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REVIEW ARTICLE

Prevention of Port-Site Metastasis in Gynecologic Malignancies

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ABSTRACT

Port-site metastasis is a major complication of surgical laparoscopy for gynecologic oncology and has been reported in literature with an incidence of 1.1 to 16%. Factors that contribute for development of port site can be divided in three categories: operative related, wound related and tumor related. With this review, the authors pretend to report the ideal surgical conditions, laparoscopic environment and means of prevention to decrease risk of port-site metastases in gynecologic malignancies.

Keywords: Port-site metastasis, Prevention, Gynecologic malignancies.

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INTRODUCTION

Laparoscopy is an established technical option for the diagnosis, staging and treatment of several oncologic pathologies.[1] The early optimism after the introduction of this approach was followed by the doubts based on the observation of port-site metastasis after laparoscopic surgery for neoplastic diseases.[2] In 1978, port-site metastasis was defined for the first time, subsequent to laparoscopy in a patient with ovarian cancer. Port-site metastasis is a major complication of surgical laparoscopy for gynecologic oncology and has been reported in literature with an incidence of 1.1 to 16%.[3] Prospective studies show that it is possible to keep the incidence of abdominal wall metastases to about 1% comparable to open surgery.[4] Etiology of port-site metastases is multifactorial. Factors can be divided in three categories: operative related, wound related and tumor related. Operative-related factors include the gas used, the effect of gas turbulence in long laparoscopic procedures, the high pressure pneumoperitoneum, long-operative procedure, tumor manipulation, local trauma and individual surgical skills. Wound-related factors are forced extraction of unprotected tissue and contamination from instruments during tumor dissection. Tumor-related factors are the biologic properties of the tumor, embolization of exfoliated cells and tumor stage.[1,3,5-8]

AIM

The aim of this review is to report ideal surgical conditions, laparoscopic environment and means of prevention to decrease risk of port-site metastases in gynecologic malignancies.

MATERIALS AND METHODS

The authors searched in Medline database for English-language and French-language articles using the keywords 'laparoscopic port-site metastases', 'prevention of laparoscopic port-site metastases', 'laparoscopic port-site metastases in ovarian cancer', 'laparoscopic port-site metastases in endometrial cancer', 'laparoscopic port-site metastases in cervical cancer' and 'laparoscopic port-site metastases in borderline ovarian tumors'.

Additional articles were obtained based on the bibliographic cross-reference of the initial articles reviewed.

There were identified >400 articles in English published during the last 51 years regarding the history, incidence, etiology and prevention of port-site metastases. According to the aim of this revision, 28 articles were selected and reviewed.

RESULTS

The development of port-site metastases following laparoscopic resection of various malignancies continues to be a disturbing issue for laparoscopic surgeons.[9]

Mostly studies intend to investigate the factors potentially responsible for the spread of cancer cells in laparoscopic surgery.

Based on experimental studies and clinical reports, many theories have been proposed to account for the ability of tumor to spread to surgical wounds. The tumor cell entrapment hypothesis, which was proposed in 1989, suggests that free cancer cells are able to implant on raw tissue surfaces including damaged peritoneal surfaces. Postoperatively, these areas become covered by a fibrinous exudate which could serve to protect the tumor cells from destruction by the normal defense mechanisms. This theory is supported by studies that have demonstrated tumor cells at concentrations of up to 26% in wound washings and have shown the recovery of tumor cells from the gloves and instruments used during surgery. Hypotheses specific to laparoscopy include exfoliation and spread of tumor cells by laparoscopic instruments, direct implantation at the trocar site by frequent changes of instruments, direct implantation from the passage of the specimen, the presence of the pneumoperitoneum, which can create a 'chimney effect'

that causes an increase in the passage of tumor cells at port sites and preferential growth of malignant cells at areas of laparoscopic peritoneal perforation.[10,11]

A study performed to evaluate the variables in the spread of tumor cells to port sites in swines demonstrated that some strategies, such as increasing insufflation pressure, reducing episodes of desufflation and gas leaks, and using frequent intra-abdominal lavage may help to reduce the numbers of viable tumor cells displaced to port sites during laparoscopic surgery for intra-abdominal malignancy.[12]

Another study performed in rat model evaluated the effects of carbon dioxide (CO_2) pneumoperitoneum and wound closure technique on port-site tumor implantation. This study suggests that closure technique (skin closure alone *vs* all three layers) may influence the rate of port- site tumor implantation. The rate of tumor implantation was found to be significantly higher for skin closure alone.[13] Another experimental study in rat model proved that the choice of helium as insufflation gas reduces the incidence of port-site metastases and the degree of intraperitoneal tumor spread.[14] However, the use of helium carries a possible risk of lethal gas embolism.[4]

Several clinical reports have suggested that gasless laparoscopy may aid in the prevention of port-site metastases by reducing tumor dissemination created by the carbon dioxide CO_2 pneumoperitoneum. However, *in vitro* research involving a laparoscopic model performed on colorectal cancer cells showed that malignant cells were not identified in the CO_2 exhaust, but were found on the laparoscopic instruments used. Similarly, a study of the instruments, port cannula, and CO_2 gas of 12 patients undergoing staging laparoscopy for pancreatic cancer showed extremely low levels of free-floating tumor cells when compared with the cell content found on the cannula and instruments. In both cases, the authors concluded that the finding of malignant cells on the ports was a result of direct contamination by the instruments and not from dispersion of malignant cells by the CO_2 gas.[15] In a prospective randomized study in rats using a xenograft ovarian cancer model, port-site metastases were found to be significantly higher in the gasless laparoscopy group compared with that in a group that had laparoscopy with a CO_2 pneumoperitoneum.[16]

An article that reviewed all reported cases of laparoscopic port-site metastases in patients with gynecological malignancies revealed that 71% of port-site recurrences were isolated in the tissue-manipulating port.[8] This observation also highlights the importance of the usage of protected tissue retrieval.

Other studies were performed to evaluate if the irrigation of port sites are efficient for the prevention of port-site metastases.[17]

One study evaluated the effect of topical application of oxaliplatin on the development of port-site metastases in an experimental murine model. Intramuscular topical application of oxaliplatin did not decrease the incidence of port-site metastasis, but a tendency of declination was observed.[9]

In another article reported the results of incidence of port-site metastases with the irrigation after completion of the pneumoperitoneum with povidone-iodine, a mixture of taurolidine and heparin or sodium chloride in rat models. No difference in tumor growth at trocar wounds was found between any type of irrigation and controls in both experiments.[18] However, another study has shown a significant reduction in port-site metastases when diluted povidone-iodine was instilled in the peritoneal cavity in a rat model.[16]

Cell adhesion molecules integrin and CD44 play an important role in the development of port-site metastasis. According to an investigative study in a murine model, intraperitoneal injection of antiadhesion molecules can prevent port-site metastasis.[19]

Another study investigated the antiproliferative effect of aspirin and indomethacin on tumor cells *in vitro* and *in vivo* and the potential of these drugs to inhibit port-site and intraperitoneal metastases. Despite promising *in vitro* studies, this study does not suggest any clinical therapeutic value associated the use of aspirin or indomethacin for the prevention of the spread of tumor following the spillage of cells into the peritoneal cavity at laparoscopic surgery.[20]

Several authors have suggested that the presence of ascites may be a contraindication to performing laparoscopy in patients with known or suspected malignancy. Specifically, a review of the literature of all cases of port-site metastases demonstrated the presence of ascites to be significantly associated with the early occurrence of port-site metastases, and another study has demonstrated that patients with ovarian cancer who developed port-site metastases after undergoing laparoscopy tended to have larger amounts of ascitic fluid present at the time of surgery.[21] Specific factors that were shown to be significantly associated with the rapid development of port-site metastases postoperatively included the diagnosis of ovarian malignancy, the presence of ascites and noncurative surgery. The early onset of postoperative chemotherapy has been advocated by several authors that have suggested that patients with a longer duration between laparoscopy and postoperative chemotherapy may be more likely to develop port-site metastases.[22]

A recent study presented clinical evidence to prove that port-site metastases are likely to be due to the hematogenous spread of tumor cells. In this same study, the authors propose

that port-site metastasis could be a likely existence of circulating tumor cells at the time of surgical trauma of penetrating nature, i.e. port site or injection site, which manifest in some patients depending upon their immune response.[23]

DISCUSSION

Proper surgical technique in tumor handling following rigorous oncological principles is the key to good surgery with low recurrences and excellent survival rates. Some unusual cases reported in literature highlight the important role that tumor and host biologic mechanisms play in the development of port-site metastasis.[24] Whether or not patients with malignancy would benefit from a gasless laparoscopy approach remains controversial and further research is needed in this area.[16]

According to the review of literature, the prophylactic measures proposed to avoid the development of port-site metastases after laparoscopy in gynecologic malignancies are as follows:

- Preoperative measures[7,25]
  - Proper patient selection
  - Avoidance of laparoscopic surgery, if ascites is present
  - Compliance guidance and adequate equipment for advanced laparoscopic surgery
  - Knowledge of the principles of prevention in the event of intraoperative discovery of malignant disease
  - Adequate duration of the procedure
  - Proper training of the surgeon
- Technical measures[1,3,25-28]
  - Protected puncture of ovarian cyst
  - Resection without rupture of an ovarian cyst (in case of rupture-aspiration and extensive washing)
  - Minimal tumor manipulation
  - Resection of the tumor with adequate margin
  - Peritoneal lavage with heparin in order to avoid adhesion of free cells or lavage with cytocidal solutions
  - Use of protective bags for tissue retrieval
  - Avoiding CO_2 leaks and sudden desufflations
  - Use of heated and humidified CO_2
  - Exsufflation of the peritoneum before removal of the ports
  - Drainage placement, if needed, before abdomen deflation
  - Irrigation of ports with heparin or povidone-iodine solution before removal
  - Administration systemic or intraperitoneal of methotrexate
  - Closure of all abdominal layers including the peritoneum
  - Early chemotherapy.

CONCLUSION

Laparoscopic port-site metastases are a potential complication of laparoscopy in patients with gynecological malignancies, even in patients with early-stage disease.

Although the etiology is not yet understood, a number of factors are contributory. All efforts should be made to prevent port-site metastases.

The risk of port-site metastases remains low, provided that surgeons rigorously adhere to the principles of oncological surgery.

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