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Title: Balance and physical functioning in patients after head and neck cancer post-neck dissection surgery: A Case Series

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Abstract

Background and Purpose. Rehabilitation research in people with head and neck cancer, undergoing neck dissection (ND) surgery, has been largely confined to evaluation of shoulder dysfunction. Balance and broader physical functioning variables were evaluated in this patient group.

Case Description. This case series presents four patients scheduled for ND surgery, who completed a comprehensive battery of balance and physical functioning assessments pre-operatively and six weeks post-operatively.

Outcomes. Post-ND surgery, the majority (n=3) of patients reported increased upper quadrant pain, with proprioception and neck range of motion measurements showing a decreasing trend. One patient had no neck pain or changes in proprioception. The changes for standing balance and endurance varied across the patients, with no observable trend.

Discussion. Quality of life, physical activity and a number of physical functioning measures, including proprioception and physical activity, were lower after ND surgery. This case series identifies the adverse effects of ND surgery performed prior to the start of adjuvant therapy, with many deficits noted potentially amenable to therapeutic intervention. The clinical implication of this study is that Physical Therapists should assess physical functioning variables after ND surgery and intervene early if deficits are noted.

Key words: Head and neck cancer, neck dissection, neck proprioception, standing balance, physical activity, case series

BODY OF ARTICLE

People with head and neck (HnN) cancer make up nearly 5% of the world cancer population with a mortality of 4.6%.[1] Standard medical management includes one or more of the following treatments; chemotherapy, radiotherapy and surgery.[2] These treatments decrease physical activity (PA), independence in activities of daily living and quality of life (QoL).[3-5] Neck dissection (ND) surgery is indicated in the presence of primary or residual cervical node metastases. Neck and shoulder dysfunctions are common features following this surgery.[6-12]

Patients with musculoskeletal neck pain have greater neck proprioception and standing balance deficits (i.e. postural stability).[13,14] Unexplored topics in the HnN cancer literature are the relationship between neck pain and proprioception and standing balance deficits. Damaged muscle spindles might reduce postural stability by causing a mismatch in the afferent inputs from the cervical, visual and vestibular systems.[13,14] It is hypothesized that damaged muscle spindles can reduce postural stability as afferent inputs from the cervical, visual and vestibular systems become mismatched. It is also unknown if ND surgery is associated with changes in physical activity levels after surgery but before the start of adjuvant therapy. This prospective observational study aimed uniquely to address these gaps in the literature by investigating balance, upper quadrant pain, quality of life and physical function and performance after ND. These results will promote a greater understanding of the effects of ND surgery and will help guide post-surgical rehabilitation efforts in terms of the functional deficits clinicians are likely see in this patient population.

METHODS

This prospective observational study was conducted in an acute hospital setting in Dublin Ireland, which is a dedicated cancer centre. This study was approved by the approved by the Joint Research Ethics Committee of Tallaght University Hospital/ St. James's Hospital. Written informed consent was obtained from each participant. People with head and neck cancer who were scheduled for ND surgery, with no pre-existing balance deficits were recruited and the following test battery was applied pre-operatively and 6 weeks post operatively.

1. Upper quadrant pain was measured using the Visual Analogue Scale (VAS) which is defined as the average intensity of pain experienced over the last seven days. The patient is asked to mark a place on the line corresponding to the current pain intensity from ''no pain'' at one end to ''pain as bad as it can be'[15]. The validity and reliability of the VAS has been shown previously in patients with cancer.[16-18]
2. Active neck range of motion was measured to the nearest degree (^{o}) using a universal goniometer (Baseline, Fabrication Enterprise Inc, United States of America). This method of measurement has acceptable validity and reliability.[19]
3. Neck Proprioception was assessed using the head repositioning accuracy to neutral head position method[20] as shown in Fig.1. A laser pointer was used to obtain the absolute error value (i.e. distance between the start "neutral" position, reference as zero and returned "neutral" position, in centimetres) after an active movement. Neck proprioception was tested three times, unless compensatory movements were observed, and the mean used for analysis. This method has fair to excellent reliability regardless of the devices used and sufficient validity in identifying positional error.[21]
4. Endurance was assessed using the 6-minute walk test (6MWT)[22], a validated and reliable tool to assess functional capacity in healthy in patients with cancer.[23,24] The

minimally important difference for deterioration of the 6MWD in lung cancer is between 22 m and 42 m, or a change of 9.5%.[25]

5. Physical activity level was measured using the International Physical Activity Questionnaire (IPAQ) – long form. Descriptive information of performance across four domains - work, transport, garden/yard and leisure, and sitting were collected and processed following the standard criteria (http://www.ipaq.ki.se) to generate a continuous score in MET-minutes/week for domains of activity and a total score was also generated. The validity and reliability of the IPAQ has been established in adults[26] and elderly populations.[27]
6. Quality of life was measured using the University of Washington Quality of Life questionnaire (UWQoLv4). This questionnaire comprises 12 Likert-type questions with 3-5 statements each (scored between 0 – worse to 100 – best) and generates a global composite score as well as physical and social-emotional subscale scores. This questionnaire is validated and reliable tool.[28] The minimal clinical important difference of the global composite score is seven.[29]
7. Standing balance was also assessed using a Wii Balance Board (Nintendo, Japan), using a program described by Clark in 2010, which was developed in accordance with Holmes (2013)[30, 31.] The Nintendo Wii Balance board (Nintendo, Kyoto, Japan), was interfaced with a laptop computer (Lenovo Flex 2-14, Lenovo PC HK Limited, China) using a custom-written software (Labview 8.5 National Instruments, Austin, Texas, United States of America). The board was calibrated[30] and standing balance (i.e. postural stability) was assessed by recording changes in centre of pressure (CoP) co-ordinates[31] during two conditions. The two conditions are shown in Fig. 2. In condition 1 the position was double leg stance, eyes open and neck neutral. In condition 2 the position was double leg stance, eyes open and neck extended. Due to the myriad of CoP

measures available and to avoid spurious type one errors and model overfitting, results a-priori focused on CoP velocity (speed of movement, in centimetres per second), and amplitudes (maximal distance travelled, in centimetres), in anterior-posterior (AP) and medial-lateral (ML) directions. Higher values indicate greater postural instability. A recent systematic review shows this system is valid and reliable[32], and it has been used previously to detect subtle impairments in people with neck pain[33,34].

FIGURE 1 ABOUT HERE FIGURE 2 ABOUT HERE

DESCRIPTION OF CASES

Case 1

A 60-year old male presented with a 9-month history of left facial palsy. He was an ex-smoker with a body mass index (BMI) of 42.7 and age-adjusted Charleston co-morbidity index (CCI) of six points. Further demographic detail is provided in Table 1. Subsequent investigations diagnosed him with adenocarcinoma of the left parotid gland and cervical metastases (pT2N2b) and a second primary non-small cell lung cancer. He underwent a left parotidectomy, left modified ND and sural nerve graft. Detailed results of physical functioning variables are shown in Tables 2-4. At the six-week time-point, he reported an increased pain intensity of 2.3cm. Neck flexion, ipsilateral lateral flexion and ipsilateral rotation range of movements (ROM)s were below acceptable ranges pre-operatively.[34] These ROMs were further reduced post-operatively, with a marked decrease of 15° in flexion. This deficit in flexion was substantially more than other ranges tested. Proprioception errors following each ROM increased 7% - 83% post-ND except contralateral rotation, which decreased by 48% (9.7cm to 5.0cm). All measures of standing balance decreased following surgery indicating greater postural instability. Average six minute walk test distance declined post surgically but remained above age and gender based predicted distances.[35] Total PA levels decreased markedly by 67% (2604 MET-min/week to 872 MET-min/week), All vigorous PA ceased (from 960 MET-min/week pre-surgery to 0MET-min/week post-surgery) and moderate PA declined by 970 MET-min/week (from 1050 MET-min/week pre-surgery to 80 MET-min/week post-surgery). Quality of life values were lower with a decreased in global UWQoL composite scores from a mean of 84.1 to 76.5.

TABLE 1 ABOUT HERE

Case 2

A 60-year old female smoker with a BMI of 30.9 and an age-adjusted CCI of three points presented with an ulcerative lesion and was subsequently diagnosed with cancer at the floor of mouth (pT4N0) and concurrent papillary thyroid cancer. She had a left floor of mouth resection and bilateral selective ND with reconstruction using a left nasolabial flap. She underwent oral re-excision due to unclear margins. During the post-operative assessment, she reported a 4.2 cm pain intensity. Changes in ROMs post-surgery varied with decrements of 3% - 25% in flexion, ipsilateral LF and contralateral rotation. Absolute proprioception errors following active flexion, extension and ipsilateral rotation increased by 50% - 170% post-ND while the remaining ROM movements decreased these errors by 21% - 38%. All parameters of standing balance decreased post-ND except total and ML velocity in the neck neutral condition. Amplitudes were lower with the neck extended, indicating better postural stability during neck extension. Total PA levels and 6-minute walk test distance were low and remained largely unchanged post-ND. Total MET-minutes decreased by 4.2% (-31.5 MET-minutes) and the distance covered in the six minute walk test increased by 5.1% (+23.3m). Quality of life (UWQoL) global composite scores were below normative values and decreased from a mean of 70.2 to 64.7.

TABLES 2-4 ABOUT HERE

Case 3

Case 3 was a 74-year old male ex-smoker with a history of heavy alcohol intake (36-units weekly) and a BMI of 26.9 and age-adjusted CCI of five points. He presented with a lump in his neck, later identified to be a malignant tumour at the left submandibular gland with cervical metastases (pT3N2b). He was also diagnosed with concurrent papillary thyroid

cancer. Following a left submandibular gland resection and left selective ND, pain intensity increased from 1.4 cm pre-surgery to 3.5 cm post-surgery. All pre-surgical neck ROMs increased 20% to 105% following surgery, except for ipsilateral lateral flexion which decreased from 29.3 cm to 28.7 cm. Absolute proprioceptive error following ipsilateral lateral flexion decreased by 24% (-1.7 cm) whilst errors following extension and contralateral flexion increased by 386 % (+9.0 cm) and 157% (+7.3 cm) respectively. All balance-related measures during neck neutral condition increased post-ND. Both AP and ML amplitudes then were greater compared to the neck extended condition. Total PA levels and 6-minute walk test distances were below expected values for age matched healthy individuals at both time points. His pre-surgical six-minute walk test distance was largely unchanged post-surgically (+2%, 10m). Total PA levels, excluding vigorous PA (which was 0 at both time points), decreased by 64% (from 4416 MET-min/week to 1572 MET-min/week) as both moderate PA and walking PA decreased by 2580 MET-min/week and 264 MET-min/week respectively. Global UWQoL composites scores decreased from a mean of 84.8 to 66.1.

Case 4

A 78-year old male was reviewed for and underwent a right modified ND after residual cervical metastases were identified following completion of neo-adjuvant therapy for right supraglottic cancer (T3N2b). He was a smoker and drank 10-units weekly. His BMI was 25.3 and age-adjusted CCI was five points**.** He sustained extensive fractures to his right lower limb during childhood which required his use of a walking stick. He reported no pain at either time-point. Neck flexion and lateral flexion were below normal ranges[34] pre-operatively with contralateral and ipsilateral lateral flexion increasing 138% (29.0^{o}) and 50% (10.0^{o}) respectively. Proprioceptive errors remained unchanged except for improvements for

error following flexion and contralateral rotation. Standing balance could not be compared due to equipment failure during post-ND assessment. Six-minute walk test distance declined from 130m to 104m, he took three rest-breaks during each test due to lower limb fatigue. Total PA composed of only moderate PA, decreased from 2340 MET-min/week to 735 MET-min/week while global UWQoL composite score increased from a mean of 86.8 to 88.3.

DISCUSSION

Local musculoskeletal dysfunction tends to be the primary physical therapy-focused concern after ND surgery[36]. This case series took the unique approach of evaluating the balance and physical function of patients who had undergone surgery for the treatment of head and neck tumors using a comprehensive battery of clinically based balance and physical functioning tests. Principal findings were that a broad range of physical functioning measures declined in the majority of participants, and a number of deficits persisted at the 6-week time-point after ND surgery. Many of these deficits would be amenable to physical therapy intervention. This implies that Physical Therapists should consider broadening their assessment and treatment strategies of this patient group to capture these deficits.

A trend of increased upper quadrant pain (shoulder) was observed in three patients. Case 4 differed in that he reported no pain, improved QoL and neck ROM that did not worsen. Unlike the other patients, Patient no. 4 received neo-adjuvant chemoradiotherapy. Anecdotally he was very well informed about his condition, potentially due to his more prolonged treatment course thus far increasing his exposure to health professional education which may have contributed to his improved status. If true, this notion advocates for more comprehensive patient education where possible which may positively influence how

symptoms are experienced. Changes in neck ROM post-ND among the four patients were non-uniform, though the majority (n=3) had decreased ipsilateral lateral flexion and/or contralateral rotation. These observations were similar to those assessed in patients at sixth-week and one-year post-ND[6-8] which highlights the possible utility of a 6-week observation time-point in this patient group. Increased neck ROMs were observed in two patients, which may be attributed to physical therapy interventions received as part of their care plans[37] or a less extensive surgery. [6-8]

A common trend of worsening neck proprioception errors following neck extension and ipsilateral rotation was observed post-ND. These errors may be attributed to pain and changes in muscle length[38,39]. It is possible that damaged muscle spindles can reduce postural stability as afferent inputs from the cervical, visual and vestibular systems become temporally mismatched. This appeared to be supported by the results of the first three patients with neck pain and then also supported by the fourth patient who did not have neck pain and did not have deficits in proprioception. Neck proprioception errors were larger than those seen in both healthy individuals and those with neck pain.[40,41] In contrast, these previous studies reported significantly worse proprioceptive error following neck flexion motion, possibly due to differences in mechanism of "injury" and muscles affected. Neck dissections may be unilateral and affect the sternocleidomastoid and trapezius muscles[42] but neck pain of other origins commonly affect bilateral flexor and extensor neck muscles[43,44], with presentation of weakness and stiffness.

Standing balance measurements varied substantially and no trend could be observed. This could be due to the small sample size or to a lack of sensitivity of the test protocol for this population. It was hypothesized that the trend of increased pain and joint position errors would lead to a decreased postural stability as demonstrated in earlier studies.[45,46] The absence of decrement may also have been related to well-controlled pain.[47,48] Kogler et al in

2000[49] described how standing condition with neck extension seemed to increase postural instability. Instead results of the present study were similar to Adamo in 2013[50], who found postural stability to be similar during both conditions. Perhaps the limited neck extension ROM achieved post-ND (<45^{o}) neither increased stretch-related activity in the cervical muscles nor disrupted input from the vestibular receptors.[49,50] Ultimately maintaining postural stability is multifactorial and patients may have compensated with other strategies which requires further study.

Total PA scores decreased in participants, with none meeting recommended levels of PA post-ND.[51] This level of inactivity is in agreement with the findings from previous studies which reported that cancer survivors engaged in decreasing amounts of PA.[3,52-55] The trend of PA observed here prior to commencement of adjuvant therapy, highlights a further decrease in PA levels with accompanying health consequences.[4]

UWQoL global composite scores tended to decline after ND, a change reported in previous studies.[56,57] Six weeks after surgery, these patients tended to have greatest concern over control and physical self-efficacy due to necessity for adjustment and adaptation following post-treatment changes.[5,58] Three patients achieved 6MWD within 90% of their predicted value.[18] Although the 6-minute walk test is widely used, it was only validated in people with cancer recently[59,60] hence there is a lack of comparative data within the same population. The minimal (less than 6%) difference post-ND was similar to patients with gastrointestinal cancer[61], indicating that there had been very limited loss of function and thus little to recover.

The main clinical implications of this study are firstly, the need to surveil the physical function of patients post ND-surgery and begin a rehabilitation program as soon as it is safe when deficits are noted. The time between surgery and initiation of adjuvant treatment is a window of opportunity to help these patients both recover and prepare for the next phase of their treatment.

A number of strengths and limitations pertained to this study. Firstly, recruitment was a challenge during this study due to a short time frame between admissions to surgery, as well as the comprehensive test battery which was time consuming to conduct, hence the small number of participants in this study. Nonetheless, this observational study appears to be the first to assess patients with HnN cancer with a comprehensive battery of tests, beyond those related to shoulder dysfunction. Furthermore, the assessments conducted six-weeks post-operatively, which were well tolerated, provided new insight into patients' health-related status prior to adjuvant therapy.

CONCLUSION

This appears to be the first prospective observational study in which a broad physical functioning test battery was used to assess the impact of surgery on patients with HnN cancer. Quality of life, and several physical functioning measures including proprioception and physical activity declined after ND, highlighting the effects of surgery prior to adjuvant therapy. Physical therapists should assess physical functioning following surgery and initiate a rehabilitation program expediently if deficits are noted. Future studies should evaluate longer terms functional deficits to assess if changes are persistent or improve over time to help guide assessment and rehabilitation in this population. The test battery implemented in this study was feasible and should be evaluated on a larger scale. The possible link between damaged muscle spindles and proprioception also deserves consideration in larger studies. This would provide for a more comprehensive analysis of the effects of ND surgery in patients with HnN cancer and may guide rehabilitation needs.

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Table 1: Patient demographics

	Gender	Age	Pre-BMI	Age-adjusted CCI	Smoking status	Alcohol /week	Tumour site	TNM stage	ND	SAN	Recon.	Neo-adjuvant therapy
Case 1	Male	60	41.67	6	Ex	No	Left parotid	pT2N2b	Left modified	Preserve	Sural nerve graft	Nil
Case 2	Female	60	30.90	3	Yes	No	Left FOM	pT4N0	Bilateral selective	Remove	Left NLF	Nil
Case 3	Male	74	26.94	5	Ex	36 units	Left submandibular joint	pT3N2b	Left selective	Preserve	Nil	Nil
Case 4	Male	78	25.20	5	Yes	10 units	Right supraglotic recurrence	T3N2b	Right modified	Preserve	Nil	CRT

BMI; body mass index, CCI; Charleston co-morbidity index, TMN; tumour, metastases, nodal, ND; neck dissection, SAN; spinal accessory nerve, Recon; reconstruction, FOM; floor of mouth, NLF; nasolabial flap, CRT; chemoradiotherpy, NSCLC; non-small cell lung cancer

Table 2 Upper quadrant pain (VAS score in cm), quality of life (UWQoLv4 global composite and subscale scores), and endurance capacity (m) pre and post-surgery

	Upper Quadrant Pain			Quality of life									Endurance capacity		
	VAS Pre	VAS Post	Δ VAS	Global Score Pre	Global Score Post	Δ Global Score	PF Pre	PF Post	Δ PF	SEF Pre	SEF Post	Δ SEF	6MWT Pre	6MWT Post	Δ 6MWT
Case 1	0.00	2.30	+2.30	84.08	76.50	-7.58	86.17	84.83	-1.34	82.00	68.17	+13.83	532.73	518.10	-14.63
Case 2	0.00	4.15	+4.15	70.17	64.67	-5.5	77.83	68.17	-9.66	62.50	61.17	-1.33	456.70	480.00	+23.30
Case 3	1.40	3.45	+2.05	84.75	66.08	-18.67	89.00	55.67	-33.33	80.50	76.50	-4.00	464.70	475.20	+10.50
Case 4	0.00	0.00	0.00	86.83	88.25	+1.42	87.50	90.33	+2.83	86.17	86.17	0.00	130.00	104.00	-26.00

Δ; difference between pre-surgery and post-surgery, PF; physical function, SEF; social-emotional function, 6MWT; six-minute walk test

Table 3 Range of motion (°) pre and post-surgery

	Flexion Pre	Flexion Post	Δ Flexion	Ext Pre	Ext Post	Δ Ext	Contra LF Pre	Contra LF Post	Δ Contra LF
Case 1	30.00	15.00	- 15.00	30.33	30.00	+ 0.33	42.00	34.00	- 8.00
Case 2	40.00	30.00	- 10.00	33.33	35.00	+ 1.67	50.00	50.00	0.00
Case 3	20.00	25.67	+ 5.67	30.67	36.67	+ 6.00	24.67	30.00	+ 5.33
Case 4	30.00	32.33	+ 2.33	39.00	40.00	+ 1.00	21.00	50.00	+ 29.00
	Ipsi LF Pre	Ipsi LF Post	Δ Ipsi LF	Contra Rot Pre	Contra Rot Post	Δ Contra Rot	Ipsil Rot Pre	Ipsil Rot Pre	Δ Ipsil Rot
Case 1	38.33	27.67	- 10.66	63.33	56.67	- 6.66	50.00	46.67	-3.33
Case 2	53.33	43.33	- 10.00	68.33	66.00	- 2.33	51.67	60.00	- 8.33
Case 3	29.33	28.67	- 0.66	20.00	41.00	+ 21.00	36.33	60.00	+ 23.67
Case 4	20.00	30.00	+ 10.00	61.67	50.00	- 11.67	53.33	54.00	- 0.67

Δ; difference, Contra; contralateral, Ipsi; ipsilateral, LF; lateral flexion, Rot; rotation, Ext; extension, NS; non-significant

Table 4 Physical Activity levels (MET-min/week) and sitting (minutes/day) pre and post-surgery

	Mod PA Pre	Mod PA Post	Δ Mod PA	Vig PA Pre	Vig PA Post	Δ Vig PA	Total PA Pre	Total PA Post	Δ Total PA	Sitting Pre	Sitting post	Δ Sitting
Case 1	1,050.00	80.00	-970.00	960	0.00	-960.00	2,604.00	872.00	-1732.00	420.00	240.00	-180.00
Case 2	540.00	360.00	-180.00	0.00	0.00	0.00	738.00	706.50	-31.50	171.43	222.86	+51.43
Case 3	4,020.00	1,440.00	-2580.00	0.00	0.00	0.00	4,416.00	1,572.00	-2844.00	240.00	240.00	0.00
Case 4	2340.00	735.00	-1605.00	0.00	0.00	0.00	2340.00	735.00	-1605.00	398.57	360.00	-38.57

Δ; difference, PA; Physical activity

Table 5A Results of standing balance velocity (centimetres/seconds) for condition 1 (neck neutral) and condition 2 (neck extended)

		Total velocity Pre	Total velocity Post	Δ Total velocity	AP velocity Pre	AP velocity Post	Δ AP velocity	ML velocity Pre	ML velocity Post	Δ ML velocity
Condition 1	Case 1	1.47	3.36	-1.89	1.25	3.03	+1.78	0.54	1.06	+0.52
	Case 2	1.25	1.28	+0.03	0.94	0.86	-0.08	0.67	0.76	+0.09
	Case 3	0.95	1.08	+0.13	0.63	0.86	+0.23	0.57	0.47	-0.10
Condition 2	Case 1	1.57	3.66	+2.09	1.24	3.28	+2.04	0.61	1.19	+0.58
	Case 2	1.64	1.20	-0.44	1.10	0.97	-0.13	0.96	0.50	-0.46
	Case 3	1.49	1.26	-0.23	1.25	1.11	-0.14	0.54	0.43	-0.11

Δ; difference, AP; antero-posterior, ML; mediolateral

Table 5B Results of standing balance amplitude (centimetres) for condition 1 (neck neutral) and condition 2 (neck extended)

		AP amplitude Pre	AP amplitude Post	Δ AP amplitude	ML amplitude Pre	ML amplitude Post	Δ ML amplitude
Condition 1	Case 1	2.66	4.95	+2.29	1.01	2.55	+1.54
	Case 2	2.86	1.75	-1.11	1.91	1.77	-0.14
	Case 3	2.65	2.40	-0.25	1.67	2.69	+1.02
Condition 2	Case 1	2.20	3.31	+1.11	1.34	1.86	+0.52
	Case 2	2.23	1.88	-0.35	1.88	1.21	-0.78
	Case 3	2.63	1.78	-0.85	1.35	0.98	-0.37

Δ; difference, AP; antero-posterior, ML; mediolateral

Fig. 1 Demonstration of head positioning accuracy to neutral, with laser pointer integrated in cap

Fig. 2 Assessment of Standing balance, showing test positions; Condition 1 (left) and Condition 2 (right)