Relationship between pain, tightness, heaviness, perceived limb size, and objective limb size measurements in patients with chronic upper-limb lymphoedema

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Key words

Upper-limb lymphoedema, quality of life, holistic care, lymphoedema measurement, lymphoedema symptoms

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Abstract

Background: Lymphoedema has a significant effect on patient quality of life due to the daily experience of limb symptoms such as pain, tightness and heaviness. While treatment of lymphoedema often focuses on reduction in objective limb measures, there is minimal evidence to support that this reduces subjective limb symptoms. **Aims:** This study aimed to investigate the relationship between subjective arm symptoms and objective limb size measurements in patients with chronic upper-limb secondary lymphoedema. **Methods:** A retrospective audit of previously conducted clinical trial data was undertaken, comparing objective measures of bio-impedance spectroscopy and perometry with Likert-scale data, pre- and post-interventions. **Results:** There is some evidence that reduction in objective limb measures reduces limb symptoms, but limb symptoms were also reduced without reducing limb size in a yoga intervention. Thus, there is some element of subjective experience that is independent of limb size. **Conclusions:** This work supports current treatment of lymphoedema, but serves to remind practitioners of the importance of holistic care in chronic disease.

Lymphoedema is a chronic, progressive disease of lymphatic system dysfunction, resulting in the affected body part becoming swollen due to accumulation of interstitial fluid (Földi et al, 2003). It is a recognised complication in a significant number of patients having breast cancer surgery.

Apart from the swollen limb, chest or breast, women may experience many other symptoms of lymphoedema, such as pain, tightness, heaviness, aching, throbbing and burning sensations (Badger et al, 1988; Moffatt et al, 2003; Tsuchiya et al, 2008). These symptoms lead to a decreased physical functioning(Bendova, et al, 1988; Tsuchiya et al, 2008), negative psychosocial effects such as decreased ability to work, the need to wear compression garments, and negative reactions to the swollen limb from both the patient themselves and from their friends (Bendova et al, 1988; Moffatt et al, 2003; Tsuchiya et al, 2008). Overall, this leads to decreased quality of life, social interactions and psychosocial wellbeing (Moffatt et al, 2003; Heiney et al, 2007; Tsuchiya et al, 2008; Cormier et al, 2009; Klernas et al, 2010; MacLean et al, 2010).

The drastic effect of lymphoedema on overall quality of life, social interaction and psychosocial wellbeing indicates that the daily experience of the patient living with lymphoedema should be of a high importance when suggesting or providing treatment (McWayne and Heiney, 2005).

Increased burden of arm symptoms correlates with increased disability for the patient (Hayes et al, 2010). Similarly, treatment of arm swelling has been documented to improve the subjective symptoms associated with lymphoedema (Carroll and Rose, 1992; Kirshbaum 1996; Kim et al, 2007) and quality of life (Hormes et al, 2010).

When treating any patient with lymphoedema, objective measurements are often utilised to monitor the patient's condition. However, the patient's own experience of the condition may be just as or more important in influencing the effectiveness of treatment than changes in objective measures, due to the impact of this chronic disease on everyday quality of life.

This study aims to investigate the relationship between subjective arm symptoms (perceived limb size, pain, tightness and heaviness), and objective limb size measurements in patients with chronic upper-limb secondary lymphoedema.

Methods

Data from trials previously conducted at the Lymphoedema Assessment Clinic, Flinders Medical Centre, were audited for this investigation. Each trial investigated

the effect of a different intervention on secondary lymphoedema of upper limbs, as a result of previous breast cancer surgery.

Three groups of patients were established, and the effect of treatment with different 4-week interventions was investigated. Two groups received a traditional 'physical therapy' intervention, and one group participated in a yoga intervention. Each group of patients had available perometry, bioimpedance spectroscopy (BIS), and self-rated Likert-scale questionnaire data on severity of pain, tightness, limb size and heaviness.

This study was approved by the Southern Adelaide Clinical Human Research Ethics Committee.

Objective measures

Perometry and bioimpedance spectroscopy (BIS) were used to objectively measure limb size. Perometry uses an optoelectric device to measure total limb volume, whereas BIS measurements reflect the amount of fluid in the limb measured by the resistance to current flow at low frequencies. These techniques have been validated and are accepted as near gold standard measurements for measuring overall limb volumes and fluid content respectively (Stanton et al, 1997; Piller, 2010).

Perometry and BIS measurements at baseline and after 4 weeks of intervention were compared. The difference between measurements of affected and unaffected arms was calculated at baseline and post-intervention. The change in limb size over the intervention period was expressed as both absolute and percentage reduction. Although there are many ways to calculate the percentage reduction in limb size over the treatment period, we used the method used by McNeely et al (2004).

Subjective measures

Although the literature describes many different subjective symptoms experienced by women with lymphoedema, this study uses pain, heaviness, tightness and perceived limb size difference as subjective measures. These symptoms were described in the literature as commonly experienced by women with lymphoedema (Badger et al, 1988; Carroll and Rose, 1992; Armer et al, 2003; Moffatt et al, 2003; Tsuchiya et al, 2008; Cormier et al, 2009). All patients scored their experience of these symptoms on 10-point self-rated Likert scale (1=no symptom and 10=worst imaginable experience).

Statistical analysis

All statistical analyses were performed using STATA version 12.0 (StataCorp, 2011) and R version 2.13.2 (R-Development-Core-Team 2011). Descriptive statistics used for objective measures were mean and standard deviation (SD), whereas median (MED) and inter-quartile range (IQR) were calculated for subjective measures. Paired t-test and Wilcoxon signed rank test were used for significant differences of objective and subjective measurements between baseline and post-intervention.

A multilevel mixed-effect linear regression was applied in STATA using the xtmixed command to fit linear mixed models of the continuous objective measures outcome. Mixed models account for fixed and random effects when fitting a linear regression. The fixed effects are analogous to standard regression coefficients and are estimated directly.

To assess associations with change in the objective measures outcome across time, the outcome measured at follow- up was modelled in the multilevel random regression equation, corrected for baseline objective measures. The model included the main effects of subjective measures and also interactions between subjective measures and follow-up time.

Results

Table 1 shows the percentage reduction in BIS and perometry measurements for each trial, over the intervention period. Interventions 1 and 2 were based on a physical intervention like massage or manual lymphatic drainage. The third intervention was a yoga programme. *Table 2* shows the baseline and post-intervention subjective symptom scores for pain, heaviness, tightness and perceived limb size, and whether or not any difference was significant.

Intervention 1 (n=24) reduced the BIS score by 29.3% (P<0.001) and perometry measurements by 17.6% (P<0.001). This intervention also showed significant improvements in heaviness and perceived limb size. Although there were no changes to median values, the pain and tightness scores showed significant differences (P<0.01) between baseline and post-intervention period. These significant differences could occur from the large drop of the third quarter scores in the post intervention (*Table 2*).

Intervention 2 (n=21) reduced BIS score by 24.8% (P<0.001) and perometry score by 20.3% (P<0.001). This intervention did not significantly affect the experience of pain symptoms as measured by change in median score (*Table 2*), but was found

Table 1. Changes in bioimpedance spectroscopy and perometry for 4-week interventions targeting secondary upper-limb lymphoedema

Outcome	Intervention	Baseline mean (SD)	Post intervention mean (SD)	% change	*P*-value	Post intervention effect
Bioimpedance spectroscopy	1	558.3 (296.5)	394.6 (233.4)	−29.3%	<0.001	Improved
	2	644.8 (526.3)	485.2 (342.5)	−24.8%	<0.001	Improved
	Yoga	269.0 (346.0)	275.3 (357.1)	+2.3%	0.12	Worse**
Perometry	1	668.8 (360.3)	551.3 (323.5)	−17.6%	<0.001	Improved
	2	825.0 (428.6)	657.4 (344.2)	−20.3%	<0.001	Improved
	Yoga	497.8 (448.3)	508.8 (423.3)	+2.2%	0.27	Worse**

SD=Standard deviation; ** denotes result is not statistically significant (P>0.05)
P values are based on paired t-test for baseline and post intervention comparison

Table 2. Changes in subjective limb symptoms for 4-week interventions targeting secondary upper-limb lymphoedema

Symptom	Intervention	Baseline score median (IQR)	Post intervention score median (IQR)	P-value	Post intervention effect†
Pain	1	1.0 (1.0–2.5)	1.0 (1.0–1.0)	0.01	No change
	2	1.0 (1.0–4.0)	1.0 (1.0–1.0)	0.04	No change
	Yoga	2.5 (1.0–4.0)	2.0 (1.0–3.0)	0.12	Improved**
Heaviness	1	2.8 (1.0–5.0)	1.0 (1.0–1.0)	<0.001	Improved
	2	3.0 (1.0–5.0)	1.0 (1.0–1.0)	<0.01	Improved
	Yoga	3.5 (2.0–6.0)	3.0 (2.0–4.5)	<0.01	Improved
Tightness	1	1.0 (1.0–5.0)	1.0 (1.0–1.0)	<0.01	No change
	2	2.0 (1.0–7.0)	1.0 (1.0–1.0)	<0.01	Improved
	Yoga	3.5 (2.0–6.0)	3.0 (2.0–4.0)	0.04	Improved
Perceived limb size	1	5.0 (5.0–7.5)	2.3 (2.0–4.0)	< 0.001	Improved
	2	6.0 (5.0–8.0)	2.0 (2.0–3.0)	< 0.001	Improved
	Yoga	5.0 (3.0–7.0)	4.0 (3.0–5.0)	0.07	Improved**

IQR= Inter-quartile range (1st quarter–3rd quarter)
** denotes result is not statistically significant (P>0.05)
P values are based on non parametric Wilcoxon Signed Rank test for baseline and post intervention comparison
† Post intervention effect is based on the median values.

to do so in the mixed model analysis (*Table 3*). It was effective in reducing heaviness, tightness and limb size.

Although the yoga intervention (n=35) was not effective at reducing objective measures (BIS score increased by 2.3%; P=0.12 and perometry score increased by 2.2%; P=0.27), this intervention was successful in reducing all subjective symptoms. Pain, heaviness, tightness and perceived limb size were all reduced, despite the lack of reduction of limb size by objective measures. Only the reduction in heaviness and tightness were statistically significant.

Importantly, none of the four interventions worsened the severity of pain, heaviness, tightness or perceived limb size.

The multilevel mixed-effects linear regression model was undertaken to determine whether changes in objective limb measurements could predict alterations in subjective symptoms (*Table 3*).

The changes in BIS in intervention 2 only were predictive of the effects on all four subjective measures [pain (P=0.02), heaviness (P<0.001), tightness (P<0.01) and limb size (P=0.02)]. The relationship between changes in BIS and each symptom was a positive linear relationship, as described in *Table 3*.

Changes in perometry scores in intervention 1 were also positively predictive of heaviness (P=0.02), tightness (P=0.04) and limb size (P<0.01) whilst for intervention 2, changes in perometry scores were positively predictive of changes in heaviness (P<0.01) and limb size only (P<0.01).

No linear relationships were found for the yoga data because no significant change in the objective measurements occurred with this intervention.

Discussion

The aim of this study was to investigate the potential relationship between objective measurements used clinically to monitor lymphoedema treatment (perometry and BIS), and subjective symptoms comprising a patient's experience of lymphoedema (pain, tightness, heaviness and perceived limb size). As lymphoedema is a chronic, incurable condition that greatly impacts on quality of life, it is important that treatment addresses the patient's symptom burden as well as reducing limb size.

No consistent relationships were identified between objective limb measurements and subjective symptoms amongst the three intervention groups. However, several relationships were identified that may become more prominent in a study of a larger sample size, or a prospectively designed study; these are seen in *Tables 2 and 3*.

Subjective limb heaviness and perceived size of the limb were the symptoms most often reduced by a reduction in objectively measured limb volume. A linear relationship was found between reductions in limb volume, measured by perometry, and decreased heaviness and perceived limb size scores, in interventions 1 and 2 (*Table 3*). Tightness was also significantly reduced with reduced limb volume in intervention 2 (*Table 3*). These results suggest that the experience of these symptoms is linked to limb volume, and thus treatments targeting a reduction in limb volume, such as manual lymphatic drainage (MLD) should be effective in reducing their incidence. These results are similar to those reported by Armer et al (2003), who reported that feelings of heaviness and limb swelling were the best predictors of the presence of lymphoedema, in work looking at subjective indicators for lymphoedema.

Furthermore, intervention 2 demonstrated that a reduction in limb fluid, as measured by BIS, led to statistically significant reductions in pain, heaviness, tightness and perceived limb size (*Table 3*). This was not demonstrated in the other manual-type intervention nor the yoga

Table 3. Changes in subjective limb symptoms for 4-week interventions targeting secondary upper-limb lymphoedema

		Bio-impedance spectroscopy			Perometry		
Subjective measure	Intervention	Coefficient (β)	95% CI	P-value	Coefficient (β)	95% CI	P-value
Pain	1	−28.4	−63.1–6.2	0.11	10.3	−13.6–34.1	0.40
	2	37.8	5.7–69.9	0.02	5.6	−24.4–35.5	0.72
	Yoga	−6.4	−26.0–13.1	0.52	−12.1	−44.4–20.2	0.46
Heaviness	1	2.1	−21.3–25.5	0.86	17.5	2.8–32.2	0.02
	2	54.1	21.9–86.2	<0.001	43.1	14.4–71.8	<0.01
	Yoga	2.4	−13.8–18.6	0.77	−2.5	−29.7–24.6	0.85
Tightness	1	7.0	−15.1–29.1	0.54	13.8	0.7–26.9	0.04
	2	33.4	6.8–59.9	<0.01	13.7	−11.1–38.5	0.28
	Yoga	−1.9	−16.4–12.5	0.79	−19.8	−42.5–3.0	0.09
Perceived limb size	1	22.1	−7.1–51.2	0.14	29.0	10.0–48.1	<0.01
	2	47.9	7.3–87.5	0.02	46.2	11.1–81.2	<0.01
	Yoga	13.0	−6.8–32.9	0.20	7.4	−32.3–47.1	0.72

CI = confidence interval; No interaction was found between time (pre-post) and each subjective measure.

intervention. This interesting result suggests that extracellular fluid burden is a significant factor in the subjective symptom experience. This was the only significant relationship that included a reduction in pain. This relationship validates treatment modalities that seek to reduce fluid burden in order to control lymphoedema.

The results of the yoga intervention suggest that factors other than objective limb size or volume are important in the symptom experience of lymphoedema. This intervention recorded no significant change in limb volume, however improvements across all subjective symptoms analysed were found (*Table 2*). Not all results were significant with $P<0.05$, as the sample size for this intervention group was small; results may improve with a larger sample size. The improvement in symptoms despite the lack of change in objective measures suggests the importance of holistic care provision for lymphoedema patients, and suggest that the traditional treatments aimed only at reduction of limb volume may not be effective in alleviating all symptoms experienced by the patient. Tsuchiya et al (2008) suggest that the presence of subjective symptoms in the absence of objective symptoms suggests a psychological component to the symptom experience.

Although our results indicate that pain may be reduced by reductions in objective limb measurements, it seems to be the symptom least likely affected. Pain is a complex symptom, thus it is likely that psychosocial factors and illness behaviour may have a bearing on the experience of pain, beyond that contributed by the limb size and fluid volume.

Cormier et al (2009) suggest that subjective symptoms generally become worse with increasing limb volume. In support of this, our study has identified positive linear relationships between objective measures of limb size and subjective symptoms experienced in lymphoedema.

The assessment of a subjective symptom experience is difficult. The literature describes the pain associated with lymphoedema as having components such as aching, boring, burning, bursting, heaviness, throbbing, tenderness and firmness (Badger et al, 1988; Moffatt et al, 2003; Cormier et al, 2009). Assessing the subjective experience of lymphoedema is difficult, as different women will describe their symptoms in different ways, thus it is difficult to assess what 'pain' or 'tightness' mean for different people.

This study was intended to explore possible links between subjective symptoms and objective measurements used in the treatment of lymphoedema. Whilst some interesting findings have emerged, we believe that many more results of statistical significance could be attained with a larger sample size. Also, for the sake of this investigation, only four different subjective indicators were chosen, and the intervention period was 4 weeks. The retrospective nature of the study meant that data from different trials could not be combined, and thus has limited statistical power. Future studies could investigate the subjective symptoms more broadly, though this brings increased study complexity.

Conclusion

The results of this study support goals of reduction in limb size and volume in the treatment of lymphoedema, as an effective way to reduce subjective symptom burden. Reduction in objective limb measures should not be the only focus of treatment; reduction in the symptom burden of lymphoedema should be seriously considered. Non-traditional therapies such as yoga may have a role in lymphoedema treatment and aid in decreasing limb pain.

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