HYS Ngan 顏婉嫦
KF Tam 譚家輝
TY Ng 吳東耀

Prevention of lymphoedema using omentoplasty after pelvic lymphadenectomy: a prospective randomised controlled trial

Key Messages

1. In a randomised controlled trial involving 97 women undergoing pelvic lymphadenectomy, lower limb lymphoedema was detected using clinical and objective measurements in 11% of women.
2. In this study, omentoplasty, ie mobilising a pedicle of omentum to cover the pelvic raw area, did not decrease the occurrence of lower limb lymphoedema when compared to a control group in whom omentoplasty was not performed.
3. The lack of difference could be due to an inadequate sample size since only 5 to 7% of lymphoedema was found in our control group compared to the 40% reported in a pilot study on which the sample size calculation was based.
4. A larger study is required to confirm that omentoplasty does not prevent lymphoedema.

Hong Kong Med J 2008;14(Suppl 5):S43-6

Department of Obstetrics and Gynaecology, Queen Mary Hospital, University of Hong Kong, Hong Kong SAR, China
HYS Ngan, KF Tam, TY Ng

HSRF project number: 01030361

Principal applicant and corresponding author:
Prof Hextan YS Ngan
Department of Obstetrics and Gynaecology, The University of Hong Kong, 6/F, Professorial Block, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong SAR, China
Tel: (852) 2855 4518
Fax: (852) 2855 0947
E-mail: hysngan@hkucc.hku.hk

Introduction

Pelvic lymphadenectomy is the removal of the lymphatic systems around pelvic vessels as part of the staging procedure in the treatment of a number of gynaecological cancers. The purpose is to assess whether the tumour has spread to the lymphatic vessels. In early-stage cervical cancer this is performed along with a radical hysterectomy. In endometrial cancers, it is performed with a total hysterectomy and bilateral salpingoophorectomy and other staging procedures. Though there are complications associated with radical hysterectomy or total hysterectomy, the complications specific to pelvic lymphadenectomy are lymphoedema and lymphocysts. Lymphoedema and its associated complications, such as cellulites, may affect the patient's quality of life. This study aimed to explore the use of omentoplasty as a means of reducing the incidence of lymphoedema after pelvic lymphadenectomy.

Methods

Study design and randomisation

Patients admitted to the Department of Obstetrics and Gynaecology, Queen Mary Hospital, The University of Hong Kong for a pelvic lymphadenectomy were recruited. An informed consent was obtained in compliance with the Institutional Review Board of the Hospital and University. Subjects were randomised to two groups: one group would have an omentoplasty using the technique described by Patsner and Hackett,[1] whereas the other group would have no omentoplasty and thus act as controls. Randomisation was performed using stratification by type of cancer, ie cervical and endometrial cancers. Sealed opaque envelopes containing the randomised treatment allocation were prepared and kept by the research assistant prior to commencing patient recruitment. It was calculated that 32 patients were required for each arm to give a power of 80% for a difference in lymphoedema rates of 30% with a two-sided test at significance level α=0.05. Therefore it was estimated that a sample size of 70 was needed, taking into account a likely 10% drop out rate.

Assessment of lymphoedema

Lymphoedema was assessed using clinical and objective measurements. The clinical classification laid down by the International Society of Lymphology was used. Grade 1 refers to no or minimal fibrosis, ie the oedema pits on pressure and reduces on limb elevation; grade 2 refers to substantial fibrosis clinically, ie the oedema does not pit nor reduces with limb elevation, and grade 3 refers to grade 2 plus elephantine changes. Patients were followed up at 3, 6, 9 and 12 months then at 4 to 6 monthly intervals during the second year after surgery.

Objective measurements were made according to the system described by Stranden.[2] Standardised circumferential measurements were made at seven specific points on each lower limb, ie at the foot, ankle, lower calf, upper calf, knee, lower thigh, and upper thigh. The volume was calculated using the truncated cone formula: volume $=[\Sigma(x^2 + y^2 + xy)]/3\pi]$; where x indicates the distance from the tip of the cone to the base and y indicates the circumference

Table 1. Clinical characteristics

	Control	Omentoplasty	P value (control vs omentoplasty)
Mean age (range)	52.2 (30-79)	48.5 (25-70)	0.13*
Cancer			
Endometrial	25	29	0.22†
Cervical	26	17	
Stage			
I	47	37	1.0†
II and above	4	9	
Type			
Squamous cell carcinoma	13	16	0.26†
Adenocarcinoma	28	26	
Others	10	4	
Hysterectomy			
Simple	22	15	0.30†
Radical	29	31	
Radiotherapy			
No	34	29	0.83†
Postoperative	17	17	
Mean, median (range) of pelvic nodes removed	34.5, 33 (7-81)	34.7, 31 (14-64)	0.90*
Pelvic node metastasis			
Positive	7	10	0.28†
Negative	44	35	
Estimated 4-year disease-free survival	84%	88%	0.50‡
Estimated 4-year overall survival	88%	91%	0.64‡

* Student's *t* test

† Chi squared test

‡ Log rank test

of the cone at distance x. The limbs were assessed prior to surgery, then at 3, 6 and 12 months after by a team of dedicated physiotherapists blinded to the patient's assigned group.

Patients recruited

Between January 2002 and December 2005, 201 patients were approached and 58 refused to join the study. Of the 143 patients recruited, 32 patients did not undergo lymphadenectomy. Fourteen withdrew from the study, mainly because they found the follow-up visits too frequent. A total of 97 patients entered the study.

Clinical characteristics

The entire group ranged in age from 25 to 79 years with a mean of 50.4 years. Fifty-four patients had endometrial cancer and 43 had cervical cancer; 84 patients had stage I, four had stage II, and nine had stage III or higher (staged according to the FIGO [International Federation of Gynecology and Obstetrics] system) endometrial or cervical cancer. Twenty-nine had squamous cell carcinoma; 54 had adenocarcinoma, and 14 other cell types such as adenosquamous cell carcinoma, clear cell carcinoma or sarcoma. Thirty-seven had a total hysterectomy and 60 had a radical hysterectomy together with a pelvic lymphadenectomy. The total number of pelvic nodes removed ranged from 7 to 81 with a mean of 34.5 and a median of 33. Thirty-four patients required postoperative radiotherapy. The clinical parameters did not differ significantly between the two groups (Table 1). Thirteen patients had recurrent disease and 10 of these died. The interval between treatment and latest follow-up date for patients still living ranged from 3 to 55 months (median, 31 months.) The interval from treatment to death ranged from 5 to 26 months. The estimated 4-year disease-free survival rate was 85% and overall survival was 89%.

Statistical analysis

Statistical analysis was performed using the SPSS version 11. The chi squared test, Fisher's exact test, Student's *t* test, Mann-Whitney test, Kaplan Meier estimation and log rank test were used when appropriate. A P value of <0.05 was considered significant.

Results

Lymphoedema and omentoplasty

Objective lower limb lymphoedema (LLL)—a more than 20% increase in volume compared to the preoperative measurement—was found in five patients. Three were in the control group and two in the omentoplasty group. In four patients the oedema affected the lower limb below the knee and one had involvement of the whole leg. There was no statistical difference in the rates of LLL between the control and omentoplasty groups (Fisher's exact test, P=0.83). The objective measurement changes in these five patients are shown in Table 2.

Clinical LLL was detected in seven patients—four in the control group and three in the omentoplasty group. There was no statistical difference in the rates of LLL between the control and omentoplasty (Fisher's exact test, P=1.0). Clinical LLL was detected during the follow-up assessments done at 1, 4, 11, 13, 14, 18, and 20 months. Three patients had lympoedema in the left leg, two had it in the right leg

Table 2. Changes in objective measurement of limb volume in five patients with an increase of more than 20% over the preoperative measurement

	Postoperative			Clinical oedema
	3 months	6 months	12 months	
Left calf	33%	10%	-3%	Yes
Right calf	5%	9%	24%	No
Left calf	27%	24%	15%	No
Right leg	24%	29%	32%	No
Right calf	-13%	-15%	39%	No

and two had bilateral lymphoedema. All had grade-one lymphoedema. The objective percentage changes in the measurements taken in six patients ranged from -13 to 19%. Only one patient had both clinical and objective LLL. She had a 33% increase in volume on measurement at 3 months after surgery which decreased to 10% at 6 months and -3% at 12 months with corresponding clinical improvement.

Since only one patient had LLL on both clinical and objective measurements, using the data from both clinical and objective measurement, LLL was found in 11 patients in this study—six in the control and five in the omentoplasty group. There was no statistical difference in LLL between the control and omentoplasty groups (Fisher's exact test, P=1.0). The median time for detecting LLL either by clinical or objective methods was 12 months.

Lymphoedema with other clinical factors

Taking both clinical and objective lymphoedema together, no significant association was found with postoperative radiotherapy (Fisher's exact test, P=0.51). No association was found between the occurrence of lymphoedema and the total number of pelvic nodes removed (Mann-Whitney test, P=0.32); positive pelvic node metastases (Fisher's exact test, P=0.10), with types of surgery (Fisher's exact test, P=0.53); squamous or adenocarcinoma tumours (Fisher's exact test, P=0.44) and stage cancer stages (Fisher's exact test, P=0.22). There was no significant difference in the disease-free survival and the overall survival of patients with or without oedema (log rank test, P=0.68, P=0.39 respectively).

Discussion

Lower limb lymphoedema is a complication of pelvic lymphadenectomy. Disruption of the locoregional lymphatic drainage leads to swelling of the lower limbs. The incidence varies from 1 to 40% after a radical hysterectomy.[3,4] The incidence in this study was 11% when both clinical and objective assessments were used. Using objective measurement, three (60%) of the five patients were found to have LLL at 3 months with one resolving at 6 months, one at 12 months, and one persisting at 12 months. On the other hand, two patients were found to have developed LLL at 12 months. Using clinical assessment, two (29%) of the seven patients were found to have LLL before 6 months. Three (43%) of these seven patients were found to have LLL around 12 months and two (29%) at and after 18 months. Our study showed that LLL can develop quite early after surgery, however, over half of our patients developed it after 1 year, an unusual finding although late development of LLL has been reported. It is hence important to look for LLL not only during the first year of follow-up but also the second year after surgery.

None of the risk factors in association with LLL were found in this study. The relationship between postoperative radiotherapy and LLL is controversial. One study found a 3-fold increase in the incidence of LLL (5% vs 15%) in irradiated patients but another found, as we did, that there was no significant association with postoperative radiotherapy.[5,6] Age, stage and type of hysterectomy had no association with LLL, a finding supported by other studies.[4] We also found that other factors such as histology, type of cancers, total number of pelvic nodes removed, metastases in pelvic nodes, recurrence, and death were not associated with LLL. Hence, it is difficult to predict which patient is more likely to develop LLL after surgery.

Though most LLL detected was mild, complications like cellulitis tend to resolve more slowly in patients with lymphoedema, thus prevention is the best approach. A pilot study of omentoplasty in gynaecological patients showed that clinical LLL occurred in 40% of patients in the control group and 8% in the omentoplasty group.[3] A later study performed by Patsner and Hackett[1] on 140 patients showed that omentoplasty was safe. No LLL was detected in his cohort. Though omentoplasty has promise as a means of preventing LLL, our randomised control trial failed to show a difference in the incidence of LLL in the control and omentoplasty groups. This could be attributed to the method used for the detection of LLL. More sensitive methods such as magnetic resonance imaging and dynamic lymphoscintigraphy may be more objective and sensitive but are costly. Hence, we used a less sophisticated objective method—leg measurement—in addition to clinical assessment. It has been shown that surface measurement has accuracy comparable to water displacement as a means of measuring leg volume.[2] Using this objective measurement, LLL was only detected in 5% of patients. This could be due to the early cessation of objective measurement, since, as shown by the clinical assessment data, most patients with LLL were found to have developed it after 12 months. On the other hand, LLL was detected in 7% of patients using clinical assessment, a finding compatible with other studies using clinical assessment.[1,2] Our finding of a low rate (5-7%) of LLL in the control arm using both objective and clinical assessments suggests that the sample size was probably too small to detect a significant difference. Hence, a larger clinical study may be needed to show whether omentoplasty is an effective method of lowering the rate of LLL.

Conclusions

The current study showed that the incidence of LLL

assessed by clinical and objective measurement after pelvic lymphadenectomy was 11%, which was lower than reports from some studies. Omentoplasty has not been shown to decrease the incidence of LLL. A larger study is required for confirmation.

Acknowledgements

This study was supported by the Health Services Research Fund (HSRF: 01030361), Food and Health Bureau, Hong Kong SAR Government. We thank the Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China. The investigators also thank Miss Yuk-fung Tong, Miss Gladys Collier, Miss Yvonne CK Yue from the Department of Physiotherapy who performed all the objective measurements. Miss Ann MW Yip, research nurse and Miss Man-yin Tsang, research assistant, who recruited all the patients. We thank Dr LC Wong, Dr YM Chan, and Dr KKL Chan who performed some of the operations in this study in the Department of Obstetrics and Gynaecology.

References

1. Patsner B, Hackett TE. Use of the omental J-flap for prevention of postoperative complications following radical abdominal hysterectomy: report of 140 cases and literature review. Gynecol Oncol 1997;65:405-7.
2. Stranden E. A comparison between surface measurements and water displacement volumetry for the quantification of leg edema. J Oslo City Hosp 1981;31:153-5.
3. Logmans A, Kruyt RH, de Bruin HG, Cox PH, Pillay M, Trimbos JB. Lymphedema and lymphocysts following lymphadenectomy may be prevented by omentoplasty: A pilot study. Gynecol Oncol 1999;75:323-7.
4. Abu-Rustum NR, Alektiar K, Iasonos A, et al. 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 2006;103:714-8.
5. Soisson AP, Soper JT, Clarke-Pearson DL, Berchuck A, Montana G, Creasman WT. Adjuvant radiotherapy following radical hysterectomy for patients with stage IB and IIA cervical cancer. Gynecol Oncol 1990;37:390-5.
6. Snijders-Keilholz A, Hellebrekers BW, Zwindeman AH, van de Vijver MJ, Trimbos JB. Adjuvant radiotherapy following radical hysterectomy for patients with early-stage cervical carcinoma (1984-1996). Radiother Oncol 1999;51:161-7.