Laparoscopy versus laparotomy for FIGO Stage I ovarian cancer (Review)

Medeiros LRF, Rosa DD, Bozzetti MC, Rosa MINES, Edelweiss MI, Stein AT, Zelmanowicz A, Ethur AB, Zanini RR

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2008, Issue 4

http://www.thecochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Laparoscopy versus laparotomy for FIGO Stage I ovarian cancer

Lídia RF Medeiros[1], Daniela D Rosa[2], Mary C Bozzetti[3], Maria INES Rosa[4], Maria I Edelweiss[5], Airton T Stein[6], Alice Zelmanowicz[7], Anaelena B Ethur[8], Roselaine R Zanini[9]

[1]Social Medicine/Epidemiology, Post-graduation Program in Medical Sciences, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil. [2]Hospital Femina - Grupo Hospitalar Conceicao, Porto Alegre, Brazil. [3]Social Medicine, Faculty of Medicine at Federal University of Rio Grande do Sul, Rio Grande do Sul, Brazil. [4]Medical School, Universidade do Extremo Sul Catarinense, Criciuma, Brazil. [5]Pathology, Faculty of Medicine at Federal University of Rio Grande do Sul, Rio Grande do Sul, Brazil. [6]Department of Public Health, Universidade Federal de Ciências da Saúde, Porto Alegre, Brazil. [7]Cancer Prevention Centre, Complexo Hospitalar Santa Casa, Rio Grande do Sul, Brazil. [8]Postgraduate Program in Epidemiology, Federal University of Rio Grande do Sul, Rio Grande do Sul, Brazil. [9]Postgraduate Program in Epidemiology at Federal University of Rio Grande do Sul, Federal University of Rio Grande do Sul, Rio Grande do Sul, Brazil

Contact address: Lídia RF Medeiros, Social Medicine/Epidemiology, Post-graduation Program in Medical Sciences, Universidade Federal do Rio Grande do Sul, Jose de Alencar 1244, 1009 Menino Deus, Porto Alegre, Rio Grande do Sul, 90880-480, Brazil. lidia.rosi@terra.com.br. lidiarosi@hotmail.com.

Editorial group: Cochrane Gynaecological Cancer Group.
Publication status and date: Edited (no change to conclusions), published in Issue 12, 2010.
Review content assessed as up-to-date: 20 July 2008.

Citation: Medeiros LRF, Rosa DD, Bozzetti MC, Rosa MINES, Edelweiss MI, Stein AT, Zelmanowicz A, Ethur AB, Zanini RR. Laparoscopy versus laparotomy for FIGO Stage I ovarian cancer. *Cochrane Database of Systematic Reviews* 2008, Issue 4. Art. No.: CD005344. DOI: 10.1002/14651858.CD005344.pub2.

ABSTRACT

Background

Over the past ten years laparoscopy has become an increasingly common approach for the surgical removal of early stage ovarian tumours. There remains uncertainty about the value of this intervention. This review has been undertaken to assess the available evidence of the benefits and harms of laparoscopic surgery for the management of early stage ovarian cancer compared to laparotomy.

Objectives

To evaluate the benefits and harms of laparoscopy in the surgical treatment of FIGO stage I ovarian cancer (stages Ia, Ib and Ic) when compared with laparotomy.

Search methods

Trials were identified by searching the Cochrane Gynaecological Cancer Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), The Cochrane Library Issue 2, 2007, MEDLINE (January 1990 to November 2007), EMBASE (1990 to November 2007), LILACS (1990 to November 2007), BIOLOGICAL ABSTRACTS (1990 to November 2007) and Cancerlit (1990 to November 2007). We also searched our own publication archives, based on prospective handsearching of relevant journals from November 2007. Reference lists of identified studies, gynaecological cancer handbooks and conference abstract were also scanned.

Selection criteria

Studies including patients with histologically proven stage I ovarian cancer according to the International Federation of Gynaecology and Obstetrics (FIGO).

Studies comparing laparoscopic surgery with laparotomy for early stage ovarian cancer were only available from 1990. It was anticipated that a very small number of randomised controlled trials (RCTs) were conducted studying the management of early stage ovarian cancer. Therefore, non-randomised comparative studies, cohort studies and case-controls studies, but not studies with historical controls, were also considered.

Data collection and analysis

Data extraction was performed independently by five review authors (LRM, DDR, MIR, MCB and MIE) who assessed study quality and quality of extracted data. Extracted data included trial characteristics, characteristics of the study participants, interventions and outcomes. The quality of non RCTs was assessed using appropriate quality evaluations tools from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and from the Newcastle-Ottawa tool for observational studies (NOS).

Main results

No RCTs were identified. Three observational studies were identified.

Authors' conclusions

This review has found no evidence to help quantify the value of laparoscopy for the management of early stage ovarian cancer as routine clinical practice.

PLAIN LANGUAGE SUMMARY

Laparoscopy versus laparotomy for FIGO Stage I ovarian cancer

Controversial discussion has arisen among endoscopists and oncologists about the laparoscopic management of early stage ovarian tumours. This systematic review found no evidence to help quantify the value of laparoscopy for the management of early stage ovarian cancer in clinical practice.

BACKGROUND

Malignant ovarian neoplasms are responsible for four per cent of all cancer affecting women and are the second most common cause of death from gynaecological cancer and the fourth most common cause of death from all types of cancer affecting women (Yancik 1993). Diagnosis of early stage ovarian cancer (limited to the ovaries) is rare and is mainly made by accidental discovery at the time of routine ultrasonography or during laparoscopy. The incidence of managing an unexpected ovarian cancer by laparoscopy is 6.5 in 1000 women with an adnexal mass (Wenzl 1996).

Most cancers of the ovary are epithelial. The most common histologic subtype is serous (40 to 70% of all types); endometrioid tumours are the second most common, (20% to 25% of all cases). Mucinous epithelial tumours are rarer, comprising 5% to 20% of all cases (Kosary 1994).

Borderline ovarian tumours constitute approximately 5.9% of low malignant potential (Medeiros 2005).

The diagnosis of borderline ovarian tumours is more difficult due to variations in the histopathologic criteria used among different countries for the differential diagnosis between borderline and malignant lesions (Burger 2000). Stromal and germ cell tumours comprise 1.1% to 1.7% of all cases of malignant ovarian tumours (Medeiros 2005).

The prognosis of all ovarian tumours is independently affected by the following factors: stage of cancer at diagnosis, histological subtype, tumoral grading and the volume of residual disease after surgery (Benedet 2000). Current standard treatment for patients with early stage ovarian cancer is a laparotomy with a longitudinal

median incision to allow the required surgical staging (Benedet 2000; Hand 1993; Kosary 1994). The primary tumour, if limited to the ovary, must be examined to look for capsular rupture (Benedet 2000). There is evidence that the overall survival rate can be higher when the transformed cells are confined to the ovaries (Crayford 2000).

For patients with borderline tumours with obvious limited disease (stage Ia) and normal examination of the opposite ovary conservative therapy can be administered when there is a desire to maintain fertility (Benedet 2000; Vinatier 1996). For patients with FIGO stage Ia, Ib or Ic, the proposed surgical treatment includes total hysterectomy and bilateral salpingo-oophorectomy and all obvious sites of tumour must be removed (Benedet 2000; Vinatier 1996). Furthermore, the omentum, pelvic and para-aortic lymph nodes should be removed for histological examination in order to obtain accurate staging (Benedet 2000; Vinatier 1996).

Recently two parallel RCTs, the International Collaborative Ovarian Neoplasm 1 (ICON1) (Trimbos 2003) and the Adjuvant Chemotherapy in Ovarian Neoplasm (ACTION) (Trimbos 2004) in early-stage ovarian cancer compared platinum-based adjuvant chemotherapy with observation following surgery. They showed that adjuvant chemotherapy may provide further benefits for women with stage I ovarian cancer. ICON1 reported an improvement in overall survival of 8% and in recurrence-free survival of 11% in patients treated with adjuvant platinum-based chemotherapy compared with observation only (Trimbos 2003).

However, ACTION also showed that adjuvant chemotherapy significantly improved the overall and the disease-free survival only in inadequately staged patients (Trimbos 2004), though this was a post hoc sub group analysis. In addition, a systematic review led by Elit *et al.* found similar results, especially when patients were not submitted for lymphadenectomy as part of the surgical staging (Elit 2004). Therefore in the patients who had undergone optimal surgical staging, adjuvant chemotherapy may have had no effect on the prognosis (Trimbos 2004; Vergote 2003). Many physicians believe that the best policy for the treatment of patients with early stage ovarian cancer is to make efforts to achieve optimal surgical staging and to save adjuvant chemotherapy for those patients in whom optimal staging is not feasible (Trimbos 2004). However, there are no RCTs addressing optimal staging or surgery.

Laparoscopy has been restricted to patients with pre-operative evidence of a benign diagnosis (Vergote 2004). The inappropriate treatment of a malignant condition by endoscopy is associated with worse prognosis (Lehner 1998). Rupture of an ovarian malignant tumour should be avoided at the time of surgery for an early stage ovarian cancer (Vergote 2004). Some endoscopic procedures are performed using CO2 laser techniques, and this is considered by some authors to increase the risk of activating cell enzymes which may lead to mitosis and an increase in the production of tumour growth factors. If the duration of laparoscopic surgery is prolonged there may also occur mechanical or chemical damage of the mesothelium which, in some cases of malignancy may be inadvertently treated as a benign lesion, increasing the risks of metastases in the abdominal cavity (Greene 1995; Volz 1999). However, reports addressing the selective use of laparoscopic techniques in the management of malignant gynaecologic disease have been published with increasing frequency (Chi 1999; Dottino 1999; Kadar 1997; Vinatier 1996), although it still remains controversial whether laparoscopy is a good choice for the management early stage ovarian cancer (Vergote 2004).

It is not yet established whether laparoscopy is as good as or better than the conventional surgical approach for the treatment of ovarian tumours which are assumed to be malignant. Given the limited evidence from randomised trials in this area of surgery, and the concerns that have arisen over quality, an objective analysis of the literature requires evaluation of both randomised and non-randomised studies. We performed a systematic review to compare laparoscopy with laparotomy as surgical approaches for the treatment of early stage ovarian cancer.

OBJECTIVES

To evaluate the benefits and harms of laparoscopy in the surgical treatment of FIGO stage I ovarian cancer (stages Ia, Ib and Ic) when compared with laparotomy.

The following issues were addressed in this review:

- Is laparoscopy (intervention group) effective in improving overall survival (OS) (compared with laparotomy (control group) in patients with FIGO stage I ovarian cancer?

- Is laparoscopy (intervention group) effective in improving progression free survival (PFS) compared with laparotomy (control group) in patients with FIGO stage I ovarian cancer?

- Does primary laparoscopy result in less surgical complications than laparotomy (control group) in patients with FIGO stage I ovarian cancer?

- Does primary laparoscopy (intervention group) result in more local recurrence (port site) than laparotomy (control group) in midline incision in patients with FIGO stage I ovarian cancer?

- Does primary laparoscopy (intervention group) result in more distant recurrence than laparotomy (control group) in patients with FIGO Stage I ovarian cancer?

- Does primary laparoscopy (intervention group) result more tumour spillage at the time of surgery than laparotomy (control group) in patients with FIGO stage I ovarian cancer?

- Does primary laparoscopy (intervention group) result in less cost than laparotomy (control group) in patients with FIGO stage I ovarian cancer?

METHODS

Criteria for considering studies for this review

Types of studies

Inclusion criteria

Studies of patients with histologically proven stage I ovarian cancer according to the International Federation of Gynaecology and Obstetrics (FIGO) were included.
Studies comparing laparoscopic surgery with laparotomy for early stage ovarian cancer were only available from 1990.
It was anticipated that a very small number of RCTs would have been conducted analysing patients with early stage ovarian cancer. Therefore, non-randomised comparative studies, cohort studies and case-controls studies, but not studies with historical controls, were also considered.

Exclusion criteria

All studies regarding patients with early stage ovarian cancer who desired to remain fertile, treated by conservative surgery (unilateral salpingo-oophorectomy).
All studies where ovarian cancer was inadequately staged.

Types of participants

Patients with early stage ovarian cancer was included, i.e. patients with disease confined to the ovaries, no lymph node involvement or distant metastases.
The International Federation of Gynaecology and Obstetrics (FIGO) distinguishes patients with stage I ovarian cancer as follows (Scully 1999):
Stage Ia: unilateral tumours
Stage Ib: bilateral tumours
Stage Ic: identifies tumour spillage, tumour capsular penetration, positive peritoneal cytology
No lymph node involvement or distant metastases
Whenever possible the results were stratified by: histological subgroups of ovarian cancer.
Histological sub grouping for malignant ovarian tumours were considered whenever possible (Scully 1999):
(1) Surface epithelial-stromal tumours:
(a) serous type (borderline and malignant)
(b) mucinous type (borderline and malignant)
(c) endometrial type
(2) Germ cell tumours:
(a) teratoma (immature and monodermal types)
(b) dysgerminoma
(c) yolk sac tumour
(d) embryonal carcinoma
(e) carcinoid tumours
(3) Sex cord-stromal tumours:
(a) granulosa-stromal cell tumours
(b) sertoli-stromal cell tumours (androblastoma)
(c) sex cord tumour with annular tubules
(d) gynandroblastoma
(e) unclassified sex cord-stromal tumour
(f) steroid (lipid) cell tumour

Types of interventions

Two surgical approaches used for the management of FIGO stage I ovarian cancer were compared: laparoscopy (intervention group) and laparotomy (control group).

Types of outcome measures

Primary outcomes

(1) Survival at five years
(2) Progression free-survival (PFS) at five years

Secondary outcomes

(1) Tumour spillage at the time of surgery.
(2) Local recurrence: laparoscopy (porte site) and laparotomy (midline incision).
(3) Distant recurrence.
(4) Surgical outcome:
(a) Surgical complications (immediate and delayed):
(i) injury (to the bladder, urether, vascular, small bowel and colon injuries);
(ii) presence/complication of adhesions;
(iii) fever;
(iv) intestinal obstruction;
(v haematoma;
(vi) infection;
(vii) rate of conversion to laparotomy.
(b) Systemic complications:
(i) chest infection;
(ii) deep venous thrombosis;

(iii) pulmonary embolism;
(iv) cardiac failure;
(v) cardiac ischemias;
(vi) cerebrovascular accident
(c) Operative time.
(d) Recovery from surgery: length of hospital stay and re-admission rates.

Search methods for identification of studies

Electronic searches

Searches was conducted to identify all published and unpublished RCTs and non RCTs comparing laparoscopy and laparotomy for early stage ovarian cancer. The search strategies identified studies in all languages and, when necessary, non English language papers were translated so that they could be fully assessed for potential inclusion in the review.
Trials were identified by searching the Cochrane Gynaecological Cancer Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), The Cochrane Library Issue 2, 2007, MEDLINE (January 1990 to November 2007), EMBASE (1990 to November 2007), LILACS (1990 to November 2007), BIOLOGICAL ABSTRACTS (1990 to November 2007) and Cancerlit (1990 to November 2007).

MEDLINE was searched using the following strategies:
1. Randomized controlled trial. pt.
2. Controlled clinical trial.pt
3. Randomizes controlled trials/
4. random allocation/
5. double -blind method/
6. single-blind method/
7. or/1-6
8. clinical trial.pt
9. exp clinical trials/
10. (clin$ adj25 trial$).ti,ab,sh.
11. ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or masks$)).ti,ab,sh.
12. placebos/
13. placebo$.ti,ab,sh
14. random$.ti,ab,sh.
15. Research design/
16. or/8-15
17. (animal not human).sh
18. 16 not 17
19. comparative study.sh
20. exp evaluation studies
21. follow up studies.sh
22. prospective studies
23. (control$ or prospectiv$).mp or volunter$.ti.ab.
24. exp cohort studies/
25. cohort.tw
26. exp longitudinal studies/
27. (cohort adj5 (stud$ or trial$)).tw
28. (prospectiv$ adj5 (stud$ or trial$)).tw
29. (longitudinal adj5 (stud$ or trials)).tw
30. or/18-29
31. exp Ovarian Neoplasms/
32. (ovar$ adj5 tumo?r).tw
33. (ovar$ adj5 neoplas$).tw
34. (ovar$ adj5 cancer$).tw
35. (ovar$ adj5 carcino$).tw
36. exp Adnexal Diseases/
37. exp Ovarian Cancer/
38. or/31-37
39. exp “early ovarian cancer”/
40. exp “early ovarian neoplasm”/
41. “stage I ovarian cancer”/
42. or/ 39-41
43. 38 and 42
44. exp SURGERY/
45. surg$.tw.
46. laparo$.tw.
47. exp Surgical procedures, Operative/
48. or/44-47
49. 43 and 48
50. 30 and 49
See Appendix 1 for further electronic search strategies

Searching other resources

The citation list of relevant publications, abstracts of scientific meetings and list of included studies were checked through hand searching and experts in the field contacted to identify further reports trials. The results of handsearching of the following conferences/publications were searched:
Gynecologic Oncology
International Journal of Gynaecological Cancer
British Journal of Cancer
British Cancer Research Meeting
Annual Meeting of the International Gynaecologic Cancer Society
Annual Meeting of the American Society of Gynecologic Oncologist
Annual Meeting of the European Society of Medical Oncology (ESMO)
Annual Meeting of the American Society of Clinical Oncology (ASCO)

Data collection and analysis

Selection of studies

All eligible studies were assessed for their methodological quality and relevance to the review objectives. Study selection was undertaken by the review authors. No effort was made to blind the review authors for names of authors, institutions and journals. The reason for this is that all review authors were very familiar with the literature on early stage ovarian cancer treatment. As it was known that no RCTs have been published, we decided to incorporate other types of studies in this review, i.e. cohort studies and case-control studies, but not studies with historical controls.

Data extraction and management

All studies were assessed with the aid of a critical review form. Three different critical review forms were used: one for RCTs (Table 1). One for case control studies and one for cohort studies (Table 2; Table 3, Table 4). The critical review forms were filled out independently by the review authors to assess whether the studies meet the inclusion criteria. Extracted data included trial characteristics, characteristics of the study participants, interventions and outcomes (Table 1). The quality of non RCTs were assessed using appropriate quality evaluations tools by STROBE (Strengthening the Reporting of Observational studies in Epidemiology) (Vandenbroucke 2007) and Newcastle-Ottawa tool for observational studies (NOS) (Wells 2007). A"star system" has been developed in which a study was judged based on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of the exposure and outcome of interest for case control and cohort studies. The goal of this project was to develop an instrument providing an easy and convenient tool for quality assessment of non randomised studies to be included in a systematic review (Wells 2007).
Differences were resolved by discussion. When a paper contained insufficient information to make a decision about eligibility or when additional information was required we contacted the author/ principal investigator asking for further information.

Data synthesis

Statistical analysis was performed in accordance to the guidelines developed by the Cochrane Gynaecological Cancer Group. All trials were initially included in one analysis of surgical laparoscopy and laparotomy for early stage ovarian cancer. However, it was impossible to performed the meta-analysis due the methodological difference between the studies (design and quality of report). For that reason we performed qualitative systematic review. We assessment of the quality of each studies using NOS and STROBE. NOS use a 'star system' developed on the following broad perspectives: the selection of the study groups; comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control of cohort studies respectively. The STROBE statement is a checklist of 22 items that we consider essential for good reporting of observational studies (cohort and case-control).

RESULTS

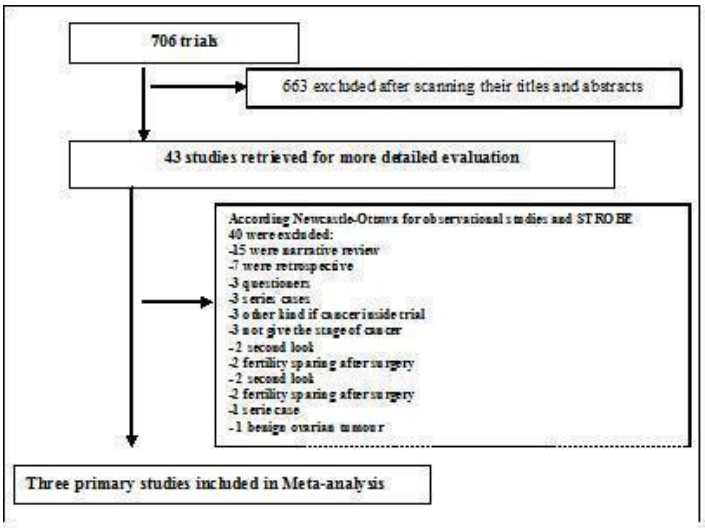
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The initial search identified 706 citation, of which 663 were excluded and 43 were retrieved for detailed examination. Only three published trials met the inclusion criteria, one cohort (Tozzi 2004) and two case-control studies (Ghezzi 2007; Hua 2005) (Figure 1). No RCTs were identified.

Figure 1. Study selection process



Included studies

Settings

The three included studies were of single-centre design, conducted in Italy (Ghezzi 2007; Tozzi 2004) and China (Hua 2005) which was translated from Chinese to Portuguese.

Designs

One case-control study compared ten consecutive patients submitted to laparoscopy for early stage ovarian cancer with eleven patients with the same diagnosis who underwent laparotomy (Hua 2005). Another case-control study compared 15 patients with early stage ovarian cancer submitted to laparoscopy with another group of 19 patients with the same diagnosis submitted to laparotomy (Ghezzi 2007).

We found one prospective cohort study with 42 patients eligible to enter the study with ovarian cancer FIGO stage IA to IB and follow up around 46.4 months (SD 16.25; range 2 to 72 months), initially submitted to laparoscopy (Tozzi 2004). However, 18 patients were excluded due to tumour rupture (n = 5) not explained if occurred during or before surgery, presence of peritoneal implants (n = 3), ovarian surface invasion (n = 4), or microscopic invasion at frozen section analysis (n = 2), tumour size large than 11 x 8 cm, which is the largest diameter of the endobag (n = 4). In these,18 cases laparoscopy was converted to laparotomy.

Participants

All women included in the trials had malignant ovarian tumours and underwent a preliminary workup, including ultrasonography, CA 125, and colour Doppler ultrasonography followed by surgery (laparoscopy or laparotomy).

In the cohort study (Tozzi 2004) 24 patients were submitted to laparoscopy, the median age was 36.8 years (SD 13.5, range 19 to76) and histological results were as follows: 20.8% serous, 12.5%, respectively, were mucinous, and dysgerminoma, 8,3% were endometrioid, and 4,1%, respectively, clear cell, yolk sack tumour, teratoma and granuloma cells. Histological grading was G1, G2 and G3, in 50%, 33% and 16,6%, respectively. Tumour stage was 50% IA, 20.8% IB and 29.2% IC. (Tozzi 2004).

Thirty-four patients with apparent early stage ovarian cancer were submitted for surgery . In the case-control study (Ghezzi 2007) 15 patients undergoing a comprehensive laparoscopic staging were compared with 19 patiens that were submitted to laparotomy. Age in the laparoscopy group: 55 years (SD 13.5; range 13 to 70). Age in the laparotomy group: 61 years (standard deviation (SD) 0.58; range 44 to 70), the body mass index 23.8 (SD 4.2) in the

laparoscopy group and 25.8 (SD 3.1) in the laparotomy group. The histopathologic study of the surgical specimens in the laparoscopic group showed: seven serous cystadenocarcinoma, three mucous cystadenocarcinoma, three endometrioid tumours, one dysgerminoma and one carcinosarcoma. Tumour was - 53.3% G2 and 46.6% G3. In the laparotomy group there were: 14 serous cystadenocarcinoma , 2 mucous cystadenocarcinoma, 1 endometrioid tumour, 1 small cell carcinoma in a mature teratoma. Tumour grading was 5.2% G1, 26.3 G2 and 68.4% G3. Final stage in the laparoscopy group: Ia (n = 5); Ic (n = 6), IIIa (n = 2), IIIc (n = 2); final stage in the laparotomic group: Ia (n = 8); Ic (n = 5), IIIa (n = 3), IIIc (n = 3).Controls were selected from consecutive women who underwent laparotomy for an apparent early stage ovarian cancer between 1997 to 2003, and who met the same criteria for eligibility as the laparoscopy group. Patients were operated in all cases by the same surgeons, with extensive training and experience both in gynaecologic oncology and in advances laparoscopic procedures. All patients received a single dose of prophylactic antibiotic one hour prior to the intervention (ampicillin/sulbactam 1.5 g intravenously) as well as anti-thrombotic prophylaxis with heparin(Ghezzi 2007).

In the case-control study (Hua 2005) 10 patients with early stage ovarian cancer underwent laparoscopic surgery and 11 patients with the same diagnosis underwent laparotomy. Age in the laparotomy group:42 (SD 6). Age in laparoscopy group: 40 years (SD 8). In the laparoscopy group nine were epithelial tumour and one was stromal; in the laparotomy group nine were epithelial and two cases were stromal, and all cases had tumour grading G3

Interventions

In the cohort study patients in the laparoscopy group were submitted to bilateral salpingo-oophorectomy with laparoscopic assisted vaginal hysterectomy, pelvic lymphadenectomy, infrarenal para-aortic lymphadenectomy, complete resection of the infundibulopelvic-pelvic ligament, appendectomy and partial omentectomy (Tozzi 2004). In the case-control studies, the patients in the laparoscopy group were submitted to bilateral salpingo-oophorectomy with laparoscopic assisted vaginal hysterectomy, pelvic lymphadenectomy, infrarenal para-aortic lymphadenectomy, complete resection of the infundibulopelvic-pelvic ligament, appendectomy and partial omentectomy; in the laparotomy group the patients were submitted the same procedures (Hua 2005, Ghezzi 2007). Frozen section analysis was performed in all included studies.

Outcomes

In the cohort study: survival at five years, PFS at five years, intraoperative complications, blood transfusions, operative time for completeness of staging and primary surgery, number of pelvic lymph nodes resected, presence of trocar site metastasis (Tozzi 2004).

In the case control study: survival, PFS at five years, operative time, intraoperative blood loss, intraoperative complications, number of pelvic lymph nodes resected, (Hua 2005; Ghezzi 2007).

Excluded studies

Please see Characteristics of excluded studies. Thirty nine studies were excluded often for more than one reason. The most common causes for exclusion were design other than a RCT, a narrative review, a series of cases or a retrospective studies.

Risk of bias in included studies

Inter-rater agreement for quality assessment was good (Cohen's kappa = 0.78). Initial disagreements were solved through discussion in all cases. The quality of non-RCTs was assessed using appropriate quality evaluations tools by NOS (Wells 2007) (Table 2 and Table 3) and by STROBE (Vandenbroucke 2007) (Table 4)

Cases control studies (Hua 2005, Ghezzi 2007) (Newcastle-Ottawa)

Selection

(a) Is the case definition adequate? Yes,with independent validation = yes*
(b) Representative of the cases: consecutives series of cases = yes*
(c) Selection controls: hospital control with the same disease
(d) Definition of controls: history of disease with the same diagnosis that in the laparoscopy group (treatment) = yes*

Comparability

(a) controls for early stage ovarian cancer treated by laparoscopy or laparotomy the most important factor was selected (survival) = Yes* for Ghezzi 2007, and no for Hua 2005
(b) controls for any additional factor (surgery complications, operative time, blood transfusion, number of pelvic lymph nodes resected, trocar site metastasis, recurrence) = yes*

Exposure

(a) Assessment of outcome: secure record (surgical records)=yes*
(b) Same method of ascertainment for cases and controls=yes*
(c) Non-response rate: rate different and no designation
We found six stars in the two case-control studies. The studies have good quality assessment by NOS (Table 2)

Cohort study (Tozzi 2004) (Newcastle- Ottawa)

Selection

(a) Representative of the exposed cohort: the population represented the average patients with early stage ovarian cancer described in the community = yes*.
(b) Draw from the same community as the exposed cohort = yes*
(c) Ascertainment of exposure: surgical records = yes*
(d) Demonstration that the outcome of interest was not present at the start of the study = yes*

Comparability

(a) Controls for early stage ovarian cancer treated by laparoscopy or laparotomy - the most important factor was select (survival)= yes*
(b) Controls for any additional factor (surgery complications, operative time, blood transfusion, number of pelvic lymph nodes resected, trocar metastasis, recurrence)=yes*

Outcomes

(a) Assessment of outcome: record linkage = yes*
(b) Was the follow up long enough for the occurrence of outcomes? yes (46,4 months) = yes*
(c) Subjects lost from follow up unlikely to introduce bias - small number lost > 100% (selected and adequate%) follow up, or description provide of those lost = yes*
We found nine stars in the cohort study, the corresponding to an excellent quality by NOS (Table 3).

Evaluation of quality by STROBE (Vandenbroucke 2007) of three included studies

From a checklist of 22 items, all three studies showed problems with seven items: title, variables, bias, statistical methods, participants, main results and other analysis (Table 4). The studies (Ghezzi 2007;.Hua 2005; Tozzi 2004) did not give information about potential confounders and effects modifiers (item 7) and did not describe potential sources of bias (item 9). In the statistical methods there was no description for the control of confounding factors and, the subgroups and interactions were not described in the sensitivity analysis (item 12). In the results there was no consideration for the use of a flow diagram (item 13). In the main results unadjusted estimates were not given and, when applicable, confounder-adjusted estimate and their precision were not describe (e.g., 95% confidence intervals [CI]) (item 16). There was no reported on subgroup analysis, interactions and sensitivity analysis (item 17). When describing the limitations of the studies was no description of sources, directions and magnitude of potential bias. Conclusion: there were problems in important items in the STROBE, for considering a study of good quality.

Effects of interventions

A meta-analysis was not possible due to differences among studies and because STROBE has a low quality for evaluations of important outcomes. Therefore, we performed a qualitative systematic review. We used three selected observational studies (two case-control and one cohort study) (Ghezzi 2007; Hua 2005; Tozzi 2004). These three studies met the inclusion criteria with a total 97 patients with early stage ovarian cancer.

Cohort Study

(Tozzi 2004). Forty-two patients were eligible for the study and were submitted to laparoscopy. In 18 of these patients there were conversion to laparotomy due to tumour rupture in 5 cases, peritoneal implants in 3 cases, ovarian surface invasion in 4 cases, and microscopic invasion at frozen section analysis was in 2 cases, and large tumour size in 4 cases. Tozzi 2004 describe only the laparoscopy group.

Primary outcomes

Survival at five years

In Tozzi 2004 the survival for 24 patients at maximum follow up 72 months (median 46.6, SD 16.25; range 2 to 72 months) and OS was 100%.

PFS at five years

In Tozzi 2004 two patients (8.3%) had tumour recurrence in the laparoscopy group. One patient, primarily treated with surgery and chemotherapy for an epithelial ovarian cancer FIGO IB G3, had a pelvic recurrence and underwent secondary surgery with debulking and bowel resection followed by second-line chemotherapy. The second patient with a diagnosis of epithelial ovarian cancer FIGO IA G3 received six cycles of platinum and paclitaxel because of positive peritoneal biopsies at second-look laparoscopy. Disease-free survival was 91.6% in 24 cases.

Secondary outcomes

(1) Tumour spillage at the time of surgery *:* from 42 eligible patients tumour spillage occurred in 5 (11.9).
(2) Local recurrence: for the laparoscopy (porte-site) and laparotomy (midline incision) groups: until 2004 there was no trocar site metastasis in 24 cases. In 15 out of 24 patients (62.5%) a second-look laparoscopy was performed, and local recurrence occurred in 1 case.
(3) Distant recurrence: until 2004 there were no distant recurrences, there were two pelvic recurrences out of 24 cases.
(4) Surgical outcome

(a) Complications (immediate and delayed):
(i) Injury (bladder, urether, vascular, small bowel and colon injuries): did not occur.
(ii) Presence /complications and adhesions: not described.
(iii) Fever: not described.
(iv) Intestinal obstruction: did not occur.
(v) Haematoma: did not occur.
(vi) Infection: not described.
(vii) Convertion to laparotomy: from 42 patients initially eligible to laparoscopy, 18 were submitted to a laparotomy (42.8%).
(vii) Systemic complications: one patient developed chylous ascites with spontaneous evacuation of the lymphatic fluid through abdominal drainage, the patient was discharged 12 days after surgery. There were no cases of chest infection, deep venous thrombosis, pulmonary embolism, cardiac failure, cardiac ischemias or cerebrovascular accident.
(B) *Operative time:* mean operative time for all patients was 176 min (SD 48.45; range:102 to 306 min); it a took a mean of 166 min (SD 20.9 range 118 to 206 min) for complete stating and 182 (SD 39.18 ; range 141 to 306) for the primary treatment of patients who underwent LAVH (laparoscopy assisted vaginal hysterectomy) with contralateral salpingo-oophorectomy.
(c) R*ecovery from surgery:*
(i) length of hospital stay: The overall mean length of hospital stay was 7 days (SD 1.66; range 5 to12). Adjuvant treatment was proposed in five cases.
(ii) re-admission rates: not described.
(d) *Mean number of bilateral pelvic lymph nodes*:19,6 (SD 7.1; range 5 to 35).

Case Control

(Hua 2005). Ten patients with early stage ovarian cancer were submitted to laparoscopic total hysterectomy, pelvic lymph nodes dissection, bilateral adnexectomy, high ligation of the ovarian aortic and vein, omentectomy, and additional appendectomy. Eleven patients with the same diagnosis underwent the same procedure by laparotomy.

Primary outcomes

1) Survival at five years: not reported
(2) PFS at five years : not reported

Secondary outcomes

(1) Tumour spillage at time of surgery:
Laparoscopy: yes, all cases by vaginal puncture ovarian tumour
Laparotomy : not reported.
(2) Local recurrence: laparoscopy (porte site) and laparotomy (midline incision):
Laparoscopy:not reported.
Laparotomy:not reported.
(3) Distance recurrence:
Laparoscopy: not reported.
Laparotomy: not reported.
(4) Surgical outcome:
(a) Complications (immediate and delayed):
(i) Injury (bladder, urether, vascular, small bowel and colon injuries):
Laparoscopy: The right obturator nerve was injured and was sutured.
Laparotomy: did not occur.
(ii) Presence /complications and adhesions:
Laparoscopy: right obturator nerve was injured.
Laparotomy: one case of urinary retention, one case of chylous ascites.
(iii) Fever:
Laparoscopy: not reported.
Laparotomy: not reported.
(iv) Intestinal obstruction:
Laparoscopy: did not occur.
Laparotomy: did not occur.
(v) Haematoma:
Laparoscopy:did not occur.
Laparotomy:did not occur.
(vi) Infection:
Laparoscopy:did not occur.
Laparotomy: one case of wound infection.
(vii) Conversention to laparotomy: did not occur.
(vii) Systemic complications:
Laparoscopy: did not occur.
Laparotomy: did not occur.
(viii) Blood loss
Laparoscopy: 280 ml (SD 156 ml),
Laparotomy: 346 ml (SD 170 ml).There were statistically significantly differences in blood loss between the two groups ($p < 0.05$).
(b) Operative time:
Laparoscopy: 298 min (SD 60 min)
Laparotomy: 182 min (SD 43 min). There were statistically significantly differences the two groups ($p < 0.05$)
(c) recovery from surgery:
(i) length of hospital stay:
Laparoscopy: not reported.
Laparotomy: not reported.
(ii) re admissions rate:
Laparoscopy:not reported.
Laparotomy:not reported.
(d) Mean number of bilateral pelvic lymph nodes
Laparoscopy : 25 (SD 5)
Laparotomy: 27 (SD 7).There were no statistically significantly differences between the two groups ($p > 0.05$)

Case Control

(Ghezzi 2007). Fifeteen patients with early stage ovarian cancer were submitted to laparoscopic total hysterectomy, pelvic lymph nodes dissection, bilateral adnexectomy, high ligation of the ovarian aortic and vein, omentectomy, and additional appendectomy. Nineteen patients with the same diagnosis who underwent the same procedure by laparotomy served as a control group.

Primary outcomes

1) Survival at five years : The laparoscopy group had at least two years of follow up with 100% survival. For the laparotomy group survival was also 100%, but the follow up time had a median of 29 months (SD 18,5; range 14 to 92).
(2) PFS at five years: in the laparoscopy group there were no recurrences and in the laparotomy group there were 4 recurrences (7.1%).

Secondary outcomes

(1) Tumour spillage at the time of surgery:
Laparoscopy: in three cases.
Laparotomy : in two cases.
(2) Local recurrence: laparoscopy (porte site) and laparotomy (midline incision):
Laparoscopy:not reported.
Laparotomy:not reported.
(3) Distance recurrence:
Laparoscopy: not reported.
Laparotomy:not reported.
(4) Surgical outcome:
(a) Complications (immediate and delayed):
(i) Injury (bladder, urether, vascular, small bowel and colon injuries):
Laparoscopy:not reported.
Laparotomy: not reported.
(ii) Presence /complications and adhesions:
Laparoscopy:not reported
Laparotmy:not reported
(iii) Febrile morbidity:
Laparoscopy: not reported.
Laparotomy: not reported.
(iv) Intestinal obstruction:
Laparoscopy:not reported.
Laparotomy :not reported.
(v) Haematoma:
Laparoscopy: retroperitoneal haematoma requiring laparotomy and hypogastric arteries ligature occurred 7 h after surgery.
Laparotomy: there were no haematomas.
(vi) Infection:
Laparoscopy: not reported.
Laparotomy: 6 cases: urinary infection (n = 4) and wound infection (n = 2).
(vii) Convertion to laparotomy: occurred 7 h after surgery.
(vii) Systemic complications:
Laparoscopy:not reported.
Laparotomy:not reported.
(viii) Blood loss
Laparoscopy: 250 ml (SD 225; range 50 to 1000) in one patient who had a retroperitoneal haematoma and had to received six units of packed red blood cells plus four units of fresh frozen blood.
Laparotomy: 400 ml (SD 201; range 150 to 1000). Not significant.
(B) Operative time:
Laparoscopy: 377 min (SD 47 min)
Laparotomy: 272 min (SD 81 min). There were statistically significance differences between two groups ($P < 0.05$).
(C) recovery from surgery:
(i) length of hospital stay:
Laparoscopy : 3 days (SD 2.3; range 2 to 12).
Laparotomy: 7 days (SD 2.3; range 4 to 14). There were statistically significance differences between two groups ($P < 0.001$).
(ii) re-admissions rate:
Laparoscopy: not reported.
Laparotomy: not reported.
(d) Mean number of bilateral pelvic lymph nodes
Laparoscopy : 25.2 (SD 9.3)
Laparotomy: 25.1(SD 5.8).There were no statistically significant differences between the two groups ($p > 0.05$).

DISCUSSION

The challenge when trying to conduct a systematic review on surgical management by laparoscopy or laparotomy in patients with early stage ovarian cancer is that this a rare disease. It is not realistic to expect a large number of RCTs. We found only three observational studies with good quality by Newcastle- Ottawa tool (Wells 2007), although they had important problems in the STROBE checklist (Vandenbroucke 2007). Good reporting reveals the strengths and weaknesses of a study and facilitates interpretations and applications of the results. In this systematic review a meta-analysis was not possible due to differences in the quality among studies. Therefore we performed a qualitative systematic review. Egger *et al.* showed that meta-analysis of observational data may produce precise but spurious results. The statistical combination of data should therefore not be an important component of systematic reviews of observational studies (Egger 2001). However, clinical decisions may still be made on the basis of evidence derived from non-randomised observational studies, such as cohort and case-control studies. Although observational studies may provide useful results, they are limited due to unrecognised confounding factors, which may distort results (bias). Concato *et al.*, showed that results of well-designed observational studies do not overestimate the magnitude of the effects of treatments systemat-

ically as compared to results from randomised controlled trials on the same topic (Concato 2000).

Controversy has arisen between endoscopists and oncologists about the laparoscopic management of early stage ovarian tumours. Kinderman *et al.* wrote that 39% of the stage Ia ovarian cancer may spread after endoscopic procedures, demonstrating implant and metastases, even in an early follow up phase. It was harmful for the majority of patients when the subsequent laparotomy indicated due to very early implants and metastases in the pelvis, in the abdominal cavity or in the laparoscopic trocar site was delayed for more than eight days after the endoscopic procedure (Kindermann 1995). For Ramirez *et al.*, laparoscopic port-site metastases are a potential complications of laparoscopy in patients with gynaecological cancer (Ramirez 2004). Gleeson *et al.*, Childers *et al.*, Leminen *et al.* and Kadar *et al.*, reported cases of abdominal wall metastases from ovarian cancer after laparoscopy (Childers 1994; Gleeson 1993; Leminen 1999). Romagnolo *et al.*, described tumour rupture or spilling during surgery, with a statiscally significant greater incidence in the group of patients treated by laparoscopy (34.6%) when compared to laparotomy (6.6%), p < 0.0001 (Romagnolo 2006). Dembo *et al.*, performed a multivariable analysis by Cox Regression for survival analysis and found the following prognostic factors: grade, adherences and ascites. In their analysis capsular rupture, stages Ia, Ib, size and age were not significant factors for survival (Dembo 1990). In addition Sjövall *et al.* did not find differences in survival between patiens whose tumours had intact capsules and those in whom rupture occurred during surgery (78 and 85%, respectively). However, when the rupture occurred before surgery survival was only 59%. (Sjövall 1994). Volz *et al.*, analysed animal models microscopically and showed, that induction of a pneumoperitoneum caused diffuse damage to the entire mesothelial cell layer with exposure of the basal lamina and development of extensive mechanisms of repair. The exposure of the extracellular matrix proteins including laminin, fibronectin, and vitronectin to the tumour cell surface is a possible mechanism for increased tumour cell adherence. A second mechanism may be the promotion of intraperitoneal tumour cell growth by increased interleukin 1 production by the peritoneal macrophages, which are extensively involved in this unique repair mechanism (Volz 1999).

The guidelines for epithelial ovarian carcinoma FIGO stage I include both surgical and adjuvant therapeutic procedures (Sijmons 2007). Recently two parallel RCTs, ICON1 and ACTION trials showed in that adjuvant chemotherapy would provide further benefits for women with stage I ovarian cancer (Trimbos 2003). There are still no consensus on how to separate patients with surgical stage I disease who are at a higher risk of tumour recurrence and death from those with a low risk. Histological grade is considered one the most important prognostic factors in stage I epithelial ovarian cancer (Vergote 2001).Tumour rupture, capsular penetration and dense adhesions are generally believed to be associated with worse prognosis in these cases (Vergote 2001). Obermair *et al*, analysed 456 patients, with Grade 3 stage I ovarian cancer and found an, OS in five years of 87 % (95% CI 80.3 to 93.6); if CA 125 was higher than 30 U/ml OS in five years was 86% (95% CI 81.8 to 90.9) (Obermair 2007). In the staging ovarian cancer microscopic assessment of grade provide a better discriminations for the necessity of further interventions than blind biopsies. Grade and ploidy may be surrogates for genetic instability, which may be the principal determinant of prognosis. With the publication of the ICON 1 and ACTION trials plus other evidences in the literature in last few years, tumoral grade achieved the power to determine adjuvant treatment in early stage ovarian cancer and should now be incorporate to stage for treatment decisions(Green 2003).

In this systematic review, the cohort study showed out of 100% with 2 recurrences, and a follow up ranging 2 to 72 months; 42.2% were eligible initially to laparoscopy but had conversion to laparotomy. The operative time was 176 min (SD 20.9) in the laparoscopy group (Tozzi 2004). In case-control studies, Hua *et al.*, showed an operative time for the laparoscopy group of 298 min (SD 60 min) and Ghezzi *et al.*, found an time of 377 min (SD 47 min). In vitro, the ovarian carcinomatous cells exposed to carbon dioxide for 3 hours had a 52% increase in growth by 4 days after exposure. This increased cell growth had a linear relationship with the length of exposure to carbon dioxide when compared to now-exposed control cells (Smidt 2001). Three major pathways exist for the dissemination of ovarian malignancies: via bloodstream, via lymphatic channels, and spread through the abdomen and pelvis as a result of rupture of the ovarian capsule (Sugarbaker 1996). For Greene *et al.*, the mechanical effect of pneumoperitoneum and the probable result of the pressure may cause cellular dissemination. The effects of this mechanical dissemination in an already immunocompromised host sets up an ideal mechanism for growth that may be observed early in the postoperative evaluation of the violated abdominal wall (Greene 1995).

On the other hand, there are a number of reports in the literature describing the use of operative laparoscopy in patients with early stage ovarian cancer (Childers 1994). Pelvic and para-aortic laparoscopic lymphadenectomy, appear to be feasible and adequate, although there may occur a mechanical effect caused by the pneumoperitoneum damage in the mesothelial cell layer. According to the FIGO, the prognosis of all ovarian tumours are independently affected by the following factors: stage of cancer at diagnosis, histological subtype grade and volume of residual disease after surgery (Benedet 2000). Therefore, the staging laparotomy is the most important part of the early management of ovarian tumours. Benedet et al, showed that laparoscopy is more appropriate if the suspicion favours a benign diagnosis in a young woman with normal levels of tumoral (Benedet 2000). Canis *et al.* showed that the incidence of spread of ovarian cancer after laparoscopy surgery is difficult to establish and the prognostic relevance trocar site metas-

tasis is not known (Canis 2001). The authors concluded that the laparoscopic management of ovarian cancer remains controversial and that; it should be performed only in prospective clinical trials (Canis 2001). Until the results of such studies become available, an immediate vertical midline laparotomy remains the gold standard if a malignant tumour is found (Canis 2001).

AUTHORS' CONCLUSIONS

Implications for practice

According to FIGO the primary surgery for patients with early stage ovarian cancer should be a vertical abdominal incision, with sampling from the peritoneal fluid and the entire peritoneal surface of the abdominopelvic wall; inspection and palpation of the cavity from the pelvis to the diaphragm is recommended in the search for tumoral implants (Benedet 2000). We did not find any good evidence for the recommendation of laparoscopy for the routine management of patients with early stage ovarian cancer. This review does not support the use of laparoscopy in the routine practice for the management early stage ovarian cancer.

Implications for research

Further trials should carefully address the methods of randomisation as blinding is impractical in these kind of studies. Future research should include specific patient subgroups and include additional outcomes such as surgical efficacy, tumour recurrence, patient satisfaction, quality of life, costs, survival at five years and PFS at five years. The follow up period should provide more information on recurrence, and on the potentially harmful effects of laparoscopy. For evaluation of costs it would be helpful if it were reported separately for the preoperative, intraoperative and postoperative periods.

Survival data for patients with gynaecologic malignancies managed by laparoscopy are still lacking. It is imperative that the survival is not compromised by employing new surgical techniques.

These and other important issues should be addressed by future trials before the role of laparoscopy in gynaecological oncology can be determined.

ACKNOWLEDGEMENTS

We would like to thank the members of the Cochrane Gynaecological Cancer Review Group based at the Royal United Hospital. Bath, UK for their help, advice and support throughout the review process: G Quinn, CJ Williams,C Jess and A Oestmann.

REFERENCES

References to studies included in this review

Ghezzi 2007 *{published data only}*
Ghezzi F, Cromi A, Uccella S, Bergamini V, Tomera S, Franchi M, et al.Laparoscopy versus laparotomy for the surgical management of apparent early stage ovarian cancer. *Gynecologic Oncology* 2007;**105**(2):409–13.

Hua 2005 *{published data only}*
Hua KQ, Jin FM, Xu F, Zhu ZL, Lin JF, Feng YJ. Evaluations of laparoscopic surgery in the early stage malignant tumor of ovary with lower risk. *Zhonghua Yi Xue Za Zhi* 2005;**85**(3):169–72.

Tozzi 2004 *{published data only}*
* Tozzi R, Köeler C, Ferrara A, Schneider. Laparoscopy treatment of early ovarian cancer:surgical and survival outcomes. *Gynecologic Oncology* 2004;**93**:199–203.

References to studies excluded from this review

Amara 1996 *{published data only}*
Amara DP, Nezhat C, Teng N, Nezhat F, Nezhat C, Rosati M. Operative laparoscopy in the managment of ovarian cancer. *Surgical Laparoscopy and Endoscopy* 1996;**6**(1): 38–45.

Berman 2003 *{published data only}*
Berman ML. Future directions in the surgical managment of ovarian cancer. *Gynecologic Oncology* 2003;**90**(2):S33–S39.

Bristow 2000 *{published data only}*
Bristow RE. Surgical standards in management of ovarian cancer. *Current Opinion in Oncology* 2000;**12**:474–80.

Canis 1994 *{published data only}*
Canis M, Gerard Mage, Pouly JL, Wattiez A, Manhes H, Bruhat MA. Laparoscopic diagnosis of adnexal cystic masses: a 12 year experience with long term follow up. *Obstetrics and Gynecology* 1994;**83**(5):707–12.

Canis 1997 *{published data only}*
Canis M, Pouly JL, Wattiez, Mage G, Manhes H, Bruhat A. Laparoscopic managment of adnexal masses suspicious at ultrasound. *Obstetrics and Gynecology* 1997;**89**(5):679–83.

Canis 2000 *{published data only}*
Canis M, Mage G, Wattiez A, Pouly JL, Sonteara SS, Bruhat MA. A simple management program for adnexal masses. *Gynecologic Oncology* 2000;**7**:113–8.

Chapron 1998 *{published data only}*
Chapron C, Dubuisson JB, Kadadoch O, Capela-Allouc. Laparoscopic management of organic ovarian cysts: is there a place for frozen section diagnosis?. *Human Reproduction* 1998;**13**:324–9.

Childers 1995 *{published data only}*
Childers JM, Lang J, Surwit EA, Hatch K. Laparosocpic surgical staging of ovarian cancer. *Gynecologic Oncology* 1995;**59**:25–33.

Childers 1996 *{published data only}*
Childers JM, Nasseri A, Surwit EA. Laparoscopic management of suspicious adnexal masses. *American Journal of Obstetrics and Gynecology* 1996;**175**(6):1451–59.

Darai1998 *{published data only}*
Darai E, Teboul J, Fauconnier A, Scoazec JY, Benifla JL, Madelenat P. Management and outcome of borderline ovarian tumors incidentally discovered at or after laparoscopy. *Acta Obstetricia et Gynecologica Scandinavica* 1998;**77**:451–7.

Dottino 1999 *{published data only}*
Dottino PR, Levine DA, Ripley DL, Cohen CJ. Laparoscopic management of adnexal masses in premenopausal and postmenopausal women. *Obstetrics and Gynecology* 1999;**93**(2):223–7.

Fauvet 2005 *{published data only}*
Fauvet R, Bocara J, Dufournet C, Poncelet C, Darai E. Laparoscopic managment of borderline ovarian tumors results of a French multicenter study. *Annals of Oncology* 2005;**16**:403–10.

Goff 2006 *{published data only}*
Goff BA, Matthews BJ, Wynn M, Muntz HG, Lisher DM, Baldwin LM. Ovarian cancer: patterns of surgical care across the United States. *Gynecologic Oncology* 2006;**103**: 383–90.

Kadar 1995 *{published data only}*
Kadar N. Laparosocpic surgery for gynaecological malignancies in women aged 65 years or more. *Gynaecological Endoscopy* 19995;**4**:173–6.

Klindermann 1995 *{published data only}*
Klindermann G, Maassen V, Kuhn W. Laparoscopic preliminary surgery of ovarian malignancies. Experiences from 127 German gynecologic clinic. *Gerburtshilfe Frauenheikd* 1995;**55**(12):687–94.

Leblanc 2004 *{published data only}*
Lebalnc E, Querleu D, Narducci F, Occelli B, Papageorgiou T, Sonada Y. Laparoscopic restaging of early stage invasive adenexal tumors a 10 year experience. *Gynecologic Oncology* 2004;**94**:624–9.

Leblanc 2006 *{published data only}*
Lebalnc E, Sonoda Y, Narducci F, Ferron G, Querleu D. Laparoscopic staging of early ovarian carcinoma. *Current Opinion in Obstetrics and Gynecology* 2006;**18**:407–12.

Lécuru 2004 *{published data only}*
Lécuru F, Desfeux P, Camatte S, Bissery A, Robin F, Blanc B. Satge I ovarian cancer: comparison of laparoscopy and laparotomy on staging and survival. *European Journal of Gynaecological Oncology* 2004;**25**:571–6.

Maiman 1991 *{published data only}*
Maiman, Seltzer V, Boyce J. Laparoscopic excision of ovarian neoplasms subsequentetly found to be malignant. *Obstetrics and Gynecology* 1991;**77**:563–5.

Malik 1998 *{published data only}*
Malik E, Böhm W, Stoz F, Nitsch D, Rossmanith WG. Laparoscopic managment of ovarian tumors. *Surgical Oncology* 1998;**12**:1326–33.

Maneo 2004 *{published data only}*
Maneo A, Vignali M, Chiari S, Colombo A, Mangioni C, Landoni F. Are bordeline tumors of the ovary safely treated by laparoscopy?. *Gynecologic Oncology* 2004;**94**:387–92.

Manolitsas 2001 *{published data only}*
Manolitsas T, Fowler JM. Role of laparoscopy in the management of the adnexal mass and staging of gynecologic cancers. *Clinical Obstetrics and Gynecology* 2001;**44**(3): 495–521.

Mehra 2004 *{published data only}*
Mehra G, Weekes ARL, Jacobs IJ, Visvanathan D, Menon U, Jeyarajah AR. Laparoscopy extraperitoneal paraaortic lymphadenectomy a study of its applications in gynecological malignancies. *Gynecologic Oncology* 2004;**93**: 189–93.

Nezhat 1992 *{published data only}*
Nezhat F, Nezhat C, Welander CE, Benigno B. Four ovarian cancers diagnosed during laparoscopic managment of 1011 women with adnexal masses. *American Journal of Obstetrics and Gynecology* 1992;**167**(3):790–6.

Parker 1990 *{published data only}*
Parker WP, Berek JS. Management of selected cystic adnexal masses in posmenopausal women by operative laparoscopy. *American Journal of Obstetrics and Gynecology* 1990;**63**(5): 1574–77.

Pomel 1995 *{published data only}*
Pomel C, Provencher D, Dauplat J, Gauthier P, Le Boueded G, Drouin P, et al.Laparoscopy staging of early ovarian cancer. *Gynecologic Oncology* 1995;**58**:301–6.

Poncheville 2001 *{published data only}*
Poncheville L, Perrrotin F, Lefrancq T, Lansac J, Body G. Does paraaortic lymphadenectomy have a benefit in the treament of ovarian cancer that is apparently confined to the ovaries?. *European Journal of Cancer* 2001;**37**:210–15.

Querleu 2003 *{published data only}*
* Querleu D, Papageorggiou TH, Lambaudie E, Sonoda Y, Narducci F, LeBlanc E. Laparoscopic restaging of bordeline ovarian tumours - results of 30 cases initially presumed as stage IA bordeline ovarian tumours. *British Journal of Obstetrics and Gynaecology* 2003;**110**:201–4.

Querleu 2006 *{published data only}*
Querleu D, Leblanc E, Cartron G, Narducci F, Ferron G, Martel P. Audit of preoperative and early complications of laparoscopic lymph node dissection in 1000 gynecologic cancer patients. *American Journal of Obstetrics and Gynecology* 2006;**195**(5):1287–92.

Querleu 2006 *{published data only}*
Querleu D, Leblan E, Ferron G, Narducci F. Laparoscopic surgery in gynaecological oncology. *European Journal of Surgical Oncology* 2006;**32**:853–8.

Reich 1990 *{published data only}*
Reich H, MyGlynn F, Wilkie W. Laparoscopic management of stage I ovarian cancer. *Journal of Reproductive Medicine* 1990;**35**(6):601–5.

Romagnolo 2006 *{published data only}*
Romagnolo C, Gadducci A, Sartori E, Zola P, Magggino T. Managment of bordeline ovarian tumors: results of an Italian mulcenter study. *Gynecologic Oncology* 2006;**101**: 255–60.

Rouzier 2005 *{published data only}*
Rouzier R, Pomel C. Update on the role of laparoscopy in treatment of gynecological malignancy. *Current Opinion in Obstetrics and Gynecology* 2005;**17**:77–82.

Spirtos 2005 *{published data only}*
Spirtos MN, Eisekop SM, Boike G, Schlaerth HB, Cappellari JO. Laparoscopic staging in patients with incompletely staged cancers of the uterus, ovarian, fallopian tube, and primart peritoneum: a Gynecologic Oncology Group (GOG) study. *American Journal of Obstetrics and Gynecology* 2005;**193**:1645–9.

Tozzi 2005 *{published data only}*
Tozzi R, Schneider A. Laparoscopic treatment of early ovarian cancer. *Current Opinion in Obstetrics and Gynecology* 2005;**17**:354–8.

Tropé 2006 *{published data only}*
Tropé C, Kaern J. Primary surgery for ovarian cancer. *European Journal of Surgical Oncology* 2006;**32**:844–52.

Vaisbuch 2005 *{published data only}*
Vaisbuch E, Dgani R, Ben-Arie A, Hagay Z. The role of laparoscopy in ovarian tumors of low malignant potencial and early-stage ovarian cancer. *Obstetrical and Gynecological Survey* 2005;**60**(5):326–30.

Vergote 2003 *{published data only}*
Vergote I, Trimbos BJ. Treatment of patients with early epithelial ovarian cancer. *Current Opinion in Oncology* 2003;**15**:452–55.

Vinatier 1996 *{published data only}*
Vinatier D, Cosson DM, Querleu D. Laparoscopy in gynaecological cancer. *Surgical Oncology* 1996;**5**:211–20.

Volz 1996 *{published data only}*
Voltz J, Köster S, Schaeff. Lapaparoscopic managment of gynaecological malignancies:time to hesitate. *Gynaecology Endoscopy* 1996;**6**:145–6.

Wenzl 1996 *{published data only}*
Wenzl R, Leihner R, Husslein P, Sevelda P. Laparoscopy surgery in cases of ovarian malignancies: an Austria-wide Survey. *Gynecologic Oncology* 1996;**63**:57–61.

Additional references

Benedet 2000
Benedet JL, Bender H, Jones H 3rd, Ngan HY, Pecorreli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. *International Journal of Gynaecology and Obstetrics* 2000;**70**(2):209–62.

Burger 2000
Burger CW, Prinssen HM, Baak JPA, Wagenaar N, Kenemans P. The management of borderline epithelial tumors of the ovary. *International Journal of Gynecological Cancer* 2000;**10**:181–97.

Canis 2001
Canis M, Rabischong B, Botchorishvili R, Tamburro S, Wattiez A, Mage G, et al.Risk of spread of ovarian cancer after laparoscopic surgery. *Current Opinion in Obstetrics Gynecology* 2001;**13**:9–14.

Chi 1999
Chi DS, Curtin JP. Gynecologic cancer and laparoscopy. *Obstetrics and Gynecology Clinics of North America* 1999;**26** (1):201–15.

Childers 1994
Childers JM, Aqua KA, Surwit EA, Hallum AV, Hatch KD. Abdominal-wall tumor implantation after laparoscopy for malignant conditions. *Obstetrics and Gynecology* 1994;**84** (5):765–9.

Concato 2000
Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies and the hierarchy of research designs. *NEJM* 2000;**342**:1887–92.

Crayford 2000
Crayford TJB, Campbell S, Bourne TH, Rawson HJ, Collins WP. Benign ovarian cysts and ovarian cancer: a cohort study with implications for screening. *Lancet* 2000; **355**:1060–3.

Dembo 1990
Dembo AJ, Davy M, Stenwing AE, Berle EJ, Bush R, Kjorstad K. Prognostic factors in patients with stage I epithelial ovarian cancer. *Obstetrics and Gynecology* 1990;**75** (2):263–72.

Dottino 1999
Dottino PR, Tobias DH, Beddoe A, Golden AL, Cohen CJ. Laparoscopic lymphadenectomy for gynecologic malignancies. *Gynecologic Oncology* 1999;**73**:383–8.

Egger 2001
Egger M, Smith GD, Schneider M. Systematic review of observational studies. *Systematic reviews in Health care - Meta-analysis in context* 2001;**2**:211–227.

Elit 2004
Elit L, Chambers A, Fyles A, Covens A, Carey M, Fung MF. Systematic review of adjuvant care for women with stage I ovarian carcinoma. *Cancer* 2004;**101**(9):1926–35.

Gleeson 1993
Gleeson N, Nicosia SV, Mark JE, Hoffman MS, Cavanagh D. Abdominal wall metastases from ovarian cancer after laparoscopy. *American Journal of Obstetrics and Gynecology* 1993;**169**(3):522–3.

Green 2003
Green JA. Early ovarian cancer - time for a rethink on stage? . *Gynecologic Oncology* 2003;**90**:235–7.

Greene 1995
Greene FL. Principles of cancer biology in relation to minimal access surgical techniques. *Seminars in Laparoscopic Surgery* 1995;**2**:155–7.

Hand 1993
Hand R, Fremgen A, Chmiel JS, Recant W, Berk R, Sylvester J, et al.Stanging procedeures, clinical management, and survival outcome for ovarian carcinoma. *JAMA* 1993; **269**:1119–22.

Kadar 1997
Kadar N. Laparoscopic management of gynecological malignancies. *Current Opinion in Obstetrics and Gynecology* 1997;**9**:247–55.

Kindermann 1995
Kindermann G, Maasen V, Kuhn W. Laparoscopic preliminary surgery of ovarian malignancies. Experiences from 127 German gynecologic clinics. *Geburtshilfe Frauenheilkd* 1995;**55**(12):687–94.

Kosary 1994
Kosary CL. FIGO stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system: an analysis of 1973-87 SEER cases of cancers of the endometrium, cervix, ovary, vulva and vagina. *Seminars in Surgical Oncology* 1994;**10** (1):31–46.

Lehner 1998
Lehner R, Welzl R, Heinzl H, Husslein P, Sevelda P. Influence of delayed staging laparotomy after laparoscopy removal of ovarian masses later found malignant. *Obstetrics and Gynecology* 1998;**92**:967–71.

Leminen 1999
Leminen A, Lehtovirta P. Spread of ovarian cancer after laparoscopic surgery: report of eight cases. *Gynecologic Oncology* 1999;**75**:387–90.

Medeiros 2005
Medeiros LR, Rosa DD, Edelweiss MI, Stein AT, Bozzetti MC, Zelmanowicz A, et al.Accuracy of frozen-section analysis in the diagnosis of ovarian tumors: a systematic quantitative review. *International Journal of Gynecological Cancer* 2005;**15**:1–11.

Obermair 2007
Obermair A, Fuller A, Lopez-Varela, van Gorp, Vergote I, Eaton L, et al.A new prognostic model for FIGO stage I epithelial ovarian cancer. *Gynecologic Oncology* 2007;**104**: 607–11.

Ramirez 2004
Ramirez PT, Frumovitz M, Wolf JK, Levenback C. Laparoscopic port-site metastases in patients with gynecological malignancies. *International Journal of Gynecologic Cancer* 2004;**14**:1070–77.

Scully 1999
Scully RE. Histological typing of ovarian tumours. *World Health Organization International histological classifications of tumors*. Second Edition. Springer, 1999:45–6.

Sijmons 2007
Sijmons EA, van Lankveld MAL, Witteveen PO, Peeters PHM, Koot VCM, van Leeuwen. Compliance to clinical guidelines for early-stage epithelial ovarian cancer in relation to patients outcome. *European Journal of Obstetrics and Gynecology* 2007;**131**:203–08.

Sjövall 1994
Sjövall K, Nilson B, Einhorn N. Differents types of rupture of the tumor capsule and the impact on survival in early ovarian carcinoma. *Internatiional Journal of Gynecological Cancer* 1994;**4**:333–6.

Smidt 2001
Smidt VJ, Sings DM, Hurteau JA, Hurd WW. Effects of carbon dioxide on human ovarian carcinoma cell growth. *American Journal of Obstetrics and Gynecology* 2001;**185**: 1347–7.

Sugarbaker 1996
Sugarbaker T, Chang D, Koslowe P, Sugarbaker PH. Pathobiology of peritoneal carcinomatosis from ovarian malignancy. *Cancer Treatment and Research* 1996;**81**:63–74.

Trimbos 2003
Trimbos BJ, Parmar M, Vergote I, Guthrie D, Bolis G, Colombo N et al. International Collaborative Ovarian Neoplasm 1, European Organisation for Reseach and Treatment of Cancer Collaborators-Adjuvant Chemotherapy in Ovarian Neoplasm. International Collaborative Ovarian Neoplasm trial 1 and Adjuvant Chemotherapy in Ovarian Neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. *Journal of the National Cancer Institute* 2003;**95**(2):105–12.

Trimbos 2004
Trimbos BJ, van der Burg ME. Adjuvant chemotherapy in patients operated on for early ovarian carcinoma. *Nederlands Tijdschriftvoor Geneeskunde* 2004;**148**(18):874–8.

Vandenbroucke 2007
Vandenbrouke JP, von Elm E, Altman D, Gotzsche PC, Mulrow CD, Pocock SJ. Strenghthening the reporting of observational studies in Epidemiology (STROBE): explanation and elaboration. *Annals of Internal Medicine* 2007;**147**(8):163–94.

Vergote 2001
Vergote I, De Brabanter J, Fyles A, Bertelsen K, Einhorn N, Sevelda P, et al.Pronogstic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma.. *Lancet* 2001;**375**:176–82.

Vergote 2003
Vergote I, Trimbos BJ. Treatment of patients with early epithelial ovarian cancer. *Current Opinion in Oncology* 2003;**15**(6):452–5.

Vergote 2004
Vergote I. Role of surgery in ovarian cancer: an update. *Acta Chirurgica Belgica* 2004;**104**(3):246–56.

Vinatier 1996

Vinatier D, Cosson DF, Querleu D. Laparoscopy in gynaecological cancer. *Surgical Oncology* 1996;**5**:211–20.

Volz 1999

Volz J, Köster S, Spacek A, Paweletz N. The influence of pneumoperitoneum used in laparoscopic surgery on an intraabdominal tumor growth. *Cancer* 1999;**86**(5):770–4.

Wells 2007

GA Wells, B Shea, D O'Connell, J Peterson, V Welch, M Losos, P Tugwell. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical˙epidemiology/oxford.htm.

Wenzl 1996

Wenzl R, Lehner R, Husslein P, Sevelda P. Laparoscopic surgery in cases of ovarian malignancies: an Austria-wide survey. *Gynecologic Oncology* 1996;**63**:57–61.

Yancik 1993

Yancik R. Ovarian cancer. Age contrasts in incidence, histology, disease stage at diagnosis, and mortality. *Cancer* 1993;**71**:517–23.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ghezzi 2007

Methods	Case and control study. No Data on sample size calculation and power. The study was carried in 2003 in Department of Obstetrics and Gynecology, University of Insubria, Del Ponto Hospital, Piazza Biroldim I, Vareses , Italy and in Department of Obstetrics and Gynecology, University of Verona, Italy
Participants	34 patients with apparent early ovarian cancer was submitted for surgery . 15 patients undergoing a comprehensive laparoscopic stating and were compared with 19 patients that were submitted for laparotomy. All women were submitted for preliminary workup, including ultrasonography, CA 125, as well as colour Doppler ultrasonography. Age (years) in the laparoscopy group: 55 years (SD 13.5; range 13-70). Age (years) in the laparotomy group: 61 (SD 0.58; range 44-70), body mass index 23.8 (SD 4.2) in the laparoscopy group and 25.8 (SD 3.1)
Interventions	Laparoscopic and laparotomy for treatment early ovarian cancer. Intraoperative mass rupture was defined as any rupture, intentional, or unintentional, that results in spill of cysts contents into the peritoneal cavity. retrieved via an endobag to avoid contact with the port sites and submitted for frozen section. After the diagnosis of malignancy, multiple random peritoneal were performed. Bilateral lymphadenectomy was performed as previously described and all patients, external iliac, internal iliac and obturator lymphonodes were removed. Common iliac and paraaortic lymphadenectomy were performed. Total infracolic omentectomy was than performed using scissors and bipolar coagulation. Appendicectomy were performed. Salpingo-oophorectomy and total laparoscopic hysterectomy were performed
Outcomes	Postoperative complications were defined as adverse events occuring within 30 days of surgery as a result of the procedure. Febrile morbidity was defined two temperatures > 38, hospital stay, blood loss, blood transfusions, pelvic lymph nodes, paraaortic lymphnodes
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Hua 2005

Methods	Case and control study. The study was carried out between September 2002 to may 2004 in Department of Gynecology, Fudan University, Gynecology and Obstetric Hospital, Shangai 200011, China
Participants	21 patients with early ovarian cancer were evaluated. 10 were submitted the laparoscopic operation and 11 were submitted the laparotomy. Mean age in laparoscopy group was 40 (SD8). Mean age in laparotomy group was 42 (SD6)

Hua 2005 (*Continued*)

Interventions	Laparoscopic in 10 patients with early ovarian cancer who underwent laparoscopic total hysterectomy, pelvic lymph nodes dissection, bilateral adnexectomy, ovarian aortic and vein high ligation, omentectomy, and additional appendicectomy Laparatomy in 11 patients with early ovarian cancer who underwent the same procedure. Frozen section method during operation proved the diagnosis of ovarian cancer and cytological examination proved negative result of the peritoneal irrigation liquid
Outcomes	Operative time, intraoperative blood loss, number of pelvic lymph node resected, surgical complications
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Tozzi 2004

Methods	Cohort prospective. No data on sample size calculation and power and precision. The study was carried out between May 1996 until June 2003 in Departament of Gynecology, Friedrich Shiller, Jena, Germany
Participants	Forty two patients were eligible to enter the study, but 18 patients were excluded because of tumor rupture (n=5), presence of peritoneal tumor implants (n=3), ovarian surface invasion either macroscopic (n=4), or microscopic at frozen (n=2) or because of tumor size (n=4), exceeding 11 x 8 cm , which is the diameter of biggest endobag. All these conditions managed conversion to laparotomy. Thus, 24 patients with FIGO stage IA-B underwent either primary treatment or completation of staging by laparoscopy. All women were submitted a preliminary workup, including ultrasonography, CA 125, as well as colour Doppler ultrasonography. Age (years) in the laparoscopy group: 36.8 (SD 13.5; range 19-76) and body mass index 27.3 (SD 4.37; 20.2-38.6). I
Interventions	24 patients with ovarian FIGO stage IA-B were managed by laparoscopy. All patients underwent bowel preparation. The procedure was started by laparoscopy with peritoneal washing and careful inspection of the entire abdomen including diaphragm, liver, gallbladder, small bowel, reto-sigmoide colon, paracolic gutter and abdominal wall. Any suspicious lesion was biopsied and sent for frozen section. All specimens were retrieved via endobag to avoid contents with port site. If necessary, puncture and drainage were performed in the endobag. The integrity of endobag was checked after extraction from the abdomen and the tumor was sent frozen section. Once the diagnosis of cancer was confirmed, intraperitoneal spread was excluded by laparoscopy and tumor rupture avoided and laparoscopic assisted vaginal hysterectomy (LAVH) with contralateral salpingo-oophorectomy, appendectomy, partial resection of the omentum, pelvic lymphadenectomy and infrarenal para aortic bilateral lymphadenectomy. Also appendectomy was performed
Outcomes	Operative complications, surgery time, mean number of pelvic lymph nodes, hospital stay, survival and PFS at five years

Tozzi 2004 (*Continued*)

Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Amara 1996	Series of cases.
Berman 2003	Narrative review.
Bristow 2000	Narrative review.
Canis 1994	Narrative review.
Canis 1997	Not give the stage of ovarian cancer (Ia, Ib or Ic). They wrote about 10 cases of low malignant potential tumour and 15 cases of cancer, but without stage
Canis 2000	Not give the stage of ovarian cancer (Ia, Ib or Ic). Only related about 28 cases of cancer and borderline tumor
Chapron 1998	Narrative review.
Childers 1995	Case control trial, but with second look laparoscopy to evaluate both intraperitoneal cavity and retroperitoneal lymph nodes
Childers 1996	The stage of ovarian cancer (Ia, Ib or Ic) not given. Only related about 19 cases of cancer
Darai1998	Retrospective trial.
Dottino 1999	Another ovarian disease, wrote about ovarian cancer, they gave stage IIC, IIIa abd IV for ovarian cancer
Fauvet 2005	Retrospective study.
Goff 2006	Narrative review.
Kadar 1995	Not randomised. Other kind of cancer (endometrial, cervical, ovarian)
Klindermann 1995	A questionnaire was mailed to 237 German Department Gyn/obs. A response rate 46% (127 hospital) concerning the Endoscopicall technique used for cancer operation

(*Continued*)

Leblanc 2004	Cohort with other types of cancer (fallopian tube carcinoma), and in patients that were inadequately staged at the time of initial surgery for invasive ovarian carcinoma
Leblanc 2006	Narrative review.
Lécuru 2004	Retrospective and multi centric study.
Maiman 1991	Members and candidate members of the Society of Gynecologic Oncologists responded to a survey concerning the "laparoscopy management of ovarian neoplasm subsequently found be malignant"
Malik 1998	Retrospective study.
Maneo 2004	Criteria of exclusion: 62 patients had fertility -sparing after surgery
Manolitsas 2001	Narrative review.
Mehra 2004	To describe experience of laparoscopy extraperitoneal paraaortic in 32 patients with cervical, ovarian and endometrial carcinomas
Nezhat 1992	Series cases.
Parker 1990	Only benign ovarian cysts.
Pomel 1995	Patients with I ovarian carcinoma underwent a laparoscopic procedure to complete their staging
Poncheville 2001	Retrospective study.
Querleu 2003	Retrospective study.
Querleu 2006	Many types of tumors (cervical, vaginal, endometrial, and ovarian carcinoma)
Querleu 2006	Narrartive review.
Reich 1990	Series of cases.
Romagnolo 2006	Patients affected by ovarian mass suspected of borderline ovarian tumor are operated - primary laparoscopic, but 46.9% have no for exclusion of SR, because a fertility-sparing surgical treatment was chosen
Rouzier 2005	Narrative review.
Spirtos 2005	Other kinds of gynecological cancer.
Tozzi 2005	Narrative review.
Tropé 2006	Narrative review.
Vaisbuch 2005	Narrative review.

(*Continued*)

Vergote 2003	Narrative review.
Vinatier 1996	Narrative review.
Volz 1996	Narrative Review.
Wenzl 1996	A questionnaire was sent to all 97 Departaments of Gynecology in Austria was to determine the frequency of discovering a malignant ovarian mass when laparoscopy is uses to manage an adnexal mass

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. Newastle-Ottawa Quality Assessment Scale Case Control Study

Numbered item	Hua 2005	Ghezzi 2007
SELECTION		
1) Is the case definition adequate?		
(a) Yes, with independent validation?*	Yes*	Yes*
(b) Yes, e.g., record linkage or based on self reports		
(c) No description		
2) Representativeness of the cases		
(a) Consecutive or obviously representative series of cases*	Yes*	Yes*
(b) Potential for selection biases or not stated		
3) Selection of Controls		
(a) Community controls *		
(b) Hospital controls	Yes	Yes
(c) No description		
4) Definition of controls		
(a) No history of disease (endpoint)*	Yes*	Yes*
(b) No description of source		
COMPARABILITY		
1) Comparability of cases and controls on the basis of design or analysis		
(a) Study controls for ___selected the most important factor.*	Yes*	Yes*

Table 1. Newastle-Ottawa Quality Assessment Scale Case Control Study (*Continued*)

(b) Study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor)	Yes*	Yes*
EXPOSURE		
1) Ascertaiment of exposure		
(a) Secure record (e.g., surgical records) *	Yes*	Yes*
(b) Strutured interview where blind to case/control status*		
(c) Interview not blinded to case/controls status		
(d) Written self report or medical record only		
(e) No description		
2) Same method of ascertainment for cases and controls		
(a) Yes *		
(b) No	No	no
3) Non-response rate		
(a) Same rate for both groups*	No	No
(b) No respondents described	-------	--------
(c) Rate different and no designation	Yes	Yes

Table 2. Newastle-Ottawa Quality Assessment Scale Cohort Study

Numbered item	**Tozzi 2007**
SELECTION	
1) Representative of the exposed cohort	
(a) Truly representative of the average _____ (describe) in the community.*	Yes*

Table 2. Newastle-Ottawa Quality Assessment Scale Cohort Study (*Continued*)

(b) Somewhat representative of average _____ in the community*	
(c) Select group of users e.g., nurses, volunteers	
(d) No description of the derivation of the cohort	
2) Selection of the non exposed cohort	
(a)Drawn from the same community as the exposed cohort *	Yes*
(b) Drawn from a different source	
(c) No description of the derivation of the non exposed cohort	
3) Ascertainment of exposure	
(a) Secure record (e.g., surgical records) *	Yes*
(b) Strutured interview*	
(c) Writen self report	
(d) No description	
4) Demonstration that outcome of interest was not present as start of study	
(a) Yes *	Yes*
(b) No	
COMPARABILITY	
1) Comparability of cohorts on the basis of design or analysis	
(a) Study controls for _____(selected the most important factor) *	Yes*
(b) Study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor)*	Yes*
OUTCOMES	
1) Assessment of outcome	
(a) Independently blind assessment *	

Table 2. Newastle-Ottawa Quality Assessment Scale Cohort Study (*Continued*)

(b) Record linage *	Yes*
(c) self report	
(d) no description	
2) Was follow up enough for outcomes to occur	
(a) Yes (selected adequate follow up period for outcome of interest)*	Yes*
(b) No	
3) Adequacy of follow up of cohorts	
(a) Complete follow up - all subjects accounted for *	Yes*
(b) Subjects lost to follow up unlikely to introduce bias - small number lost >____% (select an adequate%) follow up, or description provide of those lost *	
(c) Follow up rate < _____% (selected an adequante %) and no description of those lost	
(d) No statement	

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

Item	Item number	Recomendations	Guezzi 2007	Hua 2005	Tozzi 2004
Title and Abstract	1	(a) indicate the study's design with a commonly used term in the title or the abstract	No	No	No
		(b) provide in the abstract and informative and balaced summary of what was done and what was found	Yes	Yes	Yes
Introduction/ Background	2	Explain the scientific background and rationale for the investigations being re-	Yes	Yes	Yes

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

		ported			
Objetives	3	State specific objetives, including any prespecified hypotheses	Yes	Yes	Yes
Methods					
Study design	4	Present key elements of study design early in paper.	Yes	Yes	Yes
Settings	5	Describe the settings, locationsm and relevant dates, including periods of recruitement, exposure colection	Yes	Yes	Yes
Participants	6	(a)Cohort study: give eligi- bility criteria, and the sources and methods of selection or participants methods of follow up	----------	---------	Yes
		(b) Case control study: give the eligibility criteria, and the sources and methods of case ascertaiment and control selection	Yes	Yes	___
Variables	7	Clearly define all outcomes, exposures, predictors, potencial confunders, and effect modifiers	No	No	No
Data sources/measuments	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparavility of as-	Yes	Yes	Yes

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

		sessment methods if there is more than one group. Give such information separately for cases and controls studies, and, if applicable, for exposed and unexposed groups in cohort and cross sectional studies			
Bias	9	Describe any efforts to address potencial sources bias.	No	No	No
Study Size	10	Explain how the study size was arrived at.	No	No	No
Quantitaive variables	11	Explain how quantitative variables were handled in the analysis. If applicable, describe which groupings were chosen and why	Yes	Yes	Yes
Statistical Methods	12	(a) Describe all statistical methods, including those used to control for confunding	No	No	No
		(b) Describe any methods used to examine subgroups and interations	No	No	No
		(c) Explain how missing data were adderessed.	No	No	No
		(d) Cohort study: if applicable, explain how loss to follow up was addressed	____	____	No
		Case-control study, if applicable, explain how matching	No	No	_____

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

		of cases and controls was adderessed			
		(e) Describe any sensibility analysis	No	No	No
Results / Participants	13*	(a) report the number of individuals at each stage of the study- e.g. , numbers potencially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow up, and analysis	Yes	Yes	Yes
		(b) give reasons for non-participation at each stage	Yes	Yes	Yes
		(c) consider use of a flow diagram	No	No	No
		*give such information separately for cases and controls in case control studies, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies			
Results/ Descripitive data	14*	(a) give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders/	Yes	Yes	Yes
		(b) indicate the number of participants with missing data for each variable of interest	No	No	No

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

		(c) Cohort study: summarize follow up time - e.g., average and total amount	___	_____	Yes
		*give such information separately for cases and controls in case control studies, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies			
Results/Outcome data	15*	(a) Cohort studies: reported numbers of outcome events or summary measures of exposure	___	_____	Yes
		(b) Case- control study: reported numbers in each exposure category or summary measures of exposure	Yes	Yes	----------
		*give such information separately for cases and controls in case control studies, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies			
Results/ Main Results	16	(a) give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence intervals) . Make clear which confounders were adjusted for and why they were included	No	No	No

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

		(b) report categories boundaries when continuous were categorized	———	-----	-----
		(c) If relevant, consider translating estimates or relative risk into absolute risk for a meaningful time period	No	No	No
Results/ Other Analysis	17	Report other analysis done, e.g., analysis of subgroups and interactions and sensibility analysis	No	No	No
Discussion					
Key results	18	Summarize key results with reference to study objectives	Yes	Yes	Yes
Limitations	19	Discuss limitations of the study , talking into account sources of potential bias or impression. Discuss both directions and magnitude of any potential bias	No	No	No
Interpretation	20	Give a cautions overall interpretation or results considering objectives, limitations, multiplicity of analysis, results from similar studies, and other relevant evidence	Yes	Yes	Yes
Generalization	21	Discuss the generalization (external validity) of the study results	Yes	Yes	Yes
Other information					

Table 3. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (*Continued*)

Funding	22	Give the source of funding and the role of funders for the present study and, if applicable, for the original study on which the present article is based	Yes	Yes	Yes

Table 4. Case controls studies and outcomes

Outcomes	Laparoscopy Hua	Laparotomy Hua	p	Laparoscopy Ghezzi	Laparotomy Ghezzi	p
Operative time	298 min (SD 60 min)	182 min (SD 43 min)	<0.05	377 min (SD 47 min)	272 min (SD 81 min)	0.002
Blood loss (ml)	280 ml (SD 280 ml)	346 ml (SD 170 ml)	<0.05	250 ml (SD 225;range 50-1000 ml)	400 ml (SD 201; range150-1000 ml)	0.28
Number pelvic lymph nodes	25 (SD 5)	27 (SD 7)	>0,05	25.2 (SD 9.3)	25.1 (SD 5.8)	>0.05
Post-operative complications	2 (20%)	7 (72.7%)	0,05	2 (13.3%)	8 (42.1%)	0.13
Number of patients	10	11		15	19	

APPENDICES

Appendix 1. Electronic search strategies

EMBASE was searched using the following strategies:
1. Controlled study/or Randomized Controlled trial/
2. double blind procedure/
3. single blind procedure/
4. crossover procedure/
5. drug comparison/
6. placebo/
7. random$.ti,ab,hw,tn,mf.
8. latin square.ti,ab,hw,tn,mf.
9. crossover.ti,ab,hw,tn,mf.
10. cross-over.ti,ab,hw,tn,mf.
11. placebo$.ti,ab,hw,tn,mf.
12. ((doubl$ or singl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).ti,ab,hw,tn,mf.
13. (comparative adj5 trial$).ti,ab,hw,tn,mf.
14. (clinical adj5 trial$).ti,ab,hw,tn,mf.
15. or/ 1-14
16. nonhuman/
17. (animal not human)/
18. or/16-17
19. 15 not 18
20. comparative study.ti,ab,hw,tn,mf.
21. follow up studies.ti,ab,hw,tn,mf.
22. prospective studies.ti,ab,hw,tn,mf.
23. (control$ or prospectiv$).mp or volunteer$.ti.ab.
24. cohort studies/
25. cohort.ti,ab,hw,tn,mf.
26. longitudinal studies.ti,ab,hw,tn,mf.
27. (cohort adj5 trial$).ti,ab,hw,tn,mf.
28. (prospectiv$ adj5 trial$).ab,hw,tn,mf.
29. (longitudinal adj5 trials).ti,ab,hw,tn,mf.
30. or/19-29
31. exp Ovarian Neoplasms/
32. (ovar$ adj5 tumo?r).tw
33. (ovar$ adj5 neoplas$).tw
34. (ovar$ adj5 cancer$).tw
35. (ovar$ adj5 carcino$).tw
36. exp Adnexal Diseases/
37. exp Ovarian Cancer/
38. or/ 31-37
39. exp “early ovarian cancer”/
40. exp “early ovarian neoplasm”/
41. “stage I ovarian cancer”/
42. or/39-41
43. 38 and 42
44. exp SURGERY/
45. surg$.tw.
46. laparo$.tw.
47. exp Surgical Technique
48. or/43-46

49. 43 and 48
50. 30 and 49
CENTRAL (Issue 2, 2007) The Cochrane Library, the National Research Register (NRR) and Clinical Trials Register were also searched in all fields using the following words: ovarian cancer, laparotomy, laparoscopy, ovarian surgery.

WHAT'S NEW

Last assessed as up-to-date: 20 July 2008.

Date	Event	Description
9 November 2010	Amended	Author contact details amended
14 May 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 2005

Review first published: Issue 4, 2008

CONTRIBUTIONS OF AUTHORS

Lidia Medeiros: Took the lead in writing the protocol, developed background, initial objectives, selection criteria, methods, search strategy.

Daniela Dorneles Rosa: Took the lead in writing the protocol, developed background, initial objectives, selection criteria, methods, search strategy. Anaelena Ethur: Took the lead in writing the protocol and statistical analysis. Roselaine Zanini: Took the lead in writing the protocol and statistical analysis. Mary Clarisse Bozzetti: Took the lead in writing the protocol, developed background and initial objectives.

Airton Stein: Contributed to background section, selection criteria, initial objectives, methods and search strategy. Maria Isabel Edelweiss: developed background and initial objectives. Alice Zelmanowicz: Took the lead in writing the protocol, developed background, initial objectives, selection criteria, methods, search strategy. Maria Ines Rosa: Took the lead in writing the protocol, developed background, initial objectives, selection criteria.

DECLARATIONS OF INTEREST

None.

INDEX TERMS

Medical Subject Headings (MeSH)

*Laparoscopy; *Laparotomy; Ovarian Neoplasms [pathology; *surgery]

MeSH check words

Female; Humans