



Research Report

Severe lymphoedema in gynaecological cancers: Impact of pneumatic compression on quality of life

Aoife Freyne^a, Niamh O. Donoghue^{a,b}, Yulia Shahabuddin^a, Roisin Baker^c, Claire Murtagh^a, Noreen Gleeson^{a,b,*}

^a Department of Gynaecology, St James's Hospital, Dublin, Ireland

^b School of Medicine, Trinity College Dublin, Dublin, Ireland

^c Royal College of Surgeons, St Stephen's Green, Dublin 2, Ireland

ARTICLE INFO

Keywords:

Gynaecological cancer
Lymphoedema
Quality of life

ABSTRACT

Objective: Good survival rates from gynaecological cancers focus our attention on the quality of survivorship. Lymphoedema is a common complication that affects many aspects of quality of life (QOL). We undertook a prospective audit of QOL of patients with higher grade lymphoedema using home compression pneumatic devices. The aim of this study was to assess QOL in a mixed gynaecological cancer cohort before and after at least eight weeks of home compression treatment.

Methods: Thirteen patients with the most severely disabling lower limb lymphoedema based on routinely collected QOL scores or a history of hospital admissions with related infection were invited to participate. QOL was assessed using the EORTC QLQ-C30 Version 3.0 and a supplementary gynaecological cancer-specific lymphoedema questionnaire. Home compression therapy was introduced not sooner than 3 months after primary cancer treatment. All patients applied compression treatment for at least one hour per day. Descriptive statistics and Wilcoxon signed-rank test were applied. A p-value < 0.05 was considered statistically significant.

Results: All participants' functional and symptom scores improved with compression therapy with the exception of sexual function.

Conclusions: Self-management with pneumatic compression devices at home is a useful adjunct in the management of severe lymphoedema. Our preliminary experience showed a substantial improvement in most QOL parameters. We cannot say if domiciliary treatment with this compression device would have broader application or a role in primary or secondary prevention of lymphoedema if introduced at an earlier stage.

1. Introduction

Gynaecological cancer accounts for more than one in eight cancers arising in Irish women. According to the National Cancer Registry of Ireland Report (Cancer in Ireland 1994), 12.5% of female malignancies are genital tract: body of uterus (4.8%), ovary (3.7%), cervix (2.7%), and others including vulva (1.3%). With the exception of ovarian cancer, survival rates for genital tract malignancy are good and this together with the early median age at diagnosis for many of these cancers is reflected in their high ranking at second place with 15% (13,610) after breast cancer at 43.6% (39,539) in the estimated complete prevalence (90,591) of women living with cancer in Ireland to end 2016. Good survival rates focus the carers of these women on the quality of their survivorship.

Cancer specific impediments to quality of survivorship arise from the disease itself and the adverse sequelae of treatments. Multiple modalities of treatment are often applied to enhance cure rates of gynaecological cancer. Surgery is the mainstay of staging and treatment for most gynaecological cancers. Many patients will also undergo radiation and/or chemotherapy. The lymphatic system is a common site for collateral damage. Lymph flow from the lower limbs, vulva and pelvis through the lymphatics of the groins and pelvis can be impaired by cancer metastases or injury arising from these modalities of treatment. Lymphoedema is the abnormal accumulation of interstitial fluid and deposition of fibroadipose tissue that results from obstruction to lymph flow (International Society of Lymphology, 2013; Kerchner et al., 2008). In women with genital tract cancer, the lymph flow in previously healthy lymph channels can be impaired after treatment by direct interruption of

* Corresponding author at: Department of Gynaecology, St James's Hospital, James Street, Dublin 8, Ireland.

E-mail address: noreengleeson@dubgyn.org (N. Gleeson).

<https://doi.org/10.1016/j.gore.2021.100902>

Received 31 August 2021; Received in revised form 27 October 2021; Accepted 1 December 2021

Available online 7 December 2021

2352-5789/© 2021 The Authors.

Published by Elsevier Inc.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

channels at organ dissection and lymphadenectomy, and by inflammation induced by radiation and infection. Lymph node excision for staging and treatment is a major contributor (Yost et al., 2014; Ryan et al., 2003). Obesity and other inflammatory conditions compound lymph stasis.

Localised interruption to flow, typically at the site of lymphadenectomy results in the accumulation of fluid as lymphoceles, also called lymphocysts (but without a true capsule) in the pelvis or groin (Weingold et al., 1967). They can reach a large size and cause compression of adjacent structures or the overlying skin and/or become infected and require intervention by drainage. When the flow impairment is more widespread, the resulting lymphoedema causes varying degrees of cosmetic distortion and dysfunction of the lower limbs, pelvis and vulva. Clinical sequelae range from skin tightness, swelling, aching pain, restricted movement and clothing, to severe immobility and recurring infections and/or sepsis. The impact on body image, psychological and sexual functioning can be profound.

Various grading schemes are described for lymphoedema based on the softness/firmness of skin and limb volume change (International Society of Lymphology, 2013). Cellulitis and lymphangitis can arise with alarming speed especially when there is bullous or papillary change in the skin. Lymphoedema of the vulva may carry a high risk of infection, even when the skin is intact, and this is reflected in the St James's Hospital Gynaecology Cancer Care Team grading of lymphoedema (Fig. 1). Studies on the impact of lymphoedema on quality of life (QOL) predominantly relate to upper limb lymphoedema in breast cancer patients (Muluk et al., 2013) and while physical symptoms may impact an individual's mobility and therefore their ability to perform activities of daily living, psychological distress is also common (Finnane et al., 2011; Chachaj et al., 2010). Penha et al suggested that the negative effect of upper limb lymphoedema on QOL of breast cancer patients could potentially negate the benefit of reconstructive surgery (Lopez Penha et al., 2011). Those studies which included lower limb lymphoedema are not exclusive to gynaecological cancers and high grade lymphoedema (Finnane et al., 2011).

Treatment of established lymphoedema that does not reduce

spontaneously with elevation, SJH LE3 grade or higher, presents a substantial challenge. Strict attention to skin and nail care, prompt treatment of infections, manual lymph drainage and compression bandaging are the mainstay of management. Specialist-provided manual lymph drainage and compression bandaging are a limited resource in our health service and complete/complex physical decongestive therapy is only available in specialised clinics abroad. Pneumatic compression devices (PCD) have been shown to reduce the cost of lymphoedema care (Brayton et al., 2014) and Muluk et al showed a reduction in limb volume with PCD and an associated improvement in QOL⁷. We now offer PCD that include full length garments and pumps for patients with the most severe impairment to QOL or recurring infections. The fitted zippered garments extend from toes to groin. Pressure of 100 mmHg is recommended with application for at least one hour per day in the woman's home. The aim of this study was to assess the QOL in an exclusively gynaecological cancer cohort before and after at least eight weeks of home pneumatic compression treatment of severe lower limb lymphoedema.

2. Methods

This prospective, interventional study was conducted in St James's Hospital Gynaecological Cancer Centre. Ethical approval was granted from the St. James's Hospital/Adelaide and Meath incorporating the National Children's Hospital Joint Research Ethics Committee. Patients with the most severe lower limb lymphoedema based on routinely collected QOL scores or a history of hospital admissions with related infection were invited to participate. Those who consented underwent preliminary ankle-brachial index to out rule peripheral vascular disease. Detailed examination was performed and recurrent cancer and active infection were ruled out. Eligible patients were offered the pneumatic compression devices (PCD) for application at home and were required to complete a further QOL assessment after at least eight weeks of treatment. The women were advised to apply the PCD to their bare lower limb but to continue all their baseline special skin care measures including bandaging throughout the trial period. They were further advised to stop PCD and seek urgent clinical assessment if infection arose.

Quality of life was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core Questionnaire (EORTC QLQ-C30 version 3.0). This is a 30 item, validated, self-report tool developed to assess QOL in cancer patients (Supplementary Material). It comprises multi-item and single-item measures including five functional scales (physical, social, role, cognitive and emotional), three symptom scales (fatigue, pain, nausea and vomiting), six single item scales (dyspnoea, sleeping disturbances, appetite loss, constipation, diarrhoea and financial impact) and a global health status/QOL scale (Aaronson et al., 1993). Response choices range from 1 (not at all) to 4 (very much), with the exception of the two items of the global QOL scale, where responses range from 1 (very poor) to 7 (excellent).

The EORTC Quality of Life Group has developed a number of supplementary disease and treatment specific modules including gynaecological cancer specific modules, which may be used in conjunction with the EORTC QLQ-C30 (Supplementary Material Fig. 1). Although some of these include questions related to lymphoedema e.g. cervical cancer module (EORTC QLQ-CX24), there is no dedicated EORTC gynaecological cancer-related lymphoedema module. As this was a mixed gynaecological cancer cohort, a supplementary lower limb lymphoedema questionnaire was developed for and piloted in this study (Supplementary Material Fig. 2). It consisted of 6 items and included functional and symptom measures namely body image, sexual activity and enjoyment, lymphoedema, tingling and numbness and muscle and joint pain. Questions and response choices mirrored those used in the EORTC QLQ-C30. Questionnaires were completed by participants before and after treatment with the PCD.

St James's Hospital Gynaecology Cancer Care Centre Lymphoedema Grading	
SJH LE1	Mild pitting oedema, soft smooth skin, swelling reduces with elevation
SJH LE2	Non-pitting oedema, tense smooth skin, swelling reduces with elevation
SJH LE3	Non-pitting oedema, sclerotic skin, fails to reduce with elevation
SJH LE4	Non pitting oedema, sclerotic skin, fails to reduce with elevation, hyperkeratosis
SJH LE5	Non pitting oedema, sclerotic skin, fails to reduce with elevation, hyperkeratosis and bullae or papillae
SJH LE6	Vulval/pubuc lymphoedema +/- lower limb lymphoedema
SJH LE7	Vulval/pubuc lymphoedema with sclerosis +/- lower limb lymphoedema
SJH LE8	Vulval/pubuc lymphoedema with sclerosis and hyperkeratosis +/- lower limb lymphoedema
SJH LE9	Vulval/pubuc lymphoedema with sclerosis, hyperkeratosis, bullae or papillae +/- lower limb lymphoedema

Fig. 1. St James's Hospital Gynaecological Cancer Care Lymphoedema Grading.



Fig. 2. Compression garment (a) frontal and (b) lateral aspect.

The pneumatic compression pump used in this study was a Hydroven 12 LymphAssist (Huntleigh HC, Cardiff, U.K.) on which the sequential setting at a pressure of 100 mmHg was recommended for at least one continuous hour daily. The garments are full length extending from toes to groin (Fig. 2a and b) and consist of 12 chambers through which pressure is applied sequentially from the feet towards the groins. The cost of a pump and two garments is circa €3000 (\$3600).

Planned clinical review was performed and follow up QOL scores were recorded no sooner than eight weeks after starting treatment.

Descriptive statistics were used to report demographic and clinical data. Quality of life scoring was applied according to the EORTC Manual. All scale scores were linearly transformed to a 0–100 scale. For the functional scales and the global QOL scale, a higher score represents a higher level of function or QOL. For the symptom scales, a higher score represents greater symptom burden. QOL scores were reported as mean and standard deviation. A Wilcoxon signed-rank test was used to

compare quality of life scores before and after leg compression pump therapy. Analysis was completed using Microsoft Excel 2013 and Statistical Package for the Social Sciences (SPSS) Version 26. A p-value < 0.05 was considered statistically significant.

3. Results

Twelve of 13 sequential patients with SJH-LE grade 3 or higher accepted the invitation to participate. One patient considered the equipment too cumbersome and reverted to a further course of MLD instead. All patients had attended the hospital's physiotherapy facility and were using high grade compression stockings. The demographic profile of the participants is shown in Table 1. Patients ranged in age from 37 to 72 years. Their primary cancer diagnoses were cervix (n = 6) of whom five had adjuvant radiotherapy after radical surgery, endometrial (n = 3) of whom one had chemotherapy and radiotherapy after

Table 1
Demographics and clinical characteristics (n = 12).

Participant No.	Age	Primary site	FIGO Stage	Primary treatment	Time since completing primary treatment (years)	Laterality	SJH-LE Grade	Cellulitis (in prior 6 months)	Hospitalisation due to infection
1	37	Cervix	IA	Radical trachelectomy, PLND	6.5	Bilateral	4	0	0
2	62	Endometrial	IA	TH, BSO, PLND	5	Bilateral	4	0	0
3	57	Endometrial	IIIA	TH, BSO, PLND	7.75	Bilateral	3	2	1
4	63	Cervix	IB	RH, PLND, XRT	1	Bilateral	3	1	0
5	54	Cervix	IB	RH, PLND	15	Unilateral	5	3	0
6	63	Endometrial	IIIA	TH, BSO, PPLND, CT, XRT	11	Bilateral	4	1	0
7	45	Vulva	IB	RV, BGLND	7.25	Unilateral	5	1	0
8	47	Vulva	IB	RV, BGLND	0.25	Bilateral	3	0	0
9	38	Cervix	IB (pT2b, N0)	RH, BS, PPLND, XRT	3.25	Unilateral	5	2	1
10	72	Vulva	IB	RV, BGLND	2.75	Unilateral	4	0	0
11	56	Cervix	IB (pT1b, N1)	RH, PPLND, CT, XRT	18.5 *	Bilateral	9	4	2
12	49	Cervix	IB	RH, PLND, XRT	11.75*	Bilateral	9	3	2

Abbreviations: (P)PLND, (*para*-aortic) pelvic lymphadenectomy; TH, total hysterectomy; BSO, bilateral salpingo-oophorectomy; RH, radical hysterectomy; CT, chemotherapy; XRT, radiotherapy; RV, radical vulvectomy; BIFLND, bilateral inguino-femoral lymph node dissection.

* 2 patients had interval single site relapse in *para*-aortic lymph nodes treated with lymphadenectomy and XRT 9 and 6 years after primary treatment.

staging surgery with lymphadenectomy, and vulva (n = 3) all of whom had full inguino-femoral lymphadenectomy. Two patients' lymphoedema arose after successful salvage lymphadenectomy and radiotherapy for *para*-aortic recurrence of cervical squamous cell cancers.

The lymphoedema was bilateral lower limb in 8 (75%), unilateral in 4 (25%) and in addition involved the pubis or vulva in 2 (17%) patients. We graded the lymphoedema (Fig. 1) SJH LE3 (25%), SJH LE4 (33%), SJH LE5 (25%), SJH LE7 (8%), SJH LE9 (8%). Lymphadenectomy and radiotherapy of the *para*-aortic region was associated with the highest grades. Eight patients had related infections, namely cellulitis or lymphangitis within the preceding six months and four had been hospitalised for this complication at least once.

All patients used the PCDs for at least one hour per day. Eight patients reported more than once daily application. The subjective experience was relaxing and comfortable for 11 patients. One patient reported slight pins and needles in one foot. She was advised to reduce the pressure to 75 mmHg for a couple of days and then gradually increase it back to 100 mmHg. We found no other adverse effects.

Supplementary Tables 1 and 2 present a comparison of QOL at baseline and at least 8 weeks after commencing compression pump therapy. The mean global health score of participants following compression pump therapy was 75 ± 9.62 , significantly higher than pre-therapy ($p < 0.01$) (Supplementary Table 1). Participants' functioning as measured with physical, role, emotional, cognitive and social scales, all improved significantly with compression therapy (Fig. 3a). Participants were most symptomatic with pain and fatigue at baseline; both improved significantly with therapy ($p < 0.01$) (Fig. 3b).

The gynaecological cancer-related lymphoedema questionnaire identified body image as the scale which improved most after therapy ($p < 0.05$) (Fig. 4). Participants were most symptomatic of leg swelling of lymphoedema per se. The improvement in lymphoedema with therapy was significant ($p < 0.01$). Unlike the other scales and symptoms, sexual activity and enjoyment scored poorly at baseline and also following compression therapy. No patient had a further hospital admission for cellulitis.

4. Discussion

Lymphoedema is a common adverse outcome of gynaecological cancer treatments that can progress to being irreducible at varying rates. Women with SJH LE3 stage or higher merit the attention of a specialist lymphologist/physiotherapist. They are at risk of substantial long term health impairment and recurring infections. An estimated 1451 patients a year are admitted to Irish hospitals with cellulitis related to lymphoedema with an average length of stay of 11 days and at a cost, estimated at €13.6 (\$16.6) million (Health Service Executive Policy Document, 2018). That amounts to an average cost of €9373 (\$11,150)

per patient admission. Cost aside, episodes of cellulitis can be life threatening. Patients with sclerotic lymphoedema are recommended manual lymph drainage and compression bandaging and complete, complex physical decongestive therapy is offered by specialised clinics abroad. It combines manual lymph drainage with limb compression using multi-layered padding materials and short-stretch bandages applied repetitively. Surgical interventions aim to restore lymph flow and excise the excess subcutaneous fibro-adipose tissue (Doscher et al., 2012; Hoffner et al., 2018). Lymph venous bypass and lymph node microsurgical transplantation have been reported to substantially reduce episodes of cellulitis mainly or exclusively in the upper limbs (Chang et al., 2013; Ozturk et al., 2016). Its value in women who have undergone irradiation to groins or pelvis remains to be established so surgical treatment of lower limb lymphoedema remains experimental. Cold laser therapy, a photochemical treatment that may decrease fibrosis, stimulate macrophages and promote lymphangiogenesis has been described in small trials in upper limb lymphoedema with conflicting results (Carati et al., 2003; Kozanoglu et al., 2009; Kaviani et al., 2006).

In addition and in part due to physical deformity and disfigurement, lower limb lymphoedema impairs psychological health and QOL. Emotional, social, sexual and financial well-being are compromised⁸. Given the limitations of compression therapies and lack of access to either complete decongestive therapy or surgery in our health service, we considered PCDs might be beneficial in women with severe lymphoedema following gynaecological cancer treatments. Peripheral vascular disease, venous thrombosis, active infection and recurrent cancer were excluded before commencing treatment. This is a report of the quality of life outcomes of the first cohort of women so treated.

The majority of women had undergone pelvic surgery followed by radiotherapy or full groin lymphadenectomy. This profile fits with our clinical experience that dual modality pelvic treatment carries a high risk and some degree of lymphoedema is expected after full groin lymphadenectomy (Abu-Rustum et al., 2006; Gaarenstroom et al., 2003; Rossi et al., 2017). That risk of lymphoedema is one of the incentives for curtailing lymphatic disruption through sentinel lymph node mapping and analysis (Rossi et al., 2017; Holloway et al., 2017; Van der Zee et al., 2008; Lécuru et al., 2011). Lymphoedema was unilateral in the lower limbs in only one third of patients. Vulval lymphoedema was present only in those who had undergone pelvic and *para*-aortic lymphadenectomy.

Only one patient rejected the compression device and boots as too cumbersome. The remaining twelve were all compliant with daily application by their own report. They found the massaging effect comforting. There were no adverse effects associated with PCD use. No patient had a further hospital admission for cellulitis in the six months after initiating treatment. Patient wellbeing aside, the financial savings in

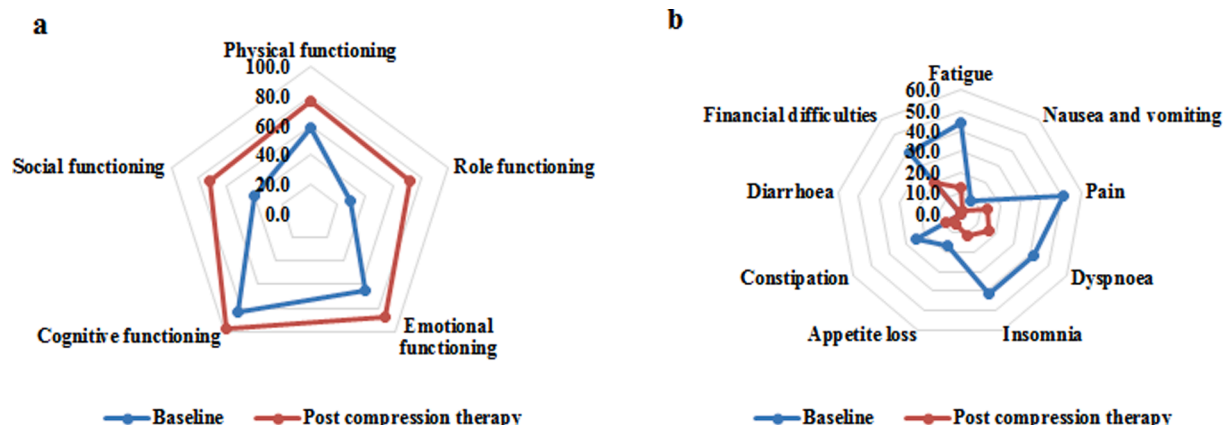


Fig. 3. EORTC QLQ-C30 mean functional scale scores (a) and symptom and single item scale scores (b) before and after compression therapy.

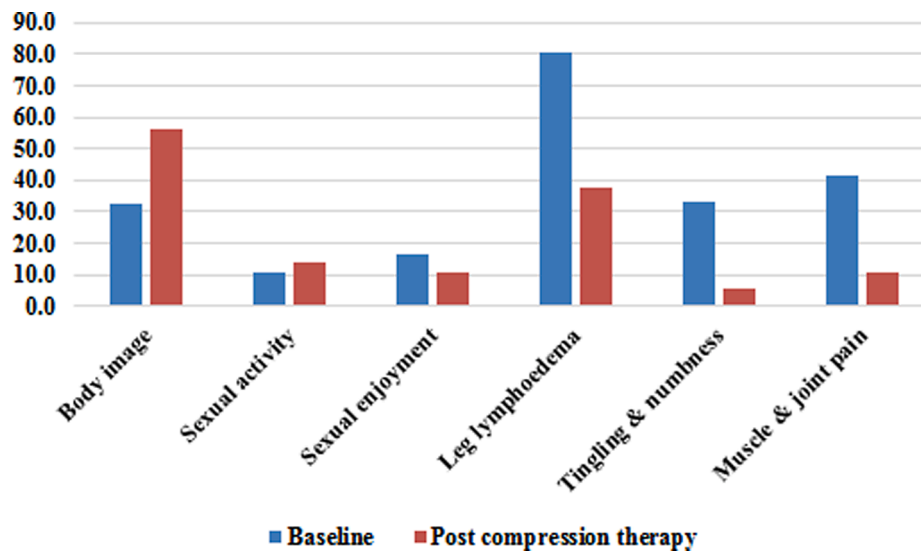


Fig. 4. Gynaecological cancer-related lymphoedema module mean functional and symptom scores before and after compression therapy.

reduced hospital admissions for infections could offset the cost of the equipment.

The importance of QOL evaluation in cancer populations is increasingly recognised both in clinical practice and clinical trials and this comes to the fore with longer survivorship. Given the considerable morbidity associated with gynaecological cancer diagnosis and its treatment and the complex psychological impact on body image and sexuality, integration of QOL measurement is strongly recommended in the follow-up of these patients. QOL is multidimensional. The EORTC QLQ-C30 is a tool widely applied to assess patient-reported QOL. It encompasses global QOL, symptoms and functional scales including physical, role, social, cognitive and emotional. This study focused on the impact of a home intervention for lower limb lymphoedema on QOL. Serial EORTC QLQ-C30 scoring confirmed substantial benefit to all patients. Pain and fatigue are commonly reported symptoms across the cancer trajectory. Participants in this study also reported pain and fatigue as the most commonly experienced symptoms. Both improved significantly following home compression therapy, as did all functional scales.

In addition to the EORTC QLQ-C30, a supplementary tool was developed from EORTC QLQ of gynaecological site specific cancer sites and piloted in an effort to capture the symptoms closely associated with lower limb lymphoedema in this patient cohort. A number of lymphoedema questionnaires exist (Coriddi et al., 2020; Keeley et al., 2010; Devoogdt et al., 2014; Augustin et al., 2005; Weiss and Daniel, 2015) but none within the EORTC format. Although participants were predictably most symptomatic of lymphoedema, muscle and joint pain and paraesthesia, symptoms often associated with chemotherapy, also scored highly. Sexual activity and enjoyment scored poorly at baseline and was the exception in not improving with the reduction in lymphoedema despite a significant improvement in body image. Sexual dysfunction remains as one of the major and most challenging aspects of collateral damage in the treatment of genital tract cancers.

There were strengths and limitations to this study. A detailed itemised QOL questionnaire was used in order to comprehensively assess QOL at baseline in patients with severe lymphoedema and after starting domiciliary treatment with PCD. The QOL assessor was blinded to the clinical status of the participants. We demonstrated an improvement in all QOL parameters with the exception of sexual function. However, this is a small cohort of patients in a single cancer centre who were selected by their treating clinicians based on the clinical impression that their lymphoedema was severe and impacting adversely on their QOL. All had severe lymphoedema and many had previous hospital admissions for

related infections. We did not undertake serial measurements of the limbs, but limb volume has previously been shown to improve with PCD⁷ and interobserver error limits its reliability (Casley-Smith, 1994; Deltombe et al., 2007). Our focus was on QOL. The standard EORTC QLQ-C30 was supplemented by additional questions, all of which were drawn from other EORTC gynaecological cancer-specific modules. This pilot expanded QOL questionnaire would need further validation.

5. Conclusions

A domiciliary intervention that facilitates the self-management of lymphoedema is attractive because of patient control and convenience and potential lower cost than the labour intensive methods of professional massage and bandaging. The methods may be complementary. Our preliminary experience showed a substantial improvement in most quality of life parameters (with the exception of sexual function). We recommend that peripheral vascular disease, venous thrombus and recurrent disease are excluded prior to starting the home compression therapy for established lymphoedema. We cannot say if domiciliary treatment with this pneumatic compression device would have broader application or a role in primary or secondary prevention of lymphoedema if introduced at an earlier stage, for example after full inguino-femoral lymphadenectomy for vulval cancer.

CRedit authorship contribution statement

Aoife Freyne: Conceptualization, Validation, Project administration, Writing – original draft. **Niamh O. Donoghue:** Methodology, Resources, Validation, Formal analysis, Writing – review & editing. **Yulia Shahabuddin:** Project administration. **Roisin Baker:** Project administration. **Claire Murtagh:** Data curation. **Noreen Gleeson:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We are grateful to Support GynaeCancerCare at the St James's

Hospital Foundation (www.supportstjames.ie) and the Emer Casey Foundation (www.emercaseyfoundation.com) for their continuing financial support of the Lymphoedema Project.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gore.2021.100902>.

References

- Aaronson, N.K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N.J., Filiberti, A., Flechtner, H., Fleischman, S.B., Haes, J.C.J.M.d., Kaasa, S., Klee, M., Osoba, D., Razavi, D., Rofe, P.B., Schraub, S., Sneeuw, K., Sullivan, M., Takeda, F., 1993. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J. Natl. Cancer Inst.* 85 (5), 365–376. <https://doi.org/10.1093/jnci/85.5.365>.
- Abu-Rustum, N.R., Alektiar, K., Iasonos, A., Lev, G., Sonoda, Y., Aghajanian, C., Chi, D.S., Barakat, R.R., 2006. The incidence of symptomatic lower-extremity lymphedema following treatment of uterine corpus malignancies: a 12-year experience at Memorial Sloan-Kettering Cancer Center. *Gynecol. Oncol.* 103 (2), 714–718. <https://doi.org/10.1016/j.ygyno.2006.03.055>. Epub 2006 Jun 5 PMID: 16740298.
- Augustin, M., Bross, F., Földi, E., Vanscheidt, W., Zschocke, I., 2005. Development, validation and clinical use of the FLQA-L, a disease specific quality of life questionnaire for patients with lymphedema. *VASA. J Vasc Dis* 34 (1), 31–35.
- Brayton, K.M., Hirsch, A.T., O'Brien, P.J., Chevillat, A., Karaca-Mandic, P., Rockson, S.G., 2014. Lymphedema prevalence and treatment benefits in cancer: impact of a therapeutic intervention on health outcomes and costs. *PLoS ONE* 9 (12), e114597. <https://doi.org/10.1371/journal.pone.0114597>. PMID: 25470383; PMCID: PMC4255037.
- Cancer in Ireland 1994–2016 with estimates for 2016–2018: Annual Report of the National Cancer Registry.
- Carati, C.J., Anderson, S.N., Gannon, B.J., Piller, N.B., 2003. Treatment of postmastectomy lymphedema with low-level laser therapy: a double blind, placebo-controlled trial. *Cancer* 98 (6), 1114–1122. <https://doi.org/10.1002/cncr.11641>. Erratum. In: *Cancer*. 2003 Dec 15;98(12):2742 PMID: 12973834.
- Casley-Smith, J.R., 1994. Measuring and representing peripheral oedema and its alterations. *Lymphology*. 27 (2), 56–70. PMID: 8078362.
- Chachaj, A., Malyszczak, K., Pyszel, K., Lukas, J., Tarkowski, R., Pudeiko, M., Andrzejak, R., Szuba, A., 2010. Physical and psychological impairments of women with upper limb lymphedema following breast cancer treatment. *Psychooncology*. 19 (3), 299–305. <https://doi.org/10.1002/pon.1573>. PMID: 19399782.
- Chang, D.W., Suami, H., Skoracki, R., 2013. A prospective analysis of 100 consecutive lymphovenous bypass cases for treatment of extremity lymphedema. *Plast. Reconstr. Surg.* 132 (5), 1305–1314. <https://doi.org/10.1097/PRS.0b013e3182a44626>. PMID: 24165613.
- Coriddi, M., Dayan, J., Sobti, N., Nash, D., Goldberg, J., Klassen, A., Pusic, A., Mehrara, B., 2020. Systematic review of patient-reported outcomes following surgical treatment of lymphedema. *Cancers (Basel)*. 12 (3), 565. <https://doi.org/10.3390/cancers12030565>. PMID: 32121343; PMCID: PMC7139674.
- Deltombe, T., Jamart, J., Recloux, S., Legrand, C., Vandebroek, N., Theys, S., Hanson, P., 2007. Reliability and limits of agreement of circumferential, water displacement, and optoelectronic volumetry in the measurement of upper limb lymphedema. *Lymphology*. 40 (1), 26–34. PMID: 17539462.
- Devoogdt, N., De Groef, A., Hendrickx, A., et al., 2014. Lymphoedema functioning, disability and health questionnaire for lower limb lymphedema (Lymph-ICF-LL): Reliability and validity. *Phys. Ther.* 94, 705–721.
- Doscher, M.E., Herman, S., Garfein, E.S., 2012. Surgical management of inoperable lymphoedema, the re-emergence of abandoned techniques. *J. Am. Coll. Surg.* 215 (2), 278–283. <https://doi.org/10.1016/j.jamcollsurg.2012.03.020>.
- Finnane, A., Hayes, S.C., Obermair, A., Janda, M., 2011. Quality of life of women with lower-limb lymphedema following gynecological cancer. *Exp. Rev. Pharmacoecon. Outcomes Res.* 11 (3), 287–297. <https://doi.org/10.1586/erp.11.30>.
- Gaarenstroom, K.N., Kenter, G.G., Trimbos, J.B., Agous, I., Amant, F., Peters, A.A.W., Vergote, I., 2003. Postoperative complications after vulvectomy and inguinofemoral lymphadenectomy using separate groin incisions. *Int. J. Gynecol. Cancer*. 13 (4), 522–527. <https://doi.org/10.1046/j.1525-1438.2003.13304.x>.
- Health Service Executive Policy Document, 2018. Lymphoedema and Lipoedema Treatment in Ireland A Model of Care for Ireland – A Working Group Report 2018.
- Hoffner, M., Ohlin, K., Svensson, B., et al., 2018. Liposuction gives complete reduction of arm lymphedema following breast cancer treatment-A 5-year prospective study in 105 patients without recurrence. *Plast. Reconstr. Surg. Glob. Open*. 6 (8), 10. <https://doi.org/10.1097/GOX.0000000000001912>. Published 2018 Aug 16.
- Holloway, R.W., Abu-Rustum, N.R., Backes, F.J., Boggess, J.F., Gotlieb, W.H., Jeffrey Lowery, W., Rossi, E.C., Tanner, E.J., Wolsky, R.J., 2017. Sentinel lymph node mapping and staging in endometrial cancer: A Society of Gynecologic Oncology literature review with consensus recommendations. *Gynecol. Oncol.* 146 (2), 405–415. <https://doi.org/10.1016/j.ygyno.2017.05.027>.
- International Society of Lymphology, 2013. The diagnosis and treatment of peripheral lymphedema: 2013 Consensus Document of the International Society of Lymphology. *Lymphology*. 46, 1.
- Kaviani, A., Fateh, M., Yousefi Nooraie, R., Alinagi-zadeh, M.R., Ataie-Fashtami, L., 2006. Low-level laser therapy in management of postmastectomy lymphedema. *Lasers Med. Sci.* 21 (2), 90–94. <https://doi.org/10.1007/s10103-006-0380-3>. Epub 2006 May 4 PMID: 16673054.
- Keeley, V., Crooks, S., Locke, J., et al., 2010. A quality of life measure for limb lymphedema (LYMQOL). *J. Lymphoedema* 5 26–37, 12.
- Kerchner, K., Fleischer, A., Yosipovitch, G., 2008. Lower extremity lymphedema update: pathophysiology, diagnosis, and treatment guidelines. *J. Am. Acad. Dermatol.* 59 (2), 324–331. <https://doi.org/10.1016/j.jaad.2008.04.013>.
- Kozanoglu, E., Basaran, S., Paydas, S., Sarpel, T., 2009. Efficacy of pneumatic compression and low-level laser therapy in the treatment of postmastectomy lymphoedema: a randomized controlled trial. *Clin Rehabil.* 23 (2), 117–124. <https://doi.org/10.1177/0269215508096173>. PMID: 19164399.
- Lécure, F., Mathevet, P., Querleu, D., Leblanc, E., Morice, P., Daraï, E., Marret, H., Magaud, L., Gillaizeau, F., Chatellier, G., Dargent, D., 2011. Bilateral negative sentinel nodes accurately predict absence of lymph node metastasis in early cervical cancer: results of the SENTICOL study. *J. Clin. Oncol.* 29 (13), 1686–1691. <https://doi.org/10.1200/JCO.2010.32.0432>. Epub 2011 Mar 28 PMID: 21444878.
- Lopez Penha, T.R., Slangen, J.J.G., Heuts, E.M., Voogd, A.C., Von Meyenfeldt, M.F., 2011. Prevalence of lymphoedema more than five years after breast cancer treatment. *Eur. J. Surg. Oncol.* 37 (12), 1059–1063.
- Muluk, S.C., Hirsch, A.T., Taffe, E.C., 2013. Pneumatic compression device treatment of lower extremity lymphedema elicits improved limb volume and patient-reported outcomes. *Eur. J. Vasc. Endovasc. Surg.* 46 (4), 480–487.
- Ozturk, C.N., Ozturk, C., Glasgow, M., Platek, M., Ashary, Z., Kuhn, J., Aronoff, N., Lohman, R., Djohan, R., Gurunluoglu, R., 2016. Free vascularized lymph node transfer for treatment of lymphedema: a systematic evidence based review. *J. Plast. Reconstr. Aesthet. Surg.* 69 (9), 1234–1247. <https://doi.org/10.1016/j.bjps.2016.06.022>. Epub 2016 Jul 1 PMID: 27425000.
- Rossi, E.C., Kowalski, L.D., Scalici, J., Cantrell, L., Schuler, K., Hanna, R.K., Method, M., Ade, M., Ivanova, A., Boggess, J.F., 2017. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. *Lancet Oncol.* 18 (3), 384–392. [https://doi.org/10.1016/S1470-2045\(17\)30068-2](https://doi.org/10.1016/S1470-2045(17)30068-2).
- Ryan, M., Stainton, M.C., Slaytor, E.K., Jacorelli, C., Watts, S., Mackenzie, P., 2003. Aetiology and prevalence of lower limb lymphoedema following treatment for gynaecological cancer. *Aust. N. Z. J. Obstet. Gynaecol.* 43 (2), 148–151. <https://doi.org/10.1046/j.0004-8666.2003.00040.x>. PMID: 14712972.
- Van der Zee, A.G., Oonk, M.H., De Hullu, J.A., Ansink, A.C., Vergote, I., Verheijen, R.H., Maggioni, A., Gaarenstroom, K.N., Baldwin, P.J., Van Dorst, E.B., Van der Velden, J., Hermans, R.H., van der Putten, H., Drouin, P., Schneider, A., Sluiter, W.J., 2008. Sentinel node dissection is safe in the treatment of early-stage vulvar cancer. *J. Clin. Oncol.* 26 (6), 884–889. <https://doi.org/10.1200/JCO.2007.14.0566>. PMID: 18281661.
- Weingold, A.B., Olivo, Ee, Marino, J., 1967. Pelvic lymphocyst: diagnosis and management. *Arch. Surg.* 95 (2), 304–307. <https://doi.org/10.1001/archsurg.1967.01330140142032>.
- Weiss, J., Daniel, T., 2015. Validation of the lymphedema life impact scale (LLIS): A condition-specific measurement tool for persons with lymphema. *Lymphology*. 48 (3), 128–138. PMID: 26939160.
- Yost, K.J., Chevillat, A.L., Al-Hilli, M.M., et al., 2014. Lymphedema after surgery for endometrial cancer: prevalence, risk factors, and quality of life. *Obstet. Gynecol.* 124, 307.