



Trends in port-site metastasis after laparoscopic resection of incidental gallbladder cancer: A systematic review

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Background. The risk of port-site metastasis after laparoscopic removal of incidental gallbladder cancer was previously estimated to be 14–30%. The present study was designed to determine the incidence of port-site metastasis in incidental gallbladder cancer in the modern era (2000–2014) versus the historic era (1991–1999). We also investigated the site of port-site metastasis.

Methods. Using PRISMA, a systematic review was conducted to identify papers that addressed the development of port-site metastasis after laparoscopic resection of incidental gallbladder cancer. Studies that described cancer-specific outcomes in ≥ 5 patients were included. A validated quality appraisal tool was used, and a weighted estimate of the incidence of port-site metastasis was calculated.

Results. Based on data extracted from 27 papers that met inclusion criteria, the incidence of port-site metastasis in incidental gallbladder cancer has decreased from 18.6% prior to 2000 (95% confidence interval 15.3–21.9%, $n = 7$) to 10.3% since then (95% confidence interval 7.9–12.7%, $n = 20$) ($P < .001$). The extraction site is at significantly higher risk than nonextraction sites.

Conclusion. The incidence of port-site metastasis in incidental gallbladder cancer has decreased but remains high relative to other primary tumors. Any preoperative finding that raises the suspicion of gallbladder cancer should prompt further investigation and referral to a hepato-pancreato-biliary specialist. (*Surgery* 2017;161:618-27.)

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THE LANDSCAPE OF OPERATIVE MANAGEMENT of gallbladder disease was significantly changed after the advent of laparoscopy. In the United States, the proportion of cholecystectomies performed

laparoscopically increased from 2.5% to 76.6% for elective cases and from 0.7% to 67.5% for urgent cases between the years 1988 and 1997.¹ Though some surgeons expressed concerns about insufficiently mature and objective data regarding complications and unexpected sequelae, this rapid adoption was fuelled largely by improved patient-reported outcomes.²

Shortly after the initial application of the laparoscopic approach to cancer resection in the 1990s, there were an alarming number of early reports of recurrence within an access port wound, coined port-site metastasis (PSM). This pattern of recurrence has now been observed in gastrointestinal, gynecologic, urologic, and thoracic malignancies.³

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Reports of PSM after laparoscopic resection of gallbladder cancer seemed to be especially frequent, prompting a literature review by Paolucci⁴ in which he attempted to estimate the incidence of PSM in gallbladder cancer case series and reports published up to January 2000. His review of 4 international surveys plus 75 case reports concluded that PSM occurred in 14–30% of patients after laparoscopic cholecystectomy for presumed benign conditions, in whom gallbladder cancer was discovered postoperatively (so-called incidental gallbladder cancer [IGBCA]). The incidence of IGBCA in gallbladders removed laparoscopically is in turn estimated to be 0.2–3.3%.⁵

In the United States, approximately 3,700 new cases of gallbladder cancer are documented annually, 50% of which are diagnosed as IGBCA after laparoscopic cholecystectomy.^{6,7} This represents a large cohort of patients who are potentially at risk for PSM. This is important because the development of PSM is an indicator of poor prognosis and may contribute to inferior outcomes. In a study of 113 patients with IGBCA, median survival in patients with T2/T3 disease who developed PSM was 17 months, compared to 42 months in similar patients without PSM.⁸ The presence of PSM may also contribute to the burden of intractable symptoms in such patients.

No cases of PSM after resection of IGBCA had been reported prior to 1991. Paolucci's review⁴ of cases that had been described in papers published between 1991 and 1999 has been frequently cited and was important in raising awareness of the high incidence of PSM in gallbladder cancer, possibly precipitating changes in operative technique (eg, routine use of a specimen retrieval bag, avoidance of bile spillage). It was not clear whether the incidence of PSM subsequently declined.

In the present systematic review, we sought to determine whether the incidence of PSM has changed from the *historic era* (1991–1999) to the *modern era* (2000–2014). We also examined the relative incidence of extraction and nonextraction site PSMs, a comparison that might provide a mechanistic clue to inform the development of future strategies to reduce the risk of PSM.

METHODS

With the collaboration of a Health Sciences library information specialist (M.E.), search strategies were designed to retrieve all published articles and abstracts related to wound recurrence after cancer resection. Five electronic databases were searched from inception until August 14, 2014, limited to human studies published in English: Cochrane

Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Embase, Medline, and Medline In-Process. The detailed search strategy can be found online in [Supplementary Figure 1](#).

The search strategy was validated with 10 test articles that were independently identified while manually surveying the literature. The titles and abstracts yielded by the search were screened by 2 independent reviewers (D.B.R., T.R.C.), and only those related to wound recurrence in gallbladder cancer were retained. The full-text manuscripts of retained studies were obtained for comprehensive review. If an article cited another publication that described wound recurrence in gallbladder cancer that had not been captured by our search strategy, we included the latter for analysis if it met inclusion criteria. If only the abstract of a study was available, it was retained if the relevant data were provided in the abstract itself. Although the search was limited to English language publications, some non-English articles had English abstracts and were captured by our search strategy; if the relevant data were provided in English, the study was retained.

We sought to compare the incidence of PSM after laparoscopic resection of unsuspected gallbladder cancer reported in papers published in the historic era (1991–1999) and the modern era (2000–2014). For this purpose, the inclusion criteria were English language papers that reported the presence or absence of PSM following a minimum of 5 laparoscopic cholecystectomies in which the gallbladder was found to harbor an unsuspected adenocarcinoma. Papers that explicitly reported no PSM after laparoscopic cholecystectomy in the setting of IGBCA were included in the analysis of PSM incidence. Multiple publications by the same author(s) were closely reviewed to eliminate duplicate cases. Individual cases that were converted from laparoscopic to open resections were excluded from subsequent analysis. Within each manuscript, only cases of unsuspected gallbladder cancer were retained for estimating the incidence of PSM.

In addition to reporting a raw, pooled incidence of PSM in IGBCA, to compensate for the different levels of quality among manuscripts, we used a validated quality appraisal tool for case series.⁹ We included 18 of the 20 elements of the checklist for our analysis and excluded 2 that were not relevant to case series reporting the incidence of PSM in IGBCA. This quality appraisal tool does not suggest a cut-off to distinguish high- from low-quality papers; interpretation of results is left to the tool user. Therefore, we separated the 18 elements

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