Assessment of hand function in women with lymphadenopathy after radical mastectomy

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Background. Breast cancer related 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 particularly 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 Jebsen-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 management of impairment associated with hand strength and function. Future studies that evaluate hand grip strength and function in a larger sample which includes a more diverse age group of women with BCRL are warranted to confirm the current findings.

Assessment of Hand Function in Women with lymphadenopathy after radical mastectomy

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Abstract

Background. Breast cancer related 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 particularly 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 Jebsen-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,

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 management of impairment associated with hand

42   strength and function. Future studies that evaluate hand grip strength and function in a larger

43   sample which includes a more diverse age group of women with BCRL are warranted to confirm

44   the current 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 between left and right handgrip

71 strengths was found in women with BCRL (*Gomes et al., 2014*). Another study reported a

72 significantly impaired muscle strength and function in women with breast cancer who underwent

73 chemotherapy, or a radical mastectomy as compared to healthy women (*Klassen et al., 2017*).

74 More recently, *Winters-Stone et al. (2019)* reported a significantly lower handgrip strength and

75 function in older 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*), as their outcome measures.

80   While most studies have used subjective measures to evaluate hand function in women with

81   BCRL, few studies have used objective measure of hand function (*Smoot et al., 2010; Wong et al.,*

82   *2019; Dollar et al., 2014; Kärki et al., 2005; Cantarero-Villanueva et al., 2012*). For instance,

83   *Smoot et al. (2010)* used both subjective and objective measures such as DASH questionnaire and

84   a handheld dynamometer to evaluate hand function and strength, respectively in women with or

85   without BCRL. *Cantarero-Villanueva et al. (2012)* examined handgrip strength as an objective

86   measure of function in breast cancer survivors. It is important to objectively assess hand grip

87   strength and hand function so that appropriate and complete clinical assessment and intervention

88   can be implemented to address any impairments or functional limitations in women with BCRL

89   (*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 healthy control. 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 hypothesizes that grip strength

97   and objectively measured hand function will be impaired in women with BCRL compared to

98   women without BCRL.

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 convenience 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 healthy control (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 each 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 each 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: 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*). Results were

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, σ 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.

Results

154   A total of 31 women with BCRL and 31 age-matched healthy women were included in the study

155   (Table 1). Out of 31 subjects, 21 subjects had right hand lymphedema and 10 subjects had left

156   hand lymphedema. Sixty-eight percent women with BCRL and 58% healthy women were right

157   hand dominant. Mean age of the patients and healthy control groups were 55.5 (± 8.4) and 55.7 (±

158   8.1) years, respectively.

159   Table 2 presents the result of power grip and precision grip strength of right and left hands.

160   Compared to healthy controls, there were significant reductions of both power and precision grip

161   strengths p<0.05. 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 in women with BCRL when compared to

166   the healthy controls (p<0.05). Reduction in hand function in women with BCRL were clinically

167   meaningful as indicated by moderate to large effect sizes (Cohen's d = 0.54 to 3.02, respectively)

168   in all variables of hand functions.

Discussion

169

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 the control group 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, which could reduce the strength of grip. A study conducted

187 by *Dawes et al. (2008)* found similar results where women with BCRL had lesser hand grip

188 strength, and shoulder ROM and other hand morbidities, which led to impairment. In precision

189 grip strength, the activity of tip, key and tripod pinch requires much finer motor control and is

190 more dependent on intact sensation. In case of women with BCRL, it is also seen that there is

191 involvement of kinesthetic sense of wrist joint and small joints which reduces the force generation

192   during gripping activities (*Karadibak & Yavuzsen, 2015; Smoot et al., 2010*), this could be the

193   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. For the JTHFT when administered to the women with BCRL, the

199   duration of each activity like writing, picking up small common objects, and picking up large

200   objects, card turning, simulated feeding, and stacking checkers performance was increased. The

201   overall time taken for completion of tasks was 68.8 seconds for right hand dominant and 100.3

202   seconds for left 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 and lack of movement in articulation could

214 also add to the reasons for impaired hand function (*Karadibak & Yavuzsen, 2015; Rietman et al.,*

215 *2003; 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) reported reduced daily functional skills, lack of energy and motivation, and reduced

221 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 evaluate hand function during and after

226 rehabilitation of women with BCRL are warranted to examine changes in hand grip strength and

227 function as compare to age matched healthy individuals. Second, the results of this study were

228 limited to the specific age groups (i.e., 35 to 65 years), hence generalization of this results in

229 younger (e.g., < 35 years) or older (e.g., > 65 years) women with BCRL need caution. Further

230 studies that included a more diverse age group (e.g., young to elderly) are required to examine

231 influence of age on hand grip strength and function in women with BCRL. Third, although the

232 current study estimated a 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 management of impairment associated with hand strength and

238   function. Future studies that evaluate hand grip strength and function in a larger sample with a

239   more diverse age group of women with BCRL population are warranted to confirm the current

240   findings.

241   **Competing interest**

242   "The authors declare that they have no competing interests".

243

244   **References**

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341

Participants characteristics.

1   **Table 1** Participants characteristics.

Variables	Women with BCRL Mean ± SD	Women without BCRL Mean ± SD	P (t)
Age (years)	55.5 ± 8.4	55.7 ± 8.1	0.890 (0.138)
Body mass index (kg/m^2)	24.5 ± 0.7	24.4 ± 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 ± 3.4		
Treatment of cancer			
Surgery	11		
Surgery and chemotherapy	11		
Surgery and radiotherapy	9		
Number of nodes removed	10.4 ± 2.1		
BCRL: Breast Cancer related Lymphedema			

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

	RIGHT				LEFT			
Variables	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)								

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)