

Port-site Metastasis after Minimally Invasive Surgery for Urological Malignancy: A Review of Literature

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ABSTRACT

Introduction: Port-site metastasis (PSM) has been a concern with the common use of minimally invasive surgery, especially laparoscopy in urologic oncology. We conducted this study to provide a review of PSMs reported after minimally invasive surgery in managing urologic malignancies, possible contributing factors and preventive measures.

Materials and methods: An electronic search of MEDLINE, PubMed, Google Scholar, and HighWire Press with the combined keywords "port-site metastasis" and "urology" was carried out.

Results: A total of 40 articles comprising almost 60 cases addressing PSM after minimally invasive surgery for urological malignancy were identified.

Conclusion: Port-site metastasis in urological laparoscopic surgery is rare and is preventable. Risk can be minimized by applying open surgery oncological procedural principles.

Keywords: Laparoscopy, Port-site metastasis, Robotic, Urological malignancy.

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INTRODUCTION

In recent years, questions have been raised about the oncologic safety of laparoscopic and robotic approach.¹ Even though a large number of specialized centers around the world perform laparoscopy for urologic cancer,^{2,3} local recurrence and PSM still remain a concern.⁴

When PSMs occur, they often do so in the presence of advanced disease, but it is not uncommon for them to occur in isolation.^{5,6}

The first known report of a PSM was by Dobronze et al⁷ in 1978. The authors reported implantation of

malignant ovarian cystic adenoma in penetration sites of the pneumo-needle and trocar. Some specific procedures and tumors have been associated with a higher incidence of PSM or tumor seeding; however, the precise incidence of PSM and its etiology and pathogenesis have not been well defined in urologic laparoscopy.⁸

Since the first successful laparoscopic nephrectomy in 1991,¹ minimally invasive approaches have been increasingly used in tumor resection and lymph node dissection for urologic cancers. This approach has multiple advantages, including decreased length of hospitalization, decreased pain, faster recovery, and improved cosmesis.² Laparoscopic surgery has equivalent oncologic outcomes to open procedures; however, PSM is rare, troubling, and often an unexplained occurrence. The first known occurrence of PSM after a urologic procedure was in 1994, when Stolla et al⁹ reported a case of subcutaneous metastasis of bladder transitional cell carcinoma (TCC) after laparoscopic pelvic lymph node dissection. Since then, about 50 PSMs have been reported in the setting of urologic surgery.¹⁰

Port-site metastasis is a multifactorial phenomenon with an as-yet undetermined incidence. Etiological factors include natural malignant disease behavior, host immune status, local wound factors, laparoscopy-related factors, such as aerosolization of tumor cells (the use of gas, type of gas, insufflation and desufflation, and pneumoperitoneum) and sufficient technical experience of the surgeons and operating team (adequate laparoscopic equipment, skill, minimal handling of the tumor), surgical manipulation, wound contamination during instrument change, organ morcellation, and specimen removal.⁹

MATERIALS AND METHODS

An electronic search of MEDLINE, PubMed, Google Scholar, and HighWire Press of the published literature up to 2017 was carried out using the combined key words "port-site metastasis" and "Urology."

Duplicate references, as well as repeated references to the same data sets, were removed. The articles and case reports directly addressing PSM after minimally invasive surgery for urological malignancy were reviewed.

RESULTS

Table 1¹¹⁻¹⁶ shows the case reports found on MEDLINE, PubMed, Google Scholar, and HighWire Press; search of

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Table 1: Search results on MEDLINE, PubMed, HighWire Press, Google Scholar, and SciELO compiled according to the date of publication

Author	Procedure	Tumor type, stage, and grade	Number of cases
Shimokihara et al ³⁵	Laparoscopic radical nephrectomy	Clear cell RCC—metastatic RCC on histopathological examination	1
Johnson ⁵	Robotic radical cystectomy	TCC	1
De Bruyne et al ¹¹	Prostatic adenocarcinoma	Prostatic adenocarcinoma T3b, Gleason 7	1
Shiozaki et al ¹²	Laparoscopic nephroureterectomy	Rt upper ureter carcinoma T2N0M0 grade III	1
Song et al ¹³	Robot-assisted partial nephrectomy	RCC	1
Javali et al ¹⁴	Laparoscopic radical nephrectomy	Chromophobe RCC T2N0M0	1
Kumar et al ⁶	Laparoscopic radical nephrectomy	1. T2N0M0 RCC 2. T1N0M0 RCC	2
Huang et al ³⁶	Laparoscopic radical cystectomy and pelvic lymph node dissection	NA	1
Wen and Yin ³	Hand-assisted retroperitoneoscopic nephroureterectomy and bladder cuff excision	Left renal urothelial carcinoma	1
Yasuda et al ¹⁵	Laparoscopic nephroureterectomy	Upper urinary tract carcinoma. T2N0M0 grade II>3	1
Greco et al ¹⁶	Laparoscopic partial nephrectomy	Renal clear cell papillary carcinoma pT1a, high grade	1
Spermon and Witjes ³⁷	Laparoscopic retroperitoneal lymph node dissection	Stage IIb nonseminomatous germ cell tumor (histology-yolk sac and teratoma elements)	1
Masterson and Russo ³⁸	Laparoscopic partial nephrectomy	T1bNxM0 RCC	1
Segawa et al ³⁹	Laparoscopic nephroureterectomy and cystectomy	Invasive bladder cancer with bone metastasis. Grade NA	1
Cresswell et al ⁴⁰	Laparoscopic retroperitoneal lymph node dissection	Stage 1 nonseminomatous germ cell tumor. Grade NA	1
Castillo and Vitagliano ⁴¹	Laparoscopic retroperitoneal lymph node dissection	Mixed germ cell tumor T3N0M0	1
Muntener et al ⁴²	(A) Laparoscopic radical nephroureterectomy (B) Laparoscopic partial nephrectomy	Upper tract TCC. Stage T1, high grade RCC T1N0M0G3	1 1
Manabe et al ⁴³	Laparoscopic nephroureterectomy	Upper tract TCC without distant metastases	1
Dhobada et al ⁴⁴	Laparoscopic nephrectomy	RCC T2N0M0G3	1
Kobori et al ⁴⁵	Laparoscopic nephrectomy	Papillary adenocarcinoma of pelvis. Stage and grade unavailable	1
El-Tabey and Shoma ⁴⁶	Laparoscopic cystectomy (robot assisted)	Bladder TCC T3bN0M0G3	1
Porpiglea et al ⁴⁷	Laparoscopic adrenalectomy	Adrenal metastasis from nonsmall-cell lung carcinoma	1
Chueh et al ⁴⁸	Laparoscopic bilateral nephroureterectomy	Grade II renal TCC with pelvic muscular invasion and bladder metastasis	1
Naderi et al ⁴⁹	Laparoscopic nephroureterectomy	Kidney TCC cT1N0M0	1
Micali et al ⁸	(A) Laparoscopic retroperitoneal lymph node dissection (B) Laparoscopic simple nephrectomy (C) Laparoscopic nephroureterectomy (D) Laparoscopic adrenalectomy (E) Laparoscopic pelvic lymph node dissection	Nonseminomatous germ cell tumor Incidental TCC in each instance—pT1/G2; pT1/G3; pT2/G3; NA pT3/G3 Penile cancer	1 4 3 4 1
Iwamura et al ⁵⁰	(A) Laparoscopic retroperitoneal nephrectomy (B) Laparoscopic Adrenalectomy (C) Laparoscopic pelvic lymph node dissection	RCC T1bN0M0 Lung metastases pT4/G3 (3); Adrenocortical Ca-grade and stage NA (1) Squamous penile Ca	1 4 1
Matsui et al ⁵¹	Laparoscopic retroperitoneal nephroureterectomy	SCC pT3N0M0	1
Saraiva et al ⁵²	Laparoscopic adrenalectomy	Metastatic melanoma of adrenal gland. Grade unavailable	1
Rassweiler et al ¹⁰	(A) Laparoscopic adrenalectomy (B) Laparoscopic retroperitoneal lymph node dissection	Small-cell lung carcinoma adrenal metastasis NA	1
Chen et al ⁵³	Laparoscopic nephrectomy (hand-assisted)	RCC T2N0M0	1
Wang et al ⁵⁴	Laparoscopic cystectomy	Incidental finding of SCC in ovarian dermoid cyst	1
Castilho et al ⁵⁵	Laparoscopic nephrectomy	RCC T1N0G2	1

(Cont'd...)

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Author	Procedure	Tumor type, stage, and grade	Number of cases
Landman and Clayman ⁵⁶	Laparoscopic nephrectomy	RCC T1N0G2	1
Fentie et al ⁵⁷	Laparoscopic nephrectomy	RCC T3N0G4	1
Otani et al ⁵⁸	Laparoscopic nephrectomy	Incidental finding of TCC, G3 within tuberculous atrophic kidney	1
Ahmed et al ⁵⁹	Laparoscopic nephrectomy	Kidney TCC T3G3-G4	1
Altieri et al ⁶⁰	Laparoscopic pelvic lymph node dissection	Bladder TCC T3G2	1
Bangma et al ⁶¹	Laparoscopic pelvic lymph node dissection	PCa T3N1	1
Andersen et al ⁶²	Transperitoneal laparoscopic bladder biopsy	Bladder TCC T1G2	1
Stolla et al ¹⁷	Laparoscopic pelvic lymph node dissection	Bladder TCC pT3G2	1

the published literature up to 2017 recovered 40 articles comprising almost 60 cases for the words “port-site metastasis” and “urology.”

Etiological factors have been categorized into three main categories: Tumor-related, wound-related, and surgical technique-related factors. Surgical technique-related factors have been categorized into two main categories: Manipulation is the principal factor acting in tumor dissemination. Extraction of the surgical specimen is determined by the surgeon. The possible preventive measure has been categorized into two main categories: Active measures and measures for reducing the risk of laparoscopic PSM in urological surgery.

DISCUSSION

In urothelial cancers, port-site recurrence has been reported in a total of 13 cases, as reviewed by Micali et al⁸ in an international survey of 19 urologic laparoscopic centers performing a total of 18,750 laparoscopic procedures for urologic malignancies. The incidence was 0.12% (13 of 10,912). Majority of port-site recurrences reported in this survey represented TCC. Of these 13 cases, there were 4 metastatic adrenal carcinomas, 4 urothelial carcinomas, 3 nephroureterectomy cases of upper urothelial carcinoma, 1 case of retroperitoneal lymph node resection for testicular cancer, and 1 case of lymph node resection for penile cancer. Port-site metastasis after laparoscopic extirpative surgery for renal-cell carcinoma (RCC) is extremely rare. Micali et al⁸ identified no instances of port-site recurrence in 2,604 cases of laparoscopic radical nephrectomy for RCC.

Port-site metastasis is a rare complication of laparoscopic intervention in urologic malignancies. Of the more than 50 reported cases of PSM in the urologic oncology literature, only 10 have occurred after surgery for RCC.¹³ First case of camera PSM after robot-assisted partial nephrectomy was reported by Song et al.¹² The estimated incidence of PSM for robotic cystectomy is <0.5%. This is higher than the overall PSM rate for urologic cancers (0.09%).⁵ The incidence of tumor seeding in general laparoscopic surgery ranges from 0.8 to 21%.^{8,9}

Tsivian and Sidi⁹ alone reported nine cases of PSMs after urologic laparoscopy, and Rassweiler et al¹⁰ published eight local recurrences observed in 1,098 laparoscopic procedures for urologic malignancies. Single case of PSM after prostatic adenocarcinoma has been reported by De Bruyne et al¹¹ and usually associated with poor prognosis.

For port-site tumor recurrence to occur, several conditions must be present. There must be release of viable cancer cells from the tumor. There must be a mechanism by which these tumor cells are transported to the port site. Lastly, implantation of the tumor cells at the port site and subsequent growth must occur. It has been hypothesized that several factors may aid in this process, namely (1) the biologic aggressiveness of the tumor, (2) local wound factors, (3) host immune responses, and (4) laparoscopic surgical techniques.¹³

Biological aggressiveness of the tumor, represented by grade and stage, plays a decisive role in possible tumor seeding determination, explaining why grades II and III TCCs represent the majority of PSMs in urological procedures.¹³

Local wound factors help in the implantation and proliferation of tumor cells at the port site.¹³ Cancer cells have high proliferation potential within healing skin incisions or intestinal anastomosis.¹⁷ Tumor cells implant more easily and successfully during early wound healing, adhering to fibrin deposited at the site of surgical wound as a part of normal healing.¹⁸ The presence of growth factors at the wound site promotes the survival and propagation of these cancer cells. As suggested by few animal studies, the port-site incision is more conducive than the laparotomy incision for tumor seeding.¹⁹ Aoki et al²⁰ suggest that repair of the peritoneum at the trocar entry site may reduce the risk of tumor implantation and subsequent recurrence.

Immune depression of the peritoneum occurs during laparoscopic insufflation as demonstrated by macrophage function alteration, resulting in tumor recurrence and metastasis.²¹⁻²⁵ Overall, immune function is diminished

in the perioperative period because of factors like anesthetic agents, opioids, surgical trauma, blood transfusions, temperature changes, pain, and psychological stress.²³ Some studies showed a better preservation of cell-mediated immunity after laparoscopic surgery.³⁴ However, these benefits are not applied to the peritoneal level, possibly related to the hypoxic environment due to pneumoperitoneum pressure and secondary effect of the carbon dioxide in the peritoneal macrophage response.³⁴

Factors related to laparoscopic surgical technique contribute to port-site recurrence.²⁶ These include the use of pneumoperitoneum, trocar site contamination, organ and tumor morcellation, and the method of specimen retrieval. The direct dissemination of tumor cells from contaminated material or from extraction with an open bag has been reported.^{5,6,23} Several studies have suggested that CO₂ insufflation has an impact on the movement of tumor cells within the peritoneal cavity and subsequent implantation at port sites.^{12,27} Wittich et al²⁶ found that aerosolization of tumor cells occurs during CO₂ laparoscopy. According to the chimney effect hypothesis,²⁸ the continued leakage of gas around and through the trocar results in a cumulative buildup of tumor cells at the port site, thus promoting PSM. Tseng et al²⁸ demonstrated that tissue trauma at trocar sites, combined with leakage of CO₂, leads to enhanced tumor growth at these sites. In addition to the potential effects of pneumoperitoneum on the transfer of tumor cells, it has also been proposed that malignant cells may be transferred from the tumor to the port site by the aggressive manipulation of the tumor with laparoscopic instruments and the subsequent withdrawal and reinsertion of these contaminated instruments. Hewett et al²⁷ were the first to demonstrate this concept in a pig model. The importance of minimizing tumor manipulation is first detailed by Greco et al.¹⁶ Irrigating port sites with povidone iodine may lower the risk of port-site recurrence.²⁹ Local application of cytotoxic agents, such as methotrexate and cyclophosphamide, is also found to be effective.³⁰ Javali¹⁴ suggested that positron emission tomography and computed tomography could be a useful adjunct in diagnosing port-site recurrence especially in cases presenting within a short span of time following laparoscopic surgery for urological malignancy, wherein induration due to surgical factors at scar site may be confused with port-site recurrence.

Measures suggested in the Literature to prevent Urologic Port-site Metastasis³¹

- Avoidance of laparoscopic surgery if ascites is present^{9,31}
- Avoidance of gas leakage along the trocar³¹
- Avoidance of tumor-boundary violation

- Use of an impermeable bag if morcellation is done¹⁵
- Use of a bag for intact specimen removal
- Placement of drain if needed before abdominal deflation³²
- Povidone-iodine irrigation of the laparoscopic instruments, trocar, and port-site wounds.²⁹ Local application of cytotoxic agents, such as methotrexate and cyclophosphamide, is also found to be effective³⁰
- Suturing all port sites ≥ 10 mm^{9,31}

Burns et al³³ demonstrated on an animal model that port-site tumor implantation was significantly increased when only skin was closed compared with closure of all three layers. The authors proved that closure technique may influence the rate of port-site tumor implantation.

CONCLUSION

Port-site metastasis in urological laparoscopic surgery is rare and is preventable. Risk can be minimized by applying open surgery oncological procedural principles.^{31,34-62}

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