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Perioperative enhanced recovery programmes for gynaecological cancer patients (Review)

Lu D, Wang X, Shi G

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TABLE OF CONTENTS

[Intervention Review]

Perioperative enhanced recovery programmes for gynaecological cancer patients

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ABSTRACT

Background

Gynaecological malignancies contribute to 10% to 15% of cancers in women internationally. In recent years, a trend towards new perioperative care strategies has been documented as 'Fast Track (FT) surgery', or 'Enhanced Recovery Programmes' to replace some traditional approaches in surgical care. The FT multimodal programmes may enhance the postoperative recovery by means of reducing surgical stress. This systematic review aims to assess fully the beneficial and harmful effects of FT programmes in gynaecological cancer care.

Objectives

To evaluate the beneficial and harmful effects of FT programmes in gynaecological cancer care.

Search methods

We searched the following databases, The Cochrane Gynaecological Cancer Review Group's Trial Register, the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 4, 2009, MEDLINE and EMBASE to November 2009. In addition, all reference lists of included trials were searched and experts in the gynaecological oncology community were contacted in an attempt to locate trials. This search was updated and re-run in May 2012 and November 2014.

Selection criteria

All randomised controlled trials (RCTs) comparing any type of FT programmes for surgery in gynaecological cancer to conventional recovery strategies were included.

Data collection and analysis

Two review authors independently screened studies for inclusion. Since no RCTs were identified, data collection and analysis could not be performed.

Main results

No studies were identified that met the inclusion criteria.

Authors' conclusions

We currently have no evidence from high-quality studies to support or refute the use of perioperative enhanced recovery programmes for gynaecological cancer patients. Further well-designed RCTs with standard FT programmes are needed. This review has been updated in 2012 and 2014. The results of the original review published in 2010 remain unchanged.

PLAIN LANGUAGE SUMMARY

Perioperative enhanced recovery programmes for women with gynaecological cancer

Gynaecological cancers lead to a significant amount of morbidity and mortality internationally. In recent years, a trend towards new perioperative care strategies has been documented. These 'Fast Track (FT) surgery' or 'Enhanced Recovery Programmes' replace traditional approaches in surgical care management. The FT multimodal programmes may enhance the postoperative recovery period by reducing surgical stress. The review authors found no high-quality studies to support or refute the use of perioperative enhanced recovery programmes for gynaecological cancer patients.

BACKGROUND

Description of the condition

Gynaecological malignancies consist of vulval, vaginal, cervical, uterine, fallopian and ovarian cancers, and contribute to 10% to 15% of cancers in women with differing incidence and prognoses often dependent on international geographical location (Kehoe 2006). Cervical cancer is the second most common form of cancer in women, and approximately 80% of these cancers occur in developing countries (Boyle 2003). It is the most prevalent cancer in women living in sub-Saharan Africa, Central and South America, and South-East Asia. Ovarian cancer, the sixth most common cancer in women, accounts for the most frequent cause of death from gynaecological malignancies in the western world (Boyle 2003). The incidence differs depending on the geographical location, with the highest incidence in Scandinavian countries (at over 20/100,000) and lowest in Japan (3/100,000) (Kehoe 2006). Cancer Research UK reports that in the UK the incidence of ovarian cancer over a women's lifetime is 1 in 50 (Cancer Research UK 2009).

Surgery plays a pivotal role in gynaecological cancer therapy (Kehoe 2006); other treatments include chemotherapy and radiotherapy, with multiple modalities also given. Postoperative care includes postoperative fluid restriction, early removal of indwelling urinary catheter and postoperatively enhanced ambulation. The choice of postoperative care often varies between medical centres. As the postoperative recovery period is influenced by specific care paths, it is important to re-examine the traditional approaches for perioperative care, and to establish if current practice is supported by clinical evidence (Chase 2008).

Postsurgical patients may remain hospitalised as a precautionary measure to prevent and monitor for early complications such as haemorrhage. However, it may be unnecessary for patients to remain hospitalised to monitor for delayed complications such as wound infection and prolonged ileus (disruption of normal propulsive gastrointestinal motor activity that occurs most commonly after abdominal surgery). Sharma 2007 indicates that a longer hospital stay is associated with a lower quality of life (QoL) and poorer functional well-being in patients who had undergone surgery for colorectal cancer. More recently, well-designed trials of perioperative care have been performed. These evidence-based results have shown that many of the traditional approaches to pre- and postsurgical care are unnecessary or even harmful. These include preoperative bowel preparations, postoperative use of nasogastric tubes and drainage tubes, enforced bed rest and graduated diets (Kehlet 2002; Kehlet 2003; Verma 2007).

Description of the intervention

In recent years, a trend towards new perioperative care strategies has been documented as 'Fast Track (FT) surgery', or 'Enhanced Recovery Programmes', or 'Enhanced Recovery After Surgery (ERAS)' to replace some traditional approaches in surgical care (Spanjersberg 2009). This multimodal FT surgery care team requires not only surgeons but also anaesthesiologists, nurses and physiotherapists (Kehlet 2002; Kehlet 2003). FT programmes focus on a number of techniques that facilitate early recovery after major surgery, by means of preserving preoperative host (patient's) composition and organ functions. Techniques include epidural or local anaesthesia, minimally invasive techniques, optimal pain control and aggressive postoperative rehabilitation (Wilmore 2001). Kehlet 2008 incorporated these strategies in elective colonic surgery in the mid-1990s to enhance postoperative recovery and to reduce common impedance to early hospital discharge, such as the need for analgesics or fluids, delayed patient mobilisation, postoperative complications and lack of home care.

The main elements of FT programmes in colonic surgery consist of many evolving approaches that differ from traditional care. These include: preoperative education of postoperative care, avoidance of bowel preparation, no routine use of prophylactic antibiotics, absence of preoperative fasting (carbohydrate-loaded liquids are administered two hours before surgery), tailored anaesthesiology encompassing epidural anaesthesia and short-acting anaesthetics, perioperative high inspired (inhaled) oxygen concentrations, avoidance of perioperative fluid overload, short incisions, use of non-opioid analgesics, no routine use of drains and nasogastric tubes, early removal of bladder catheters, use of standard laxatives and prokinetics (drugs that enhance the passage of intraluminal contents of the gastrointestinal tract), and early/enhanced postoperative feeding and mobilisation (Wind 2006).

Apart from elective bowel surgery, FT programmes have been successfully applied in other fields of elective surgery, such as aortic aneurysm (Podore 1999) and pulmonary lobectomy (Tovar 1998). FT programmes were found to reduce hospital stays to three days and one to two days, respectively. Furthermore, laparoscopic gastro-oesophageal reflux surgery has been reported to be successful in an ambulatory setting (outpatient surgery) using FT programmes (Trondsen 2000). Although these principles of care also appear to succeed in open abdominal hysterectomy for benign disease (Møller 2001), ovarian cancer (Marx 2006) and vaginal prolapse surgery (Ottesen 2002; Ottesen 2003), high-quality evidence is still scarce for different types of gynaecological malignancies. In addition, some single-core FT elements have been shown to be successful in patients with gynaecological cancers. One Cochrane systematic review concluded that early drinking and eating on the first day after major abdominal gynaecological surgery is safe but is associated with the increased risk of nausea (Charoenkwan 2007).

How the intervention might work

Surgical stress can cause physical response and multiple organ dysfunctions, including pain, catabolism (the metabolic breakdown of complex molecules into simpler ones, often resulting in a release of energy), immuno-dysfunction, nausea, vomiting, ileus, impaired pulmonary function, increased cardiac demands, coagulatory-fibrinolytic (clot forming or dissolving) dysfunction, cerebral dysfunction, fluid homeostasis alteration, sleep disturbances and fatigue (Kehlet 2008). Stress reduction during an elective surgical procedure not only provides a rational basis for increased recovery but also diminishes the risk of organ dysfunction and complications (Kehlet 2006; Wilmore 2002).

Multimodal FT programmes may contribute to the reduction of surgical stress by various means such as afferent neural blockade (decreasing postoperative neuroendocrine stress response by blocking the painful stimulus from organs to brain), non-opioid multimodal analgesia, minimal invasive surgery, prevention of intraoperative hypothermia and intraoperative fluid restriction. However, the relationship between FT programmes and surgical stress needs further clarification. The comparable contribution of each of the elements in the FT programmes remains uncertain;

however, removal of the nasogastric tube at the time of extubation is widely accepted as beneficial, as is no bowel preparation (Nelson 2007; Slim 2004). Limited evidence currently available indicates that FT surgery appears to be safe and shortens hospital stay for colonic surgery (Wind 2006).

In some studies (Basse 2004; Khoo 2007; King 2006; Schwenk 2006), FT programmes were shown to lead to significantly reduced postoperative organ dysfunction and a shortened hospital stay. Importantly, these studies indicate that FT surgery accounts for the reduced risk of perioperative complications; in terms of cost-effectiveness, Delaney et al reported decreased costs in FT surgery (Delaney 2003). Although there is mounting evidence that FT programmes account for enhanced recovery and reduced need for hospitalisation, initial concerns on safety have not been clarified (Kehlet 2008). Nevertheless, re-admission rates, which are important in the overall assessment of FT, have not increased (Andersen 2007).

Why it is important to do this review

In colonic surgery, implementation of FT programmes is supported by two published systematic reviews (Eskicioglu 2009; Wind 2006) and one randomised controlled trial (RCT) (Khoo 2007). These evidence-based multimodal FT programmes offer a new approach to surgeons of all disciplines, and a consensus has been reached in colonic surgery. Although these principles of practice also appear to be successful in open abdominal hysterectomy for benign disease (Møller 2001) and vaginal prolapse surgery (Ottesen 2002; Ottesen 2003), no evidence-based decision is available on major surgery for gynaecological malignancies. Therefore, this Cochrane systematic review aims to assess fully the beneficial and harmful effects of FT programmes for gynaecological cancers and also aims to determine whether there is a better way to achieve 'stress, pain, and risk-free operations' (Kehlet 2008).

OBJECTIVES

To evaluate the beneficial and harmful effects of FT programmes in gynaecological cancer care.

METHODS

Criteria for considering studies for this review

Types of studies

Only RCTs were included. Trials were eligible irrespective of blinding, number of patients randomised and language of the article. Quasi-randomised or non-randomised studies (NRS) were reviewed but not considered for inclusion.

Types of participants

Patients with indications for elective surgical treatment in gynaecological cancer. Both laparoscopic and open surgical techniques were eligible for inclusion.

Types of interventions

We compared any type of FT programme with conventional recovery strategies.

The eligible FT recovery strategy was defined as consisting of at least four FT elements: preoperative counselling, preoperative feeding, no bowel preparation, no premedication, fluid restriction, perioperative high O_2 concentrations, active prevention of hypothermia, epidural analgesia, minimally invasive/transverse incisions, no routine use of nasogastric tubes, no routine use of drains, enforced postoperative mobilisation, enforced postoperative oral feeding, no systemic morphine use, standard laxatives and early removal of bladder catheter (Wind 2006).

Types of outcome measures

Primary outcomes

- Postoperative length of overall hospital stay.
- Postoperative complications, for example: acute confusion, nausea and vomiting, postoperative fever, secondary haemorrhage atelectasis (the lack of gas exchange within alveoli owing to blood consolidation), pneumonia, wound infection, wound or anastomosis dehiscence (breakdown of the stitches), embolism and deep vein thrombosis, acute urinary retention, bowel obstruction owing to fibrinous adhesions, paralytic Ileus, incisional hernia, persistent fistula (an abnormal connection or passageway between two organs or vessels that normally do not connect).
- Early and late mortality (early mortality is defined as death within 30 days; late mortality is defined as death within three months).

Secondary outcomes

- Re-admission rate.
- Bowel function.
- QoL, measured by a validated scale.

Search methods for identification of studies

Electronic searches

The following electronic databases were searched:

- the Cochrane Gynaecological Cancer Review Group's Trial Register
- the Cochrane Central Register of Controlled Trials (CENTRAL)
- MEDLINE
- EMBASE

For MEDLINE we developed a search strategy based on the terms related to the review topic (Appendix 1).
For databases other than MEDLINE, the search strategy was adapted accordingly, these can be found in Appendix 2 and Appendix 3. Databases were searched from 1950 to 25 Novemeber 2014.

All relevant articles found were identified on PubMed and using the 'related articles' feature. An updated search will be carried out for newly published articles every year.

Searching other resources

Unpublished and Grey literature

MetaRegister, Physicians Data Query, www.controlled-trials.com/rct, www.clinicaltrials.gov and www.cancer.gov/clinicaltrials were searched for ongoing trials. The main investigators of the relevant ongoing trials were contacted for further information, as well as the major co-operative trials groups active in this area.

Handsearching

The reference lists of all relevant trials obtained by this search were handsearched for further trials.

Correspondence

Authors of relevant trials were contacted to ask if they knew of further published and unpublished data.

Language restrictions

Papers in all languages were sought and translations carried out if necessary.

Data collection and analysis

Selection of studies

All titles and abstracts retrieved by electronic searching were downloaded to the reference management database Endnote, duplicates were removed and the remaining references were examined by two review authors independently. Those studies that clearly did not meet the inclusion criteria were excluded and copies of the full text of potentially relevant references were obtained. The eligibilities of retrieved papers were assessed independently by two review authors. Disagreements were resolved by discussion between the two review authors and if necessary by a third review author. Reasons for exclusion were documented.

Data extraction and management

Since no eligible study was included, no data could be extracted. We will update this section when potential studies emerge in the future. The following information will be extracted from the included studies.

Trial characteristics

- Trial design: multicentre or single centre; single phase or cross-over design.
- Number of patients randomised, excluded and analysed.
- Duration, timing and location of the trial.
- Source of funding.

Baseline characteristics of the studied groups

- Type of gynaecological cancer.
- Age of the patients.
- Investigative work-up.
- Body mass index (BMI) and American Society of Anaesthesiology (ASA) classification.
- Type of surgical procedures.
- The prognostic factors for surgical recovery, for example smoking, co-morbidities, obesity.

Intervention

1. Randomisation number.
2. Type of intervention and control.
3. Other identical perioperative care in both groups.

Outcomes

1. Outcomes reported.
2. How were outcomes defined?
3. How were outcomes measured?
4. Timing of outcome measurement

All data will be extracted independently by two review authors using forms adhering to Cochrane guidelines. Additional information will be sought on trial methodology or actual trial data from the authors of trials that appear to meet the eligibility criteria but have aspects of methodology that are unclear or data in an unsuitable form for meta-analysis. Differences of opinion will be registered and resolved by consensus or a third review author.

For binary outcomes, we will record the number of participants experiencing the event in each group of the trial. For continuous outcomes, for each group we will extract the arithmetic means and standard deviations. If the data are reported using geometric means we will extract standard deviations on the log scale. Medians and ranges will be extracted and reported in tables.

Assessment of risk of bias in included studies

In future updates, the risk of bias in included RCTs will be assessed using The Cochrane Collaboration's tool and the criteria specified in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2009). This will include assessment of:

- sequence generation;
- allocation concealment;
- blinding (assessment of blinding will be restricted to blinding of outcome assessors, since it is generally not possible to blind participants and personnel to surgical interventions);
- incomplete outcome data;
- selective reporting of outcomes;
- other possible sources of bias (e.g. a potential source of bias related to the specific study design used, or stopped early owing to some data-dependent process, extreme baseline imbalance, etc.).

The risk of bias tool will be applied independently by two review authors and differences resolved by discussion. Results will be presented in the 'Risk of bias' table and also in both a 'Risk of bias' graph and a 'Risk of bias' summary section. Results of meta-analyses will be interpreted in light of the findings with respect to risk of bias.

Measures of treatment effect

- For dichotomous outcomes (e.g. complications), we will extract the number of patients in each group (e.g. patients who did/did not get abdominal sepsis) who experienced the outcome of interest and the number of patients assessed at end point, in order to estimate a risk ratio (RR).
- For continuous outcomes (e.g. QoL measures), we will extract the final value and standard deviation of the outcome of interest and the number of patients assessed at end point in each treatment arm at the end of follow-up, in order to estimate the mean difference between treatment arms and its standard error.
- For time-to-event data (e.g. early and late mortality), we will extract the hazard ratio (HR) and its variance from trial reports; if these are not presented, we will extract the data required to estimate them using Parmar's methods (Parmar 1998), for example number of events in each arm and log-rank P value comparing the relevant outcomes in each arm, or relevant

data from Kaplan-Meier survival curves. If it is not possible to estimate the HR, we will extract the number of patients in each treatment arm who experienced the outcome of interest and the number of participants assessed, in order to estimate a RR.

Where possible, all data extracted will be those relevant to an intention-to-treat analysis, in which participants are analysed in groups to which they were assigned.

Unit of analysis issues

No cross-over trials and cluster-randomised trials will be included.

Dealing with missing data

We will attempt to extract data on the outcomes only among participants who were assessed at end point. We will not impute missing outcome data. For the primary outcome, if data are missing or only imputed outcome data are reported, we will contact trial authors to request data on the outcomes among participants who were assessed.

Assessment of heterogeneity

Heterogeneity between studies will be assessed by visual inspection of forest plots, by estimation of the percentage heterogeneity between trials that cannot be ascribed to sampling variation (Higgins 2003), by a formal statistical test of the significance of the heterogeneity (Deeks 2001), and if possible by subgroup analyses (Subgroup analysis and investigation of heterogeneity). If there is evidence of substantial heterogeneity, the possible reasons for this will be investigated and reported.

Assessment of reporting biases

Funnel plots corresponding to meta-analysis of the primary outcome will be used to assess the potential for small study effects such as publication bias. If these plots suggest that treatment effects may not be sampled from a symmetric distribution, as assumed by the random-effects model, further meta-analyses will be performed using fixed-effect models.

Data synthesis

If sufficient clinically similar studies are available, their results will be pooled in meta-analyses.

- For any dichotomous outcomes (e.g. complications), RRs will be pooled using the inverse-variance random-effects method.
- For continuous outcomes (e.g. QoL measures), the mean differences between the treatment arms at the end of follow-up will be pooled if all trials measured the outcome on the same scale, otherwise standardised mean differences will be pooled.

For trials with multiple treatment groups, the 'shared' comparison group will be divided into the number of treatment groups and comparisons between each treatment group and the split comparison group will be treated as independent comparisons.
Random-effects models with inverse variance weighting will be used for all meta-analyses (DerSimonian 1986).
If possible, studies making different comparisons will be synthesised using the subgroup methods of Bucher 1997.

Subgroup analysis and investigation of heterogeneity

Subgroup analyses will be performed, grouping the trials by:

- different kinds of surgical procedures;
- different types of gynaecological cancer;
- different FT elements contributing to FT programmes.

Factors such as age, stage, length of follow-up and adjusted/unadjusted analysis will be considered in interpretation of any heterogeneity.

Sensitivity analysis

Sensitivity analyses will be performed excluding studies at high risk of bias.

RESULTS

Description of studies

Results of the search

A total of 1651 citations were initially obtained, of which full texts of 19 citations were sought for detailed assessment. Handsearching of reference lists and journals resulted in a retrieval of a further eight citations. Of these 27 reports, one described 'fast track' as referral pattern, five discussed benign gynaecological diseases and 17 performed only one FT element. The remaining four reports on three trials were excluded as they were not RCTs (see Characteristics of excluded studies). In the 2012 update, the new search found 446 citations, and four out of them were sought for further assessment. However, none of them were eligible for inclusion owing to only one FT element being used. In the 2014 update an additional 679 citations were screened. Three of these were further assessed and added to the excluded studies as they did not meet the inclusion criteria.

Included studies

No eligible RCTs were included.

Excluded studies

Eberhart 2008 was stated as a prospective study that assigned consecutive participants into different groups at a time point. Gerardi 2008 and Marx 2006 were partially prospective studies with a retrospective control group.

Risk of bias in included studies

No eligible RCTs were included.

Effects of interventions

In the absence of any eligible RCTs, we were unable to perform any analysis. We summarised the main results of the NRS in Table 1 and Table 2.

DISCUSSION

Owing to the lack of RCTs, there is currently no evidence to support or refute the use of perioperative enhanced recovery programmes for gynaecological cancer patients.

Summary of main results

Although no analysis was performed in this Cochrane review, we have presented the main results of the three excluded studies in Table 2. These NRS show the potential benefits of perioperative enhanced recovery programmes for gynaecological

cancer patients. Both Gerardi 2008 and Marx 2006 stated that FT programmes could shorten the length of hospital stay; it was found that FT programmes had similar postoperative complications, mortality and re-admission rates as the conventional perioperative care procedures. Moreover, bowel function recovery was enhanced in Eberhart 2008 and Gerardi 2008. Eberhart 2008 concluded that the programmes could improve postoperative QoL, while shortened hospital stay could lead to a significant reduction in hospital-related cost in Gerardi 2008. However, we are currently unable to ascertain any definitive conclusions from these low-quality studies.

Overall completeness and applicability of evidence

No evidence is available from RCTs at present. The NRS we presented only studied ovarian cancer. Other types of gynaecological cancer (e.g. uterine cervical cancer or endometrial cancer) were studied for the perioperative enhanced recovery programmes. Moreover, standard guidelines of FT programmes have not been unified, which means these multimodal programmes are different in every study. This could potentially amplify the heterogeneity in results.

Potential biases in the review process

To prevent bias in the review process, the search was guided and developed by the Cochrane Gynaecological Cancer Review Group. No restrictions such as language were applied to the search. The study selection was conducted independently by two review authors. Any disagreement was resolved by discussion with the third review author.

AUTHORS' CONCLUSIONS

Implications for practice

The updated searches carried out in Novemeber 2014 concluded that there is still no evidence from RCTs to support or refute the use of perioperative enhanced recovery programmes in gynaecological cancer patients.

Implications for research

Well-designed and well-conducted RCTs are necessary to evaluate FT perioperative programmes. We recommend any such investigators use the standard FT programmes in future studies (Kehlet 2008).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Study	Reason for exclusion
Belavy 2013	RCT, only examined epidural analgesia
Eberhart 2008	NRS, 'prospective study'
Feng 2008	Phase III multi-centre RCT, investigated early enteral feeding only
Gerardi 2008	NRS, prospective FT group with retrospective control group
Janda 2014	RCT, investigated early oral intake only
Marx 2006	NRS, prospective FT group with retrospective control group

ADDITIONAL TABLES

Table 1. Characteristics of the excluded studies

Study ID	Participants	Intervention	Control	Outcomes	Note
Eberhart 2008	Ovarian cancer undergoing major abdominal surgery	The multimodal fast-track algorithm group (N = 46)	The traditional algorithm group (N = 40)	• PPP33-questionnaire (a quality of life tool) • Recovery • Postoperative complications	The full text could not be retrieved
Gerardi 2008	FIGO Stages II-IV epithelial ovarian or primary peritoneal cancer undergoing primary cytoreductive surgery.	The postoperative management dictated by a prescribed clinical pathway (N = 19)	The postoperative management directed by the preference of individual surgeon (N = 45)	• Time to flatus • Time to tolerance of diet • ICU stay • Postoperative complications • Length of hospital stay • Hospital cost • 30-day re-admission rate	The clinical pathway included rapid diet advancement, early discontinuance of nasogastric suction, criteria-based utilisation of parenteral nutrition, selective laboratory testing and deferring initiation of chemotherapy until after discharge
Marx 2006	Ovarian cancer undergoing surgery	Perioperative multimodal rehabilitation (N = 69)	Perioperative conventional care (N = 72)	• Postoperative complications • Re-operations • Re-admissions • Mortality • Primary hospital stay	Multimodal rehabilitation included: no preoperative sedatives, no bowel preparation, continuous epidural analgesia, no nasogastric tube, early oral feeding, early mobilisation

FIGO: International Federation of Gynecology and Obstetrics.

Table 2. Outcomes of the excluded studies

Outcomes	Eberhart 2008	Gerardi 2008	Marx 2006
Primary outcomes			
Length of hospital stay (days)	-	Intervention group: 7.0 (95% CI 3 to 27) Control group: 10.0 (95% CI 5 to 30) P = 0.010	Intervention group: 5 (95% CI 2 to 31) Control group: 6 (95% CI 2 to 64) P < 0.05
Postoperative complications	"rare and did not differ between both groups"	Intervention group: 57.9% Control group: 62.2% P = 0.746	Intervention group: 24.6% Control group: 31.9% P > 0.05
Early and late mortality	-	Only 1 mortality in control group at day 17	Intervention group: 0% Control group: 2.8% P > 0.05
Secondary outcomes			
Re-admission rate	-	Intervention group: 21.1% Control group: 33.3% P = 0.326	Intervention group: 2.9% Control group: 12.5% P > 0.05
Time to flatus (days)	"Patients in fast-track group rated their recovery to be faster than patients treated by the traditional concept"	Intervention group: 6.0 (95% CI 4 to 20) Control group: 6.0 (95% CI 2 to 15) P = 0.630	-
Time to tolerance of diet (days)	-	Intervention group: 3.0 (95% CI 1 to 20) Control group: 6.0 (95% CI 1 to 14) P = 0.013	-
QoL	"Several dimensions of the PPP33-questionnaire ("autonomy", "physical complaints", and "postoperative pain") were improved by the multimodal "fast-track" rehabilitation programme"	-	-
Cost	-	Intervention group: 19,700 (95% CI 11,010 to 84,170) Control group: 25,110 (95% CI 11,980 to 78,150) P = 0.043 *	-

Table 2. Outcomes of the excluded studies *(Continued)*

Re-operation	-	-	Intervention group: 4.3% Control group: 12.5% P > 0.05

* 2006 US dollars
CI: confidence interval; QoL: quality of life.

APPENDICES

Appendix 1. MEDLINE search strategy

MEDLINE Ovid 1950 to May 2012

1 exp Uterine Neoplasms/
2 exp Ovarian Neoplasms/
3 exp Fallopian Tube Neoplasms/
4 exp Vaginal Neoplasms/
5 exp Vulvar Neoplasms/
6 ((endometr* or uter* or cervi* or ovar* or vagin* or fallopian* or vulva* or gynae* or gyne*) adj5 (cancer* or neoplas* or carcinom* or malignan* or tumor* or tumour*)).mp.
7 1 or 2 or 3 or 4 or 5 or 6
8 surgery.fs.
9 exp Gynecologic Surgical Procedures/
10 exp Laparoscopy/
11 (surg* or operat* or laparoscop* or hysterectomy or ovariectomy or salpingostomy).mp.
12 8 or 9 or 10 or 11
13 7 and 12
14 exp Perioperative Care/
15 exp Preoperative Care/
16 exp Convalescence/
17 exp "Length of Stay"/
18 ERAS.mp.
19 fast track.mp.
20 ((enhanced or early) and (rehabilitat* or recover* or convalesc*)).mp.
21 14 or 15 or 16 or 17 or 18 or 19 or 20
22 13 and 21
23 randomized controlled trial.pt.
24 controlled clinical trial.pt.
25 randomized.ab.
26 placebo.ab.
27 drug therapy.fs.
28 randomly.ab.
29 trial.ab.
30 groups.ab.
31 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32 (animals not (humans and animals)).sh.
33 31 not 32
34 22 and 33

key: mp=title, original title, abstract, name of substance word, subject heading word, fs=floating subheading, ab=abstract, sh=medical subject heading

Appendix 2. EMBASE search strategy

EMBASE Ovid 1980 May 2012

1 exp uterus cancer/
2 exp ovary tumor/
3 exp uterine tube tumor/

4 exp vagina tumor/
5 exp vulva tumor/
6 ((endometr* or uter* or cervi* or ovar* or vagin* or fallopian* or vulva* or gynae* or gyne*) adj5 (cancer* or neoplas* or carcinom* or malignan* or tumor* or tumour*)).mp.
7 or/1-6
8 su.fs.
9 exp gynecologic surgery/
10 exp laparoscopy/
11 (surg* or operat* or laparoscop* or hysterectomy or ovariectomy or salpingostomy).mp.
12 or/8-11
13 7 and 12
14 exp perioperative period/
15 exp preoperative care/
16 exp peroperative care/
17 exp postoperative care/
18 exp "length of stay"/
19 ERAS.mp.
20 fast track.mp.
21 ((enhance or early) and (rehabilitat* or recover* or convalesc*)).mp.
22 exp convalescence/
23 or/14-22
24 13 and 23
25 exp controlled clinical trial/
26 randomized.ab.
27 placebo.ab.
28 dt.fs.
29 randomly.ab.
30 trial.ab.
31 groups.ab.
32 or/25-31
33 24 and 32

key:

mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name, ab=abstract, fs=floating subheading

Appendix 3. CENTRAL search strategy

CENTRAL Issue, 4 May 2012

#1 MeSH descriptor Uterine Neoplasms explode all trees
#2 MeSH descriptor Ovarian Neoplasms explode all trees
#3 MeSH descriptor Fallopian Tube Neoplasms explode all trees
#4 MeSH descriptor Vaginal Neoplasms explode all trees
#5 MeSH descriptor Vulvar Neoplasms explode all trees
#6 (endometr* or uter* or cervi* or ovar* or vagin* or fallopian* or vulva* or gynae* or gyne*) near/5 (cancer* or neoplas* or carcinom* or malignan* or tumor* or tumour*)
#7 (#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8 Any MeSH descriptor with qualifier: SU
#9 MeSH descriptor Gynecologic Surgical Procedures explode all trees
#10 MeSH descriptor Laparoscopy explode all trees
#11 surg* or operat* or laparoscop* or hysterectomy or ovariectomy or salpingostomy
#12 (#8 OR #9 OR #10 OR #11)
#13 (#7 AND #12)
#14 MeSH descriptor Perioperative Care explode all trees
#15 MeSH descriptor Preoperative Care explode all trees
#16 MeSH descriptor Convalescence explode all trees
#17 MeSH descriptor Length of Stay explode all trees
#18 ERAS
#19 fast track
#20 (enhanced or early) and (rehabilitat* or recover* or convalesc*)
#21 (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20)

#22 (#13 AND #21)

WHAT'S NEW

Date	Event	Description
15 November 2018	Amended	The Editors are looking for contributors to update and maintain this Cochrane Review. Contact ruh-tr.gnoc-cochrane@nhs.net for further information.

HISTORY

Protocol first published: Issue 1, 2010
Review first published: Issue 6, 2010

Date	Event	Description
19 March 2015	New citation required but conclusions have not changed	No new studies identified for inclusion.
19 March 2015	New search has been performed	Searched update November 2014. Text updated accordingly.
5 November 2012	New citation required but conclusions have not changed	No new studies identified.
1 May 2012	New search has been performed	A new search was run in May 2012.

CONTRIBUTIONS OF AUTHORS

Donghao Lv: drafting of protocol and review; search for trials; data entry into RevMan; extraction of data; selection of trials for inclusion/exclusion.
Huan Song: extraction of data; selection of trials for inclusion/exclusion; obtaining copies of trial reports; extraction of data.
Gang Shi: all correspondence; drafting of protocol and review; interpretation of results.

DECLARATIONS OF INTEREST

Authors declare that all the analyses and interpretation reflect the opinions of the authors; no pharmaceutical company was involved in the analysis or interpretation of data, or in the writing of this systematic review.

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External sources

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INDEX TERMS

Medical Subject Headings (MeSH)

Genital Neoplasms, Female [*surgery]; Length of Stay; Perioperative Care [*methods]; Program Evaluation

MeSH check words

Female; Humans