

Diagnostic accuracy of upper limb neurodynamic tests in the diagnosis of cervical radiculopathy

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1 **Introduction**

2 Cervical radiculopathy (CR) is a relatively common neurological disorder caused by
3 mechanical compression from a disc or other space-occupying lesion or from inflammation to
4 the nerve root (Anekstein et al, 2012) The annual incidence of CR is 107.3 per 100,000 for
5 men and 63.5 per 100,000 for women (Radhakrishnan et al, 1990). The clinical manifestations
6 of cervical radiculopathy may include pain, sensory deficits, motor deficits, diminished
7 reflexes, or combinations of these. Cervical radiculopathy typically is self-limiting with 75%–
8 90% of patients achieving symptomatic improvement or resolution within a year with
9 conservative care (Woods et al, 2015)

10 Although no gold standard exists as a reference standard for cervical radiculopathy,
11 magnetic resonance imaging (MRI) is the preferred diagnostic method (Mink et al, 2003),
12 since it can differentiate tumors, inflammation, visualize trauma, and the extensiveness of
13 disc, arthritic, neural, and vascular cervical pathologies. Electrodiagnostic tests are capable of
14 detecting clinically significant problems in many patients as well, although they are operator
15 dependent and variable methods and normative values are used in practice (Reza Soltani et al,
16 2014). Furthermore it may be negative if performed before denervation has occurred or when
17 re-innervation is complete (Ashkan et al, 2002). Cervical radiculopathy is considered a
18 ‘clinical diagnosis with imaging confirmation’, and it is important to match valid clinical
19 signs with MRI findings and/or electrodiagnostic test results (Carette and Fehlings, 2005 ;
20 Kuijper et al, 2009).

21 There are numerous clinical tests used to diagnose cervical radiculopathy. Upper Limb
22 neurodynamic tests ((ULNT) 1, 2a, 2b and 3), or also called upper limb tension test (ULTT),
23 initially described by Elvey (Elvey, 1986), Butler (Butler, 2000) and Shacklock (Shacklock
24 1996), involve targeted sequences of movement that provoke mechanosensitivity of the nerve.
25 The tests are performed by placing and releasing progressively more tension on the proposed

26 component of the nervous system that is being tested. A recent systematic review (Thoomes
27 et al, 2017) concluded that “limited evidence for accuracy of physical examination tests for
28 the diagnosis of CR” exists.

29 Moreover, neurodynamic test procedures in studies that populated the aforementioned
30 systematic review used a variety of testing methods and results to determine a positive
31 finding. Three criteria has been advocated when testing: 1) reproduction of neurogenic pain-
32 burning or lightning-like pain, tingling sensation in the neck and arm (Apelby-Albrecht et al,
33 2012), the patient’s symptoms reproduced (Wainner et al, 2003), or reproduction of pain
34 (Ghasemi et al, 2013); 2) side to side range of motion difference (Wainner et al, 2003) or
35 side-to-side difference in painful radiation (Apelby-Albrecht et al, 2012); and 3)
36 increased/decreased symptoms with structural differentiation (Apelby-Albrecht et al, 2012) or
37 cervical structural differentiation with cervical spine movement alone (Wainner et al, 2003).
38 Interestingly, there is inconsistency in what is advocated to measure including conflicting
39 evidence for reproduction of any pain or discomfort (Apelby-Albrecht et al, 2012 ; Ghasemi
40 et al, 2013); and side to side range of motion comparisons (Nee et al, 2012). Most studies
41 advocate the use of structural differentiation, which involves directional movement of a
42 defined body region (e.g., neck side flexion) away from the area assessed to evaluate the
43 effect of mechanical force on the nervous system and its impact on the patient’s symptoms.

44 In clinical practice, many clinicians have assessed the accuracy of neurodynamic tests
45 on two criteria as recommended by Nee et al (Nee et al, 2012) : 1) familiar patient’s
46 pain/symptoms reproduced and 2) increased/decreased symptoms with structural
47 differentiation. Since we are unfamiliar with any studies that have included both findings in
48 the assessment of CR, we investigated the accuracy of four ULNTs in comparison against a
49 reference standard of medical history and MRI confirmation in patients with and without CR.
50 We hypothesized that the findings may provide insight on the role of ULNTs (e.g., screening

51 or confirmation) and that the more rigid definition of a positive test should improve the
52 specificity of the test findings. Further, combinations of test findings should result in more
53 diagnostic accuracy than individual tests alone.

54

55 **Materials and Methods**

56 The study was a diagnostic accuracy study (prospective) design in which clinical
57 testing occurred in a state of diagnostic uncertainty. The study followed the updated 2015
58 STARD reporting standards (Bossuyt et al, 2015). Patients were informed about the study and
59 they gave their consent for participation before inclusion. The study was conducted in
60 accordance with the Ethical principles and the Helsinki Declaration on research involving
61 human subjects and was approved the French regulatory and ethics rules (n°2212189v0).

62 Participants were recruited from consecutive patients referred to a Neurosurgery
63 Department by a general practitioner or specialist from September 2017 to September 2019.
64 Each patient had a suspected neck disorder. Referred patients provided information and
65 questionnaires about pain intensity and neck disability. To be included patients had to be aged
66 18 to 65 years, reporting arm pain with or without neck pain of at least 3-months in duration.
67 In addition, they were required to have a self-reported pain score of at least 30mm and less
68 than 80 on a 100 mm visual analogue scale (VAS) (Horn et al, 2016) during the previous 24
69 hours, and had a self-reported score of at least 20% on the Neck Disability Index
70 questionnaire (NDI) (Masaracchio et al, 2013).

71 Subjects were excluded if they were unable to understand French, had suffered from a
72 significant neck trauma at the time of the study (i.e., recent cranio-cervical trauma including
73 cervical spine fracture), had a history of neck or arm surgery, inflammatory joint
74 condition/arthritis, fibromyalgia, diabetes, pregnancy, cardiovascular, neurological, neoplastic
75 or psychiatric pathology, cervical myelopathy, pyramidal or extrapyramidal pathology.

76

77 *Reference Standard:* The diagnosis of CR or a competing diagnosis was made by a
78 single neurosurgeon with 15 years of experience from the consecutive patients included.
79 Cervical radiculopathy is a clinical diagnosis that is confirmed through imaging verification,
80 thus the diagnosis of CR was based on the following criteria: 1) history and presence of
81 dermatomal radicular pain and/or symptoms (dysesthesia, muscle weakness or altered
82 reflexes) attributable to a CR and 2) presence of MRI findings. MRI findings were specific
83 in their confirmation of nerve root compression or irritation by disc herniation or stenosis in
84 pre- or intra-foraminal space narrowing on the ipsilateral side and at the same or adjacent
85 level of radicular pain (Kuijper et al, 2008). The reference standard results were interpreted
86 without knowledge of the results of ULNT.

87 Index tests : Approximately one hour after the reference standard was provided by the
88 neurosurgeon, a single physiotherapist with 10 years of experience in neck pain management,
89 and advanced certification for orthopedic assessment evaluated the ULNT on each participant.
90 No intervention was allowed between the index test(s) and reference standard. The
91 physiotherapist was blind to the patient history, clinical/MRI findings and the diagnosis. The
92 index test results were interpreted without knowledge of the results of the reference standard
93 and the presence of CR. Before the tests, patients were instructed to communicate the onset
94 of any sensation such as stretch, tingling or pain anywhere in the arm or neck (Schmid et al,
95 2009). The patient was positioned supine without a pillow (Walsh 2005). The examiner
96 performed the ULNTs for that are purported for the median (ULNT1 and ULNT2a), radial
97 (ULNT2b) and ulnar (ULNT3) nerves (Figure 1) in randomized order using randomization
98 software. Upper limb neurodynamic testing was operated according to the standardized
99 sequence previously described (Butler, 2000; Nee et al, 2012 ; Schmid et al, 2009), with a 5-
100 minute break between each test to avoid any pain sensitization by repeating tests (Walsh

101 2005). Passive movements were achieved to the end of range or until symptoms were
102 produced (Schmid et al, 2009). The non-symptomatic side was tested first for each ULNT for
103 familiarization with sensation/pain induced by tests. A ULNT was considered as positive if
104 both of the two following criteria were met:

- 105 - Reproduction of a familiar symptomatic complaint of arm pain and/or neck pain at
106 least partially (pain or dysesthesia including burning, or lightning-like pain, or
107 tingling sensation) (Nee et al, 2012);
- 108 - Structural differentiation: Once such a familiar complaint was provoked, structural
109 differentiation between neurogenic and non-neurogenic sources was performed by
110 the addition of sensitizing movements at a site distant to the pain: ipsilateral- or
111 contralateral cervical lateral flexion, elbow or wrist extension/flexion, or shoulder
112 girdle elevation (Appendix A) (Nee et al, 2012);

113 Tests were considered negative if each failed to meet the positive criteria identified above or
114 indeterminate if the patient was unable to tolerate the test of position to allow complete
115 execution of the test.

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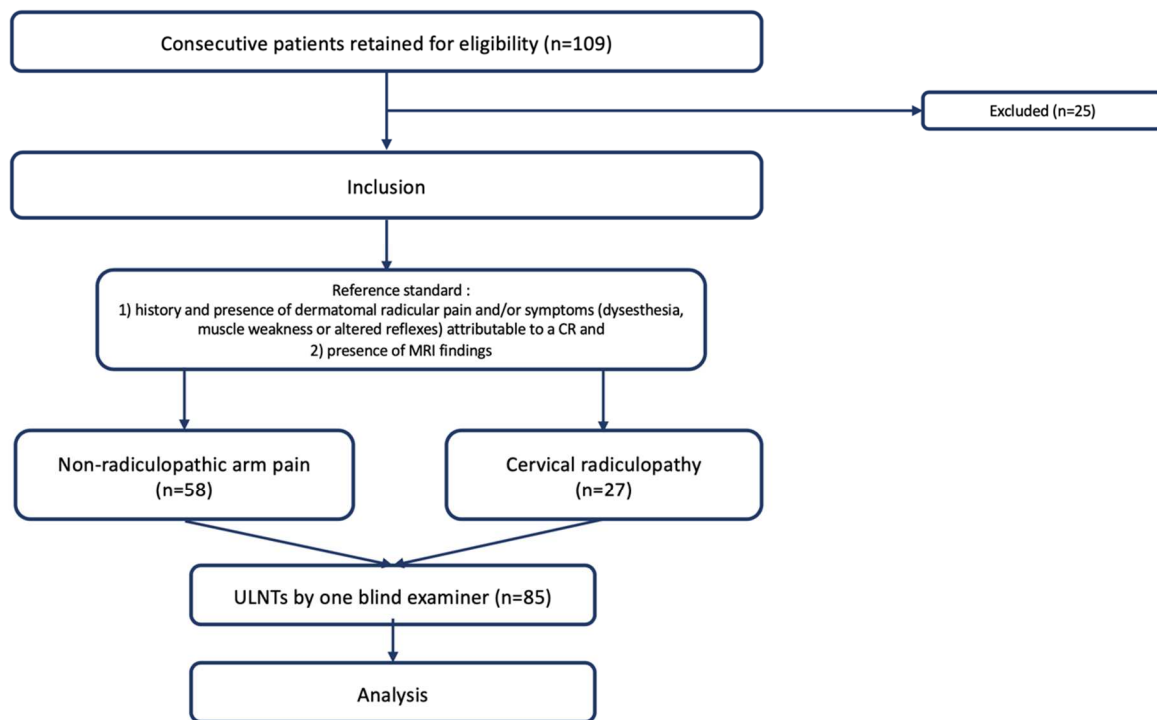
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123 **Figure 1. Flow chart**



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126 Results

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128 Statistical analysis were carried using SPSS (IBM SPSS, Version 26.0. IBM Corp.

129 Armonk, NY). Variables normality was tested with Shapiro-Wilk test for continuous data.

130 Nonparametric continuous variables were described as medians and interquartile ranges and

131 differences were tested using the Wilcoxon Mann Whitney test. Gaussian variables were

132 described with means and standard deviations and differences were tested using the Student's

133 t-test. Categorical variables were described as numbers and percentages. They were compared

134 using Chi square test or Fisher's exact test, as appropriate. P-value significance level was set

135 at .05 and all tests were bilateral. Two by two tables were created for each ULNT measure.

136 ULNT test performances were analyzed using calculations for sensitivity, specificity, positive

137 likelihood ratios (LR+), and negative likelihood ratios (LR-). Sensitivity is the percentage of

138 people whose test is positive for a specific disease among a group of people who have the

139 disease (Cook et al, 2020). Specificity is the percentage of people whose test is negative for a

140 specific disease among a group of people who do not have the disease [22]. LR+ are the
141 probability of a person with the disease testing positive divided by the probability of a person
142 without the disease testing positive (Cook et al, 2020). LR- are the probability of a patient
143 who has the condition of testing negative divided by the probability of a patient without the
144 disease, testing negative (Cook et al, 2020).

145 We also calculated pretest probability, which is the probability of the condition being
146 present before the diagnostic result is known and is sample specific for those enrolled in our
147 study, and post-test probability with a positive and a negative finding on the ULNTs. Post-test
148 probability is the percentage chance of the condition being present after a positive or negative
149 finding for a ULNT. Generally, a positive test will increase the post-test probability of
150 diagnosing the condition (otherwise known as ruling in the diagnosis). In contrast, a negative
151 finding will generally decrease the post-test probability of diagnosing the condition
152 (otherwise known as ruling out the condition) (Cook et al, 2020).

153 We calculated sensitivity/specificity, LR+/LR-, and post-test probabilities with a
154 positive and a negative finding for the four individual ULNT tests and combinations of these
155 tests. When calculating combinations of findings, the clusters of tests were placed in
156 “conditions” (e.g., 1 of 4 is positive, 2 of 4 is positive, etc.) and evaluated for their abilities to
157 influence post-test probability change with each defined condition. For all analyses, we also
158 evaluated post-test probability change, which is the difference between the pre-test prevalence
159 and the post-test finding with a positive or a negative result (Cook et al, 2020). Since the
160 purpose of a test is to change the post-test probability of an accurate diagnosis, larger post-test
161 probability changes were considered to have the highest clinical utility. 95% confidence
162 intervals (95%CI) were calculated for all of these features.

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164 Between September 2016 to December 2018, 85 participants, from 109 individuals

165 who were screened, were enrolled in the study. Of the 85 participants, 27 (31.7%) were
 166 diagnosed with CR, 42 with neck and non-radiculopathic arm pain, 12 with peripheral nerve
 167 entrapment, and 4 with diffuse shoulder pain (Table 1). All participants received the same
 168 reference standard and were included for analysis (Figure 1). Diagnostic accuracy of the
 169 four individual ULNTs are presented in Table 2. All four of the tests were more specific,
 170 than sensitive, with the ULNT3 demonstrating the highest specificity. None of the four tests
 171 markedly influenced post-test probability with a positive or a negative finding, with post-test
 172 probability changes from baseline prevalence ranging from 41.58% with a positive for
 173 ULNT3 to 15.72% with a negative for ULNT 2a.

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175 **Table 1:** Baseline characteristics of the subjects (n=85)

	Cervical radiculopathy	Non-radiculopathic arm pain	
Age*	43.96 (8.94)	45.27 (9.74)	p = 0.61
Height (m)	1.66 (0.09)	1.67 (0.08)	p = 0.54
Body Mass Index *	24.73 (3.91)	24.88 (4.97)	p = 0.74
Duration (self-report) in months *	93.25 (98.41)	70.51 (62.31)	p = 0.69
Visual Analogue Scale for Pain*	5.14 (1.58)	5.03 (1.53)	p = 0.73
Neck Disability Index (%)	38.16 (14.14)	43.07 (13.90)	p= 0.19

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179 **Table 2:** Diagnostic Accuracy of Individual Upper Limb Neurodynamic Tests. Pre-test
 180 Prevalence = 31.7%.

Sensitivity	Specificity	LR+ (95% CI)	LR- (95% CI)	Post-test Probability	Post-test Probability with
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					with a Positive Finding (95% CI)	a Negative Finding (95% CI)
ULNT 1	59.26 (38.80, 77.61)	75.86 (62.83, 86.13)	2.46 (1.41-4.27)	0.54 (0.33-0.87)	53.30 (39.55-66.46)	20.04 (13.28-28.76)
ULNT 2a	70.37 (49.82, 86.25)	72.41 (59.10, 83.34)	2.55 (1.57-4.14)	0.41 (0.22-0.75)	54.20 (42.15-65.77)	15.98 (9.26-25.82)
ULNT 2b	55.56 (35.33, 74.52)	75.86 (62.83, 86.13)	2.30 (1.30-4.06)	0.59 (0.38-0.92)	51.63 (37.63-65.33)	21.49 (14.99-29.92)
ULNT 3	40.74 (22.39, 61.20)	93.10 (83.27, 98.09)	5.91 (2.07, 16.87)	0.64 (0.46-0.88)	73.28 (48.99-88.65)	22.95 (17.59-28.99)

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183 Diagnostic accuracy of test conditions for combinations of ULNTs are presented in
184 Table 3. Characteristically, with lower conditions (e.g., 1 of 4 is positive) values exhibit
185 high sensitivity and low specificity, whereas higher conditions (4 of 4 are positive) values
186 exhibit low sensitivity and high specificity. As expected, the condition of 1 out of 4 ULNT
187 tests positive was the most sensitive combination whereas the condition of 4 out of 4 ULNT
188 tests was the most specific. The condition of 1 out of 4 tests positive has the ability to “rule
189 out” CR (LR-=0.08), exhibiting a post-test probability change of 28.12% with a negative
190 finding. The condition of 4 of 4 tests positive had an infinite LR+ but there were only 3
191 cases in which all four tests were positive. The condition of 3 of 4 tests positive occurred in
192 12 of the 27 patients with CR and provided a LR+ of 12.89 and a post-test probability of
193 85.71 (post-test probability change of 54.01%). No adverse events from performing the
194 index test or the reference standard were observed.

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200 **Table 3.** Diagnostic Accuracy of Clustered Upper Limb Neurodynamic Test findings
201 (Conditions). Pre-test Prevalence = 31.7%.
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Sensitivity	Specificity	LR + (95%	LR- (95% CI)	Post-test Probability	Post-test Probability with
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	CI				with a Positive Finding (95% CI)	a Negative Finding (95% CI)
1 of 4 Positive	96.30 (81.03, 99.91)	46.55 (33.34, 60.13)	1.80 (1.40, 2.32)	0.08 (0.01, 0.56)	45.51 (39.38-51.84)	3.58 (0.46-20.62)
2 of 4 Positive	85.19 (66.27, 95.81)	74.14 (60.96, 84.74)	3.29 (2.07, 5.23)	0.20 (0.08, 0.50)	60.42 (48.99-70.82)	8.49 (3.59-18.83)
3 of 4 Positive	44.44 (25.48-64.67)	96.55 (88.09-99.58)	12.89 (3.10-53.62)	0.58 (0.41, 0.81)	85.71 (59.06-96.14)	23.237 (18.57-28.82)
4 of 4 Positive	11.11 (2.35, 29.16)	100.00 (93.84, 100.00)	Inf.	0.89 (0.78, 1.02)	100	29.23 (26.58-32.13)

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205 **Discussion**

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This study sought to determine the diagnostic accuracy of four ULNTs in identifying

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CR in comparison with a reference standard of clinical diagnosis with MRI confirmation.

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The study was performed in a situation of diagnostic uncertainty and used a more rigid

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definition of what constitutes a positive test compared to previous studies [12-14]; the tests

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also more closely matched how the tests are used in clinical practice. Findings were that

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ULNTs when used in isolation did not lead to acceptable LR-, LR+ or post-test probability.

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However, 3 out of 4 tests positive can rule in CR with a LR+ of 12.89. One of four positive

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tests provided a LR- of 0.08 indicating that CR can be ruled out if no tests are positive. Of

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the four tests, the ULNT3 influenced post-test probability the most with a positive test

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(73.28%), whereas the ULNT2a influenced post-test probability the most with a negative

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test (15.98%).

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Each ULNT provided stronger LR+ values than LR-, thus influencing post-test probability

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with a positive finding more notability than a negative finding. Our findings are markedly

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different than those from Wainner et al. who found very low values of LR+ (<1.3) -

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suggesting that they did not rule in - and moderately low LR- values (>0.12) - suggesting

224 they are better for ruling out (Wainner et al, 2003). Ghasemi and colleagues [14] failed to
225 report a LR+ (or a LR-) (Ghasemi et al, 2013) and our calculations from their sensitivity and
226 specificity values yielded LR+ values similar or worse than those of Wainner and associates
227 (Wainner et al, 2003). The differences in findings compared to those of others (Wainner et
228 al, 2003 ; Ghasemi et al, 2013) are likely related to the way we defined a positive index test
229 (familiar compliant that was altered by structural differentiation). In Wainner and
230 colleagues' study, an ULNT was defined as positive if only one of the following criteria
231 were present: reproduction of the patient's symptoms, or side to side range of motion deficit,
232 or structural differentiation using the cervical spine (Wainner et al, 2003). Ghasemi et al.,
233 reported a positive finding if 'pain' occurred during testing (hasemi et al, 2013). Basing the
234 test outcome on one criterion alone as identified by those authors could lead to an increase
235 in false positive findings, thus decreasing specificity, and worsening the LR+ value
236 (Schiffman et al, 2014). Apelby-Albrecht et al. defined as positive if all the three following
237 criteria were met: reproduction of neurogenic symptoms according to a dermatomal pattern,
238 increased or decreased symptoms with structural differentiation, and a difference in painful
239 radiation between sides (Apelby-Albrecht et al, 2013). Our LR+ values are very similar to
240 previous findings by a recent systematic review (Thoomes et al, 2017) calculated from data
241 reported by Apelby-Albrecht et al (Apelby-Albrecht et al, 2013). However, in our study
242 ULNT was defined as positive according to two criteria and we include a more mixed
243 control group population (58 neck or shoulder pain, thoracic outlet syndrome and carpal
244 tunnel syndrome) than Apelby-Albrecht (only 18 subjects with neck pain or carpal tunnel
245 syndrome) (Apelby-Albrecht et al, 2013). These findings highlight the importance to
246 clinicians of determining a positive ULNT based on symptom reproduction together with the
247 effects of structural differentiation, at least in diagnosing cervical radiculopathy.

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249 In their recent systematic review of diagnostic tests for CR, Koulidis et al [25] concluded
250 that ULNTs could only be used as a “ruling out” strategy (Koulidis et al, 2019) based on
251 Apelby-Albrecht et al’s data (Apelby-Albrecht et al, 2013). Conversely, in our sample,
252 ULNT when used in isolation were better at ruling in CR versus ruling out, yet clustering
253 the ULNT findings produced large changes in post-test probability with either a negative
254 finding or a positive finding. The condition of one of four positive tests yields a LR- of 0.08
255 (95%CI=0.01-0.56). This means that when none of the four ULNTs are positive it can rule
256 out CR with only a 3.58% chance that the patients in this sample had CR. Moreover, using
257 multiple combination of ULNT demonstrated that the condition of 3 of 4 positive tests
258 yielded a LR+ of 12.89 (95%CI=3.10-53.62) which means it can rule in CR with a post-test
259 probability of 85.71%. We recommend the use of 3 of 4 conditions over 4 of 4, since this
260 finding was uncommon and because the confidence intervals crossed 1.0 for the LR-
261 analyses.

262 We are also the first to report post-test probability of a positive and negative finding with an
263 ULNT, an analysis omitted from past works (Apelby-Albrecht et al, 2013; Ghasemi et al,
264 2013). Post-test probability provides a better understanding of how markedly one’s decision
265 is influenced by single, or combined, positive or negative test results. This is of particular
266 importance since the reporting of individual sensitivity and specificity values is not
267 recommended (Hegedus and Stern, 2009 ; Baeyens et al, 2019) and may yield conflicting
268 results for ruling in or ruling out conditions.

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270 *Study limitations*

271 Although there is notable debate on an appropriate sample size for a diagnostic
272 accuracy study (Hajian-Tilaki, 2014 ; Bujang and Adnan, 2016), we feel compelled to

273 identify our sample of 85 (including 27 CR) as a potential limitation. A smaller sample size
274 may lead to less precision (e.g., wide confidence intervals). Only one clinician was involved
275 in determining the reference standard and another was involved in determining the ULNT.
276 Although the ULNT tester was blinded to the diagnosis of the patient, the transferability of
277 their findings is unknown, since we did not test interrater agreement. Future research is
278 needed to assessed the validity of ULNT with a larger sample of patients with CR and a
279 larger control group with similar symptoms (thoracic outlet syndrome, neck/shoulder pain,
280 peripheral nerve entrapment, *etc.*), and with more examiner and reference standards
281 including magnetic resonance neurography and small fiber function (Schmid et al, 2013).

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284 **Conclusions**

285 Our results support past findings that the singular use of ULNT to rule in or rule out
286 CR is not recommended. When combinations are used, findings have higher clinical utility.
287 When all ULNTs are negative, CR can be ruled out, whereas when 3 of 4 tests are positive,
288 CR can be ruled in. As such, we recommend the use of ULNT tests as combinations only.
289 Our study does not test the validity of ULNT tests for specific nerve trunks, which it is
290 hypothesized to perform.

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296 **Table 1:** Baseline characteristics of the subjects (n=85)

297 * *Wilcoxon rank sum test*

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300 **Table 2:** Diagnostic Accuracy of Individual Upper Limb Neurodynamic Tests. Pre-test

301 Prevalence = 31.7%.

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303 95%CI: Confidence interval at 95%

304 LR+: Positive likelihood ratio

305 LR-: Negative likelihood ratio

306 ULNT: Upper limb neurodynamic test

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309 **Table 3.** Diagnostic Accuracy of Clustered Upper Limb Neurodynamic Test findings

310 (Conditions). Pre-test Prevalence = 31.7%.

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312 95% CI: Confidence interval at 95%

313 LR+: Positive likelihood ratio

314 LR-: Negative likelihood ratio

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329 **Appendix A.** Standard sequence of joint movements and suggested structural differentiation
330 maneuvers (sensitizing movements at a site distant to the pain) for each ULNT (Nee et al,
331 2012)

ULNT 1 (median nerve) :

- Shoulder girdle stabilization
- Shoulder abduction
- Wrist/finger extension
- Forearm supination
- Shoulder external rotation
- Elbow extension
- Structural differentiation:
Cervical side bending or release wrist extension



ULNT 2a (median nerve) :

- Shoulder girdle depression
- Elbow extension
- Shoulder external rotation and forearm supination
- Wrist/finger extension
- Shoulder abduction
- Structural differentiation:
Cervical side bending, or release shoulder girdle depression or release wrist extension



ULNT 2b (radial nerve) :

- Shoulder girdle depression
- Elbow extension
- Shoulder external rotation and forearm pronation
- Wrist/finger flexion
- Shoulder abduction
- Structural differentiation :
Release shoulder girdle depression or release wrist flexion



ULNT 3 (ulnar nerve) :

- Wrist/finger extension
- Forearm pronation
- Elbow flexion
- Shoulder external rotation
- Shoulder girdle depression
- Shoulder abduction
- Structural differentiation :
Cervical side bending, or release shoulder girdle depression or release wrist extension



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335 **Abbreviations :**

336 CR : Cervical radiculopathy

337 ULNT : Upper limb neurodynamic tests

338 MRI : magnetic resonance imaging

339 LR+ : Positive likelihood ratio

340 LR- : Negative likelihood ratio

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