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The location of the primary colon cancer has no impact on outcomes in patients undergoing cytoreductive surgery for peritoneal metastasis ☆

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ABSTRACT

Background: The impact of the location of colorectal cancer on patient outcomes has been reported in several settings. The objective of this study was to assess the prognostic impact of the location of the primary colon cancer among patients with colorectal cancer peritoneal metastases undergoing complete cytoreductive surgery.

Methods: Using the prospectively maintained clinical and biological digestive peritoneal metastasis database of the BIG-RENAPE network, we identified 796 patients treated by a complete cytoreductive surgery between January 2004 and January 2017 for colorectal cancer peritoneal metastases in 16 different institutions. The 2 primary endpoints were overall survival and progression-free survival. To evaluate the impact on overall survival and progression-free survival of potential prognostic factors (including the location of the primary colorectal cancer), these factors were included in univariate and multivariate Cox proportional hazard models.

Results: Right-sided colorectal cancers were more often *BRAF* mutated and had microsatellite instability, whereas the frequency of *RAS* mutation was similar between right-sided and left-sided colorectal cancers. After a median follow-up time of 3.3 years, there was no significant difference in overall survival or progression-free survival according to tumor side. The lack of effect of tumor location on overall survival and progression-free survival was consistent across subgroups.

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Conclusion: Among patients undergoing complete cytoreductive surgery for peritoneal metastases, the site of the primary colorectal cancer was not associated with differences in progression-free survival or overall survival. Tumor side should not be used as a stratification factor in trials of colorectal cancer peritoneal metastases and should not be used in the selection process of patients for cytoreductive surgery.

Introduction

Colorectal cancers (CRCs) can be characterized by their primary location within the colon and rectum.[1] Biologic characteristics of left-sided (LS) CRC and right-sided (RS) CRC differ substantially. Differences in the microbiome[2] and carcinogenesis[3] have been reported according to tumor sidedness. As a consequence, RS CRC more commonly display mucinous histologic characteristics, microsatellite instability (MSI), and activating mutations of *KRAS, BRAF,* and *PIK3CA* genes[4,5] and, less often, *NRAS* and *p53* mutations.[5,6]

The impact of CRC location on patient outcomes has been reported in the settings of both localized and metastatic disease. Large population-based studies have found that survival after resection of colon cancer differs by tumor location; patients with stage III RS colon cancers have a worse prognosis.[7–9] In the metastatic setting, LS CRC is also associated with a significantly decreased risk of death[10,11]; these observations appear to be independent of the mutational spectrum within these CRCs.[11–14]

Some patients with CRC peritoneal metastases are candidates for surgery with the potential for long-term survival and cure.[15,16] The location of the primary CRC might be used as an aid in determining appropriate treatment strategies for patients with peritoneal metastasis secondary to CRC; however, the prognostic implication of the location of the primary CRC has not yet been examined in patients with resectable peritoneal metastases. The objective of this study was to assess the prognostic impact of the location of the primary CRC among patients with peritoneal metastases undergoing a complete cytoreductive surgery.

Material and methods

Study design and patient selection

A retrospective study of patients treated by a complete cytoreductive surgery between January 2004 and January 2017 for CRC peritoneal metastases was performed among 16 different institutions, 14 from the French national network of peritoneal surface malignancies (BIG-RENAPE) and 2 from Canada. The query was performed September 2017 on the BIG-RENAPE hybrid clinical database on digestive peritoneal metstases.[17]

Inclusion criteria were histologically proven CRC, synchronous or metachronous peritoneal metastases at time of operation, and a first complete cytoreductive surgery, defined as a completeness of cytoreduction (CC) score reported in the operative report of 0 or 1.[18] Patients were excluded when the side of the CRC was not reported or located on transverse colon or mid- and low rectum, when multiple primary sites of CRC were reported, and when the peritoneal carcinoma index (PCI) at the time of the cytoreductive surgery was 0 but there were nonresectable, synchronous, extraperitoneal metastases.

Study protocol

Detailed information was obtained on age, sex, site of the primary CRC, synchronicity between primary tumor and peritoneal metastases, *RAS* and *BRAF* mutational status, MSI, pathologic subtype, operative details such as duration of the operation and hyperthermic intraperitoneal chemotherapy (HIPEC), PCI,[18] major surgical complications, history and type of perioperative chemotherapy, and operative details.

The primary location of the CRC was determined by endoscopic, pathologic, or operative reports. To be consistent with previous studies, primary CRCs located in the cecum, ascending colon, and transverse colon were defined as RS CRCs, and those located in the splenic flexure, descending colon, sigmoid colon, and rectum were defined as LS CRCs.[19] *RAS* and *BRAF* mutations have been tested in most patients since late 2008, according to French clinical practice.[20] The duration of the operation was defined as the time between the start and the end of the cytoreduction, counting the time of HIPEC when performed using an open abdomen technique. Based on center protocol, HIPEC was performed either using an open ("coliseum") or closed technique, with the goal of reaching an intra-abdominal temperature of 43°C. The cytotoxic agents used were either oxaliplatin (360 mg/m^2 for 30 minutes) or mitomycin C (35 mg/m^2 for 90 minutes). PCI was scored during the cytoreductive surgery and extracted from the operative reports.[18] Postoperative morbidity and mortality were evaluated 90 days after cytoreductive surgery and graded by local investigators using the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 3.0. Major surgical complications were defined as any adverse event with a grade $\geq$ 3 according to the National Cancer Institute Common Terminology Criteria for Adverse Events. The type of perioperative chemotherapy was decided on by the center's specialized multidisciplinary team.

According to French guidelines, patients were followed with clinical examinations and surveillance imaging every 3 months for the first 3 years, then every 6 months for the next 2 years, and then annually.[21] Long-term outcomes were recorded, and the 2 primary endpoints were overall survival (OS) and progression-free survival (PFS). OS was assessed from the date of cytoreductive surgery until death from any cause. PFS was assessed from the date of cytoreductive surgery until death or relapse, whichever occurred first. Relapse was confirmed either on pathologic examinations or on radiologic examinations when peritoneal nodules appeared or increased in size. If relapse or death did not occur before the cutoff date, data were censored at the time of the last valid assessment. Progression was defined according to treating physicians in the 16 institutions.

Data analysis

Quantitative variables were expressed as median and 25th to 75th percentiles. Categorical variables were summarized as number and percentages. The nonparametric Mann-Whitney *U* test or Fisher exact test was used as appropriate to compare distributions of continuous and categorical variables between the 2 groups according to primary location of the CRC. OS and PFS were estimated by the Kaplan-Meier method and compared using the log-rank test according to primary location of the CRC.

To evaluate the impact on OS and PFS of potential prognostic factors (including primary location of the CRC), these factors were included in univariate Cox proportional hazard models. Continuous variables were modeled as binary using the most clinically

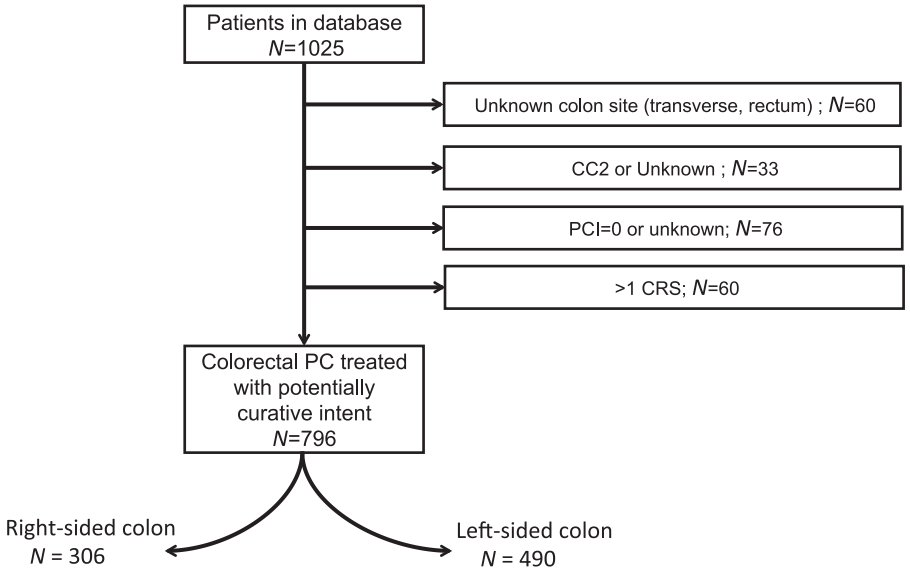

Fig. 1. Flow chart. *CC,* completeness of cytoreduction; *CRS,* cytoreductive surgery; *PC,* peritoneal carcinomatosis; *PCI,* peritoneal carcinoma index.

relevant thresholds. The proportional hazards assumption was assessed using the scaled Schoenfeld residuals. Variables considered as clinically relevant or yielding *P* values <.1 by univariate analysis were retained for multivariate model analysis. The objective of the multivariate analysis was to assess the independent effect of primary tumor side on survival outcomes. The added value of primary tumor side in the multivariate model was evaluated using a likelihood ratio test; the likelihood scores of the model evaluated with and without primary tumor side were compared, considering that lesser likelihood scores indicate better fitting models. All testing was 2-tailed. Subgroup analyses were performed to assess the impact of primary tumor side on OS and PFS in subgroups defined according to age; date of cytoreductive surgery; synchronicity between primary tumor and peritoneal metastasis; *RAS, BRAF,* and MSI status; CC score; HIPEC; PCI; duration of operation; major surgical complications; history and number of cycles of preoperative chemotherapy; and history of postoperative chemotherapy. Tests to determine interactions of the primary tumor side with covariates were used to identify predictive factors by assessing whether there was a significant difference in the primary tumor side effect on PFS and OS between subgroups.

Statistical analyses were performed with R Software Version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics

From January 2004 and January 2017, 1,025 patients undergoing a cytoreductive surgery for CRC peritoneal metastasis were included in the BIG-RENAPE database. Sixty patients were excluded because of multiple tumors or an unknown primary site, 33 were excluded because the completeness of the cytoreductive surgery was insufficient (CC2) or not reported, 76 were excluded because the PCI was 0 or not scored, and 60 were excluded because the procedure was not the first complete cytoreductive surgery (Fig 1). Among the 796 patients included in the study, 306 had RS CRC and 490 had LS CRC.

Patients with RS CRC were more likely to present with synchronous peritoneal metastases and to harbor signet cell pathologic characteristics. Patients with RS CRC also more often had a *BRAF* mutation (22% vs 11%, $P=.018$) and MSI (23% vs 10%, $P=.0096$), whereas the frequency of *RAS* mutation was similar between RS and LS CRCs. There was no significant difference in PCI, CC score, HIPEC administration, or a history and type of preoperative chemotherapy between RS and LS tumors. The duration of cytoreductive surgery was somewhat greater among patients with LS CRCs (median of 342 minutes vs 363 minutes, $P=.018$), whereas the administration of postoperative chemotherapy tended to be more common among patients with RS CRCs (71% vs 63%, $P=.055$). The rate of missing data was low for covariates associated with patient characteristics and treatment strategy (age, sex, PCI, CC score, HIPEC, preoperative chemotherapy) but was more prevalent for tumor characteristics (35% for *RAS* status, 62% for *BRAF* status, 73% for MSI status, and 33% for pathologic subtype) and for administration of postoperative chemotherapy (28%) (Table 1).

Overall survival

The median follow-up time was 3.3 years (95% confidence interval [CI] 3.0 months–3.7 years). There was no difference in duration of follow-up according to tumor side (median follow-up = 3.6 years in the RS group versus 3.2 years in the LS group, $P=.36$). The analysis of OS was based on 320 deaths (40% of patients), including 126 in the RS group (32%) and 194 in the LS group (40%). The median OS in the RS group was 3.5 years (95% CI 3.0–4.1 years) versus 4.0 years in the LS group (95% CI 3.5–4.4 years). The OS hazard ratio (HR) was 0.99 (95% CI 0.79–1.23, $P=.90$) (Fig 2, *A*).

In univariate analyses, patients' recent date of cytoreductive surgery, *BRAF* wild-type status, CC0, PCI ≤ 14, duration of the cytoreductive surgery <6 hours, absence of major surgical complications, and history of postoperative chemotherapy were associated with a better OS (Table 2). In the adjusted analysis using a multivariate Cox proportional hazard model, PCI ≤ 14 and absence of major surgical complications were independent factors associated with better OS. The side of the primary CRC was not associated with OS after adjustment on covariates (Table 2).

No significant effect of tumor side on OS was found across all subgroups. The duration of the operation was the only subgroup in which an impact of tumor side on OS was seen (<6 hours: HR 0.74; 95% CI 0.52–1.0, tending to favor the LS tumor group [$P=.096$]; ≥6 hours: HR 1.20; 95% CI 0.82–1.75; but a $P=.35$); the interaction test, however, was not statistically significant ($P=.055$) (see Supplemental Materials).

Table 1
Patient characteristics according to primary tumor location

Variable	*Data not available*	*All* (n = *796*)	*Location of primary CRC*		*P*
			Right sided (n = *306*)	*Left sided* (n = *490*)	
Age, y, median (25th–75th)	0	59 (51-65)	59 (51–65)	59 (51–65)	0.82
Sex male *(%)*	0	387 (49%)	147 (48%)	240 (49%)	0.85
Synchronous peritoneal metastases (%)	37	389 (51%)	162 (57%)	227 (48%)	0.017
Date of cytoreductive surgery Jan 1, 2012 or later (%)	0	427 (54%)	167 (55%)	260 (53%)	0.71
RAS mutation (%)	276	269 (52%)	110 (56%)	159 (49%)	0.15
BRAF mutation (%)	494	46 (15%)	24 (22%)	22 (11%)	0.018
MSI (%)	582	32 (15%)	19 (23%)	13 (10%)	0.0096
Signet-ring cells (%)	263	22 (4%)	14 (7%)	8 (2%)	0.011
Completeness of cytoreductive score (%)	60				0.94
CC0		702 (95%)	274 (95%)	428 (96%)	
CC1		34 (5%)	14 (5%)	20 (4%)	
HIPEC (%)	0	745 (94%)	284 (93%)	461 (94%)	0.57
PCI, median (25th–75th)	—	8 (4–13)	7 (4–14)	8 (4–13)	0.83
PCI > 14 (%)	0	194 (24%)	82 (27%)	112 (23%)	0.23
Duration of operation, median (25th–75th)	197	360 (282-450)	342 (262-449)	363 (300–450)	0.018
Major surgical complication (%)	58	351 (48%)	140 (49%)	211 (47%)	0.60
Preoperative chemotherapy (%)	0	709 (89%)	272 (89%)	437 (89%)	0.91
>6 preoperative chemotherapy cycles (%)	144	307 (47%)	103 (43%)	204 (49%)	0.12
Preoperative oxaliplatin (%)	282	249 (54%)	93 (53%)	156 (54%)	0.92
Preoperative irinotecan (%)	282	165 (32%)	65 (33%)	100 (32%)	0.85
Preoperative anti-EGFR (%)	282	31 (6%)	13 (7%)	18 (6%)	0.71
Preoperative antiangiogenic (%)	282	119 (23%)	43 (22%)	76 (24%)	0.52
Postoperative chemotherapy (%)	223	380 (66%)	152 (71%)	28 (63%)	0.055

Table 2
Prognostic factors of overall survival in univariate and multivariate analysis (Cox model)

				Cox proportional hazards regression for overall survival			
				Unadjusted analysis		*Adjusted analysis*	
	Data not available	N *(%)*	*3-y OS rate (%) (95% CI)*	*HR (95%CI)*	P	*HR (95% CI)*	P
Tumor side							
Right side	0	306 (38%)	57 (51–64)	REF	.90	REF	.21
Left side		490 (62%)	62 (57–68)	1.0 (0.8–1.2)		0.8 (0.6–1.1)	
Age (y)							
<60	0	422 (53%)	57 (52–63)	REF	.15	NI	NI
≥60		373 (47%)	64 (58–70)	0.8 (0.7–1.1)			
Date of cytoreductive surgery							
Before 2012	0	369 (46%)	57 (51–62)	REF	.034	REF	.051
2012 or later		427 (54%)	66 (60-72)	0.8 (0.6–1.0)		0.7 (0.5–1.0)	
Carcinomatosis							
Metachronous	37	370 (49%)	62 (57–68)	REF	.21	NI	NI
Synchronous		389 (51%)	61 (56–67)	1.2 (0.9–1.5)			
Pathologic subtype							
No signet-ring cells	263	511 (96%)	62 (57–67)	REF	.28	NI	NI
Signet-ring cells		22 (4%)	56 (38–82)	1.4 (0.8–2.4)			
Completeness of cytoreduction score							
CC0	60	702 (95%)	61 (57–66)	REF	.0034	REF	.45
CC1		34 (5%)	39 (25–61)	1.9 (1.1–2.8)		1.2 (0.7–2.2)	
HIPEC							
No	0	51 (6%)	60 (47–76)	REF	.75	NI	NI
Yes		745 (94%)	60 (56–65)	1.1 (0.7–1.6)			
PCI							
≤14	0	602 (76%)	68 (63–72)	REF	<.0001	REF	.00012
>14		194 (24%)	39 (32–48)	2.3 (1.8–2.9)		2.0 (1.4–2.8)	
Duration of operation							
<6 h	197	327 (55%)	64 (58–70)	REF	.0054	REF	.18
≥6 h		272 (45%)	49 (42–57)	1.4 (1.1–1.8)		1.3 (0.9–1.8)	
Major surgical complication							
No	58	387 (52%)	64 (58–70)	REF	.00023	REF	.042
Yes		351 (48%)	53 (47–60)	1.5 (1.2–1.9)		1.4 (1.0–1.9)	
Preoperative chemotherapy							
No	0	87 (11%)	60 (49–73)	REF	.92	NI	NI
Yes		709 (89%)	60 (56–65)	1.0 (0.7–1.4)			
No preoperative cycles							
≤6	144	345 (53%)	59 (53–66)	REF	1.0	NI	NI
>6		307 (47%)	62 (56–68)	1.0 (0.8–1.3)			
Postoperative chemotherapy	223						
No		193 (34%)	58 (50–66)	REF	.043	REF	.35
Yes		380 (66%)	58 (52–65)	0.8 (0.6–1.0)		0.9 (0.6–1.2)	

NI, not included; *REF*, reference.

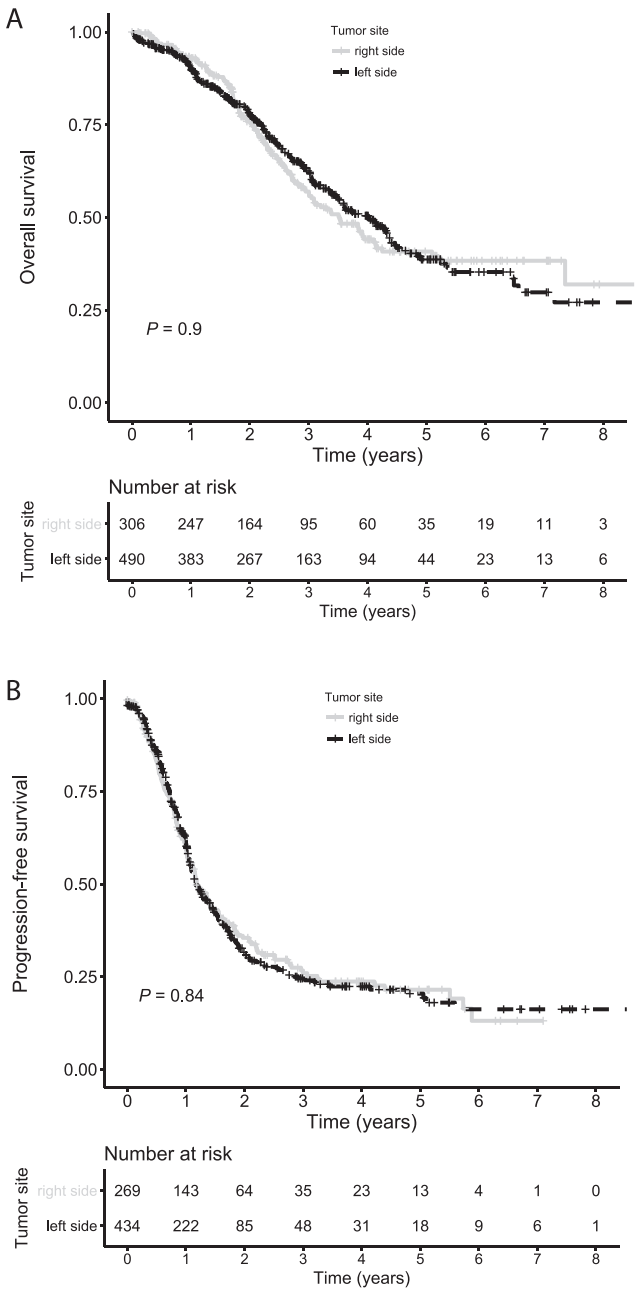

Fig. 2. Survival of patients according to the side of the primary CRC. A, Overall survival according to the side of the primary tumor. B, Progression-free survival according to primary tumor side.

Progression-free survival

Follow-up imaging data were missing for 93 patients, and the PFS analysis was performed on the remaining population of 703 patients. The PFS analysis was based on 453 progressions or deaths (64% of patients), including 178 in the RS group (66%) and 275 in the LS group (63%). The median PFS in the RS group was 1.2 years (95% CI 1.1–1.5 years) versus 1.2 years in the LS group (95% CI 1.1–1.4 years). The PFS HR was 1.02 (95% CI 0.85–1.23, $P = .84$) (Fig 2, *B*).

In univariate analyses, patients age > 60 years, a more recent date of cytoreductive surgery, CC0, PCI ≤ 14, absence of a major surgical complication, number of preoperative chemotherapy cycles ≤ 6, and a history of postoperative chemotherapy were associated with a better PFS (Table 3). In the adjusted analysis using a multivariate Cox proportional hazard models, a more recent date of cytoreductive surgery, PCI ≤ 14, absence of a major surgical complication, number of preoperative chemotherapy cycles ≤ 6, and history of postoperative chemotherapy were independent factors associated with better PFS. The side of the primary CRC was not associated with PFS after adjustment on covariates (Table 3).

No significant effect of tumor side on PFS was identified across all subgroups (see Supplemental Materials).

Discussion

This large, multicenter study of prospectively collected data found that the side of the primary CRC had no impact on long-term outcomes for patients with peritoneal metastases undergoing a complete cytoreductive resection. In particular, there was no impact on OS and PFS, and this result was consistent across all subgroups. According to previous published evidence, RS CRCs were more often *BRAF* mutated and had MSI compared with LS CRCs.[4] These different molecular features between RS and LS CRCs was identified also among the patients with peritoneal metastases included in this study.

For patients with stage IV CRC, RS CRCs have been associated consistently with worse outcome among patients treated with exclusive supportive care[22] and palliative chemotherapy[10,11,23] and in those undergoing curative resection of liver metastases.[24–26] The unfavorable outcomes of patients with RS CRCs have been reported among *RAS* wild-type (WT) patients.[25,27] Moreover, for patients with RAS WT CRCs, the left side is also predictive of a greater efficacy of anti–epidermal growth factor (EGFR) treatment.[27,28] Despite these observations, the conclusions that can be derived from studies including mostly patients with liver and lung metastases cannot always be applied to patients with peritoneal metastasis. As an example, *RAS* mutations are associated with significantly worse outcomes among patients operated for liver metastasis,[29–31] but these same *RAS* mutations do not affect outcomes among patients undergoing resection of CRC peritoneal metastasis.[29] In this study we found no impact of side of the primary CRC on outcomes after complete cytoreductive surgery for a peritoneal metastases, whatever the status of *RAS* and *BRAF* mutation. Given the high rate of missing data regarding the type of perioperative chemotherapy and the low number of patients treated with anti-EGFR therapy, no formal recommendations can be offered from these data regarding the choice of the optimal perioperative chemotherapy. We acknowledge that the general assumption that patients with RS, metastatic, *RAS* WT CRC may benefit more from initial treatment with bevacizumab in combination with chemotherapy and those with LS primary CRCs should receive first-line treatment with anti-EGFR therapies[11,19,32,33] seems disputable in the context of peritoneal metastasis.

Prognostic factors and scores have been developed to guide selection of patients for operative intervention based on favorable tumor biology.[34,35] The independent prognostic value of the side of the primary CRC makes it an eligible biomarker for patient selection. Among selected patients undergoing liver resections for metastatic CRCs, tumor side affected OS, but the reported cure rates were not different according to tumor side,[24,36] suggesting that the location of the primary CRC should not change decision making concerning resection of CRC liver metastases. Our results suggest that among selected patients undergoing a complete cytoreductive surgery for peritoneal metastases secondary to CRC, OS and cure rate are not different according to the side of the primary CRC. From our data, we maintain that there is no reason to include the side of the primary CRC in the selection of patients for peritoneal cytoreductive surgery.

Table 3
Prognostic factors of progression-free survival in univariate and multivariate analysis (Cox model)

				Cox proportional hazards regression for progression-free survival			
				Unadjusted analysis		*Adjusted analysis*	
	Data not available	N *(%)*	*3-y PFS rate (%) (95% CI)*	*HR (95%CI)*	P	*HR (95% CI)*	P
Tumor side							
Right side	0	306 (38%)	26 (20–32)	REF	.84	REF	.24
Left side		490 (62%)	24 (20–30)	1.0 (0.8–1.2)		0.9 (0.7–1.1)	
Age (y)							
<60	0	422 (53%)	23 (19–29)	REF	.036	REF	.26
≥60		373 (47%)	27 (22–34)	0.8 (0.7–1.0)		0.9 (0.7–1.1)	
Date of cytoreductive surgery							
Before 2012	0	369 (46%)	21 (16–26)	REF	.019	REF	.021
2012 or later		427 (54%)	31 (25–37)	0.8 (0.7–1.0)		0.8 (0.6–1.0)	
Carcinomatosis							
Metachronous	37	370 (49%)	28 (22–34)	REF	.15	NI	NI
Synchronous		389 (51%)	24 (19–29)	1.1 (1.0–1.4)			
Pathologic subtype							
No signet-ring cells	263	511 (96%)	27 (23–33)	REF	.56	NI	NI
Signet-ring cells		22 (4%)	20 (8–48)	1.1 (0.7–1.8)			
Completeness of cytoreduction score							
CC0	60	702 (95%)	24 (21–29)	REF	.018	REF	.40
CC1		34 (5%)	7 (2–26)	1.6 (1.1–2.4)		1.2 (0.8–2.0)	
HIPEC							
No	0	51 (6%)	20 (11–35)	REF	.94	NI	NI
Yes		745 (94%)	26 (22–30)	1.0 (0.7–1.4)			
PCI							
≤14	0	602 (76%)	30 (25–35)	REF	<.0001	REF	<.0001
>14		194 (24%)	13 (8–20)	1.8 (1.5–2.2)		1.7 (1.3–2.2)	
Duration of operation							
<6 h	197	327 (55%)	25 (20–31)	REF	.57	NI	NI
≥6 h		272 (45%)	30 (24–39)	0.9 (0.7–1.2)			
Major surgical complication *NA=58*							
No		387 (52%)	30 (25–36)	REF	.00027	REF	.012
Yes		351 (48%)	19 (14–26)	1.4 (1.2–1.8)		1.3 (1.1–1.7)	
Preoperative chemotherapy							
No	0	87 (11%)	24 (16–37)	REF	.99	NI	NI
Yes		709 (89%)	25 (22–30)	1.0 (0.8–1.3)			
No preoperative cycles							
≤6	144	345 (53%)	28 (22–35)	REF	.014	REF	.015
>6		307 (47%)	23 (18–29)	1.3 (1.1–1.6)		1.3 (1.1–1.7)	
Postoperative chemotherapy							
No	223	193 (34%)	25 (19–33)	REF	.0027	REF	.010
Yes		380 (66%)	25 (20–32)	0.7 (0.6–0.9)		0.7 (0.6–0.9)	

NI, not included; *REF*, reference.

In the PRODIGE 7 phase III trial, patients were treated with cytoreductive surgery plus HIPEC with oxaliplatin or cytoreductive surgery alone in association with systemic chemotherapy. There was no significant impact of HIPEC with oxaliplatin on long-term outcomes.[37] Most of the patients included in this series were treated before the presentation of the results of this trial and received HIPEC; however, given the absence of interaction between HIPEC and tumor side in this study and given the absence of any impact of HIPEC with oxaliplatin on long-term outcomes in the PRODIGE 7 trial, it is unlikely that tumor side would affect the prognosis of patients treated with cytoreductive surgery without HIPEC.

The limitations of our study include the heterogeneity of patients in the RS and LS groups, a relatively uncontrolled selection of patients for cytoreductive surgery, and the high rate of missing data concerning biologic tumor characteristics and perioperative treatment types. Nevertheless, the consistent lack of impact of the side of the primary CRC across all subgroups analyzed enhances our confidence in this result. Furthermore a consensus appears to exist on favoring classification of CRC based on molecular characteristics rather than sidedness.[38] Given the present results, the impact on survival of this molecular classification should be further investigated in the setting of peritoneal metastases. We want to point out that patients not amenable to cytoreductive surgery and patients with incomplete cytoreductive surgery were excluded from this survey, and thus the results cannot be applied to these patient populations.

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Supplementary materials

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