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REVIEW ARTICLE

Incidence and prognostic significance of positive peritoneal lavage in colorectal cancer

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Abstract
Purpose The significance of peritoneal lavage cytology as a prognostic marker has been examined in various types of cancer. However, the meaning of positive peritoneal lavage cytology in colorectal cancer is still controversial. The aim of this review is to evaluate the prognostic significance of positive peritoneal lavage cytology in colorectal cancer.
Methods An English literature search was performed on all studies published between 1998 and 2014 that compared the detection of peritoneal free cancer cells with survival or recurrence.
Results Eighteen articles met the inclusion criteria. All studies employed one (or more) of the three techniques used to detect free cancer cells in the peritoneal cavity: (1) conventional cytology, (2) immunocytochemistry or (3) polymerase chain reaction. The incidence of positive peritoneal lavage cytology ranged from 2.2 to 47.2 % across the studies. The factors correlated with positive peritoneal lavage cytology were tumor penetration and metastases (lymph node, liver and peritoneum). In nine studies, positive lavage findings were associated with a worse survival, and it was associated with increased recurrence in 13 studies.
Conclusion Positive peritoneal lavage cytology seems to be an indicator of a poor prognosis in colorectal cancer patients. Further studies are needed to clarify the prognostic impact of peritoneal lavage cytology, by comparing the different methods used for the collection of the peritoneal lavage.

Keywords Peritoneal lavage · Colorectal cancer · Survival · Recurrence

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Purpose

Colorectal cancer is the third most commonly diagnosed cancer in males and the second most common in females. Each year, more than 1.2 million new cases of colorectal cancer are diagnosed worldwide [1]. During the past three decades substantial developments and advances have been made in the screening, diagnosis, staging and treatment of this neoplastic condition. However, worldwide, the disease-specific mortality rate of colorectal cancer is still nearly 33 % [1].

Complete removal of the tumor is the most effective primary treatment for carcinoma of the colon and rectum. However, recurrence after curative resection of an apparently localized tumor is common. The most common mechanisms of metastasis in large-bowel cancer are lymphatic spread to regional lymph nodes and hematogenous spread to the liver via the portal vein, and these are thought to occur due to undetected local, peritoneal, lymphatic or hematogenous micrometastases present prior to surgical resection or due to inadequate tumor resection [2, 3].

Local recurrence may be the result of inadequate local excision or unresected lymphatic permeation [4]. It is widely accepted that the liver, lung, pelvis and peritoneum are the most common sites of recurrence and metastasis. For liver or lung metastases, hepatectomy or pulmonary resection have been aggressively conducted. For local

recurrence, aggressive surgical resection may be beneficial [5]. Peritoneal recurrence is less common than recurrence to other sites, and therefore, is prognostically less important than other sites of recurrence [5]. Moreover, peritoneal recurrence is often diagnosed at the terminal stage because there is no effective treatment for peritoneal metastases [6, 7]. Therefore, it is of great importance to predict peritoneal recurrence at an early stage and to adopt a strategy to prevent its progression.

Furthermore, despite recent advances in the knowledge of various clinical, biological and pathological features related to the prognosis of colorectal carcinoma, the degree of tumor penetration into the bowel wall and lymph node involvement have been regarded as the main prognostic factors for patients with colorectal cancer, and these factors are used for prognostic classification in both Dukes staging and TNM classification.

The significance of peritoneal cytology as a prognostic marker has been examined in various types of cancer. The detection of free cancer cells by peritoneal cytology at the time of surgery has been reported to be one of the most accurate prognostic factors. It has been especially well studied in gastric cancer [8–10]. According to the TNM classification, gastric cancer with positive cytology is classified as Stage IV [11]. Peritoneal cytology has also been shown to be a useful prognostic marker for pancreatic, esophagogastric, lung and gynecological malignancies [12–18]. However, the meaning of positive peritoneal cytology in colorectal cancer is still controversial [19] and examining the peritoneal cytology is not presently an established standard procedure. Therefore, cytological evaluation of peritoneal fluid is not routinely performed, and peritoneal fluid has not been considered a reliable clinical indicator. In fact, the presence of free cancer cells in the peritoneal cavity does not currently influence the decision regarding the use of adjuvant therapy.

The aim of this review was to evaluate the prognostic significance of positive peritoneal lavage cytology in colorectal cancer, and to compare the different techniques used for the detection of exfoliated cancer cells, in terms of the ability to identify patients with a worse prognostic risk following curative colorectal cancer resection.

Methods

Study selection, eligibility and exclusion criteria

To investigate the association between the detection of free peritoneal cancer cells with survival or recurrences following the resection of colorectal cancer, a PubMed MEDLINE search was performed on all clinical studies published from 1998 to 2014. The following keywords were used for the search: peritoneal cytology/peritoneal lavage cytology/peritoneal washing cytology and colorectal cancer/recurrence/survival/prognosis. Only human studies were considered for inclusion. The "related articles" function was used to expand the search from each relevant study identified, and further studies were identified from manual searches of reference lists. Non-English language articles, case reports, letters, commentaries, conference proceedings and abstracts were excluded. In order to be included in the analysis, studies had to: (1) Compare prognostic outcomes (survival or/and recurrences) with the presence or absence of free peritoneal cancer cells in patients undergoing colorectal cancer surgery. Studies which involved patients undergoing non-curative resection were only included in the analysis of outcomes for patients undergoing curative surgery alone were able to be discerned from the results; (2) clearly document whether the detection of free cancer cells was done pre- or post-resection; (3) contain a previously unreported patient group. When more than one study was reported by the same institution with overlapping time periods, the more recent publication was included in the analysis; (4) studies using any validated method for the detection of free cancer cells were included. Studies were excluded from the analysis if: (1) the outcomes of interest were not reported or it was impossible to calculate these from the published results, focused solely on the method used; (2) lavage cytology was not included in the analysis of peritoneal cytology; (3) it was impossible to separate the results for colorectal cancer from those for other malignancies.

Data extraction

The following data from each study were extracted: (1) baseline data: first author, year of publication, location of study, number of patients examined, male/female ratio, mean age, cancer stages included, length of follow-up, (2) specific outcome data: number of positive results and associated or non-associated clinicopathological parameters, method used for free cancer cell detection in peritoneal cavity, timing of lavage fluid collection (pre- and/or post-tumor resection), survival (overall or cancer-specific survival), recurrence (overall, peritoneal/local and/or distant recurrence), association between positive peritoneal lavage cytology and the outcomes.

Results

Studies selected

After application of the inclusion and exclusion criteria, the literature search identified 18 studies that compared the

Table 1 A summary of the characteristics of the studies and the method(s) used for cancer cell detection

References	Location	Patients *n* (M:F)	Method of tumor cell detection
Nishikawa et al. [20]	Japan	410 (232:178)	Conventional cytology (Pap)
Noura et al. [21]	Japan	697 (427:270)	Conventional cytology (Pap, Giemsa)
Fujii et al. [22]	Japan	298 (168:130)	Conventional cytology (Pap, Giemsa)
Yamamoto et al. [23]	Japan	189 (96:93)	Conventional cytology (Pap, Giemsa)
Katoh et al. [24]	Japan	226 (127:99)	Conventional cytology (Pap, PAS)
Hase et al. [25]	Japan	140 (76:64)	Conventional cytology (Pap, Giemsa, PAS, Alcian blue)
Homma et al. [19]	Japan	771 (411:360)	Conventional cytology (Pap, PAS, Giemsa)
Gozalan et al. [26]	Turkey	88 (46:42)	Conventional cytology (Pap, Giemsa)
Kanellos et al. [27]	Greece	98 (44:51)	Conventional cytology (Pap, Giemsa)
Bosch et al. [28]	Switzerland	53 (24:29)	Conventional cytology (Pap)/immunostaining (Ber-Ep4, Ks20.8)
Wind et al. [3]	France	88 (38:50)	Conventional cytology (Pap, Giemsa)
Temesi et al. [29]	Hungary	145 (95:50)	Conventional cytology (H&E)
Vogel et al. [9]	Germany	90 (unknown)	Conventional cytology (H&E), immunocytology (anti-HEA 125)
Kamiyama et al. [30]	Japan	51 (35:16)	Quantitative methylation-specific PCR (CDH1, CDKN2A(p16), MGMT, APC)
Hara et al. [31]	Japan	126 (71:55)	qRT-PCR (CEA, CK20)
Lloyd et al. [32]	Australia	125 (unknown)	Immunobead RT-PCR (CEA, LAMγ2, EphB4, MAT, CK20)
Lee et al. [33]	Korea	189 (120:69)	Conventional cytology (Pap, Giemsa, H&E), immunohistochemistry (CEA, calretinin, CA19-9)
Rossi Del Monte et al. [34]	Italy	48 (22:26)	Cytology (Pap, Giemsa), immunofluorescence (EpCAM/CD326, CEA), qRT-PCR (CEA,CK20)

prognostic outcomes (survival and/or recurrences) with the presence or absence of free cancer cells detected by any of the three methods used (conventional cytology, immunocytochemistry or polymerase chain reaction (PCR)), either pre-resection or pre- and post-resection of colorectal cancer.

Methods used to detect free cancer cells, and the incidence of positive peritoneal lavage

In the 18 studies, the incidence of positive peritoneal lavage cytology ranged from 2.2 to 47.2 % [3, 9, 20–34]. There were variations in the methods used to detect free cancer cells, the timing, volume, type of lavage fluid and site of fluid collection.

With regard to the methods used for the detection of free cancer cells, all studies employed one (or more) of three techniques, as summarized in Table 1. In most studies, conventional cytology was performed after staining with Papanicolaou and Giemsa stains [3, 21–23, 26, 27, 34]. In some studies, conventional cytology studies were performed after staining with periodic acid-Schiff (PAS) and/or Alcian blue stain, in addition to the Papanicolaou and Giemsa staining [19, 25]. In some studies, only staining with hematoxylin-eosin (H&E) to identify tumor cells was performed. Various staining methods were used to detect tumor cells. If at least one tumor cell was identified, the cytology was considered positive. In conventional cytology, the detection rate of positive peritoneal lavage ranged from 0 to 35.5 %. One study revealed no detection of positive peritoneal lavage cytology using conventional cytology, whereas positive findings were obtained by immunofluorescence (17 %) and qRT-RCR (42 %) [34]. No significant difference in the incidence of peritoneal lavage cytology was observed according to the type of staining performed.

In some studies, conventional peritoneal cytology was described as the preferred method for the detection of cancer cells, because it is a universal and inexpensive method that can be easily performed at any institution worldwide [20, 21, 23, 25]. Immunocytochemistry with various monoclonal antibodies evaluating Ber-EP4, Ks20.8, HEA125, CEA, CA19-9, calretinin and EpCAM/CD326 has been proposed to increase the sensitivity of cytology studies [9, 28, 33, 34]. Using this technique, the positive rate of peritoneal lavage cytology ranged from 5.2 to 47.2 %. Molecular methods, such as RT-PCR, can also be applied for the detection of messenger RNA in the lavage fluid, using CEA, CK20, LAMγ2, EphB4 and MAT as the markers [31, 32, 34]. One study used methylation-specific PCR to detect abnormal methylation of specific colorectal cancer-related genes [CDH1, CDKN2A(p16), MGMT, APC] [30]. The detection rate of positive peritoneal lavage cytology used this molecular technique ranged from 28.8 to 42 %.

The detection rates of free cancer cells in peritoneal lavage cytology using either immunocytochemistry or RT-PCR were relatively high. However, there has been some

Table 2 The methods used for lavage collection

References	Lavage	Site of lavage fluid	Timing of lavage (pre-/post-resection)
Nishikawa et al. [20]	200 ml saline	Douglas cavity	Pre-resection
Noura et al. [21]	100 ml saline (37 °C)	Douglas cavity	pre-resection
Fujii et al. [22]	200 ml saline and 500 U of heparin	N/A	Pre-resection
Yamamoto et al. [23]	50 ml saline	The abdominal cavity over the tumor site	Pre-resection
Katoh et al. [24]	100 ml warm saline	The abdominal cavity over the tumor site	Pre-resection
Hase et al. [25]	100 ml saline	Peritoneal cavity	Pre- and post-resection
Homma et al. [19]	20 ml saline	Douglas cavity	Pre-resection
Gozalan [26]	50 ml saline	The abdominal cavity over the tumor site	Pre-resection
Kanellos et al. [27]	100 ml saline	The abdominal cavity over the tumor site	Pre-resection
Bosch et al. [28]	700 ml Ringer lactate	N/A	Pre- and post-resection
Wind et al. [3]	50 ml saline	Into the paracolonic gutters and pelvis	Pre-resection
Temesi et al. [29]	50 ml saline	Adjacent to the tumor or Douglas cavity	Pre- and post-resection
Vogel et al. [9]	100 ml warm saline	The abdominal cavity over the tumor site	Pre-resection
Kamiyama et al. [30]	50 ml saline	Douglas cavity	Pre-resection
Hara et al. [31]	100 ml saline	Douglas cavity and paracolon cavity near the tumor	Pre-resection
Lloyd et al. [32]	50 ml saline	The tumor bed and the pelvic floor	Pre- and post-resection
Lee et al. [33]	1000 ml saline	Peritoneal cavity	Pre-resection
Rossi Del Monte et al. [34]	250 ml saline	The abdominal cavity over the tumor site	Pre-resection

criticism about the cost and the complexity of the immunocytochemistry and RT-PCR techniques. According to Rekhraj et al. [2] "The increased sensitivity offered by immunocytology and PCR techniques must be balanced with the increased cost and complexity associated with these, and perhaps these techniques may play a greater role when the use of peritoneal free cancer cells detection becomes more accepted in colorectal cancer resection". The target genes and antigens tested in immunochemical and molecular techniques varied among the studies, so further studies are needed to identify which target genes and/or antigens in peritoneal lavage cytology could more accurately predict a worse prognosis in colorectal cancer patients.

In Asian studies, the incidence of positive peritoneal lavage cytology in conventional cytology studies ranged from 2.2 to 15.7 % [20–25, 33], while in other studies, it ranged from 14.7 to 35.5 % [3, 9, 26–29]. Therefore, the detection rates of free cancer cells in peritoneal lavage cytology in Asian studies were relatively low, which may have been influenced by the differences in the diagnostic criteria in different countries, or possibly ethnic variations in the course of colorectal cancer.

In all studies, the collection of lavage fluid was performed immediately after the laparotomy (pre-resection), while in four studies, it was also collected after the resection of the tumor (post-resection) (Table 2). Some studies found cases where positive peritoneal lavage cytology was detected only in post-resection samples, but not in pre-resection samples, reflecting the fact that a problem with performing a cytology study after resection might be the possibility of the outflow of cancer cells from the serosa, colon lumen or the lymphatics cut, meaning that the type of surgery performed might influence the results [35].

The volume of lavage fluid instilled varied from 50 to 1,000 ml, but most studies proposed that a small amount of liquid (50–200 ml) as the most effective (Table 2). One study used Ringer's lactate as lavage fluid, while the remaining studies used saline solution (NaCl 0.9 %). And in most studies, liquid was instilled into the peritoneal cavity over the tumor site and/or the Douglas cavity, because it was most likely that free cancer cells would be more effectively detected in that particular area. Some investigators aspirated the full volume and others aspirated only a certain amount. However, no evident association with the

incidence of positive peritoneal cytology was observed based on the volume aspirated.

Factors correlated with positive peritoneal lavage fluid

The factors that were significantly correlated or were not correlated with positive peritoneal lavage cytology are summarized in Table 3. In all analyses, the associations between the factors were considered to be significant for values of $P < 0.05$. Overall, the factors most commonly associated with positive peritoneal lavage cytology were the depth of invasion and presence of metastases (lymph node, liver, and peritoneum). Although no correlation has been found between the presence of free tumor cells in the peritoneal cavity and the grade of colon cancer, a cytological examination was more likely to be positive in patients with liver metastases, peritoneal metastases or serosal involvement. No differences in the factors associated with positivity were found between conventional peritoneal lavage cytology and molecular techniques. No significant association was found between the age, gender or tumor site and peritoneal lavage fluid findings, while the association between the histological grade, lymphatic invasion, venous invasion and peritoneal lavage cytology is still controversial.

Some studies showed positive peritoneal lavage cytology in T2 patients [9, 19, 22, 26, 27]. There are two plausible explanations for the presence of free cancer cells in patients without microscopic evidence of serosal involvement. One possibility is that the histological examination of the depth of invasion is not always performed at a spot where the cancer infiltration is the most profound. The other possibility is that cancer cells may be shed through the lymphatics, from the metastatic lymph nodes or through the lymphatic canals via the omentum and the peritoneum [19].

The survival rates according to the peritoneal cytology findings

Among the 18 studies, 14 reported the relationship between positive peritoneal lavage cytology and survival, as summarized in Table 4. Nine studies revealed that positive peritoneal lavage cytology was predictive of a worse survival in colorectal cancer patients, while five studies did not show such an association. All studies using RT-PCR showed the association of positive peritoneal lavage cytology with a worse prognosis. Rossi Del Monte et al. used a combination of immunofluorescence and qRT-PCR, and demonstrated that positive qRT-PCR findings, but not immunofluorescence findings, were significantly associated with a worse prognosis. Furthermore, Lloyd et al., using immunobead RT-PCR, showed that the presence of free marker-positive cells in post-resection, but not pre-resection, peritoneal lavage fluid was associated with significantly worse survival. Only one of three studies using the immunocytochemistry technique showed the effectiveness of positive peritoneal lavage cytology in predicting a worse survival. Concerning the conventional cytology alone, four of eight studies showed the predictive value of positive peritoneal lavage cytology on the survival. However, three of the four Japanese studies revealed an association of positive peritoneal lavage cytology with a worse survival. Although the incidence of positive peritoneal lavage cytology was lower in Japan, it was more strongly associated with a worse survival, which means that it has a lower sensitivity but a higher specificity.

The influence of positive peritoneal lavage fluid on the development of recurrences

The viability of exfoliated cancer cells has been confirmed in a previous study [36]. These viable exfoliated cancer cells may implant and proliferate in the peritoneum, which results in peritoneal dissemination of the tumor. The influence of positive peritoneal lavage cytology on the development of recurrences (local, peritoneal, liver and lung) was investigated in most of the studies included in this review (17 of 18 studies, Table 4). Thirteen studies demonstrated an association between positive peritoneal lavage cytology and recurrences. The detection of free tumor cells in the peritoneal lavage was associated with a higher recurrence and may lead to the identification of patients who are more likely to develop recurrence. All studies using the RT-PCR technique showed the association of positive peritoneal lavage cytology with recurrences, and consequently, with worse survival rates.

As noted above, 13 studies demonstrated an association between recurrence and positive peritoneal lavage cytology, but only five studies using the conventional cytology methods described the association between positive peritoneal lavage cytology and higher local/peritoneal recurrence (Table 4). Peritoneal dissemination is considered to result from two steps: first, the cancer cells shed from the serosal surface of the primary tumor and are transported into the peritoneal cavity; then, these free cancer cells in the peritoneum preferentially attach to other sites, such as the omentum and mesenterium, and subsequently grow and disseminate into the peritoneal cavity [31]. Therefore, the low incidence of peritoneal recurrence in colorectal cancer patients may be due to either the low incidence and limited exfoliation of free cancer cells from the primary tumors, or to the low metastatic potential of colorectal cancer cells in the peritoneal cavity [31]. The abundant free tumor cells detectable by the low-sensitivity conventional cytology methods may lead, at least in part, to peritoneal recurrence, but the

Table 3 The factors correlated and not correlated with positive lavage findings

References	Positive rate	Factor(s) correlated with positive lavage	Factor(s) not correlated with positive lavage
Nishikawa et al. [20]	31 (7.6 %)	Macroscopic peritoneal dissemination, depth of invasion histological high grade, non-R0 resection	Age, gender, tumor site
Noura et al. [21]	15 (2.2 %)	Depth of invasion, positive lymph nodes, stage, lymphatic invasion, venous invasion	Age, gender, tumor size, tumor site, histological grade
Fujii et al. [22]	18 (6.0 %)	Macroscopic peritoneal dissemination, hepatic metastasis, non-R0 resection	Histological grade, invasion depth, lymph node metastasis, lymphatic invasion, venous invasion
Yamamoto et al. [23]	11 (5.8 %)	None	Gender, age, tumor site, histological grade, pTNM classification
Katoh et al. [24]	33 (14.6 %)	Positive lymph nodes, elevated preoperative CA19-9, macroscopic peritoneal dissemination	Gender, age, tumor site, histological grade, pTNM classification, lymphatic invasion, venous invasion, preoperative CEA, distant metastasis.
Hase et al. [25]	22 (15.7 %) (both 10 (7.1 %), pre 11(7.9 %), post 1 (0.7 %)	Macroscopic peritoneal dissemination, liver metastasis, 20 ml < ascites, macroscopic type, depth of invasion, circumferential involvement, lymphatic invasion,	Tumor site
Homma et al. [19]	21 (2.7 %)	Depth of invasion, venous invasion	Age, gender, tumor site, histological grade, stage, lymphatic invasion
Gozalan et al. [26]	13 (14.7 %)	Macroscopic peritoneal dissemination, ascites, multi: necrosis, depth of invasion, histological high grade	Gender, age, tumor site, tumor size, vascular invasion, neural invasion, tumor penetration, lymph node metastasis
Kanellos et al. [27]	25 (26.3 %), CEA32 (32.6 %)	Stage	Location, histological grade, lymph node metastasis
Bosch et al. [28]	13 (25 %), CC10 (18.9 %), IC 11 (20.8 %) (9 before, 2 during, 7 after)	N/A	N/A
Wind et al. [3]	25 (28 %)	None	Age, gender, tumor site, tumor size, histological grade, tumor depth, lymph node metastasis, hepatic metastasis, perinervous spread, vascular spread, lymphatic spread
Temesi et al. [29]	25 (17.2 %) (pre 17, both 6, post 2)	Depth of invasion, positive lymph nodes	Gender, age, tumor site
Vogel et al. [9]	CC 32/90 (35.5 %), IC 17/36 (47.2 %)	CC: depth of invasion, metastases, IC: metastases	N/A
Kamiyama et al. [30]	16/45 (35.6 %)	None	
Hara et al. [31]	29/126 (29 %)	Univariate analysis (uni): hepatic metastasis, positive lymph nodes, multivariate analysis (multi): histological high grade, depth of invasion	Distant meta, cytology (Pap)
Lloyd et al. [32]	36 (28.8 %) (pre 15, post 26)	N/A	N/A
Lee et al. [33]	15 (7.9 %) (6 (40 %) Pap, Giemsa, 11 (73.3 %) HE, 10 (66.7 %) immuno)	Uni: positive lymph node, macroscopic peritoneal metastasis, stage, multi: depth of invasion, histological high grade	Peritoneal effusion, obstruction, circumferential involvement, lymphatic invasion, perineural invasion, venous invasion, liver metastasis
Rossi Del Monte et al. [34]	CC0## %, immuno 17 %, PCR 42 %	N/A	N/A

Table 4 The outcome data from the studies

References	Survival	Recurrence	Peritoneal recurrence
Nishikawa et al. [20]	Positive	Positive (peritoneal recurrence only)	Positive
Noura et al. [21]	Positive	Positive (peritoneal recurrence only)	Positive
Fujii et al. [22]	Negative	Negative	CY + high tendency towards P rec, not statistically significant
Yamamoto et al. [23]	Positive	Positive (*P*, others)	Positive
Katoh et al. [24]	Positive (2–4, strongly with Stage III)	Positive (distant)	Negative, $P = 0.077$
Hase et al. [25]	N/A	Positive	N/A
Homma et al. [19]	N/A	Positive	N/A
Gozalan et al. [26]	Negative	Negative	N/A
Kanellos et al. [27]	Negative	Positive (local)	N/A
Bosch et al. [28]	Positive	Positive	N/A
Wind et al. [3]	Negative	Negative	N/A
Temesi et al. [29]	N/A	Positive	N/A
Vogel et al. [9]	Negative	Negative	N/A
Kamiyama et al. [30]	N/A	Positive	N/A
Hara et al. [31]	Positive	N/A	No peritoneal recurrence in this study
Lloyd et al. [32]	Positive	Positive	N/A
Lee et al. [33]	Positive	Positive	N/A
Rossi Del Monte et al. [34]	Positive	Positive	N/A

small number of intraperitoneal free tumor cells detected using only the highly sensitive immunohistochemistry or qRT-PCR methods may not result in peritoneal recurrence in colorectal patients, suggesting that the prognostic significance depends on the number of disseminated intraperitoneal free tumor cells.

Hase et al. have shown a greater influence of post-resection lavage cytology on postoperative local recurrence compared to the pre-resection findings, and the local recurrence rate for positive post-resection cytology was significantly higher than that of negative post-resection cytology, regardless of the pre-resection cytology findings [25]. Cells spilled during surgical manipulation may explain some recurrences observed after the resection of colon carcinoma, especially those involving the suture line, abdominal wound or laparoscopic port site [37]. To avoid local recurrence, the serosal site of cancer infiltration should be covered during the operation to prevent the exfoliation of tumor cells, and it is also necessary to exercise care to prevent injury to the bowel by surgical manipulations. Further studies are needed to demonstrate the best timing of peritoneal lavage fluid collecting, by comparing the post-resection and pre-resection lavage findings, because two of the four studies that performed post-resection lavage showed an association of the post-resection, but not pre-resection, lavage fluid with a worse prognosis in terms of the recurrence [25] and survival [32].

Noura et al. demonstrated that patients who received intraperitoneal chemotherapy had a significantly better peritoneal recurrence-free survival and cancer-specific survival than did the patients who did not receive intraperitoneal chemotherapy in the positive peritoneal cytology group [5]. Further studies are needed to examine the effects of adjuvant treatment in patients with positive peritoneal lavage cytology.

Conclusion

Positive peritoneal lavage cytology seems to be a prognostic factor associated with higher recurrence and lower survival rates in patients with colorectal cancer. Since the heterogeneity of the lavage techniques makes the comparison between studies difficult, further studies including multi-institutional prospective studies, and comparing the different collection methods, are needed to clarify the true prognostic impact of peritoneal lavage cytology. Since the detection of free cancer cells in the peritoneal cavity seems to be associated with a worse prognosis, peritoneal lavage may prove to be beneficial to identify which patients should receive adjuvant treatment, in addition to the TNM classification. Additionally, further studies are needed to examine whether adjuvant treatment can improve the prognosis of patients with positive peritoneal lavage cytology.

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