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ORIGINAL ARTICLE

Hospital stay for temporary stoma closure is shortened by C-reactive protein monitoring: a prospective case-matched study

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Abstract

Background C-reactive protein (CRP) has been suggested as a satisfactory early marker of postoperative complications after colorectal surgery. The aim of this study was to assess the impact of a CRP monitoring-driven discharge strategy, after stoma reversal following laparoscopic sphincter-saving surgery for rectal cancer.

Methods Eighty-eight patients who had stoma reversal between June 2016 and April 2018 had CRP serum level monitoring on postoperative day (POD) 3 and, if necessary, on POD5. Patients were discharged on POD4 if the CRP level was < 100 mg/L. Patients were matched [according to age, gender, body mass index, neoadjuvant pelvic irradiation, type of anastomosis (stapled or manual), and adjuvant chemotherapy] to 109 identical control patients who had stoma reversal between 2012 and 2016 with the same postoperative care but without CRP monitoring.

Results Postoperative 30-day overall morbidity [CRP group: 12/88 (14%) vs controls: 11/109, (10%), $p = 0.441$] and severe morbidity rates (i.e. Dindo 3–4) [CRP group: 2/88 (2%) vs controls: 2/109 (2%), $p = 0.838$] were similar between groups. Mean length of stay was significantly shorter in the CRP group (CRP group: 4.6 ± 1.3 vs controls: 5.8 ± 1.8 days; $p < 0.001$). Discharge occurred before POD5 in 59/88 (67%) CRP patients vs 15/109 (14%) controls ($p < 0.001$). The unplanned rehospitalization rate [CRP group: 6/88 (7%) vs controls: 4/109 (4%), $p = 0.347$] was similar between groups.

Conclusions In patients having temporary stoma closure after laparoscopic surgery for rectal cancer, postoperative CRP monitoring is associated with a significant shortening of hospital stay without increasing morbidity or rehospitalization rates.

Keywords Stoma closure · Postoperative CRP monitoring · Length of hospital stay · Dosage-driven-strategy

Introduction

Proctectomy with total mesorectal excision (TME) is the gold standard for rectal cancer management [1]. Although this procedure is associated with optimal oncologic outcomes, it is associated with a significative risk of anastomotic leakage (AL), with reported rates as high as 27% [2–5]. AL has been demonstrated to be a risk factor for increased risks of postoperative mortality [6], definitive stoma [7, 8], impaired functional outcomes [9], and long-term tumour recurrence [10]. Diverting stoma has been demonstrated to be associated with reduced postoperative AL rate [2, 11], and is now recommended following restorative rectal cancer surgery [1].

Stoma reversal (SR) is usually considered as a safe procedure with limited postoperative morbidity risk. In a meta-analysis including 6107 patients, Chow et al. reported a postoperative mortality rate as low as 0.4% and a postoperative morbidity rate of 17%, mainly comprising minor complications [12]. However, the authors also highlighted a surprisingly long mean postoperative length of stay (LoS) of up to 5.1 days [12]. Waiting for bowel action and observation for potential postoperative intra-abdominal septic complications, such as AL, may be a reason for this surprisingly long LoS.

In this setting, the development of biomarkers able to early predict postoperative intra-abdominal septic complications following SR might allow a selective discharge strategy, leading to reduced LoS in low-risk patients. Several studies have focused on biomarkers as predictor of septic complication following colorectal surgery, and especially

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C-reactive protein (CRP) [13–16]. CRP is an acute-phase protein produced by the hepatocytes as part of the stress response associated with inflammation, surgery, and infection [17]. Some authors developed a postoperative clinical–biological score, including CRP levels, able to predict the occurrence of a postoperative septic complications following colorectal resection with anastomosis [18]. However, no study to date has focused on postoperative CRP monitoring after elective SR following laparoscopic sphincter-saving surgery for rectal cancer.

Our aim was to prospectively evaluate a postoperative discharge strategy using CRP monitoring, in patients undergoing SR following laparoscopic sphincter-saving surgery for rectal cancer.

Materials and methods

Study population

All patients having SR after laparoscopic surgery for rectal cancer between June 2016 and April 2018 in our institution were prospectively included and constituted the CRP group. Exclusion criteria were: patients presenting with synchronous metastasis, patients with rectal adenocarcinoma complicating inflammatory bowel disease or a familial adenomatous polyposis, and patients operated on for pelvic recurrence after a primary surgery.

Stoma closure

All resections had been performed according to the latest French rectal cancer guidelines [1]. In all patients, rectal surgery was carried out laparoscopically and a stapled colorectal or a hand-sewn coloanal anastomosis was performed, according to the tumour distance from the anal verge. In all cases, a diverting ileostomy was fashioned at the end of the operation. Diverting SR was planned 6–8 weeks after rectal surgery, in the absence of anastomotic leakage on a computed tomography (CT) scan with contrast enema.

No mechanical bowel preparation was performed before SR. Surgery was performed according to a standardized procedure for all the patients. Briefly, all patients were operated on through an elective, peristomial, approach under general anesthesia. All patients received a prophylactic intravenous antibiotic (cefoxitin, 2 g) as recommended by the Société Française d'Anesthésie Réanimation (SFAR) guidelines [19]. The procedure started with an adequate mobilization of the two small bowel segments. A hand-sewn end-to-end anastomosis was then performed using 5-0 polydioxanone (PDS®, Ethicon, Somerville, NJ, USA). In all patients, the abdominal wall was closed in two layers using a continuous absorbable suture (Vicryl® 1, Ethicon, Somerville, NJ, USA). The skin was partially left open using a purse-string technique with a 4.0 poliglecaprone suture (Monocryl®, Ethicon, Somerville, NJ, USA).

Postoperative CRP monitoring-driven strategy management

Postoperative discharge was planned according to the results of postoperative CRP monitoring in all CRP group patients, as described in Fig. 1. The CRP level was measured on postoperative day (POD) 3. Patients with a CRP level ≤ 100 mg/L were discharged on POD4, in the absence of any sign of postoperative complications, and if bowel function and feeding was normal. Patients with a CRP level > 200 mg/L on POD3 had immediate abdominopelvic CTscan to rule out postoperative intra-abdominal sepsis. In patients with a CRP level between 100 and 200 mg/L, discharge was postponed, and the CRP level was measured again on POD5. Discharge was then allowed on POD6 in all patients presenting with reduction in the CRP level of > 30% between POD3 and POD5, in the absence of any sign of postoperative complications, and if bowel function and feeding were normal. An abdominopelvic CT scan was performed on POD5 in all other patients.

Following discharge, all patients from the CRP group received telephone-delivered supportive care to exclude late complications and fulfil potential unmet needs. All patients from the CRP group were routinely seen in the outpatient clinic, 4–6 weeks after SR.

Control population

All patients from the CRP group were individually matched to all identical patients who had SR following laparoscopic sphincter-saving surgery for rectal cancer between January 2012 and May 2016, according to age (± 10%), gender, body mass index (BMI, ± 10%), neoadjuvant pelvic irradiation, type of anastomosis (stapled or manual), and adjuvant chemotherapy. These patients received the same postoperative care as patients from the CRP group, but did not have any postoperative CRP monitoring. All control patients were seen in the outpatient clinic, 4–6 weeks after SR.

Outcome measures

Primary outcome was postoperative LHS. Secondary outcomes were rehospitalization rate, 30-day postoperative overall morbidity, 30-day postoperative severe morbidity, and postoperative hospital costs. Overall 30-day postoperative morbidity included all postoperative complications and was defined and graded according to the Clavien–Dindo classification [20]. Severe postoperative morbidity included all complications graded 3 or 4 [20]. Hospital costs included costs of the

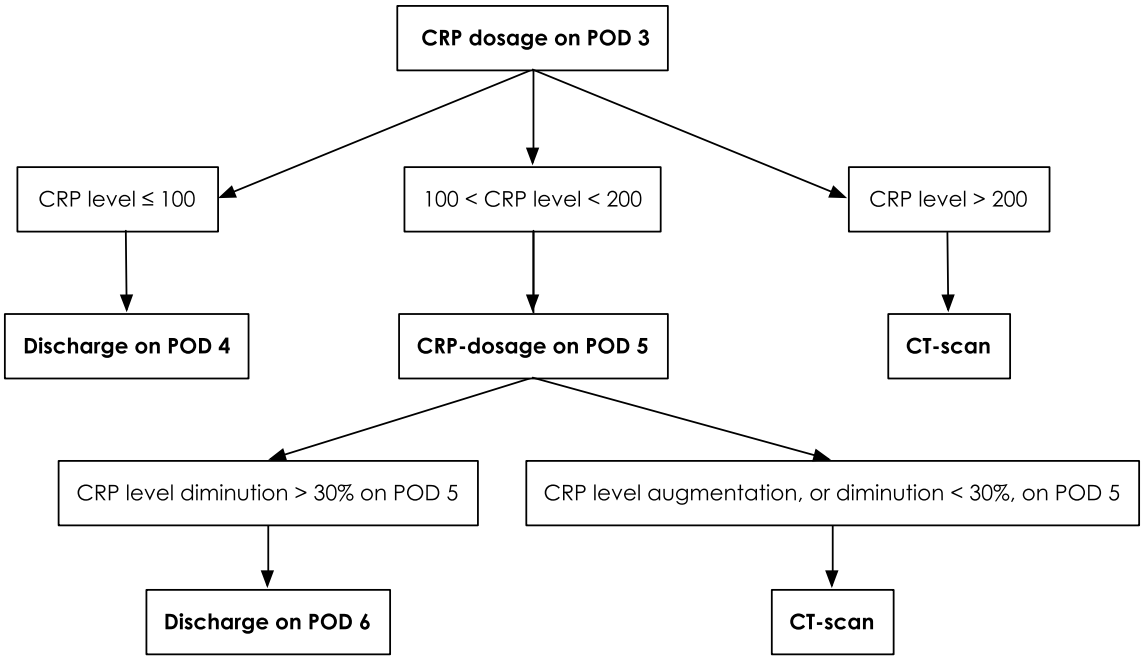

Fig. 1 Postoperative CRP monitoring-driven discharge strategy after stoma reversal following laparoscopic sphincter-saving surgery for rectal cancer

surgical procedure, the primary hospitalization, and potential rehospitalization and reintervention. All costs were extracted from our administrative records and established according to the French national medical classification for clinical procedures (Classification Commune des Actes Médicaux, CCAM).

Statistical analysis

Quantitative data were reported as mean ± standard deviation (range) and were compared using the Mann–Whitney *U* test. Qualitative data were reported as number of patients (percentage of patients) and compared using either the Pearson χ^2 test or the Fisher exact test, depending on the sample size. All tests were two sided with a level of significance set at $p < 0.05$. All analyses were performed using SPSS for Mac OSX (version 22.0, IBM Corp, Armonk, NY, USA).

This study was approved by our institutional review board, conducted according to the ethical standards of the Committee on Human Experimentation of our institution, and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [21].

Results

CRP group

A total of 88 patients had SR following laparoscopic surgery for rectal cancer between June 2016 and April 2018 and these constituted the CRP group. In all patients, postoperative discharge was planned according to the previously defined postoperative CRP monitoring-driven strategy.

Patient demographics and characteristics of primary rectal surgery are provided in Table 1. A total of 50/88 (57%) patients were males, with a mean age of 61 ± 13 (22–84) years, and a mean body mass index (BMI) of 26 ± 5 (18–43) kg/m^2. The majority had neoadjuvant pelvic irradiation ($n = 66/88$, 75%) before rectal cancer surgery. A total of 67/88 (76%) patients had a mid or a low rectal tumour, and an intersphincteric resection was performed in 27/88 (31%). The anastomosis was stapled in 61 patients (69%) and hand-sewn in 27 patients (31%). A side-to-end anastomosis was performed in the majority of the cases ($n = 59/88$, 67%). During SR, an elective hand-sewn end-to-end ileo-ileal anastomosis was performed. No patients required conversion to a midline incision.

Following SR, postoperative mortality was nil. Overall 30-day postoperative morbidity was observed in 12/88 patients (14%) including minor complications graded 1–2 according to the Clavien–Dindo classification in 9/88 (10%) patients (hypokalemia, $n = 2$; rectal bleeding, $n = 1$; pulmonary atelectasia, $n = 1$; prolonged ileus, $n = 1$; acute renal failure, $n = 1$; acalculous cholecystitis, $n = 1$; wound abscess, $n = 1$; pancytopenia, $n = 1$, and an enterocutaneous fistula related to anastomotic leakage treated conservatively, $n = 1$) and severe complications graded 3–4 in 2/88 patients (2%), diagnosed after discharge, and comprising an intra-abdominal hematoma requiring CT-guided drainage, diagnosed on

Table 1 Baseline characteristics of 197 patients who underwent stoma reversal following laparoscopic sphincter-saving surgery for rectal cancer

	Overall ($n=197$)	CRP group ($n=88$)	Control group ($n=109$)	p value
Sex				0.143
Female	74 (38)[a]	38 (51)	36 (49)	
Male	123 (62)	50 (57)	73 (67)	
Age, years	62 ± 12[b]	61 ± 13	62 ± 10	0.626
Body mass index, kg/m^2	25 ± 5	26 ± 5	25 ± 4	0.936
ASA score				
ASA score 1–2	181 (92)	78 (89)	103 (94)	0.134
ASA score 3–4	16 (8)	10 (11)	6 (6)	
Neoadjuvant radiotherapy				0.747
Yes	151 (77)	66 (75)	85 (78)	
No	46 (23)	22 (25)	24 (22)	
Tumour location				0.265
Upper rectum	40 (20)	21 (24)	19 (17)	
Mid/Low rectum	157 (80)	67 (76)	90 (83)	
Anastomosis type				0.451
Hand-sewn Coloanal	66 (33)	27 (31)	39 (36)	
Stapled Colorectal	131 (66)	61 (69)	70 (64)	
Anastomosis construction				0.494
Side-to-end	137 (70)	59 (67)	78 (72)	
End-to-end	60 (30)	29 (33)	31 (28)	
pT stage				0.499
T3–T4	91 (46)	43 (49)	48 (44)	
T0-Tis-T1–T2	106 (54)	45 (51)	61 (56)	
pN Stage				0.343
N +	56 (28)	28 (32)	28 (26)	
N0	141 (72)	60 (68)	81 (74)	

[a]Number of cases (percentage of cases)

[b]Mean ± standard deviation

CRP C-reactive protein, *ASA* American society of anesthesiologists

POD11, and an anastomotic leak requiring reintervention, diagnosed on POD29.

Mean CRP level on POD3 was 50 ± 41 (range 6–284) mg/L POD3 CRP level was significantly increased in patients who presented with postoperative complications, vs without [43 ± 31 (range 6–149) mg/L, $p<0.001$].

A total of 80/88 patients (91%) had a CRP level < 100 mg/L on POD3, allowing discharge on POD3 in 2/88 (2%) patients, who were discharged 24 h earlier for administrative reasons, and on POD4 in 57/88 (65%) patients. Discharge was delayed after POD4 in 21 patients despite a CRP level < 100 mg/L on POD3 for social reasons ($n=11$), minor complications ($n=6$), ileus ($n=4$), or postoperative pain ($n=1$). A total of 7/88 patients (8%) presented with a CRP level between 100 and 200 mg/L on POD3, and were discharged on POD6, because the CRP level decreased more than 30% on POD5 in 7/7 patients (100%). Finally, 1/88 patient (1%) presented with a CRP level on POD3 > 200 mg/L and was discharged on POD14 because of prolonged ileus. This CRP monitoring-driven strategy led to a mean LHS of 4.6 ± 1.3 (range 3–14) days.

A total of 6/88 (9%) patients required rehospitalization within 30 days following SR because of late minor complications ($n=6$) or severe complications ($n=2$), as reported before.

Control group

CRP group patients were matched with 109 control patients (Table 1): 73/109 (67%) were males, with a mean age of 62 ± 10 (range 34–85) years, and a mean BMI of 25 ± 4 (range 17–42) kg/m^{2,} and 85/109 (78%) received neoadjuvant radiochemotherapy before rectal cancer surgery. A total of 90/109 (83%) patients had a mid or a low rectal tumour, and an intersphincteric resection was performed in 39/109 (36%). Anastomosis was stapled in 70/109 patients (64%) and handsewn in 39/109 patients (36%). A side-to-end anastomosis was performed in the majority of the cases

($n=78/109$, 72%). During SR, an elective hand-sewn end-to-end ileo-ileal anastomosis was performed in all patients. No patients required conversion to midline incision.

Following SR, postoperative mortality was nil. Overall 30-day postoperative morbidity was observed in 11/109 patients (10%) including minor complications graded 1–2 according to the Clavien–Dindo classification in 9/109 (8%) patients (prolonged ileus, $n=4$; acute urinary retention $n=2$; portal thrombosis $n=1$; intra-abdominal abscess $n=1$; wound abscess $n=1$), and severe complications graded 3–4 (intra-abdominal abscess requiring CT-guided drainage) in 2/109 patients (2%). A total of 2/109 (2%) patients were discharged on POD 3 and 13/109 (12%) were discharged on POD 4, leading to a mean LHS of 5.8 ± 1.8 (range 3–14) days and 4/109 (4%) patients required rehospitalization because of minor ($n=2$) or severe ($n=2$) complications, as reported above.

Comparative outcomes

As shown in Table 2, there was no difference between the 2 groups regarding 30-day postoperative overall ($p=0.441$) and severe morbidity ($p=0.838$). However, patients from the CRP group were more likely to be discharged on POD4 than those from the control group: CRP group: 59/88 (67%) vs control group: 15/109 (14%) ($p<0.001$). The mean LHS was significantly shorter in the CRP group, as compared to the control group: CRP group: 4.6 ± 1.3 (range 3–14) days vs control group: 5.8 ± 1.8 (range 3–14) days ($p<0.001$). The rehospitalization rate was similar between groups [CRP group: 6/88 (7%) vs control group: 4/109 (4%) ($p=0.347$)].

The mean overall cost was significantly lower in the CRP group, than in the control group [CRP group: 4849€ ± 4017 (3454–40177) vs control group: 5291€ ± 2062 (3516–15007) ($p<0.001$)].

Discussion

We prospectively evaluated the possible impact of postoperative CRP monitoring on hospital stay after temporary stoma closure following laparoscopic sphincter-saving surgery for rectal cancer. Our comparative case-matched study showed that: (a) mean hospital stay was significantly lower in patients with postoperative CRP monitoring; (b) a significant reduction of total costs was also noted in CRP group; and (c) this CRP-driven strategy was not associated with a higher rate of unscheduled rehospitalizations or morbidity.

In various studies, postoperative CRP levels have been measured after colorectal surgery to predict the occurrence of postoperative intra-abdominal septic complications. All these non-randomized studies were included in four meta-analyses published between 2012 and 2017 that highlighted satisfactory positive and negative predictive values of CRP level regarding the occurrence of postoperative complications [13–16]. Despite these good results, the real

Table 2 Postoperative outcome of 197 patients who underwent stoma reversal following laparoscopic sphincter-saving surgery for rectal cancer

	Overall ($n=197$)	CRP group ($n=88$)	Control group ($n=109$)	p value
Postoperative overall morbidity				0.441
Yes	23 (12)[a]	12 (14)	11 (10)	
No	174 (88)	76 (86)	98 (90)	
Postoperative severe morbidity				0.838
Yes	4 (2)	2 (2)	2 (2)	
No	193 (98)	86 (98)	107 (98)	
Rehospitalization within 30 days				0.347
Yes	12 (6)	6 (7)	4 (4)	
No	185 (94)	82 (93)	105 (96)	
Mean length of hospital stay, days	5.2 ± 1.7	4.6 ± 1.3[b]	5.8 ± 1.8	< 0.001
Discharge on POD 4				
Yes	74 (38)	59 (67)	15 (14)	< 0.001
No	123 (62)	29 (33)	94 (86)	
Rehospitalization within 30 days				0.347
Yes	12 (6)	6 (7)	4 (4)	
No	185 (94)	82 (93)	105 (96)	

CRP C-reactive protein, *POD* postoperative day

[a]Number of patients (percentage of patients)

[b]Mean ± standard deviation

patient-related potential benefit of postoperative CRP levels is still to be demonstrated. No study to date has compared the outcome of patients operated on with or without CRP monitoring-driven discharge strategy.

Data regarding postoperative CRP level after SR are scarce. Only a few SR patients were included in previously published studies focusing on postoperative CRP levels [18, 22, 23], but these studies also included patients having other colorectal procedures, making analysis of the possible benefit of CRP monitoring after SR impossible. To the best of our knowledge, the present study is the first that only monitors postoperative CRP monitoring after SR.

However, as has already been demonstrated for patients having colorectal resections, SR patients could benefit from postoperative CRP monitoring. If the morbidity rate is low (17%), with a very low rate of peritonitis [12], shortening the postoperative hospital stay seemed feasible in low-risk patients without postoperative complications selected by CRP monitoring. These points prompted the present study.

Our postoperative CRP dosage-driven discharge strategy, based on previously described CRP cutoffs, allows satisfactory prediction of postoperative complication. In previous studies, after colorectal resection, mean CRP levels on POD 3 ranged from 100 [24] to 135 mg/L [25] in uncomplicated patients, but from 163 [26] to 257 mg/L [27] in patients with postoperative complications. We, therefore, defined low-risk patients as patients with a CRP level < 100 mg/L on POD3 and high-risk patients as patients with a CRP level > 200 mg/L, thus defining a "grey-zone" for patients with a CRP level between 100 and 200 mg/L. For patients within the grey-zone on POD3, we believe that if, on POD5, diminution reduction of > 30% in the CRP level is observed, the patients are probably at low risk of complications, and discharge the day after, on POD6, is feasible. This strategy is mainly based on a meta-analysis published in 2014 that suggested that the CRP level did not rapidly decrease after POD3 in complicated patients [15]. This probably reflects that postoperative CRP production is a dynamic process, and the rate of change and the balance between production and consumption is of primary importance. The results we obtained suggested that our CRP monitoring-driven discharge strategy is safe, as the only two patients in the CRP group requiring rehospitalization for Clavien–Dindo 3–4 morbidity presented with very late complications, diagnosed on POD11 and POD29, and were likely to have been discharged even in the absence of CRP monitoring. Our strategy might allow a significant reduction of both mean LHS and overall costs, therefore, justifying the slightly increased cost induced by CRP monitoring for all patients. It may be that time to discharge can be safely further reduced without the need for CRP monitoring, as other groups have reported a safe day case discharge protocol for SR in patients suitable for the same day discharge [28].

Limitations of this study were its retrospective control group.

Conclusions

Our results suggest that a postoperative discharge strategy using CRP monitoring, in patients having SR following laparoscopic sphincter-saving surgery for rectal cancer, is associated with reduced length of hospital stay and overall costs, without jeopardy to patients' short-term outcome. In our opinion, this strategy could now be routinely adopted after temporary stoma closure.

Compliance with ethical standards

Conflict of interest The authors declare that they have no financial disclosure or conflict of interest.

Ethical approval This study was approved by our institutional review board, conducted according to the ethical standards of the Committee on Human Experimentation of our institution, and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Informed consent For this type of study formal consent is not required.

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