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Randomised trial of drains versus no drains following radical hysterectomy and pelvic lymph node dissection: a European Organisation for Research and Treatment of Cancer-Gynaecological Cancer Group (EORTC-GCG) study in 234 patients

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ABSTRACT

Drainage, following radical hysterectomy and pelvic lymph node dissection to prevent postoperative lymphocyst formation and surgical morbidity, is controversial. To study the clinical significance of drainage, 253 patients were registered and 234 patients were randomised into two arms. In one arm ($n = 117$) postoperative drainage was performed, in the other arm ($n = 117$) no drains were inserted. In both arms closure of the peritoneum of the operating field was omitted. The main exclusion criteria were blood loss of more than 3000 ml during surgery or persistent oozing at the end of the operation. Clinical and ultrasound or CT-scan evaluation was done at one and 12 months postoperatively. The median follow-up amounted to 13.3 months. No difference in the incidence of postoperative lymphocyst formation or postoperative complications was found between the two study arms. The late (12 months) incidence of symptomatic lymphocysts was 3.4% (drains: 5.9%; no drains: 0.9%). The difference showed a p -value of 0.06 in Fisher's Exact test. The operating time was related to the occurrence of postoperative lymphocyst formation. It was concluded that drains can be safely omitted following radical hysterectomy and pelvic node dissection without pelvic reperitonisation in patients without excessive bleeding during or oozing at the end of surgery.

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1. Introduction

Lymphocyst formation is a well-known complication following pelvic lymph node dissection^{1,2} that can lead to leg oedema, deep venous thrombosis, ureteral obstruction, pain and secondary infection.^{3,4} Retroperitoneal drainage of the operating field has been advocated to prevent lymphocyst formation and febrile morbidity, but with the recent tendency to leave the peritoneum open and allow for transperitoneal resorption of lymph fluid throughout the abdominal cavity⁵, this policy has been challenged in retrospective⁶ as well as randomised studies.^{7,8} The general conclusion from these studies was that drainage may be omitted, but the use of postoperative drainage for the prevention of lymphocysts is still advocated⁹. Furthermore, the few prospective randomised trials undertaken so far have only studied limited numbers of patients.^{7,8}

These considerations led the Gynaecological Cancer Group (GCG) of the European Organization of Research and Treatment of Cancer (EORTC) to undertake a multicenter randomised clinical trial to compare the incidence of lymphocyst formation and postoperative morbidity between two groups of patients who underwent radical hysterectomy and pelvic lymph node dissection. In one group, pelvic drainage was performed and in the other group no drains were placed during surgery. Peritonisation of the operating field was omitted in both groups. The results of this trial (EORTC 55962) are reported here.

2. Materials and methods

Between February 1998 and July 2000, patients were entered in the EORTC trial 55962. The patients underwent radical hysterectomy and pelvic lymphadenectomy in twelve European cancer centres. The patients were randomised to either pelvic drainage or no drainage following surgery in order to define the significance of drainage in the prevention of lymphocyst formation and surgical morbidity following radical hysterectomy. Stratification was performed per centre. Exclusion criteria for randomisation included blood loss during surgery exceeding 3000 ml, persistent oozing at the end of the procedure requiring postoperative drainage, concomitant urinary or bowel injury or derivation or surgical procedures for urinary incontinence, pregnancy, application of abdominal mass or preoperative radiotherapy or chemotherapy.

The pelvic peritoneum was left open in all patients and the vaginal cuff was primarily closed. In the drainage arm 2 passive or active suction drains were placed in the retroperitoneal fossa and inserted via the vagina or the abdominal route, according to the institution's policy. Drains were removed when fluid loss was less than 50 ml in 24 h. Prophylactic antibiotics and prevention of thrombo-embolism was mandatory and was also performed according to the institution's protocol.

All patients were seen one month after surgery and at 3 months intervals during the first postoperative year. At 1 and 12 months postoperatively, imaging was performed by ultrasonography or computerised tomography (CT)-scan. The primary end-point of the study was lymphocyst incidence and secondary end-points were other postoperative

complications. Postoperative complications were defined according to the French-Italian glossary of 1993.¹⁰

Equivalence between the two study-arms was defined as less than doubling the rate of lymphocysts in the no drainage arm. With a one sided type I error of 0.05 and a power of 80%, the number of patients needed to show equivalence on the basis of the expected incidence of lymphocysts was calculated at 214. Analysis of the results was on an intention to treat basis.

3. Results

A total of 253 patients were registered. Nineteen patients were ineligible for randomisation because of various forms of protocol violation: (lymph node dissection aborted: 4, inoperability: 8, excessive blood loss: 2, administrative problems: 5) leaving 234 patients for randomisation: 117 in the drains-arm and 117 in the no drains-arm. Median follow-up amounted to 13.3 months (drains-arm: 14.0 months, no drains-arm: 13.1 months).

Baseline characteristics of the patients in both arms are given in Table 1 and were comparable between the two arms. The same was true for clinical parameters related to the surgical treatment (Table 2).

During the study period 13 patients died, six in the drains-arm and 7 in the no drains-arm. In the drains-arm, death was due to the primary cancer in three patients, in the no drains-arm this was the case in 6 patients. There was one patient with a postoperative death due to haemorrhage, allocated to

Table 1 – Baseline characteristics of 234 eligible patients randomised to drainage or no drainage following radical hysterectomy and pelvic lymph node dissection^a

	Drains (n = 117)	No drains (n = 117)	Total (n = 234)
Median age yrs ^b (range)	46.5 (27.7–80.6)	45.5 (27.6–79.3)	46.2 (25.7–80.6)
Median weight (range)	65 (42–115)	65 (47–110)	64 (42–115)
WHO performance status			
0	113	112	225
1	4	4	8
2	–	1	1
Primary tumour			
Cervical cancer	97	101	198
Endometrial cancer	19	16	35
Vaginal cancer	1	–	1
Cervical cancer FIGO stage			
Ia1	–	1	1
Ia2	5	2	7
Ib1	65	70	135
Ib2	11	13	24
IIa	16	15	31
Total	97	101	198

a All variables: not significant.

b yrs: years.

Table 2 – Clinical parameters related to surgical treatment between the drains arm and the no drains-arm

	Drains (n = 117)	No drains (n = 117)	Total (n = 234)
Median number of lymph nodes Removed (range)	27 (7–62)	25.5 (10–75)	26 (7–75)
Para-aortic nodes Removed (patients)	15	9	24
Median duration of surgery (min, range)	240 (75–450)	245 (135–440)	240 (75–450)
Transposition of ovaries (patients)	19	12	31
Median time to resumption of bowel sounds (days)	2	2	2
Lymph node metastasis (%)	20.9	19.8	20

the drains-arm. Overall actuarial survival and disease free survival was not different between the two arms: 5 years overall survival in the drains-arm and the no drains-arm 73.7% (95% CI: 48.0–99.3) and 89.9% (95% CI: 81.7–98.3), respectively. Actuarial 5 years disease free survival in the drains-arm and the no drains-arm: 90.5% (95% CI: 84.9–96.2) and 78.1% (95% CI: 57.1–99.2), respectively.

Postoperative complications are listed in Table 3. Again, there were no significant differences between the two study-arms. All together (1 month evaluation, 12 months evaluation, symptomatic and asymptomatic), lymphocysts were found in 30.8% of patients in the drains-arm and 37.6% of patients in the no-drains arm. The most relevant clinical parameter relating to the occurrence of lymphocysts would be long-term symptomatic cysts. Table 4 shows the presence of lymphocysts at 12 months postoperatively. Symptomatic lymphocysts were seen in 5.9% of patients in the drains-arm versus 0.9% in the no drains-arm. This difference represented a *p*-value of 0.06 using Fisher's Exact Test. On the basis of preset statistical criteria, the equivalence in the incidence of lymphocysts between the drains and no drains-arm could not be rejected, leading to the conclusion that postoperative drainage does not result in less lymphocysts formation.

The presence of metastatic nodes was not related to the incidence of lymphocysts and neither was the number of lymph nodes removed. The operating time, however, showed a significant relation to the incidence of lymphocysts (odds ratio 0.996; 95% CI: 0.993–0.999; *p* = 0.037) but the magnitude of this effect was small.

4. Discussion

This study showed that drainage following radical hysterectomy and pelvic lymphadenectomy does not lead to a decrease of lymphocyst formation when following the study protocol. This protocol prescribed prophylactic antibiotics, thromboprophylaxis and non-closure of the peritoneum.

Table 3 – Postoperative complications following radical hysterectomy and pelvic lymphadenectomy in the drains group and no drains group

	Drains (n = 117)	No drains (n = 117)	Total (n = 234)
Fever for two consecutive days	7	4	11
Wound infection (patients)	1	8	9
Drain site infection (patients)	1	–	–
Pelvic infection G1-2 (patients)	–	2	2
Urinary tract infection (patients)	45	54	99
Respiratory tract infection (patients)	4	2	6
Deep venous thrombosis/embolism	1	1	2
Bowel obstruction requiring surgery	–	2	2
Recto vaginal fistula requiring surgery	1	–	1
Vesico vaginal fistula requiring surgery	1	–	1
Uretero vaginal fistula requiring surgery	1	2	3
Ureteral stenosis requiring surgery	0	2	2

Table 4 – Long term (12 months) incidence of lymphocysts in the drains arm and no drains-arm following radical hysterectomy and pelvic lymphadenectomy

	Drains (n = 117)		No drains (n = 117)		Total (n = 234)	
Missing	2	1.7%	–	–	2	0.9%
No lymphocysts	86	73.5%	97	82.9%	183	78.2%
Asymptomatic lymphocysts	22	18.8%	19	16.2%	41	17.5%
Symptomatic lymphocysts	7	5.9%	1	0.9%	8	3.4%

The latter requirement is probably important because it enables free drainage of lymphatic fluid to the intraperitoneal cavity and resorption by the peritoneum, omentum and diaphragm^{1,11,12}.

At 12 months evaluation the incidence of symptomatic lymphocysts was even less in the no drains-arm (0.9%) as compared to the drains-arm (5.9%) and this difference almost reached statistical significance (*p* = 0.06).

The incidence of complications was comparable between the two arms as were survival and disease-free survival.

The only prognostic factor for the occurrence of lymphocyst formation that could be demonstrated was the duration of surgery, but the effect of this relation was of borderline significance.

The conclusion that drainage of the operating site adds no favourable effect to the result and sequelae of radical hysterectomy and pelvic lymphadenectomy confirms the results of previous studies^{5–7,13}, but our study is the largest randomised trial undertaken so far. The incidence of lymphocysts found in our study is within the range of the findings of others^{5,7}. However, the figure of 20.9% total lymphocysts at 12 months postoperatively may seem formidably high, but it should be realised that the vast majority of these cysts were asymptomatic. Furthermore, it cannot be excluded that the ultrasonographic diagnosis of a lymphocyst might actually represent an intraperitoneal pseudocyst caused by postoperative adhesions and filled with peritoneal fluid.

In the end, the overall conclusion from this randomised clinical trial is that drains to prevent lymphocyst formation can safely be omitted following radical hysterectomy and pelvic lymphadenectomy in patients with no excessive bleeding during surgery or oozing at the end of the operation. This conclusion adds valuable information to earlier trials because in most of the earlier reported studies no systematic imaging was performed after 1 year.

Conflict of interest statement

No actual or potential conflicts of interest on behalf of the authors of this paper do exist.

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