Original Article

2b or Not 2b? Shoulder Function After Level 2b Neck Dissection: A Double-Blind Randomized Controlled Clinical Trial

Peter T. Dziegielewski, MD [1,2,3]; Margaret L. McNeely, PhD[4]; Nigel Ashworth, MBChB[5]; Daniel A. O'Connell, MD[3]; Brittany Barber, MD[3]; Kerry S. Courneya, PhD [6]; Brock J. Debenham, MD[7]; and Hadi Seikaly, MD[3]

BACKGROUND: Selective neck dissection (SND) is a mainstay of head and neck cancer treatment. A common sequela is shoulder syndrome from spinal accessory nerve (SAN) trauma. Extensive dissection in neck levels 2 and 5 leads to SAN dysfunction. However, it is not known whether limited level 2 dissection reduces SAN injury. The purpose of this double-blind randomized controlled trial was to determine whether omitting level 2b dissection would improve shoulder-related quality of life and function. **METHODS:** Patients with head and neck cancers undergoing surgery were randomized 1:1 to SND without level 2b dissection (group 1) or with it (group 2) on their dominant-hand side. Patients, caregivers, and assessors were blinded. The primary outcome was the change in the Neck Dissection Impairment Index (NDII) score after 6 months. An a priori calculation of the minimally important clinical difference in the NDII score was determined to establish a sample size of 15 patients per group (power = 0.8). Secondary outcomes included shoulder strength and range of motion (ROM) and SAN nerve conduction. The trial was registered at ClinicalTrials.gov (NCT00765791). **RESULTS:** Forty patients were enrolled, and 30 were included (15 per group). Six months after the surgery, group 2 demonstrated a significant median decrease in the NDII from the baseline (30 points) and in comparison with group 1, whose NDII dropped 17.5 points ($P = .02$). Shoulder ROM and SAN conduction demonstrated significant declines in group 2 ($P \leq .05$). No adverse events occurred. **CONCLUSIONS:** Level 2b should be omitted in SND when this is oncologically safe and feasible. This allows for an optimal balance between function and cancer cure. ***Cancer* 2020;126:1492-1501**. *© 2019 American Cancer Society*.

KEYWORDS: head and neck cancer, neck dissection, quality of life, shoulder dysfunction, shoulder syndrome, spinal accessory nerve.

INTRODUCTION

Head and neck cancers of the oral cavity, pharynx, and larynx have a propensity for lymph node metastases in the neck. Lymphatic spread portends significant drops in survival. The majority of cases are treated with primary surgery, which includes neck dissection to remove diseased and at-risk lymph node groups. Historically, all groups were removed in a radical neck dissection.[1] Today, selective neck dissections (SNDs) are routinely practiced because they reduce morbidity while maintaining oncologic efficacy.[2]

The most common long-term complication of neck dissection is shoulder dysfunction due to the dissection of, or injury to, the spinal accessory nerve (SAN).[3] The result is shoulder syndrome, which includes chronic pain, weakness, limited range of motion (ROM), shoulder droop, and impaired shoulder-related quality of life (QOL).[4-6] Despite a tincture of time and dedicated physical therapy (PT), shoulder impairments may become permanent and lead to profound effects on activities of daily living, hobbies, employment status, and personal independence.[5,7]

The SAN traverses the neck from the skull base to the trapezius muscle via neck levels 2 and 5. Level 5 is preserved in SND; level 2 is universally included. SND can be modified to preserve level 2b, and this may lessen shoulder morbidity.[8-11] Level 2b is often dissected in node-positive (N1-N3) necks[12]; in node-negative (N0) necks, this is surgeon-dependent.[2,5,11,12] Proponents for including level 2b cite the fact that occult nodal metastases may be missed if these nodes are not removed.[13-15] Opponents argue that the risk of occult disease in level 2b is too low to provide an oncologic benefit, but increased dissection will cause physical dysfucntion.[9,12,16,17]

There are minimal data on SAN function after level 2b dissection.[3,8,9,18] As with any cranial nerve, it appears that SAN function deteriorates after surgical dissection.[19,20] However, the effect of nerve dysfunction on patient-perceived

Corresponding Author: Peter T. Dziegielewski, MD, Department of Otolaryngology, University of Florida, 1345 Center Dr, Room MSB M2-228, Gainesville, FL 32610 (peter.t.dz@gmail.com).

[1]Department of Otolaryngology, University of Florida, Gainesville, Florida; [2]University of Florida Health Cancer Center, University of Florida, Gainesville, Florida; [3]Division of Otolaryngology–Head and Neck Surgery, Department of Surgery, University of Alberta, Edmonton, Alberta, Canada; [4]Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Alberta, Canada; [5]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; [6]Faculty of Physical Education and Recreation, University of Alberta, Edmonton, Alberta, Canada; [7]Department of Radiation Oncology, University of Alberta, Edmonton, Alberta, Canada

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shoulder-related QOL and functional outcomes has not been evaluated in a vigorous trial.

This randomized controlled trial (RCT) is the first to examine the effect of level 2b dissection on shoulder function as determined by clinically meaningful measures. The primary objective was to determine the impact of level 2b dissection on shoulder function–related QOL. Secondary outcomes included objective physical assessments of shoulder function as well as electromyography (EMG) measurements of SAN function.

MATERIALS AND METHODS

Health research ethics board approval was obtained on October 12, 2008, at the University of Alberta (HREB007527). The trial was registered with ClinicalTrials.org (NCT00765791) on November 10, 2008. Patient enrollment occurred from November 17, 2008, to January 31, 2012.

The Clinical Trials Office at the University of Alberta provided trial management/support. The authors were responsible for the trial design, data analysis, data integrity, and content of this article.

Trial Design

This double-blind RCT with parallel arms was conducted at a tertiary-care academic center (University of Alberta). Each arm was allocated 1:1 in a randomized fashion. No changes were made to the protocol (Supporting Materials A) after commencement.

Enrollment

Untreated patients with head and neck cancer were assessed with the following criteria:

Inclusion criteria

1. Age ≥ 18 years.
2. Biopsy-proven mucosal head and neck cancer.
3. Plan for primary surgical tumor resection with bilateral SND.
4. Plan for postoperative external-beam radiation therapy (XRT).
5. N0 neck on dominant-hand side.

Exclusion criteria

1. Previous neck surgery with dissection at level 2 or 5.
2. Previous neck XRT, including level 2 or 5.
3. Documented shoulder neuropathy, myopathy, or arthropathy.
4. Cardiac pacemaker (ie, a contraindication to nerve conduction testing).
5. Positive neck disease on a randomized side found intraoperatively (ie, necessitating comprehensive neck dissection, including levels 2b and 5).

Patients meeting the criteria were offered trial participation. The operating surgeon (H.S.) explained the trial; those interested signed an informed consent form and were enrolled by the trial coordinator. Data were collected as they became available by the trial coordinator, who was not involved in the protocol design or the data analysis. Primary data collection and verification were completed in January 2013. Patients were followed for 5 years after their surgery to determine tumor recurrence rates, with data collection being finished in February 2017.

Intervention

Bilateral SND, including levels 2 to 4, was performed at the time of tumor resection. Patients were randomized to one of the following:

1. Group 1 (not 2b): Level 2b was not dissected (SND [2a-4]).
2. Group 2 (2b): Level 2b was dissected (SND [2ab-4]).

Surgical Procedure

The standardized SND (2-4) technique (Supporting Materials B) was performed by a single surgeon (H.S.). Levels 1, 3, and 4 were dissected in the typical fashion.[5,21] In group 1 (SND [2a-4]), the SAN was dissected only on its inferior border, and this left fascia covering ~270 degrees of the nerve. In group 2 (SND [2ab-4]), the SAN was dissected 360 degrees, and level 2b contents were passed under the nerve. Retraction was limited to the sternocelidomastoid muscle (SCM) and was not applied directly to the SAN. At the completion of SND, the integrity of the SAN was assessed visually and with a Vari-Stim nerve stimulator at 0.5 mA (Medtronic, Jacksonville, Florida).

After surgery, patients were admitted to the head and neck surgical oncology ward and followed a standardized care protocol.[22] During and after their hospital stay, all patients underwent standardized shoulder rehabilitation PT.[23,24]

Outcomes

Primary

The change in the Neck Dissection Impairment Index (NDII) (supporting Materials C) score[5] from before the surgery to 6 months after the surgery was the primary outcome. The NDII was chosen because it is the only neck dissection–specific shoulder/neck function and QOL instrument.[5] The 10-item NDII test-retest correlation is 0.91 ($P < .001$) with an internal-consistency Cronbach α coefficient of .95. Individual items are scored from 1 (a lot) to 5 (not at all), with higher scores representing higher QOL (Supporting Materials B). The total score is scaled to a 100-point cumulative score, with higher scores indicating better QOL. This questionnaire is patient-centered and is well applicable to activities of daily living.[25]

Secondary

1. Surgical:
   a. SAN injury: Cautery, compression, and transection injuries were monitored intraoperatively.
   b. Operative time: This was measured from the beginning to the end of level 2 dissection.
2. Oncologic:
   a. Lymph node yield and cancer incidence in level 2 according to standard histology: Immunostains such as p40, s100, Ki-67, and cytokeratin AE1/AE3 were used in cases in which histology did not provide a clear answer for the cancer status.
   b. Long-term locoregional recurrence rates.
3. Shoulder function:
   a. Shoulder ROM: Active and passive shoulder ROM was determined with a universal goniometer by a single assessor.[23,24]
   b. Shoulder strength: Participants performed a 1-repetition maximum seated row test to evaluate changes in shoulder retraction muscle group strength.
   c. Shoulder muscular endurance: A seated row was performed at 50% of the 1-repetition maximum.
   d. Shoulder height: The standing resting position of the shoulder tip was measured from the floor in centimeters.

   A single exercise physiologist (independent assessor) performed all assessments.
4. SAN function: Data were collected on a Viking Select machine (Nicolet, Madison, Wisconsin), which was operated by the same electromyographer (N.A.). Measurements were obtained according to the Buschbacher technique.[26-28] The primary onset latency, negative peak amplitude, and negative peak area of the compound motor amplitude and needle EMG were determined.

Outcomes were measured preoperatively and 4 and 6 months postoperatively. Four months was chosen because this is the typical time in which patients finish adjuvant XRT and undergo a milestone PT evaluation. Six months was chosen because shoulder function typically shows the majority of recovery by this point.[11,23] Even with more extensive neck dissections, including level 5, most recovery occurs within 6 months.[11] Moreover, this is the time frame in which patients are most likely to comply with a PT regimen.[29,30] Outcome measurement details are described in the protocol.

Minimally Important Clinical Difference

An a priori calculation was performed to determine the minimally important clinical difference (MICD) in the NDII[31] via an anchor-based approach.[32] Before this study, no such value was established. A list of all patients who had undergone SND (2ab-4) in the preceding 12 months was generated from operating room records. Forty-one patients were identified and were at least 6 months out from surgery. A chart review was performed to confirm that SND (2ab-4) was performed on the patient's dominant-hand side. Twenty-five patients met the criteria and were contacted to participate in a phone survey. Patients were asked to complete the NDII. They were then asked to complete the same questionnaire but for each question were asked the following: "What would your score need to be for you to notice a shoulder function–related improvement in your quality of life or for you to choose a different treatment?" The average difference was 18.1 points.

Sample Size Calculation

The MICD was used to calculate the sample size with a power of 0.8 and an α value of .05. The necessary sample size to meet the desired power was 15 participants in each group. It was decided that 40 patients were to be enrolled to account for an expected 25% attrition rate.

Randomization and Masking

Forty cards labeled either "2b" or "not 2b" were created on opaque cardboard. The card order was determined by a block-randomized, computer-generated random number sequence, which was created by an investigator not affiliated with the trial (SPSS version 23; IBM, Chicago, Illinois). A 1:1 ratio of the 2b and not 2b designations was assigned with random blocks of 2, 4, 6, and 8. The cards were folded in half and placed in numbered radio-opaque envelopes stored in the order of the generated sequence. The primary surgeon (H.S.), the physical therapist (M.L.M.), and the elctromyographer (N.A.) were not aware of how many randomization cards were created.

Randomization occurred immediately before level 2 dissection. The circulating nurse opened the envelope on the top of the stack and pulled out the next card, which was announced to the primary surgeon (H.S.).

Blinding

Participants were not made aware of whether level 2b was dissected until the completion of 6-month testing. The physical therapists providing PT, the exercise physiologist (an independent assessor), and the electrophysiologist (N.A.) were blinded to which neck side was randomized and to which group the patients belonged. They tested both shoulders and did not have access to patients' surgical records.

Statistical Analysis

The normalcy of the patient distribution was determined with the Kolmogorov-Smirnov test as well as skewness and kurtosis tests. All variables were not normally distributed; thus, nonparametric tests of comparison were used. For continuous variables, the Mann-Whitney U test was used, and for categorical variables, the Fisher exact test was used. The central tendency was measured as the median. Analyses were performed with SPSS version 23.0 (IBM).

RESULTS

Forty patients were enrolled and randomized. Figure 1 shows participant flow and follow-up. Five patients were excluded from each group because of patient withdrawal or positive neck disease found intraoperatively on the side to be randomized. Six, citing that testing was too time-consuming, withdrew postoperatively. Two withdrew postoperatively because of fractured arms from unrelated falls. These occurred after hospital discharge and were not considered adverse treatment events. Six were unable to complete EMG testing because of excessive shoulder pain. Patients were analyzed in an intent-to-treat fashion based on the group to which they were assigned.

Table 1 shows baseline characteristics and demonstrates no significant differences; randomization was successful. Twenty-nine patients had squamous cell carcinoma, and 1 had a carcinoid tumor (group 1). All patients were at clinical stage III or IV and planned to undergo XRT postoperatively. Ten patients in group 1 received XRT, and 2 received chemo-XRT; 13 in group 2 received XRT, and 3 received chemo-XRT ($P > .05$). XRT was given 6 to 10 weeks postoperatively with 60 to 70 Gy to the primary site and 54 to 60 Gy to the neck.

The median level 2 lymph node yield was 6 (range, 3-18) in group 1 and 11 (range, 4-26) in group 2. No level 2 nodes in randomized necks harbored occult cancer. All final surgical margins were negative.

There were no adverse events, including intraoperative SAN or other cranial nerve injuries, major vascular injuries, physical testing injuries, and EMG injuries. All SANs were stimulated strongly (visible trapezius contraction) after neck dissection with the nerve stimulator set at 0.5 mA.

The median operative time was 4.0 ± 1.0 minutes (interquartile range, 3-5 minutes) for group 1 (not 2b) and 7.0 ± 1.0 minutes (interquartile range, 4-8 minutes) for group 2 (2b; $P = .006$).

All participants completed NDII questionnaires preoperatively and 6 months postoperatively (Table 2). The differences between 6-month postoperative scores and preoperative scores were statistically significant for both groups (group 1, $P = .002$; group 2, $P = .001$). A post hoc analysis for study power showed a power of 0.88 for the NDII data (primary outcome).

All participants attended PT sessions and completed physical testing (Tables 3 and 4). All patients reported performing at-home exercises in accordance with a standardized schedule. The median change in the body mass index was -2.3 kg/m^2 for group 1 and -2.8 kg/m^2 for group 2 ($P = .87$).

Nerve conduction results are presented in Table 5. There were no significant changes in distal motor latency ($P > .05$); however, the median action potential amplitudes demonstrated significant drops within and between groups ($P \leq .05$). The area under the EMG curves significantly decreased in both groups but especially in group 2 ($P \leq .05$).

All participants were followed every 3 months by H.S. for a planned 5 years with no losses to follow-up. Follow-up ranged from 0.5 to 7.5 years. Patients who did not make it to 5 years died of either concurrent disease or recurrent cancer. No patient had a neck recurrence. One patient had a recurrence at the skull base 6 months after surgery. Two patients had local recurrences (1 in each group), and both were salvaged with surgery.

DISCUSSION

SND limits lymph node dissection to preserve shoulder function.[16,19,33,34] SAN dysfunction in SND occurs with level 2a/2b dissection.[16,35] Thus, can level 2b–sparing SND further improve shoulder outcomes?

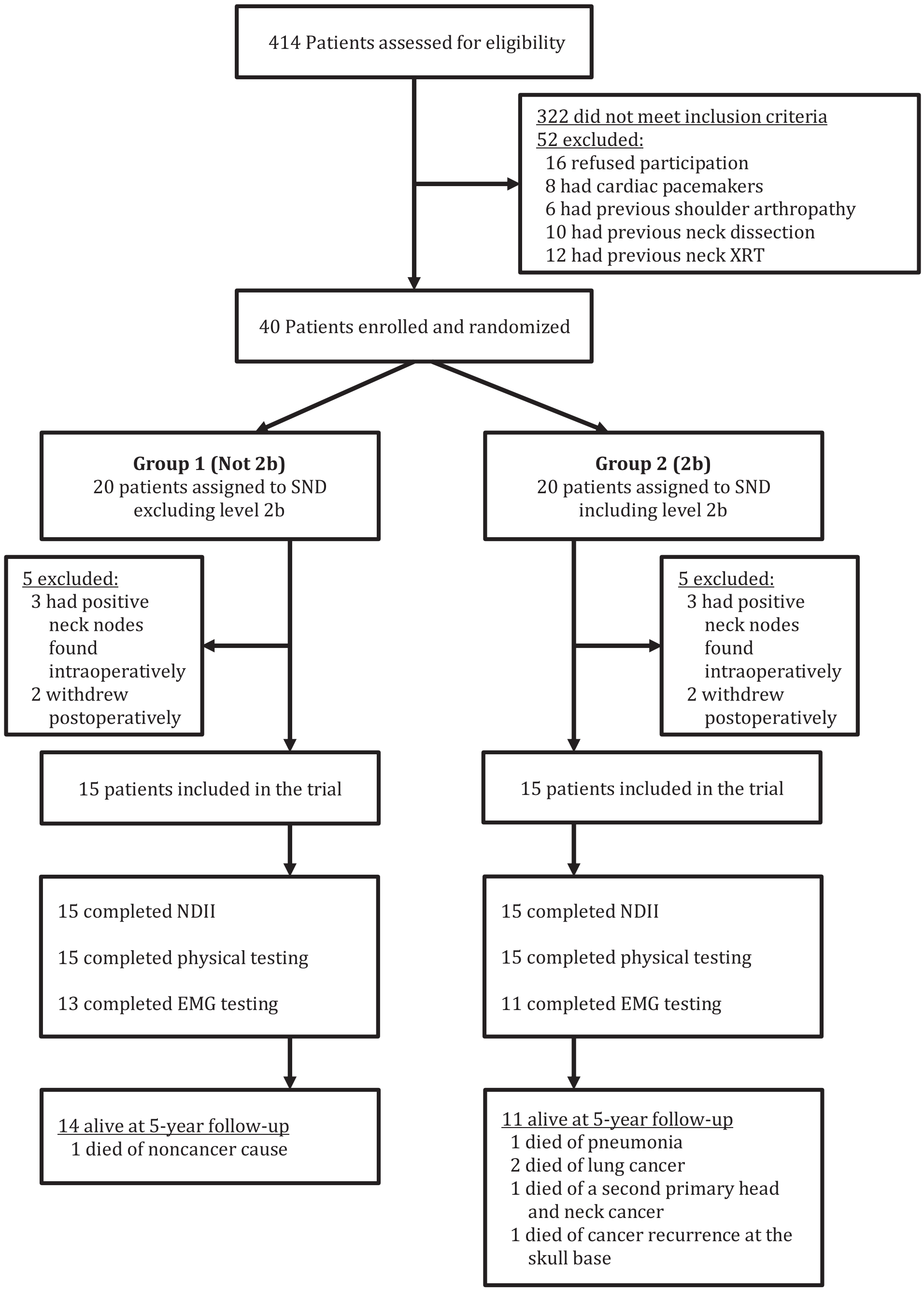

Figure 1. Randomization, enrollment, and follow-up of trial participants. EMG indicates electromyography; NDII, Neck Dissection Impairment Index; SND, selective neck dissection; XRT, external-beam radiation therapy.

Yes. This study convincingly shows that SND (2a-4) causes less shoulder impairment than SND including 2b. Shoulder-related QOL at 6 months postoperatively was 17 points lower than the baseline with 2b-sparing dissection (group 1). This drop is statistically but not clinically significant. For patients with level 2b dissected (group 2), the decline was 30 points at 6 months, which is statistically and clinically significant. Moreover, the difference in 6-month scores between the groups was significant ($P = .008$).

The results show that even minimal dissection of the SAN (SND [2a-4]) will cause patient-perceived shoulder impairment; however, this does not become clinically meaningful until level 2b is dissected. The dysfunction

TABLE 1. Baseline Characteristics of the Study Participants

Characteristic	Group 1: Not 2b (n = 15)	Group 2: 2b (n = 15)	*P*
Age, median (range), y	59.8 (48.6-78.8)	64.3 (44.0-76.4)	.76
Sex: male:female, No.	14:1	12:3	.30
Primary cancer site, No.			.12
Oral cavity	5	8	
Oropharynx	9	3	
Larynx	1	4	
pT classification, No.			.08
Tx	1	0	
T1	2	0	
T2	9	5	
T3	2	4	
T4	1	6	
pN classification, No.			.97
N0	8	9	
N1	2	2	
N2a	2	2	
N2b	3	2	
Overall AJCC stage, No.			.45
II	6	3	
III	3	3	
IV	6	9	
CCI score, median (range)	5 (2-6)	4 (2-7)	.69
Smoking history, median (range), pack-y history	20 (0-50)	30 (0-50)	.46
Preoperative BMI, median (range), kg/m^2	25.2 (19.8-38.7)	27.6 (17.1-36.1)	.36

Abbreviations: AJCC, American Joint Commission on Cancer; BMI, body mass index; CCI, Charlson Comorbidity Index.
All measurement values are presented as medians.

TABLE 2. Perioperative NDII Scores per Group

Perioperative Time Period	NDII Score, Median ± SE (IQR)		*P*
	Group 1: Not 2b	Group 2: 2b	
Preop	100 ± 1.7 (92.5 to 100)	97.5 ± 2.4 (92.5 to 100)	.49
4 mo postop	71.3 ± 6.7 (48.1 to 81.3)	62.5 ± 6.3 (28.8 to 68.8)	.19
6 mo postop	77.5 ± 4.6 (72.5 to 90.0)	65.0 ± 4.9 (55.0 to 75.0)	**.008**
Median change (6 mo – preop)	−17.5 ± 3.8 (−22.5 to −2.5)	−30 ± 5.1 (−40.0 to −25.0)	**.02**

Abbreviations: IQR, interquartile range; NDII, Neck Dissection Impairment Index; postop, postoperative; preop, preoperative; SE, standard error.
All measurement values are presented as medians. Bolded values denote statistical significance ($P \leq .05$).

TABLE 3. Perioperative Shoulder ROM per Group

Perioperative Time Period	ROM, Median (IQR), Degrees		*P*
	Group 1: Not 2b	Group 2: 2b	
Active flexion			
Preop	162 (148 to 166)	154 (147 to 162)	.51
4 mo postop	143 (118 to 158)	136 (115 to 146)	.25
6 mo postop	148 (131 to 152)	140 (115 to 154)	.31
Change (6 mo – preop)	−14 (−16 to −16)	−34 (−48 to −4)	.07
Active abduction			
Preop	161 (143 to 164)	157 (150 to 162)	.68
4 mo postop	151 (89 to 166)	87 (69 to 145)	**.04**
6 mo postop	154 (114 to 166)	93 (84 to 155)	**.046**
Change (6 mo – preop)	−7 (−28 to 4)	−61 (−88 to 4)	.06
Active internal rotation			
Preop	70 (55 to 100)	85 (50 to 100)	.98
4 mo postop	67.5 (44 to 84)	55 (43 to 65)	.12
6 mo postop	65 (40 to 80)	50 (30 to 68)	.22
Change (6 mo – preop)	−18 (−30 to 0)	−20 (−35 to −10)	.23
Active external rotation			
Preop	60 (35 to 90)	75 (41 to 81)	.68
4 mo postop	58 (41 to 74)	40 (28 to 55)	**.02**
6 mo postop	50 (35 to 75)	43 (28 to 50)	.29
Change (6 mo – preop)	−10 (−15 to 5)	−13 (−30 to −5)	.22
Passive flexion			
Preop	166 (163 to 171)	161 (159 to 170)	.46
4 mo postop	160.5 (147 to 172)	160 (153 to 166)	.70
6 mo postop	165 (150 to 170)	162 (143 to 171)	.79
Change (6 mo – preop)	−3 (−13 to 4)	−1 (−31 to 3)	.84
Passive abduction			
Preop	173 (165 to 175)	162 (154 to 174)	.13
4 mo postop	168 (128 to 177)	172 (141 to 176)	.80
6 mo postop	171 (153 to 180)	169 (142 to 172)	.41
Change (6 mo – preop)	−1 (−17 to 6)	−8 (−32 to 20)	.90

Abbreviations: IQR, interquartile range; postop, postoperative; preop, preoperative; ROM, range of motion.
All measurement values are presented as medians. Bolded values denote statistical significance ($P \leq .05$).

observed even with SND (2a-4) is potentially related to the partial devascularization of the SAN on the superior aspect of level 2a.[8] It could also be due to an SAN injury when the level III/IV contents are pulled up under the SCM. The SAN is in close proximity and can be grossly injured or overstimulated during this part of the dissection if the surgeon is not careful. However, the technique used within this trial minimized any cautery or blind dissection during this part of the SND. In addition, all SANs were stimulated strongly with a low current at the end of SND; this supports the idea that the dysfunction from SND (2a-4) is more likely due to ischemia than technique.

All patients experienced decreases in self-perceived shoulder function after SND (2-4). Partial recovery occurred at 6 months, as expected, but none returned to the baseline.[24,30] This was despite all patients being enrolled in a progressive resistance exercise training program.[24,30] Similar results showing a universal drop in NDII scores have been shown for more extensive neck dissections and those exposed to XRT.[8,19,33,36]

This is the first study to establish the MICD for NDII scores (18.1 points). The value defines how much change in shoulder-related QOL is meaningful to patients. Moreover, this allows the current data to show clinically significant improvements in shoulder-related QOL when level 2b is spared in SND. Future trials may use this value in studying shoulder function after neck dissection.

TABLE 4. Perioperative Shoulder Strength Testing per Group

	1 Repetition Maximum, Median (IQR), lbs		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	70 (48 to 100)	80 (50 to 90)	.72
4 mo postop	70 (53 to 100)	80 (50 to 100)	.99
6 mo postop	70 (47 to 100)	70 (34 to 95)	.55
Change (6 mo – preop)	0 (0 to 0)	0 (0 to 0)	.49
	Muscular Endurance, Median (IQR), Repetitions		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	20 (17 to 24)	21 (19 to 23)	.78
4 mo postop	10 (7 to 13)	8 (5 to 13)	.45
6 mo postop	11 (10 to 19)	11 (10 to 15)	.43
Change (6 mo – preop)	−7 (−11 to −3)	−9 (−16 to −4)	.41
	Shoulder Height, Median (IQR), cm		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	150 (145 to 152)	151 (139 to 153)	.78
4 mo postop	152 (147 to 154)	151 (140 to 155)	.49
6 mo postop	149 (147 to 152)	151 (142 to 153)	.94
Change (6 mo – preop)	−0.1 (−2 to 0.7)	−1 (−1 to −1)	.99

Abbreviations: IQR, interquartile range; postop, postoperative; preop, preoperative.
All measurement values are presented as medians.

TABLE 5. Perioperative Spinal Accessory Nerve Conduction Studies on the Randomized Neck

	Distal Motor Latency, Median (IQR), ms		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	2.2 (2.0 to 2.4)	2.2 (2.0 to 2.4)	.86
4 mo postop	2.1 (1.6 to 3.0)	2.2 (1.9 to 3.6)	.43
6 mo postop	2.2 (0.9 to 2.4)	2.6 (1.8 to 2.8)	.05
Change (6 mo – preop)	0.1 (−1.4 to 0.4)	0.2 (−0.1 to 0.9)	.25
	Action Potential Amplitude, Median (IQR), mV		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	8.1 (7.9 to 9.7)	7.9 (7.1 to 10.3)	.60
4 mo postop	7.8 (4.2 to 8.5)	2.3 (0.9 to 4.7)	**.04**
6 mo postop	7.6 (4.4 to 8.8)	1.4 (0.7 to 3.3)	**.002**
Change (6 mo – preop)	−0.4 (−3.6 to 0.1)	−5.6 (−9.3 to −4.0)	**.004**
	Area, Median (IQR), mVms		
Perioperative Time Period	Group 1: Not 2b	Group 2: 2b	*P*
Preop	76.7 (68.9 to 86.3)	78.7 (58.8 to 96.9)	.92
4 mo postop	73.5 (24.5 to 79.2)	21.1 (8.1 to 41.8)	**.04**
6 mo postop	61.2 (29.5 to 74.6)	24.4 (10.1 to 43.5)	**.04**
Change (6 mo – preop)	−14.4 (−46.8 to 1.3)	−47.1 (−100.8 to −32.6)	.05

Abbreviations: IQR, interquartile range; postop, postoperative; preop, preoperative.
All measurement values are presented as medians. Bolded values denote statistical significance ($P \leq .05$).

All active ROM measures declined in both groups from the baseline to 6 months. Although most patients showed a partial recovery, no patient experienced a full recovery. Previous studies support the idea that the most significant ROM disruption is in abduction when both level 5[15,16] and level 2b are dissected.[8] Active abduction was most affected. Patients with level 2b dissected lost a median of 61 degrees in abduction, which was significantly worse than that for their counterparts at 6 months ($P = .049$). The decline of 61 degrees from the baseline very likely represents a clinically meaningful difference but only approached statistical significance

($P = .06$). In a feasibility study, Parikh et al[8] also found that patients with level 2b dissected experienced the most ROM disruption in abduction. This is similar to what Celik et al[11] showed, with abduction tending to show the majority of its improvement 6 months after surgery.

Because both groups received identical PT interventions postoperatively, it was possible to control for differences in outcomes that would have been influenced by rehabilitation services.[37] Passive ROM was not significantly affected by level 2b dissection, and this suggests that the loss of active ROM was not due to mechanical contractures in the shoulder joint. Rather, the loss of motion was linked to losses in nerve function. Although the progressive resistance exercise training program helps to minimize fibrotic changes and preserve shoulder-joint/soft-tissue mobility, it cannot fully compensate for the loss of nerve function.[33]

Both groups maintained shoulder strength, endurance, and shoulder height. This is likely attributable to the development of compensatory musculature in the shoulder girdle, as has previously been described.[23,24,30]

EMG changes showed markedly worse nerve function in group 2 (2b). Compound motor amplitude potentials and negative peak areas, which are directly proportional to axon numbers, fell. Distal motor latencies remained unchanged within and between groups, and this suggests that SAN myelin is undamaged. This points to axonotmesis and not neuropraxia as the main mechanism of nerve injury, which is consistent with a stretch or ischemic injury (vs compression). There was a significant difference between groups at all time points and especially in the change from baseline. Similar results have been reported in nerve conduction amplitude drops after extensive level 5 SAN dissection.[8,35] Despite the use of a technique that avoids direct stretch to the SAN, the SCM requires retraction to expose level 2b. Through this retraction, it is conceivable that indirect SAN stretch occurs. It is possible that different neck dissection techniques could result in various degrees of nerve disruption. A future study could be performed to compare different methods of level 2 and SAN dissection.

Some claim that level 2b dissection is difficult and time-consuming.[8,38,39] Level 2b dissection required 3 additional minutes of surgical time in this study. Although this was statistically significant, it was certainly not a clinically meaningful difference. This was the first study to show the time needed to complete level 2b dissection.

The lymph node yield of level 2b averaged 6 nodes, which was on par with previous reports.[38] Moreover, there were no neck recurrences after 5 years. Thus, it was ensured that appropriately thorough dissections were performed.

Limitations included a low sample size; however, the trial met the a priori power calculation for the primary outcome and had high post hoc power. It was, however, limited in numbers for nerve conduction testing because some patients opted out on account of ongoing neck pain/discomfort or difficulty in attending appointments. Recruiting patients for this trial was challenging because the strict criteria made many patients ineligible.

Parikh et al[8] conducted a similar study in which patients were randomized to different SNDs. This pilot study also found patient attrition to be an issue. Their study focused on EMG results, which are likely the most objective measure of SAN function after neck dissection, but it did not focus on patient-reported outcomes. Moreover, their study lacked the rigorous controls of the current trial in terms of controlling for PT intervention, arm dominance, and surgical technique (all of the current participants received a bilateral neck dissection). Lima et al[35] have shown that EMG testing can pick up subclinical SAN dysfunction. It is important that subclinical and even major EMG changes in the SAN rarely correlate with subjective findings such as QOL.[19,40] This is the first RCT to investigate shoulder function–related QOL changes when level 2b is dissected.

The current trial stopped measuring outcomes at 6 months, which is when shoulder function often begins to recover after neck dissection when level 5 is spared.[11,23] Emerging evidence demonstrates that SAN recovery and objective shoulder function may continue to slowly improve beyond 1 year after neck dissection.[41] The current data show that most recovery seems to happen after 4 months and that between 4 and 6 months, QOL and functional measures improve only minimally. This study focuses on the period of time with the most recovery and may reflect only short-term recovery. Previous studies have also shown that the majority of shoulder function improves within the first 6 months.[8,11,23] However, slow improvement may continue for a year or longer.[41] Thus, patients, especially those undergoing 2b dissection, may benefit from ongoing PT and follow-up beyond 6 months. Future studies could consider follow-up of 1 year or longer because shoulder-related QOL and functional measures may continue to improve over time. This would be especially true for patients committed to ongoing long-term shoulder rehabilitation.

Because we know that level 2b–preserving SND produces improved shoulder function, the next question is this: When is it oncologically safe to omit level 2b in SND? The long-term follow-up of this study showed that no patient had a neck recurrence. Hoyt et al[12] have shown that contralateral level 2b nodes very rarely have metastatic lymph nodes across all head and neck mucosal cancer sites. Paleri et al[41] found that only 18 of 903 patients with head and neck cancer (2%) had level 2b nodal disease. Several others have corroborated these data.[39] Thus, there is evidence to suggest when level 2b could be safely omitted in SND. However, this study was not designed or powered to answer this question.

In conclusion, SND including level 2b leads to significant long-term deterioration in QOL and active abduction and nerve conduction amplitude deficiencies. When it is oncologically sound, level 2b should be omitted from SND.

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CONFLICT OF INTEREST DISCLOSURES

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AUTHOR CONTRIBUTIONS

Peter T. Dziegielewski: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, validation, visualization, revisions, manuscript writing, manuscript reviewing, and manuscript editing. **Margaret L. McNeely:** Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, validation, revisions, manuscript writing, manuscript reviewing, and manuscript editing. **Nigel Ashworth:** Data curation, formal analysis, investigation, methodology, project administration, resources, validation, manuscript writing, manuscript reviewing, and manuscript editing. **Daniel A. O'Connell:** Formal analysis, investigation, methodology, validation, revisions, manuscript reviewing, and manuscript editing. **Brittany Barber:** Data curation, formal analysis, investigation, validation, manuscript reviewing, and manuscript editing. **Kerry S. Courneya:** Formal analysis, investigation, methodology, project administration, resources, validation, manuscript reviewing, and manuscript editing. **Brock J. Debenham:** Formal analysis, investigation, validation, manuscript reviewing, and manuscript editing. **Hadi Seikaly:** Conceptualization, formal analysis, funding acquisition, investigation, methodology, supervision, validation, revisions, manuscript reviewing, and manuscript editing.

REFERENCES

1. Crile G III. On the technique of operations upon the head and neck. *Ann Surg*. 1906;44:842-850.
2. Schmitz S, Machiels JP, Weynand B, Gregoire V, Hamoir M. Results of selective neck dissection in the primary management of head and neck squamous cell carcinoma. *Eur Arch Otorhinolaryngol*. 2009;266:437-443.
3. Gane EM, Michaleff ZA, Cottrell MA, et al. Prevalence, incidence, and risk factors for shoulder and neck dysfunction after neck dissection: a systematic review. *Eur J Surg Oncol*. 2017;43:1199-1218.
4. Nahum AM, Mullally W, Marmor L. A syndrome resulting from radical neck dissection. *Arch Otolaryngol*. 1961;74:424-428.
5. Taylor RJ, Chepeha JC, Teknos TN, et al. Development and validation of the Neck Dissection Impairment Index: a quality of life measure. *Arch Otolaryngol Head Neck Surg*. 2002;128:44-49.
6. Chepeha DB, Taylor RJ, Chepeha JC, et al. Functional assessment using Constant's Shoulder Scale after modified radical and selective neck dissection. *Head Neck*. 2002;24:432-436.
7. Remmler D, Byers R, Scheetz J, et al. A prospective study of shoulder disability resulting from radical and modified neck dissections. *Head Neck Surg*. 1986;8:280-286.
8. Parikh S, Tedman BM, Scott B, Lowe D, Rogers SN. A double blind randomised trial of IIb or not IIb neck dissections on electromyography, clinical examination, and questionnaire-based outcomes: a feasibility study. *Br J Oral Maxillofac Surg*. 2012;50:394-403.
9. Koybasioglu A, Bora Tokcaer A, Inal E, Uslu S, Kocak T, Ural A. Accessory nerve function in lateral selective neck dissection with undissected level IIb. *ORL J Otorhinolaryngol Relat Spec*. 2006;68:88-92.
10. Koybasioglu A, Tokcaer AB, Uslu S, Ileri F, Beder L, Ozbilen S. Accessory nerve function after modified radical and lateral neck dissections. *Laryngoscope*. 2000;110:73-77.
11. Celik B, Coskun H, Kumas FF, et al. Accessory nerve function after level 2b–preserving selective neck dissection. *Head Neck*. 2009; 31:1496-1501.
12. Hoyt BJ, Smith R, Smith A, Trites J, Taylor SM. IIb or not IIb: oncologic role of submuscular recess inclusion in selective neck dissections. *J Otolaryngol Head Neck Surg*. 2008;37:689-693.
13. Dziegielewski PT, O'Connell DA, Szudek J, et al. Neck metastases in oropharyngeal cancer: necessity and extent of bilateral treatment. *Head Neck*. 2013;35:1461-1467.
14. Smith R, Taylor SM, Trites JR, Smith A. Patterns of lymph node metastases to the submuscular recess. *J Otolaryngol*. 2007;36:203-207.
15. Rogers SN, Lowe D, Paleri V. A survey of head and neck surgical oncologists regarding the inclusion of level IIb in a neck dissection of the node negative neck. *Br J Oral Maxillofac Surg*. 2011;49:230-232.
16. Cappiello J, Piazza C, Nicolai P. The spinal accessory nerve in head and neck surgery. *Curr Opin Otolaryngol Head Neck Surg*. 2007;15:107-111.
17. Villaret AB, Piazza C, Peretti G, et al. Multicentric prospective study on the prevalence of sublevel IIb metastases in head and neck cancer. *Arch Otolaryngol Head Neck Surg*. 2007;133:897-903.
18. Elsheikh MN, Rinaldo A, Ferlito A, et al. Elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma: is dissection of sublevel IIB necessary? *Oral Oncol*. 2008;44:216-219.
19. Giordano L, Sarandria D, Fabiano B, Del Carro U, Bussi M. Shoulder function after selective and superselective neck dissections: clinical and functional outcomes. *Acta Otorhinolaryngol Ital*. 2012;32:376-379.
20. Orhan KS, Demirel T, Baslo B, et al. Spinal accessory nerve function after neck dissections. *J Laryngol Otol*. 2007;121:44-48.
21. Mendez A, Seikaly H, Ansari K, Murphy R, Cote D. High definition video teaching module for learning neck dissection. *J Otolaryngol Head Neck Surg*. 2014;43:7.
22. O'Connell DA, Barber B, Klein MF, et al. Algorithm based patient care protocol to optimize patient care and inpatient stay in head and neck free flap patients. *J Otolaryngol Head Neck Surg*. 2015;44:45.
23. McNeely ML, Parliament M, Courneya KS, et al. A pilot study of a randomized controlled trial to evaluate the effects of progressive resistance exercise training on shoulder dysfunction caused by spinal accessory neurapraxia/neurectomy in head and neck cancer survivors. *Head Neck*. 2004;26:518-530.
24. McNeely ML, Parliament MB, Seikaly H, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: a randomized controlled trial. *Cancer*. 2008;113:214-222.
25. Goldstein DP, Ringash J, Bissada E, et al. Evaluation of shoulder disability questionnaires used for the assessment of shoulder disability after neck dissection for head and neck cancer. *Head Neck*. 2014;36:1453-1458.
26. Buschbacher RM, Kumbhare DA, Robinson LR. Buschbacher's Manual of Nerve Conduction Studies. Demos Medical; 2016.
27. Dumitru D, Amato AA, Zwarts MJ. Electrodiagnostic Medicine. Hanley & Belfus; 2002.
28. Liveson JA, Ma DM. Laboratory Reference for Clinical Neurophysiology. FA Davis; 1992.

29. McNeely ML, Parliament MB, Seikaly H, et al. Predictors of adherence to an exercise program for shoulder pain and dysfunction in head and neck cancer survivors. *Support Care Cancer*. 2012;20:515-522.
30. McNeely ML, Parliament MB, Seikaly H, et al. Sustainability of outcomes after a randomized crossover trial of resistance exercise for shoulder dysfunction in survivors of head and neck cancer. *Physiother Can*. 2015;67:85-93.
31. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol*. 2008;61:102-109.
32. Rai SK, Yazdany J, Fortin PR, Avina-Zubieta JA. Approaches for estimating minimal clinically important differences in systemic lupus erythematosus. *Arthritis Res Ther*. 2015;17:143.
33. Guldiken Y, Orhan KS, Demirel T, Ural HI, Yucel EA, Deger K. Assessment of shoulder impairment after functional neck dissection: long term results. *Auris Nasus Larynx*. 2005;32:387-391.
34. Patel KN, Shah JP. Neck dissection: past, present, future. *Surg Oncol Clin N Am*. 2005;14:461-477, vi.
35. Lima LP, Amar A, Lehn CN. Spinal accessory nerve neuropathy following neck dissection. *Braz J Otorhinolaryngol*. 2011;77:259-262.
36. Laverick S, Lowe D, Brown JS, Vaughan ED, Rogers SN. The impact of neck dissection on health-related quality of life. *Arch Otolaryngol Head Neck Surg*. 2004;130:149-154.
37. Selcuk A, Selcuk B, Bahar S, Dere H. Shoulder function in various types of neck dissection. Role of spinal accessory nerve and cervical plexus preservation. *Tumori*. 2008;94:36-39.
38. Bhattacharya A, Adwani D, Adwani N, Sharma V. Is it worthy? Removal of level IIB nodes during selective neck dissection (I-III) for oral carcinomas. *Ann Maxillofac Surg*. 2015;5:20-25.
39. Bartella AK, Kloss-Brandstatter A, Kamal M, et al. "IIb or not IIb"—the necessity of dissection in patients with oral squamous cell carcinoma. *J Craniomaxillofac Surg*. 2016;44:1733-1736.
40. Cheng PT, Hao SP, Lin YH, Yeh AR. Objective comparison of shoulder dysfunction after three neck dissection techniques. *Ann Otol Rhinol Laryngol*. 2000;109:761-766.
41. Paleri V, Kumar Subramaniam S, Oozeer N, Rees G, Krishnan S. Dissection of the submuscular recess (sublevel IIb) in squamous cell cancer of the upper aerodigestive tract: prospective study and systematic review of the literature. *Head Neck*. 2008;30:194-200.