

# Assessment of hand function in women with lymphadenopathy after radical mastectomy (#55550)

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First revision

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# Assessment of hand function in women with lymphadenopathy after radical mastectomy

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**Background.** Breast cancer related to upper limb lymphedema (BCRL) is a common complication in post-mastectomy patients. It is known to cause upper limb disability, which subsequently may affect the grip strength and hand function. There is little evidence on the objective assessment of functional activities mainly hand function in women with BCRL. Therefore, this study objectively assesses the handgrip strength and hand functions in women with BCRL. **Method.** A cross-sectional study design was conducted on a sample of women with (n = 31) and without (n = 31) BCRL. The Handgrip strength and hand functions were measured using a dynamometer and Jepsen-Taylor hand function test, respectively. **Results.** The results showed a significantly reduced handgrip strength in women with BCRL as compared to age-matched healthy adult women for both right and left hands (p<0.05). Similarly, hand functions were significantly impaired in women with BCRL as compared to healthy adult women (p<0.05). Reduction in handgrip strength and hand function in women with BCRL were clinically meaningful as indicated by moderate to large effect sizes (Cohen's d = 0.61 to 0.99 and 0.54 to 3.02, respectively) in all outcomes except power handgrip strength in left hand (Cohen's d = 0.38). **Conclusion.** The results of this study indicate a significant reduction of hand grip strength and hand function in women with BCRL. Our findings suggest that objective measures of grip strength and function be included in the assessment of women with BCRL to better guide clinical decision making and patient care, which may include impairment associated with hand strength and function. Future studies that evaluate hand grip strength and function in a larger sample which include a more diverse age group of BCRL population are warranted to confirm the current findings.

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21

## 22 **Abstract**

23 **Background.** Breast cancer related to upper limb lymphedema (BCRL) is a common complication

24 in post-mastectomy patients. It is known to cause upper limb disability, which subsequently may

25 affect the grip strength and hand function. There is little evidence on the objective assessment of

26 functional activities ~~mainly~~ hand function in women with BCRL. Therefore, this study objectively

27 assesses the handgrip strength and hand functions in women with BCRL.

28 **Method.** A cross-sectional study design was conducted on a sample of women with (n = 31) and

29 without (n = 31) BCRL. The Handgrip strength and hand functions were measured using a

30 dynamometer and Jebsen-Taylor hand function test, respectively.

31 **Results.** The results showed a significantly reduced handgrip strength in women with BCRL as

32 compared to age-matched healthy adult women for both right and left hands (p<0.05). Similarly,

33 hand functions were significantly impaired in women with BCRL as compared to healthy adult  
34 women ( $p < 0.05$ ). Reduction in handgrip strength and hand function in women with BCRL were  
35 clinically meaningful as indicated by moderate to large effect sizes (Cohen's  $d = 0.61$  to  $0.99$  and  
36  $0.54$  to  $3.02$ , respectively) in all outcomes except power handgrip strength in left hand (Cohen's  $d$   
37  $= 0.38$ ).

38 **Conclusion.** The results of this study indicate a significant reduction of hand grip strength and  
39 hand function in women with BCRL. Our findings suggest that objective measures of grip strength  
40 and function be included in the assessment of women with BCRL to better guide clinical decision  
41 making and patient care, which may include impairment associated with hand strength and  
42 function. Future studies that evaluate hand grip strength and function in a larger sample which  
43 include a more diverse age group of BCRL population are warranted to confirm the current  
44 findings.

## 45 Introduction

46 Breast cancer related upper limb lymphedema (BCRL) is common in patients who undergo  
47 mastectomy. Lymphedema is a clinical condition in which accumulation of excess protein rich  
48 tissue fluid and tissue alterations causes oedema (*Karadibak & Yavuzsen, 2015*). The cancer  
49 registry program of twenty-five Population Based Cancer Registries (PBCRs) reports increasing  
50 trends for incidence and mortality of breast cancer in Indian women (*Malvia et al., 2017*). The  
51 cancer projection data showed that the number of breast cancer cases will increase to double by  
52 2020 (*Malvia et al., 2017*). A previous study reported 42% incidence of lymphedema in women  
53 who underwent mastectomy (*Norman et al., 2009*).

54 The major signs and symptoms lymphedema are: (a) increased limb circumference, (b)  
55 restricted range of motion of affected joints, (c) stiffness, (d) sensory impairment in the hand, and

56 (e) decrease use of affected limb for functional tasks (*Gomes et al., 2014*). Additionally,  
57 chemotherapy may cause disruption in muscle metabolism (e.g., cytokine dysregulation, adenosine  
58 triphosphate dysregulation, and deprivation of satellite cells) results muscle wasting leading to  
59 reduced muscle strength and fitness level (*Clarkson & Kaufman, 2010*).

60 Handgrip strength is essential for performing upper limb functional activities of daily living  
61 (*Rietman et al., 2003*). Women with BCRL may have impaired upper limb use during functional  
62 activities (*Noelle, 2005; Carol, 2017*). A cross-sectional study done in 2010, compared upper  
63 extremity impairment and activity following breast cancer treatment between women with or  
64 without BCRL and reported decreased grip strength and upper limb activities in women with  
65 BCRL (*Smoot et al., 2010*). BCRL is also associated with restricted range of motion in the affected  
66 limb, reduced functional ability, as well as physical disfigurement, pain, and skin problems. There  
67 is a significant negative relationship present between severity of oedema and hand function  
68 (*Karadibak & Yavuzsen, 2015*).

69 In the previous study, while left and right handgrip strengths were reduced in women with  
70 BCRL as compared to age-matched healthy women, no difference in left and right handgrip  
71 strengths in women with BCRL (*Gomes et al., 2014*). Another study reported a significantly  
72 impaired muscle strength and function in women with breast cancer who underwent chemotherapy,  
73 or a radical mastectomy as compared to healthy women (*Klassen et al., 2017*). More recently,  
74 *Winters-Stone et al. (2019)* reported a significantly lower handgrip strength and function in older  
75 women with breast carcinoma than healthy older adults.

76 Most studies that evaluated the hand functional activities and strength in women with BCRL,  
77 have used numerous types of questionnaires such as Hand Function Sort Questionnaire (HFS)  
78 (*Karadibak & Yavuzsen, T, 2015*) or Disability of Arm Shoulder Hand questionnaires (DASH)

79 (*Smoot et al., 2010*), and Hand Dynamometer (*Dawes et al., 2008*), ~~respectively~~ as their outcome  
80 measures. While most studies have used subjective measures to evaluate hand function in women  
81 with BCRL, few studies have used objective measure of hand function (*Smoot et al., 2010; Wong*  
82 *et al., 2019; Dollar et al., 2014; Kärki et al., 2005; Cantarero-Villanueva et al., 2012*). For  
83 instance, *Smoot et al. (2010)* used both subjective and objective measures such as DASH  
84 questionnaire and a handheld dynamometer to evaluate hand function and strength, respectively in  
85 women with or without BCRL. *Cantarero-Villanueva et al. (2012)* examined handgrip strength as  
86 an objective measure of function in breast cancer survivors. It is important to objectively assess  
87 hand grip strength and hand function so that appropriate and complete clinical assessment and  
88 intervention can be implemented to address any impairments or functional limitations in women  
89 with BCRL (*Mak et al., 2015; Rietman et al., 2004; Hayes et al., 2010; Park et al., 2012*).

90 There is limited research to determine objective assessment of hand function after surgery and  
91 chemotherapy treatment in women with breast cancer. Therefore, the purpose of this study is to  
92 (1) evaluate the hand grip strength and hand functional activities using objective outcome measures  
93 in women with BCRL; and (2) to compare findings in women with BCRL to ~~normative data~~. In  
94 women with BCRL, objective assessment of hand function will provide greater clarity and  
95 precision regarding performance of functional activities of daily living than subjective assessment  
96 alone, which will better guide clinical practice. The current study hypothesize that grip strength  
97 and objectively measured hand function will be impaired in women with BCRL compared to ~~those~~  
98 ~~who do not had~~ BCRL.

## 99 **Materials & Methods**

100 This study was an observational cross-sectional design with convenience sampling. All the  
101 subjects were recruited from Ramaiah Medical College Hospital and HCG MSR Cancer Centre,



102 Bengaluru, India. An ethical clearance was obtained from the Ethical Committee of Ramaiah  
103 Medical College and Hospital (MEU-PT/EC/12/2018). Purpose of the study was explained to each  
104 individual and a written informed consent was obtained.

105 The subjects were included based on the following criteria: (1) age between 35-65 years, (2)  
106 had completed chemotherapy/surgery  $\geq 6$  months, (3) women with BCRL for more than 3 months  
107 old, (4) affecting the dominant hand and (5) self-reported pain score of seven or less on visual  
108 analogue scale (because  $\geq 7$  pain score might influence handgrip strength and function)  
109 (*Cantarero-Villanueva et al., 2012*). Subjects were excluded if they were receiving radiotherapy,  
110 who had a history of fracture or surgery in upper limb in last 3 months or had neuromuscular or  
111 musculoskeletal disorders that would have prevented assessment of hand grip strength and  
112 function. The control group included a convenient sample of 31 healthy age-matched women  
113 without history of breast carcinoma.

#### 114 **Objective Measures**

115 A hand dynamometer and pinch gauge/pinch meter were used to measure power grip and precision  
116 grip strength and the Jebsen-Taylor hand function test (JTHFT) (*Mak et al., 2015*) tool kit was  
117 used to assess hand function. Hand dynamometer and pinch gauge are valid instruments to assess  
118 grip strength (*Neumann et al., 2017; Lindstrom-Hazel et al., 2009; Shin et al., 2012*). Handgrip  
119 strength and function of both patient (i.e., women with BCRL) and normal healthy (i.e., women  
120 without BCRL) samples were evaluated in a similar fashion.

#### 121 **Measurement of Power Grip Strength of Hand**

122 A baseline hand dynamometer was used to assess the power grip. Individuals were asked to hold  
123 the hand dynamometer, where the elbow was in 90 degrees flexion and shoulder in neutral position.

124 The individuals were asked to press the hand dynamometer as hard as they can, three times, and  
125 the best value was taken from ~~both the~~ hand (*Smoot et al., 2010*).

### 126 **Measurement of Precision Grip strength of Hand**

127 For assessing the precision grip, pinch gauge was used (*Smoot et al., 2010*). Individuals were asked  
128 to hold the pinch gauge and press it in three different position, Tip of thumb to tip of index finger,  
129 thumb pad to lateral aspect of index finger, and thumb pad to pad of index finger and pad of middle  
130 finger (Tripod pinch). Individuals sat on a chair, their elbow was in 90 degrees flexion and shoulder  
131 in neutral position. Instructions were given to the patients to press the pinch gauge in three different  
132 position (Tip to tip, Key pinch, and Tripod pinch) as hard as they can. Each precision grip was  
133 performed three times and the best value was taken from ~~both the~~ hand.

### 134 **Assessment of Hand Function**

135 For assessing bilateral hand function, the Jebsen-Taylor hand function test (JTHFT) (*Mak et al.,*  
136 *2015*) tool was used. It is a valid and reliable tool which objectively measures the hand function  
137 (*Mak et al., 2015*). It is a task specific tool, consisting of 7 tasks for assessing hand functions. The  
138 tasks are ~~u~~ writing, picking up small common objects, and picking up large objects, card turning,  
139 simulated feeding, and stacking checkers. Each task was measured by calculating time (*Mak et al.,*  
140 *2015*).

### 141 **Statistical analysis**

142 The data were tabulated in Microsoft Excel and the statistical program for social science software  
143 for Window (version 17, SPSS Inc, Chicago, IL) was used for the statistical analyses. Descriptive  
144 statistics was used to calculate the mean and standard deviation of the patient's age. A student t-  
145 test was used to determine statistical difference of grip strength and hand function between  
146 normative data and patient data. Additionally, the effect sizes were calculated using the Cohen's

147 d for each variable to evaluate clinically meaningful changes. Effect size were defined as: small ( $d$   
148 =  $<0.5$ ), medium ( $d = 0.50$  to  $0.80$ ), and large ( $d = >0.80$ ) (*Gärtner et al., 2010*). ~~Data was~~  
149 considered statistically significant if  $p < 0.05$ . The sample size was calculated using estimation of  
150 means from the formula ( $n = [Z_{\alpha}\sigma / d]^2$ ). Where  $Z_{\alpha}$  is 95% confidence level,  $\sigma$  is standard deviation,  
151 and  $d$  is the margin of error. The  $Z_{\alpha}$  was 1.96, the Standard deviation was 2.1 of writing in JTHFT  
152 and the margin of error was 0.75 (*Voogd et al., 2003*). The estimated sample size came to 31.

## 153 Results

154 ~~Total~~ 31 women with BCRL and 31 age-matched healthy women were included in the study (Table  
155 1). Out of 31 subjects, 21 subjects had right hand lymphedema and 10 subjects had left hand  
156 lymphedema. Sixty-eight percent women with BCRL and 58% healthy women were right hand  
157 dominant. Mean age of the patients and healthy groups were 55.5 ( $\pm 8.4$ ) and 55.7 ( $\pm 8.1$ ) years,  
158 respectively.

159 Table 2 presents the result of power grip and precision grip strength of right and left hands.  
160 There were significant reductions of both power and precision grip strengths  $p < 0.05$  ~~when~~  
161 ~~compared to normative data~~. Reductions in handgrip strength in women with BCRL were clinically  
162 meaningful as indicated by moderate to large effect sizes (Cohen's  $d = 0.61$  to  $0.99$ ) in all handgrip  
163 strength except power handgrip strength in left hand (Cohen's  $d = 0.38$ ).

164 Table 3 compares the activities of hand functions in women with and without BCRL. The hand  
165 functions were significantly reduced across all activities ~~when compared with normative data~~  
166 ( $p < 0.05$ ). Reduction in hand function in women with BCRL were clinically meaningful as  
167 indicated by moderate to large effect sizes (Cohen's  $d = 0.54$  to  $3.02$ , respectively) in all variables  
168 of hand functions.

## 169 Discussion

170 The present study examined the hand grip strength and hand functional activities in women with  
171 BCRL. Findings of the study indicate significant reduction in the power grip and precision grip  
172 strengths in women with BCRL as compared to age-matched healthy adult women. The results of  
173 the hand function also showed significantly increased time to complete the task performance.  
174 Reduction in handgrip strength and hand function in women with BCRL were also clinically  
175 meaningful as determined by moderate to large effect sizes (Cohen's  $d = 0.61$  to  $0.99$  and  $0.54$  to  
176  $3.02$ , respectively) in all outcomes except power handgrip strength in left hand (Cohen's  $d = 0.38$ ).

177 Reduced strength has been known to have debilitating effects on women with BCRL. Most  
178 studies demonstrate that upper limb lymphedema negatively affects the hand grip strength (*Wong*  
179 *et al.*, 2019). The same was found to be true among women with BCRL in the current study, mean  
180 of the dominant right-hand power grip was 23.8 kg and dominant left hand was 22.2 kg when  
181 compared to normative data of 29.4 and 25.5, respectively. The reduction of grip strength could  
182 be due to swelling in hand and wrist which in turn leads to decreased wrist and finger range of  
183 motion (ROM) and reduction of initiation of wrist extension and finger flexion (*Smoot et al.*, 2010).  
184 The position of producing a power grip for normal individual is, wrist in slight extension and elbow  
185 in 90 degrees of flexion, in BCRL patients the wrist extension is reduced due to swelling resulting  
186 in active insufficiency of hand muscles, ~~this active insufficiency~~ could reduce the strength of grip.  
187 A study conducted by *Dawes et al.* (2008) found similar results where women with BCRL had  
188 lesser hand grip strength, and shoulder ROM and other hand morbidities, which led to impairment.  
189 In precision grip strength, the activity of tip, key and tripod pinch requires much finer motor control  
190 and is more dependent on intact sensation. In case of women with BCRL, it is also seen that there  
191 is involvement of kinesthetic sense of wrist joint and small joints which reduces the force

192 generation during gripping activities (*Karadibak & Yavuzsen, 2015; Smoot et al., 2010*), this could  
193 be the probable reason for the reduced precision grip strength in the studied subjects.

194 BCRL and its complications involving impaired upper limb function are well established  
195 sequelae among breast cancer survivors. About 13 – 28% of breast cancer survivors post treatment  
196 when surveyed have reported limitations in daily activities (*Voogd et al., 2003*). The present  
197 participants when objectively assessed (JTHFT) for their hand function showed similar results to  
198 that available in literature. The JTHFT when administered to the women with BCRL, the duration  
199 of each activity like writing, picking up small common objects, and picking up large objects, card  
200 turning, simulated feeding, and stacking checkers performance was increased. The overall time  
201 taken for completion of tasks was 68.8 seconds for right hand dominant and 100.3 seconds for left  
202 hand dominant.

203 While performing JTHFT, the tasks require power grip and precision grip equally, like picking  
204 up large and heavy objects, handwriting, simulated feeding etc. Reduced power grip strength and  
205 precision grip strength will have implications on activity performance. Our subjects also showed  
206 reduced strength and task time was increased, thereby we can assume that strength does play a role  
207 in performing of hand functions. A study conducted by *Dawes et al. (2008)* reported that when  
208 DASH questionnaire along with grip strength assessment of women with BCRL was analyzed, the  
209 scores were higher in women who had self-reported symptoms of lymphedema, indicating activity  
210 limitation and participatory restriction. This reduction of hand function could be because of the  
211 reduction in power grip strength and precision grip strength and reduction of kinesthetic sense  
212 (*Karadibak & Yavuzsen, 2015*), thus suggesting that impairment in hand grip strength plays a part  
213 in performing hand function. Loss of muscle strength, lack of movement in articulation could also

214 add to the reasons for impaired hand function (*Karadibak & Yavuzsen, 2015; Rietman et al., 2003;*  
215 *Smoot et al., 2010; Dawes et al., 2008; Kärki, 2005*).

216 BCRL or hand oedema significantly affects functional mobility and activities of daily livings  
217 of upper extremity (*Karadibak & Yavuzsen, 2015; Rietman et al., 2003; Smoot et al., 2010; Dawes*  
218 *et al., 2008*). Additionally, women with BCRL may develop weaknesses and restriction of shoulder  
219 muscles and range of motion and reduced quality of life (*Karadibak & Yavuzsen, 2015*). Voogd et  
220 al. (2003) ~~examined the quality of life in women with BCRL and they~~ reported reduced daily  
221 functional skills, lack of energy and motivation, and reduced quality of life.

## 222 **Limitations and directions for future research**

223 The current study acknowledged some limitations. First, this study used a cross-sectional design,  
224 therefore, a causal relationship between BCRL, and hand grip strength and function could not be  
225 established. Future prospective longitudinal studies that evaluated hand function during and after  
226 rehabilitation of women with BCRL are warranted to examine hand grip strength and function as  
227 compare to age matched healthy individuals. Second, the results of this study were limited to the  
228 specific age groups (i.e., 35 to 65 years), hence generalization of this results in younger (e.g., < 35  
229 years) or older (e.g., > 65 years) women with BCRL need caution. Further studies that included a  
230 more diverse age group (e.g., young to elderly) are required to examine influence of age on hand  
231 grip strength and function in women with BCRL. Third, although the current study estimated a  
232 priori sample size, larger sample might give better results.

## 233 **Conclusions**

234 The results of this study indicate a significant reduction of hand grip strength and hand function in  
235 women with BCRL. Our findings suggest that objective measures of grip strength and function be  
236 included in the assessment of women with BCRL to better guide clinical decision making and

237 patient care, which may include impairment associated with hand strength and function. Future  
238 studies that evaluate hand grip strength and function in a larger sample ~~which include~~ a more  
239 diverse age group of BCRL population are warranted to confirm the current findings.

## 240 **Competing interest**

241 “The authors declare that they have no competing interests”.

242

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340

**Table 1** (on next page)

Participants characteristics.

1 **Table 1** Participants characteristics.

Variables	Women with BCRL Mean $\pm$ SD	Women without BCRL Mean $\pm$ SD	P (t)
Age (years)	55.5 $\pm$ 8.4	55.7 $\pm$ 8.1	0.890 (0.138)
Body mass index (kg/m <sup>2</sup> )	24.5 $\pm$ 0.7	24.4 $\pm$ 0.8	0.842 (0.201)
Hand dominance (% of right)	68%	58%	0.439 (0.779)
Side of BCRL (right/left)	21/10		
Duration of BCRL (months)	8.7 $\pm$ 3.4		
Treatment of cancer			
Surgery	11		
Surgery and chemotherapy	11		
Surgery and radiotherapy	9		
Number of nodes removed	10.4 $\pm$ 2.1		

BCRL: Breast Cancer related Lymphedema

2

**Table 2** (on next page)

Comparison of grip strength between women with and without breast cancer related lymphedema

1 **Table 2** Comparison of grip strength between subjects with and without BCRL

Variables	RIGHT				LEFT			
	Women with BCRL Grip strength (Kg.) Mean ± SD	Women without BCRL Grip strength (Kg.) Mean ± SD	p value (<0.05)	Effect size (Cohen's d)	Women with BCRL Strength Mean ± SD	Women without BCRL Grip strength (Kg.) Mean ± SD	p Value (<0.05)	Effect size (Cohen's d)
Power grip	23.8 ± 9.9	29.4 ± 8.3	0.019	0.61	22.2 ± 9.3	25.5 ± 7.9	0.013	0.38
Precision grip								
Tip pinch	4.1 ± 1.1	5.2 ± 1.7	0.004	0.76	3.9 ± 1.1	5.0 ± 1.7	0.004	0.77
Key pinch	6.1 ± 1.3	7.5 ± 2.6	0.013	0.68	5.9 ± 1.3	7.3 ± 2.9	0.033	0.62
Tripod pinch	5.4 ± 1.1	7.5 ± 2.8	0.001	0.98	5.2 ± 1.1	7.3 ± 2.8	0.001	0.99

BCRL: Breast Cancer related Lymphedema; Effect size: small (0.20), medium (0.50), large (0.80)

2

**Table 3** (on next page)

Comparison of hand functions between women with and without breast cancer related lymphedema



**Table 3** Comparison of hand functions between subjects with and without BCRL

Variables	RIGHT				LEFT			
	Women with BCRL Hand function (Sec) Mean ± SD	Women without BCRL Hand function (Sec) Mean ± SD	p value (<0.05)	Effect size (Cohen's d)	Women with BCRL Hand function (Sec) Mean ± SD	Women without BCRL Hand function (Sec) Mean ± SD	p value (<0.05)	Effect size (Cohen's d)
Card turning	7.5 ± 2.5	4.3 ± 1.6	0.010	1.53	8.2 ± 2.7	4.9 ± 1.4	0.001	1.53
Picking up small objects	7.1 ± 1.7	4.9 ± 1.1	0.002	1.54	7.4 ± 2.1	5.2 ± 1.5	0.021	1.21
Simulated feeding	8.4 ± 1.4	5.1 ± 0.8	0.003	2.89	9.7 ± 1.4	5.9 ± 1.1	0.003	3.02
Stacking checkers	3.8 ± 0.9	3.3 ± 0.6	0.035	0.65	4.1 ± 1.4	3.5 ± 0.7	0.001	0.54
Picking up large objects	4.3 ± 1.0	2.9 ± 0.6	0.001	1.70	5.3 ± 2.5	3.1 ± 1.4	0.001	1.09
Picking up heavy objects	4.3 ± 0.9	2.9 ± 0.6	0.023	1.83	5.2 ± 1.9	3.2 ± 1.1	0.001	1.29
Handwriting	33.2 ± 26.4	21.2 ± 12.2	0.025	0.58	64.5 ± 32.1	39.8 ± 10.1	0.001	1.04

BCRL: Breast Cancer related Lymphedema; Effect size: small (0.20), medium (0.50), large (0.80)