PRIORITY BRIEFING

The purpose of this briefing paper is to aid Stakeholders in prioritising topics to be taken further by PenCLAHRC as the basis for a specific evaluation or implementation research project.

Does laparoscopy improve diagnosis and treatment decision-making in suspected ovarian cancer?

Question ID: 9

Question type: Intervention

Question: Does laparoscopy improve diagnosis and treatment decision-making in suspected ovarian cancer?

Population: Women who have suspected ovarian cancer

Intervention: Laparoscopy once ovarian cancer is suspected. The technique would enable biopsy to achieve a diagnosis, and enables assessment of the abdomen to decide whether surgery or chemotherapy are the best initial treatments.

Control: Current practice is to perform a CT scan or ultrasound. If the disease looks operable, a laparotomy is done to achieve both the diagnosis and deliver initial treatment. If not operable, diagnosis is achieved with ascites cytology or image guided biopsy, and treatment given in the form of chemotherapy. The problem with this approach is that there is evidence that imaging is only about 60% reliable at predicting operability. This means that up to 40% of patients are potentially having the wrong initial treatment.

Outcome: 1. Diagnosis in a shorter space of time. 2. Fewer cases of no diagnosis or uncertain diagnosis after initial investigations. 3. Data about the correlation between laparoscopy findings and imaging in this institution. 4. Establish safety of laparoscopy in this context. 5. Fewer unnecessary operations done and fewer possible operations left undone (ie better treatment selection). 6. Cost effectiveness. 7. Patient experience.

Laparoscopy: A laparoscopy is a surgical procedure that allows the surgeon to access the inside of the abdomen and the pelvis. The surgeon does not have to make large incisions (cuts) in the skin. This is made possible with an instrument called a laparoscope. A laparoscope is a small flexible tube that contains a light source and a camera. The advantages of this technique over traditional open surgery is that people who have a laparoscopy have: a faster recovery time, less pain after the operation, and minimal scarring. A laparoscopy is generally regarded as a very safe procedure. Serious complications as a result of surgery are rare and occur in an estimated 1 in a 1,000 cases.

Ovarian Cancer: The main risk factor for ovarian cancer is age (being over the age of 50) but others include a strong family history of ovarian or breast cancer,

obesity, use of hormone replacement therapy (HRT), and infertility and fertility treatments. Most ovarian cancers are a type called epithelial cancer. There are several types of epithelial cancers of the ovary. The most common types are: serous and endometrioid. Less common types of epithelial ovarian cancer are: mucinous, clear cell, and undifferentiated or unclassifiable. They are currently all treated in a similar way.

The Health Problem:

NICE report that ovarian cancer is the fifth commonest cancer in women in the UK after breast, colorectal, lung and uterus. Approximately 6,700 new cases of ovarian cancer were diagnosed every year in United Kingdom between 2004 and 2007 accounting for approximately 1 in 20 cases of cancer in women. The lifetime risk of women being diagnosed with ovarian cancer is 1 in 48. Overall 90% of the ovarian cancer recorded in the UK in 2007 were in women aged 45 years and above. Approximately 4,300 women die from ovarian cancer each year in the UK which makes it the leading cause of death in gynaecological cancers. It accounts for 6% of all cancer deaths in women. The reason for the high mortality rate in ovarian cancer may be because most women are diagnosed with advanced ovarian cancer at the time of detection.

A recent trial (Vergote et al, NEJM 2010) has demonstrated that advanced (stage 3 and 4) ovarian cancer can be treated initially with surgery followed by chemotherapy, or chemotherapy followed by surgery, with no difference in mortality. Surgery first, however, is associated with higher morbidity and surgical risk. The recommendation is that chemotherapy is therefore given first in advanced ovarian cancer. The problem is that if the patient is not to have initial surgery, how do you a) make the diagnosis quickly and reliably and with low risk, and b) how do you confirm that disease is advanced (stage3 or 4) rather than early (stage 1 or 2). Current ways involve staging with CT and biopsy with image guided needle biopsy, or fluid cytology. CT is unreliable (see JCO paper), and biopsy is time consuming and a significant minority fail and have to be repeated. The result is long delays, and potentially the wrong decision due to inaccurate staging. Laparoscopy has the potential to both diagnose and stage the disease in one episode, provide quicker and more accurate diagnoses and be more cost effective. If early stage is evident, treatment surgery can be undertaken straight away.

Guidelines:

Guidelines are currently being developed by NICE on Ovarian cancer: the recognition and initial management of ovarian cancer. In these draft guidelines the recommendations for secondary care of patients with suspected ovarian cancer are to Use biopsy rather than cytology to obtain tissue for diagnosis if surgery has not been performed, to use percutaneous image-guided biopsy if this is feasible and to use laparoscopy only if percutaneous image-guided biopsy is not feasible or has not produced an adequate sample.

The Cancer Reform Strategy (DoH, 2007) states that cancer diagnosis should occur in the shortest possible time (with attendant waiting targets), and with maximal use of minimal access surgery (such as laparoscopy).

NHS Priority:

Regional

SW SHA Priorities framework 2008-11

- The southwest SHA has undertaken to achieve the 5 year goals of the cancer reform strategy in 3 years.
- Match highest life expectancy in Europe by 2013
- Reduce mortality rates from cancer in people under 75 years
- Cancer patients will receive earlier diagnosis

Local

- Increase life expectancy (all localities in the peninsula)
- Reduce cancer mortality (CIOSPCT)

Existing Research:

Published research

No systematic reviews were identified on this topic area. Seven articles appear to investigate the effectiveness of using laparoscopy to stage, diagnose and in some cases treat ovarian cancer. All of the studies included here report positive potential for the use of laparoscopy in this area although study samples range from 55-98 patients. One study suggests that use of laparoscopy can reduce the risk of further explorative lararotomies from 30% down to 18%[1]. Another study suggests that laparoscopy is more sensitive to detecting peritoneal carcinosis than CT with a sensitivity of 100% and 47.8% respectively[5]. And another reports that the overall accuracy rate of laparoscopy in assessing optimal cytoreduction as 90%[7]. Other studies have also looked at the impact of using a score alongside laparoscopy to try and improve its effectiveness[3,6]. These studies conclude that using a simplified scoring system based on laparoscopy was also reliable in assessing chance of optimal cytoreduction.

Ongoing research

No ongoing research was identified in this topic area.

Feasibility:

There is a capability to perform this study in Exeter. There is also the potential to perform it regionally.

References:

1) A. Fagotti, F. Fanfani, G. Vizzielli, V. Gallotta, A. Ercoli, A. Paglia, B. Costantini, M. Vigliotta, G. Scambia, G. Ferrandina (2009). Should laparoscopy

be included in the work-up of advanced ovarian cancer patients attempting interval debulking surgery?
Objectives. Primary: To investigate whether S-LPS could contribute to a better identification of patients to submit to IDS. Secondary: To identify the most appropriate level of laparoscopic index value (PIV) to identify inoperable patients in this subset of patients. Methods. A prospective single-institutional study including patients with advanced ovarian/peritoneal cancer (FIGO stage IIIC–IV) to be submitted to IDS after NACT. Patients have been considered eligible for surgical exploration in case of complete/partial radiological or serological response; stable disease if primary surgery had been performed in a different hospital; progressive radiological disease in the presence of serological response, young age, and good performance status (ECOG b1); and progressive serological disease with stable clinical and radiological disease. A laparoscopic assessment for each patient has been performed. Results. Ninety-eight consecutive AOC patients submitted to NACT have been eligible for the study. With the addition of S-LPS to the RECIST criteria, a surgical exploration is performed in all patients and the percentage of explorative laparotomies drops to about 10%. The use of S-LPS after the GCIG criteria can reduce the risk of both explorative laparotomies from 30% to 13%, and inappropriate unexplorations from 18% to 0%. Moreover, at a PIV N4 the probability of optimally resecting the disease at laparotomy is equal to 0. Conclusions. Present data suggest that S-LPS can play a relevant role to discriminate patients with partially/stable disease or referred from other Institutions after NACT, which can be susceptible of successful IDS.

2) Brun, J. L., R. Rouzier, et al. (2009). "Neoadjuvant chemotherapy or primary surgery for stage III/IV ovarian cancer: contribution of diagnostic laparoscopy." BMC Cancer 9: 171.
BACKGROUND: The aims of this retrospective study were to evaluate laparoscopic triage of patients with advanced ovarian cancer towards primary surgery or neoadjuvant chemotherapy, and to analyze outcome according to the treatment. METHODS: Between January 2001 and December 2006, 55 patients with stage III - IV ovarian cancer underwent diagnostic laparoscopy. Primary surgery was performed when complete cytoreduction was considered feasible, while the other patients received neoadjuvant chemotherapy (platinum-based combination with taxanes) and interval surgery. All the patients received adjuvant chemotherapy. RESULTS: Patients treated with neoadjuvant chemotherapy (n = 29) had a higher mean body mass index (P = 0.048), higher serum CA 125 levels (P = 0.026), and more metastases (P = 0.045) than patients treated with primary surgery (n = 26). In patients treated with primary surgery, complete cytoreduction and a residual tumour size <or= 2 cm were obtained in respectively 54% and 77% of cases. Complete cytoreduction was achieved in respectively 100% and 33% of cases when primary surgery was performed by an oncologic gynaecologist and by a non-oncologic gynaecologist (P = 0.002). Interval surgery yielded complete cytoreduction and a residual tumour size <or= 2 cm in respectively 73% and 85% of cases. With a median follow-up of 24 months

(range 7 - 78 months), the survival rates after primary surgery and interval surgery were 61% and 66% respectively. CONCLUSION: Diagnostic laparoscopy is useful for identifying patients with stage III/IV ovarian cancer who qualify for primary cytoreduction. Surgeon experience was a determining factor for the success of complete cytoreduction.

3) Jean-Luc Brun, Roman Rouzier, Serge Uzan, Emile Daraï. (2008) External validation of a laparoscopic-based score to evaluate resectability of advanced ovarian cancers: Clues for a simplified score
Background. The relevance of laparoscopy-based score in identifying patients with advanced ovarian cancer for optimal cytoreductive surgery has been evaluated. Methods. 55 patients with stage III–IV ovarian cancer, having undergone both laparoscopy and laparotomy for cytoreductive surgery, were retrospectively analyzed. Seven parameters were assessed: omental cake, peritoneal carcinosis, diaphragmatic carcinosis, mesenteric retraction, bowel infiltration, stomach infiltration, liver metastases. Each parameter was assigned 2 points if present and 0 if not (Fagotti score). Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and accuracy were calculated for each parameter. Receiver Operating Characteristic (ROC) curve analysis was used to predict the surgical outcome. Results. A laparoscopy-based score of ≥8 was associated with suboptimal cytoreduction with sensitivity, specificity, PPV, NPV, and accuracy of 46%, 89%, 89%, 44%, and 60% respectively. ROC curve analysis gave an Area Under the Curve (AUC) of 0.74. A modified score was set up by selecting 4 of the 7 parameters which satisfied the inclusion criteria in our population: diaphragmatic carcinosis, mesenteric retraction, stomach infiltration, liver metastases. Thirteen patients (12%) had a modified score of ≥4 and 42 patients (88%) had a score of b4 with an optimal cytoreduction rate of 0% and 43% respectively (P=0.002). A modified score of ≥4 was associated with suboptimal cytoreduction with sensitivity, specificity, PPV, NPV, and accuracy of 35%, 100%, 100%, 43%, and 56% respectively. ROC curve analysis gave an AUC of 0.68. Conclusion. This simplified laparoscopy-based score was at least as accurate as the Fagotti score to predict resectability.

4) Angioli, R., I. Palaia, et al. (2006). "Diagnostic open laparoscopy in the management of advanced ovarian cancer." Gynecol Oncol 100(3): 455-61.
OBJECTIVE: Optimal primary cytoreductive surgery (OPCS) plus adjuvant chemotherapy (AC) represents the standard management for patients with advanced ovarian cancer (AOC). Recently, some authors have suggested the use of neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) in patients with unresectable AOC. This study has been started to evaluate the role of diagnostic open laparoscopy (DOL) in predicting who are the best candidates to OPCS. METHODS: All patients newly diagnosed as affected by AOC were submitted to DOL in order to establish the possibility of OPCS considered as no residual tumor left after operation. Patients considered not susceptible of OPCS were submitted to three cycles of NACT, administered every 3 weeks (Carboplatin, targeted AUC = 6, plus paclitaxel 175 mg/mq),

followed by IDS and adjuvant chemotherapy. RESULTS: From January 2000 to March 2004, 87 patients with AOC underwent DOL. Fifty-three patients (61%) were judged operable and therefore submitted to primary cytoreductive surgery (Group A). Optimal debulking rate in this group of patients was 96%. Thirty-four patients were judged affected by disease not cytoriducible to absent residual tumor and therefore scheduled for NACT-IDS-AC (Group B). Twenty-five patients were judged with partial clinical response and were therefore scheduled for IDS and AC. Optimal debulking rate (no residual tumor) in Group B patients was 80%. No major perioperative complications, due to laparoscopy, occurred. All Group B patients received the first cycle of chemotherapy the day after DOL. In 34 patients (39%), an explorative laparotomy was avoided. With a median follow-up of 22 months (range 2-49 months), the proportions surviving were 87% and 60% in Group A and Group B patients, respectively. CONCLUSION: DOL could be considered a valid diagnostic tool in evaluating the extent of disease in AOC. Our data suggest that the use of DOL leads to decrease the rate of primary cytoreductive surgery for AOC; on the other hand, a higher optimal debulking rate (no residual tumor) at primary surgery is achieved.

5) Denzer, U., S. Hoffmann, et al. (2004). "Minilaparoscopy in the diagnosis of peritoneal tumor spread: prospective controlled comparison with computed tomography." Surg Endosc 18(7): 1067-70.
BACKGROUND: Early diagnosis of peritoneal spread in malignant disease prevents unnecessary laparotomies. Minimally invasive laparoscopy with the patient under conscious sedation is a new, easily feasible diagnostic technique. This study compares prospective and controlled diagnostic minilaparoscopy with computed tomography (CT) scan for the diagnosis of peritoneal metastases. METHODS: In this study, 56 patients with malignant disease were prospectively investigated with diagnostic minilaparoscopy and CT scan. RESULTS: The study criteria were fulfilled by 54 patients. Minilaparoscopy detected peritoneal carcinosis in 28 of 54 cases, whereas CT detected the disease in 14 of 54 cases. For 36 patients, the diagnosis could be verified by histologic examination of peritoneal biopsies or laparotomy. In this group, minilaparoscopy detected peritoneal carcinosis in 25 of 36 cases, whereas CT detected the disease in 12 of 36 cases. CONCLUSIONS: Minilaparoscopy was more sensitive than CT in detecting peritoneal carcinosis (100% vs 47.8%; $p < 0.01$). Considering its low grade of invasiveness and superior sensitivity, minilaparoscopy should be regarded as the procedure of choice for the early detection of peritoneal carcinosis.

6) Anna Fagotti, Gabriella Ferrandina, Francesco Fanfani, Alfredo Ercoli, Domenica Lorusso, Marco Rossi, and Giovanni Scambia. A Laparoscopy-Based Score To Predict Surgical Outcome in Patients With Advanced Ovarian Carcinoma: A Pilot Study (2006)
Background: Our objective was to set up a more objective quantitative laparoscopy-based model in predicting the chances of optimal cytoreductive surgery in advanced ovarian cancer patients. Methods: Sixty-four advanced

ovarian cancer patients were submitted to both laparoscopy and standard longitudinal laparotomy sequentially, to define the chances of optimal debulking surgery (residual disease £1 cm). Three patients could not be evaluated by laparoscopy because of the presence of multiple and tenacious adherences. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated for each laparoscopic parameter. On the basis of the statistical probability of each factor to predict surgical outcome, seven laparoscopic features were selected for inclusion in the final model. Each parameter was assigned a numerical score based on the strength of statistical association, and a total predictive index value was tabulated for each patient. Receiver operating characteristic curve analysis was used to assess the ability of the model to predict surgical outcome. Results: After debulking surgery, 41 (67.2%) of 61 patients were left with optimal residual disease. The presence of omental cake, peritoneal carcinosis, diaphragmatic carcinosis, mesenteric retraction, bowel and/or stomach infiltration, and liver metastases satisfied the basic inclusion criteria and were assigned a final predictive index value of 2. In the final model, a predictive index score ‡8 identified patients undergoing suboptimal surgery with a specificity of 100%. The positive predictive value was 100%, and the negative predictive value was 70%. Conclusions: The reliability of laparoscopy in assessing the chance of optimal cytoreduction can be improved by using a simple scoring system.

7) Anna Fagottia, Francesco Fanfania, Manuela Ludovisib, Roberto Lo Voib, Giuseppe Bifulcoa, Antonia Carla Testab, Giovanni Scambiaa,(2004) Role of laparoscopy to assess the chance of optimal cytoreductive surgery in advanced ovarian cancer: a pilot study

Objective. To investigate whether laparoscopy can be considered as adequate and reliable as standard laparotomy in predicting optimal cytoreduction (RT V 1 cm) in patients with advanced ovarian cancer. Methods. From March to November 2003, 95 patients with suspected advanced ovarian or peritoneal cancer have been evaluated. Thirtyone cases were excluded due to an anesthesiological class of risk ASA III–IV (51.6%) and for the presence of a large size mass reaching the xiphoid (48.4%). Sixty-four patients completed the study. All patients were submitted to preoperative clinico-radiological evaluation and then to both laparoscopy and standard longitudinal laparotomy, sequentially. Some specific preoperatively defined parameters were analyzed during each procedure in order to obtain the most accurate evaluation on the possibility to get an optimal cytoreduction. Results. The overall accuracy rate of laparoscopy in assessing optimal cytoreduction was 90%. The negative predictive value (NPV) of the clinical–radiologic evaluation corresponded to 73%, whereas in no case was the judgment of unresectable disease obtained by laparoscopy changed by the laparotomic approach (NPV 100%). On the contrary, an optimal debulking was achievable in 34 of 39 cases (87%) selected as completely resectable by explorative laparoscopy. Conclusions. Laparoscopy can be considered super imposable to standard longitudinal laparotomy in identifying not optimally resectable advanced ovarian cancer patients.