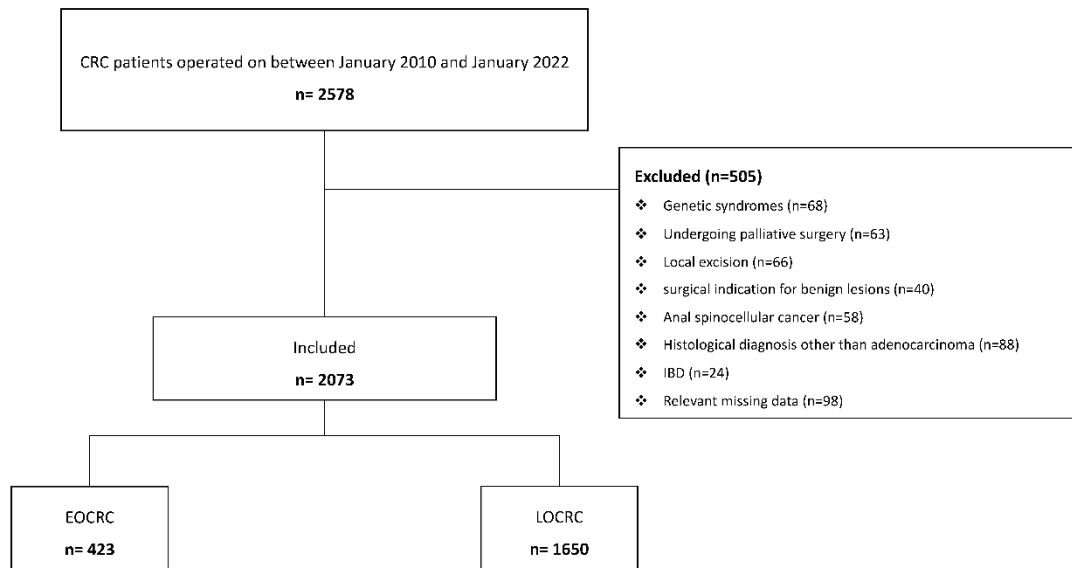


**Table S1. Detailed list of the variables included in the prospective institutional database and the variables selected to be analyzed in the study**

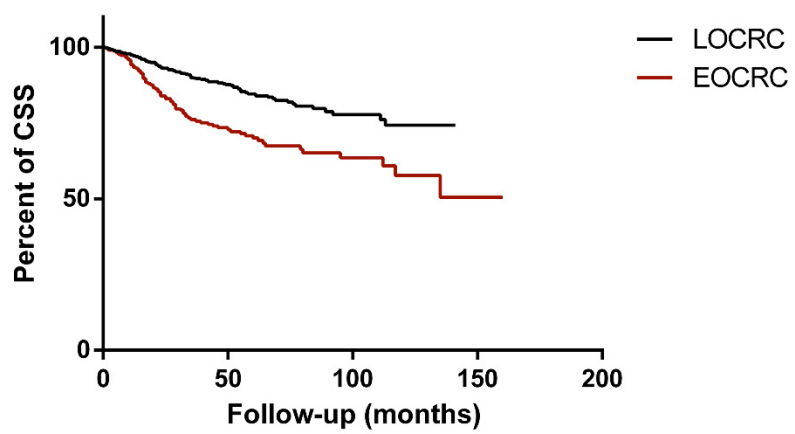
<b>Variable category</b>	<b>Prospective institutional database</b>	<b>Selected variables</b>
<b>Demographic</b>	Date of birth; Place of birth; Gender; Date of diagnosis; Age at diagnosis.	Gender; Age at diagnosis
<b>Clinical information</b>	Weight; Height; BMI; Previous medical history; CCI; Previous and concomitant medications; Previous surgeries; Smoking status; Alcohol addiction; Relevant infections; Tumor location; Family history of CRC (and degree relatives); Family history of tumor (and degree relatives); Known history of genetic syndromes; Type of genetic syndrome.	BMI; Previous medical history; CCI; Smoking status; Tumor location; Family history of CRC (and degree relatives); Family history of tumor (and degree relatives); Known history of genetic syndromes (if yes, patients were excluded).
<b>Therapeutics information</b>	Preoperative chemo or chemoradio treatment; Hospital of treatment; Start date and end date of treatment; Type of treatment; Indication for treatment; Adverse reactions related to treatment.	Preoperative chemo or chemoradio treatment.
<b>Preoperative scores and scales</b>	MUST score; HADS score; PSS score; EORTC-CR30/C29; LARS score (whenever possible).	
<b>Radiological/endoscopic information</b>	Date of colonoscopy; Colonoscopy findings; Date of MRI; MRI findings; Date of CT scan; CT scan findings; Preoperative evidence of distal metastasis; Metastasis sites; Preoperative evidence of synchronous CRC; Synchronous CRC localization; cTNM; Mesorectal fascia involvement; Date of restaging (if indicated); Type of restaging; cTNM of restaging.	Preoperative evidence of distal metastasis; Preoperative evidence of synchronous CRC; Synchronous CRC localization.
<b>Surgical data</b>	Date of surgery; Type of surgery; Surgery denomination; Start time; End time; Operative time; Surgery setting; Surgical approach; Type of anesthesia; Ileostomy/colostomy construction; Additional resections (e.g. hepatic resections); Surgical-related complications; EBL; Intraoperative transfusion; Drain placement.	Type of surgery; surgery denomination; operative time; surgery setting; surgical approach; Additional resections (e.g. hepatic resections).
<b>Postoperative outcomes</b>	Date of admission; Date of discharge; LOS; Discharge setting; 90-day postoperative complications; Clavien-Dindo classification (of the most severe complication); CCI (all complications); 48-h and 72-h postoperative pain (VAS scale); 24-h, 48-h, and 72-h CRP; Opioid medications; Time to first flatus; Time	LOS; 90-day postoperative complications; Clavien-Dindo classification (most severe complication); 90-day reoperation.

	to first bowel movement; Daily drain volumes (if applicable); 90-day reoperation; type of reoperation; 90-day readmission.	
<b>Pathological data</b>	pTNM classification; Tumoral stage (AJCC 8 <sup>th</sup> edition); Grade of regression Dworak (if applicable); Number of harvested lymph nodes; Number of positive lymph nodes; Lymph nodes ratio; Circumferential margin positivity; Distance of the tumor from the distal margin; Resection margins; Mucinous phenotype; Signet-ring cells phenotype; Microsatellite status; Grade of differentiation; Extramural invasion; Perineural invasion; Lymphovascular invasion; Mutations test; mutated gene; type of mutation.	pTNM classification; Tumoral stage (AJCC 8 <sup>th</sup> edition); Grade of regression Dworak (if applicable); Number of harvested lymph nodes; Number of positive lymph nodes; Lymph nodes ratio; Circumferential margin positivity; Distance of the tumor from the distal margin; Resection margins; Mucinous phenotype; Signet-ring cells phenotype; Microsatellite status; Grade of differentiation; Extramural invasion; Perineural invasion; Lymphovascular invasion; Mutations test.
<b>Postoperative scores and scales</b>	30-day: MUST score; HADS score; PSS score; EORTC-CR30/C29; LARS score (whenever possible). 6-month: MUST score; HADS score; PSS score; EORTC-CR30/C29; LARS score (whenever possible). 12-month: MUST score; HADS score; PSS score; EORTC-CR30/C29; LARS score (whenever possible).	
<b>Postoperative treatment information</b>	Adjuvant therapy; Type of adjuvant therapy; Start date; End date; Therapy duration; Hospital of therapy; Adverse reactions related to therapy; Withdrawal; Reason for withdrawal; Stoma closure (if applicable); Date of stoma closure.	Adjuvant therapy.
<b>Oncological outcomes</b>	Date of last follow-up; Status at last follow-up (alive/dead); Date of death; Cause of death; Cancer-related death; Time from surgery to death; Recurrence; Progression; Site of recurrence/progression; Date of recurrence or progression; Time from surgery to recurrence/progression; Time from surgery to last follow-up; Therapy for recurrence/progression; Type of therapy; Surgery for recurrence/progression; Type of surgery; Date of surgery for recurrence; Metachronous CRC tumors; Date of metachronous CRC	Status at last follow-up (alive/dead); Cancer-related death; Time from surgery to death; Recurrence; Progression; Time from surgery to recurrence/progression; Time from surgery to last follow-up; Metachronous CRC tumors; Other neoplasms.

	tumor diagnosis; Other neoplasms; Date of other neoplasm diagnosis.	
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**Figure S1:** study inclusion flowchart.



**Figure S2:** CSS (Cancer specific-free survival) of EORC (Early-onset colorectal cancer) (red line) and LORC (Late-onset colorectal cancer) (black line) patients. Data were compared with Kaplan-Meier analysis and Log-rank (Mantel-Cox) test (HR=2.09; 95% CI: 1.77-3.46;  $p < 0.0001$ ). The CSS proportion in EOCRC patients at 36 months was 76% versus 89% in the LOCRC group (150/344 versus 501/1636 subjects at risk).