


Lymph nodal recurrence in levels IV and V in oral squamous cell carcinoma after neck dissection

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Introduction

Oral squamous cell carcinoma (OSCC) is the most common cancer in the oral cavity.¹ The 5-year-survival rate is between 64.4% and 79.3%.² However, prognosis worsens if nodal metastases appear and the survival rate drops down to 50%.³ The guidelines recommend removal of level I–III lymph nodes,⁴ if necessary on both sides, as an elective neck dissection, even if the lymph nodes appear clinically inconspicuous. In case of suspicious lymph nodes, levels IV and V can be removed additionally, but no strict guidelines exist.⁵ The prevalence of lymph node metastases in levels IV and V seems to be around 3% and 1%, respectively, when elective neck dissection of levels I–III is performed.⁶ Most of the metastases appear in level II, and for this reason, the lymph nodes in this level are known as high-risk nodes.⁷

Complications after removal of levels IV and V can have a high impact on patients' quality of life. Nerve traction is the most common complication after performing neck dissection and can

Abstract

Background: The aim of the study was to determine the risk of lymph node recurrence in levels IV and V after tumour resection and neck dissection of level I–III and level I–V.

Methods: Data from 228 patients suffering from OSCC were analysed retrospectively. Patients with level I–III neck dissection were compared to those with level I–V neck dissection in terms of number and location of nodal recurrence.

The incidence of level IV–V recurrence in patients who had received level I–III neck dissection was compared with that of patients who had received level I–V neck dissection. The incidence of level IV–V recurrence was also compared between patients with pN0 and pN+ necks.

Results: Overall, 19 patients developed metastases. Only in two cases appeared nodal recurrence in levels IV or V. There was no statistically significant difference between both groups.

Conclusions: Neck dissection of levels I–III seems to be sufficient treatment in cases of unsuspected lymph nodes in levels IV and V, even in cases of positive nodes in levels I–III if adjuvant radiation therapy is applied. However, 5-year-disease free survival rate is lower in patients with nodal metastases in levels IV and V than in patients with metastases located in levels I–III.

severely detract the quality of life in patients. Especially the accessory nerve is endangered if level V is removed.⁸ Even if the nerve is not damaged during surgery, patients can suffer from shoulder pain and be limited in their movements when lifting the arm and shoulder because side branches can be injured during surgery.^{9–11} Furthermore, the thoracic duct or right lymphatic duct can be injured during level IV removal resulting in chyle leakage. A high volume of chyle leakage can be a potentially lethal complication after neck dissection.¹¹

The aim of this study, which includes 228 patients treated with resection of OSCC and primary neck dissection, was to analyse the lymph node recurrence in levels IV and V after previous neck dissection in levels I–III and levels IV and V.

Material and methods

The study was conducted in accordance with the Declaration of Helsinki, and approved by the institutional Ethics Committee of the

Table 1 Preoperative staging

Number of patients	Staging after the UICC 2017
99	T1N0M0
56	T2N0M0
13	T3N0M0
1	T1N1M0
1	T1N2bM0
3	T2N1M0
1	T2N2aM0
4	T2N2bM0
3	T2N2cM0
4	T3N1M0
2	T3N2aM0
30	T4aN0M0
3	T4aN1M0
4	T4aN2M0
1	T4aN3M0
1	T4bN3 M0

University Hospital of Munich, Germany (Munich, Germany; 20-1096, 4 January 2021).

This study includes 252 patients who underwent surgical resection of OSCC and neck dissection between 2013 and 2019.

Following parameters were documented and analysed: localization of the tumour, staging (using the UICC system), grading, perineural invasion, tumour thickness and diameter, bone invasion, surgical margins, number and levels of resected lymph nodes, number of positive lymph nodes, localization of positive lymph nodes, the diameter of metastases and localisation of lymph nodal recurrence.

To avoid selection bias, all patients with immunosuppressive therapy were excluded. Patients who underwent chemotherapy after

primary surgery were also excluded. A total of 24 patients were excluded, resulting in a total of 228 patients enrolled in the study. One hundred and thirty-nine patients were male and 89 female. The average age was 64.9 (ranging from 30 to 93 years).

Patients with level I–III neck dissection (group 1) were compared to those with level I–V neck dissection (group 2) in terms of the number and location of nodal recurrence. In each group, the postoperative lymph node status after primary neck dissection was considered. Subgroups of patients with involved lymph nodes (N+) after primary neck dissection and patients with tumour-free lymph nodes (N0) were determined and compared.

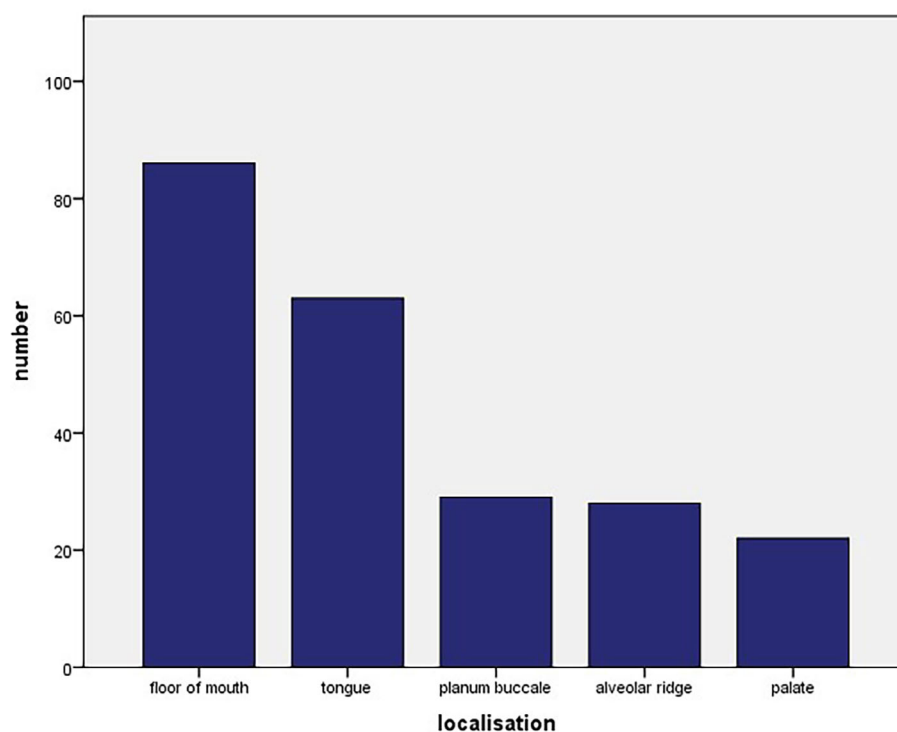
Statistical analysis

We used Fisher's exact test to compare the incidence of level IV–V recurrence between patients who received level I–III neck dissection and those with level I–V neck dissection.

Fisher's exact test was also implemented to search for significant differences regarding recurrence in levels IV–V between patients with a pN0 and those with a pN+ nodal status after primary level I–III neck dissection.

Results

Overall, 228 patients suffering from OSCC were included in this study. Data regarding the preoperative tumour staging is shown in Table 1. The median tumour diameter for all patients was 24.12 mm (range from 3 to 97 mm). The median depth of invasion for all patients was 8.23 mm (range from 1 to 35 mm). Figure 1 gives an overview of tumour localisations.

Fig. 1. Localisation of primary tumour site.

On average, 21.7 lymph nodes were resected during primary neck dissection (ranging from 8 to 64). Altogether 75 patients (32.9%) suffered from histologically proven lymph nodal metastasis after primary neck dissection. Overall, 19 patients (7.4%) had a recurrence in lymph nodes during the follow-up. The average follow-up-time amounted to 5.3 years. All patients underwent preoperative staging with computed tomography of the head and neck. Forty-seven patients (29.7%) with postoperative N0 status had suspicious lymph nodes in preoperative computed tomography. In 60 patients (85.7%) with N+ status after primary neck dissection, suspicious lymph nodes have been detected in preoperative computed tomography.

In 10 cases (4.3%) the resection margins were involved and a secondary resection was performed to achieve healthy margins according to the guidelines. Perineural invasion was found in 28 patients (7.9%), lymphovascular invasion in 41 cases (18%).

Nineteen of the 228 (8.3%) patients suffered from lymph nodal recurrence during follow-up. The median tumour diameter in this group of patients was 27.47 mm (range from 8 to 97 mm). The median depth of invasion amounted to 8.5 mm (4–12 mm). R1-resection of the primary tumour was found in 4 cases for this group of patients. Eight patients with lymph nodal recurrence had negative lymph nodes (N0) in primary neck dissection, 11 had primary N+ neck dissection. Six of the 19 patients with lymph nodal recurrence were radiologically inconspicuous concerning their primary lymph nodal staging, 8 of them had suspicious lymph nodes in the primary staging in level IB, 2 in level IA, 1 in level I–III,

I in level III and one in level I–III on both sides. Table 2 gives an overview of all 19 patients suffering from lymph nodal recurrence considering age, staging, localization, grading, tumour diameter, extent of neck dissection and localization of lymph nodal recurrence.

In 17 cases (7.5%), lymph nodal recurrence appeared again in level I–III. Four patients with recurrence in levels I–III had primary level I–V neck dissection and all 4 had positive lymph nodes after primary neck dissection. Recurrence in level I–III appeared in 13 patients (5.7%) who underwent primary level I–III neck dissection. Six of them were in the N+ subgroup and 7 in the N0 subgroup.

In 2 cases (0.9%) patients developed recurrence of metastases in levels IV and V. Both patients had previous Level I–III neck dissection. One of the patients belonged to the N+ subgroup and the other one to the N0 subgroup. In one patient, recurrence occurred in both levels IV and V. In the other patient, recurrence occurred only in level V. Primary cancer was located on the lateral tongue in both cases. Figs. 2 and 3 give an overview of all patients, levels of performed neck dissection and recurrence.

Overall, 72 (31.6%) patients received adjuvant radiation after surgical treatment. Seventeen of 32 patients (53.1%) who had a neck dissection in levels I–V received radiotherapy.

Fifty-five of 196 patients (28.1%) who had neck dissection in levels I–III received adjuvant radiotherapy. Seven of the 19 patients (36.8%) suffering from lymph nodal recurrence received adjuvant radiation. In further 7 cases, radiotherapy was recommended from

Table 2 Data of all patients suffering from lymph nodal recurrence

Age	Neck dissection	Tumour diameter	Localisation R = Right L = Left	grading	TNM (after primary resection)	Localisation of metastases in primary surgery	Localisation of lymph nodal recurrence	Survival in years
82	I–IV both sides	22 mm	Floor of mouth R	2	T4aN3bM0	Level I left side	Level II left side	4
60	I–V both sides	20 mm	Soft palate L	2	T2N3bM0	Level I–II left side	Level III left side	2
73	I–III right side and I–II left side	38mm	Hard palate L	2	T2N2bM0	Level IB right side, II–III left side	Level II left side	1
81	I–III bothsides	15 mm	Tongue L	3	T1N1M0	I–II rightside	Level III	1
72	I–III both sides	35 mm	Floor of mouth R	1	T4aN0M0	No metastases	Level I–III right side	2
75	I–III both sides	36 mm	Tongue R	1	T2N0M0	No metastases	Level III left side	1
77	I–III both sides	18 mm	Tongue R	2	T1N0M0	Level Ib right side	Level IV and V right side	5
86	I–III both sides	22 mm	Alveolar ridge L	2	T2N1M0	Level Ib left side	Level III left side	2
65	I–III both sides	22 mm	Tongue R	2	T2N0M0	No metastases	Level II right side	1
66	I–III both sides	25 mm	Tongue R	3	T2N1M0	Level Ib right side	Level V right side	2
84	I–III both sides	19 mm	Planum buccale R	3	T1N1M0	Level Ib right side	Level III right side	3
57	I–III both sides	37 mm	Tongue L	2	T1N2M0	Level II right side	Level II–III right side	2
93	I–III both sides	8 mm	Planum buccale L	2	T1N2bM0	Level I–b and III left side	Level II right side	alive
75	I–III both sides	47 mm	Floor of mouth R	2	T3N2cM0	Level II–III left side, level II right side	Level III left side	2
68	I–III both sides	20 mm	Lower lip L	2	T1N0M0	No metastases	Level Ib right side	1
58	I–III both sides	17 mm	Floor of mouth R	3	T1N0M0	No metastases	Level II right side	alive
65	I–III both sides	19 mm	Hard palate R	2	T1N0M0	No metastases	Level I right side	3
72	I–III both sides	8 mm	Alveolar ridge L	2	T1N0M0	No metastases	Level II left side	alive
61	I–III right side, I–IV left side	97 mm	Floor of mouth R	2	T3N3bM0	Level Ib left side	Level Ib left side	2

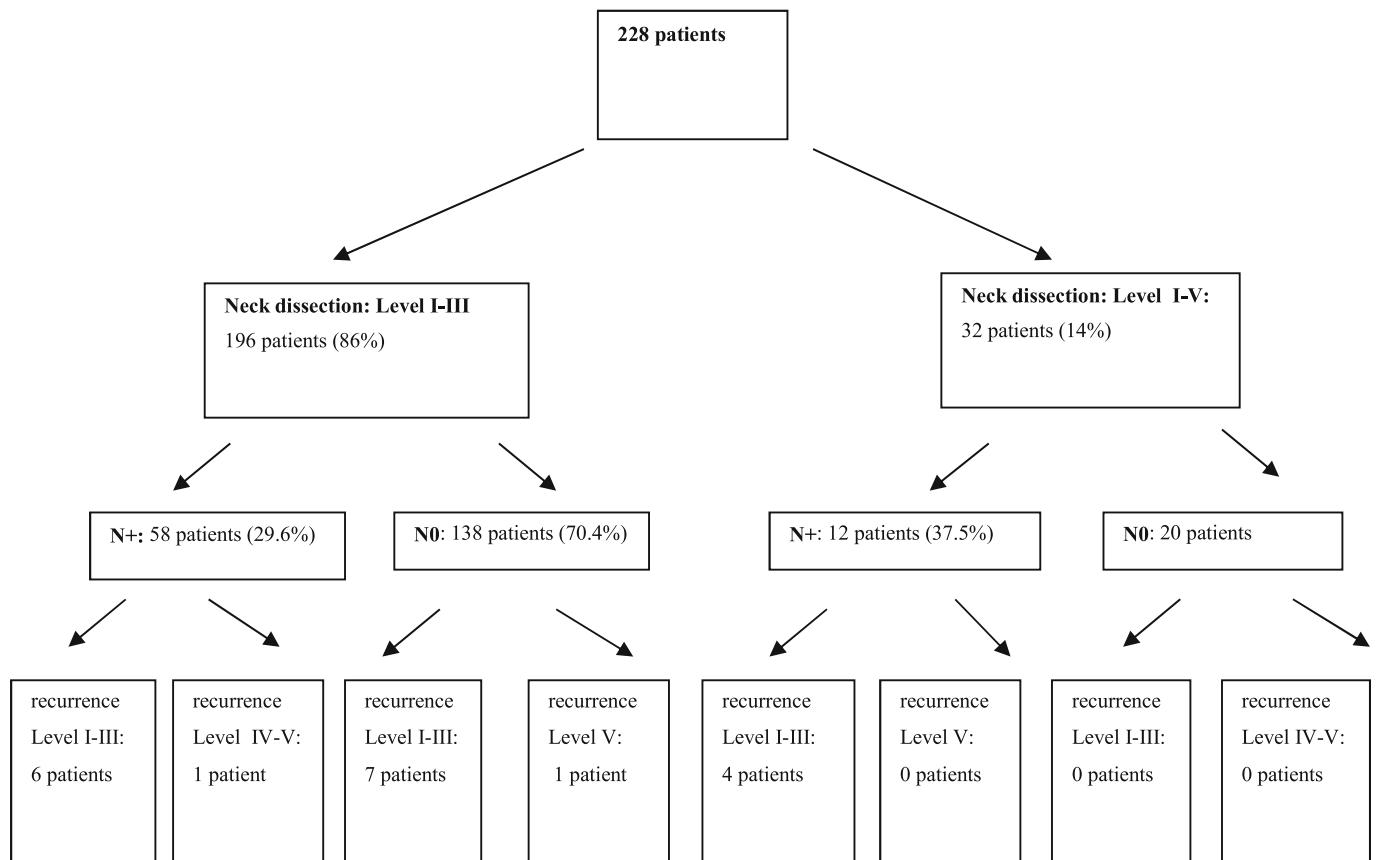
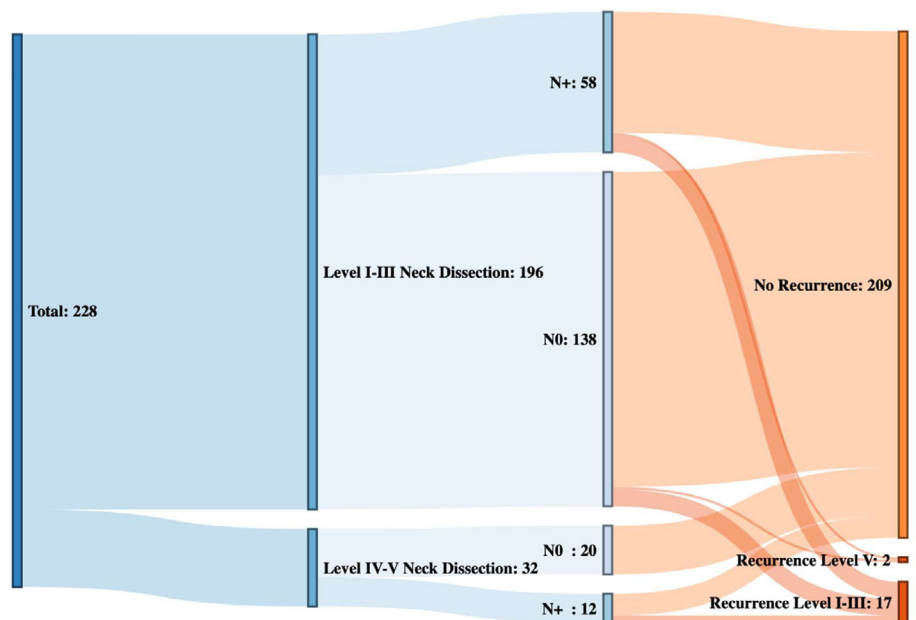


Fig. 2. Overview of neck dissection.

interdisciplinary tumour conference, but the patients refused further treatment. In our department radiation is recommended in patients with bone infiltration and T4 staged tumours receive irradiation as well as patients suffering from lymph nodal spreading or close

margins <5 mm. Also patient suffering from perineural invasion get the recommendation for irradiation. Of the 60 patients with N+ neck, 59 patients received adjuvant radiotherapy and one patient refused adjuvant radiotherapy. Both patients suffered from lymph

Fig. 3. Overview of all patients and metastases (Sanky blot).



nodal recurrence in levels IV and V did not receive adjuvant radiation after primary surgery. Neck dissection of levels IV and V and adjuvant radiation was performed after the diagnosis of lymph nodal recurrence in both cases. Prognosis in both cases was poor as both patients died 15 months and 13 months after diagnosis of lymph nodal recurrence.

Statistical analysis using Fisher's exact test revealed no statistical significance between patients who received level I–III neck dissection and those who had primary level I–V neck dissection concerning the appearance of level IV and V recurrence ($P = 0.566$). There was also no statistically significant difference between patients with negative lymph nodes after primary level I–III neck dissection and patients with positive lymph nodes after primary level I–III neck dissection in terms of level IV and V recurrence ($P = 0.552$).

Discussion

Nodal metastases from OSCC mainly occur in levels I to III. Lea *et al.* report that 85% of all metastases appear in level IIA.¹² Level IV is only involved in 3% of cases and level V in only 1%.¹³ If nodal metastases are present in Level I to III in the primary neck dissection, level IV can be involved in 7%–17% and Level V in only 0.6% of the patients.⁶

Hence, the question arises whether surgical resection of level IV and V is indicated in cases with clinical and radiological unsuspecting lymph nodes in level IV and V. Especially, given the fact that in cases of involved lymph nodes in level I to III, adjuvant radiation therapy is performed.¹⁴ In the present study, only 8.3% of all patients suffered from recurrent nodal metastases. Overall, 7.4% of the patients with OSCC presented with recurrence in level I–III and only 0.9% of all patients had a recurrence in level IV and or V.

A systematic review including 498 patients showed similar results with involvement of 2.8% of levels IV and V in lymph nodal recurrence.¹⁵ Therefore, the authors recommended neck dissection of levels I–III in cases without clinical or radiological suspicious lymph nodes in levels IV and V.

Complications after removal of lymph nodes in levels IV and V can have a high impact on patients' quality of life. Especially the accessory nerve is endangered, if level V is removed.¹⁶ Another study showed that 40.5% of all patients suffered from complications after neck dissection, with 10% of them having an injury of the spinal accessory nerve.¹⁷ Even if the nerve itself does not get any substantial damage during surgery, side branches can be injured and vascular supply may get lost.⁷ Patients report shoulder pain and limitation in certain movements. McGarvey *et al.* reviewed 59 patients after neck dissection and found an overall prevalence of accessory nerve shoulder dysfunction of 36.86%.¹⁸ A prospective quality of life study found postoperative radiotherapy and level V neck dissection to be predictors of poor shoulder function after 6–9 months. Outcomes in the level I–III neck dissection group were significantly better and recovering time was shorter at 3–6 months. The authors also reported neck irritation in addition to bad shoulder abduction as side effects.¹⁶

Furthermore, chyle leak can appear in case of level IV removal, and a high volume of chyle leakage is a potentially lethal complication after neck dissection.¹⁹ In cases of low flow fistulas, conservative treatment

such as fat-free diet, total parenteral nutrition and drainage is recommended. However, chyle leak is known to lead to prolonged hospitalization and, therefore, could delay adjuvant radiation therapy.²⁰

Byers *et al.* describe a risk of 3% for skip metastases in level IV.²¹ Especially the tongue as localisation of the primary tumour is reported to have a higher risk for metastases occurring in levels IV and V. In the present study, both patients with lymph nodal recurrence in levels IV and V had a tumour located on the tongue. However, skip metastasis did not occur, but neck dissection in level I–III has been performed before. In a study by Zhien *et al.*, including 637 patients, the authors stated that metastases in levels I–III were common, while metastases in levels IV and V were very rare. No skip metastases or recurrence in levels IV and V were found.²²

Adjuvant postoperative radiation reduces the risk of lymph nodal recurrence. A study by Kolli *et al.* reported a recurrence rate of 27% in the group of patients who received selective neck dissection alone, compared with a recurrence rate of 7% in patients who received postoperative radiotherapy after selective neck dissection.²³ In our study, only 36.8% of all patients suffering from lymph nodal recurrence received adjuvant radiation after primary surgery. The two patients suffered from recurrence in levels IV and V did not receive radiation after primary surgery, although the interdisciplinary tumour board recommended adjuvant radiation. Roy *et al.* show similar results.¹³ They report a low level of lymph nodal spreading in levels IIB, IV and V. Radiation could be an alternative to surgical treatment of levels IV and V.²⁴ Of course the higher number of irradiated patients in the I–V group could affect the recurrence rate. This is surely a weakness of this study and would be better to compare in a prospective study.

In the present study, there was no statistically significant difference between patients who received level I–V neck dissection and patients who received level I–III neck dissection in terms of level IV and V recurrent lymph nodes. Neither was there any statistically significant difference between patients who received level I–III neck dissection with postoperatively no positive nodes and patients who received level I–III neck dissection with postoperatively positive nodes in terms of level IV and V recurrent lymph nodes. Hence, the benefit of level IV and V neck dissection for patients with OSCC and no suspicious lymph nodes in levels IV and V is highly questionable. On the other hand, 5-year-disease free survival rate is lower in patients with nodal metastases in levels IV and V than in patients with metastases located in levels I or II.²⁵

Conclusion

The risk of nodal metastases in levels IV and V from OSCC is generally low. Selective neck dissection of levels I, II and III seems to be a sufficient treatment option in cases of clinically and radiologically unsuspecting lymph nodes in levels IV and V. Even in cases of positive nodes in levels I, II and III adjuvant radiation therapy without the removal of levels IV and V could be a sufficient treatment option. Still this decision should always be made individually in interdisciplinary cooperation with oncologists, pathologists, radiologists and surgeons in review of all patients' findings. However, five-year-disease free survival rate is lower in patients with nodal metastases in levels IV and V than in patients with metastases

located in levels I or II. Therefore, further prospective studies are necessary to determine which patients benefit from elective Level IV and V neck dissection.

Author contributions

Katharina Theresa Obermeier: Conceptualization; data curation; formal analysis; methodology; writing – original draft. **Paris Liokatis:** Conceptualization; data curation; supervision; writing – review and editing. **Selgai Haidari:** Investigation; methodology; writing – review and editing. **Tamara Katharina Kakoschke:** Methodology; writing – review and editing. **Moritz Kraus:** Formal analysis; software; validation; visualization. **Wenko Smolka:** Conceptualization; project administration; writing – original draft; writing – review and editing.

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Conflict of interest statement

None declared.

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