Anaesthesia for gynaecological oncological surgery

Monica Morosan FRCA
Philip Popham BSc MBBS FRCA MD

Gynaecological malignancy surgery can be eventful for both anaesthetists and surgeons. Surgical access for pelvic malignancy may be difficult; gynaecological tumours often have non-specific features, present late for treatment, and can achieve an impressive size before they are investigated. Proximity of the gynaecological tumour to other abdominal structures such as the kidneys or rectum may require input from other surgical specialties. Neurovascular bundles and lymph nodes are often adherent to the pelvic side wall, making dissection difficult. Finally, surgical staging is required for most cancers as microscopic disease cannot be determined through radiological investigations.

Overview of gynaecological cancers

Cervical cancer

Globally, cervical cancer is the second commonest cancer in women. The introduction of a cervical screening programme using Pap smear testing improved diagnosis, access to management, and prognosis of the condition. Eighty to ninety per cent of cases are squamous cell tumours, the remainder being tumours of epithelial or mesenchymal tissue. Spread typically occurs via vaginal mucosa, myometrium, and the paracervical lymphatics, but may also spread directly via the obturator fascia and involve other pelvic organs such as bladder and rectum. The FIGO classification (International Federation of Gynecology and Obstetrics) includes data derived from both clinical and pathological postoperative staging. Investigations will be dictated by the presentation, and may include i.v. pyelogram, colposcopy, cystoscopy, and computerised tomography (CT) or magnetic resonance imaging (MRI) of the pelvis. Haematogenous spread generally involves the lung, liver, and bone. Patients with early invasive disease generally undergo simple hysterectomy, whilst those with later stages undergo radical hysterectomy which involves removal of the uterus, 25% of vagina, the uterosacral and uterovesical ligaments, parametrium and pelvic node dissection. Thirty per cent of patients are of reproductive age, and in those preservation of ovaries and vagina is often expected.

Endometrial cancer

In the developed world, endometrial cancer is the commonest cancer of the female genital tract. (For individual risk factors and incidences please refer to Tables 1 and 2.) Diagnosis is either by dilatation and curettage or biopsy. In 2008, FIGO updated the classification of endometrial carcinoma to include surgical staging. Histologically, the cancer involves epithelial, stromal, or mesenchymal tissue that may lead to adenocarcinoma (the commonest), adenosquamous, serous papillary, clear cell or undifferentiated cancers. Spread is by local invasion, or tubal (leading to peritoneal metastases), lymphatic, and haematogenous spread (lung, liver, brain, and bone). Treatment consists of total abdominal hysterectomy and bilateral salpingo-oophorectomy with full pelvic lymphadenectomy.

Ovarian cancer

Patients with ovarian cancer have the poorest survival, probably because of late presentation that occurs in two-thirds of cases. Histological examination shows epithelial involvement is commonest (90%), the remainder being stromal, sex cord, or germ-cell tumours. One of the unique features of ovarian cancer is that it spreads to pelvic organs with no boundaries (peritoneal carcinomatosis). Complete tumour removal is associated with improved survival; hence, treatment is complex, highly invasive surgery.

Owing to its particular pattern of spread, ovarian cancer requires surgical staging either through a laparoscopic or an open surgical approach. Malignant cells exfoliate easily and travel along surfaces of the peritoneal cavity, frequently to the paracolic gutters, right hemidiaphragm,
Table 1 Risk factors in gynaecological cancers

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian</td>
<td>Age, Ovulation, Family history, Nulliparity, Polycystic ovary, Pelvic inflammatory disease, Diet (fats)</td>
</tr>
<tr>
<td>Uterine</td>
<td>Hormonal, High BMI, Diabetes, Physical activity, Smoking</td>
</tr>
<tr>
<td>Cervix</td>
<td>Sexual practice, HPV infection, Smoking, Oral contraceptive pill, Diet, Immunosuppression</td>
</tr>
<tr>
<td>Vulvar</td>
<td>Age, Dyethilstilberstrol, HPV infection, Sexual history, Smoking</td>
</tr>
</tbody>
</table>

Table 2 Incidence, survival, and mortality of gynaecological cancers in UK (adapted from Cancer Research UK; data reproduced with permission)

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Incidence(^a) AS (per 100 000)</th>
<th>Survival(^b) 5-y RS (%)</th>
<th>Mortality(^a) AS (per 100 000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian</td>
<td>17.1</td>
<td>42.9 (England 2005–2009)</td>
<td>9.1</td>
</tr>
<tr>
<td>Uterine</td>
<td>20.3</td>
<td>77.3 (England 2005–2009)</td>
<td>3.9</td>
</tr>
<tr>
<td>Cervix</td>
<td>8.4</td>
<td>66.6 (England 2005–2009)</td>
<td>2.3</td>
</tr>
<tr>
<td>Vulval</td>
<td>2.5</td>
<td>58.0 (England and Wales 1996–1999)</td>
<td>0.7</td>
</tr>
<tr>
<td>Vaginal</td>
<td>0.6</td>
<td>58.0 (England and Wales 1996–1999)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

\(^a\)AS European age-standardized.

Ovarian cancer can be familial in 5–10% of cases. Carriers of BRCA type 1 or 2 genes are offered surgery after the age of 35. Ovarian and pelvic cancers can be secondaries from other cancers, such as bowel or breast cancer.

Vaginal/vulval cancer

Vaginal cancer is rare. The majority are secondaries from other pelvic cancers, particularly uterus, ovaries, or rectum, possibly as a consequence of occult disease or radiation-induced carcinogenicity. Histologically, the tumours are squamous, adenocarcinoma, melanoma, small cell, lymphoma, and undifferentiated. Spread follows a direct path to the pelvis, or via the lymphatics to lungs, liver, and bone. Depending on staging, treatment involves partial vaginectomy and lymphadenectomy, followed by radiotherapy.

Vulval cancer is also uncommon and, predominantly, consists of squamous cell type. Spread is by direct invasion of the vagina, urethra, and anal canal, with lymphatic spread to inguinal, pelvic and femoral nodes, and distant spread to bone, liver, and lungs. Depending on staging, treatment involves block dissection of vulva, groin, and lymph nodes.

Anaesthetic considerations

Preoperative

Preoperative assessment should follow general principles, paying particular attention to general risk factors (obesity, increased age, and smoking) and quantification of distant cancer spread. Assessment of cardiovascular function and pulmonary complications is guided by the history and examination findings. Preoperative dyspnoea is difficult to investigate as it can also be the result of ascites. Eighty-nine per cent of stage III–IV ovarian cancer patients will have ascites. This leads to a wider distribution of cancerous cells, which may implant in recesses such as the upper abdominal subdiaphragmatic spaces, rather than surfaces that undergo peristalsis. Rapidly accumulating ascites, high bowel obstruction or multiple levels of bowel obstruction are contraindications to surgery. Depending on co-morbidities such as severe ischaemic heart disease, end-stage renal failure, advanced valvular lesions, or end-stage lung disease, consideration should be given to changing from a laparoscopic to an open surgical procedure.

The following paraneoplastic syndromes have been described in gynaecological cancers:

- Ovarian cancer: cerebellar degeneration, nephritic syndrome, retinopathy, cauda equina syndrome.
- Uterine: hypercalcaemia, retinopathy, peripheral neuropathy, encephalitis, myelitis, dermatomyositis.

Preoperative investigations should include full blood count, clotting, urea and electrolytes, liver function tests, group and save or cross-match, chest X-ray, and electrocardiogram. Recent guidance from the Advisory Committee on the Safety of Blood, Tissue and Organs (SaBTO) stressed the need to obtain valid consent for blood transfusion, which should be documented in the patient’s record.

Preoperative MRI of the abdomen and pelvis may allow the prediction of expected blood loss, and the need for ureteric stents, percutaneous nephrostomies, or bowel resection. In advanced cancers, MRI imaging also helps to evaluate musculo-skeletal and pelvic sidewall involvement.

Some patients have neoadjuvant chemotherapy before cytoreductive surgery and present for interval debulking. Chemotherapy with platinum-based drugs such as carboplatin and cisplatin is used in ovarian cancer.
Microlax™ enemas are administered before operation, and if bowel involvement occurs with ovarian cancer, osmotic sodium phosphate laxatives (Fleet™) may be given. Omental spread leads to anorexia and nausea and vomiting, and these patients benefit from i.v. fluid therapy during the preoperative fast.

Communication with the patient and her family should concentrate on giving adequate information on the anaesthetic plan, possible risks, or complications, and the potential need for high dependency or intensive care nursing.

**Intra-operative considerations**

Surgical techniques in this field evolve continuously. Laparoscopic surgery has the advantages of identifying small lesions through lens magnification, formation of fewer adhesions, and improved recovery compared with open surgery. In a few centres, robotic surgery is generally performed in recurrent cancers after radiotherapy, but may be used as a palliative procedure for symptom control. Since 1948, when it was first performed, mortality has decreased from 23% to 3–5%. Surgery in patients with previous pelvic radiotherapy poses particular risks.

In ovarian cancer, leaving minimal residual disease confers a survival benefit. This has led to more radical procedures being used. Maximal surgical debulking may involve radical oophorectomy with/without recto-sigmoid colectomy, bowel resection, splenectomy, diaphragmatic perinecicomy, omentectomy, and liver resection, via an abdominal incision from xiphoid to pubis. Diaphragmatic surgery relies on complete mobilization of liver through resection of the falciform and round ligaments. If there is invasion near hepatic veins, clamping of suprahepatic and infrahepatic vena cava, hepatic vein and hilum may reduce bleeding. Liver mobilization during perinecitectomy is the only predictor for post-operative pleural effusions, which led to a routine chest drain placement in some centres.¹

The principles of fast track surgery have been well publicized recently.² Although it has been attempted in gynaec-oncology, a Cochrane review identified only two studies addressing its use in surgery for ovarian malignancy.³ Currently, enhanced recovery programmes in gynaec-oncology are not well defined. They can be used for staging laparoscopy, hysterectomy, or second-look laparoscopy after chemotherapy. The potential benefits include less infectious exposure, rapid return to community and cost savings.

**Practical considerations**

Regarding mode of anaesthesia, radical vulvectomies without dissections extending above the inguinal ligament are the only procedures amenable to a single-shot spinal anaesthetic. In all other procedures, a general anaesthetic technique is required.

In our institution, laparoscopic hysterectomies (including bowel resection) are performed using premedication with i.v. midazolam, followed by standard induction of anaesthesia with fentanyl, propofol, and atracurium or rocuronium. Intraoperative analgesia includes administration of an appropriate dose of morphine, paracetamol and, if there are no contraindications to non-steroidal medication, an i.v. dose of parecoxib. After operation, these patients will require a patient-controlled analgesia system (PCA) of morphine. If the patient is morbidly obese or has a history of obstructive sleep apnoea, then a PCA of morphine or fentanyl and high-dependency monitoring are used.

When a Pfannenstiel or vertical infraumbilical incision is planned and the patient does not have any risk factors for significant postoperative pain, then we would perform a standard anaesthetic and analgesic technique, together with an ultrasound (USS)-guided transversus abdominis plane (TAP) block at the end of the procedure.

Patients with risk factors for significant postoperative pain development (previous chemotherapy, presence of biosocial risk factors or extensive surgery with large tissue destruction, or nerve involvement) are given Gabapentin in a dose of 600 mg 1 h before surgery. Concurrent intraoperative use of other sedative drugs needs to be avoided. Our practice is to continue gabapentin after operation for 4 days. The dose should be halved in patients with renal dysfunction. We would consider an intra- or postoperative ketamine infusion in patients with a history of chronic pain conditions with ambulatory opioid exposure or illicit i.v. drug use.

If the incision involves a supra umbilical incision to improve access in para-aortic lymphadenectomy, a subcostal USS-guided approach for TAP blocks is used. If the surgery involves upper abdomen resections (macroscopic disease surrounding liver or spleen), a low thoracic epidural is sited before induction of anaesthesia. These patients will have a planned postoperative admission to the high dependency unit.

For all major cases we use intraoperative bispectral index monitoring, in addition to standard monitoring. Invasive arterial blood pressure is used in cases where we anticipate major blood loss or the patient is super-morbidly obese or has significant cardio-respiratory comorbidities.

Antibiotic prophylaxis should be administered at induction of anaesthesia. In prolonged procedures, a repeat dose can be given. The choice of antibiotic should follow local protocols.

Thromboprophylaxis must be considered in every case. Overall risk of deep vein thrombosis (DVT) is 7–45%, and is associated with fatal embolism in 1%.⁴ Thrombo-embolic events may be the presenting feature of the cancer, and hence may complicate surgical planning. Gynaecological cancers lead to an increased risk of thrombo-embolism through several mechanisms that include:

- Tumour cells release tissue factor (TF) and pro-coagulant which have direct pro-coagulant properties
- Other pro-coagulant substances are released after the interaction between tumour cells, platelets, monocytes, and macrophages
A pelvic tumour compressing major vessels may cause venous stasis
- Immobilization
- Ovarian clear cell is more commonly associated with DVT
- Presence of a central venous cannula; upper limb thrombosis risk 27–66%
- Chemotherapy leads to a 2- to 6-fold increase in thromboembolic risk, most likely as a result of endothelial damage, reduced concentrations of circulating plasma protein C and S, expression of TF and release of inflammatory cytokines. Radiotherapy has inflammatory effects on the vasculature with endothelial disruption, cytokine release, and increased platelet aggregation.
- Treatment of anaemia with erythropoietin stimulating agents has been associated with an increased rate of thromboembolism and poor surgical outcome. A postulated mechanism is that erythropoietin receptors may exist on tumour cells.

Thromboprophylaxis should start before operation and continue after operation according to local protocols. Mechanical prophylaxis and pharmacological agents may be used together. Occasionally patients may be receiving therapeutic anticoagulation as a result of recurrent thrombotic episodes. Haematology advice before surgery should be sought and a plan for recommencement of therapeutic anticoagulation after operation should be in place. Such considerations may have implications for perioperative bleeding and the choice of analgesia technique.

Preparation for significant blood loss should be guided by the individual case and the amount of tumour invasion. This will also dictate the need for invasive monitoring.

Use of cell salvage in gynaecological surgery is controversial. Previously contraindicated in malignancies, its use in gynaecological surgery has been studied in a prospective study, where blood transfusion requirements were reduced in patients undergoing radical hysterectomy. The use of leucocyte depletion filters leads to complete removal of viable, nucleated tumour cells. In our practice, cell salvage is not offered routinely in oncological procedures, but is considered in Jehovah’s Witness patients.

Obesity is a risk factor in gynaecological cancers. A recent study looking at outcomes of obese patients with endometrial cancer found that 41.7% were morbidly obese and 18.7% were super morbidly obese. Hover-mattresses or slide sheets can be used for transferring to the operating table. Anti-slide sheets or bean bags should be used if lithotomy head down position is required (see Fig. 1). When a HoverMatt™ is used for transfer, we would remove it before surgery to reduce the chance of patients sliding when in the head down lithotomy position. Changes in position at the same time as pneumoperitoneum can significantly impair ventilation in morbidly obese patients or patients with decreased lung compliance.

Thermoregulation should be considered. An upper body forced air mattress and fluid warmer, together with continuous temperature monitoring should be used in every case. Padding of the arms and access to the drips and arterial line will depend on the patient’s body habitus and availability of equipment; arms may be wrapped by the side, tucked on chest, or placed on arm boards. The precise position may be guided by surgical needs. In open procedures, we would place the patient’s arms out on arm boards, while in lithotomy head down position for laparoscopic procedures, arms are wrapped by the patient’s side, aiding surgical, but limiting anaesthetic access.

In laparoscopic hysterectomies, a sudden, temporary loss of pneumoperitoneum upon removal of specimen together with the uterine manipulator must be accompanied by appropriate changes in ventilation. Careful assessment of the airway before extubation should be made, as prolonged, steep head down procedures can compromise the airway through oedema. Patients at risk should be placed first on the list.

Advanced ovarian cancer surgery can be associated with significant fluid shifts. Individually tailored intra-operative fluid management, guided by the use of cardiac output monitoring devices, aims to optimize the total volume of fluid administered. Using a goal-directed algorithm in ovarian cytoreductive surgery, fluid therapy with a balanced starch solution was associated with better haemodynamic stability, reduced requirement for fresh frozen plasma, and preservation of renal function in the short term, when compared with crystalloid. Stroke volume optimization has led to patients receiving more colloid compared with standard therapy. This occurs at a time when excessive fluid administration has detrimental effects on tissue perfusion. To date, studies using starch solutions in the perioperative period have not included long-term mortality as an outcome.

Postoperative admission to high dependency or intensive care unit (ICU) management may be required. A study of critically ill gynaecological cancer patients identified an ICU mortality of 17.3%, while overall mortality of cancer patients admitted to ICU is 47%. Vasopressor use, sepsis-related admission, and Acute Physiology and Chronic Health Evaluation (APACHE) II score more than 15 were found to be independent predictors of mortality.

Fig 1  Laparoscopic hysterectomy in a patient with a BMI of 45, smoker and asthmatic. The angle of the head down positioning cannot be fully appreciated because of upper body Bair Hugger™ (reproduced with patient’s consent).
Postoperative

Immediate anaesthetic issues include acute pain management, postoperative nausea and vomiting (PONV), delirium in geriatric patients, and surgical complications.

Postoperative analgesia should be a continuation of the intraoperative analgesia, using a multimodal approach where possible. Standard pain management after laparoscopic or open hysterectomy includes PCA using opioids with subsequent conversion to oral controlled-release oxycodeine. Procedure-specific postoperative pain management website (PROSPECT) has issued recommendations for abdominal hysterectomies (evidence included published reviews up to 2006). In patients with high risk of developing significant postoperative pain, epidural analgesia is recommended (Grade A level of evidence from randomized clinical trials, in accordance with Oxford Centre for Evidence-Based Medicine 2003). In low-risk patients, strong opioids and wound infiltration are recommended (Grade A).

Recent developments include intra- and postoperative i.v. lidocaine and ketamine infusions (together with PCAs) in open hysterectomies. Neither has influenced recovery in a recent trial, which stopped at interim analysis. Abdominal pain in peritoneal carcinomatosis can be refractory to opioid administration. Animal studies have linked up-regulation of substance P and down-regulation of μ-opioid receptor in dorsal root ganglia as possible mechanisms. Glucocorticoids exert an opioid sparing effect by acting on the cyclooxygenase pathway, and this appears to be dose dependent. Dexamethasone in a single dose of either 15 mg before operation or 10 mg after operation reduced opioid consumption during the first 24 h post hysterectomy.

Postoperative confusion has been studied in patients over the age of 60 undergoing gynae-oncology surgery. Delirium occurred in 17.5% of patients, more commonly in the elderly and those with hypoalbuminaemia, associated co-morbidities, postoperative blood transfusion, and immobility.

Risk factors for PONV should be identified before operation. Gynaecological surgery is known to be a risk factor for PONV, although this may be because of a population selection effect. Multivariate analysis in large trials failed to show an association. Preventive strategies aimed at decreasing the baseline risk such as the use of intra-operative regional analgesia, the avoidance of volatile agents or nitrous oxide, and use of antiemetic drugs should be applied. Additional treatment in the postoperative period should include serotonin antagonists, dexamethasone, and dopamine antagonists. Aprepitant is a new agent, licensed for chemotherapy-induced nausea and vomiting, and has been used as an oral dose before operation in PONV prevention. It is as effective as the other classes of antiemetics.

Surgical complications can present after operation with injuries to blood vessels, ureters, bladder, and rectum. Depending on severity, they might lead to an unplanned high dependency admission.

Surgery with pelvic exenteration presents an increased risk of septic complications and small bowel obstruction. Radical procedures involving the upper abdomen are noted for postoperative pulmonary complications.

Late issues

Recent studies have attempted to assess an association between recurrence in gynaecological malignancy and mode of anaesthesia. Surgery, anaesthetic agents, and opioid medication suppress immune function in the perioperative period. In a retrospective analysis of anaesthetic technique in ovarian adenocarcinoma, the authors concluded that patients offered epidural anaesthesia had improved 3- and 5-y survival.

Chronic pain after abdominal hysterectomy ranges in incidence between 5 and 32%. These studies also included benign conditions and endometriosis patients. The surgical process is responsible for 22% of chronic pain overall. Various approaches in hysterectomy (laparoscopic or open) are not associated with an increased incidence of chronic pain development. Important contributing factors include poorly controlled pre- or postoperative pain and anxiety. Studies in gynaecological oncology surgery have investigated quality of life indicators, but not chronic pain. Patients attending follow-up clinics frequently report it, and research is needed in this area.

Conclusions

Acute management of patients presenting with malignancies requires multidisciplinary involvement and avoiding fragmentation of care. Information on the type of cancer, prognosis, previous treatment, patients’ wishes for resuscitation, and end-of-life care should be summarized into a portable patient folder; this should ease communication and decision-making in the event of a pre-terminal acute event.

References

10. Abdominal Hysterectomy. PROSPECT Recommendations. www.postoppain.org (accessed on 5 April 2013)

Please see multiple choice questions 13–16.