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ORIGINAL ARTICLE

Simultaneous colorectal and hepatic procedures for colorectal cancer result in increased morbidity but equivalent mortality compared with colorectal or hepatic procedures alone: outcomes from the National Surgical Quality Improvement Program

Osama H. Hamed, Neil H. Bhayani, Gail Ortenzi, Jussuf T. Kaifi, Eric T. Kimchi, Kevin F. Staveley-O'Carroll & Niraj J. Gusani

Program for Liver, Pancreas and Foregut Tumors, Penn State Cancer Institute, Penn State College of Medicine, Hershey, PA, USA

Abstract

Background: Simultaneous colorectal and hepatic surgery for colorectal cancer (CRC) is increasing as surgery becomes safer and less invasive. There is controversy regarding the morbidity associated with simultaneous, compared with separate or staged, resections.

Methods: Data for 2005–2008 from the National Surgical Quality Improvement Program (NSQIP) were used to compare morbidity after 19 925 colorectal procedures for CRC (CR group), 2295 hepatic resections for metastatic CRC (HEP group), and 314 simultaneous colorectal and hepatic resections (SIM group).

Results: An increasing number of simultaneous resections were performed per year. Fewer major colorectal and liver resections were performed in the SIM than in the CR and HEP groups. Patients in the SIM group had a longer operative time and postoperative length of stay compared with those in either the CR or HEP groups. Simultaneous procedures resulted in higher rates of postoperative morbidity and major morbidity than CR procedures, but not HEP procedures. This difference was driven by higher rates of wound and organ space infections, and a greater incidence of septic shock. Mortality rates did not differ among the groups.

Conclusions: Hospitals in the NSQIP are performing more simultaneous colonic and hepatic resections for CRC. These procedures are associated with increases in operative time, length of stay and rate of perioperative complications. Simultaneous procedures do not, however, increase perioperative mortality.

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Correspondence

Niraj J. Gusani, Program for Liver, Pancreas and Foregut Tumors, Section of Surgical Oncology, Department of Surgery, Penn State College of Medicine, 500 University Drive, Mail Code H070, PO Box 850, Hershey, PA 17033-0850, USA. Tel: + 1 717 531 5965. Fax: + 1 717 531 3649. E-mail: ngusani@psu.edu

Introduction

Colorectal cancer (CRC) is the fourth most frequently diagnosed malignancy worldwide[1,2] and is the second leading cause of cancer-related death.[1] One third of patients with CRC present with stage IV disease with synchronous liver metastasis.[3] Over the last few decades there have been significant improvements in the management of CRC with liver metastasis, resulting in the near-doubling of 5-year survival from 30–35% in the 1980s and 1990s to 50–65% in the current era.[4,5] This improvement is related to multiple factors, including advanced technical strategies which have increased the feasibility and safety of resection of colorectal liver metastases (CRLM),[6] in combination with significant improvements in systemic chemotherapy and targeted therapy.[7] Complete resection of all liver metastases is a key factor in achiev-

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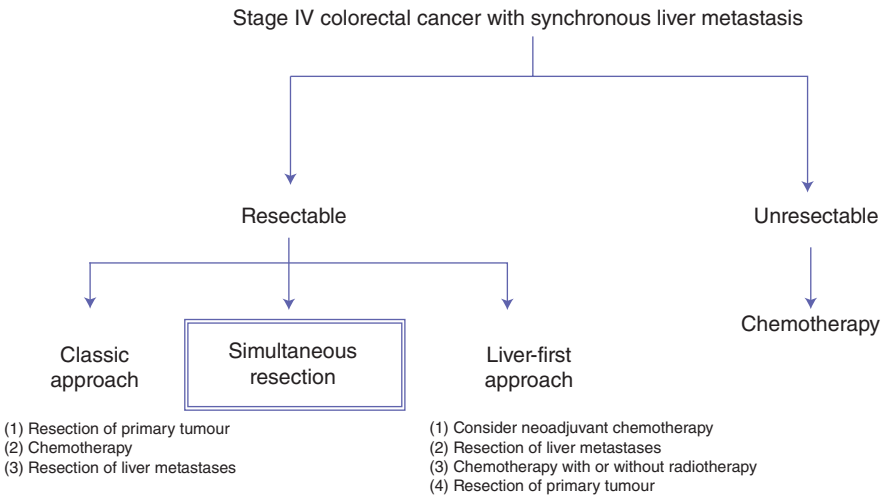

Figure 1 Management of colorectal cancer with synchronous liver metastasis

ing this result.[8] Only 20% of patients with synchronous CRLM have resectable disease at diagnosis.[2] In line with a better understanding of the disease, the new trends shift management strategies away from initial resection of the primary tumour (the classic approach) towards protocols in which treatment of the liver disease is the primary goal. Liver resection can be carried out prior to or simultaneously with colorectal surgery[9] (Fig. 1).

Simultaneous resection of CRLM along with the colorectal primary tumour has multiple advantages. First, simultaneous resection involves a single surgical procedure and general anaesthetic, which lower the overall hospital cost and length of stay (LoS) compared with those of two separate procedures and hospitalizations.[10] In addition, removal of all neoplastic foci at once may result in interruption of the metastatic cascade and avoid tumour progression that may occur as a result of postoperative immunosuppression associated with the staged approach.[11] Finally, the simultaneous approach may avoid the occurrence of delays and interruptions in chemotherapy administration. The disadvantage of simultaneous resection is that there is a potential increase in morbidity as a result of combining two major abdominal procedures, one clean and the other clean-contaminated.[12] There have also been some concerns regarding an increased risk for anastomotic leak as a result of splanchnic congestion associated with pedicle clamping (Pringle manoeuvre) during liver resection, inadequate surgical exposure through a single incision, and the difficulty of coordinating two separate surgical teams.[10]

Over the last decade, multiple single-institution series have consistently demonstrated the safety of simultaneous colorectal resections and minor hepatic resections. Studies have shown similar, and sometimes improved, rates of perioperative mortality and morbidity, intraoperative blood loss, operative time and hospital LoS in comparison with those associated with the classic staged approach.[13–16] By contrast, there is conflicting evidence about the safety of performing colorectal procedures simultaneously with major liver resections: some reports have demonstrated an acceptable safety profile[14,17–20] and others have shown a significant increase in perioperative mortality and morbidity compared with the staged approach.[21,22]

With the exception of a multi-institution study by Reddy *et al.*,[21] most published reports constitute single-institution experiences with small numbers of patients, which limits the ability to make definitive conclusions regarding the feasibility and safety of simultaneous resection. The American College of Surgeons' National Surgical Quality Improvement Program (ACS NSQIP) is an important surgical quality programme for general and vascular surgery in the USA.[23] Data are risk-adjusted and case mix-adjusted. For each patient, over 136 pre-, intra- and postoperative variables are prospectively collected by trained nursing staff for 30 days after surgery and data are audited annually for accuracy and completeness.[24] The ACS NSQIP has hundreds of participating hospitals and includes large numbers of patients, and thus its database can provide an excellent opportunity to study the 30-day outcomes of the simultaneous approach to resection of CRLM on a national level. The aim of this study was to compare morbidity and mortality in the simultaneous resection of primary CRC and hepatic metastases with those in colorectal and hepatic resections, respectively, using ACS NSQIP data.

Materials and methods

For this study, de-identified ACS NSQIP Participant Use File (PUF) data for 2005–2008 were utilized. During the study period, the ACS NSQIP collected detailed patient data for individuals undergoing general surgical procedures in 211 participating university and community hospitals. This study was approved by the Penn State Hershey Medical Center Institutional Review Board. The ACS NSQIP and the hospitals participating in the ACS

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NSQIP represent the source of the data used herein; these institutions have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the present authors.

Patients and procedures

All patients who underwent colon and liver resection were identified by primary Current Procedural Terminology (CPT) codes (Appendix 1). Postoperative diagnoses of CRC or secondary liver cancer were identified using International Classification of Diseases [Version 9 (ICD-9)] codes (Appendix 2). To identify patients undergoing simultaneous colorectal and liver resection, secondary CPT codes were reviewed, for which NSQIP has two categories: 'other' CPT codes, designed for additional procedures performed by the same surgical team, and 'concurrent' CPT codes, designed for additional procedures performed by a different surgical team.

A total of 22 534 patient records that met these definitions were identified. These included records for 19 925 (88.4%) patients who underwent colorectal procedures alone for primary colorectal malignancy (CR cohort), 2295 (10.2%) patients submitted to hepatic resections alone for colorectal neoplasms (HEP cohort), and 314 (1.4%) patients who underwent simultaneous colorectal and hepatic resections for primary colorectal malignancy (SIM cohort). In order to compare surgical complexity, 'major' colorectal resections were considered to include low anterior resection, total colectomy and total proctocolectomy. 'Major' hepatic resections were considered to include hemi-hepatectomy and trisegmentectomy.

Statistical analysis

Mean and median values were used to describe continuous data, with discrete variables displayed as totals and frequencies. For bivariate analyses, two-tailed *t*-tests and Mann–Whitney *U*-tests were used to compare continuous data, whereas the Fisher exact or chi-squared tests were used for categorical variables. A *P*-value of <0.05 was considered to indicate statistical significance. All statistical analyses were performed using SPSS Statistics Version 19.0.0 (IBM Corp., Armonk, NY, USA).

Outcomes definitions

Rates of 30-day mortality, minor and major morbidity, and hospital LoS were examined. Minor morbidity included superficial surgical site infections, urinary tract infections and deep vein thrombosis or thrombophlebitis. Major morbidity followed the definition outlined by Borja-Cacho *et al.*,[25] and included deep incisional surgical site infection, organ or organ space surgical site infection, wound disruptions, pneumonia, need for re-intubation, pulmonary embolism, progressive renal insufficiency, acute renal failure, cerebrovascular accidents, coma, peripheral nerve injury, cardiac arrest, myocardial infarction, graft or flap failure, sepsis, septic shock, need for return to the operating room, and >48 h on a ventilator. Mortality was defined as death from any cause at any time from the date of the procedure to 30 days after the procedure.

Results

Demographics and preoperative characteristics

Demographics and preoperative comorbidities of the study population can be found in Table 1.

Operative and perioperative data

The frequency of simultaneous colorectal and hepatic resections increased over time. Overall, SIM group patients accounted for 12.0% of all hepatectomies in the 4-year sample. The proportion of SIM cases, as a percentage of hepatectomies, increased from 8.4% in 2005 to 12.7% in 2008.

Colorectal surgery in SIM group patients was left-sided in 135 cases (43.0%), sigmoid or rectal in 45 cases (14.3%), right-sided or transverse colonic in 94 cases (30.0%), and of an unspecified colorectal primary in 40 cases (12.8%). Hepatic and colorectal resections were performed by the same surgical team in 74.8% ($n = 235$) of patients in the SIM group. The complexity of surgical procedures performed in the CR, HEP and SIM groups is shown in Table 2.

Postoperative outcomes

The overall 30-day mortality rate was 2.2%; there was no difference in this outcome among the three groups (Table 3). The overall incidence of postoperative morbidity was 25.0%. The SIM group had a significantly higher incidence of postoperative morbidity compared with the HEP group (29.3% versus 20.3%; $P < 0.001$), but not compared with the CR group (29.3% versus 25.0%; $P = 0.094$). Major morbidity was also higher in the SIM compared with the HEP group (20.4% versus 14.9%; $P = 0.011$), but not compared with the CR group (20.4% versus 16.7%; $P = 0.103$).

Within the SIM group, postoperative outcomes in patients undergoing major versus minor colorectal procedures and major versus minor hepatectomy procedures were compared. Rates of complications for each combination of procedure types are shown in Table 4. When outcomes in patients undergoing major and minor hepatectomy procedures within the SIM group were compared, no significant difference was noted in rates of morbidity (26.7% versus 30.3%; $P = 0.578$), major morbidity (21.7% versus 20.1%; $P = 0.784$) or mortality (1.7% versus 1.6%; $P = 0.959$).

Discussion

Synchronous CRLM is found in 20–30% of patients with CRC at the time of presentation.[3] Although such presentation is a negative prognostic indicator,[26] it is not a contraindication for surgical resection if the disease can be removed.[27] The management of resectable synchronous CRLM represents a challenge to the multidisciplinary team, especially in patients with an asymptomatic small primary tumour. The simultaneous resection of liver metas-

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Table 1 Population description and comorbidities in the study population (n = 22 534)

	CR group (n = 19 925, 88.4%)	HEP group (n = 2295, 10.2%)	SIM group (n = 314, 1.4%)	CR versus SIM *P*-value	HEP versus SIM *P*-value
Age, years, median (range)	68 (16–90)	61 (21–90)	62 (26–90)	< 0.001	0.024
Female, *n* (%)	9 672 (48.5)	1 029 (44.8)	158 (50.3)	0.532	0.067
Body mass index, kg/m^2, median (range)	26.9 (9.6–88.4)	27.2 (10.0–79.2)	26.3 (17.0–72.6)	0.074	0.004
Tobacco use, *n* (%)	2 983 (15.0)	273 (11.9)	57 (18.2)	0.117	0.002
Ascites, *n* (%)	295 (1.5)	11 (0.5)	6 (1.9)	0.532	0.003
Functions independently, *n* (%)	19 080 (95.8)	2 278 (99.3)	306 (97.5)	0.289	0.002
Chronic pulmonary disease, *n* (%)	1 158 (5.8)	56 (2.4)	16 (5.1)	0.590	0.007
Dyspnoea, *n* (%)	2 804 (14.1)	189 (8.2)	32 (10.2)	0.043	0.200
Percutaneous coronary intervention, *n* (%)	1 336 (6.7)	107 (4.7)	9 (2.9)	0.007	0.148
Cardiac surgery, *n* (%)	1 390 (7.0)	93 (4.1)	13 (4.1)	0.050	0.941
Hypertension, *n* (%)	10 918 (54.8)	1 059 (46.1)	151 (48.1)	0.018	0.517
Diabetes, *n* (%)	3 361 (16.7)	329 (14.3)	38 (12.1)	0.079	0.537
Heart failure, *n* (%)	259 (1.3)	4 (0.2)	2 (0.6)	0.302	0.108
Dialysis, *n* (%)	93 (0.5)	6 (0.3)	0	0.225	0.364
Weight loss, *n* (%)	1 328 (6.7)	91 (4.0)	38 (12.1)	< 0.001	< 0.001
Chemotherapy, *n* (%)	514 (2.6)	304 (13.2)	24 (7.6)	< 0.001	0.005
Radiation therapy, *n* (%)	1 962 (9.8)	37 (1.6)	43 (13.7)	0.024	< 0.001
ASA score of ≥3, *n* (%)	10 739 (53.9)	1 625 (70.8)	203 (64.6)	< 0.001	0.025

CR, colorectal surgery only; HEP, hepatic surgery only; SIM, simultaneous hepatic and colorectal surgery; ASA, American Society of Anesthesiologists.

Table 2 Operative complexity and details in the study population (n = 22 534)

	CR group (n = 19 925, 88.4%)	HEP group (n = 2295, 10.2%)	SIM group (n = 314, 1.4%)	CR versus SIM *P*-value	HEP versus SIM *P*-value
Major colorectal resection, *n* (%)	5169 (25.9)	–	68 (21.7)	0.932	–
Major hepatic resection, *n* (%)	–	771 (33.6)	60 (19.1)	–	< 0.001
Operative time, min, median (range)	148.0 (6–1614)	216.0 (20–991)	265.5 (65–832)	< 0.001	< 0.001
Blood transfusion, units, median (range)	0 (0–23)	0 (0–40)	0 (0–40)	< 0.001	0.185

CR, colorectal surgery only; HEP, hepatic surgery only; SIM, simultaneous hepatic and colorectal surgery; Major colorectal resection: low anterior resection, total colectomy and total proctocolectomy; Major hepatic resection: hemi-hepatectomy and trisegmentectomy.

tasis along with the colorectal primary tumour is one option available in synchronous CRLM and current data indicate the increasing utilization of such an approach in ACS NSQIP hospitals over the study period. This trend coincides with an increased number of publications demonstrating the safety and feasibility of this approach.[15–17,19,22,28,29]

The current study shows that patients in the SIM group had longer operative times compared with those in the HEP and CR groups. Previously published literature describes shorter operative times in the simultaneous compared with the staged approach,[13–16] but these studies combined the operative times for separate colorectal and hepatic procedures in the staged group. By contrast, the current results are based on comparisons of the SIM group with the CR and HEP groups separately. No comparison with outcomes in the CR and HEP groups combined could be made in this study because these groups represent different sets of patient procedures performed at different institutions and by different surgical teams. This also explains why the SIM group was found to have a longer postoperative hospital stay compared with the CR and HEP groups, respectively.

By contrast with previously published studies that showed similar or even lower rates of postoperative morbidity after simultaneous resection compared with staged resection,[14,17–19,30] this study found significantly higher rates of overall and major morbidity in the SIM group compared with the HEP group, but not with the CR group. However, as with operative times and for the same reasons, data for the SIM group could not be compared with outcomes in the CR and HEP groups combined.

The driver of the increased morbidity in the SIM group was infectious or septic complications. This finding echoes data cited in the existing literature.[12,31] One theory attributes this to the combination of a clean case, liver resection, with a clean-

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Table 3 Postoperative morbidity in the study population (n = 22 534)

	CR group (n = 19 925, 88.4%)	HEP group (n = 2295, 10.2%)	SIM group (n = 314, 1.4%)	CR versus SIM *P*-value	HEP versus SIM *P*-value
Mortality, *n* (%)	471 (2.4)	23 (1.0)	5 (1.6)	0.371	0.341
Morbidity, *n* (%)	5075 (25.5)	466 (20.3)	93 (29.3)	0.094	< 0.001
Major morbidity, *n* (%)	3367 (16.9)	341 (14.9)	64 (20.4)	0.103	0.011
LoS, days, median (range)	6 (1–187)	5 (1–138)	7 (1–108)	< 0.001	< 0.001
Superficial SSI, *n* (%)	1713 (8.6)	92 (4.0)	30 (9.6)	0.549	< 0.001
Deep SSI, *n* (%)	313 (1.6)	13 (0.6)	10 (3.2)	0.024	< 0.001
Organ SSI, *n* (%)	682 (3.4)	107 (4.7)	23 (7.3)	< 0.001	0.042
Dehiscence, *n* (%)	322 (1.6)	15 (0.7)	8 (2.5)	0.196	0.001
Sepsis, *n* (%)	552 (2.8)	58 (2.5)	17 (5.4)	0.005	0.004
Reoperation, *n* (%)	1243 (6.2)	80 (3.5)	18 (5.7)	0.713	0.050
Pneumonia, *n* (%)	620 (3.1)	70 (3.1)	10 (3.2)	0.941	0.897
Re-intubation, *n* (%)	531 (2.7)	61 (2.7)	10 (3.2)	0.571	0.591
Pulmonary embolism, *n* (%)	162 (0.8)	28 (1.2)	5 (1.6)	0.130	0.580

CR, colorectal surgery only; HEP, hepatic surgery only; SIM, simultaneous hepatic and colorectal surgery; LoS, length of stay; SSI, surgical site infection.

Table 4 Morbidity by complexity of surgery at simultaneous resection in 314 patients

	Minor CR and minor HEP (n = 203, 64.6%)	Major CR and minor HEP (n = 51, 16.2%)	Minor CR and major HEP (n = 43, 13.7%)	Major CR and major HEP (n = 17, 5.4%)
Mortality, *n* (%)	4 (1.3%)	0	1 (0.3%)	0
Morbidity, *n* (%)	60 (19.1%)	17 (5.4%)	12 (3.8%)	4 (1.3%)
Major morbidity, *n* (%)	37 (11.8%)	14 (4.5%)	10 (3.2%)	3 (1.0%)

CR, colorectal surgery; HEP, hepatic surgery.

contaminated case, colorectal resection. Longer operative time is also a risk factor for postoperative infection and may play a role in its increased incidence. A study by de Santibanes *et al.* found that simultaneous resection was associated with a high incidence of overall postoperative morbidity (64%), particularly anastomotic leak (21%).[18] The authors identified longer operative time (> 8 h) and increased intraoperative blood loss as independent risk factors for septic complications.[18] The increased postoperative morbidity found in the SIM group did not translate to increased mortality, a finding consistent with reports in the existing literature.[15,16,32,33] In a review of outcomes in three large hepatobiliary centres, Reddy *et al.*[21] found that simultaneous colorectal and major hepatic resections increased morbidity compared with major hepatectomy alone. Others have shown that major hepatectomy can be performed in a simultaneous fashion with no added mortality or morbidity.[17,34] This controversy may contribute to the aversion of some surgeons to the performance of major resection during simultaneous procedures. The current data demonstrate that major hepatectomy was less common in the SIM group compared with the HEP group. However, analysis of data for the SIM group shows that there were no differences in morbidity or mortality between those undergoing major and minor hepatectomy, respectively. Neither did the combination of major colectomy and major hepatectomy increase morbidity.

In 2009, Robertson *et al.*[35] analysed survival after hepatic resection for CRLM using the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER)–Medicare database. They found the incidence of simultaneous resection (resection of colon primary and liver metastases in the same hospitalization) to be 32%, which is higher than the 13.2% noted by the current study in the ACS NSQIP database. Robertson *et al.* reported crude 30-day and 90-day mortality rates after hepatic resection of 4.0% and 8.2%, respectively.[35] In patients who underwent simultaneous resection, the mortality rate was much higher (13.5%).[35] Multivariate analysis showed simultaneous resection to be an independent factor for the increase in 90-day mortality.[35] Although these numbers are similar to those cited in a previously published SEER–Medicare analysis,[36] they are higher than the present findings in the ACS NSQIP database (30-day mortality rates: 1.0% in the HEP group, 1.6% in the SIM group), which are consistent with the mortality rates of 0–3% reported in the literature.[7,37,38]

The current study has several limitations, most of which arise from the nature of the NSQIP dataset. This study was able to analyse only 30-day outcomes after colorectal, hepatic and simultaneous resections; this is an inherent limitation of the ACS NSQIP database. Recently, there has been increasing evidence that 90-day postoperative follow-up gives a more accurate indication of outcomes after hepatic resection.[39] The majority of previously

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published articles on the subject looked primarily at the short-term postoperative outcomes of simultaneous resection to prove its feasibility and safety. Less evidence is available on the longterm oncologic outcomes, but recently published articles have analysed both short- and longterm outcomes and found similar rates of 3- and 5-year survival in simultaneous resection and the staged approach.[18,40] This dataset also lacks preoperative laboratory values for many patients.[41] Although this is more common in healthier patients undergoing low-risk procedures, the lack of data is not random. As a result of this limitation, preoperative laboratory values were not included in the analysis.

Conclusions

The current study is one of the first to evaluate the outcomes of simultaneous resection of CRLM in a population-based database. This study notes an increase in the proportion of simultaneous procedures performed over the years of the study period at ACS NSQIP hospitals. Although simultaneous resection did not increase 30-day mortality, it was associated with increases in operative time, postoperative LoS and rate of septic complications compared with separate colorectal surgery and hepatectomy.

Conflicts of interest

None declared.

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Appendix 1 Current Procedural Terminology (CPT) codes

Colorectal procedure codes	
44140–44147	Partial removal of the colon
44150	Removal of the colon
44151–44156	Removal of the colon with ileostomy
44157	Colectomy with ileoanal anastomosis
44158	Colectomy with neo rectum pouch
44160	Removal of the colon
44204	Laparoscopic partial colectomy
44205	Laparoscopic partial colectomy with ileum
44206	Laparoscopic partial colectomy with stoma
44207	Colectomy with coloproctostomy
44208	Colectomy with coloproctostomy
45110	Partial removal of the rectum
45111	Partial removal of the rectum
44210	Laparoscopic total proctocolectomy
44211	Laparoscopic colectomy with proctectomy
44212	Laparoscopic total proctocolectomy
45160	Excision of rectal lesion
45170	Excision of rectal lesion
45395	Laparoscopic removal of the rectum
45397	Laparoscopic removal of the rectum with pouch
45112	Removal of the rectum
45113	Partial proctectomy
45114	Partial removal of the rectum
45116	Partial removal of the rectum
45119	Removal of the rectum with reservoir
45120	Removal of the rectum with reservoir
45121	Removal of the rectum and colon
45123	Partial proctectomy
45550	Repair of the rectum and removal of sigmoid
Hepatectomy procedure codes	
47120	Partial removal of the liver
47122	Extensive removal of the liver – trisegmentectomy
47125	Partial removal of the liver – left lobectomy
47130	Partial removal of the liver – right lobectomy
47370	Laparoscopic ablation of liver lesion – radiofrequency
47371	Laparoscopic ablation of the liver – cryoablation
47379	Laparoscopic liver procedure
47380	Open ablation of the liver – radiofrequency
47381	Open ablation of liver tumour – cryoablation
74399	Liver surgery procedure

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Appendix 2 International Classification of Diseases (ICD-9) codes

153	Malignant neoplasm of the colon
153.1	Malignant neoplasm of the transverse colon
153.2	Malignant neoplasm of the descending colon
153.3	Malignant neoplasm of the sigmoid colon
153.4	Malignant neoplasm of the cecum
153.6	Malignant neoplasm of the ascending colon
153.7	Malignant neoplasm splenic flexure
153.8	Malignant neoplasm other sites in the colon
153.9	Malignant neoplasm unspecified site in the colon
154	Malignant neoplasm at the rectosigmoid junction
154.1	Malignant neoplasm of the rectum
154.8	Malignant neoplasm other sites rectosigmoid junction
197.5	Secondary malignant neoplasm of large intestine and rectum
197.7	Malignant neoplasm of liver, secondary

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