

Prophylactic antibiotics at the time of tracheotomy lowers the incidence of pneumonia

Nicklas Järvelä Johansen¹ & Christoffer Holst Hahn²

ABSTRACT

INTRODUCTION: Nosocomial pneumonia in relation to tracheotomy is a well-known complication. The aim of the present study was to study prophylactic antibiotics at the time of tracheotomy as a protective factor against nosocomial pneumonia.

METHODS: A retrospective follow-up study was conducted on otorhinolaryngeal cancer patients requiring a surgical tracheotomy over a four-year period. Data were extracted from a digital record system. The inclusion criteria included a cancer diagnosis in the otorhinolaryngeal area; and the tracheotomy had to be the primary operation. A total of 88 patients were eligible for inclusion, forming a group without antibiotics (n = 53) treatment and a group with antibiotics (n = 35) treatment.

RESULTS: In the group without antibiotics, 67% (n = 34) developed pneumonia (not including aspirational) versus 44% (n = 14) in the group with antibiotics (p = 0.04). The 30-day mortality was 10% (n = 9), and the one-year mortality was 58% (n = 42) for the total population, with no statistically significant differences between the groups. Pneumonia after tracheotomy prolonged the hospitalisation time regardless of grouping. In the group without antibiotics, the median was seven days for patients without pneumonia compared with 12.5 days for patients with pneumonia (p < 0.01). Within the group with antibiotics, the median was ten days for the patients without pneumonia versus 16 days for those with pneumonia (p = 0.02).

CONCLUSION: The present study indicates that prophylactic antibiotics administration at the time of tracheotomy lowers the incidence of pneumonia in otorhinolaryngeal cancer patients.

FUNDING: not relevant.

TRIAL REGISTRATION: not relevant.

Each year many tracheotomies are performed in Denmark as well as internationally. In the US alone, the count was 113,653 in 2006, with an overall complication rate of 3.2% and an in-hospital mortality of 19.6% [1]. The complications range from acute complications such as nosocomial pneumonia, subcutaneous emphysema and post-operative bleeding, to late complications like tracheal stenosis and dysphagia [2, 3]. To the best of our knowledge, only one otorhinolaryngeal study has directly studied the risk of nosocomial pneumonia in relation to tracheotomy [4].

Many patients with head and neck cancer require a tracheotomy due to upper airway obstruction. They have a minimal need for mechanical ventilation and may require a surgical tracheotomy due to the location of the cancer at the surgical site. In the critical care literature, the subject has been scrutinised with varying results over the years. De Leyn et al [2] reviewed the existing literature and concluded that it was controversial whether tracheotomy is a risk factor for pneumonia or not.

In the critical care literature focus is on ventilator-associated-pneumonias (VAP) as many patients at the intensive care units (ICU) are mechanically ventilated for a long time. Furthermore, percutaneous tracheotomies are recommended as the procedure of choice [2].

The lack of relevant otorhinolaryngeal literature, the differences between ICU- and head and neck cancer patients, and the ensuing difficulties in comparing the results all demonstrate the need for further studies. Our hypothesis is that the administration of prophylactic antibiotics (AB) at the time of tracheotomy may lower the risk of post-operative, nosocomial pneumonia. As of today, no official guidelines on the use of prophylactic AB prior to tracheotomy exist in Denmark in the field of otorhinolaryngology. Our primary aim was to estimate the prevalence of nosocomial pneumonia after tracheotomy in patients with a head and neck cancer, and to evaluate whether prophylactic AB given around the time of tracheotomy lowers the risk of pneumonia.

METHODS

Patients

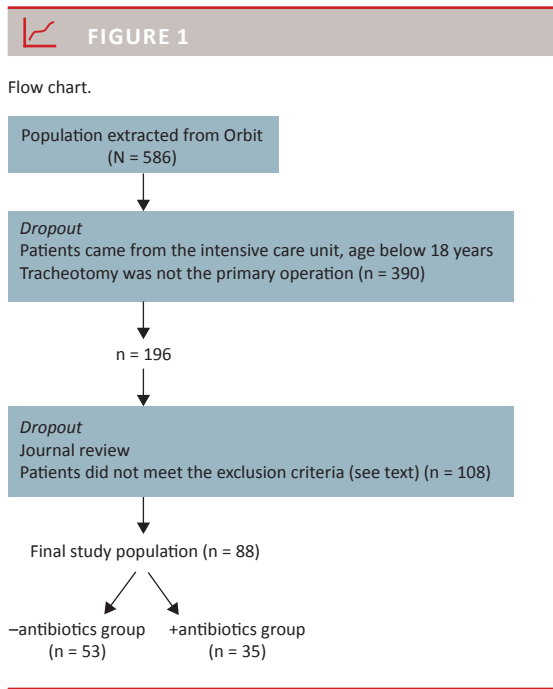
A retrospective follow-up study was conducted at the Ear, Nose and Throat Department, Rigshospitalet, Denmark in the spring of 2014. A total of 586 patients were found in Orbit (a digital registration system for operations) where we searched for a surgical tracheotomy as the primary operation in the period from January 2010 to February 2014. Of these 586 patients, 196 (33%) were initially found to be eligible for inclusion. A journal review excluded another 108 patients, which gave rise to the final study population (n = 88) (Figure 1).

The enrolled patients were assigned to two subgroups depending on whether AB had been given within the last four days before tracheotomy. These groups were the –prophylaxis group without antibiotics (n = 53) and the +prophylaxis group with antibiotics (n = 35).

ORIGINAL ARTICLE

1) Department of Medicine, Amager Hospital
2) Department of Otolaryngology, Rigshospitalet, Denmark

Dan Med J
2015;62(7):A5107



The inclusion criteria of the study were a minimum age of 18 years, a diagnosis of cancer in the head and neck area or in the airways, no primary hospitalisation at the ICU around the time of tracheotomy, and, finally, the tracheotomy had to be registered as the primary operation.



New tracheotomy.

The exclusion criteria included records not allowing a 30-day follow-up, intubation or mechanical ventilation for more than 24 hours before the procedure, suspicion or diagnosis of pneumonia one week before the tracheotomy and, finally, an already existing tracheotomy.

Definitions

During the medical records study, 14 primary parameters with subgroups were registered. These included age, gender, diagnosis, co-morbidity, indication, time from cancer diagnosis to tracheotomy, former radiation therapy and time from radiation to tracheotomy, tracheotomy complications, pneumonia parameters, time until pneumonia, hospitalisation time, 30-day mortality and one-year mortality.

Table 1 and **Table 2** show all of these parameters including the subgroups. The cancer diagnosis and the date it was made were based on the histology answer of the Danish Pathology Databank. All timespans excluding those for cancer and radiation therapy were registered from the day of the tracheotomy. Complications were registered within the first 30 days after surgery.

Our diagnosis of pneumonia was defined as AB prescribed after tracheotomy on suspicion of pneumonia as it reflected the treating physician's assessment. However, the patients in the +prophylaxis group were already given AB after tracheotomy. Therefore, the new AB after tracheotomy had to be prescribed independently of the AB prior to tracheotomy, or the old AB indication had to be changed to pneumonia.

Statistical analysis

The statistical analysis was carried out with IBM SPSS Statistics 22 using a t-test on the mean age, and the Mann-Whitney test on all other numerical outcomes. The binary outcomes were analysed with the chi-squared test or Fisher's exact test, as appropriate. The statistical significance was calculated using a two-tailed p-value < 0.05, and the mean \pm standard deviation (SD) or median \pm interquartile range (IQR) are shown as needed. During the medical records study, some of the parameters were not registered for all patients in the digital record system. The statistical analysis of these parameters has been made with the available data, and {n} marks the number of patients used for this in all of the tables.

Trial registration: not relevant.

RESULTS

Table 1 presents the characteristics of the study population. For the total population, the mean age was 68.3 years, and 69% were males. No statistically significant differences between the -prophylaxis and +prophylaxis group were found for any of the data.



TABLE 1

	–prophylaxis ^a (N = 53)	+prophylaxis ^b (N = 35)	Total (N = 88)	p-value	Characteristics of the study population.
Age, yrs, mean ± SD	68.5 ± 10.4	68.0 ± 9.1	68.3 ± 9.9	0.81	
Gender, n (%)				0.20	
Male	34 (64)	27 (77)	61 (69)		
Female	19 (36)	8 (23)	27 (31)		
Diagnosis, n (%)				0.29	
C. laryngis	12 (23)	9 (26)	21 (24)		
C. rhinopharyngis	0	1 (3)	1 (1)		
C. hypopharyngis	15 (28)	9 (26)	24 (27)		
C. oropharyngis	4 (8)	5 (14)	9 (10)		
C. cavum oris	6 (11)	7 (20)	13 (15)		
C. oesophagei	6 (11)	0	6 (7)		
C. thyroidea	7 (13)	4 (11)	11 (13)		
C. pulmonis	2 (4)	0	2 (2)		
Cervical metastasis	1 (2)	0	1 (1)		
Co-morbidity, n (%)				0.35	
None	40 (76)	26 (74)	66 (75)		
COPD	5 (9)	4 (11)	9 (10)		
Asthma	0	2 (6)	2 (2)		
Diabetes mellitus	3 (6)	2 (6)	5 (6)		
Apoplexia with sequelae	5 (9)	1 (3)	6 (7)		
Total co-morbidity	13 (25)	9 (26)	22 (25)	0.90	
Indication, n (%)				0.45	
Stridor	45 (85)	32 (91)	77 (88)		
Respiratory insufficiency	2 (4)	0	2 (2)		
Prophylactic before radiation therapy	6 (11)	3 (9)	9 (10)		
Time from cancer diagnosis to tracheotomy, days, median (IQR)	100 (29-310)	128 (39-497.5)	115 (30.5-369.5)	0.49	
Former radiation therapy, n (%)	36 (68)	26 (74)	62 (71)	0.52	
Time from radiation to tracheotomy, days, median (IQR) (n)	126.5 (12.5-363) {36}	332 (28-825) {26}	160 (20-704) {62}	0.14	

(n) = number of patients with data available for statistical analysis due to lack of registration in the records; AB = antibiotics; C = cancer; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; SD = standard deviation.

a) AB was not given within the last 4 days before tracheotomy.

b) AB was given within the last 4 days before tracheotomy.

Table 2 presents the outcomes of the –prophylaxis group vs. the +prophylaxis group.

As shown in Table 2, 67% (n = 34) developed non-aspirational pneumonia in the –prophylaxis group versus 44% (n = 14) in the +prophylaxis group (p = 0.04). Including the aspirational pneumonias, the p-value was 0.07. The median time of hospitalisation in the –prophylaxis group was ten days versus 14 days in the +prophylaxis group (p = 0.09).

The administration of AB after tracheotomy was highest in the –prophylaxis group where 76% (n = 40) received this versus 54% (n = 19) in the +prophylaxis group (p = 0.04). No other pneumonia parameters showed any statistically significant difference between the groups.

As for the total study population, the 30-day mortality was 10% (n = 9), the one-year mortality was 58% (n = 42) and the median time until pneumonia was four days. There were no statistically significant differences between the groups.

The median time of hospitalisation was shorter for –pneumonia patients than for +pneumonia patients, regardless of prophylaxis. The median time was seven days for the –pneumonia patients versus 12.5 days for the +pneumonia in the –prophylaxis group (p < 0.01). Within the +prophylaxis group, the median was ten days for the –pneumonia patients versus 16 days for the +pneumonia (p = 0.02). The results are not shown in Table 2, but accounted for in the text.

Male gender was not associated with pneumonia, and a diagnosis of pneumonia did not affect the 30-day or the one-year mortality.

DISCUSSION

This study suggests that patients without AB prophylaxis have a higher prevalence of pneumonia than patients with prophylaxis. Furthermore, pneumonia increased the length of hospitalisation regardless of AB prophylaxis.

 TABLE 2

Outcomes of the group without antibiotics versus the group with antibiotics.

	–prophylaxis (N = 53)	+prophylaxis (N = 35)	Total (N = 88)	p-value
<i>Tracheotomy complications, n (%) {n}</i>				
Post-operative bleeding	8 (15)	3 (9)	11 (13)	0.52
Subcutaneous emphysema	3 (6)	1 (3)	4 (5)	1.00
Urinary tract infection	0	1 (3)	1 (1)	0.40
Wound infection	6 (11)	3 (9)	9 (10)	1.00
Pneumonia	34 (67) {51}	14 (44) {32}	48 (58) {83}	0.04
Aspirational pneumonia	2 (11) {19}	3 (14) {21}	5 (13) {40}	1.00
Total pneumonia	36 (68)	17 (49)	53 (60)	0.07
<i>Pneumonia parameters, n (%) {n}</i>				
Antibiotics after tracheotomy	40 (76)	19 (54)	59 (67)	0.04
Stethoscopia pulmonis	19 (36)	16 (46)	35 (40)	0.36
Thoracic X-ray	17 (53) {32}	7 (37) {19}	24 (47) {51}	0.26
Tracheal secretion	15 (48) {31}	8 (73) {11}	23 (55) {42}	0.29
CRP > 25 mg/dl	47 (98) {48}	30 (88) {34}	77 (94) {82}	0.16
Time until pneumonia, days, median (IQR)	4(2-6)	5 (2-9)	4 (2-7)	0.60
Hospitalization time, days, median (IQR)	10 (7-15)	14 (8.5-26)	12 (7-20.5)	0.09
30-day mortality, n (%)	6 (11)	3 (9)	9 (10)	1.00
1-yr mortality, n (%) {n}	23 (52) {44}	19 (66) {29}	42 (58) {73}	0.26

{n} = number of patients with data available for statistical analysis due to lack of registration in the records; CRP = C-reactive protein concentration; IQR = interquartile range.

Our results indicate that AB may be a protective factor against nosocomial pneumonia following tracheotomy. As mentioned before, only one otorhinolaryngeal study has directly evaluated this topic. One other otorhinolaryngeal study has included pneumonia as a tracheotomy complication. However, as it did not provide data on how pneumonia was defined, or whether AB had been used in connection with the tracheotomy, we cannot compare our results with the results reported from this study [5]. We therefore discuss our findings primarily by comparing them with the critical care literature.

Sepehr et al [4] evaluated tracheotomies as a risk factor for pneumonia in an otorhinolaryngeal setting. Tracheotomy was found to be a risk factor ($p < 0.01$). However, a short course of AB < 4 days versus a long course of > 4 days showed no statistically significant differences ($p = 0.69$). This is the study that compares best with ours, but a number of problems arise when comparing the two studies.

Firstly, our study investigates studies the lack of prophylactic AB as a risk factor for developing pneumonia. Sepehr et al studied tracheotomy as a risk factor and all patients apparently received prophylactic AB. Secondly, it was not clearly stated whether AB was started before, around or after tracheotomy. Finally, it is unclear whether the tracheotomy was the primary operation, whereas in our study this was an inclusion criterion.

As mentioned in the Introduction, it is heavily debated in the critical care literature if tracheotomy is a risk factor for VAP. One study found no difference in the frequency of respiratory infections before or after tracheotomy [6]; however, other studies recognised the association [7, 8].

Speculations have been made as to whether AB could be a risk factor for VAP. One study found that AB given during an ICU stay was associated with VAP in multivariate analysis ($p < 0.01$) [9]. Another study showed no influence of AB given prior to tracheotomy on VAP incidence; however, their goal was to investigate the effect of selective decontamination of the digestive tract on VAP incidence [10]. Finally, some studies find AB to be protective against pneumonia in mechanically ventilated patients [11-13].

Interestingly, Cavalcanti et al propose a bimodal effect of AB offering protection against early-onset VAP, but predisposing to late-onset VAP due to selection of resistant microorganisms [14].

The pathophysiology of VAP must be considered too when comparing our results to the critical care literature. The endotracheal intubation tube is an entryway for bacteria that colonise the upper airways, possibly forming biofilm on the tube. It also allows for aspiration of contaminated oropharyngeal secretions into the lungs [14]. The tracheotomy negates this, but bypasses the upper airways' filter function on the inspired air, marking the importance of tracheotomy management [2].

Despite the above, prophylactic AB two hours before tracheotomy is recommended in the ICU setting [2]. Georges et al [15] found that AB treatment on the day of surgical tracheotomy lowered the risk of early nosocomial pneumonia for mechanically ventilated patients in a univariate analysis ($p < 0.03$). These results support our findings and hypothesis, even though they evaluated the risk of VAP.

The shortest median time of hospitalisation was observed in the –prophylaxis group, but the pneumonia prevalence was also highest here. These results seem contradictory. One explanation may be that the patients in the +prophylaxis group were given AB in the last four days before tracheotomy. The indication could be sepsis or other serious infections meaning that the patients in this group may have been more ill and therefore hospitalised for a longer period.

We found a statistically significantly longer mean time of hospitalisation among the patients with pneumonia regardless of AB prophylaxis or not. Several studies in the critical care literature confirm the association between VAP and a longer mean time of hospitalisation, ICU stay and an increase in mortality [6-8, 15]. Our study showed no difference between the 30-day

and the one-year mortality. To the best knowledge of the authors, no otorhinolaryngeal studies regarding this have yet been performed.

Our paraclinical diagnostic tools could not be evaluated due to lack of registration in the digital records system.

Finally, we found that 69% of the study population was male. The male gender seems to be overly prevalent among patients requiring tracheotomy, but gender has not been confirmed as a risk factor for nosocomial pneumonia in our study. However, male gender as a VAP risk factor has been reported in the critical care literature [11, 13].

In the critical care literature, several other risk factors than tracheotomy and different ways of preventing VAP have been identified. These factors may also be considered in the otorhinolaryngeal field.

AB as a risk versus protective factor has been discussed in the above. Early versus late tracheotomy in relation to mechanical ventilation has not been shown to be associated with a decrease in VAP. However, it may shorten the length of mechanical ventilation, ICU stay and hospitalisation time [2, 9, 16-18]. Finally, hyperthermia around tracheotomy and prolonged sedation > 24 hours following tracheotomy have been associated with an increase in VAP [15].

Protective measures against VAP include the possible benefit of an early tracheotomy, selective decontamination of the digestive tract [10] and, finally, the conclusion that the prevention of VAP is a continuous multidisciplinary process [19, 20].

Our study has several limitations. First, the retrospective design poses a problem due to the difficulties in matching the groups, e.g. no standardised choice of AB drug, dose or timing. Second, the study population is far too small for the study to gain significant statistical power. Third, our diagnosis of pneumonia relied on the assessment of the treating physician. Fourth, only 88 patients of the original 586 were eligible for inclusion, which introduces the possibility of selection bias. For example, patients primarily hospitalised at the ICU leading up to tracheotomy were discarded. The no-inclusion of head and neck cancer patients from the ICU may dwarf our results since these patients could be more likely than others to catch pneumonia. Finally, the study was conducted at a single department making it difficult to generalise the results.

CONCLUSION

Our results suggest a protective effect of AB prior to tracheotomy and confirm the lengthening of hospitalisation following pneumonia.

The lack of relevant otorhinolaryngeal studies outside the ICU setting and the limitations concerning the

strength of the results of this study warrant further studies in the future, preferably a randomised controlled trial evaluating the effect of prophylactic AB at the time of tracheotomy.

CORRESPONDENCE: Nicklas Järvelä Johansen, Medicinsk Afdeling, Amager Hospital, Italiensvej 1, 2300 Copenhagen S, Denmark.
E-mail: jarvela@gmail.com

ACCEPTED: 4 May 2015

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

- Shah RK, Lander L, Berry JG et al. Tracheotomy outcomes and complications: a national perspective. *Laryngoscope* 2012;122:25-9.
- De Leyn P, Bedert L, Delcroix M et al. Tracheotomy: clinical review and guidelines. *Eur J Cardiothorac Surg* 2007;32:412-21.
- Epstein SK. Late complications of tracheostomy. *Respir Care* 2005;50:542-9.
- Sepehr A, Santos BJG, Chou C et al. Antibiotics in head and neck surgery in the setting of malnutrition, tracheotomy, and diabetes. *Laryngoscope* 2009;119:549-53.
- Fiorine FR, Santoro R, Deganello A et al. Is open tracheotomy performed by residents in otorhinolaryngology a safe procedure? A retrospective cohort study. *Eur Arch Otorhinolaryngol* 2015;272:1483-9.
- Sole ML, Talbert S, Penover DA et al. Comparison of respiratory infections before and after percutaneous tracheostomy. *Am J Crit Care* 2014;6:80-7.
- Apostolopoulou E, Bakakos P, Katostaras T et al. Incidence and risk factors for ventilator-associated pneumonia in 4 multidisciplinary intensive care units in Athens, Greece. *Respir Care* 2003;48:681-8.
- Alp E, Güven M, Yildiz M et al. Incidence, risk factors and mortality of nosocomial pneumonia in intensive care units: a prospective study. *Ann Clin Microbiol Antimicrob* 2004;3:17.
- Nseir S, Di Pompeo C, Jozefowicz E et al. Relationship between tracheotomy and ventilator-associated pneumonia: a case control study. *Eur Respir J* 2007;30:314-20.
- Veelo DP, Bulut T, Dongelmans DA et al. The incidence and microbial spectrum of ventilator-associated pneumonia after tracheotomy in a selective decontamination of the digestive tract-setting. *J Infect* 2008;56:20-6.
- Bornstain C, Azoulay E, De Lassence A et al. Sedation, sucralfate, and antibiotic use are potential means for protection against early-onset ventilator-associated pneumonia. *Clin Infect Dis* 2004;38:1401-8.
- Rello J, Diaz E, Roque M et al. Risk factors for developing pneumonia within 48 hours of intubation. *Am J Respir Crit Care Med* 1999;159:1742-6.
- Cook DJ, Walter SD, Cook RJ et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. *Ann Intern Med* 1998;129:433-440.
- Cavalcanti M, Valencia M, Torres M. Respiratory nosocomial infections in the medical intensive care unit. *Microbes Infect* 2005;7:292-301.
- Georges H, Leroy O, Guery B et al. Predisposing factors for nosocomial pneumonia in patients receiving mechanical ventilation and requiring tracheotomy. *Chest* 2000;118:767-74.
- Diaz E, Rodríguez AH, Rello J. Ventilator-associated pneumonia: issues related to the artificial airway. *Respir Care* 2005;50:900-6.
- Möller MG, Slaikeu JD, Bonelli P et al. Early tracheostomy versus late tracheostomy in the surgical intensive care unit. *Am J Surg* 2005;189:293-6.
- Shan L, Hao P, Xu F et al. Benefits of early tracheotomy: a meta-analysis based on 6 observational studies. *Respir Care* 2013;58:1856-62.
- Eid RC, Domingues F, Silva Barreto JK et al. Successful prevention of tracheostomy associated pneumonia in step-down units. *Am J Infect Control* 2011;39:500-5.
- Marra AR, Cal RGR, Silva CV et al. Successful prevention of ventilator-associated pneumonia in an intensive care setting. *Am J Infect Control* 2009;37:619-25.