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Effect of elective neck dissection versus sentinel lymph node biopsy on shoulder morbidity and health-related quality of life in patients with oral cavity cancer: A longitudinal comparative cohort study

Gerben van Hinte [a,*], Tolunay Sancak [b], Willem L.J. Weijs [b], Matthias A.W. Merkx [b,c], Ruud A. Leijendekkers [a,e,f], Maria W.G. Nijhuis-van der Sanden [a,d], Robert Takes [f], Caroline M. Speksnijder [b,g,h]

[a] Radboud University Medical Center, Radboud Institute for Health Sciences, Department of Rehabilitation, Nijmegen, the Netherlands
[b] Radboud University Medical Center, Department of Oral and Maxillofacial Surgery, Nijmegen, the Netherlands
[c] Comprehensive Cancer Organisation Netherlands, Utrecht, the Netherlands
[d] Radboud University Medical Center, Radboud Institute for Health Sciences, IQ Healthcare, Nijmegen, the Netherlands
[e] Radboud University Medical Center, Radboud Institute for Health Sciences, Orthopaedic Research Laboratory, Nijmegen, the Netherlands
[f] Radboud University Medical Center, Department of Otorhinolaryngology, Head and Neck Surgery, Nijmegen, the Netherlands
[g] University Medical Center Utrecht, Department of Oral and Maxillofacial Surgery and Special Dental Care, University of Utrecht, Utrecht, the Netherlands
[h] University Medical Center Utrecht Cancer Center, Department of Head and Neck Surgical Oncology, University of Utrecht, Utrecht, the Netherlands

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ABSTRACT

Objective: To research the difference in shoulder morbidity and health-related quality of life between patients with $cT_{1\text{-}2}N0$ oral cavity squamous cell carcinoma that undergo either elective neck dissection (END) or a sentinel lymph node biopsy (SLNB) based approach of the neck.
Materials and methods: A longitudinal study with measurements before surgery, 6 weeks, 6 months, and 12 months after surgery. Shoulder morbidity were determined with measurements of active range of motion of the shoulder and patient-reported outcomes for shoulder morbidity (SDQ, SPADI) and health-related quality of life (HR-QoL) (EQ5D, EORTC-QLQ-HN35). Linear mixed model analyses were used to analyze differences over time between patients that had END, SLNB or SLNB followed by complementing neck dissection.
Results: We included 69 patients. Thirty-three patients were treated with END. Twenty-seven patients had SLNB without complementing neck dissection (SLNB), and nine were diagnosed lymph node positive followed by completion neck dissection (SLNB + ND). Ipsilateral shoulder abduction ($P = .031$) and forward flexion ($P = .039$) were significantly better for the SLNB group at 6 weeks post-intervention compared to the END and SLNB + ND group. No significant differences for shoulder morbidity, or health-related quality of life were found at 6 weeks, 6 months, and 12 months between the three groups.
Conclusion: With oncologic equivalence for the END and SLNB as strategies for the cN_0 neck already demonstrated, and the SLNB being more cost-effective, our demonstrated benefit in short-term shoulder function strengthens the choice for the SLNB as a preferred treatment strategy.

Introduction

Oral cavity squamous cell carcinoma (OCSCC) is the most common type of oral cavity neoplasm with a worldwide approximate incidence of 354,864 patients in 2018 [1]. Early-stage $T_{1\text{-}2}$ tumors account for almost half of this population [2]. The surgical removal of the primary tumor is complemented by a (therapeutic) neck dissection (ND) when regional lymph node metastases are detected pre-operatively (cN_+). When no local lymph node metastases are detected with the pre-operative diagnostic procedures, this is classified as cN_0. However, patients with a cN_0 neck are still at risk of regional recurrence because occult undetected lymph node metastases are present in 20–30% of these patients [3]. The

* Corresponding author at: Department of Rehabilitation, Radboud University Medical Center, Radboud Institute of Health Sciences, Reinier Postlaan 4, 6525 GC Nijmegen, the Netherlands.
E-mail address: gerben.vanhinte@radboudumc.nl (G. van Hinte).

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three most frequently used strategies to manage regional disease recurrence in patients with a cN_0 neck are elective neck dissection (END), sentinel lymph node biopsy (SLNB), and a "wait and see" strategy with patient observation (PO) [4]. Patients diagnosed as lymph node positive with SLNB are treated with ND, a procedure comparable to that of the END strategy.

The question of which strategy for the treatment of cN_0 neck is most optimal is currently one of the most heavily debated subjects in head and neck oncology. A systematic review published in 2020 showed significantly better results for recurrence rate, disease-specific and overall survival for END compared to PO [5]. Both a systematic review and a randomized clinical trial (RCT) published in 2020 showed that END and SLNB are comparable on recurrence rate, disease-specific and overall survival, favoring these over PO [6,7]. However, with occult lymph node metastasis present in only 20–30% of the patients, END causes overtreatment of 70–80% of the $cT_{1\text{-}2}N_0$ OCSCC patients in comparison to completion neck dissection after a positive SLNB only [8]. In addition, the SLNB is a less invasive and more cost-effective procedure compared to END [9]. With PO performing worse, and oncologic equivalence for the END and SLNB, the optimal strategy for the cN_0 neck is, however, still open for debate. Differences in treatment-related morbidity and health-related quality of life (HR-QoL) between cN_0 locoregional management strategies are therefore important outcomes to determine the preferred choice. An important part of treatment-related morbidity of surgical procedures in the neck is experienced by patients in limitations and pain in shoulder function [10,11]. A recent systematic review including five observational studies showed less shoulder morbidity for the SLNB strategy compared to the END strategy [6]. A more recent RCT showed that this benefit for SLNB was only present at 6 months follow-up and not at longer follow-up [7]. Although closely related to treatment-related morbidity, up till now research found no significant differences in HR-QoL between the END and SLNB strategies [6,7,12]. High-quality longitudinal research on shoulder morbidity and HR-QoL that compares both strategies with the inclusion of SLNB, diagnosed lymph node positive, followed by complementing neck dissection (SLNB + ND) patients is scarce. Moreover, adequate physical performance measurements on shoulder AROM are missing. Further research is needed to determine which locoregional management strategy is more beneficial for patients, using models corrected for covariates that are known to influence shoulder morbidity and HR-QoL as for example age, sex, and the extent of the ND [11,13,14]. Therefore, our aim is to study the difference in shoulder morbidity and HR-QoL between patients with $cT_{1\text{-}2}N_0$ oral squamous cell carcinoma that undergo END, SLNB, or SLNB + ND. We expect patients in the SLNB group to experience less shoulder morbidity and better HR-QoL in comparison to patients undergoing END and patients in the SLNB + ND group.

Materials and methods

Study setting and patients

A prospective longitudinal comparative study was conducted between January 2014 and June 2020 at the Radboud University Medical Center. The locoregional management strategy for patients with cN_0 transitioned from END to the SLNB strategy during the end of 2015 and the start of 2016 providing the opportunity for a natural comparative study. We identified three separate groups, including the Elective Neck Dissection (END) group, SLNB (SLNB) group, and SLNB with complementing neck dissection (SLNB + ND) group. Patients treated with the END were included between January 2014 and 2016. Patients treated with the SLNB (SLNB and SLNB + ND) were included between 2015 and 2019. Both SLNB groups underwent SLNB where dual -labelled (tc99m-ICG) nanocolloid was injected *peri*-tumoral. Lymphoscintigraphy and SPECT-CT were used to detect the sentinel lymph node on imaging. During surgery, the ICG near-infrared signal and radioactivity were respectively detected by a near-infrared camera system and gamma detection probe. The sentinel lymph node was surgically removed and histopathologically examined using stepped serial sectioning and immunohistochemistry. In the case of a negative lymph node, no complementing neck dissection treatment is necessary (SLNB group while a positive lymph node is followed in most cases by ND (SLNB + ND). In some cases of SLNB, diagnosed lymph node positive, patients could be treated with radiotherapy. These patients were analyzed in the SLNB group because no complementing neck dissection was performed.

Inclusion criteria were: 1) a clinically confirmed early-stage OCSCC ($cT_{1\text{-}2}$) with a clinically negative neck (cN_0) and 2) 18 years or older. Exclusion criteria were: 1) inability to read Dutch, 2) cognitive impairments, 3) prior history of oral oncology treatment, and 4) prior history of shoulder trauma or shoulder surgery. The study was conducted according to the principles of the Declaration of Helsinki (64th version, October 19th, 2013). The research protocol was approved by the Ethical Commission of the Radboud University Medical Center (NL2014-2019). All patients signed informed consent forms before measurements. This study followed guidelines provided by the Strengthening The Reporting of OBservational Studies in Epidemiology (STROBE) statement and checklist [15].

Study procedure

Patients were measured at baseline before surgery (M0), 6 weeks (M1), 6 months (M2), and at 12 months (M3) after surgery. The outcomes of this study were shoulder morbidity and HR-QoL. Active Range of Motion (AROM) measurements of the shoulder were performed in a standardized order and according to a standardized measurement protocol by a senior physiotherapist. Shoulder AROM was expressed as the ipsi- or contralateral side of neck intervention.

Patient characteristics, demographic and clinical data

The demographic and clinical data were obtained from the patient during the baseline measurement and/or from medical records. These data included treatment modality (END, SLNB, SLNB + ND), age, sex, body mass index (BMI), smoking status (non-smoker, former smoker, current smoker), pack-years, alcohol usage (no alcohol use, one or more units daily), ASA score, tumor location (lip, tongue, gingiva, floor of the mouth, cheek, retromolar trigonium, palatum durum), clinical T-stage score, pathologic T- and N-stage score, number of lymph nodes resected, if level 2b was resected (yes/no), surgical reconstruction of the oral cavity (no reconstruction, local flap, free skin or myocutaneous revascularized flap), postoperative radiotherapy (yes/no), local recurrence during the first 12-months post-intervention (yes/no), survival during first 12 month post-intervention (yes/no), and number of physical therapy sessions.

Shoulder morbidity

Shoulder morbidity was defined as shoulder AROM and patient-reported shoulder pain and limitations in daily life. We obtained the AROM of abduction, forward flexion, and external rotation of the shoulder. Shoulder abduction and forward flexion was measured with a digital inclinometer (Baseline© Digital Inclinometer, Fabrication Enterprises Inc., White Plains, New York, USA) [16]. External rotation of the shoulder was measured with a goniometer (Universal goniometer, Mathys Synthes, Bettlach, Switzerland) [16].

Shoulder pain and limitations were measured with the Shoulder Disability Questionnaire (SDQ) and Shoulder Pain and Disability Index (SPADI). The SDQ contains 16 questions regarding physical activities in the last 24 h that could provoke possible shoulder complaints. This questionnaire addresses physical, emotional, and social impairment due to shoulder complaints or incapability of performing an activity by the usage of a 3-point scale (1: Yes, I experience complaints, 2: No, I do not experience complaints, 3: The question does not apply to me). An overall

score was calculated by dividing the number of given answers as "Yes" by the total amount of answers without the "does not apply to me" answers. The test–retest reliability of the SDQ was good in head and neck cancer (HNC) patients (ICC = 0.84) [17]. The SPADI is a validated 13-item questionnaire with two main categories regarding pain (5 items) and impairment in daily activities (8 items) based on an 11-point scale (0–10) for each item. A higher score indicates more pain or impairment due to the treatment of the shoulder [17]. An overall score for each category and a total score was calculated. The test–retest reliability showed excellent reliability (ICC = 0.91) in HNC patients [17].

Health-related quality of life

The EQ-5D-3L is a validated HR-QoL questionnaire that explores 5 items of health status regarding mobility, self-care, daily usual activities, pain/discomfort, and anxiety/depression. The questionnaire also includes a Visual Analogue Scale (VAS) from 0 to 100 mm to get an impression about the current health status, which we used as an outcome measurement for general HR-QoL for this study. Higher scores on the VAS indicate a better HR-QoL [18]. The EQ-5D-3L showed good psychometric properties [19].

The European Organization for Research and Treatment for Cancer Quality of Life Questionnaire – Head and Neck 35 questions (EORTC-QLQ-HN35) is an HNC-specific Quality of Life Questionnaire. This questionnaire contains 35 items that can be transformed into a score from 0 to 100. For the function scales, a score of 100 means the perfect quality of life, whereas for the symptom scales it indicates a heavy burden [20]. The EORTC-QLQ-HN35 showed good psychometric properties [20].

Statistical analysis

Categorical patient characteristics are presented as numbers and percentages, while continuous characteristics are presented as means and standard deviations (SDs). In the case of non-normally distributed variables, outcomes are presented as medians and 25th and 75th percentiles. Differences between baseline characteristics of patients in the 3 groups were analyzed with a Chi-square test for nominal and ordinal data, one-way ANOVA for normally distributed continuous data, and a Kruskal-Wallis test for non-normal distributed continuous data. Longitudinal data regarding shoulder AROM and overall scores of the questionnaires were analyzed using linear mixed models analysis. For this analysis, a random intercept for the subject was used. For fixed factors, the time of measurement (M0-M3), treatment group (END, SLNB, SLNB + ND), and their interaction were used. The additional fixed factors or covariate factors included in the model were based on known effects on shoulder morbidity or HR-QoL reported in research: age, sex, postoperative radiotherapy, TNM-classification, BMI, dissection of cervical level IIb, the amount of dissected cervical levels, and smoking status (in pack-years) [11,13,14,21]. Differences between the three groups were tested by the likelihood ratio test. Furthermore, time effects within groups were analyzed using the linear mixed model. The individual ordinal sub-items of the questionnaires were analyzed with Generalized Linear Models analysis with the same random and fixed factors. The individual ordinal sub-items of the questionnaires were analyzed with Generalized Linear Models analysis for the same random and fixed factors. Data analysis was performed using IBM SPSS Software Version 26.0 (SPSS, Inc., Chicago, Illinois, United States).

Results

In total, the data of 69 patients was used in this study (Fig. 1) of which 33 belonged to the END group, 27 to the SLNB group, and 9 to the SLNB + ND group Proportionally there were fewer T2-stage patients in the SLNB group compared to both the END and SLNB + ND groups (P = .001) (Table 1).

Shoulder morbidity

Within groups analyses for shoulder AROM are depicted in Table 2, showing that ipsilateral forward flexion was lower at 6 weeks post-intervention for the END group and SLNB + ND group compared to baseline (P = .002). Ipsilateral forward flexion recovered between 6 weeks and 6 months after treatment for the END and SLNB + ND group (P = .003). Ipsilateral shoulder abduction deteriorated at 6 weeks (P = .000) and recovered at 6 months (P = .002) for the END group. External rotation of the shoulder deteriorated between 6 and 12 months for the END group (P = .003). Visualization of the within differences for shoulder AROM is depicted in Fig. 2.

Within groups analyses for patient-reported shoulder morbidity are presented in Table 3. Shoulder morbidity was higher compared to baseline at 6 weeks in the END group for SPADI (P = .001) and SDQ (P =

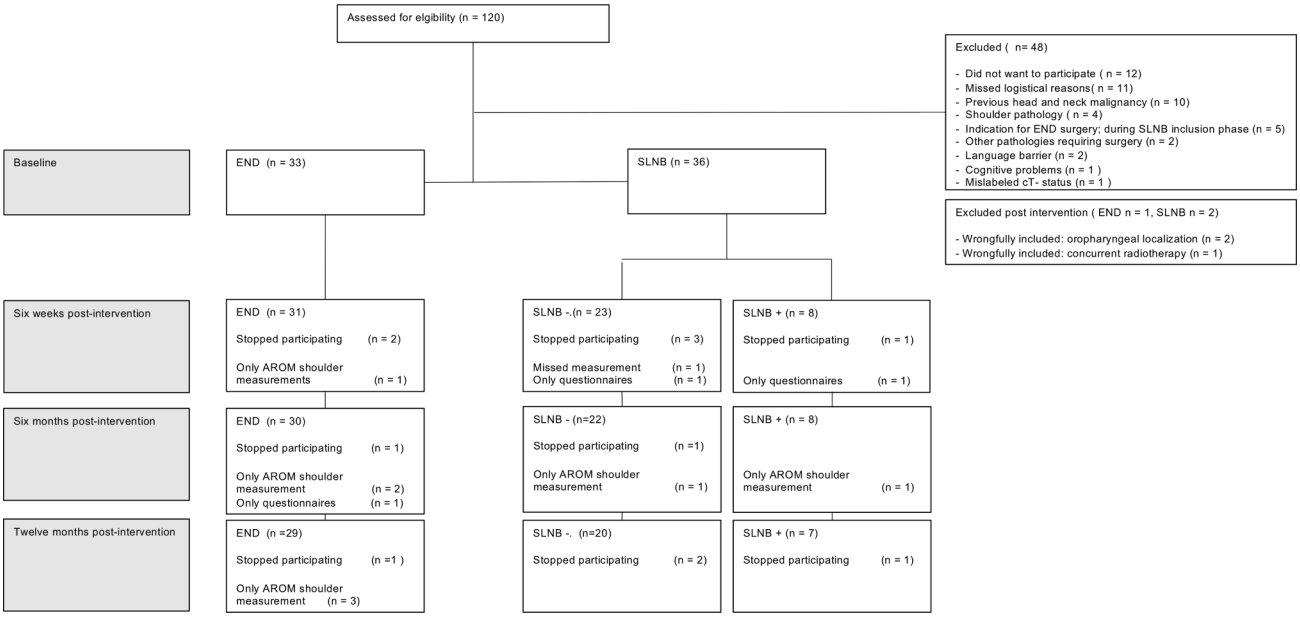

Fig. 1. Participant recruitment and follow-up.

Table 1
Demographic and clinical characteristics.

Patient characteristics, n (%)		END (N = 33)	SLNB (N = 27)	SLNB-ND (N = 9)	*P*-value
Sex	Female	19 (57.6)	12 (44.4)	5 (55.6)	0.584†
	Male	14 (42.4)	15 (55.6)	4 (44.4)	
Age (years), mean (SD)		64.5 (10.2)	64.5 (11.0)	66.3 (11.3)	0.893¥
BMI; mean (SD)		25.0 (5.5)	26.5 (4.9)	25.0 3.6)	0.513¥
Smoking (daily)	Non-smoker	17 (51.5)	11 (40.7)	2 (22.3)	
	Former smoker	7 (21.2)	8 (29.6)	3 (33.3)	0.596†
	Current smoker	9 (27.3)	8 (29.6)	4 (44.4)	
Pack years, median (25th–75th PCTL)		0 (0–41)	5 (0–45)	30 (1–43.5)	0.713
Alcohol use (daily)	No alcohol use	15 (45.5)	11 (40.7)	6 (66.7)	0.596†
	One or more unit(s) daily	18 (54.5)	16 (59.3)	3 (33.3)	
ASA classification	ASA I	8 (24.2)	5 (18.5)	0 (0)	0.097†
	ASA II	22 (66.7)	13 (48,1)	7 (77.8)	
	ASA III	3 (9.1)	9 (33.3)	2 (22.2)	
Localisation tumor	Tongue	18 (54.5)	16 (59.3)	4 (44.4)	0.195†
	Floor of the mouth	7 (21.2)	5 (18.5)	4 (44.4)	
	Cheek	6 (18.2)	1 (3.7)	1 (11.1)	
	Trigonum retromolare	0 (0.0)	3 (11.1)	0 (0.0)	
	Lip	0 (0.0)	1 (3.7)	0 (0.0)	
	Gingiva	2 (6.1)	1 (3.7)	0 (0.0)	
	Palatum durum	0 (0.0)	0 (0.0)	0 (0.0)	
cT	cT_1	7 (21.2)	18 (66.7)	2 (22.2)	0.001*†
	cT_2	26 (78.8)	9 (33.3)	7 (77.8)	
pTN	pT_1	13 (39.4)	20 (74.1)	3 (33.3)	0.054†
	pT_2	18 (54.5)	5 (18.5)	6 (66.7)	
	pT_3	2 (6.1)	1 (3.7)	0 (0.0)	
	pT_4	0 (0.0)	1 (3.7)	0 (0.0)	
	pN_0	26 (78.8)	23 (85.2)	0 (0.0	0.000†
	pN_1	3 (9.1)	2 (7.4)Ω	8 (88.9)π	
	pN_2	4 (12.1)	2 (7.4)Ω	1 (11.1)	
Number of nodes resected, median (25th–75th PCTL)		5 (5–5)	2 (1–3)	6 (5–10)	0.000*‡
Level 2B resected (yes)		33 (100.0)	22 (81.5)	9 (100.0)	0.065†
Reconstruction	Primary Closure	18 (54.5)	9 (70.4)	4 (44.4)	0.525†
	Local Flap/ Thiersch	11 (33.3)	7 (25.9)	4 (44.4)	
	Bone graft/ Free vascularized flap	4 (12.1)	1 (3.7)	1 (11.1)	
		22 (66.7)	24 (88.9)	7 (77.8)	0.127†
Radiotherapy post-intervention		0 (0.0)	1 (3.7)	0 (0.0)	NA
Mortality		1 (3)	0 (0.0)	4 (44.4)	NA
Local Recurrence		0 (0–0)#	0 (0–5)#	0 (0–0)	0.516‡
Number of PT treatments, median (25th–75th PCTL)					

*p: < 0.001; †: Chi-Square; ¥: ANOVA; U; ‡: Kruskal-Wallis.
#: Four END patients received more than 20 treatments, 1 SLNB patient received more than 20 treatments.
Π: Five out of 8 patients labeled as pN_1 had a positive lymph node in the SLNB but did not have any positive lymph nodes in the complementing neck dissection.
Ω Patients diagnosed lymph node positive but treated with radiation therapy and therefore analyzed in the SLNB without complementing neck dissection group (SLNB).
ASA-score: American society of anesthesiologists physical status - classification system, BMI: body mass index, cT: clinical tumor stage, END: elective neck dissection, IQR: interquartile range, NA: not applicable, pTN: pathologic tumor node stage; PT: physical therapy; SD: standard deviation; SLNB: sentinel lymph node biopsy.

.029), and for the SDQ ($P = .024$) in the SLNB + ND group. Between the 6 and 12 months measurements, the END group showed recovery of the SPADI ($P = .006$) and SDQ ($P = .025$). A visualization of the within differences for patient-reported shoulder morbidity is depicted in Fig. 2.

Between groups analysis of the AROM scores showed that ipsilateral forward flexion ($P = .039$), and ipsilateral shoulder abduction ($P = .031$) were lower for the END group and SLNB + ND group compared to the SLNB group at 6 weeks post-intervention (Table 2). No significant differences between groups in external rotation of the shoulder (AROM) and morbidity (SPADI and SDQ) were found (Table 3).

Health-related quality of life

The within groups analyses (Table 3) showed lower head and neck-specific HR-QoL at 6 weeks post-intervention compared to baseline for all three groups: the END group ($P = .034$), the SLNB group ($P < .001$), and the SLNB + ND group ($P = .002$). The SLNB group ($P < .001$) and SLNB + ND group ($P = .045$) recovered between the 6 weeks and 6 months measurements (Table 3). The HR-QoL (EQ-5D) improved significantly between the 6 and 12 months in the END group to an above baseline measurement score ($P = 0.015$). Visualization of the within differences for shoulder patient-reported morbidity and HR-QoL is depicted in Fig. 2. No between group differences were found for HR-QoL between the three groups (Table 3).

Discussion

This study found that shoulder AROM expressed in ipsilateral forward flexion and abduction is better for patients in the SLNB group at 6 weeks post-intervention compared to both patients undergoing END and patients diagnosed SLNB positive followed by complementing neck dissection (SLNB + ND). No differences in patient-reported shoulder morbidity (SDQ and SPADI), HNC specific HR-QoL (EORTC-QLQ-HN35), and cancer generic HR-QoL (EQ-5D) were found between the 3 groups. This confirms our hypothesis that patients without pre-operatively detected regional lymph node metastasis (cN_0) can benefit from the SLNB strategy due to less short-term shoulder morbidity. With 70 to 80% of $T_{1\text{-}2}$ clinically negative OCSCC expected to be diagnosed lymph node negative with SLNB, this short-term benefit in shoulder

Table 2
Shoulder range of motion: between and within differences for three intervention groups analyzed with mixed model analysis.

	M0	M1	M2	M3	Mixed model Within groups P-value	Mixed model Within groups P-value	Mixed model Within groups P-value	Mixed model Between groups P-value
Active Range of Motion Shoulder (degrees, SD)		END (n = 33)			M0-M1	M1-M2	M2-M3	
Forward flexion	169 (18)	160 (17)	170 (20)	168 (21)	0.002**	0.003**	0.833	0.039*
Abduction	168 (26)	150 (32)	166 (32)	167 (27)	0.000***	0.002**	0.468	0.031*
External rotation	56 (21)	52 (19)	60 (23)	52 (23)	0.201	0.092	0.033*	0.836
		SLNB - (n = 27)						
Forward flexion	175,0 (13)	175 (12)	176 (12)	173 (17)	0.868	0.662	0.351	0.039*
Abduction	175 (25)	170 (14)	178 (30)	175 (18)	0.302	0.081	0.466	0.031*
External rotation	56 (16)	60 (17)	55 (17)	54 (18)	0.438	0.387	0.986	0.836
		SLNB + (n = 9)						
Forward flexion	175 (20)	157 (26)	174 (14)	176 (17)	0.017*	0.016*	0.963	0.039*
Abduction	183 (25)	165 (26)	181 (21)	191 (22)	0.079	0.114	0.477	0.031*
External rotation	51 (19)	59 (16)	60 (11)	53 (10)	0.506	0.689	0.427	0.836

* P < 0.05; **p < 0.01; ***p < 0.001.
END: elective neck dissection, SD: standard deviation, SLNB: sentinel lymph node biopsy.
All range of motion outcomes are presented in degrees and with standard deviation for the ipsilateral side.

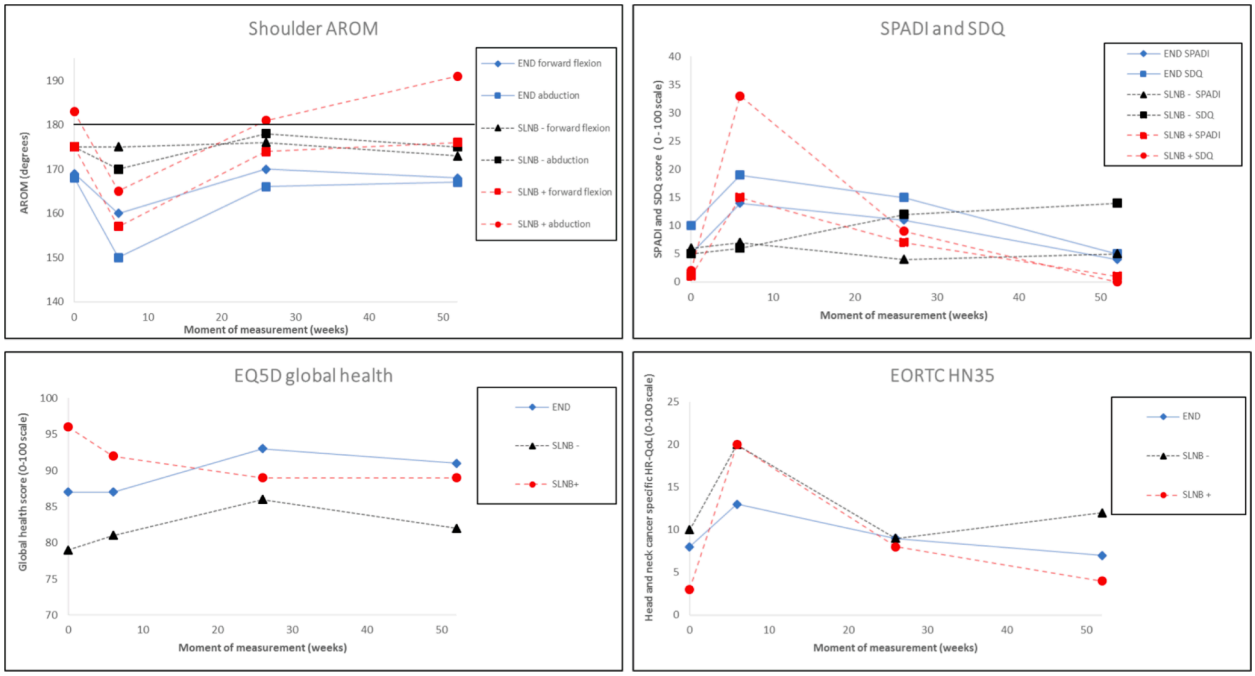

Fig. 2. Visualization of the within differences for shoulder patient-reported morbidity and Health-related Quality of life.

AROM could strengthen the choice for SLNB as a preferred treatment strategy. The SLNB + ND group, although small (n = 9), was included because this gives the most optimal representation of patient trajectories in both the END and SLNB strategies. Other studies chose to include the SLNB + ND as a representative for END patients [12] or to exclude them [22,23] which limits a true representation of the strategies. Only one other randomized study described the three different groups, but chose not to correct for possible confounding variables in the analysis, lacked a baseline measurement, and dichotomized shoulder AROM measurements [7]. Our longitudinal study thereby used a complete set of physical and patient-reported measurements [16,17]. These findings provide new insights into treatment-related shoulder morbidity and HR-QoL that can be used to substantiate the choice between END and SLNB as strategies for patients with CN_0) OCSCC.

Shoulder morbidity

A better ipsilateral forward flexion and abduction of the shoulder at 6 weeks for SLNB group patients is in line with the hypothesis that the less invasive procedure causes less shoulder morbidity. It also confirms the hypothesis that these benefits are to be expected in the first year after medical intervention as demonstrated by Garrel et al. [7]. This latter study also found better outcomes for shoulder morbidity at 4, 6, and 12 months after intervention which we didn't find but the differences are possibly related to the larger group sizes in that study. This is also confirmed by our previous cross-sectional study in which no significant differences were demonstrated between the END and SLNB strategies after more than 1-year of follow-up [24]. Other long-term cross-sectional studies found better results for SLNB compared to END at long-term follow-up, but the differences were small and limited in clinical relevance [12,22,23,25].

Table 3
Patient reported outcome measurements on health-related quality of life and shoulder morbidity: between and within differences for three intervention groups analyzed with mixed model analysis

	M0	M1	M2	M3	Mixed model Within groups P-value	Mixed model Within groups P-value	Mixed model Within groups P-value	Mixed model between groups P-value
Questionnaire		END (n = 33)			M0-M1	M1-M2	M2-M3	
EORTC-QLQ HN-35	8 (8)	13 (10)	9 (10)	7 (9)	0.034*	0.092	0.654	0.693
EQ5D	87 (16)	87 (19)	93 (18)	91 (15)	0.942	0.015*	0.509	0.930
SPADI	5 (12)	14 (22)	11 (19)	4 (8)	0.001**	0.537	0.006**	0.568
SDQ	10 (28)	19 (27)	15 (23)	5 (12)	0.029*	0.318	0.025*	0.246
		SLNB- (n = 27)						
EORTC-QLQ HN-35	10 (12)	20 (19)	9 (8)	12 (16)	0.000***	0.000***	0.218	0.693
EQ5D	79 (23)	81 (21)	86 (24)	82 (23)	0.916	0.424	0.860	0.930
SPADI	6 (14)	7 (18)	4 (10)	5 (10)	0.770	0.542	0.947	0.568
SDQ	5 (20)	6 (18)	12 (24)	14 (30)	0.684	0.433	0.664	0.246
		SLNB+ (n = 9)						
EORTC-QLQ HN-35	3 (8)	20 (16)	8 (7)	4 (8)	0.002**	0.045*	0.816	0.693
EQ5D	96 (8)	92 (15)	89 (15)	89 (13)	0.727	0.677	0.613	0.930
SPADI	1 (12)	15 (21)	7 (17)	1 (14)	0.095	0.220	0.312	0.568
SDQ	2 (5)	33 (33)	9 (18)	0 (35)	0.024*	0.067	0.780	0.246

* $P < 0.05$; **$p < 0.01$; ***$p < 0.001$.
END: elective neck dissection, EORTC-QLQ-HN35: european organization for research and treatment of cancer quality of life questionnaire head & neck module, EQ-5D: euroqoL five-dimensional instrument, SLNB: sentinel lymph node biopsy, SDQ: shoulder disability questionnaire, SNLB: sentinel lymph node biopsy, SPADI: shoulder pain and disability index.

The within groups analysis showed a significant decline in shoulder range of motion and an increase in shoulder morbidity at the 6-week measurement for the END group. This progressively recovered up to baseline values at 6 and 12 months after oral oncological treatment. This initial deterioration in shoulder morbidity is comparable to previous research in patients undergoing ND [10,11,26]. Remarkably, the modelled shoulder AROMs for all strategies are above age and gender stratified reference values, indicating no limitations in shoulder and neck AROM for the 3 groups [16]. This could possibly be related to overcorrecting the modeled scores. This was confirmed when we analyzed the raw data on mean shoulder range of motion. Mean range of motion scores for forward flexion and abduction of the shoulder were approximately 5–10 degrees lower than the modelled scores. In contrast to this, four END patients received more than 20 physiotherapy sessions for problems regarding neck and shoulder function in comparison to one patient in the SLNB group. The relatively high variance in the modeled outcomes also indicates that possible outliers in shoulder morbidity could be present in both the END and SLNB groups. The higher variance could also be explained by the relatively high measurement error in measurements on shoulder range of motion in patients with head and neck cancer [16]. This means that adequate identification of patients at risk is still of importance.

Health-related quality of life

We found no differences in cancer generic or HNC specific HR-QoL between the three groups. This is in contrast with the previous research that found better health utility scores (EQ-5D) for SNLB compared to END representing HR-QoL [23]. The results we found are in line with the study by Flach et al. who described no significant difference between END and SLNB [12]. Within group analyses showed a significant deterioration in HNC-specific HR-QoL at the 6 week measurement for all three strategies that improved up to baseline values at 6 months. This means that no specific effect of neck dissection (groups 1 and group 2B) on HNC-specific HR-QoL was found. The decrease in HNC specific HR-QoL experienced by all patients could therefore be related to reduced oral function caused by the surgical removal of the primary tumor.

Strengths and limitations of the study

Our study is the first to compare the END and SLNB locoregional management strategies in a longitudinal design, with a combination of objective shoulder AROM measurements and patient-reported outcomes. The use of mixed model analysis strengthens the validity of the outcomes taking into account the effect of the repeated measurements, the influence of patient and treatment characteristics, and its ability to correct for missing data strengthens the outcomes. No formal power analysis or simulation was performed because the study was a natural comparative study dependent on the change of treatment strategy. However, the modelled outcomes and the reported variance allow for adequate interpretation, except for the third small group. Information on the accessory nerve status objectified with electromyography (EMG) of patients in this study is lacking. Accessory nerve status can explain about 50% of the limitations in shoulder function, in addition to providing prognostic information to patients and physical therapists [26,27]. Information on the type of physiotherapy treatment and the level of experience of the physiotherapist is missing which could have given more insight into the problems as experienced by patients.

Conclusion

SLNB patients treated without complementing neck dissection (SLNB) have better postoperative shoulder AROM at 6 weeks after the intervention compared to patients undergoing the END strategy or diagnosed lymph node positive SLNB + ND followed by completion neck dissection (SLNB + ND). Shoulder morbidity as measured with patient-reported outcomes and quality of life is comparable for the END, SLNB and SLNB + ND groups. With oncologic equivalence for the END and SLNB as strategies for the cN_0 neck already demonstrated, and the SLNB being more cost-effective, our demonstrated benefit in short-term shoulder morbidity strengthens the choice for the SLNB as a preferred treatment strategy.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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