)	<0.001
Day 8	0.7 (0.5, 0.8)	1.4 (1.1, 1.8)	<0.001
Day 9	0.6 (0.5, 0.8)	1.5 (1.1, 1.8)	<0.001
Day 10	0.6 (0.4, 0.8)	1.2 (0.8, 1.7)	0.012

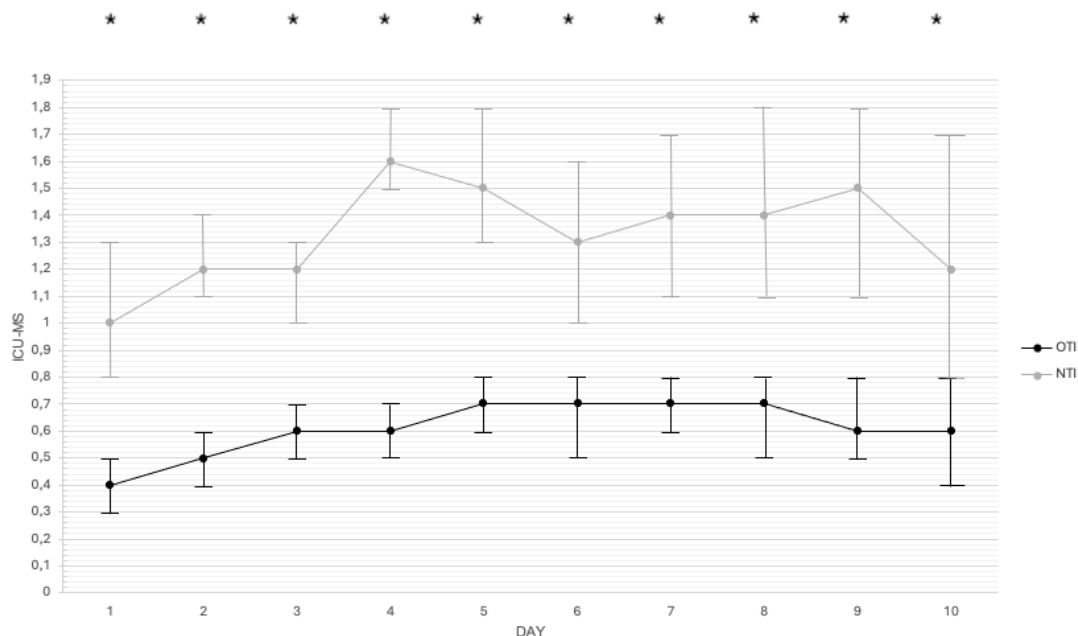


Figure 14. Average scores on the ICU Mobility Scale for day 1-10. Error bars represent 95% confidence interval.

On day one, there were no records of physiotherapy for more than half the patients of both groups. To be exact seven hundred and eighty-one (60.5%) of the OTI patients and one hundred and eighty-two (56%) of the NTI patients did not receive physiotherapy. In the orotracheally intubated group three hundred and sixty-seven patients and seventy-eight nasotracheally intubated patients received physiotherapy of the category zero which is defined as passive movement. Category one defined as any activity in bed was achieved by one hundred and twenty OTI and thirty NTI patients. Two OTI and one NTI patient were passively moved to a chair (category two). Category three describes sitting over the edge of the bed and was managed by

sixteen orotracheally intubated patients and twenty-two nasotracheally intubated patients. Three patients from the OTI group and four patients from the NTI group were able to stand which translates to category four. One OTI and five NTI patients were able to attain category five and another one orotracheally intubated patient, and three nasotracheally intubated patients marched on the spot (category six). No patient in either cohort was able to perform the extent of movement required for categories seven to ten ($p < 0.001$).

Table 19. Scores on the ICU Mobility Scale on day 1. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 1291)	Nasotracheal intubation (n = 325)
0	367	78
1	120	30
2	2	1
3	16	22
4	3	4
5	1	5
6	1	3
No physiotherapy	781	182

On day two, seven hundred and eight (54.8%) OTI patients and one hundred and sixty-five (50.8%) NTI patients did not participate in a physiotherapy session. Again, this is more than 50% of patients in each group. The exact split can be seen in table 20. On the second day of observation, there were no records of patients walking with the assistance of two people (category seven). However, one orotracheally intubated person walked with the assistance of one person (category eight). One nasotracheally intubated patient managed to walk without assistance but with a gait aid (category nine) and one NTI patient walked independently without the assistance of a person or a gait aid (category ten).

Table 20. Scores on the ICU Mobility Scale on day 2. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 1292)	Nasotracheal intubation (n = 325)
0	403	84
1	136	31
2	1	0
3	36	26
4	2	7
5	3	10
6	2	0
7	0	0
8	1	0
9	0	1
10	0	1
No physiotherapy	708	165

On the third day of observation, six hundred (52.1%) orotracheally intubated patients and one hundred and forty-three (50.7%) nasotracheally intubated patients did not receive a physiotherapy session which again is about half the patients in each group. No patient in either group performed exercises of the categories two, seven, eight, and nine, yet one OTI patient walked without the assistance of a person or gait aid (category ten). The exact distribution is listed in table 21.

Table 21. Scores on the ICU Mobility Scale on day 3. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 1151)	Nasotracheal intubation (n = 282)
0	367	72
1	123	27
3	50	27
4	4	7
5	2	5
6	4	1
10	1	0
No physiotherapy	600	143

On the fourth day of observation, 50% of NTI patients (one hundred and thirteen) and 51.3% of OTI patients (four hundred and seventy-four) did not partake in a physiotherapy session. Again, there were no records of patients achieving the level of movement required for categories seven, eight, nine, and ten. Moreover, there were no patients who were moved to a chair (category two). The extent of movement on day two ranged from passive movement in bed to marching on the spot.

Table 22. Scores on the ICU Mobility Scale on day 4. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 924)	Nasotracheal intubation (n = 226)
0	292	57
1	114	15
3	36	27
4	5	3
5	2	4
6	1	7
No physiotherapy	474	113

Day five is the first day during the observation period on which more than 50% of OTI patients received physiotherapy. No physiotherapy was recorded for 364 (48.6%) OTI patients and 88 (53%) of the nasotracheally intubated patients. The exact degree of movement that took place during sessions is depicted in table 23.

Table 23. Scores on the ICU Mobility Scale on day 5. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 749)	Nasotracheal intubation (n = 166)
0	251	43
1	83	12
3	41	13
4	7	2
5	1	3
6	2	5
No physiotherapy	364	88

On the sixth day of observation, three hundred and thirty-four (54.5%) of the oro-tracheally intubated patients and fifty-six (47.9%) of the nasotracheally intubated patients did not receive a physiotherapy session. The majority of patients in both groups who took part in a session was moved passively in bed without any active participation. Table 24 shows the range of movement during physiotherapy on day six.

Table 24. Scores on the ICU Mobility Scale on day 6. ($p = 0.001$)

ICU-MS category	Orotracheal intubation (n= 613)	Nasotracheal intubation (n = 117)
0	193	32
1	59	15
2	1	1
3	19	6
4	3	3
5	3	1
6	0	2
8	0	1
9	1	0
No physiotherapy	334	56

The scores on the ICU Mobility Scale for day seven of the observation period can be seen in table 25. There were no records of physiotherapy sessions for two hundred thirty-four OTI patients (45.9%) and forty-six NTI patients (49.5%). More than half the patients did do physiotherapy on that day, the range of extent is shown in table 25.

Table 25. Scores on the ICU Mobility Scale on day 7. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 510)	Nasotracheal intubation (n = 93)
0	193	24
1	56	7
2	0	1
3	23	13
4	1	1
5	3	0
9	0	1
No physiotherapy	234	46

On day eight of observation, two hundred and seven of the orotracheally intubated patients (50.6%) and thirty-two of the nasotracheally intubated patients (47.8%) did not have a physiotherapy session. Of those who did partake in a session the exact split of activity is listed in table 26.

Table 26. Scores on the ICU Mobility Scale on day 8. ($p = 0.008$)

ICU-MS category	Orotracheal intubation (n= 409)	Nasotracheal intubation (n = 67)
0	148	20
1	40	6
2	0	1
3	12	7
6	1	0
9	1	1
No physiotherapy	207	32

One hundred and seventy-seven orotracheally intubated patients (53.8%) and twenty-two nasotracheally intubated patients (40%) did not partake in a physiotherapy session on the ninth day of observation. The level of movement of those patients who did receive a session is listed in table 27.

Table 27. Scores on the ICU Mobility Scale on day 9. ($p < 0.001$)

ICU-MS category	Orotracheal intubation (n= 329)	Nasotracheal intubation (n = 55)
0	113	18
1	29	5
2	0	1
3	8	7
4	1	0
5	1	1
9	0	1
No physiotherapy	177	22

On the last day of the observation period one hundred and forty-four (54.5%) of the OTI patients and twenty-four (52.2%) of the NTI patients did not receive a physiotherapy session.

Table 28. Scores on the ICU Mobility Scale on day 10. ($p = 0.14$)

ICU-MS category	Orotracheal intubation (n = 264)	Nasotracheal intubation (n = 46)
0	86	10
1	23	5
2	1	0
3	8	7
5	2	0
No physiotherapy	144	24

4. Discussion

The objective of this retrospective, single-center study was to compare nasotracheal and orotracheal intubation in critically ill patients who received mechanical ventilation for at least 48 hours. The results show that patients intubated nasotracheally were more alert and were able to perform to a greater extent during physiotherapy sessions, as they received lower doses of sedative medication as well as vasopressors.

The Richmond Agitation Sedation Scale is used to quantify the level of awareness and subsequently the depth of sedation of ICU patients (Sessler et al., 2001, Ely et al., 2003). The recommended RASS range of 0 or -1 correlates with a state of being alert and calm, or drowsy (Sessler et al., 2001). These levels of awareness represent the ideal state for endotracheally intubated patients as recommended by, *inter alia*, German guidelines, because patients are awake and able to communicate while receiving sufficient doses of analgetic and sedative medication to avoid pain or agitation (S3-Leitlinie). Deep sedation during mechanical ventilation has been shown to correlate with delayed extubation and therefore a lengthier time of invasive mechanical ventilation, longer ICU and overall hospital stays, and higher mortality (Shehabi et al., 2013, Stephens et al., 2018, Kress et al., 2000, Balzer et al., 2015, Aragón et al., 2019). The results yielded by this study are mostly congruent to those mentioned above, although the length of the overall hospital stay was not ascertained. The length of the ICU stay did not differ significantly between the two groups, the length of intubation however did. The latter is attributable to our theory, that an evaluation regarding extubation versus prolonged ventilation requiring a tracheostomy could be conducted at an earlier stage during the ICU stay for patients intubated nasotracheally. During weaning from mechanical ventilation doses of sedative medication are decreased in order to evaluate the possibility for extubation (Quintard et al., 2017, Vagionas et al., 2019). As NTI patients in this study required lower doses of sedative medication it is likely the evaluation took place earlier in time as no or little gradual reduction of sedative medication compared to the OTI group had to take place.

The results of this study show that patients intubated nasotracheally spent more time in the optimal RASS range, which correlates with a score of 0 or -1 on the Richmond Agitation Sedation Scale, compared to those intubated orotracheally. Furthermore, it

is apparent that there was an association between orotracheal intubation and mortality. Patients intubated orotracheally initially showed significantly higher scores on the SOFA-score, though values for the other mortality prediction scores APACHE II, and SAPS II did not differ significantly. The higher mortality rate in the OTI group is therefore possibly in part due to the difference in the depth of sedation and not directly resulting from the route of intubation. Rather it is due to the secondary effects caused by orotracheal intubation.

Patients intubated orotracheally spent a higher percentage of time with a RASS of +1, -2, -3, -4, and -5, which, respectively, translates to a state of being restless, lightly sedated, moderately sedated, deeply sedated, and unarousable (Sessler et al., 2002). The average score on the Richmond Agitation Sedation Scale was significantly higher in the NTI group during the entire observation period.

This goes hand in hand with our findings regarding the doses of sedative medication administered in the two groups. Patients intubated nasotracheally received considerably lower doses of Propofol and Sufentanil compared to orotracheally intubated patients. According to Kress et al patients who received daily interruptions in the continuous administration of sedative drugs had a shorter overall intubation period (Kress et al., 2000). This is supported by results yielded from other studies (Vagionas et al., 2019, Kollef et al., 1998). The difference in doses of sedative medication administered is most likely explicable due to the triggering of an oropharyngeal stimulus when intubated orotracheally, causing discomfort, which in turn leads to a need for heavier sedation. In their meta-analysis, Adly and colleagues also found this to be the case when comparing sedation levels in endotracheally intubated patients versus patients who had received a tracheostomy (Adly et al., 2018). More recent studies have also shown a significant difference in the doses of sedative medication required prior to a tracheostomy compared to after the tracheostomy has been established, with a lesser need of sedatives in the latter state (Wallen et al., 2022, Morton et al., 2022). The pharyngeal reflexes are triggered in the areas of the posterior pharyngeal wall, soft palate, tonsillar area, and the base of the tongue (Miller, 2002, Sivakumar and Prabhu, 2023). Patients with tracheostomy do not experience pharyngeal stimuli as the tracheal tube is placed below the area in which pharyngeal reflexes are triggered. When comparing nasotracheal and orotracheal intubation, tubes placed nasotracheally cause less triggering of the pharyngeal reflex. No or little triggering of reflexes in turn explains why overall less

sedation is required in the nasotracheal group. The nasotracheal tube has a smaller diameter than the orotracheal tube and even though the tube is also placed pharyngeally it does not cause a pharyngeal reflex as the tube does not touch any of the sensitive areas apart from the posterior pharyngeal wall which it is positioned parallelly to (Atanelov et al., 2023). Once more, this is the most likely explanation for the significant difference of sedative medication required in the two groups.

The rate of spontaneous ventilation was significantly higher in the NTI group which again may be explained by the lower doses of sedative medication. In this study, the doses of Propofol, Sufentanil, and Midazolam were assessed, all three of which can cause dose-dependent respiratory depression as an adverse effect when used for sedation purposes (Folino et al., 2022, Monk et al., 1988, Lingamchetty et al., 2021). As the patients in the NTI group received lower mean doses of sedatives it is likely this is the reason for the higher level of spontaneous ventilation in this group.

Presumably, the actual route of intubation was therefore not the main determinant for the difference in rates of spontaneous breathing, but it was rather due to adverse effects caused by the sedatives. Another explanation for our results may be that patients ventilated mechanically who also breathe spontaneously require less sedation (Spinelli et al., 2020). This is also reflected in the results yielded by this study, as the NTI group had higher rates of spontaneous breathing compared to the lower rates in the OTI group.

Spontaneous respiration during mechanical ventilation has positive physiological effects such as maintaining a certain diaphragmic muscle tone. Without spontaneous breathing the diaphragm is prone to atrophy and dysfunction which in turn can cause complications after stopping mechanical ventilation (Levine et al., 2008, Putensen et al., 2001, Yoshida et al., 2017, Schepens et al., 2020). Diaphragmatic atrophy and dysfunction can hinder a successful extubation, leading to a need for prolonged mechanical ventilation, and correlates with poor patient outcome and should therefore be avoided if possible (Schepens et al., 2020, Goligher et al., 2018).

Mechanical ventilation is associated with decreased ventilation of the dorsal lung regions leading to atelectasis formation whereas spontaneous breathing leads to a more even distribution of gas which is the reason why spontaneous breathing during mechanical ventilation is beneficial for lung health in the long run (Putensen et al., 2006, MacIntyre, 2016).

As previously mentioned, NTI patients required less vasopressor therapy, namely Noradrenaline, compared to the OTI group. An adverse effect of Propofol is hypotension (Folino et al., 2022, Claeys et al., 1988, Wadbrook, 2000). Therefore, the higher doses of Propofol are consistent with an increased requirement for Noradrenaline in the OTI group to counteract the drop in blood pressure during sedation with Propofol. The reason why patients intubated orotracheally have a greater requirement of vasopressor therapy is therefore not necessarily determined primarily by the route of intubation but is a result of adverse effects of sedative medication, which the OTI group receives more of due to the reasons discussed above.

Patients intubated nasotracheally were able to perform at significantly higher levels during physiotherapy sessions throughout the ten-day observation time. As discussed above, patients in the nasotracheal intubation group received lower average doses of sedative medication leading to a higher mean score on the Richmond Agitation Sedation Scale, which in turn is favorable during physiotherapy. The deeper level of sedation in orotracheally intubated patients may well coincide with the decreased performance during physiotherapy, as orotracheally intubated patients performed no or minimal active movement during these sessions with an average level of exercise of 0 to 1 on the ICU Mobility Scale.

The length of ventilation in nasotracheally intubated patients was significantly lower in the NTI than in the OTI group, and the rate of tracheostomy was higher in the NTI group, even though not significantly. Both are most likely attributable to the fact that NTI patients were sedated less heavily and therefore an assessment regarding the possibility of a successful extubation or the need for long-term ventilation could be conducted at an earlier point in time than with orotracheally intubated patients. Tracheostomy in long-term ventilation has several advantages including a lower requirement of sedative drugs, and easier oral hygiene, as well as increased patient comfort and mobility (Wallen et al., 2022, Bösel, 2014, Freeman, 2017). In a metanalysis comparing early versus late tracheostomy in critically ill patients it was suggested that early tracheostomy, so a tracheostomy withing the first ten days of intubation, was most likely superior to late tracheostomy (Andriolo et al., 2015). This again highlights the advantage of an early evaluation regarding the potential need of a tracheostomy. Failure to extubate and therefore unsuccessful extubation leading to

reintubation has a significant impact on patients' prognosis, as an association with increased mortality rates, prolonged mechanical ventilation, and complications linked with endotracheal ventilation, such as ventilator-associated pneumonia exists (Thille et al., 2013, Torres et al., 1995, Thille et al., 2011, Ferrera and Hayes, 2023, Quintard et al., 2017).

Therefore, it is beneficial for the patient on many levels if an evaluation regarding the possibility of an extubation or the need for long-term ventilation and therefore a tracheostomy can be performed early and adequately.

The main reason why orotracheal intubation has been favored over the past decades is due to the high incidence of sinusitis in nasotracheally intubated patients (Salord et al., 1990). Having said this, the assertion was refuted in a study conducted by Holzapfel et al. comparing patient groups intubated either orotracheally or nasotracheally on the occurrence of sinusitis. They found that there was no significant difference in the incidence of clinically relevant cases of sinusitis between the two groups (Holzapfel et al., 1993). It is conceivable that the hygienic measures and medical possibilities of today's medicine enable nasotracheal intubation without the increased risk of sinusitis compared to the orotracheal group which had posed a more paramount danger in the past.

In our study, there were merely a handful of cases of sinusitis and the difference of incidences between the two groups was not significant. However, we did not screen proactively for sinusitis, and it was merely a diagnosis made retrospectively by means of the available documentation. The same can be said for ventilator-associated pneumonia. Nineteen percent of patients intubated orotracheally, and twenty percent of the nasotracheally intubated patients showed signs of a ventilator-associated pneumonia, the difference was not significant. The risk for ventilator-associated pneumonia increases the longer patients are being ventilated mechanically (Zolfaghari and Wyncoll, 2011). In purely statistical terms, the risk for the development of ventilator-associated pneumonia should be greater in the OTI group as they were intubated for a longer period of time.

This study has its limitations. Firstly, only data from a single center was obtained and analyzed, limiting the generalizability of the results. The retrospective design makes it impossible to know for sure if all incidences of sinusitis, ventilator-associated pneumonia, and complications associated with endotracheal intubation and

mechanical ventilation were recorded as these parameters were not automatically transferred into the electric patient file but rather had to be documented separately by the doctor or healthcare professional. Furthermore, it is not possible to differentiate between actual and incidental causality and the existence of unidentified confounders cannot be excluded fully.

5. Summary

Orotracheal airway management is the preferred route of intubation in the ICU although nasotracheal intubation may also be used for long-term ventilation in critically ill patients. During the last three decades, nasotracheal intubation has been widely replaced by tracheostomy. However, therapy concepts in the ICU have changed since then and more recent data indicate potential benefits of nasotracheal intubation (Hariri et al., 2018). This doctoral thesis was conducted as a retrospective, single-center, exploratory cohort-study at the University Medical Center Hamburg-Eppendorf to test the hypothesis that patients intubated nasotracheally are more alert, show higher levels of spontaneous ventilation, are able to participate more actively during physiotherapy, and require lower doses of vasopressors and sedatives compared to patients who are intubated orotracheally. Data was obtained from the electronic database and was statistically analyzed. The observational period was from January 1, 2018, to December 31, 2020. Adult patients who were admitted to one of the twelve intensive care units (140 beds), received tracheal intubation in an ICU setting, and were mechanically ventilated for a ≥ 48 hours were included. Patients who received nasotracheal intubation due to a difficult airway, for surgery or other procedures were excluded. According to the route of intubation, patients were assigned to either the nasotracheal (NTI) or the orotracheal intubation group (OTI). The length of intubation, doses of sedatives and vasopressors, fraction of time with RASS 0 or -1, and rate of spontaneous ventilation were examined for both groups over a 10-day period or until extubation if this occurred earlier.

1209 patients met the inclusion criteria. 1627 instances of tracheal intubation were recorded, of those 1298 were orotracheal and 329 nasotracheal. Patients in the NTI group received overall lower doses of vasopressors and sedatives, spent significantly more time in the recommended RASS range, received significantly less controlled ventilation, and were intubated for a significantly shorter period of time. This patient collective was also able to perform at a significantly higher level during physiotherapy sessions compared to orotracheally intubated patients.

This study was conducted to generate hypotheses for further studies. The promising results yielded by this doctoral thesis have led to the launch of a study with a similar objective but conducted prospectively. Should the results of the prospective study be congruent to our results this could lead to an increase of nasotracheal intubation which in turn could improve patient outcome.

Das orotracheale Atemwegsmanagement ist der bevorzugte Weg der Intubation im intensivmedizinischen Setting. Die nasotracheale Intubation kann auch für die Langzeitbeatmung kritisch kranker Patienten zum Einsatz kommen, jedoch wurde diese in den letzten drei Jahrzehnten weitgehend durch die Tracheotomie ersetzt. Allerdings haben sich die intensivmedizinischen Therapiekonzepte seither geändert und neuere Daten weisen auf potenzielle Vorteile der nasotrachealen Intubation hin (Hariri et al., 2018). Diese Dissertation wurde als retrospektive, monozentrische, explorative Kohortenstudie am Universitätsklinikum Hamburg-Eppendorf durchgeführt, um folgende Hypothese zu prüfen: nasotracheal intubierte Patienten sind wacher, atmen häufiger spontan, können aktiver an Physiotherapiesitzungen teilnehmen und benötigen geringere Dosen an Vasopressoren und Sedativa als Patienten, die orotracheal intubiert werden. Die Daten wurden aus der elektronischen Datenbank entnommen und statistisch ausgewertet. Der Beobachtungszeitraum war vom 1. Januar 2018 bis zum 31. Dezember 2020. Es wurden erwachsene Patienten eingeschlossen, die auf einer der zwölf Intensivstationen (140 Betten) lagen, eine tracheale Intubation im intensivmedizinischen Setting erhielten und ≥ 48 Stunden lang mechanisch beatmet wurden. Ausgeschlossen wurden Patienten, die aufgrund eines schwierigen Atemweges, wegen chirurgischer Eingriffe oder diagnostischer oder interventioneller Verfahren nasotracheal intubiert wurden. Abhängig der Intubationsroute wurden die Patienten entweder der nasotrachealen (NTI) oder der orotrachealen Intubationsgruppe (OTI) zugeordnet. Es wurden die Intubationsdauer, die Dosis der Sedativa und Vasopressoren, der Anteil der Zeit mit RASS 0 oder -1 und die Rate der Spontanatmung für beide Gruppen über einen Zeitraum von 10 Tagen oder bis zur Extubation, falls diese früher erfolgte, untersucht.

1209 Patienten wurden in die Studie eingeschlossen. Es wurden 1627 endotracheale Intubationen erfasst, von diesen waren 1298 orotracheal und 329 nasotracheal. Die Patienten in der NTI-Gruppe erhielten insgesamt niedrigere Dosen an Vasopressoren und Sedativa, verbrachten signifikant mehr Zeit im empfohlenen RASS-Bereich, wurden signifikant weniger kontrolliert beatmet und die Intubationsdauer war signifikant kürzer. Dieses Patientenkollektiv nahm zudem signifikant aktiver während Physiotherapiesitzungen teil als orotracheal intubierte Patienten.

Diese Studie wurde durchgeführt, um Hypothesen für weitere Studien zu generieren. Die vielversprechenden Ergebnisse dieser Doktorarbeit führten dazu, dass eine

prospektive Studie mit ähnlicher Zielsetzung gestartet wurde. Sollten die Ergebnisse der prospektiven Studie mit unseren Ergebnissen übereinstimmen, könnte dies zu einer Zunahme nasotrachealer Intubationen führen, was wiederum das Patientenoutcome verbessern könnte.

6. Abbreviations

ICU = intensive care unit

OTI = orotracheal intubation

NTI = nasotracheal intubation

BMI = body mass index

GCS = Glasgow Coma Scale

SAPS II = Simplified Acute Physiology Score II

APACHE II = Acute Physiology and Chronic Health Evaluation Score

SOFA = Sepsis-related / Sequential Organ Failure Assessment

RASS = Richmond Agitation and Sedation Scale

VAP = ventilator-associated pneumonia

SPSS = Statistical Package for the Social Sciences

CPR = cardiopulmonary resuscitation

n = natural number

kg = kilogram

cm = centimeter

kg/m² = kilogram per square meter

d = day(s)

h/d = hours per day

µg/kg/min = micrograms per kilogram per minute

mg/d = milligrams per day

µg/d = micrograms per day

7. References

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9. Lebenslauf

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Vorträge

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Oktober 2022 “Influence of nasotracheal versus orotracheal intubation on sedation and ventilation – a retrospective cohort study” auf der 35. Jahrestagung der European Society of Intensive Medicine

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