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RESEARCH ARTICLE

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Peritoneal recurrence after resection for Stage I–III colorectal cancer: A population analysis

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Abstract

Background: Colorectal cancer (CRC) often recurs in the peritoneum, although the pattern of peritoneal recurrence (PR) has received less attention. We sought to describe the presentation and risk factors for PR following CRC resection.

Methods: We performed a cohort study of patients undergoing resection of Stage I–III CRC from 2006 to 2007 using merged data from a Commission on Cancer Special Study and the National Cancer Database. We estimated the timing, method of detection, and risk factors for isolated PR.

Results: Here, 8991 patients were included and isolate PR occurred in 77 (0.9%) patients. The median time to PR was 16.2 months (intrquartile range = 9.3–28.0 months) and most patients were identified via new symptoms (36.4%). Pathologic factors associated with increased odds of PR included higher T stage (T3 vs. T2, odds ratio [OR] = 4.8, 95% confidence interval [CI] = 1.5–15.7), N stage (N1 vs. N0, OR = 2.00, CI = 1.1–3.7), and signet ring (OR = 8.2, CI = 3.0–22.3) or mucinous histology (OR = 2.6, CI = 1.5–4.7).

Conclusions: The majority of PR was detected within 18 months and few were identified by surveillance. Advanced T/N stage and signet ring/mucinous histology were associated with increased odds of PR.

KEYWORDS

colorectal cancer, mucinous, peritoneal recurrence, signet ring

1 | INTRODUCTION

An estimated 147 950 patients were diagnosed with colorectal cancer (CRC) in 2020, with the majority undergoing potentially curative surgical resection.[1] Recurrence following surgical resection is frequent, ranging from 5% to 33% based on stage, with distant recurrence (DR) being most common.[2,3] Although less common than liver or lung, peritoneal recurrence (PR) is of particular interest due to the evolving role of management strategies such as cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Identification of factors associated with PR is critical to understand disease progression, and also to best leverage emerging treatment options.

Risk factors for PR have not been studied in a large national sample in the United States. A regional study of 11 124 CRC patients

in Sweden identified advanced T and N stage, emergency surgery, and positive surgical margins as risk factors for isolated PR or concurrent PR and DR.[4] Based on these findings, advanced T stage and perforation are commonly used as enrollment criteria for prospective studies involving second-look laparoscopy and prophylactic HIPEC.[5] Although less commonly reported, histologic factors such as mucinous or signet-ring histology have also been identified as risk factors for PR.[6,7] However, these other pathologic risk factors are not commonly used as enrollment criteria for studies involving second-look laparoscopy or prophylactic HIPEC.

As the frequency of PR is low, adequate evaluation requires a large population of patients. We aimed to study isolated PR using data from a large national data set of CRC patients annotated for recurrence. We also aimed to identify risk factors for isolated PR rather than combined PR and DR, as these patients are most likely to benefit from diagnostic and therapeutic strategies targeted to detecting and managing peritoneal disease. The objectives of this study were to describe timing, method of detection, and survival after PR diagnosis following resection for Stage I–III CRC and identify clinical and tumor related factors associated with PR.

2 | METHODS

2.1 | Patient selection

We analyzed data from a Commission on Cancer (CoC) Special Study on CRC recurrence. The study cohort consisted of adult patients (age ≥ 18 years) identified from the National Cancer Database (NCDB) that underwent definitive resection for Stage I–III CRC between January 1, 2006 and December 31, 2007. Ten patients were randomly selected and stratified by stage at diagnosis and tumor location within the colon or rectum from each CoC accredited facility for further chart abstraction to determine recurrence. Detailed data regarding surveillance, recurrence, and treatment through December 31, 2012 were collected as part of the CoC Special Study on CRC recurrence and merged with data within the NCDB. These methods have been previously described in detail.[3,8] We excluded patients with missing information on recurrence, metastatic disease at presentation, and death without documented recurrence (Figure 1). Data for the CoC Special Study on CRC recurrence were collected via a secure web form housed at the NCDB in compliance with the Health Insurance Portability and Accountability Act. Secondary analysis of this de-identified data was considered exempt by The MD Anderson Cancer Center Institutional Review Board.

2.2 | Cohorts and variables

Patients that had a recurrence were categorized as having peritoneal, other distant, or locoregional recurrence. The PR cohort consisted of patients with PR alone or concurrent peritoneal and locoregional recurrence. The other DR cohort consisted of patients with distant but not PR. The disease-free (DF) cohort consisted of patients with no documented recurrence at the date of last follow-up or the predefined cutoff of 5 years after the surveillance start date. Demographics, tumor characteristics, pathologic reports, treatment information, and facility variables were as defined by the NCDB data standards.[9] Rural versus urban residence was inferred by linking patient zip codes to US census and US Department of Agriculture Economic Research Service data as previously described.[10] Staging was based on the American Joint Committee on Cancer (AJCC) 7th edition staging manual.[11]

2.3 | Statistical methods

Clinical and demographic characteristics were compared by χ^2, t test, and Kruskal–Wallis tests as appropriate. Median time to recurrence was estimated using the Kaplan–Meier method. Only the first recurrence was analyzed. Patients were censored at the date of last follow-up or the end of the surveillance period. Differences in demographic, tumor, and facility characteristics were compared for patients with PR versus DR using bivariate and multivariable logistic regression. All variables significant on univariate analysis with a $p < 0.2$ and a priori decided clinically important variables were included in the final multivariable model. Missing information was included as a separate category. Models were tested for fit by the

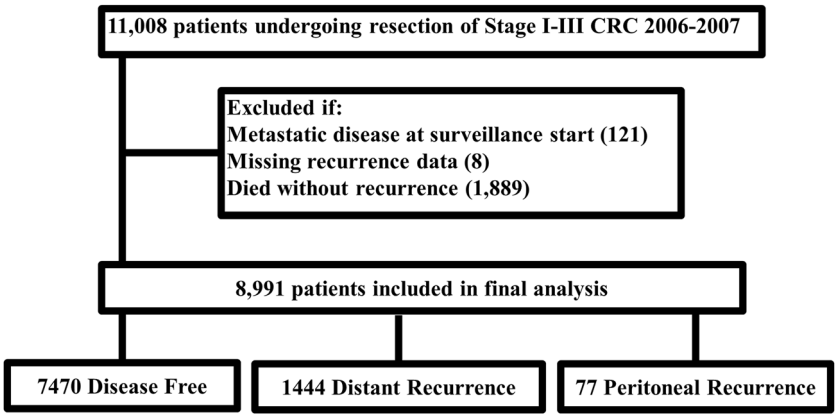

FIGURE 1 Selection of patients from of National Cancer Database (NCDB)/Commission on Cancer (CoC) cohort. CRC, colorectal cancer.

TABLE 1 Patient characteristics by PR of patients undergoing surgery for Stage 1–3 CRC (*N* = 8991)

Characteristics	DF (*N* = 7470)		Nonperitoneal DR (*N* = 1444)		PR (*N* = 77)		*p*
	N	%	*N*	%	*N*	%	
Age, year							
18–49	885	11.8	206	14.3	12	15.6	0.121
50–64	2475	33.1	479	33.2	29	37.7	
65–74	2038	27.3	379	26.2	22	28.6	
75–90	2014	27	365	25.3	13	16.9	
>90	58	0.8	15	1	1	1.3	
Sex							
Male	3537	47.3	776	53.7	45	58.4	<0.001
Female	3930	52.6	668	46.3	32	41.6	
Unknown	3	0	0	0	0	0	
Race							
White	6450	86.3	1163	80.5	67	87	<0.001
Black	679	9.1	201	13.9	7	9.1	
Others	341	4.6	80	5.5	3	3.9	
Comorbidity score*							
0	5506	73.7	1019	70.6	54	70.1	0.019
1	1541	20.6	315	21.8	20	26	
2 and more	423	5.7	110	7.6	3	3.9	
Insurance status							
Private	3109	41.6	566	39.2	31	40.3	0.03
Uninsured	245	3.3	52	3.6	4	5.2	
Medicaid	261	3.5	70	4.8	1	1.3	
Medicare	3675	49.2	710	49.2	40	51.9	
Managed Care	67	0.9	9	0.6	0	0	
Unknown	113	1.5	37	2.6	1	1.3	
Population density of residence							
Metro area	5831	78.1	1112	77	61	79.2	0.145
Urban area	1205	16.1	229	15.9	10	13	
Rural area	131	1.8	34	2.4	4	5.2	
Unknown	303	4.1	69	4.8	2	2.6	
Facility type							
Community	2023	27.1	395	27.4	22	28.6	0.975
Comprehensive	4066	54.4	773	53.5	41	53.2	
Academic/Research	1353	18.1	272	18.8	14	18.2	
Others/Unknown	28	0.4	4	0.3	0	0	
Facility location							
New England	546	7.3	93	6.4	6	7.8	0.295
Middle Atlantic	977	13.1	175	12.1	12	15.6	

Characteristics	DF (*N* = 7470)		Nonperitoneal DR (*N* = 1444)		PR (*N* = 77)		*p*
	N	%	*N*	%	*N*	%	
South Atlantic	1517	20.3	299	20.7	8	10.4	
East North Central	1549	20.7	296	20.5	16	20.8	
East South Central	490	6.6	106	7.3	5	6.5	
West North Central	603	8.1	113	7.8	10	13	
West South Central	589	7.9	127	8.8	3	3.9	
Mountain	334	4.5	51	3.5	5	6.5	
Pacific	865	11.6	184	12.7	12	15.6	

Abbreviations: CRC, colorectal cancer; DF, disease-free; DR, distant recurrence; PR, peritoneal recurrence.

*Charlson Comorbidity Index, *p* calculated via χ^2 test.

goodness of fit test. All analyses were performed using Stata MP (version 13.1; StataCorp).

3 | RESULTS

Of a total of 11 008 patients, 8991 patients met selection criteria and were included in the analysis. Recurrence of any type occurred in 1521 patients (16.9%). PR alone as the first site of recurrence occurred in 77 (0.9%) of patients, of which 22 (28.5%) also had local recurrence. Demographic data and tumor characteristics for included patients are summarized in Tables 1 and 2, respectively. At baseline there were no significant demographic differences between the groups. Patients with PR most commonly had advanced T stage (96.1% T3 or greater) and higher N stage (70.2% N1 or greater). There were also differences between the PR, DR, and DF cohorts with respect to signet ring histology (9.1% vs. 1.9% vs. 0.7%, respectively), mucinous histology (23.4% vs. 8.7% vs. 9.2%, respectively), and positive margin status (15.6% vs. 8.7% vs. 3.2%, respectively) ($p < 0.001$).

The median time to PR was 16.2 months (interquartile range = 9.3 months to 28.0 months), which was earlier than other DRs (median 21.7 months, $p = 0.003$). Most PRs (85.3%) occurred within 3 years of surgery. The most common methods of detection included new signs or symptoms (36.4%), evaluation following locoregional recurrence (20.8%), and routine surveillance imaging (14.3%, Table 3). A minority of patients (16.9%) underwent surgery for PR, 49.4% received chemotherapy alone, and 33.8% received no treatment. Survival information is shown in Figure 2. The 5-year survival rate was 22.8% in patients with PR and 32.6% in patients with DR ($p < 0.01$).

We used multivariable logistic regression to compare patients with PR to DF patients (Table 4). Tumor factors associated with increased odds of PR included higher T stage (T3 vs. T2 odds ratio [OR] = 4.82, 95% confidence interval [CI] = 1.48–15.72; T4 vs. T2 OR = 12.26, 95% CI = 3.44–43.73), higher N stage (N1 vs. N0 OR = 2.00, 95% CI = 1.08–3.73; N2 vs. N0 OR = 3.72, 95% CI 1.97–6.99), signet ring versus adenocarcinoma histology (OR = 8.22, 95% CI = 3.03–22.32), and mucinous versus adenocarcinoma histology (OR = 2.60, 95% CI = 1.45–4.65). Lymphovascular invasion, perineural invasion, and surgical margins were not significantly associated with increased odds of PR. Demographic factors associated with increased odds of PR were Medicare versus private insurance (OR = 2.55, 95% CI = 1.20–5.44), rural versus metro residence (OR = 3.63, 95% CI = 1.22–10.48), and operative year 2007 versus 2006 (OR = 1.66, 95% CI = 1.02–2.70).

Compared with patients with other DR, patients with isolated PR were independently more likely to have signet ring versus adenocarcinoma histology (OR 5.31, 95% CI = 1.82–15.49), mucinous versus adenocarcinoma histology (OR = 3.12, 95% CI = 1.70–5.72), operative year 2007 versus 2006 (OR = 1.68, 95% CI = 1.02–2.75), and receipt of adjuvant chemotherapy versus no chemotherapy (OR 2.22, 95% CI = 1.07–4.60). Advanced T and N stage were not associated with PR versus DR.

4 | DISCUSSION

In this national sample of patients undergoing surgical resection for Stage I–III CRC, most PRs occurred within 3 years of surgery and were most commonly detected based on the development of concerning symptoms or signs; relatively few were detected by surveillance imaging alone. Notable pathologic factors associated with PR were advanced T and N stage, signet ring histology, and mucinous histology. PR was not associated with tumor grade, lymphovascular or perineural invasion, or positive surgical margins. Surgical treatment for PR was uncommon, but when performed was associated with a 5-year survival of 22.8%. In contrast, 5-year OS for patients with other DR undergoing surgery was 32.6%.

We focused on patients with isolated PR, as these patients are most likely to benefit from diagnostic and therapeutic strategies targeted to detect and manage peritoneal disease. Patient or

TABLE 2 Clinicopathologic characteristics by PR of patients undergoing surgery for Stage 1–3 CRC (*N* = 8991)

	DF (*N* = 7470)		Nonperitoneal DR (*N* = 1444)		PR (*N* = 77)		
Characteristics	***N***	**%**	***N***	**%**	***N***	**%**	***p***
Cancer site							0.042
Right colon	3613	48.4	642	44.5	40	51.9	
Left colon	2860	38.3	578	40	29	37.7	
Rectum	997	13.3	224	15.5	8	10.4	
Tumor stage							<0.001
I	2383	31.9	131	9.1	0	0	
II	2649	35.5	401	27.8	23	29.9	
III	2438	32.6	912	63.2	54	70.1	
T-stage							<0.001
0/I/1	1237	16.6	49	3.4	0	0	
2	1623	21.7	152	10.5	3	3.9	
3	4088	54.7	1007	69.7	53	68.8	
4	452	6.1	226	15.7	21	27.3	
X, unknown	70	0.9	10	0.7	0	0	
N-stage							<0.001
0	4983	66.7	523	36.2	23	29.9	
1	1668	22.3	451	31.2	23	29.9	
2	729	9.8	461	31.9	31	40.3	
X, unknown	90	1.2	9	0.6	0	0	
Tumor size, mm							<0.001
<11	355	4.8	15	1	0	0	
11–20	808	10.8	97	6.7	3	3.9	
>20	5711	76.5	1244	86.1	73	94.8	
Missing	596	8	88	6.1	1	1.3	
Tumor histology							<0.001
Nonmucinous adenocarcinoma	6734	90.1	1291	89.4	52	67.5	
Signet-ring cell	50	0.7	27	1.9	7	9.1	
Mucinous	686	9.2	126	8.7	18	23.4	
Tumor grade							<0.001
Well/Moderately differentiated	6320	84.6	1141	79	51	66.2	
Poorly	1074	14.4	275	19	23	29.9	
Undifferentiated	74	1	28	1.9	3	3.9	
Unknown	2	0	0	0	0	0	
Total lymph nodes accessed							0.269
0–11	2151	28.8	409	28.3	23	29.9	
12+	5272	70.6	1023	70.8	52	67.5	
Unknown	47	0.6	12	0.8	2	2.6	

Characteristics	DF (*N* = 7470)		Nonperitoneal DR (*N* = 1444)		PR (*N* = 77)		*p*
	N	%	*N*	%	*N*	%	
Lymphovascular invasion							<0.001
Yes	1218	16.3	505	35	34	44.2	
No	4691	62.8	635	44	31	40.3	
Unknown	1514	20.3	299	20.7	11	14.3	
Not applicable	47	0.6	5	0.3	1	1.3	
Perineural invasion							<0.001
Yes	260	3.5	165	11.4	9	11.7	
No	3512	47	557	38.6	32	41.6	
Unknown	3587	48	710	49.2	33	42.9	
Not applicable	111	1.5	12	0.8	3	3.9	
Surgical margin status							<0.001
Negative	7148	95.7	1300	90	65	84.4	
Positive	241	3.2	126	8.7	12	15.6	
Unknown	81	1.1	18	1.2	0	0	

Note: *p* calculated via χ^2 test.

Abbreviations: CRC, colorectal cancer; DF, disease-free; DR, distant recurrence; PR, peritoneal recurrence.

TABLE 3 Method of detection and treatment of PR (*N* = 77)

	n (%)
Method of detection	
Patient/Physician identified sign/symptom	28 (36.4)
Elevated CEA	12 (13.0)
Asymptomatic routine imaging	11 (14.3)
As part of work up for locoregional recurrence	16 (20.8)
Incidental on unrelated imaging	8 (10.4)
Unknown	4 (5.2)
Treatment approach	
Surgery alone	7 (9.1)
Chemotherapy alone	38 (49.4)
Combined surgery/chemotherapy	6 (7.8)
None	26 (33.8)

Abbreviations: CEA, carcinoembryonic antigen; PR, peritoneal recurrence.

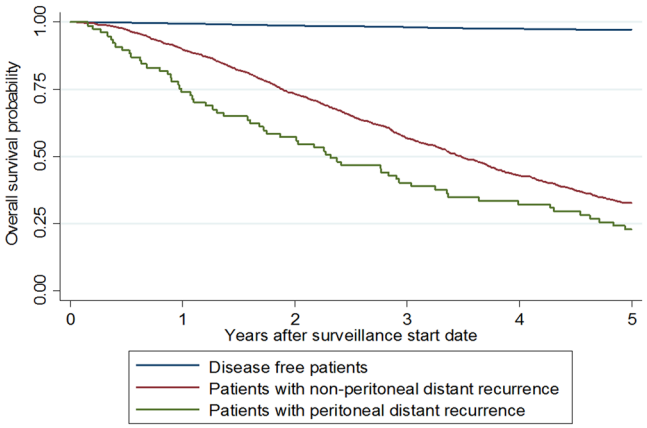

FIGURE 2 Kaplan-Meier estimates of overall survival

physician identified signs or symptoms was the most common method of detection of PR in our study, consistent with previous studies demonstrating the limited sensitivity of abdominal CT for detecting peritoneal disease, particularly for small lesions.[12,13] Detection of subclinical disease is desirable due to the increased likelihood of obtaining complete cytoreduction during subsequent CRS and HIPEC, which is predictive of survival.[14] Our results suggest that current surveillance is suboptimal for detecting most lesions at a subclinical stage. Strategies such as circulating tumor DNA (ctDNA), with or without appropriately timed second-look laparoscopy, may be considered to identify subclinical peritoneal lesions amenable to complete cytoreduction, but the effectiveness of these strategies need further investigation.[15–17]

Although the surveillance strategy for PR has not changed significantly since the study period in our analysis (2006–2007), the management of PR has evolved. We observed that 16.9% of patients underwent surgical management for PR and that the 5-year survival was 22.8%. CRS/HIPEC is now more frequently performed for PR in experienced centers, though overall evidence remains

TABLE 4 Multivariable logistic regression, factors associated with PR versus no recurrence and PR versus other DR

Variable	Odds ratio (95% confidence interval) PR compared with DF	PR compared with other DR
Age (years)		
18–49	Ref	Ref
50–64	1.12 (0.54–2.30)	1.00 (0.47–2.14)
65–74	0.49 (0.19–1.27)	0.55 (0.20–1.49)
75–90	0.28 (0.10–0.80)*	0.42 (0.14–1.27)
>90	0.61 (0.07–5.60)	0.76 (0.07–8.82)
Insurance		
Private	Ref	Ref
Uninsured	0.87 (0.29–2.67)	1.20 (0.38–3.79)
Medicaid	0.36 (0.05–2.70)	0.32 (0.04–2.45)
Medicare	2.55 (1.20–5.44)*	2.17 (1.01–4.70)
Unknown	0.98 (0.11–8.17)	0.83 (0.11–6.52)
Population density of residence		
Metro area	Ref	Ref
Urban area	0.69 (0.34–1.40)	0.77 (0.38–1.58)
Rural area	3.63 (1.22–10.78)*	2.37 (0.74–7.65)
Unknown	0.49 (0.11–2.16)	0.53 (0.12–2.29)
T-stage		
2	Ref	Ref
3	4.82 (1.48–15.72)*	2.27 (0.67–7.68)
4	12.26 (3.44–43.73)*	2.97 (0.80–11.00)
N-stage		
0	Ref	Ref
1	2.00 (1.08–3.73)*	0.92 (0.47–1.81)
2	3.72 (1.97–6.99)*	0.88 (0.44–1.73)
Tumor histology		
Nonmucinous adenocarcinoma	Ref	Ref
Signet-ring cell	8.22 (3.03–22.32)*	5.31 (1.82–15.49)*
Mucinous	2.60 (1.45–4.65)*	3.12 (1.70–5.72)*
Tumor grade		
Well/Moderately differentiated	Ref	Ref
Poorly	1.05 (0.59–1.88)	1.17 (0.64–2.12)
Undifferentiated	2.40 (0.65–8.87)	1.37 (0.34–5.47)
Total lymph nodes accessed		
0–11	Ref	Ref
12+	0.51 (0.30–0.86)*	0.77 (0.45–1.34)
Unknown	6.98 (1.23–39.45)*	2.37 (0.39–14.30)
Diagnosis year		
2006	Ref	Ref
2007	1.66 (1.02–2.70)*	1.68 (1.02–2.75)*

Variable	Odds ratio (95% confidence interval) PR compared with DF	PR compared with other DR
Surgery chemotherapy sequence		
No chemotherapy	–	Ref
Neo-adjuvant	–	1.74 (0.36–8.44)
Adjuvant	–	2.22 (1.07–4.60)*
Others	–	1.87 (0.58–6.01)
Lymphovascular invasion		
Yes	Ref	Ref
No	0.60 (0.34–1.09)	0.94 (0.52–1.69)
Unknown	0.51 (0.39–1.13)	0.53 (0.24–1.17)
Not applicable	0.99 (0.07–14.89)	0.43 (0.02–10.31)
Perineural invasion		
Yes	Ref	Ref
No	0.76 (0.33–1.75)	1.55 (0.67–3.58)
Unknown	0.67 (0.29–1.56)	1.20 (0.53–2.77)
Not applicable	2.23 (0.40–12.36)	5.29 (0.76–36.72)
Surgical margin status		
Negative	Ref	Ref
Positive	2.01 (0.96–4.17)	1.42 (0.70–2.92)

Note: Values presented as odds ratio (95% confidence interval).
Abbreviations: DF, disease-free; DR, distant recurrence; PR, peritoneal recurrence.
*$p < 0.05$.

conflicting.[18,19] Whether through CRS/HIPEC or modern chemotherapy regimens, the survival in patients with PR has improved.[20,21] The recently completed PRODIGE 7 trial observed a nearly 40% 5-year survival rate among patients undergoing CRS with or without HIPEC for PR.[22] The management and survival observed in our study may not reflect the advances in modern systemic therapy. It also may reflect the survival differences among patients in routine clinical practice compared with those enrolled in clinical trials. These differences in outcomes, however, highlight the importance of risk stratification and better detection of patients with PR as treatment approaches are improving.

Clinicians have long debated the role of prophylactic CRS/HIPEC in patients at higher risk of developing PR. Several studies have explored the role of prophylactic HIPEC and delayed second-look laparoscopy in patients at high risk of PR.[15,23,24] These studies have culminated in two recent randomized clinical trials demonstrating no benefit of adjuvant HIPEC in patients thought to be at high risk for PR.[5,25] It is important to consider our findings in the context of these trials. The PROPHYLOCHIP trial enrolled patients with local peritoneal spread, ovarian metastases, or a perforated tumor. Patients underwent prophylactic HIPEC 6 months after resection following adjuvant chemotherapy.[25] The COLOPEC trial enrolled patients with a T4 or perforated tumor and prophylactic HIPEC was performed within 2 months of resection.[5] Histology was not reported in the PROPHYLOCHIP trial and less than 15% of patients in the COLOPEC trial had signet ring or mucinous histology. Our results suggest that patients with signet ring or mucinous tumors are at increased risk for PR. In particular, signet ring and mucinous histology were associated with increased risk of PR versus DR, whereas advanced T and N stage are predictors of any DR.

An analysis of PR following CRC resection was recently conducted using a regional cross-sectional database of 11 124 CRC patients in Sweden. The authors observed a rate of metachronous PR of 4.2%.[4] This rate was higher than our observed rate, although the study included patients with concurrent PR/DR in their PR cohort, while we assessed isolated PR. Similar small retrospective studies have observed a rate of 4-5% and have also included concurrent PR/DR patients.[26–28] In these studies, 40% of patients with metachronous PR had concurrent DR, suggesting that this significantly contributed to the difference in PR rate.[27,28] A recent analysis on patients with T4 disease demonstrated a 7.9% rate of peritoneal-only recurrence.[29] In addition, we performed purposeful sampling stratified by stage and, therefore, our cohort includes a population of patients biased towards a lower stage. In our study, 31.9% of patients were of Stage I, whereas in the Swedish study, 15.8% were of Stage I. The rate of PR from our study is not representative of the general population of resected CRC patients.

The analysis has several limitations that must be taken into consideration. First, our cohort may not be reflective of all patients.

This was a stage stratified retrospective study of patients that underwent primary resection from 2006 to 2007 and frequency of recurrence cannot be generalized to all Stage I–III CRC patients. Our cohort was also limited to patients treated at CoC-accredited centers, which may not be representative of all CRC patients treated in the United States. In addition, the random sample of 10 patients from each center, regardless of volume, might over-represent smaller centers. Second, under-detection is likely given the low sensitivity of current imaging for detecting PR. Additionally, follow-up ended at first recurrence, so patients who developed PR after other DR are not recorded. Similarly, patients with initial isolated PR might not have been detected clinically until they developed DR and these patients would not have been identified as having isolated PR in our study. Finally, we could not capture all variables that might impact the probability of PR. For example, our data set did not include information regarding perforation, which has been used as high-risk enrollment criteria for previous clinical trials of adjuvant HIPEC following CRC resection.[5,25] Nonetheless, this study provides "real world" data from a large sample of patients across the United States.

This large retrospective cohort study demonstrates that while relatively uncommon, PR occurs early following CRC resection and is frequently not detected until symptoms develop. PR is associated with poor outcomes and relatively few patients underwent surgical management. We identified advanced T and N stage, signet ring histology, and mucinous histology as risk factors for PR in our cohort. Detection of PR remains a challenge and the effectiveness of emerging methods such as ctDNA, tagged imaging studies, potentially with second-look laparoscopy in selected high-risk patients warrants further investigation.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

NA.

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