Positive Peritoneal Cytology in Patients with Gastric Cancer: Natural History and Outcome of 291 Patients

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ABSTRACT

Background. Positive peritoneal cytology is a predictor of poor survival in patients with gastric cancer. Our aim is to more clearly define the natural history of this cohort.

Methods. Review of a prospectively maintained gastric cancer database of patients who had diagnostic laparoscopy with peritoneal washings. Clinicopathologic and treatment-related variables were obtained. Univariate and multivariate analyses were performed for factors associated with disease-specific survival (DSS).

Results. From January 1993 to April 2009, a total of 1241 patients with gastric cancer underwent laparoscopy with peritoneal washings; 291 (23%) had positive cytology. There were 198 patients (68%) who had visible metastases discovered at laparoscopy (M1), and 93 patients (32%) were without gross evidence of advanced disease (M1 Cyt+). The median DSS for the entire cohort was 1 year; for M1, DSS was 0.8 years, and for M1 Cyt+ , DSS was 1.3 years. At baseline, independent predictors of worse DSS were poor performance status, M1 disease, and diffuse tumors. Among the subset of patients with M1 Cyt+ disease, performance status was the strongest independent predictor of DSS. A total of 48 of the 291 Cyt+ patients had repeat staging laparoscopy after chemotherapy.

Compared with patients who had persistently positive cytology (n = 21), those who converted to negative cytology (n = 27) had a significant improvement in DSS (2.5 years vs. 1.4 years, $P = 0.0003$).

Conclusions. Patients with positive cytology as the only evidence of advanced disease exhibit a poor outcome; however, clearing of Cyt+ disease by chemotherapy is associated with a statistically significant improvement in DSS. The role for gastrectomy in patients with positive peritoneal cytology remains uncertain.

It is estimated that approximately 21,000 patients will be diagnosed with gastric cancer in the United States in 2009.¹ Many of these patients will manifest locally advanced disease ($\geq T3$ and/or node positive) and will require multimodality therapy for optimal survival.² Accurate staging of patients with locally advanced disease is critical for selecting the appropriate treatment strategy. Diagnostic laparoscopy is an important staging tool for patients with locally advanced gastric cancer and detects radiologically occult M1 disease in up to 40% of patients.^{3–6}

In addition to gross, visible M1 disease, positive peritoneal cytology has recently been included in the American Joint Committee on Cancer staging system as M1 disease.⁷ This is based on previous studies demonstrating that despite R0 resection, patients with positive peritoneal cytology have a median survival measured only in months.^{8–12} Positive cytology is a strong independent preoperative predictor of survival in patients undergoing R0 resection for gastric cancer.⁹ Despite attempts at curative resection and multimodality therapy, long-term survival in this patient cohort is exceedingly rare.

The management of patients with positive peritoneal cytology as the only evidence of M1 disease is largely unknown. At our institution, patients with locally advanced

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gastric cancer undergo staging laparoscopy with peritoneal washing for cytology as a separate procedure before consideration of therapy. Patients with positive cytology as the only evidence of M1 disease undergo systemic chemotherapy as initial therapy unless, rarely, a palliative resection is indicated. The objective of our study is to report our experience with patients with positive peritoneal cytology and focus on three specific aims: (1) to determine clinicopathologic and treatment-related variables associated with survival in patients with positive peritoneal cytology; (2) to examine the natural history of patients with positive cytology as the only evidence of M1 disease; and (3) to examine a subgroup of patients who have had repeat staging laparoscopy with washings after treatment with systemic chemotherapy.

PATIENTS AND METHODS

After institutional review board approval, patients admitted from March 1993 to April 2009 were identified from a prospectively maintained gastric cancer database at Memorial Sloan-Kettering Cancer Center. The database was queried for patients who had a diagnostic laparoscopy with peritoneal washings performed for evaluation of primary gastric cancer. Patients with recurrent gastric cancer or ascites observed on laparoscopy and patients treated with systemic chemotherapy before initial staging laparoscopy were excluded from analysis.

The medical record was reviewed for clinicopathologic variables known at the time of initial laparoscopy. Clinical variables obtained included age, sex, race, and symptoms at presentation (any reported weight loss, dysphagia, or anemia requiring transfusion). Performance status was evaluated retrospectively, and patients were grouped into Eastern Cooperative Oncology Group status 0–1 or 2–3. Results of initial esophagogastroduodenoscopy were obtained, including histologic grade and primary tumor location. Body mass index and history of smoking or alcohol use was determined. Laboratory values at initial laparoscopy were obtained and included hemoglobin and albumin.

Laparoscopic staging was performed in the standard fashion as described previously, before elective resection to exclude visible M1 disease or during the course of evaluation for extent of disease before implementation of multimodal therapy.⁴ The presence of peritoneal or visceral metastases was determined. Extent of peritoneal metastases was quantified according to the Japanese Research Society for Gastric Cancer.¹³ The extent of peritoneal disease (P status) was defined as follows: P0 = no evidence of peritoneal metastasis; P1 = limited metastases to the gastric serosal and lesser sac; P2 = limited metastasis below the

transverse colon; P3 = extensive spread of disease. Peritoneal washings were obtained as described previously.^{9,11} Approximately 150 to 200 mL of normal saline was instilled and aspirated in each of the following areas of the peritoneal cavity sequentially: the right subphrenic space, the left upper quadrant, and pelvis. Specimens were centrifuged and filter prepped, then stained using the technique described by Papanicolaou. Positive peritoneal cytology was defined as peritoneal cytology that was highly suspicious or positive for adenocarcinoma.

Treatment-related variables were also obtained including gastric resection and repeat laparoscopy with peritoneal washings after treatment with systemic chemotherapy. Outcome data obtained included disease-specific survival (DSS) for all patients and site of first recurrence for resected patients. The end point of interest was DSS, defined as the time from initial laparoscopy to death due to gastric cancer. When analyzing the timing of gastrectomy, DSS was defined as the time from gastrectomy to death due to gastric cancer. Patients who were alive or who died from other causes ($n = 14$, <5% of the cohort) were censored at last follow-up.

DSS rates were estimated by the Kaplan-Meier method, and survival curves were compared by the log rank test. Cox proportional hazard models were used to determine whether factors known at initial laparoscopy were predictive of DSS. Variables found to be significant on univariate analysis ($P < 0.1$) were considered in a multivariable model. Resection status was modeled as a time-dependent variable to account for the variability in timing of gastrectomy after initial laparoscopy. A P value of <0.05 was considered statistically significant. All statistical analyses were performed in SAS 9.2 (Cary, North Carolina).

RESULTS

Among the 1241 patients who underwent diagnostic laparoscopy for staging of gastric cancer during the time period analyzed, 300 patients (24%) had positive peritoneal cytology. After exclusion of patients with evidence of ascites at laparoscopy ($n = 3$) or who had undergone previous chemotherapy ($n = 6$), 291 patients (23%) met criteria for analysis. Clinicopathologic variables are listed in Table 1. Most patients (69%) experienced weight loss as one of their initial symptoms. Performance status was Eastern Cooperative Oncology Group (ECOG) 0–1 in 245 patients (84%), while the remaining 46 patients (16%) had poor performance status at initial presentation. Primary tumor location is shown in Table 1; of note, 39 patients (13%) had diffuse tumors. Analysis of initial biopsy samples revealed that most tumors (66%) were poorly differentiated.

TABLE 1 Clinicopathologic variables known at initial laparoscopy of 291 patients with gastric cancer and positive peritoneal cytology

Variable	Value
Age (y), median (range)	65 (31–87)
Male sex, n (%)	178 (61)
Race, n (%)	
White	227 (78)
Asian	24 (8)
Hispanic	22 (8)
Black	18 (6)
Symptoms at presentation, n (%)	
Weight loss	201 (69)
Dysphagia	81 (28)
Anemia requiring transfusion	32 (11)
Performance status, n (%)	
ECOG 0–1	245 (84)
ECOG 2–3	46 (16)
Primary tumor site	
Body, n (%)	86 (30)
Cardia, n (%)	63 (22)
Antrum, n (%)	63 (22)
Gastroesophageal junction, n (%)	40 (14)
Diffuse, n (%)	39 (13)
Poorly differentiated histology (initial biopsy sample), n (%)	193 (66)
History of smoking, n (%)	123 (42)
History of alcohol use, n (%)	42 (14)
Median body mass index (range)	24.9 (15.1–46)
Median hemoglobin (mg/dL) (range)	12.3 (4.9–12.8)
Median albumin (mg/dL) (range)	4.0 (2.3–4.9)
Peritoneal status, n (%)	
P0	102 (35)
P ≥ 1	189 (65)
Visceral metastasis, n (%)	20 (7)
M stage, n (%)	
M1 Cyt+	93 (32)
M1	198 (68)

ECOG Eastern Cooperative Oncology Group; Cyt+ positive peritoneal cytology

Diagnostic laparoscopy revealed the presence of gross peritoneal disease in 189 patients (65%) and visceral metastases in 20 patients (7%). Peritoneal disease was quantified as follows: P0 = 102 (35%); P1 = 78 (27%); P2 = 41 (14%); P3 = 70 (24%). On the basis of the presence of gross peritoneal disease (Cyt+) (n = 189) or visceral metastases (n = 9), there were 198 patients (68%) who met criteria for M1 disease, and the remaining 93 patients (32%) were M1 Cyt+.

At a median follow-up of 1 year, 232 patients (80%) had died of disease, and the median survival for the entire

cohort was 1 year (95% confidence interval, 0.9–1.1). Factors associated with DSS among all 291 patients with positive peritoneal cytology on univariate and multivariate analysis are shown in Table 2. Poor performance status, tumor location, and M1 disease were independent predictors of worse DSS. Kaplan-Meier survival curves for these factors are shown in Fig. 1.

M1 Cyt+ Patients

Among the 291 patients with positive peritoneal cytology, there were 93 patients (32%) without evidence of gross peritoneal disease or visceral metastasis (Fig. 2). Most of these patients (n = 64, 69%) were initially treated with systemic chemotherapy, most commonly cisplatin-based combination chemotherapy. There were 29 M1 Cyt+ patients (31%) who had immediate gastrectomy before their disease's cytology status was known. Among these patients, 23 (80%) of 29 underwent gastrectomy before 2005, when we changed our management strategy on the basis of results from our institution demonstrating the poor outcome among patients with positive cytology (24 of these patients were included in a previous publication). Four of the remaining six patients who had surgery from 2005 to 2009 underwent gastrectomy for palliative reasons (obstruction, hemorrhage).

Among the 64 M1 Cyt+ patients treated with systemic chemotherapy, 41 (64%) did not have a gastric resection. Twenty-three patients (56%) had disease that progressed while they were receiving chemotherapy, five patients (12%) had persistently positive cytology on restaging laparoscopy, and four patients (10%) had disease that remained locally unresectable. There was one patient (2%) whose disease experienced a complete clinical response to chemotherapy, and 2 patients (5%) were still receiving chemotherapy at the time of analysis. Six patients (15%) were lost to follow-up.

The clinicopathologic characteristics for M1 Cyt+ patients were similar to that of the entire cohort of 291 patients. We analyzed factors associated with DSS among M1 Cyt+ patients; those that were significant on univariate analysis are shown in Table 3. Gastric resection was analyzed as a time-dependent variable because patients moved from “no resection” to “resection” at variable time points through the course of their treatment with systemic chemotherapy. On multivariate analysis, poor performance status was the only independent predictor of DSS (hazard ratio [HR] 3.7, 95% confidence interval [95% CI] 1.6–8.8, $P = 0.03$). There was a trend toward significance for gastric resection (HR 0.6, 95% CI 0.3–1.5, $P = 0.06$). We compared outcome between the M1 Cyt+ patients who underwent immediate resection (n = 29) to those who were selected for gastric resection after treatment with

TABLE 2 Multivariate analysis for factors associated with disease-specific survival among 291 patients with gastric cancer and positive peritoneal cytology after staging laparoscopy

Variable	Unadjusted		Adjusted	
	HR (95% CI)	P	HR (95% CI)	P
Age (y)	1.0 (1.0–1.0)	0.67		
Sex				
Female	1.0	0.77		
Male	1.9 (0.7–1.3)			
Race				
White	1.0	0.66		
Asian	0.9 (0.5–1.5)			
Hispanic	0.7 (0.4–1.2)			
Black	1.0 (0.5–1.)			
Weight loss				
Yes	1.0	0.02	1.0	0.35
No	0.7 (0.5–1.0)		1.0 (0.8–1.4)	
Dysphagia				
Yes	1.0	0.74		
No	1.0 (0.7–1.3)			
Prior transfusion				
Yes	1.0	0.77		
No	0.9 (0.6–1.5)			
Performance status				
ECOG 0–1	1.00	<0.0001	1.0	<0.0001
ECOG 2–3	3.2 (2.23–4.48)		2.8 (2.0–4.0)	
Histology (initial biopsy sample)				
Poor	1.0	0.37		
Moderate/well	0.8 (0.6–1.2)			
Primary tumor site				
Antrum	1.0	0.002	1.0	0.03
Gastroesophageal junction	1.6 (1.1–2.6)		1.4 (0.9–2.3)	
Cardia	1.4 (1.0–2.2)		1.4 (0.9–2.2)	
Body	1.5 (1.0–2.2)		1.4 (1.0–2.1)	
Diffuse	2.5 (1.6–4.0)		2.0 (1.2–3.3)	
Body mass index	1.0 (0.4–1.0)	0.03	1.0 (1.0–1.0)	0.80
History of smoking				
Yes	1.0	0.11		
No	1.3 (1.0–1.6)			
History of alcohol use				
Yes	1.0	0.99		
No	1.0 (0.7–1.4)			
Hemoglobin	1.0 (1.0–1.0)	0.88		
Albumin	0.9 (0.7–1.2)	0.32		
M stage				
M1 Cyt+	1.0	<0.0001	1.0	<0.0001
M1	2.2 (1.6–3.0)		1.9 (1.4–2.5)	

HR, hazard ratio; 95% CI, 95% confidence interval; ECOG, Eastern Cooperative Oncology Group; Cyt+, positive peritoneal cytology
Bold values denote statistically significant ($P \leq 0.05$), Cox regression analysis

systemic chemotherapy (n = 23). From the time of gastrectomy, there was no difference in median DSS between patients who had immediate gastrectomy (0.9 years; range, 0.9–5.9 years) and those selected for resection after chemotherapy (1.7 years; range, 0.6–4.3 years) (log rank

$P = 0.76$). The M1 Cyt+ patients who initially received chemotherapy and were subsequently “selected” for resection received a median of 6 months (range, 1–16 months) of chemotherapy before elective gastrectomy. From the time of initial staging laparoscopy, patients who

FIG. 1 Disease-specific survival among 291 patients with positive peritoneal cytology. Kaplan–Meier survival curves according to Eastern Cooperative Oncology Group functional status (a), primary tumor site (b), and M stage (c)

FIG. 2 Incidence of peritoneal cytology without gross peritoneal or visceral metastases (M1 Cyt+). A total of 29 patients (31%) underwent gastrectomy without previous knowledge of positive peritoneal cytology

received initial chemotherapy had a median survival of 1.7 years (range, 0.9–4.6 years) in comparison to those patients who had immediate gastrectomy (median survival of 1.1 years (range, 0.3–5.9 years).

Among the 52 M1 Cyt+ patients who underwent resection, 39 patients (75%) experienced a known recurrence. Complete data was available for 26 of these patients. There were 29 initial sites of recurrence among the 26 patients evaluated, which included distant nodes ($n = 3$, 12%), lung/bone ($n = 4$, 15%), liver ($n = 4$, 15%), and local/peritoneum ($n = 18$, 69%). Among the 18 M1 Cyt+ patients who had a complete R0 resection, 11 (61%) had a local or peritoneal recurrence as their first site of treatment failure.

Repeat Cytology

There were 48 patients initially treated with systemic chemotherapy in the absence of disease progression who underwent repeat laparoscopy with washings during the course of their treatment. All of these patients had ECOG 0–1 performance status, and 22 patients (46%) had evidence of peritoneal disease at initial staging laparoscopy ($P1 = 9$, $P2 = 8$, $P3 = 5$). At repeat laparoscopy and cytologic analysis, 27 patients (56%) had converted to negative cytology and 21 (44%) had persistently positive cytology. Kaplan–Meier analysis for these patients is shown in Fig. 3a. Patients with repeat cytology negative had a significant improvement in DSS (median, 2.5 years; range, 0.4–4.5 years) compared to repeat positive cytology (median, 1.4 years; range, 0.6–3.9 years) (log rank $P = 0.0003$). Of note, among patients with repeat negative cytology, nine initially had peritoneal metastasis, and eight of these patients had resolution of their M1 disease along with conversion to negative cytology. Among the patients with persistently positive cytology, 13 patients initially had peritoneal metastasis, and only 1 patient had resolution of this visible disease.

TABLE 3 Clinicopathologic and treatment related variables of 93 patients with positive peritoneal cytology without gross peritoneal or visceral metastasis and multivariate analysis for factors associated with disease-specific survival

Variable	n (%)	Unadjusted		Adjusted	
		HR (95% CI)	P value	HR (95% CI)	P value
Performance status					
ECOG 0–1	85 (91)	1.0		1.0	
ECOG 2–3	8 (9)	5.1 (2.2–11.9)	0.0001	3.7 (1.6–8.8)	0.03
Primary tumor site					
Antrum	25 (27)	1.0		1.0	
Body	25 (27)	1.7 (0.8–3.4)		1.6 (0.8–3.3)	
Cardia	22 (24)	1.8 (0.9–3.8)		1.7 (0.8–3.6)	
Diffuse	5 (5)	1.8 (0.5–6.3)		1.7 (0.5–5.9)	
Gastroesophageal junction	16 (17)	3.3 (1.6–7.0)	0.04	2.7 (1.3–5.8)	0.16
Gastric resection	52 (56)	0.4 (0.3–0.8)	0.003	0.6 (0.3–1.5)	0.06

HR hazard ratio, 95% CI 95% confidence interval, ECOG Eastern Cooperative Oncology Group

Bold values denote statistically significant ($P \leq 0.05$), Cox regression analysis

We next examined subgroups of the 48 patients who had repeat staging laparoscopy with washings. Within the group of patients who converted to negative cytology, 20 (74%) of 27 were selected for gastric resection. We analyzed the outcome of these 20 patients who had repeat negative cytology and gastric resection and compared them to those with negative cytology that did not have resection ($n = 7$). Patients with repeat negative cytology selected for gastrectomy had a similar median DSS (2.5 years; range, 0.6–4.5) compared to those that had no resection (2.3 years; range, 0.4–3.1) (log rank $P = 0.76$) (Fig. 3b). Among the 26 patients (54%) selected for gastric resection, 20 patients had negative cytology and 6 had positive cytology. There was no statistically significant difference in median DSS among patients who had gastrectomy with repeat negative cytology (2.2 years; range, 0.02–4.2 years) compared to those who had gastrectomy with persistently positive cytology (1.4 years; range, 0.60–4.0 years) (log rank $P = 0.14$).

DISCUSSION

On the basis of previous studies from our institution and others, peritoneal cytology is an independent predictor of outcome in patients with gastric cancer despite R0 resection.^{8,9,11,12,14} This has affected a change in practice pattern at our institution where patients with locally advanced ($\geq T3$, node positive) undergo separate staging laparoscopy with washings before initiation of neoadjuvant chemotherapy. Patients with positive peritoneal cytology are treated with chemotherapy and are only restaged if there is no evidence of progression of disease. This practice has allowed us to carefully analyze the natural history of

patients with positive peritoneal cytology, both with and without gross evidence of M1 disease.

Factors associated with outcome among patients with advanced gastric cancer have been previously described.¹⁵ These factors include poor performance status and the presence of peritoneal or visceral metastasis. In the current study, we demonstrated that among all patients with positive peritoneal cytology, poor performance status and the presence of visible M1 disease are independently associated with worse DSS. Other factors we analyzed, such as symptoms at presentation, hemoglobin, and albumin, were not independently associated with DSS, perhaps as a result of the overwhelmingly negative impact of positive peritoneal cytology in these patients.

Patients with cytology as the only evidence for advanced disease (M1 Cyt+) represent a unique cohort of patients. We previously demonstrated that despite the absence of gross M1 disease and R0 resection, patients with positive cytology exhibit similar survival to those who have visible metastasis.¹⁶ Other groups have reported similar results and have shown that M1 Cyt+ patients have dismal outcome after curative resection.¹⁴

Our study suggests that the use of chemotherapy as initial treatment in patients with M1 Cyt+ disease is a preferred approach. In another study from our institution, Gold et al. evaluated 37 patients who underwent gastrectomy in the presence of known metastatic disease, including 12 patients with M1 Cyt+ disease.¹⁶ Patients with M1 Cyt+ disease had similar outcomes to those with visible metastasis. Of note, the patients who had cleared their cytology with systemic chemotherapy had an improved median survival compared to those with persistent metastatic disease at resection.

FIG. 3 Outcome of 48 patients who had repeat staging laparoscopy with washings. **a** Disease-specific survival (DSS) of patients whose repeat cytology was negative vs. persistently positive cytology. **b** DSS of patients whose repeat cytology was negative based on resection status. There was no difference in outcome between patients selected for gastric resection ($n = 20$) and those who were not ($n = 7$)

The role of surgery in patients with M1 Cyt+ disease who subsequently clear with chemotherapy is not clear. Our data suggest that even in this select group of patients, surgery does not seem to improve survival. Other studies, however, suggest a role for surgery in Cyt+ patients that clear their cytology. Badgwell et al. evaluated 39 patients found to have M1 Cyt+ disease at laparoscopy.¹⁷ They reported a median overall survival (13 months) that was similar to that of patients with gross disease discovered at laparoscopy (10 months, $P = 0.06$). There were 24 patients (62%) who were treated with neoadjuvant therapy and exhibited improved outcome (3-year survival, 12%) compared to those treated with palliation (0%, $P = 0.005$). There were three patients in the study treated with

neoadjuvant therapy followed by resection who were alive at 28, 65, and 89 months. Another study by Okabe et al. reported 41 patients with advanced gastric cancer treated with neoadjuvant S-1 and cisplatin.¹⁸ There were 10 M1 Cyt+ patients and 31 patients with gross peritoneal disease. Nineteen patients (46%) had resolution of their peritoneal disease after induction therapy. This included 7 (70%) of 10 of the patients with M1 Cyt+ disease that converted to negative cytology. There were 22 patients (54%) who underwent curative resection with a median survival of 43 months compared to 10 months without surgery ($P < 0.0001$). Of the 13 patients (60%) who experienced recurrence, the peritoneum was the initial site in 9 patients (69%).

It is clear that this study and the others discussed suffer from selection bias. Patients whose disease improves while they receive chemotherapy rarely require resection, unless they are undergoing palliative treatment for symptoms such as bleeding, obstruction, or perforation. Disease that responds to therapy and shows no signs of progression can be restaged with laparoscopy and washings. As demonstrated by this study and others, patients who convert to negative cytology have the best survival. However, despite these being the best group, long-term survival is rare, and patients who undergo resection have a high rate of disease recurrence, principally in the peritoneum.

A recent multicenter prospective trial randomized 88 patients with M1 Cyt+ disease to surgery alone, surgery plus intraperitoneal chemotherapy, or surgery, intraperitoneal chemotherapy, and high-volume saline lavage; all patients received adjuvant S-1.¹⁹ Patients treated with saline lavage with 10 L of dilution had 44% 5-year survival, compared to 5% 5-year survival for surgery plus intraperitoneal chemotherapy and 0% in the surgery-alone arm ($P < 0.0001$). Furthermore, peritoneal recurrence was significantly reduced with high volume lavage (40% vs. 80% for surgery plus intraperitoneal chemotherapy vs. 90% for surgery alone, $P < 0.0001$).

It is unclear at this point whether positive cytology is a predictor or governor of survival. Western series suggest that it is a predictor, with uniformly poor outcome regardless of treatment.^{9,16} The reduction in peritoneal recurrence with associated improvement in survival in the study of Kuramoto et al. suggests that an aggressive approach to peritoneum may in fact improve median and possibly long-term survival.¹⁹ This is an observation that requires confirmation.

Our current algorithm for treatment of patients with gastric cancer and positive peritoneal cytology is provided in Fig. 4. Currently, there are no level 1 data to support a specific treatment plan for patients who are M1 Cyt+. Because of the very poor outcome of patients with positive cytology, we have essentially abandoned gastrectomy as a

FIG. 4 Memorial Sloan-Kettering Cancer Center algorithm for patients with gastric cancer and positive peritoneal cytology (not supported by level 1 evidence)

primary treatment for patients who do not require palliation. However, we remain interested in these patients and continue to evaluate them during their course of treatment. If there is no evidence for radiologic or clinical progression, repeat laparoscopy with cytology is performed at 6 to 12 months after initiation of chemotherapy. This is to identify patients whose disease is responding to the current chemotherapy regimen or those with persistent or progressive disease who may benefit from a change in chemotherapy regimens. To date, there is no evidence that gastrectomy confers any benefit to patients beyond that governed by their systemic therapy. However, we continue to look for the exceptional patient whose cytology clears as a result of a favorable biology of disease, and who can thus be considered for resection.

We have demonstrated that positive peritoneal cytology, even in the absence of gross peritoneal disease, portends a poor outcome. Patients with good performance status and whose disease responds to systemic chemotherapy experience the best survival, although long-term survival is rare. The role of gastrectomy remains unclear. Future trials should include attempts at aggressive locoregional therapy to treat the peritoneum because it is the primary site of recurrence and seems to be an important determinate of survival.

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