The pathological oral cavity as a preventable source of postoperative pneumonia in thoracic surgery: a prospective observational study

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Background: Pneumonia after thoracic surgery considerably contributes to perioperative morbidity and mortality. So far, the forced expiratory volume in one second and diffusing capacity of the lungs for carbon dioxide are the most common validated prognosticators to estimate individual risk. Beyond functional parameters, modifiable risk factors for respiratory complications like pneumonia are poorly investigated in a prospective way. Thus, we aimed to assess the impact of oral health status in patients undergoing thoracic surgery and its correlation to perioperative outcomes.

Methods: A prospective observational study included adult patients undergoing elective thoracic surgery from October 2, 2018 to April 29, 2020. The day before surgery, patients were examined by a dentist. Oral health status (caries, periodontal disease, tooth loss, and regular dental visits) was correlated with perioperative outcomes.

Results: During the study period, 230 consecutive patients were included. Oral health status was poor in the study population. Postoperative complications were associated with active caries [odds ratio (OR) 2.5, $P<0.03$]. Patients with frequent dental visits and treated teeth had a lower risk for postoperative complications compared with patients without regular visits (OR 0.3, $P<0.02$). Patients with a high burden of caries had a significantly increased risk for pneumonia (OR 7.9, $P<0.002$). The forced expiratory volume in one second was a significant prognosticator for postoperative complications; however, no association between the forced expiratory volume in one second and oral health parameters was observed.

Conclusions: A pathological oral health status is a modifiable factor predicting postoperative complications and pneumonia. A prospective randomized interventional study is warranted to clarify whether an improvement in oral health status can lead to a reduction of perioperative risk.

Keywords: Tooth decay; enhanced recovery after surgery (ERAS); early recovery; oral health; caries; periodontal disease; complication

Introduction

Perioperative management in thoracic surgery is highly standardised, and with minimally invasive resections, the rate of postoperative complications in routine operations continually decreases. However, thoracic surgeons are confronted with an increasingly older collective of patients with multiple comorbidities. In the last decades, several developments like minimally-invasive approaches and enhanced recovery after surgery (ERAS) contributed to the safety profile and are of particular benefit in older patients (1). Despite all improvements, serious postoperative complications still occur (2,3). One of the most frequent severe postoperative complications is postoperative pneumonia. Although there were several attempts to minimize the risk for postoperative pneumonia, little is known about the exact origin or whether there are avoidable factors. One possible source for bacteria entry may be the oral cavity. During the staging period (e.g., via bronchoscopy), and later during intubation, bacteria may spread from the dental biofilm into the lungs. We hypothesized that the oral cavity is a source for postoperative pneumonia. Therefore, we designed a prospective observational study to analyze the link between the health status of the oral cavity and postoperative outcomes, especially postoperative pneumonia. We present the following article in accordance with the STROBE reporting checklist (4) (available at https://jtd.amegroups. com/article/view/10.21037/jtd-21-1178/rc).

Methods

We conducted a prospective observational study, which was approved by the Ethics Committee at the Medical Faculty of the University Essen (17-7822-BO). The study is registered in the German clinical trial registry (DRKS00017762), which is a WHO-recognized primary registry for Germany. All patients signed written informed consent to be eligible for study participation. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Study design

The study was designed as an investigator-initiated, prospective, single-center study to analyze the link between the occurrence of postoperative respiratory complications and the health status of the oral cavity.

Routine management

All patients underwent thoracic surgery in our department between 10/02/18 and 04/29/20. Inclusion and exclusion criteria are shown in *Table 1*. Data on demographics, preexisting conditions, and postoperative complications were recorded prospectively. We measured preoperative height and weight, which were used to calculate body mass index (BMI). All patients received a twelve-channel electrocardiogram, blood gas analysis, and blood analysis at a minimum. In cases of planned lung resection, patients also underwent functional evaluation according to the current guidelines of the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS) (5). In cases of proven or suspected lung cancer, patients were staged according to the current guidelines of ESTS and the European Society for Medical Oncology (ESMO). In these cases, patients received Fluoro-2-deoxy-D-glucose (FDG)-positron emission tomography (PET), computed tomography, brain imaging [magnetic resonance imaging (MRI) or contrast-enhanced computed tomography (CE-CT)], and if necessary, endobronchial ultrasound transbronchial needle aspirations (EBUS-TBNA) for invasive mediastinal staging. Patients were administered 1g intravenous ampicillin at the beginning of the operation. In case of lung resection, the administration was extended to the third postoperative day. 4 g/0.5 g Piperacillin/ Tazobactam was given to patients after neoadjuvant treatment. Postoperative complications and 30-day mortality were prospectively recorded.

Examination of oral cavity/dental examination

All patients who gave informed consent after screening eligibility for participation in the study were examined by an experienced dentist one day prior to surgery. The dentist was blinded to the pulmonary function testing. We evaluated the following conditions: dental caries, periodontal disease, missing teeth, teeth treated by a dentist, and undiagnosed swallowing disorders leading to an increased risk of aspiration. The health status of the oral cavity was assessed visually by using a mirror. We focused on possible sources causing postoperative pneumonia or triggering other inflammatory based events. Therefore, we were interested in the current and past caries burden. A subgroup of patients with a high caries burden (more than ten teeth with active caries) was identified based on the adapted risk model of Terpenning *et al.* (6). We recorded

Table 1 Inclusion and exclusion criteria

Inclusion	Exclusion
Elective thoracic surgical intervention	Older than 99 years
Informed consent	Pneumonia
Older than 18 years	Acute systemic infection
	Immunosuppression

Table 2 Patient characteristics

Variables	Cohort studied (N=230)
Female/male	102 (44%)/128 (56%)
Median age (years)	64 (range, 16–89)
Median FEV1 (range)	71% predicted (range, 18% to 123%)
Median BMI (kg/m^2)	25 (range, 17 to 55)
Median WBC (cells/µL)	7,600 (range, 800 to 20,000)
Median CRP (mg/dL)	0.7 (range, 0 to 29)
Median albumin (g/dL)	4.3 (range, 2.5 to 5.4)
Median creatinine (mg/dL)	0.8 (range, 0.4 to 2.4)
Smoking status	53% (N=122) ex-smoker[a]
	33% (N=77) smoker
	14% (N=31) never smoker

[a], no nicotine abuse for at least six months; FEV1, forced expiratory volume in one second; BMI, body mass index; WBC, white blood cells; CRP, C reactive protein.

active caries and the number of affected teeth. We also investigated whether periodontal disease was present in the oral cavity. Active periodontal disease, lost teeth and clinical signs of acute infection were also recorded. We also investigated if patients had regular dental visits and if there were (un-)treated teeth. Finally, we also investigated the swallowing function/undiscovered signs of Dysphagia and/or tendency for aspiration by having patients take a sip of water.

Definition of common perioperative complications and mortality

We defined perioperative mortality as death for any reason in a period of 30 days starting from the first day after operation. A postoperative complication was defined as any deviation from the normal postoperative course (7). Prolonged air leak was defined according to the definition of the ESTS as an air leak lasting longer than five days after surgery (8). Pneumonia was defined by the definition of Centers for Disease Control and Prevention criteria for nosocomial pneumonia (9). Pleural empyema was defined by purulent pleural effusion with or without detection of bacteria. For respiratory failure the definition of the ERS was used (10). The classification of Clavien-Dindo was used to grade complications (7).

Statistical analysis

Statistical analysis was conducted by using MedCalc software Version 11.6.1.0 (MedCalc software, Broekstraat 52, 9030 Mariakerke, Belgium). Statistical advice was provided by the Institute of Medical Informatics, Biometry and Epidemiology, University Medicine Essen.

The parameters of oral health and surgical outcome were analyzed by crosstabs and the Fischer's exact test. The association between patient characteristics and surgical outcome was analyzed by logistic regression. The difference between different groups or clinical parameters was analyzed by the T-test or Mann-Whitney test. Confounding factors were tested by the Cochran-Mantel-Haenszel test. The Breslow-Day-Tarone test was performed to test homogeneity of the odds ratios (OR). A P value <0.05 was considered significant. Figures were given as bars or dots.

Results

Characteristics of the study cohort

We included 230 patients [128 male (56%) and 102 female (44%)] in our study. All patient characteristics are shown in *Table 2*. The median age was 64 years (range 16 to 89 years). The study population consisted of 53% (N=122) ex-smokers (>6 months of nicotine abstinence), 33% (N=77) active smokers, and 14% (N=31) never-smokers. The median BMI was 25 kg/m^2 (range, 17 to 55 kg/m^2). The median preoperative serum CRP level was 0.7 mg/dl (range, 0 to 29 mg/dL). The median preoperative creatinine serum level was 0.8 mg/dL (range, 0.4 to 2.4 mg/dL), and the median preoperative white blood cell count (WBC) was 7,600 cells/µL (range, 800 to 20,000 cells/µL). The median preoperative serum albumin level was 4.3 g/dL (range, 2.5 to 5.4 g/dL). Preoperative lung functional assessments revealed a predicted median forced expiratory volume in one second (FEV1) of 71% (range, 18% to 123%).

Table 3 Characteristics of surgical interventions

Variables	N (total N=230)
Indication for surgery	
NSCLC	122
Metastasis	33
Pleural effusion	25
Benign nodule	20
Pneumothorax/Bulla	5
Tracheal pathology	4
Mediastinal lymphadenopathy	6
Mesothelioma	3
Adenoidcystic carcinoma	1
Port-catheter implantation for chemotherapy	4
Chest wall tumour	2
Chronic empyema	5
Type of surgical intervention	
Lobectomy	93
Extended lobectomy (with chest wall)	7
Wedge resection	27
Metastasectomy	22
Bilobectomy	4
Pneumonectomy	5
Sleeve lobectomy	8
Airway sleeve	1
Tracheal resection	4
Operation of the chest wall	5
Pneumothorax surgery/Bulla resection	5
Port-catheter implantation	4
LVRS	1
EPP or eP/D	3
Empyemectomy	5
Right/left side/both*	115/89/16
Approach	
Thoracotomy	119
RATS/VATS	101
Other	10

*, mediastinoscopy and cervical tracheal resection was not assigned to a side (N=10). NSCLC, non-small cell lung cancer; LVRS, lung volume reduction surgery; EPP, extrapleural pleuropneumonectomy; eP/D, extended pleurectomy/decortication; RATS, robotic-assisted thoracic surgery; VATS, video-assisted thoracic surgery.

Characteristics of surgical outcomes

The indication for curative intent surgery was lung cancer in 122 patients. Other indications for surgery were listed in *Table 3*.

We performed in 53% (N=123) patients a thoracotomy and in 47% (N=107) a minimal invasive approach. In total we performed 93 lobectomies, seven extended lobectomies (including resection of chest wall or vena cava), four bilobectomies five pneumonectomies, eight sleeve lobectomies and one lung sparing sleeve of the main bronchus. We also performed 49 atypical resections, four tracheal resections, five operations of the chest wall and in five times an operation for pneumothorax/Bulla. In 29 patients, we performed a minor surgery. In one case, we performed a lung volume reduction surgery (LVRS). In eight cases, we performed surgery for mesothelioma or other pleural disease.

There were no intraoperative complications and the 30-day mortality rate was 0% (*Table 4*). The rate of postoperative complications was 17% (N=35). Postoperative pneumonia occurred in 4.3% (N=10) of cases. In two cases of pneumonia, sampling of tracheal aspirates was done and in both, *Pseudomonas aeruginosa* was detected. The most common complication was prolonged air leak (>5th day after operation) with 6.1% (N=14). Other rare complications included the following: pleural effusion and reinsertion of a chest drain 2.2% (N=5), hematothorax 1.3% (N=3), postoperative empyema 1.3% (N=3), and chylothorax, renal failure, and wound infection, each 0.4% (N=1).

Health status of oral cavities

Only 38.3% (N=88) of patients attended regular dental visits and had clinical evidence of frequently treated teeth (*Table 5*). The majority of patients, 90% (N=208), had lost a minimum of one tooth, and only 10% (N=22) of patients had a complete set of teeth. A high proportion of patients [61.7% (N=142)] had active caries, and only 38.3% (N=88) of patients were free of caries. Only 17.4% (N=40) of patients had no sign of periodontal disease. Progressive/aggressive periodontal disease were detected in 42.6% (N=98) of patients, and 40% (N=92) of patients had chronic periodontal disease. In two patients, an undiagnosed tendency for aspiration with signs of dysphagia was noticed.

Patients with frequent dental visits and treated teeth had a lower risk for postoperative complications compared with patients without regular visits (OR 0.3,

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Table 4 Characteristics of complications

Variables	N (total N=230)
Intraoperative complications	None
Postoperative complications	
Prolonged air leak	14
Postoperative pneumonia	10
Collection of pleural effusion*	5
Hematothorax	3
Chylothorax	1
Wound infection	1
Renal failure	1
30-day mortality	0
Classification of Clavien-Dindo	
I	15
II	11
IIIa	5
IIIb	3
IVa	1

*, with reinsertion of a chest drain after removal of the intraoperative chest drain.

Table 5 Health status of oral cavities in the study population

Variables	N (total N=230)
Regular visits to the dentist/clinical evidence of frequently treated teeth	
Yes	88 (38.3%)
No	142 (61.7%)
Tooth lost	
Yes	208 (90%)
No	22 (10%)
Caries	
Yes	142 (61.7%)
No	88 (38.3%)
Peridontal disease	
Yes	40 (17.4%)
No	192 (82.6%)

P<0.02) (*Figure 1A*). Patients with active caries had a considerably elevated risk for postoperative complications (OR 2.5, P<0.03) (*Figure 1B*). Periodontal disease did not significantly elevate the risk for postoperative complications (OR 2.1, P=0.2) (*Table 6, Figure 1C*).

We also investigated if the risk for postoperative pneumonia was elevated for patients who regularly visited their dentist and found a strong but statistically insignificant association (OR 5.8, P=0.09). In addition, we also found no significant association between patients with active caries and postoperative pneumonia (OR 2.5, P=0.2) (*Figure 2A*).

We further analyzed the association of postoperative pneumonia in a subgroup of patients with a very high burden of caries (>ten teeth with active caries) and found a high level of association (OR 7.9, P<0.002) (*Figure 2B*).

Additionally, a logistic regression analysis was performed to evaluate whether the percent predicted FEV1, albumin, creatinine, CRP, WBC, or BMI were associated with postoperative complications (*Table 7*). Only the predicted FEV1 percent was significantly associated with postoperative complications (OR 0.9, P<0.02). Median percent predicted FEV1 values did not significantly differ in patients with active caries compared to those without (71%, range 18% to 108% *vs.* 70%, range 30% to 123%; P=0.4) and was not a confounding factor for caries in the Cochran-Mantel-Haenszel test for postoperative complications or postoperative pneumonia (*Figure 3*).

Discussion

Despite all the advances that have been made over the last decades in the field of thoracic surgery, pneumonia, respiratory insufficiency, and other postoperative complications associated with inflammatory reactions are still a relevant problem in daily practice. Several attempts have been made in the past to identify risk factors for postoperative complications. Pulmonary function testing (and in particular, percent predicted FEV1) is still one of the best evaluated and strongest predictors for the occurrence of postoperative complications (11-13).

However, functional lung testing alone is not sufficient to identify all patients who are at increased risk of developing postoperative complications, and a broad range of publications deal with other predicting factors or risk
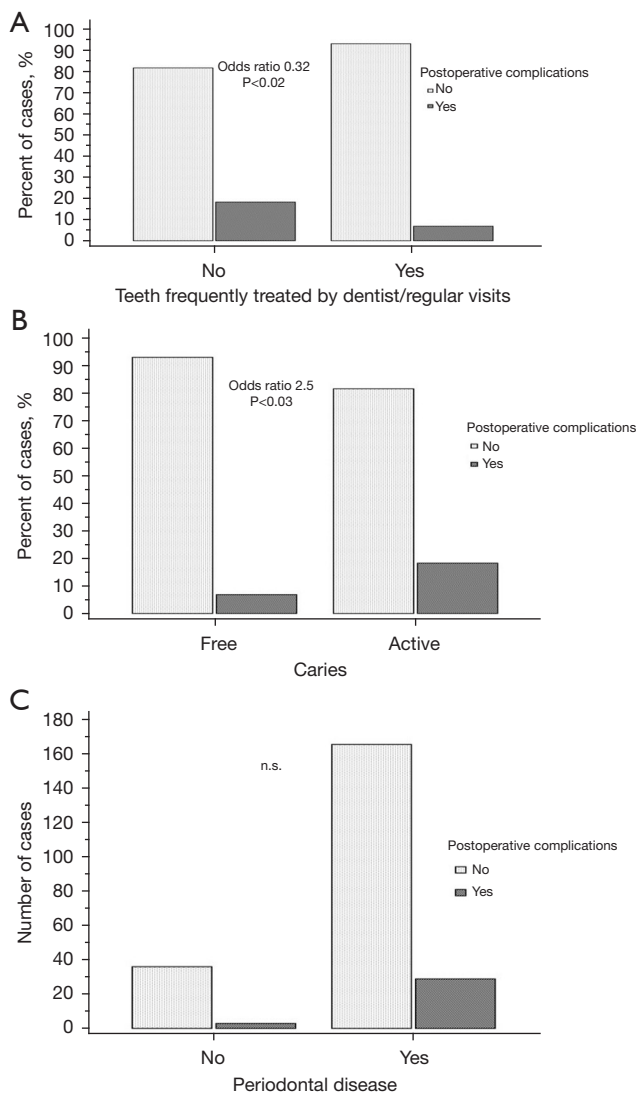
Figure 1 Oral health status is correlated with postoperative outcome. (A) Patients who regularly visit their dentist had a significantly lower risk for postoperative complications (OR 0.32, P<0.02); (B) patients with active caries had a much higher risk for postoperative complications than patients without (OR 2.5, P<0.03); (C) in contrast to patients with caries, patients with periodontal disease did not have a significantly elevated risk for postoperative complications (OR 2.1, P=0.2). OR, odds ratio. n.s., not significant.

Table 6 Relative risk and odds ratios of different health parameters of oral cavities for postoperative pneumonia

| Variables	Odds ratio	95% CI	P value
Frequently dental visits	0.3	0.1 to 0.8	<0.02
Caries	2.5	1.1 to 6.2	<0.03
Periodontal disease	2.1	0.6 to 7.2	0.2

CI, confidence interval.
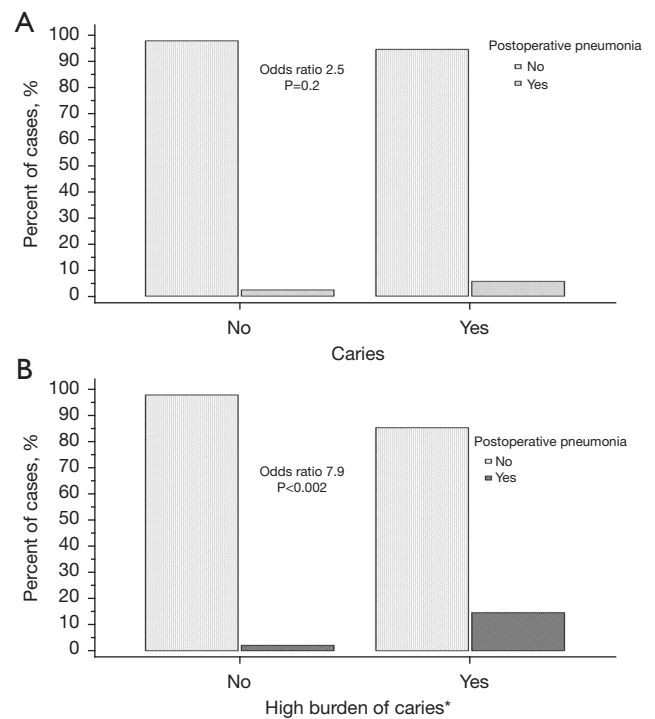
Figure 2 The existence of caries influences the rate of postoperative pneumonia. (A) There was a strong, but insignificant association between the presence of active caries and postoperative pneumonia (OR 2.5, P=0.2); (B) in a further subanalysis of patients with a high burden (*>10 teeth) of caries, we found a strong and significant association with postoperative pneumonia (OR 7.9, P<0.002). OR, odds ratio.

models (14,15). However, a clear limitation is that the majority of these factors may identify high risk patients but cannot be modified preoperatively (2). A heavy smoker with a lowered FEV1 requiring lung surgery for non-small cell lung cancer (NSCLC) may be preoperatively identified as a high-risk candidate but still needs treatment, and

the decision is frequently limited to performing surgery or choosing alternative options. Therefore, we aimed to identify factors that could be identified preoperatively and could also be modified. We hypothesized that the biofilm from the teeth and the oral cavity transfers bacteria via the trachea in the lungs and contributes to postoperative complications like pneumonia. With an increase of caries and poor dental hygiene, more bacteria are carried over,

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Table 7 Logistic regression of association with postoperative complications and different perioperative factors

Variables	Odds ratio	95% CI	Std. Error	P value
FEV1%	0.9	0.94 to 0.99	0.01	<0.02
BMI	0.9	0.8 to 1	0.04	0.7
Albumin	1	0.2 to 3	0.6	0.9
WBC	1	0.9 to 1.2	0.07	0.2
CRP	0.8	0.7 to 1	0.09	0.1
Creatinine	0.4	0.05 to 3.5	1	0.4

FEV1, forced expiratory volume in one second; BMI, body mass index; WBC, white blood cells; CRP, C reactive protein; CI, confidence interval; Std., standard.
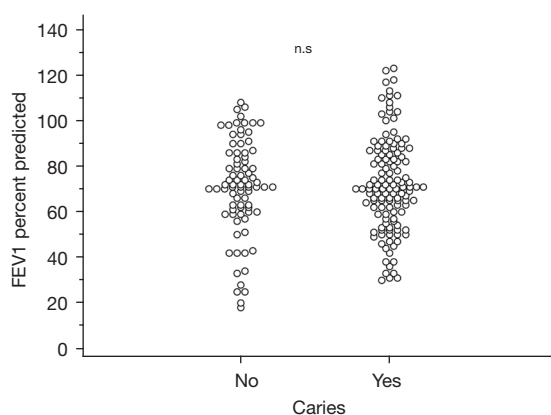
Figure 3 FEV1% predicted was equally distributed between patients with caries and those without. We found no significant imbalance (P=0.4). The same applies to patients with periodontal disease (data not shown). FEV1%, forced expiratory volume in one second percent predicted. n.s., not significant.

and the risk for postoperative complications increases (16-18). There is some evidence for this hypothesis: The direct anatomical connection between the oral cavity and the respiratory tract results in a topological continuity of the microbiome (19-21). Therefore, it is not uncommon to culture anaerobes originating from the periodontal pocket from pneumonia aspirates (22,23). Mehtonen *et al.* also demonstrated in a study with 1,592 young Finnish adults that pathological conditions of the oral cavity (like caries) in young and healthy populations are associated with a higher risk for lower respiratory tract infections (24).

In addition, there is a strong and significant link between pathological oral health and many other

pulmonary diseases (25). Chronic obstructive pulmonary disease (COPD), for example, is a widespread disease and common among patients undergoing thoracic surgery. There is robust evidence that COPD is linked to caries and periodontal disease (26). Both impact lung function and frequency of exacerbation (27,28).

In mechanically ventilated patients, protective reflexes like coughing and swallowing are suspended. Consecutive silent aspiration with oral pathogens results and may be a source of infection in the postoperative setting. In a study with 341 patients who had undergone an abdominal surgical procedure, Nishikawa *et al.* demonstrated that periodontal disease was a risk factor for infectious postoperative complications (29). The presence of periodontal disease was also associated with postoperative pneumonia in a study with patients who underwent brain surgery (30). Patients with esophageal cancer have a remarkably high risk for postoperative pneumonia, and therefore, prevention is highly relevant in the surgical management of these patients. In a prospective study from Japan, patients who underwent esophagectomy were investigated, and a positive preoperative dental plaque culture was highly predictive for the occurrence of postoperative pneumonia. Additionally there was a large overlap of pathogenic bacteria between the preoperatively sampled oral culture and the culture from the postoperative sputum sample in patients who suffered from pneumonia (31). In another large study with over 500 patients who underwent esophagectomy, Sato *et al.* demonstrated that preoperative dental examination and dental care dramatically reduced the risk for occurrence of postoperative pneumonia by 50 percent (32). Interestingly, even the rate of anastomotic leakage decreased, although it was not significant. There were several interventional studies trying to influence the rate of postoperative pneumonia by different preoperative interventions such as simple tooth brushing, professional dental care, or oral rinses with chlorhexidine (33-36). In all studies, a significant decrease in the incidence of postoperative pneumonia could be observed.

In this study, we aimed to identify the influence of pathological conditions in the oral cavity on the occurrence of postoperative pneumonia (and other inflammatory triggered complications) in patients who underwent thoracic surgery. This is the first study investigating the oral health care status in a large cohort undergoing thoracic surgery and correlating it with postoperative complications. In summary, the majority of patients had a poor oral health status. Only 39% attended regular visits to

the dentist, and caries and/or periodontal disease was often detected. Surprisingly, two patients had an undiagnosed tendency for aspiration that otherwise would not have been discovered. Patients who regularly visit the dentist had a significantly lower rate of complications. Caries was also significantly associated with a higher rate of complications, whereas the median percent predicted FEV1 was equally distributed in patients with and without caries (*Figure 3*). There was a strong but insignificant association between caries and postoperative pneumonia, which was most likely insignificant due to the group size. However, in a study with an eight-year observation period, in a large collective with more than 350 subjects, Terpenning *et al.* investigated risk factors for aspiration pneumonia and found that every decayed tooth, which is identical to dental caries, was associated with a higher risk for pneumonia (OR 1.2) (6). Therefore, we also investigated the group of patients with a high burden of caries (> ten decayed teeth) and found a high risk for postoperative pneumonia (OR 7.9, P<0.002).

We also performed a logistic regression, and neither BMI and albumin as indicators of nutritional status nor WBC, CRP, or creatinine were statistically significant for an elevated risk for postoperative complications. The only factor that was predictive for postoperative complications was percent predicted FEV1. However, this factor is, in most cases, hardly modifiable.

Limitations of the study

In this proof-of-concept study, we were able to demonstrate that the health status of the oral cavity has an influence on the postoperative outcome after thoracic surgery. This study is limited to a single European center with mainly Caucasian patients. Additionally, other factors and cofounders influencing the outcome cannot be ruled out. In the most interesting group of patients with anatomical resections, we could only detect a strong trend without significance due to the group size. Further investigations would be necessary to uncover an indirect influence.

Whether preoperative interventions impact the complications rates remains to be determined in a prospective, randomized trial.

Conclusions

Pathological conditions like caries and periodontal disease seem to have an influence on the rate of postoperative complications after thoracic surgery, especially pneumonia.

In contrast to FEV1, pathological conditions in the oral cavity are addressable. The reduction of the biofilm and of the load of bacterial contamination are feasible ways to reduce the rate of complications. An assessment of the oral microbiome and its association with respiratory infections after surgery are warranted.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1178/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1178/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1178/coif). KD reports receiving different fees for research/lectures/consulting, but all issues are not related to this study. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the University Essen (17-7822-BO). All patients signed written informed consent to be eligible for study participation.

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