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Surgical site complications of post-chemoradiotherapy neck dissection: Urgent need for standard registration

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ABSTRACT

Nowadays, a substantial number of head and neck cancer patients are treated by organ-preserving chemoradiation (CRT), with a possible increased risk of complications after planned or salvage neck dissections. We try to determine the risk pattern of surgical site complications (SSC) post-CRT.

A systematic literature search (Medline, Embase, Scopus) was performed through November 4, 2019, for studies that describe *isolated* neck dissection in patients after primary CRT for head and neck malignancies. The analyzed outcomes were SSC and required operative interventions. The quality was assessed using ROBINS-I and results were reported according to the PRISMA Statement.

Eighteen studies were included with a total of 715 patients with 804 ND procedures.

Varying complication rates are seen from 3 to 29%, in combination with a large variety of definitions of complications. On a total of 117 SSC's, surgical site infection (N = 32), wound dehiscence (N = 23) and chyle leak (N = 18) were mostly seen. Thirty-one of these complications (26.5%) required operative intervention. Meta-analysis of potential causal factors was impossible due to the missing demographic information and the heterogeneity in studies and outcome data.

Post-CRT ND is characterized by a considerable risk of SSC, in a substantial percentage requiring operative re-intervention. However, the lack of dedicated studies and the lack of uniform complication registry make it difficult to interpret the precise risk and to predict risk factors. Therefore, a standardized way to report postoperative complications in the field of head and neck surgery is highly warranted.

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1. Introduction

Since the start in the mid '90s of the combined treatment protocols of radiotherapy with (concurrent) platinum-based chemotherapy in an organ sparing setting for the treatment of advanced stages of head and neck squamous cell carcinoma (HNSCC), more patients are primarily treated non-surgically [1,2]. Because metastases to the neck seemed to be less responsive than the primary tumor to chemoradiotherapy (CRT) [3,4], cervical lymph node dissection was usually planned afterwards for optimal regional control [5,6]. This 'second part' of the therapy evolved subsequently from a radical neck dissection to a (super) selective neck dissection, targeting only the persisting or suspicious positive lymph nodes [7,8]. The timing of this neck dissection also shifted from four weeks to eight weeks after completion of therapy, to fit the ideal surgical window between acute and chronic injury post-CRT [7]. However, the planned neck dissection is abandoned as part of a standard procedure [9]. Nowadays, evaluation of the neck after primary CRT by positron-emission tomography-computed tomography (PET-CT) 12 weeks post-treatment is propagated as an alternative followed by a *salvage* therapeutic neck dissection, if indicated [10,11].

Serious tissue alterations due to chemotherapy and radiotherapy, with an increased risk of acute and late postoperative complications, make post-CRT neck dissections more at risk of developing a complication [12].

One of the acute *surgical site complications* (SSC) is surgical site infection (SSI) due to barrier function loss of the frail skin, as short-term effect or due to late term fibrosis [13,14]. Also, CRT induced vascular damage can lead to necrosis or wound dehiscence, in severe cases with the exposure of underlying vascular structures.

Head and neck surgeons should be aware of this change in complication pattern and informed consent should address more specifically the expected risks of salvage neck surgery after CRT [15].

To gain more insight into the current status of postoperative complications of neck dissection in post-CRT, we set up a systematic review of publications referring to the surgical site complications of planned or salvage lymph node dissections. The publications should have a focus on surgery of the neck to avoid any influence from complications due to the surgery at the primary site.

Our main goal is to investigate whether this review can contribute to evidence-based patient counseling regarding the risk of surgical site complications after neck dissection post-CRT and to identify risk factors.

2. Methods

2.1. Search strategy and study selection

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed for this systematic review [16].

We performed searches in three databases, Medline (Ovid), Embase and Scopus (WS). The search was performed on November 4, 2019. We searched for keywords and equivalent words in title/abstract and translated the search terms according to the standards of each separate database.

Our search blocks consisted of a combination of four elements: head and neck neoplasms, postoperative complications, neck dissection and multimodality treatment (including salvage therapy and combined treatment with chemotherapy and radiotherapy). No restrictions were applied for date or study design. The full search strategies for each database can be found in Supplementary Table 1.

The resulting articles of these searches were exported to EndNote and directly deduplicated for removal of 343 double entries. This resulted in 677 unique records.

Subsequently, titles and abstracts – and if necessary full-text – were manually screened (RH) to include treatment with both radiation and chemotherapy, for primary head and neck cancer, with neck dissection (planned or salvage) afterwards. Articles regarding up-front neck dissection followed by chemoradiotherapy and primary tumors of the esophagus and thyroid were not selected. This resulted in 58 articles.

The following selection was made by consensus of two authors (RH, AB), based on full-text articles. The following *Inclusion Criteria* were used:

- Original research with own study data.
- Malignant neoplasms of the head and neck.
- Primarily treated by radiotherapy with chemotherapy.
- Secondary treatment with *isolated* neck dissection (i.e. no other salvage surgery in continuity for primary tumor recurrence).
- Distinguishing surgical wound complications.

To keep the study population homogeneous, *Exclusion Criteria* were as follows:

- Primary tumors primary concerning thyroid or esophagus.
- Treatment with radiotherapy combined with epidermal growth factor receptor (EGFR) therapy.
- Neck dissection in the same surgical field with more extensive surgery (e.g. in-continuity resection of primary tumor).
- Studies with less than ten patients treated by *isolated* neck dissection.

In thirteen studies, there was no use of original data or only a conference abstract published. Three studies formed a group of CRT also including EGFR therapy. One study used post-CRT patients to study a distinct surgical intervention. In fifteen studies, surgical complications could not clearly be attributed to the post-CRT neck dissection, since complications were not exclusively described for different patients groups. Eight studies included fewer than ten patients with isolated neck dissection post-CRT. The remaining eighteen articles met our inclusion criteria; see Fig. 1.

2.2. Data extraction

To systematically extract data of all full text articles, a template table was designed (RH, AB). General parameters like year of publication, sample size and study design were recorded. Special attention was paid to tables, figures and supplements, to extract the number of patients with planned or salvage *isolated* neck dissection after CRT and the number of neck dissections performed. If possible, types of neck dissections were distinguished: comprehensive (extended, radical and modified radical) and selective. The time interval between primary treatment and surgery was noted as well. Total numbers of wound complications were listed and categorized into operative intervention or not and into type of complications, including surgical site infection. In case of not-reported data or when data was unfit to trace back to solitary neck dissection, the field was left blank. Focusing on wound complications, facial and accessory nerve function were not recorded. Characteristics of radiotherapy (scheme and if possible mean dose on cervical lymph nodes) and chemotherapy (type and schedule with dose) were recorded as well.

Also patient characteristics were noted for further analysis to identify a possible predictive risk profile.

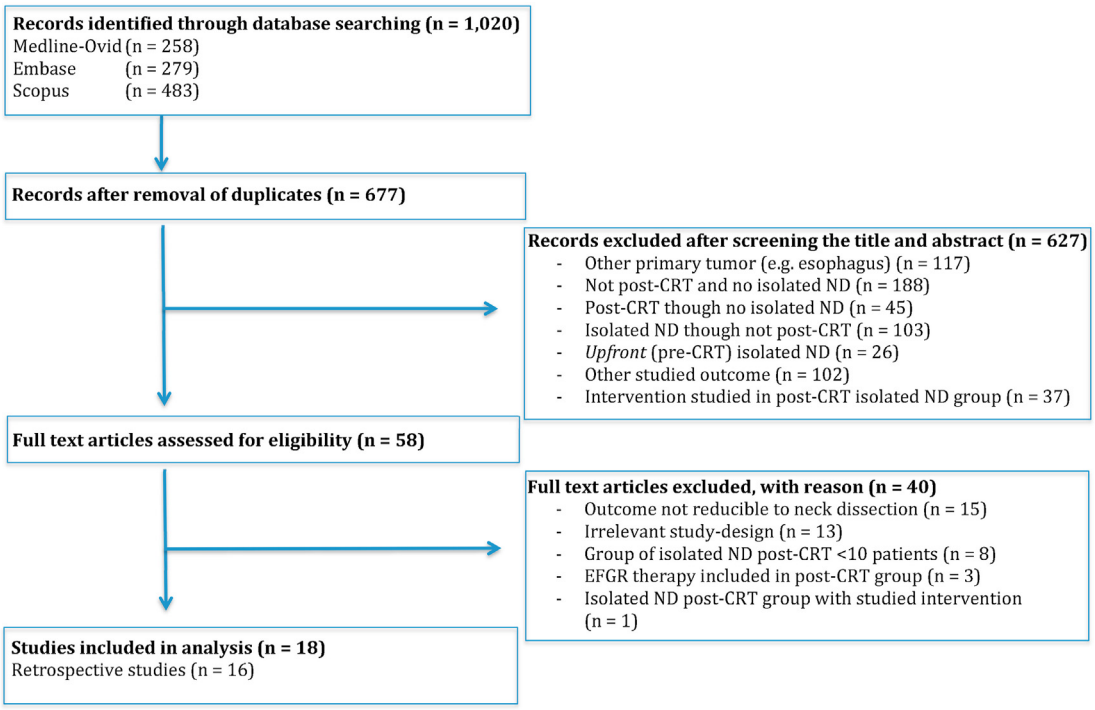

Fig. 1. Flowchart with identified, screened and included articles.

2.3. Risk of bias in individual studies

The Risk Of Bias In Nonrandomised Studies-of Interventions (ROBINS-I) tool was used to assess the risk of bias in individual studies (RH), Supplementary Table 2 [17]. The rankings in the seven separate domains are combined in an overall score for risk of bias. This score is a measure for the quality of the data and thereby for the reliability of recommendations based on this data.

3. Results

3.1. Study designs and characteristics

From 677 retrieved citations, 18 publications fulfilled the inclusion criteria (Fig. 1), with a total of 715 patients and 804 ND procedures.

Except for two publications [18,19] all studies used a retrospective design. Nine studies made use of a single group design, focusing only at post-CRT neck dissection [7,18,19–25]. The other studies consisted of multiple groups, looking also at e.g. primary site surgery or post-radiotherapy neck dissection. All studies demonstrated a serious risk of bias in more than one domain – at least for confounding and selection of participants – resulting in an overall serious risk of bias according to the ROBINS-I tool.

Sixteen studies mentioned complications (or morbidity/toxicity) in their abstract or study aim. The remaining two studies differed in purpose, with complications as an additional outcome [19,25]. Complications were graded into minor and major in eight publications [20,21,24,26–30]. Others generally categorized only in wound complications, [7,9,31,32]. Six studies made no differentiation at all [18,22,23,19,25,33]. Study characteristics and their definitions of complications are summarized in Table 1. Patient characteristics were scarcely described in the articles and therefore not listed in the table.

Seventeen articles that described their treatment protocol covered the period (1997 -2016) of evolution of cisplatin chemotherapy in combination with radiotherapy. Various schedules were used, both induction and concurrent, whether or not combined with other chemotherapeutic agents, Table 2. One study did not specifically mention which type of chemotherapy was used [31]. Radiotherapy protocols were described in all studies; each used daily fractions of 1.8–2.0 Gy, to a total dose to the involved cervical lymph nodes of 60 Gy [20,23], up to 72 Gy in grossly involved nodes [24].

Sixteen studies reported the time interval between completion of CRT and surgery, while two did not [28,31]. Intervals were based on either the time according to the protocol, or on actual median or mean values, together with the range. The interval of post-CRT neck dissection ranged from two weeks till 64.5 weeks.

Only four included articles specifically named the use of antibiotics or not. One study reported no use of antibiotics [32], the other three respectively during surgery till 24 h afterwards, for the duration of admission or a total of one week [7,26,28].

Table 3 shows a summary of the neck dissections performed. Ten studies included only planned procedures, four studies only salvage procedures and another four both. Well-defined comprehensive neck dissections were performed in 326 cases and selective neck dissections in 226. In ten publications it was not possible to categorize (all) the dissections accurately. In one study, an overview of resection per cervical lymph node level and non-lymphatic structure was made [22]. Though this could not be deduced to a specific type of neck dissection. If available, also the numbers of bilateral procedures were recorded, a specification of simultaneous or staged procedures was impossible.

3.2. Complications

Twelve studies differentiated between major, minor or wound complications. In all of these studies definitions of wound complications were different. In six studies no classification of

Table 1
Study characteristics.

Author	Year	Design	Classification	Complication definition
Newman [26]	1997	Retro	Major/minor	Major = operative intervention, ICU monitoring. Minor = non-operative, outpatient evaluation.
Lavertu [27]	1998	Retro	Major/minor	Major = fistula, operative intervention or ICU monitoring. Minor = non-operative.
Davidson [31]	1999	Retro	Wound/ systemic	Wound complication not specified.
Stenson [7]	2000	Retro	Wound	Wound complication not specified.
Grabenbauer [9]	2003	Retro	Wound	Wound complication not specified.
Proctor [32]	2004	Retro	Wound	Wound = infection (purulent drainage, dehiscence, fistula), severe edema, hemorrhage including carotid rupture.
Frank [20]	2005	Retro	Major	Major complication not specified.
Morgan [28]	2007	Retro	Major/minor	Major = pharyngocutaneous fistula and operative intervention. Minor = skin flap necrosis, seroma or wound infections.
Christopoulos [21]	2008	Retro	Major	Major complication not specified.
Nouraei [22]	2008	Retro	None	N/A
Bremke [18]	2009	Prosp	None	N/A
Hillel [23]	2009	Retro	None	N/A
Goguen [24]	2010	Retro	Major/minor	Major = operative intervention, re-admission, chyle leak. Minor = all other wound complications that necessitated outpatient treatment, i.e. minor wound infections and fluid collections, wound dehiscence and minor flap necrosis.
Pellini [29]	2013	Retro	Major/minor	Major = requiring surgical revision (massive hematoma, extended wound dehiscence, wide skin flap necrosis, and high flow chyle leak). Minor = requiring only local dressing and therapy and no further surgical procedure (slight hematoma, wound dehiscence, limited skin flap necrosis, seroma and facial swelling).
Suzuki [33]	2013	Retro	None	N/A
Pellini [19]	2014	Prosp	None	N/A
Miah [25]	2015	Retro	None	-
Taguchi [30]	2016	Retro	Major/minor	Major = required re-operation for wound trouble or significantly prolonged hospitalization. Minor = managed with local wound care or did not significantly prolong hospitalization.

Retro = retrospective, prosp = prospective. ICU = Intensive Care Unit. N/A = Not applicable.

Table 2
Characteristics of treatment.

Author	Chemotherapy	Planned therapeutic RT dose (Gy)	Interval range in weeks	Subsites	Antibiotics
Newman [26]	CisP, 5FU	66–75	2-4 (protocol)	OP, HP, LX	Yes, 24 h
Lavertu [27]	CisP, 5FU	68–72	Planned 6.8–8.4/salvage 18.3–64.5	OC, OP, HP, LX	-
Davidson [31]	-	Mean 66.4, SD 10.08	-	OC, NP, OP, HP, LX	-
Stenson [7]	Pac, 5FU/CisP, 5FU	66.5–75.5	5-17, mean 8.01	OC, NP, OP, HP, LX, UP, PT	Yes, admission
Grabenbauer [9]	CisP, 5FU	60–76, median 70	14-16, median 12	OC, OP, HP	-
Proctor [32]	CisP	63–70	8 (protocol)	OC, OP, HP, LX	None
Frank [20]	CisP	60	4-6 (protocol)	OC, OP, HP, LX	-
Morgan [28]	CisP, 5FU	59.4–72.5, mean 69.6	-	OC, NP, OP, HP, LX	Yes, 7 days
Christopoulos [21]	CisP/CarP, 5FU	70	6-8 (protocol)	OC, OP, HP, UP	-
Nouraei [22]	5FU, CisP/5FU, CarP/CisP	66	Mean 8.5, SD 3	OC, OP, HP, LX, UP	-
Bremke [18]	5FU, Mit/5FU, CisP	72	6-12, mean 9.3, SD 1.3	OP, HP	-
Hillel [23]	CisP, 5FU	60	6 3/7–21 4/7, median 10	OP	-
Goguen [24]	Carb, Pac/CisP	70–72	4-26, median 11	OC, OP, HP, LX, UP	-
Pellini [29]	CisP	70	12-14 (protocol)	-	-
Suzuki [33]	5FU, CisP/5FU, NedP	50.4–72.2, median 66.6	4-8 (protocol)	OP, HP	-
Pellini [19]	CisP	70	14.6–19.4, median, 16.4	OP	-
Miah [25]	CisP, 5FU	66	8-12 (protocol)	OP	-
Taguchi [30]	Doc, CisP, 5FU/CisP, 5FU, MTX/CarB, UFT/S1/ Doc	64–75.6	6-12 (protocol)	OP, HP, LX	-

SD = standard deviation. RT = radiotherapy. Gy = Gray.
CisP = cisplatin. CarP = carboplatin. NedP = nedaplatin. 5FU = 5-fluoruracil, Mit = mitomycin. Pac = placlitaxel. Doc = docetaxel. MTX = methotrexate. UFT = uracil/ tegafur. S-1 = tegafur/gimeracil/oteracil.
OC = oral cavity, OP = oropharynx, NP = nasopharynx, HP = hypopharynx, LX = larynx, PT = parotid, UP = unknown primary tumor. * Including 3 patients with other histologies (1 adenoid cystic carcinoma, 1 poorly differentiated mucoepidermoid carcinoma and 1 adeocarcinoma)

complications was described. Two studies registered multiple surgical complications per individual patient [24,32].

Rates of surgical site complications are shown in Table 4. Incidences varied from only one complication in 30 neck dissections (3%) [28], to five of seventeen procedures (29%) [26]. Hemorrhages were reported in only five studies, with a total of six in 219 procedures (3%). One of these was a blow-out of the carotid artery [19]. Chyle leak was mentioned in eleven studies (18 in 529 procedures; 3.4%); one study reported about five cases in 34 procedures (14.7%) [32]. Ten studies referred to wound dehiscence in their patients, with a range from 0 to 22% [23,19,27,32], with a total of 23 in 525 procedures (4.8%). Surgical site infections were described in 32 of 493 procedures (6.5%). Only three studies differentiated between superficial or deep infections [21,24,31].

Table 3
Characteristics of surgery.

Author	Number of patients	Number of neck dissections	Planned (pt.)	Salvage (pt.)	Unknown (pt.)	Comprehensive ND	Selective ND	Unknown	Bilateral ND^
Newman [26]	14	17	0	14	0	17	0	0	3
Lavertu [27]	19	23	15	4	0	15	-	8	-
Davidson [31]	-*	15	15*	0	0	-	-	15	-
Stenson [7]	69	82	69	0	0	12	70	0	14
Grabenbauer [9]	56	56	56	0	0	56	0	0	-
Proctor [32]	34	34	0	34	0	-	-	34	-
Frank [20]	39	51	39	0	0	27	24	0	12
Morgan [28]	25	30	-	-	25	-	-	30	-
Christopoulos [21]	32	35	11	21	0	14	18	3	3
Nouraei [22]	41	49	41	0	0	-	-	49	6
Bremke [18]	25	43	25	0	0	19	10	14	-
Hillel [23]	41	48	41	0	0	23	25	0	7
Goguen [24]	105	105	81	24	0	102	3	0	0
Pellini [29]	41	41	41	0	0	-	-	41	0
Suzuki [33]	36	36	0	36	0	-	-	36	-
Pellini [19]	36	37	36	0	0	37	0	0	1
Miah [25]	76	76	76	0	0	0	76	0	0
Taguchi [30]	26	26	0	26	0	-	-	26	-
Total	715	804	546 (70.5%)‡	159 (20.5%)‡	25	322 (56.2%)‡	226 (41.1%)‡	256	46 (8.5%)‡

CRT = chemoradiotherapy, ND = neck dissection. Comprehensive ND includes extended radical, radical and modified radical neck dissection. * = Actual number of patients not mentioned in study
^ = Simultaneously or staged‡ = Percentage of total neck dissections of only reporting studies.

Table 4
Overview of complications.

Author	# neck dissections	# ND with SSC (%)*	Hemorrhage	Chyle leak	Fistula	Hematoma	Seroma	Necrosis	Wound dehiscence	SSI	Operative intervention
Newman [26]	17	5 (29)		3 (17.6%)			2 (11.8%)				0 (0%)
Lavertu [27]	23	5 (22)		0					5 (21.7%)		
Davidson [31]	15	3 (20)									
Stenson [7]	82	7* (9)		0		1 (1.2%)	1 (1.2%)	0	7 (8.5%)	0	4 (4.9%)
Grabenbauer [9]	56	6 (11)	2 (3.6%)		2 (3.6%)					2 (3.6%)	2 (3.6%)
Proctor [32]	34	10* (29)	1 (2.9%)	5 (14.7%)	0				0	10 (29.4%)	
Frank [20]	51	3 (6)		1 (2.0%)		1 (2.0%)			1 (2.0%)		1 (2.0%)
Morgan [28]	30	1 (3)		1 (3.3%)			0	0		0	1 (3.3%)
Christopoulos [21]	35	4 (11)				1 (2.9%)				3 (8.6%)	1 (2.9%)
Nouraei [22]	49	3 (6)	1 (2.0%)							2 (4.1%)	
Bremke [18]	43	2 (5)	1 (2.3%)						1 (2.3%)		2 (4.7%)
Hillel [23]	48	2 (4)		2 (4.2%)		0			0		0
Goguen [24]	105	24 (23)		2 (1.9%)		2 (1.9%)	2 (1.9%)	3 (2.9%)	3 (2.9%)	12 (11.4%)	
Pellini [29]	41	10 (24)									10 (24.4%)
Suzuki [33]	36	3 (8)					3 (8.3%)				
Pellini [19]	37	2 (5)	1 (2.7%)	1 (2.7%)		0			0		
Miah [25]	76	15 (20)		2 (2.6%)		5 (6.6%)	2 (2.6%)		3 (3.9%)	3 (3.9%)	8 (10.5%)
Taguchi [30]	26	4 (15)		1 (3.8%)	0				3 (11.5%)	0	2 (7.7%)
Total	804	109 (13.6%)	6 (2.7%)^	18 (3.4%)^	2 (1.7%)^	10 (2.3%)^	10 (2.9%)^	3 (1.4%)^	23 (4.4%)^	32 (6.5%)^	31 (6.1%)^

SSC = surgical site complication, ND = neck dissection, SSI = surgical site infection. * = >1 SSC possible per procedure. ^ = Percentage of only studies reporting SSC in question

The need for operative interventions was described in eleven studies; percentages varied from 0 to 24%, while the numbers of neck dissections in these studies ranged from 17 to 82 [23,26,29].

4. Discussion

This systematic review demonstrates that the risk of surgical site complications (SSC) of patients, who undergo neck dissection (ND) after primary chemoradiotherapy (CRT), is widely varying (3-29%). The absence of dedicated studies makes it impossible to perform meta-analysis. Due to a lack of patient characteristics and a variety of tumor- and treatment data, identification of a predictive profile of patients at risk and risky procedures was not possible.

This study includes both planned and salvage neck dissections. Table 2 demonstrates that the time interval of both planned and salvage neck dissection varied. Because of the wide variation in registration of procedures in all studies it was impossible to make any correlation with timing of neck dissection or to be specific, planned or salvage neck dissection. Table 3 shows that in the planned setting *selective* neck dissection is performed, just as in the salvage setting.

Only a minority of seven studies made use of a grading system into minor and major complications. However, definition of this grading varied significantly among these studies (Table 1). Although the majority considered the necessity of an operative intervention as

a major complication, the specificity was downgraded as fistulas or even a prolonged hospital admission were grouped under major complications as well. One study even reported no occurrence of major complications, whilst they performed one time a surgical drainage in their four (11%) complications [21].

Wound dehiscence was mentioned in 56% of the studies with percentages ranging from 0 to 22%. Three studies reported an absence of wound dehiscence [23,25,32]. The next lowest incidence was in 1 out of 51 ND's (2.0%; 27 comprehensive ND's) [20], while the highest percentage of 22% (5/23) was reported in a group of at least 15 comprehensive ND's (of eight procedures type of ND was not described) [27]. No correlation could be made between the occurrence of hematoma, seroma or chyle leak on the one side and wound dehiscence on the other side.

Surgical interventions were also reported in 61% of the studies, but they did not parallel the before-mentioned reporting of wound dehiscence. The percentages ranged from 0 to 24% [23,26,29]. It was difficult to get a clear picture of the type of surgical interventions, which varied from abscess drainage to pedicled flap reconstruction.

Stenson et al. reported on a percentage of 9% surgical site complications. In four of the 82 procedures, a pedicled myofascial pectoralis flap was inserted simultaneously [7]. Only one other study mentioned the use of direct transposition of tissue in a radical neck dissection (10 of 51 procedures); 'the carotid artery was typically protected with either a dermal graft or a pectoralis muscle flap' [20]. This study showed 6% of complications.

Two of the studies with low complication incidences excluded patients with diabetes (for various reasons), which could have positively influenced the rating [18,19].

Surgical site infections are listed in 50% of the publications (range 0–29%) [9,21,30,32]. However, no correlation was found between the prophylactic use of antibiotics, which was described in a far minority of three studies [7,26,28].

Although there could be any overlap in complications, the striking differences in registration of surgical site complications make results unsuitable for meta-analysis. This was recently also encountered by others [34].

In 804 ND's, a total of 117 SSC's were seen (14.6%). Because two studies registered more SSC's per ND, a total of 109 ND's were complicated (13.6%). Among the 117 SSC's are 32 SSI's (27.4%) and 23 wound dehiscence (19.7%). Chyle leak is also frequently seen with 15.4% (18/117). Thirty-one of 117 complications (26.5%) required operative intervention.

Lessons can be learned from other fields of surgery, where a successful complication grading system in a series of >6300 patients was developed, based on the differentiation of therapeutic interventions. This grading system was called the Clavien Dindo Classification (CDC) [35], and was successfully applied in several studies analyzing the postoperative complications in surgeries outside the head and neck area. In a meta-analysis of 29 studies (2004–2007) covering gastrointestinal oncologic surgeries, the use of this grading system made it possible to assess sarcopenia as a clinically relevant risk factor for postoperative complications [36]. Also in urology, it made a systematical comparison of 2240 partial nephrectomy patients (23 studies) possible, with perioperative outcome in favor of robotic treatment [37]. Earlier, we proved it to be useful in reporting complications in parotid gland surgery [38]. By the use of interventions as parameters for the grading of complications, differences in interpretation are avoided, leading to an easy applicability and reproducible registration in retrospective cohorts.

The need for proper registration has even become more important, since the incidence of oropharyngeal squamous cell carcinoma is rising, due to human papillomavirus (HPV) associated tumors [39]. HPV-positive tumors are known for their early cervical metastasis [40], often leading to a first presentation with metastases or a large-sized – possible cystic – metastasis. Although according to the current opinion HPV-positive patients have better survival [41], an attempt to reduce cisplatinum toxicity for HPV-positive patients by switching to cetuximab was unsuccessful. So the current platinum-based protocol remains the standard for all patients [42].

Therefore, more surgery will be performed after primary chemoradiotherapy, making the need for proper counseling of CRT patients more urgent – especially adjusted to the substantial risk of surgical site complications. However, we are hampered to fulfill our duty by the lack of uniform registration in our specialty.

Based on our analysis on heterogeneous data in the literature, we are not able to recommend a specific informed consent for CRT patients undergoing salvage neck dissection.

4.1. Limitations

Together with the serious risk of bias, is the lack of homogeneous primary data about surgical site complications of the included studies the main limitation. It resulted in varying outcomes and prevented statistical analyses. Absence of demographic information in most of the included studies hampered further risk identification. Several study protocols failed to use current surgical classification of neck dissection [43], thereby forcing us to use *comprehensive* ND as category and making distinction of SSC's for type of ND impossible. The inclusions of both planned (67.9%; 546/804) and salvage ND's, could contain a selection bias of the surgeon. In two studies complications were not the primary focus, yet mentioned as an additional outcome.

5. Conclusion

In this systematic review, highly varying rates of surgical site complications were found after neck dissection post-CRT. Despite this variety, we may conclude that complications seem severe, resulting in prolonged hospital admission and substantial risk up to 24% of operative interventions. Although these observations remain rough estimates, patients should be informed about these possible risks. Further dedicated studies are necessary for a scientifically based formulation of preventive measures.

However, to reach this goal, the head and neck community should strive for a decent standardized uniform complication registration, as holds already true in other fields of surgery.

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Declaration of interest

The authors report no conflicts of interest.

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Newman [26]
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2020.10.015.

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