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The relationship between physical impairments, quality of life and disability of the neck and upper limb in patients following neck dissection

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Abstract

Purpose The purpose of this study was to examine the relationship between physical impairments, quality of life and disability in patients following neck dissection, with consideration of patient and clinical characteristics.

Methods Cross-sectional study of patients < 5 years after neck dissection for head and neck cancer. Quality of life and self-reported disability were measured with the Neck Dissection Impairment Index, Quick Disabilities of the Arm, Shoulder and Hand, and Neck Disability Index. Active neck and shoulder range of motion and isometric muscle strength were also assessed. Generalised linear modelling was used to explore relationships between variables.

Results Eighty-four participants (68% male, median age 61 years) demonstrated reduced quality of life (median (interquartile range) score = 76 (49, 93) from 0 (worst) to 100 (best)), and mild levels of upper limb (14 (2, 32)) and neck disability (14 (6, 28)) (from 0 (best) to 100 (worst)). Bilateral neck dissection was associated with reduced quality of life (coeff (95% CI) = − 12.49 (− 24.69, − 0.29)). Post-operative chemoradiation therapy was associated with reduced quality of life (− 21.46 (− 37.57, − 5.35)) and neck disability (0.71 (0.10, 1.32)). Measures of shoulder flexibility or strength were associated with quality of life and self-reported disability.

Conclusions Quality of life and musculoskeletal disability after neck dissection are associated with factors from multiple domains including physical motor function and treatment modality.

Implications for Cancer Survivors Having reduced shoulder flexibility or strength is related to functional deficits and quality of life after neck dissection for head and neck cancer.

Keywords Head and neck neoplasms · Neck dissection · Shoulder · Neck · Pain · Quality of life

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Introduction

Patients diagnosed with head and neck cancer (HNC) are treated with surgery, radiation therapy (XRT) and/or chemotherapy, with the aim of maximising survival whilst preserving physical form and function [1]. Treatment decisions can be influenced by the potential for short- and long-term side effects. Surgery commonly involves the removal of structures such as the tongue or temporomandibular joint. The resulting side effects (dysarthria, dysphagia) negatively impact upon health-related quality of life (HRQOL) [2]. Neck dissection (ND) can result in shoulder impairment and an associated reduction in HRQOL. Loss of active range of motion (AROM) at the shoulder [3] and neck [4], as well as impairments to sensation [5] and strength [6] can occur following ND. Patient-reported outcome measures specific to both HNC [7] and ND [8] have confirmed the negative impact this procedure can have on HRQOL. In addition, the presence of subjectively [9] and objectively [10] measured shoulder disability has been associated with the type of ND performed.

Radical ND (RND) removes the sternocleidomastoid muscle, the internal jugular vein and the accessory nerve as well as lymph nodes [11–13]. Considering the accessory nerve innervates the trapezius and sternocleidomastoid muscles, it is not surprising that patients can present with altered shoulder girdle function. However, impairments may still be present even when the nerve has been preserved [14]. Physical function could potentially be impaired by soft tissue trauma, subsequent scaring and post-surgical pain regardless of whether the accessory nerve was spared during ND. These side effects could be worsened with the addition of (chemo)radiation therapy ((C)XRT). Other factors that may contribute to this physical dysfunction include disuse and deconditioning, and psychosocial factors such as pain-related fear and anxiety. What remains unknown at this point is whether a relationship exists between the degree of physical impairment and reported HRQOL and disability, when the influence of other factors such as the extensiveness of the surgery and the addition of (C)XRT are also considered.

The aim of this study was to examine the relationship between physical function, HRQOL and disability in patients from 6 months to 5 years of ND for HNC, with due consideration of the effect of patient and clinical characteristics. It was hypothesised that more severe physical impairment would be associated with patient reports of poorer HRQOL and greater levels of neck and shoulder disability.

Methods

Study design, setting, participants and procedure

This cross-sectional study was conducted at two tertiary hospitals in Brisbane, Australia. Patients who received ND for HNC between 2009 and 2014 identified from hospital administrative records were eligible for this study. Invitations to participate were mailed to eligible patients, and responders were screened against exclusion criteria: under 18 years of age at surgery; pre-existing ipsilateral shoulder or neck pain or injury in the 6 months prior to surgery severe enough to limit daily function; inability to provide informed consent (e.g. due to cognitive impairment). All participants attended one assessment at their hospital with a physiotherapist (EG) during which all physical and questionnaire-based outcomes were assessed. The questionnaire-based outcomes were measures of HRQOL and self-reported disability, which prompted participants to reflect on their lives in the 1–4 weeks prior to responding to items. Ethical approval was obtained from the institutional human research ethics committees. All participants provided written informed consent. Standard post-operative clinical care at the participating hospitals included the prescription of shoulder and neck range of motion exercises immediately after surgery. Referral for ongoing outpatient physical therapy was made if shoulder pain or movement impairment was identified immediately after surgery, during post-operative XRT or at other times when considered appropriate by the treating team.

Dependent variables—measures of HRQOL and self-reported disability

Neck Dissection Impairment Index (NDII)

The NDII is a region-specific measure of HRQOL for patients following ND [15]. This patient-reported outcome measure produces a summary score ranging from 0 (worst HRQOL) to 100 (best HRQOL) and reflects the extent to which individuals experience symptoms, difficulty performing tasks and restrictions to work, social or leisure activities as a result of ND. The NDII has evidence to support its internal consistency and convergent validity against the Constant Shoulder Score and the Short Form-36 (SF-36) [15, 16] .

Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH)

The QuickDASH is an 11-item patient-reported outcome measure of functional limitations and symptoms (pain, pins and needles) in the upper limb [17]. The scores range from 0 (no impairment) to 100 (total impairment). The QuickDASH has shown both internal consistency and test–retest reliability in women with breast cancer [18] and construct validity in an orthopaedic population [17].

Neck Disability Index (NDI)

The 10-item NDI is a measure of pain-related neck disability. Questions relate to the impact of neck pain on tasks such as reading, driving and work, as well as the presence of headaches [19, 20]. The score is expressed as a percentage from 0% (no impairment) to 100% (total impairment) [21]. The NDI has evidence to support test–retest reliability, internal consistency, construct validity and concurrent validity with the McGill Pain Questionnaire in populations with neck pain [19, 20].

Explanatory variables—physical performance measures:

Resting scapular position

The scapula was defined as being upwardly (> 0°) or downwardly (< 0°) rotated in the plane of the scapula, with 0° representing a neutral position, during relaxed upright standing with the arms by the trunk [22]. A bubble inclinometer (Baseline, Fabrication Enterprises Inc., USA) was placed on the spine of the scapula to record the angle of rotation. The average of three repetitions was recorded bilaterally and the mean used for analysis.

Shoulder and neck active range of motion (AROM)

Three positions were used for measuring AROM: standing (bilateral shoulder flexion, abduction and hand-behind-back), supine lying (bilateral neck rotation and shoulder external rotation) and upright sitting (neck flexion and extension). Hand-behind-back is a combination of shoulder internal rotation, extension and adduction, and was graded on a scale from 0 (hand reaches within 5 cm of the opposite scapula) to 4 (cannot move the hand behind the trunk) [23]. All other AROM measurements were taken with a bubble inclinometer. These measurements have demonstrated moderate to high test–rest and intra-tester reliability [24–27]. Three practice trials for each movement were conducted, after which three repetitions were recorded and the mean used for analysis.

Shoulder and neck maximal isometric strength

Isometric neck and shoulder strength was measured with a dynamometer (BFG, Mecmesin, USA) attached to a rigid frame with two adjustable components. Isometric neck flexion and extension strength were tested with the participant sitting on a rigid frame, their trunk supported by an adjustable backrest and a belt across their chest (Fig. 1a, b). The adjustable resistance arm was positioned so that the dynamometer resisted neck flexion via the forehead and extension via the occiput. Participants were instructed to push with their forehead (flexion) or occiput (extension) against the resistance in an arc towards the floor in front (flexion) or behind (extension) them. Isometric shoulder flexion strength was measured with participants in standing, their back resting against a wall and their testing arm in line with the trunk (neutral) (Fig. 1c). The resistance pad of the dynamometer was applied to the anterior distal humerus just above the elbow crease with the elbow extended and forearm in full supination. Participants were instructed to perform their maximal effort into shoulder flexion against the dynamometer resistance pad.

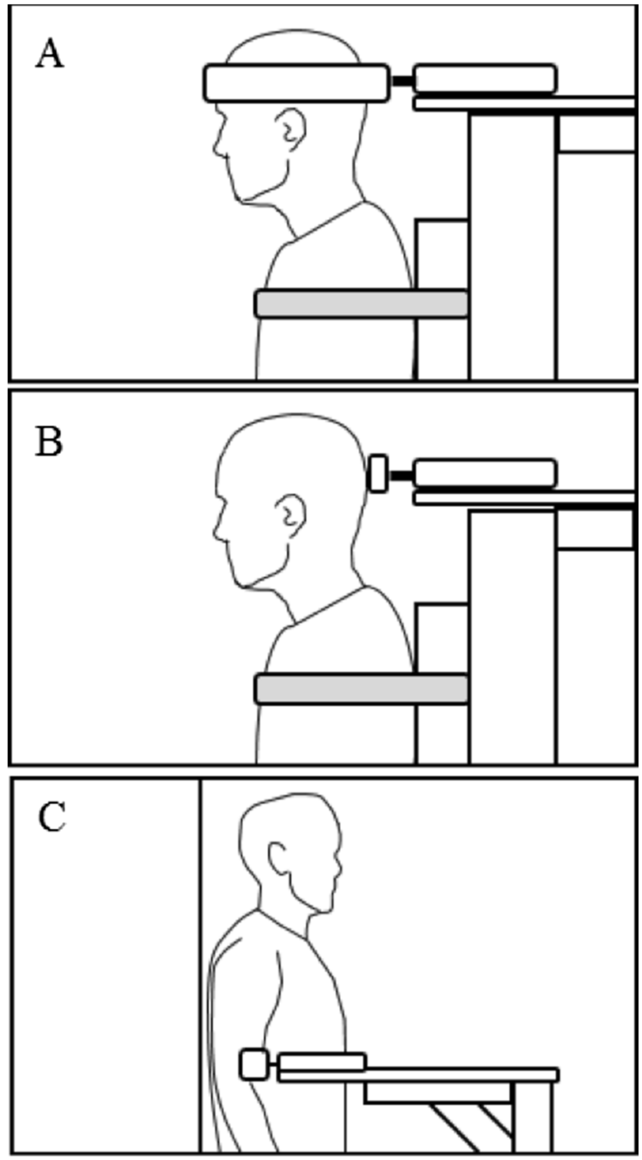

Fig. 1 The apparatus for the measurement of isometric muscle strength consisted of a specially designed ridged frame attached to a dynamometer with the participant positioned in sitting for **a** neck extension and **b** neck flexion, and standing for **c** shoulder flexion

Standard verbal encouragement was given during all strength tests, which were discontinued if pain was reported. Two submaximal contractions were conducted as a warm-up followed by up to three experimental repetitions of maximal effort, with a 1 min seated rest between repetitions. A third repetition was performed if the second repetition exceeded the first to ensure the maximal effort had been achieved. The maximum value recorded was used for analyses. The order of strength tests (neck, shoulder) was randomised across all participants to control for any effects of fatigue. At the shoulder, the non-operated arm was tested first to familiarise the participant with the test. Previous studies have shown isometric strength tests to be reliable for both the neck (ICC 0.94–0.99) [28, 29] and shoulder (0.79–0.99) [30, 31].

Explanatory variables—participant and clinical characteristics

Height and weight were self-reported by participants. Medical records were reviewed for other patient (e.g. age at time of surgery), tumour (e.g. staging) and treatment-related (e.g. adjuvant treatment) information. Type of ND was based on the classification system developed by the American Head and Neck Society [11–13]. The most recent ND was use to classify patients by type of ND if there was a history of more than one. Each participant was described as having an affected (ipsilateral to surgery) and unaffected (contralateral to surgery) side. For participants with a history of bilateral ND, the affected side was considered as either the side with the more extensive ND (if procedures were different) or most restricted shoulder AROM (if procedures were the same).

Data analysis

All statistical analyses were conducted using Stata (*Stata Statistical Software, Release 13*; StataCorp LP, College, Station, TX). Shapiro–Wilk tests and visual inspection with histograms indicated the data were not normally distributed. Therefore, Kruskal–Wallis tests were used to investigate potential differences in questionnaire outcomes between ND subgroups. Generalised linear models were used to examine whether physical impairment, patient, tumour and treatment-related variables were associated with either (1) NDII, (2) QuickDASH or (3) NDI. An identity link function was selected for the NDII model and log link functions were selected for the QuickDASH and NDI models to optimise model fit. Age, sex, body mass index, type of ND, time since surgery and accessory nerve status were included as potential explanatory variables in each model. In addition, the least absolute shrinkage and selection operator (LASSO) technique was used to guide variable selection for inclusion of other potential explanatory variables (to minimise risk of over-fitting) for the three respective generalised linear models. The additional variables considered during the LASSO technique for inclusion were affected scapular resting position, affected shoulder AROM (all directions), neck AROM (all directions), affected shoulder flexion strength (measured in kilogramme/force (kgf)), shoulder strength ratio (affected/unaffected), neck flexion and extension strength (kgf), neck strength ratio (cervical flexion/extension), T stage, N stage, tumour pathology, tumour location, history of ND and use of adjuvant therapy. Robust standard errors were used to account for the potential influence of heteroskedasticity in the generalised linear models [32, 33]. Variance inflation factors were used to rule out the potential presence of multicollinearity. To examine the potential influence of using the aforementioned LASSO variable selection technique in comparison to the selection of variables from a series of univariate regressions, a sensitivity analysis was conducted for each of the models. Variables with a p value of ≤ 0.20 in the univariate regressions were included within a generalised linear model and model outputs (coefficients and confidence intervals for significant findings) were then compared to the output from the primary analyses (and were consistent with the primary analysis and therefore have not been presented).

Results

A total of 87 patients participated in this study: 44 (51%) following unilateral SND, 24 (28%) following unilateral MRND, 16 (18%) following bilateral ND and 3 (3%) following unilateral RND. Participants with RND were not included in analyses due to the small number ($n = 3$) leaving 84 participants in the study cohort (Table 1). The median (Q1, Q3) age at the time of surgery was 61 (48, 69) years. Time since surgery ranged from a minimum of 205 days to a maximum of 2199 days, with median (Q1, Q3) values of 1277 (700, 1580) days. The majority of participants were male ($n = 57$, 68%). The largest group by pathology was squamous cell carcinoma ($n = 48$, 57%). Fifty-one participants (61%) were treated with XRT, 49 (96%) post-operatively, and 22 (26%) received chemotherapy, most of whom received it in conjunction with XRT ($n = 17$, 20%).

A summary of patient reported NDII, QuickDASH and NDI scores is presented Table 2 per type of ND with the distribution of scores for each outcome measure displayed in Fig. 2. In summary, reduced HRQOL (NDII) and mild levels of upper limb (QuickDASH) and neck disability (NDI) were present among a substantial proportion of participants. Fifty participants (60%) reported a QuickDASH score of ≥ 10, suggesting they were experiencing meaningful dysfunction. A similar number ($n = 48$, 57%) had at least a mild level of neck disability (NDI > 10%). Of those with neck disability, 29 (35%), 11 (13%) and 7 (8%) experienced mild, moderate or severe levels of neck disability, respectively. There were no significant differences in NDII, QuickDASH or NDI scores between type of ND.

Median active range of motion and strength values were lower on participants' affected side than unaffected side and are summarised in Table 3. The results of the generalised linear modelling for the (1) NDII, (2) QuickDASH and (3) NDI are presented in Table 4.

Reduced HRQOL was associated with reduced shoulder flexion AROM (coeff (95% CI) = 0.56 (0.24, 0.86)), being

Table 1 Cohort characteristics

Clinical or treatment-related factor	Whole ND cohort *N* (%)	Unilateral SND *N* (%)	Unilateral MRND *N* (%)	Bilateral ND *N* (%)
Participants	84 (100%)	44 (52%)	24 (29%)	16 (19%)
Age at surgery, years				
Median (Q1, Q3)	61 (48, 69)	62 (47, 71)	58 (49, 66)	57 (49, 68)
Length of stay, days[a]				
Median (Q1, Q3)	6 (5, 15)	6 (5, 12)	6 (5, 8)	13 (8, 18)
Time since surgery, days				
Median (Q1, Q3)	1277 (700, 1580)	1264 (792, 1550)	1305 (611, 1589)	1157 (590, 2038)
Total theatre time, h				
Median (Q1, Q3)	6.1 (4.7, 10.4)	6.4 (4.3, 9.5)	5.1 (4.5, 6.2)	10.7 (6.9, 12.9)
Body mass index, kg/m^2				
Median (Q1, Q3)	26 (23, 29)	27 (23, 29)	25 (23, 28)	25 (21, 31)
Sex—male	57 (68%)	28 (64%)	18 (75%)	11 (69%)
History of > 1 ND	11 (13%)	7 (16%)	1 (4%)	3 (19%)
Level V involved in the ND	41 (49%)	7 (16%)	24 (100%)	10 (63%)
Accessory nerve sacrificed	5 (6%)	0 (0%)	3 (13%)	2 (13%)
SCM resected in part or whole	13 (15%)	2 (5%)	6 (25%)	5 (31%)
IJV resected in part or whole	11 (13%)	2 (5%)	6 (25%)	3 (19%)
History of recurrent disease	38 (45%)	20 (45%)	13 (54%)	5 (31%)
Disease pathology				
SCC	48 (57%)	25 (57%)	13 (54%)	10 (63%)
PTC	17 (20%)	10 (23%)	1 (4%)	6 (37%)
Melanoma	11 (13%)	5 (11%)	6 (25%)	0 (0%)
Other	8 (10%)	4 (9%)	4 (17%)	0 (0%)
Location of tumour/disease				
Mucosal	31 (37%)	16 (36%)	7 (29%)	8 (50%)
Neck nodal metastases	28 (33%)	13 (30%)	13 (54%)	2 (13%)
Cutaneous	14 (17%)	9 (20%)	4 (17%)	1 (6%)
Thyroid	11 (13%)	6 (14%)	0 (0%)	5 (31%)
T stage				
T0	8 (10%)	3 (7%)	5 (21%)	0 (0%)
T1	7 (8%)	3 (7%)	2 (8%)	2 (13%)
T2	11 (13%)	8 (18%)	2 (8%)	1 (6%)
T3	5 (6%)	2 (5%)	0 (0%)	3 (19%)
T4	15 (18%)	5 (11%)	4 (17%)	6 (38%)
Tis	1 (1%)	0 (0%)	1 (4%)	0 (0%)
Tx	4 (5%)	2 (5%)	2 (8%)	0 (0%)
Not available	33 (39%)	21 (48%)	8 (33%)	4 (25%)
N stage				
N0	11 (13%)	9 (21%)	1 (4%)	1 (6%)
N1	12 (14%)	6 (14%)	2 (8%)	4 (25%)
N2	27 (32%)	8 (18%)	12 (50%)	7 (44%)
N3	1 (1%)	0 (0%)	1 (4%)	0 (0%)
rN+	30 (36%)	20 (45%)	6 (25%)	4 (25%)
rN0	3 (4%)	1 (2%)	2 (8%)	0 (0%)
XRT				
No XRT	33 (39%)	19 (43%)	8 (33%)	6 (38%)
Post-operative 60 Gy/30#	15 (18%)	6 (14%)	5 (21%)	4 (25%)
Post-operative > 60 Gy/30#	8 (10%)	3 (7%)	3 (13%)	2(13%)

Table 1 (continued)

Clinical or treatment-related factor	Whole ND cohort *N* (%)	Unilateral SND *N* (%)	Unilateral MRND *N* (%)	Bilateral ND *N* (%)
Post-operative < 60 Gy/30#	11 (13%)	6 (14%)	4 (17%)	1(6%)
Post-operative dose unknown	11 (13%)	6 (14%)	3 (13%)	2 (13%)
≥ 2 episodes of XRT	4 (5%)	3 (7%)	0 (0%)	1 (6%)
Pre-operative XRT	2 (2%)	1 (2%)	1 (4%)	0 (0%)
Chemotherapy				
No chemotherapy	62 (74%)	35 (80%)	14 (58%)	13 (81%)
Cisplatin	10 (12%)	4 (9%)	6 (25%)	0 (0%)
Other	12 (14%)	5 (11%)	4 (17%)	3 (19%)
Adjuvant treatment				
Surgery only	30 (36%)	18 (41%)	6 (25%)	6 (38%)
Surgery + XRT	32 (38%)	17 (39%)	8 (33%)	7 (44%)
Surgery + concurrent CXRT	17 (20%)	7 (16%)	7 (29%)	3 (19%)
Other[b]	5 (6%)	2 (5%)	3 (13%)	0 (0%)
Location of surgery conducted concurrently with ND				
ND only	10 (23%)	12 (15%)	1 (6%)	23 (27%)
Oral cavity, oropharynx	8 (18%)	3 (25%)	5 (31%)	16 (19%)
Pharynx and larynx	6 (14%)	4 (33%)	3 (19%)	13 (15%)
Face and skin	15 (34%)	4 (33%)	1 (6%)	20 (24%)
Neck[c]	6 (14%)	4 (33%)	8 (50%)	18 (21%)
Reconstruction	9 (2%)	3 (33%)	7 (44%)	19 (23%)
Skull base	2 (5%)	0 (0%)	0 (0%)	2 (2%)
Outside head/neck region	1 (2%)	0 (0%)	0 (0%)	1 (1%)

ND neck dissection, *SND* selective neck dissection, *MRND* modified radical neck dissection, *SCM* sternocleidomastoid, *IJV* internal jugular vein, *SCC* squamous cell carcinoma, *PTC* papillary thyroid carcinoma, *XRT* radiation therapy, *CXRT* chemoradiation therapy

[a] Length of stay as an inpatient following ND surgery

[b] Surgery with chemotherapy only or surgery with chemotherapy and XRT delivered separately

[c] For example, thyroidectomy, tracheostomy

unable to pass the hand behind the trunk (category 4 hand-behind-back) (− 37.21 (− 64.19, − 10.22)), reduced shoulder flexion strength ratio (27.19 (11.72, 42.67)), younger age at surgery (0.85 (0.56, 1.13)), greater BMI (− 1.84 (− 2.82, − 0.85)), having undergone a bilateral ND (− 12.49 (− 24.69, − 0.29)), having a history of > 1 ND (− 17.00 (− 29.37, − 4.62)) and having ND with concurrent CXRT (− 21.46 (− 37.57, − 5.35)).

Higher levels of upper limb disability were associated with reduced hand-behind-back AROM (category 1 hand-behind-back coeff (95% CI) = 0.47 (0.04, 0.89); category 4 1.08 (0.49, 1.66)) and decreased shoulder flexion strength ratio (− 1.01 (− 1.70, − 0.33)). Lower levels of upper limb disability were associated with having no T stage available (compared with T0) (coeff (95% CI) = − 0.76 (− 1.36, − 0.16)). Being of a younger age at surgery was trending towards a significant relationship with lower levels of upper limb disability (coeff (95% CI) = -22.78×10^{-3} (-46.97×10^{-3}, 1.42×10^{-3}); $p = 0.07$).

High self-reported neck disability was significantly associated with reduced AROM shoulder flexion (coeff (95% CI) =

Table 2 Results from the three primary outcomes: Neck Dissection Impairment Index (NDII), Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH), and Neck Disability Index (NDI)

Primary outcome	Whole cohort Median (Q1, Q3)	Unilateral SND Median (Q1, Q3)	Unilateral MRND Median (Q1, Q3)	Bilateral ND Median (Q1, Q3)
NDII	76 (49, 93)	83 (65, 94)	74 (39, 93)	64 (28, 84)
QuickDASH	14 (2, 32)	13 (2, 30)	11 (1, 33)	18 (7, 52)
NDI	14 (6, 28)	16 (6, 27)	12 (2, 34)	9 (8, 40)

NDII Neck Dissection Impairment Index, *QuickDASH* Quick Disabilities of the Arm, Shoulder and Hand, *NDI* Neck Disability Index, *SND* selective neck dissection, *MRND* modified radical neck dissection, *ND* neck dissection

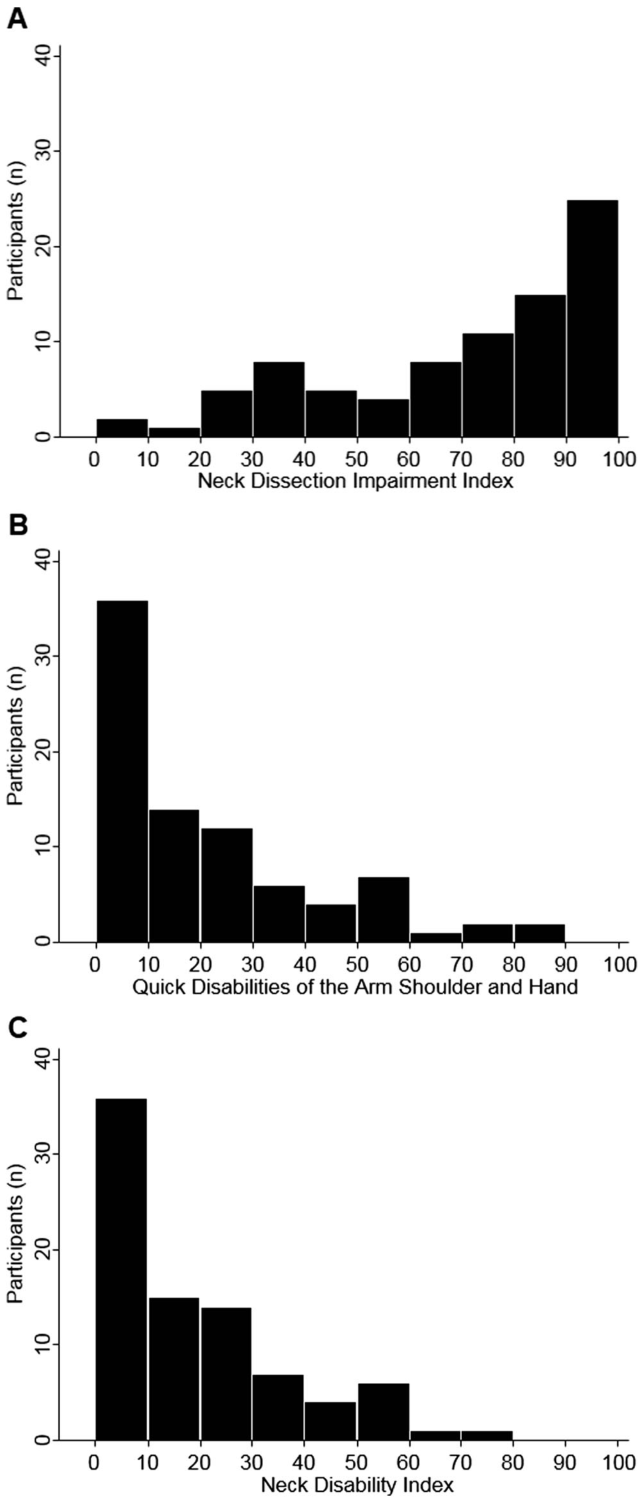

Fig. 2 Results for the three primary outcome measures: **a** Neck Dissection Impairment Index (0 worst HRQOL, 100 best HRQOL); **b** Quick Disabilities of the Arm, Shoulder and Hand (0 no upper limb impairment, 100 total upper limb impairment); **c** Neck Disability Index (0% no neck impairment, 100% total neck impairment)

− 0.01 (− 0.02, 0.00)), a younger age at surgery (− 0.05 (− 0.07, − 0.03)), greater BMI (0.05 (0.01, 0.08)), having ND with concurrent CXRT (0.71 (0.10, 1.32)) and three of the categories for restricted shoulder hand-behind-back movement (e.g. category 4 2.36 (1.05, 3.66)). Two of the T stage categories were significantly associated with neck disability (with reference to T0): having T1 disease was associated with greater neck disability (coeff (95% CI) = 0.62 (0.24, 1.01)), and having T4 disease was associated with less neck disability (− 0.49 (− 0.88, − 0.10)). Accessory nerve sacrifice was associated with less neck disability (coeff (95% CI) = − 0.92 (− 1.50, − 0.33)); however, this finding is likely spurious and should be interpreted with caution as the number of individuals with accessory nerve sacrifice was small (*n* = 5).

Discussion

This study was successful in identifying associations between physical function, HRQOL and disability in patients within 5 years of ND for HNC. Bilateral ND (in comparison to unilateral SND) and post-operative concurrent CXRT (in comparison to no adjuvant treatment) were associated with poorer HRQOL. In addition, receiving concurrent CXRT was also associated with greater neck disability. In contrast, there was no evidence for an association between type of ND and either upper limb or neck disability. A range of other patient-, tumour- and treatment-related factors were associated with reduced HRQOL, upper limb disability or neck disability. This evidence suggests the reasons for reduced HRQOL or upper limb and neck disability following ND are multi-factorial. Patients receiving bilateral ND or post-operative concurrent CXRT, or with a history of more than one ND, may require close monitoring for signs of poor recovery of HRQOL and referral to appropriate rehabilitation health professionals to address underlying concerns.

Shoulder range of motion plus strength were associated with upper limb disability in the present study. Restricted hand-behind-back AROM, rather than abduction, was associated with greater upper limb disability. Hand-behind-back is a movement essential for many key tasks of daily living (e.g. showering, drying and dressing oneself). However, it is not commonly a focus of physical rehabilitation programmes post-ND [34, 35]. Instead, programmes may primarily focus on shoulder abduction, both as an outcome measure and a target for therapy [34]. The present study also found an association between reduced shoulder strength and increased upper limb disability. Previously, progressive resistance exercise training with machine weights has been shown to improve upper body strength, which was then determined to be associated with better shoulder function [34]. Whilst both the present study and this study of exercise training show association and not causation, these results could support the importance of retraining muscular strength during rehabilitation after ND,

Table 3 Results from the physical measures of scapular resting position, neck and shoulder AROM and isometric muscle strength

Physical outcome measure	Participants ($n = 84$) Median (Q1, Q3)		
	Affected side	Unaffected side	Total range
Scapular resting position (°)	− 2 (− 8, 4)	0 (− 4, 2)	
Shoulder AROM (°)			
Shoulder flexion	150 (130, 162)	160 (144, 166)	
Shoulder abduction	145 (119, 155)	153 (139, 165)	
Shoulder external rotation	45 (35, 60)	50 (40, 60)	
Hand-behind-back	35 (42%)[a]	29 (35%)[a]	
Neck AROM (°)			
Neck rotation	65 (54, 75)	63 (51, 70)	125 (110, 142)
Neck flexion			54 (45, 60)
Neck extension			48 (40, 55)
	Affected side	Unaffected side	Ratio
Shoulder flexion strength (kg)			
Female	11.32 (7.64, 14.64)	12.38 (8.20, 14.86)	0.97 (0.83, 1.03)
Male	20.19 (13.80, 25.25)	20.56 (16.02, 27.48)	1.01 (0.81, 1.21)
	Flexion	Extension	Ratio
Neck strength (kg)			
Female	5.27 (4.26, 7.82)	9.09 (7.74, 10.20)	0.63 (0.50, 0.74)
Male	9.09 (6.35, 10.80)	11.43 (8.41, 15.31)	0.81 (0.51, 0.95)

Q1 quartile one, *Q3* quartile three, *AROM* active range of motion

[a] Number (%) of people unable to reach opposite scapula or worse (categories 1 to 4)

but also suggest hand-behind-back range ought to be considered.

Significant associations with the NDII identified in the present study have some similarities to previous research [8]. Gallagher and colleagues [8] assessed 167 patients at a median of 28.2 (range, 12–84) months following ND. NDII scores were significantly worse in patients who received MRND compared with SND, which was not the case in the present study. There was a small difference between the studies in the use of chemotherapy (present study, 24% vs. Gallagher, 16%) and XRT (present study, 61% vs. Gallagher, 75%). Despite this, both studies found associations between these adjuvant treatments and reduced HRQOL. Together, these findings highlight the potential for impairments to HRQOL to persist several years after ND, and for surgery, XRT and chemotherapy to have individual and cumulative effects on HRQOL. The presence of an association between younger age and increased neck disability (as well as quality of life (NDII) in this cohort) seems counter-intuitive, but may be related to the history of malignancy within this cohort (i.e. younger patients may not have age-related chronic diseases that have previously impaired HRQOL; therefore, the diagnosis of a life-limiting illness has a greater negative effect on their HRQOL compared with older patients). Interestingly, an association was present between T4 disease (compared with T0 disease) and lower levels of neck disability. The authors are unable to explain this observation. One theoretical and untested explanation may be that having received a poor prognosis at diagnosis, patients with T4 disease who survive their cancer may be inclined to self-report positive outcomes as a reflection of their pleasure in being alive.

In addition to an association with HRQOL, undergoing concurrent CXRT was also significantly associated with neck disability. Soft tissue side effects can occur following XRT, including fibrosis [36] and lymphoedema [37], although the evidence for an exacerbation of accessory nerve injury by XRT beyond ND has been inconsistent: some studies reported no additional burden [38–43], while others reported lower objective or subjective findings in patients who had ND and XRT [44, 45]. The most common chemotherapy agent in the present study was cisplatin, a drug delivered with XRT to patients with locally advanced disease to increase overall survival [46]. Known side effects of cisplatin and XRT include dysphagia, xerostomia and ototoxicity [47]. Fatigue is also a side effect of cisplatin [48]. Cancer-related fatigue is the most commonly reported side effect across all cancers [49]. While fatigue was not directly measured (as it was beyond the scope of the present study aims), it is plausible that cancer-related fatigue contributed to poorer HRQOL scores, particularly among people who had received cisplatin. Further prospective studies that consider XRT dose and drug type may shed light on how adjuvant treatment can impact upon musculoskeletal functioning.

Table 4 Generalised linear models for the Neck Dissection Impairment Index (NDII), Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH), and Neck Disability Index (NDI)

Explanatory variable	Model 1 NDII (link—identity)	Model 2 QuickDASH (link—log)	Model 3 NDI (link—log)
	Coefficient (95% CI); *p* value	Coefficient (95% CI); *p* value	Coefficient (95% CI); *p* value
Physical factors:			
AROM shoulder flexion[c]	0.56 (0.24, 0.86); < 0.001*	n/a	− 0.01 (− 0.02, 0.00); 0.05*
AROM shoulder abduction[c]	− 0.10 (− 0.33, 0.12); 0.37	− 9.46 (− 21.33, 2.40)[a]; 0.12	n/a
AROM shoulder HBB (reference = category 0)[d]			
Category 1	2.04 (− 8.10, 12.27); 0.70	0.47 (0.04, 0.89); 0.03*	0.59 (0.14, 1.03); < 0.01*
Category 2	0.40 (− 16.89, 17.68); 0.96	0.65 (− 0.48, 1.79); 0.26	1.26 (0.61, 1.91); < 0.001
Category 3	3.59 (− 17.83, 25.01); 0.74	0.51 (− 0.01, 1.04); 0.05	0.72 (0.08, 1.35); 0.03*
Category 4	− 37.21 (− 64.19, − 10.22); < 0.01*	1.08 (0.49, 1.66); < 0.001*	2.36 (1.05, 3.66); < 0.001*
Strength shoulder flexion ratio	27.19 (11.72, 42.67); < 0.01*	− 1.01 (− 1.70, − 0.33); < 0.001*	− 0.17 (− 0.73, − 0.39); 0.54
AROM neck extension	0.18 (− 0.15, 0.52); 0.29	n/a	− 0.01 (− 0.03, 0.00); 0.07
AROM neck rotation to the affected side	0.11 (− 0.30, 0.53); 0.60	n/a	2.40 (− 14.93, 19.73)[a]; 0.79
AROM neck rotation to the unaffected side	0.42 (− 0.08, 0.94); 0.11	n/a	n/a
Scapular resting position[c]	n/a	n/a	7.39 (− 33.48, 48.26)[a]; 0.72
Patient factors:			
Age at surgery	0.85 (0.56, 1.13); < 0.001*	− 22.78 (− 46.97, 1.42)[a]; 0.07	− 0.05 (− 0.07, − 0.03); < 0.001*
Sex (reference = female)			
Male	− 4.72 (− 12.89, 3.46); 0.26	− 0.13 (− 0.58, 0.32); 0.59	0.09 (− 0.27, 0.47); 0.62
Body mass index	− 1.84 (− 2.82, − 0.85); < 0.001*	− 0.01 (− 0.07, 0.05); 0.76	0.05 (0.01, 0.08); < 0.01*
Surgical factors:			
Time since surgery	− 2.78 (− 10.1, 4.52)[a]; 0.46	4.39 (− 25.34, 34.13)[b]; 0.77	− 23.29 (− 55.53, 8.94)[b]; 0.16
Type of neck dissection (reference = unilateral SND)			
Unilateral MRND	− 3.00 (− 11.81, 5.81); 0.50	− 0.35 (− 0.83, 0.12); 0.15	− 0.13 (− 0.81, 0.54); 0.70
Bilateral ND	− 12.49 (− 24.69, − 0.29); 0.05*	0.56 (− 0.44, 1.57); 0.27	0.17 (− 0.28, 0.62); 0.46
Status of accessory nerve (reference = preserved)			
Sacrificed	9.85 (− 4.17, 23.88); 0.17	− 0.36 (− 1.00, 0.28); 0.27	− 0.92 (− 1.50, − 0.33); < 0.01*
History of ND (reference = no)			
Yes	− 17.00 (− 29.37, − 4.62); < 0.01*	n/a	n/a
Adjuvant therapy (reference = ND only)			
ND with post-operative XRT	− 9.82 (− 22.47, 2.82); 0.13	n/a	0.40 (− 0.23, 1.02); 0.21
ND with post-operative CXRT	− 21.46 (− 37.57, − 5.35); < 0.01*	n/a	0.71 (0.10, 1.32); 0.02*
Other	− 14.86 (− 30.08, 0.37); 0.06	n/a	− 0.87 (− 1.83, 0.08); 0.07
Tumour-related factors			
T stage (reference = T0)			
T1	− 17.56 (− 37.75, 2.63); 0.09	0.09 (− 0.56, 0.74); 0.78	0.62 (0.24, 1.01); < 0.01*
T2	8.93 (− 6.61, 24.48); 0.26	− 0.44 (− 1.30, 0.42); 0.31	− 0.18 (− 0.82, 0.46); 0.58
T3	2.19 (− 21.93, 26.31); 0.86	− 0.64 (− 2.12, − 0.84); 0.40	0.35 (− 0.40, 1.10); 0.36
T4	7.94 (− 6.52, 22.40); 0.28	− 0.73 (− 1.62, 0.15); 0.11	− 0.49 (− 0.88, − 0.10); 0.01*
Tis	0.20 (− 17.02, 17.42); 0.98	− 0.55 (− 1.34, 0.24); 0.17	0.47 (− 0.24, 1.19); 0.20
Tx	7.46 (− 9.04, 23.95); 0.38	− 0.26 (− 1.58, 1.07); 0.70	− 0.02 (− 0.94, 0.90); 0.97
No T stage available	8.14 (− 6.09, 22.36); 0.26	− 0.76 (− 1.36, − 0.16); 0.01*	− 0.71 (− 1.55, 0.14); 0.10

Table 4 (continued)

Explanatory variable	Model 1 NDII (link—identity)	Model 2 QuickDASH (link—log)	Model 3 NDI (link—log)
Pathology (reference = SCC)			
PTC	4.28 (− 11.82, 20.37); 0.60	n/a	− 0.04 (− 0.67, 0.59); 0.99
Melanoma	− 0.61 (− 16.40, 15.19); 0.94	n/a	0.06 (− 0.71, 0.83); 0.88
Other	11.42 (− 5.30, 28.14); 0.18	n/a	0.18 (− 0.92, 1.28); 0.75

NDII Neck Dissection Impairment Index, *QuickDASH* Quick Disabilities of the Arm, Shoulder and Hand, *NDI* Neck Disability Index, *AROM* active range of motion, *HBB* hand-behind-back, *SND* selective neck dissection, *MRND* modified radical neck dissection, *ND* neck dissection, *XRT* radiation therapy, *CXRT* chemoradiation therapy, *SCC* squamous cell carcinoma, *PTC* papillary thyroid carcinoma

[a] Scientific notation used: this result is $\times 10^{-3}$

[b] Scientific notation used: this result is $\times 10^{-5}$

[c] This outcome refers to the affected side

[d] Categories within the HBB are as follows: 0 = hand reaches < 5 cm away from opposite scapula; 1 = hand reaches 6–15 cm away from opposite scapula; 2 = hand reaches the opposite iliac crest; 3 = hand reaches the buttock; 4 = hand unable to pass behind the trunk. *$p < 0.05$

Where coefficients are not displayed ('n/a'), the most parsimonious model did not contain this explanatory variable

This study has described key factors associated with neck disability, which have been identified as underreported in a recent systematic review [14]. Previous studies of patients with HNC have reported similar NDI scores to the present study, but were much smaller and not limited to a surgical population [50] [51]. In contrast, the NDI has been used extensively in the musculoskeletal neck pain literature [21] to measure self-reported neck disability. Younger patients with musculoskeletal neck pain often have less neck disability [52], which is in contrast to the present study where younger age was associated with greater neck disability. Accessory nerve sacrifice was associated with less neck disability in the model for the NDI; however, this finding is likely spurious and should be interpreted with caution as the number of individuals with accessory nerve sacrifice was small ($n = 5$). Overall, the results demonstrate that the neck as well as the shoulder ought to be considered as a source of dysfunction in patients managing the long-term effects of this procedure.

Other patient populations with musculoskeletal pain have also demonstrated altered axioscapular motor function during an upper limb task. Elite swimmers with shoulder pain displayed increased anterior scalene electromyography (EMG) activity compared with asymptomatic elite swimmers [53]. In addition, individuals with mechanical neck pain demonstrated altered scapular kinematics during shoulder elevation, and failed to demonstrate any adaptation in muscular activation to neck extensor muscle fatigue (unlike healthy control subjects) [54]. With regard to experimentally induced pain, localised and referred pain from hypertonic saline injection into the splenius capitis muscle has resulted in changes to trunk and axioscapular muscle EMG activity (including reduced upper trapezius activity) during elevation of the shoulder in the scapular plane [55]. It is clear from this evidence that there is a biomechanical relationship between the cervical spine and the shoulder, and that musculoskeletal pain can affect motor activation across this body region. Changes to muscular activity during functional tasks have been proposed to be a protective mechanism for painful structures [56]. Therefore, the reduction in shoulder flexion AROM found in this study may be a consequence of neck or shoulder pain, or a cause of neck or shoulder pain that, in either circumstance, is reflected in increased levels of self-perceived pain-related disability of the upper limb and neck.

Participants with a history of unilateral RND were not included in the statistical analyses within this study because this sub-group was small ($n = 3$). The HRQOL and disability scores for these $n = 3$ participants were not consistently poor (NDII range 60 to 97.5; QuickDASH range 6 to 20; NDI range 0 to 20). It is therefore not known from the present data if unilateral RND is associated with worse HRQOL or self-reported disability in comparison to unilateral SND. Previous research has demonstrated associations between RND and reduced shoulder abduction AROM [57, 58] and strength [39], shoulder and neck pain [41], and shoulder function measured with the Constant Shoulder Score [59]. However, with the rise of selective and super-selective ND [60], the frequency of RND is decreasing. Consequently, obtaining a better understanding of the long-term outcomes of patients who undergo more selective procedures is more clinically relevant in the modern Head and Neck Clinic.

There are several limitations and strengths of the present study that may influence the interpretation of the aforementioned findings. Measuring shoulder strength in a neutral position (beside the trunk) may have masked findings of reduced strength in more elevated ranges; however, this position was chosen in order to ensure all participants could complete the test. Recording muscular strength objectively is novel for this patient population, as previous studies have preferred the subjective manual muscle testing approach [6, 61, 62]. The use of strength ratios has limitations in the presence of bilateral or widespread strength deficits; therefore, the analysis considered both strength ratios and raw strength data for potential inclusion in the linear models. Another limitation of the study was that participants were from one geographical region in an industrialised nation with accessible health services, and patients from dissimilar societies may not report comparable levels of dysfunction. Regarding rehabilitation, there may have been individual variation in the treatment received depending on presenting signs and symptoms during the early recovery period that may have affected disability outcomes, but this was considered beyond the scope of the present investigation. The ever present risk of survivorship bias may have also influenced the participant sample in this cross-sectional study of patients with a life-limiting illness, in that the conclusions drawn may not reflect the lived experiences of those patients who had passed away before this study was conducted. Despite this, the findings of this study are informative to the prevention and management of neck and upper limb-related disability and HRQOL in HNC survivors.

Conclusion

Patients can experience reduced HRQOL and upper limb and neck disability following ND. Undergoing a bilateral ND is associated with worse quality of life but not upper limb or neck disability. Concurrent CXRT appears to have a negative effect on quality of life and neck disability. The patient-, tumour- and treatment-related factors associated with poorer HRQOL and greater disability of the head and neck identified in the present study may assist clinical teams in identifying patients who may require referral for rehabilitative interventions.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants This study was approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (reference no. HREC/14/QRBW/71).

Informed consent Informed consent was obtained from all individual participants included in this study.

References

1. National Comphrehensive Cancer Network (2016) Head and neck cancers, version 1.2016. https://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf. Accessed 9 Jan 2017.
2. Rathod S, Livergant J, Klein J, Witterick I, Ringash J. A systematic review of quality of life in head and neck cancer treated with surgery with or without adjuvant treatment. Oral Oncol. 2015;51(10):888–900. https://doi.org/10.1016/j.oraloncology.2015.07.002.
3. van Wilgen CP, Dijkstra PU, van der Laan BF, Plukker JT, Roodenburg JL. Shoulder complaints after neck dissection; is the spinal accessory nerve involved? Br J Oral Maxillofac Surg. 2003;41(1):7–11.
4. Teymoortash A, Hoch S, Eivazi B, Werner JA. Postoperative morbidity after different types of selective neck dissection. Laryngoscope. 2010;120(5):924–9. https://doi.org/10.1002/lary.20894.
5. Agha-Mir-Salim P, Schulte-Mattler W, Funk U, Lautenschlager C, Bloching M, Berghaus A. Origin of shoulder pain after "neck dissection". Importance of the cervical plexus. HNO. 2002;50(6):544–52.
6. Cappiello J, Piazza C, Giudice M, De Maria G, Nicolai P. Shoulder disability after different selective neck dissections (levels II–IV versus levels II–V): a comparative study. Laryngoscope. 2005;115(2):259–63. https://doi.org/10.1097/01.mlg.0000154729.31281.da.
7. Laverick S, Lowe D, Brown J, Vaughan E, Rogers S. The impact of neck dissection on health-related quality of life. Arch Otolaryngol Head Neck Surg. 2004;130:149–54.
8. Gallagher K, Sacco A, Lee J, Taylor R, Chanowski E, Bradford C, et al. Association between multimodality neck treatment and work and leisure impairment: a disease-specific measure to assess both impairment and rehabilitation after neck dissection. JAMA Otolaryngol Head Neck Surg. 2015;141(10):888–93.
9. van Wilgen CP, Dijkstra PU, van der Laan BFAM, Plukker JTM, Roodenburg JLN. Shoulder complaints after nerve sparing neck dissections. Int J Oral Max Surg. 2004;33(3):253–7.
10. Chepeha D, Taylor R, Chepeha J, Teknos T, Bradford CR, Sharma P, et al. Functional assessment using Constant's shoulder scale after modified radical and selective neck dissection. Head Neck. 2002;24:432–6.
11. Robbins KT, Clayman G, Levine PA, Medina JE, Sessions RB, Shaha A, et al. Neck dissection classification update. Arch Otolaryngol Head Neck Surg. 2002;128:751–8.
12. Robbins KT, Medina JE, Wolfe GT, Levine PA, Sessions RB, Pruet CW. Standardizing neck dissection terminology. Arch Otolaryngol Head Neck Surg. 1991;117:601–5.
13. Robbins KT, Shaha AR, Medina JE, Califano JA, Wolf GT, Ferlito A, et al. Consensus statement on the classification and terminology of neck dissection. Arch Otolaryngol Head Neck Surg. 2008;134(5):536–8. https://doi.org/10.1001/archotol.134.5.536.
14. Gane EM, Michaleff ZA, Cottrell MA, McPhail SM, Hatton AL, Panizza BJ, et al. Prevalence, incidence, and risk factors for shoulder and neck dysfunction after neck dissection: a systematic review. Eur J Surg Oncol. 2017;43:1199–218. https://doi.org/10.1016/j.ejso.2016.10.026.

15. Taylor R, Chepeha J, Teknos T, Bradford C, Sharma P, Terrell J, et al. Development and validation of the neck dissection impairment index: a quality of life measure. Arch Otolaryngol Head Neck Surg. 2002;128(1):44–9.
16. Stuiver MM, ten Tusscher MR, van Opzeeland A, Brendeke W, Lindeboom R, Dijkstra PU, et al. Psychometric properties of 3 patient-reported outcome measures for the assessment of shoulder disability after neck dissection. Head Neck. 2016;38:102–10.
17. Beaton D, Wright J, Katz J, Group TUEC. Development of the QuickDASH: comparison of three item-reduction approaches. J Bone Joint Surg. 2005;87-A(5):1038–46.
18. LeBlanc M, Stineman M, DeMichele A, Stricker C, Mao JJ. Validation of QuickDASH outcome measure in breast cancer survivors for upper extremity disability. Arch Phys Med Rehabil. 2014;95(3):493–8. https://doi.org/10.1016/j.apmr.2013.09.016.
19. MacDermid JC, Walton DM, Avery S, Blanchard A, Etruw E, McAlpine C, et al. Measurement properties of the neck disability index: a systematic review. J Orthop Sports Phys Ther. 2009;39(5):400–17. https://doi.org/10.2519/jospt.2009.2930.
20. Vernon H, Mior S. The neck disability index: a study of reliability and validity. J Manip Physiol Ther. 1991;14:409–15.
21. Vernon H. The neck disability index: state-of-the-art, 1991–2008. J Manip Physiol Ther. 2008;31:491–502.
22. Struyf F, Nijs J, Mottram S, Roussel NA, Cools AMJ, Meeusen R. Clinical assessment of the scapula: a review of the literature. Br J Sports Med. 2014;48:883–90.
23. Yang J-I, Lin J-J. Reliability of function-related tests in patients with shoulder pathologies. Sports Phys Ther. 2006;36(8):572–6.
24. Hanney WJ, George SZ, Kolber MJ, Young I, Salamh PA, Cleland JA. Inter-rater reliability of select physical examination procedures in patients with neck pain. Physiother Theory Pract, Early Online. 2013(1–8).
25. Hoving JL, Buchbinder R, Green S, Forbes A, Bellamy N, Brand C, et al. How reliably do rheumatologists measure shoulder movement? Ann Rheum Dis. 2002;61:612–6.
26. Kolber MJ, Saltzman SB, Beekhuizen KS, Cheng MS. Reliability and minimal detectable change of inclinometric shoulder mobility measurements. Physiother Theory Pract. 2009;25(8):572–81.
27. Clarkson HM. Joint motion and function assessment: a research-based practical guide. Philadelphia: Lippincott Williams & Wilkins; 2005.
28. Van Wyk L, Jull G, Vicenzino B, Greaves M, O'Leary S. A comparison of craniocervical and cervicothoracic muscle strength in healthy individuals. J Appl Biomech. 2010;26(4):400–6.
29. O'Leary S, Lorass Fagermoen C, Hasegawa H, Slettevold Thorsen A, Van Wyk L. Differential strength and endurance parameters of the craniocervical and cervicothoracic extensors and flexors in healthy individuals—technical note. J Appl Biomech. 2016;33:166–70.
30. Cadogan A, Laslett M, Hing W, McNair P, Williams M. Reliability of a new hand-held dynamometer in measuring shoulder range of motion and strength. Man Ther. 2011;16:97–101.
31. Hayes K, Walton JR, Szomor ZL, Murrell GAC. Reliability of 3 methods for assessing shoulder strength. J Shoulder Elb Surg. 2002;11:33–9.
32. Huber PJ. The behaviour of maximum likelihood estimates under nonstandard conditions. Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability. Berkeley: University of California Press; 1967. p. 221–33.
33. White H. A heretoskedasticity–consistent covariance matrix estimator and a direct test for heteroskedasticity. Econometrica. 1980;48:817–30.
34. McNeely M, Parliament M, Seikaly H, Jha N, Magee D, Haykowsky M, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. Cancer. 2008;133:214–22.
35. McGarvey A, Hoffman G, Osmotherly P, Chiarelli P. Maximizing shoulder function after accessory nerve injury and neck dissection surgery: a multicentre randomized controlled trial. Head Neck. 2015;37:1022–31.
36. Ward ECD. As-brooks CJv. Head and neck cancer: treatment, rehabilitation, and outcomes. Vol book, whole. San Diego: Plural Publishing; 2014.
37. Deng J, Ridner SH, Dietrich MS, Wells N, Wallston KA, Sinard RJ, et al. Factors associated with external and internal lymphedema in patients with head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2012;84(3):e319–28. https://doi.org/10.1016/j.ijrobp.2012.04.013.
38. Dijkstra P, Van Wilgen P, Buijs R, Brendeke W, De Goede C, Kerst A, et al. Incidence of shoulder pain after neck dissection: a clinical explorative study for risk factors. Head Neck. 2001;23(11):947–53.
39. Erisen L, Basel B, Irdesel J, Zarifoglu M, Coskun H, Basut O, et al. Shoulder function after accessory nerve-sparing neck dissections. Head Neck. 2004;26(11):967–71.
40. van Wouwe M, de Bree R, Kuik DJ, de Goede CJ, Verdonck-de Leeuw IM, Doornaert P, et al. Shoulder morbidity after non-surgical treatment of the neck. Radiother Oncol. 2009;90(2):196–201. https://doi.org/10.1016/j.radonc.2008.11.003.
41. Inoue H, Nibu K, Saito M, Otsuki N, Ishida H, Onitsuka T, et al. Quality of life after neck dissection. Arch Otolaryngol. 2006;132(6):662–6.
42. Chaplin J, Morton R. A prospective, longitudinal study of pain in head and neck cancer patients. Head Neck. 1999;21:531–7.
43. Speksnikder C, van der Bilt A, Slappendel M, de Wijer A, Merkx M, Koole R. Neck and shoulder function in patients treated for oral malignancies: a 1-year prospective cohort study. Head Neck. 2013;35:1303–13.
44. Chepeha D, Taylor R, Chepeha J, Teknos T, Bradford C, Sharma P, et al. Functional assessment using Constant's shoulder scale after modified radical and selective neck dissection. Head Neck. 2002;24(5):432–6.
45. Karaman M, Tek A, Uslu C, Akduman D, Bilac O. Effect of functional neck dissection and postoperative radiotherapy on the spinal accessory nerve. Acta Otolaryngol. 2009;129:872–80.
46. Pignon J-P, Maître AL, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomised trials and 17,346 patients. Radiother Oncol. 2009;92(1):4–14. https://doi.org/10.1016/j.radonc.2009.04.014.
47. Rivelli TG, Mak MP, Martins RE, da Costa sa Silva VT, de Castro G Jr. Cisplatin based chemoradiation late toxicities in head and neck squamous cell carcinoma patients. Discov Med. 2015;20(108):57–66.
48. Cisplatin. MacMillan Cancer Support. 2016. http://www.macmillan.org.uk/cancerinformation/cancertreatment/treatmenttypes/chemotherapy/individualdrugs/cisplatin.aspx. Accessed 20 Dec 2016.
49. Berger A, Abernathy A, A A, B AM, B WS, Cella D, et al. Cancer-related fatigue. J Natl Compr Cancer Netw. 2010;8:904–31.
50. Ghiam MK, Mannion K, Dietrich MS, Stevens KL, Gilbert J, Murphy BA. Assessment of musculoskeletal impairment in head and neck cancer patients. Support Care Cancer. 2017;25:2085–92. https://doi.org/10.1007/s00520-017-3603-1.
51. Swisher AKPTPCCS, Altaha RMD, Arbaugh JDPT, Barr KDPT, Brooks DDPT, Copeland ADPT, et al. Neck and shoulder impairments and the relationship to quality of life in head and neck cancer survivors. Rehabil Oncol. 2012;30(2):3–7.
52. Ritchie C, Hendrikz J, Kenardy J, Sterling M. Derivation of a clinical prediction rule to identify both chronic moderate/severe disability and full recovery following whiplash injury. Pain. 2013;154(10):2198–206.
53. Hidalgo-Lozano A, Calderon-Soto C, Domingo-Camara A. Fernandez-de-las-Penas C, Madeleine P, Arroyo-Morales M. Elite swimmers with unilateral shoulder pain demonstrate altered pattern

of cervical muscle activation during a functional upper-limb task. J Orthop Sports Phys Ther. 2012;42(6):552–8. https://doi.org/10.2519/jospt.2012.3875.
54. Zabihhosseinian M, Holmes MW, Howarth S, Ferguson B, Murphy B. Neck muscle fatigue differentially alters scapular and humeral kinematics during humeral elevation in subclinical neck pain participants versus healthy controls. J Electromyogr Kinesiol. 2017;33:73–82. https://doi.org/10.1016/j.jelekin.2017.02.002.
55. Christensen SW, Hirata RP, Graven-Nielsen T. The effect of experimental neck pain on pressure pain sensitivity and axioscapular motor control. J Pain. 2015;16(4):367–79. https://doi.org/10.1016/j.jpain.2015.01.008.
56. Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. Pain. 2011;152(3 Suppl):S90–8. https://doi.org/10.1016/j.pain.2010.10.020.
57. Carenfelt C, Eliasson K. Radical neck dissection and permanent sequelae associated with spinal accessory nerve injuries. Acta Otolaryngol. 1981;91(1–2):155–60.
58. Ewing MR, Martin H. Disability following radical neck dissection: an assessment based on the postoperative evaluation of 100 patients. Cancer. 1952;5:873–83.
59. Merve A, Mitra I, Swindell R, Homer JJ. Shoulder morbidity after pectoralis major flap reconstruction for head and neck cancer. Head Neck. 2009;31(11):1470–6.
60. Robbins KT, Ferlito A, Shah JP, Hamoir M, Takes RP, Strojan P, et al. The evolving role of selective neck dissection for head and neck squamous cell carcinoma. Eur Archives Oto-rhino-Laryngol. 2013;270(4):1195–202. https://doi.org/10.1007/s00405-012-2153-x.
61. Palmer MJ, Epler ME. Fundamentals of musculoskeletal assessment techniques. 2nd ed. Philadelphia: Lippincott; 1998.
62. Wang H-L. Shoulder pain after neck dissection among head and neck cancer patients. ProQuest Dissertations Publishing: Indiana University; 2009.