

Simultaneous Versus Staged Resection for Synchronous Colorectal Cancer Liver Metastases

Robert CG Martin II, MD, PhD, FACS, Vedra Augenstein, MD, Nathan P Reuter, MD, Charles R Scoggins, MD, MBA, FACS, Kelly M McMasters, MD, PhD, FACS

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- BACKGROUND:** The aim of this study was to compare postoperative outcomes of patients with synchronous colorectal liver metastases treated with either simultaneous or staged colectomy and hepatectomy.
- STUDY DESIGN:** From July 1997 to June 2008, a review of our 1,344-patient prospective hepato-pancreaticobiliary database identified 230 patients treated surgically for primary adenocarcinoma of the large bowel and synchronous hepatic metastasis. Clinicopathologic, operative, and perioperative data, complications, and grade of complications (grade 1, minor, to grade 5, death) were reviewed to evaluate selection criteria, operative methods, and perioperative outcomes. Chi-square and proportional hazard model were used to evaluate predictors of outcomes.
- RESULTS:** Seventy patients underwent simultaneous resection of colon primary and liver metastasis in a single operation; 160 patients underwent staged operations. Simultaneous resections were similar for size (median 4 cm versus 3.7 cm) and number (median 3 cm versus 3 cm) of liver metastases. Major liver resections (≥ 3 Couinaud segments) were similar between staged and simultaneous (32% versus 33%, respectively), as was type of colectomy ($p = 0.2$). Complication rates and severity were similar in both groups: 39 of 70 patients (56%) in the simultaneous group experienced 63 complications versus 88 of 160 patients (55%) with 162 complications in the staged group ($p = 0.24$). Multivariate analysis identified blood transfusion as a predictor of complication (odds ratio 2.98, $p = 0.001$). Patients having simultaneous resection required fewer days in the hospital (median 10 days versus 18 days, $p = 0.001$).
- CONCLUSIONS:** By avoiding a second laparotomy, simultaneous colon and hepatic resection reduces overall hospital stay, with no difference in morbidity and mortality rates or in severity of complications, compared with staged resection. Simultaneous resection is an acceptable option in patients with resectable synchronous colorectal metastasis. (J Am Coll Surg 2009;208:842–852. © 2009 by the American College of Surgeons)
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Synchronous liver metastasis, commonly defined as liver metastasis occurring within 12 months of the colon primary, represents 13% to 25% of 90,000 newly diagnosed colorectal liver metastases.^{1,2} Through the expansion of multidisciplinary care with advances in surgical training, surgical techniques (laparoscopy and ablation), anesthetic management, and chemotherapy, the overall survival of

these patients has significantly improved over the last 10 years when compared with historical controls.

The optimal timing for surgical resection of synchronous metastasis has been debated and continues to evolve. Referral bias, institutional bias, and patient bias still dictate the type and timing of surgical therapy in these patients. Some series reporting on the surgical management of synchronous colorectal metastasis have recommended a staged approach, with initial resection of the primary lesion followed by hepatic resection 2 to 3 months later^{3–7} (Table 1). But the paradigm for surgical management of synchronous colorectal metastasis has begun to change, with authors reporting good results for simultaneous resection of the colon and liver tumors.^{8–10} Along with this surgical paradigm change is also the challenge of deciding on the optimal timing of chemotherapy and the effects that chemotherapy has on surgical and hepatic toxicity. The primary goal of this study was to confirm that simultaneous resec-

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From the Department of Surgery, Division of Surgical Oncology, University of Louisville School of Medicine James Graham Brown Cancer Center, Louisville, KY.

Correspondence address: Robert CG Martin II, MD, PhD, FACS, Division of Surgical Oncology, University of Louisville, Norton Healthcare Pavilion, 315 East Broadway, Ste 311, Louisville, KY 40202.

Table 1. Published Results of Simultaneous Versus Staged Resection for Synchronous Colorectal Hepatic Metastasis

Author	Year	n	Type of resection, n	Morbidity, %	Mortality, %
Vogt ³⁶	1991	36	19 simul 17 staged	5.2 17.60	0
Scheele ⁴¹	1991	98	60 simul 38 staged	nr	2
Jenkins ⁴²	1993	46	22 simul 24 staged	nr	nr
Elias ¹⁰	1995	53	53 simul	19	0
Jaeck ⁵	1996	41	20 simul 21 staged	20 10	0
Nordlinger ⁴	1996	1,008	115 simul 893 other	nr	7 2
Bolton ⁴³	2000	165	50 simul 115 other	nr	12 4
Fujita ⁷	2000	97	83 simul 14 staged	58	0
Lyass ⁹	2001	112	26 simul 86 staged	27 35	0 2.3
De Santibanes ⁴⁴	2002	71	71 simul	21	0
Martin ⁴⁵	2003	240	134 simul 106 staged	49 67	2 2
Reddy ³⁹	2007	610	135 simul 475 staged	36 18	1 0.5

nr, not recorded; other, staged and metachronous resections; simul, simultaneous resection.

tion is similar to staged resection with regard to morbidity and mortality.

METHODS

A review of a 1,344-patient prospective hepato-pancreaticobiliary database at the University of Louisville, Division of Surgical Oncology, identified 230 patients who underwent resection of a primary colorectal cancer and a synchronous hepatic metastasis from July 1997 to June 2008. Synchronous hepatic metastases were defined as those identified at the time of diagnosis of the primary colon cancer. All colon and hepatic resections were performed by surgeons at the University of Louisville Department of Surgery.

The decision to perform either a staged or simultaneous resection was determined by the treating hepatobiliary surgeon or in collaboration with the colon surgeon and the hepatobiliary surgeon. Ultimately, once the oncologic decision is made that surgery is indicated, the decision to perform a synchronous resection or staged resection is based on the complexity of the hepatectomy, complexity of the colon or rectal resection, and the comorbidities of the patient. The decision to perform resection or radiofrequency ablation was determined at the discretion of the treating surgeon. In the patients undergoing hepatic resections, anatomic segmental liver resections were performed and classified as described by Couinaud.¹¹ Nonanatomic

resections were performed when judged appropriate by the attending surgeon. For patients with disease that was believed to be unresectable because of the number, distribution, or location of the tumors, or because of patient comorbid factors, ablation was performed. Our group has agreed and uses the recent Society of Surgical Oncology (SSO) and the American Hepato-Pancreato-Biliary Association (AHPBA) Consensus Conference in that the definition of resectability is the ability to resect and ablate all visible disease and leave enough liver behind for an appropriate recovery time.¹² Standard preoperative evaluation of patients with metastatic colorectal cancer included three-phase CT of the abdomen and pelvis and chest x-ray. Earlier systemic chemotherapy of any type and duration was allowed. Radiofrequency ablation was performed using intraoperative ultrasonography guidance to ensure that at least a 1-cm ablation margin was achieved around the tumors.^{13,14}

The technique for anesthetic management during hepatectomy has been previously reported.^{14,15} In principle, we use a low central venous pressure (< 5 mmHg) while maintaining a urine output of 25mL/h and a systolic blood pressure > 90 mmHg during parenchymal transection. Because of this desire, in patients who are undergoing synchronous resection, the liver resection is usually performed first so that volume can then be given during the colon resection portion of the procedure. After the specimen is

removed, crystalloid is administered IV to achieve euvolemia. Packed red blood cells and autologous blood is usually given to maintain a hemoglobin > 10 g/dL in patients with evidence of either coronary or cerebrovascular disease. Intraoperative blood products are not administered until blood loss exceeds 25% of the total blood volume.

Outflow control of the hepatic veins before parenchymal division was nearly always obtained in lobectomy or extended resections. The liver parenchyma was divided using Kelly clamps to crush liver tissue and expose bile ducts and blood vessels, which were clipped, tied, or stapled, or utilized a hemostatic assist device. Intermittent inflow vascular occlusion (the Pringle maneuver)¹⁶ was used and applied for 5- to 10- minute intervals, released briefly, and reapplied as necessary. Pringle time was recorded as the total cumulative Pringle time applied during parenchymal transection.

Postoperative complications and length of hospital stay were recorded and then graded using our standard classification scale of complications which has been reported previously.^{14,15} For patients with more than one complication, comparison of in-hospital and 90-day postoperative complications were evaluated by assigning the complication with the highest severity level for each patient. Complications were defined by published criteria.¹⁷ Earlier cardiac history was defined as a history of angina, previous coronary artery disease defined by cardiac catheterization, previous myocardial infarction, cardiac valve dysfunction requiring medication, or a history of congestive heart failure or tachyarrhythmia. Earlier pulmonary disease history was defined as abnormal pulmonary function tests, history of asthma requiring daily meter-dosed inhalers, or tobacco use greater than a 25-pack of year history. All patients were reviewed and classified using a preoperative Clinical Risk Score prognostic scoring system defined for colorectal metastasis.¹⁸ This five-point preoperative clinical score evaluates patients by five factors: disease-free interval of less than 12 months, CEA > 200 ng/ml, lymph-node positive primary, more than one hepatic lesion, and hepatic lesion > 5 cm in size.

Chi-square, Student's *t*-test, and Mann-Whitney U test for nominal, continuous, and ordinal variables were used to evaluate the association of independent variables to surgical complications. Proportional hazards analysis was performed on all variables found significant by univariate analysis. Relative risk (RR) with 95% confidence intervals was calculated as a measure of association. Differences of *p* < 0.05 were considered significant. Statistical analysis was performed using JMP software (JMP; SAS Institute Inc).

Table 2. Patient Demographics

Demographic	Staged (n = 160)	Simultaneous (n = 70)	p Value
Race, %			
Caucasian	80	86	
African American	8	8	ns
Other			
Gender, %			
Female	43	46	0.7
Male	57	54	
Age, y	61	58	0.06
Cardiac history, %			
Yes	86	87	0.8
No	14	13	
Pulmonary history, %			
Yes	5	3	0.4
No	95	97	
Diabetes, %			
Yes	10	18	0.2
No	90	82	
Alcohol history, %			
Yes	9	15	0.2
No	91	85	
Tobacco use			
Yes, %	42	47	0.6
No, %	72	72	0.9
Mean pack years: yes, n	42	47	0.6
Earlier hepatic disease, %			
Yes	0	0	ns
No	100	100	
Hypertension, %			
Yes	33	34	ns
No	67	66	
Earlier thrombotic event, %			
Yes	4	6	ns
No	96	94	
Earlier abdominal surgery, %			
Yes	13	15	0.6
No	87	85	

RESULTS

A total of 230 patients were treated for synchronous colorectal hepatic metastasis. There was an even distribution of women (staged resection, 43% versus simultaneous resection, 46%) and men (staged, 57% versus simultaneous, 54%), with a median age of 61 years (range 23 to 85 years) for staged and 58 years (range 27 to 78 years) for simultaneous. All other earlier medical history and comorbidities were similar for both the staged and simultaneous groups (Table 2). The primary colorectal adenocarcinoma was located within the right colon (staged, 33% versus simultaneous, 45%), left colon (staged, 34% versus simultaneous,

23%), or rectum (staged, 23% versus simultaneous, 30%). The majority of patients presented with rectal bleeding or anemia. A small minority presented with obstruction ($n = 15$, 7%) or perforation ($n = 3$, 1%).

Seventy patients underwent simultaneous resection of a colorectal primary and hepatic metastasis. These patients were compared with 160 patients who underwent staged resection. The extent of hepatic disease was similar, with staged patients found to have similar numbers of hepatic metastases ($p = 0.6$) and metastases ($p = 0.1$) when compared with patients undergoing simultaneous resection (Table 3). Overall, the patients subjected to a staged resection were at similar risk as the simultaneous group in terms of longterm prognosis as defined by the metastatic colorectal risk score (Table 3).

Right hemicolectomy was more common in the simultaneous group, although there were more left hemicolectomies in the staged group (Table 3). Simultaneous resection was associated with a significantly greater number of hepatic ablations and hepatic wedge resections (Table 3), with the staged group having a greater number of segmental resections, which accounted for the greatest difference in surgical procedures between the two groups. There were similar proportions of major hepatic resections (≥ 3 segments) performed for both groups. The tendency to perform major liver resections as simultaneous procedures was not significantly influenced by the location of the primary colon cancer. There was similarity in the simultaneous major hepatic resection patients who required right or left colectomy. There was also similarity among patients requiring rectal resection, and major hepatic resections were performed equally in both groups.

Overall operative duration for the staged group was a median of 235 minutes (range 70 to 400 minutes), which was longer than for the simultaneous group, whose operations lasted a median of 180 minutes (range 80 to 420 minutes, Tables 4–6). The median operative blood loss for the simultaneous group was 300 mL (range 20 to 1,500 mL), compared with the staged group, which had a median blood loss of 350 mL (range 100 to 1,500 mL) for colectomy and hepatectomy ($p = 0.9$). In the 70 patients who underwent a simultaneous resection, 35 (50%) patients received blood transfusion during their hospitalization. In the 160 patients who underwent a staged resection, 72 (45%) patients received a blood transfusion during one of their hospitalizations. The length of hospital stay was also significantly shorter for the simultaneous resections than for the combined hospitalizations of the staged colorectal and hepatic resections (Table 7). Even when patients with major liver resections (lobectomy or more) were consid-

Table 3. Extent of Disease and Resection Performed in Patients with Resectable Synchronous Hepatic Metastasis

Variable	Staged (n = 160)	Simultaneous (n = 70)	p Value
Liver lesions, n, median (range)	3 (1–8)	3 (1–16)	ns
Size of lesions, cm, median (range)	4 (0.8–13.0)	3.7 (0.3–8.8)	ns
CEA, ng/mL, median (range)	14.7 (0.8–1,300)	34.5 (1.3–597)	0.6
Primary resection, %			
Right colectomy	33	45	
Left colectomy	34	23	
Low anterior resection	15	23	ns
Abdominoperineal resection	8	7	
Total colectomy	10	10	
Node-positive colon, %			
Yes	63	68	0.5
No	37	32	
Location of lesions, segment, %*			
1	1	5	
2	19	30	
3	23	34	
4	27	32	ns
5	39	61	
6	46	50	
7	40	45	
8	31	36	
Earlier chemotherapy, %			
Yes			
5-FU	54	43	
Oxaliplatin	30	34	
Irinotecan	17	2	0.001
Other	39	43	
No	30	48	
Duration of chemotherapy, mo, n (median)	3 (0–12)	0 (0–13)	0.01
Metastatic colorectal risk score, %			
1	9	9	
2	22	16	0.83
3	55	59	
4	13	16	
5	1	0	
Liver ablation/resection*			
Ablation	46	57	
Wedge	15	36	0.2
Segmental	29	18	
$\geq$ Lobe	40	47	

*Percentages are greater than 100% because some patients presented with bilobar disease and underwent multiple types of liver ablation or resection techniques.

Table 4. Outcomes and Complications after Staged or Simultaneous Resection

Outcomes	Staged (n = 160)	Simultaneous (n = 70)	p Value
Complications, n (%)			
Yes	88 (55)	39 (56)	ns
No	72 (45)	31 (45)	
Laparotomy complications, n			
Wound infection	8	6	0.001
Ileus	10	9	
Pulmonary	16	2	
Cardiac	11	2	
Pelvic abscess	2	2	ns
Hepatic fluid/abscess	9	6	ns
Hepatic failure	8	1	ns
Operative time, min (range)	235 (70–400)	180 (80–420)	
Total blood loss, mL (range)	350 (100–1,500)	300 (20–1,500)	0.9
Transfusion			
%	45	50	ns
Units of blood, n (range)	2 (1–10)	2 (1–10)	
Length of stay, d (range)	18 (6–54)	10 (5–63)	0.001

ered, operative time, blood loss, and length of stay were significantly longer for the staged resections.

Complications after all surgical procedures occurred in 127 of 230 (55%) patients. In the simultaneous group, 39 (55%) patients sustained 63 complications. In the staged group, 88 (55%) different patients experienced 162 complications for both hospitalizations. When the types of complications were evaluated, the difference in the overall complication rates between the simultaneous and the staged groups primarily occurred from the need for a second laparotomy in the staged group (Table 4). When the specific laparotomy complications were evaluated, there was an increase in the number in staged patients (Table 4). When the hepatectomy (hepatic fluid or abscess) and colonic complications (pelvic abscess or anastomotic leak) were evaluated, there was no difference in procedure-specific complications. The overall complication rate for

Table 6. Most Severe Complication for Each Patient

Most severe grade	Staged (n = 88), %	Simultaneous (n = 39), %	p Value
Grades 1 and 2	25	16	0.1
Grades 3 and 4	21	19	0.5
Grade 5	2	2	ns

Table 5. Severity of All Complications Occurring in 127 Patients

Resection type	Complications, n	Grade 1, %	Grade 2, %	Grade 3, %	Grade 4, %	Grade 5, %
Simultaneous (n = 39)	63	17	36	45	0	2
Staged (n = 88)	162	15	53	30	2	2

simultaneous resection (56%) was similar for staged resections (55%; $p = 0.9$). This was true even when the analysis was restricted to the 97 patients who underwent major liver resection (lobectomy or greater), with the overall complications of simultaneous resections (17 of 33, 50%) being significantly less than for staged resections (38 of 64, 60%; $p = 0.04$; Table 7).

When the complications were graded by severity, the relative distribution of mild complications (grades 1 and 2), moderate complications (grades 3 and 4), and perioperative mortality (grade 5) was found to be similar between the groups, with a greater risk of grade 2 complications in the staged patients and risk of grade 3 in the simultaneous patients (Table 5). There was a greater incidence of mild complications (grades 1 and 2) in the staged group (68%) when compared with the simultaneous group (53%). An increased proportion of complications were severe (grades 3 and 4) in the simultaneous group (45%) compared with the staged group (32%). There was no significant difference in operative mortality rates (simultaneous, 1 [2%] versus staged, 3 [2%]). When only the most severe complication was considered for each patient, the relative proportion of mild (grades 1 and 2) and severe (grades 3 and 4) complications was not found to be different in the staged or simultaneous groups (Table 6).

Table 7. Outcomes and Complications after Staged or Simultaneous Resection Involving Major Liver Resections ($\geq$ Lobectomy/ $\geq$ Segments)

Variable	Staged (n = 64)	Simultaneous (n = 33)	p Value
Operative time, min (range)	268 (195–793)	202 (203–445)	0.06
Total blood loss, mL (range)	750 (250–1,500)	450 (100–1,500)	0.01
Length of stay, d (range)	18 (7–54)	12 (5–31)	0.001
Total complications, n	68	35	ns
Total patients with complications, n (%)	38 (60)	17 (50)	0.6
Total patients with grade 3 or 4 complications, n (%)	18 (28)	5 (15)	0.24
Mortality, n (%)	1 (4)	0 (0)	ns

The patient population was then analyzed for factors predictive of any complication after surgical resection. Univariate analysis did not demonstrate a significant difference in complications when age, gender, preoperative cardiac history, diabetes, preoperative pulmonary disease, albumin at the time of colectomy or hepatectomy, hemoglobin at the time of colectomy or hepatectomy, preoperative tobacco use, hypertension, type of chemotherapy, duration of chemotherapy, blood loss at the time of colectomy, duration of colectomy, type of colectomy, or Pringle time were examined (Table 8). Factors found to be significant on both univariate and logistic regression were extent of hepatic resection or ablation and blood loss at liver resection (Table 8). The trend toward an increased rate of complications stems from the greater number of patients who underwent both hepatic ablations and minor resections simultaneously, demonstrating a greater disease burden treated in these patients, in both the staged and simultaneous groups. There was an increase in complications for patients who underwent ablation, potentially related to the increased amount of hepatic parenchyma that was ablated in combination with a colectomy, but volume of ablation was not recorded in this study so this trend is unproved at this time.

DISCUSSION

Approximately 23% to 51% of the 157,000 new colorectal cancer patients will present with synchronous colorectal cancer and liver metastasis.¹⁹ Validation and optimization of established treatment criteria and oncologic guidelines are imperative to improved progress in patient survival, morbidity, mortality, and hospital stay.²⁰ Optimal management of patients with synchronous colorectal hepatic metastasis remains a multifactorial treatment strategy, based on symptoms, location and extent of disease, and the patient's performance status and underlying comorbidities. The data presented here demonstrate that simultaneous major hepatic resection ablation with colectomy is safe, with less overall morbidity, shorter overall hospital stay, and similar mortality. Additional benefits are the avoidance of a potential delay in surgical therapy for the metastatic disease and a reduction in the risk that these metastases could spread if untreated.

There are several methods for the optimal treatment of metastatic colorectal cancer that are currently in practice. All demonstrate the efficacy of combination surgical resection or ablation with chemotherapy and the addition of radiation therapy for rectal primaries. Traditional surgical training has mandated removal of the primary tumor in management of synchronous metastatic colorectal cancer to avoid obstruction or bleeding. But with the advent of colonic stents and with the significant primary tumor re-

sponse rates, this approach is dramatically changing. The optimal timing of therapy (ie, chemotherapy first, liver first, colon first, or combined resection) is less about the diagnosis of metastatic colorectal cancer and more about the extent of disease, risk of disease, and patients' performance status.

Recent reports have demonstrated the benefits of the perioperative or neoadjuvant chemotherapy approach.^{21,22} There are multiple reports demonstrating the benefits of chemotherapy before resection of the liver metastasis to downstage a patient's disease to a resectable point or to better assess the overall tumor biology²³ and determine if surgical resection will be beneficial.²⁴ But duration of chemotherapy is of utmost importance, and it should be used only to assess if there is a response, not to maximize treatment response, because of the deleterious effects of long-term chemotherapy use.²⁵⁻²⁷

In addition, neoadjuvant chemotherapy may treat microscopic disease immediately, allow for additional disease to declare itself, and assess the effectiveness of the treatment regimen.²⁸ Some also believe that chemotherapy should be given in metastatic colorectal cancer before resection of even the primary lesion. It has been reported that resection of the primary lesion gives minimal palliative benefit and in turn, can increase mortality, morbidity, and delay in beneficial chemotherapy.²⁹

In the last decade we have achieved significant advancements in hepatobiliary surgical training (far greater number of surgeons), hepatobiliary techniques (laparoscopic resections and hepatic ablation technology), anesthetic management, and overall critical care, which has made hepatic resection safer and increased overall quality of life.³⁰ Recent data have demonstrated that even major liver resections are now done with minimal morbidity and mortality.³¹ Intuitively, it appears that recovery from one major operation (open or laparoscopic) is faster than from two. Multiple studies show that performing a simultaneous colectomy and hepatectomy results in similar mortality and morbidity rates, but shorter hospital stays than for staged operations.³²⁻³⁸ In addition, the two groups have similar operative times, intraoperative blood loss, and complications.^{32,33,37}

Additional factors such as risk of undergoing general anesthesia twice and interruption of chemotherapy need to be taken into consideration when deciding whether to do a staged versus simultaneous operation. Resistance to change and to new methods of treatment is not a new phenomenon in medicine. The most current data about simultaneous colon and liver resections are still evolving. Many patients present to small centers where they are able to get only a part of their therapy and they may not be referred to another center until they have already had a resection or

Table 8. Evaluation of Factors Predictive of All Complications after Surgical Procedures

Factor	Complication	Univariate	Multivariate
Age, y, median			
Yes	60	0.6	ns
No	61		
Gender, %			
Male	50	0.3	ns
Female	44		
Cardiac history, %			
Yes	39	0.4	ns
No	48		
Pulmonary history, %			
Yes	67	0.2	ns
No	46		
Past alcohol history, %			
Yes	49	0.01	ns
No	21		
Past abdominal surgery, %			
Yes	56	0.06	ns
No	41		
Any preoperative chemotherapy, %			
Yes	60	0.1	ns
No	40		
Type of chemotherapy, %			
5-FU	44	0.06	
Irinotecan	9	0.08	ns
Oxaliplatin	29	0.5	
Other	37	0.6	
Duration of chemotherapy, mo, median			
Staged	3	0.5	ns
Simultaneous	0		
Type of colectomy, %			
Right	33	0.1	ns
Left	20		
Low anterior resection	12		
Abdominoperineal resection	8		
Extent hepatic resection, %			
<Lobe	62	0.03	1.4 (1.0–1.9)
≥Lobe	38		
Blood loss, median, mL	250	0.001	2.98 (1.5–3.2)
Timing of resection, %			
Simultaneous	56	0.3	ns
Staged	55		

Table 8. Continued

Factor	Complication	Univariate	Multivariate
Type of liver resection/ablation, %			
Ablation	44	0.02	ns
Left lateral segment	9		
Left lobectomy	8		
Right lobectomy	19		
Right posterior segment	4		
Wedge resections	15		
≥Lobe	34		

chemotherapy. General practitioners, surgeons, and oncologists need to have the understanding and the confidence that these data are the guides to optimal treatment of metastatic colorectal cancer at this time.²⁰ It takes a huge amount of coordination to treat a patient with metastatic colorectal cancer, and guidelines for treatment are essential for optimal outcomes for these patients.

In the past, several studies advocating simultaneous resections indicated that major hepatectomies should be done separately from colorectal resections.³⁹ The data showed an increased mortality with an anatomic lobectomy during a combined procedure.^{37,39} Our data showed no difference in mortality, morbidity, and severity of complications between the staged and simultaneous resection groups, even with major liver resections (Table 7). The major differences in our data when compared with data from Reddy and coworkers³⁹ are the very tight interval of this analysis (10 years versus 21 years for Reddy and colleagues' work), in which there have been significant advances in operative and anesthetic techniques, and our lack of effect from neoadjuvant chemotherapy on hepatic resection. We analyzed the severity of complications with major and minor liver resections and similar colorectal procedures and found no statistical difference between the results from the two groups. Only extent of blood loss was a significant factor of complication (odds ratio 2.98, $p = 0.001$) in these two groups.⁴⁰

The limitations of this study are that it is a retrospective review of our prospective database and demonstrates the surgical bias and training of the three lead authors (RCGM, CRS, and KMM). This has led to the equal distribution of surgical management, staged versus simultaneous, but is also confirmatory of the surgical outcomes.

In conclusion, simultaneous resection of the colon primary lesion and hepatic metastasis is safe, acceptable, and supported by our and multiple other studies. The role of chemotherapy remains in place and the optimal timing of therapy should be based on multiple factors including the patient's extent of disease, comorbidities, body habitus,

and the experience of the operating surgeon(s) to provide the best care. At initial diagnosis, metastatic colorectal cancer is best treated with a team approach including one or more surgeons (based on surgical specialty), medical oncologists, and radiation oncologist if needed. Such practice will allow for patients to have their cancer treated more quickly and efficiently and get more out of hospital time, but without increased risks.

Author Contributions

Study conception and design: Martin

Acquisition of data: Martin, Augenstein, Reuter

Analysis and interpretation of data: Martin, Augenstein, Scoggins, McMasters

Drafting of manuscript: Martin, Augenstein, Scoggins, McMasters

Critical revision: Martin, Reuter, Scoggins, McMasters

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Discussion

DR C WRIGHT PINSON (Nashville, TN): This paper retrospectively looked at 70 patients who underwent simultaneous resection versus 160 patients who underwent staged resections. And I'm going to suggest that the retrospective approach does leave us open to some selection bias; there was an application here of the surgeon's judgment. I submit that there is no difference in outcomes when that surgeon's judgment is applied. It's not the same as saying that if you take all comers there is no difference. I think we need to conclude that simultaneous resection is acceptable when in the surgeon's judgment the extent of the disease, the level of comorbidities, and the technical conduct of the operation are all favorable. That's somewhat different than the conclusion stated.

Second, I would like to ask a question about the median length of stay. Both 10 days for the liver resection and 18 days for the combined operation on a staged approach seem a little long to me, and I'd like to you comment on those lengths of stays.

Third, what order do you do the simultaneous operation in and how do you decide? Because you found that the only prediction of complication, or the only two predictions of complications were the lobectomy as a more major operation, and blood loss. I wonder if that has influenced the order that you do the operation. Would you do the liver resection first now?

My final question has to do with looking at the number of lesions removed; I noticed that in some cases they were up to 16. So I would like to hear about your indications for resection of liver metastases, and can you tell us about the median and longterm survival figures for these groups of patients?

DR BRYAN M CLARY (Durham, NC): In brief summary, this group provides yet another in a growing list of reports that detail the surgical outcomes of patients with synchronous hepatic metastasis. As Dr Martin pointed out, he is no stranger to this topic, having authored what I think is one of the seminal papers in the field.

In the experience reported today, he and his colleagues compared the outcomes of 150 patients undergoing staged resections with 70 patients who did not. This is a contemporary experience spanning 11 years, and it is important to emphasize that the colorectal resection of all staged patients was performed at Louisville. This fact represents, I think, the strength of this report and is in contrast to many reports on the topic originating from tertiary hepatic experiences where the primary tumor resection was not necessarily performed in the same institution.

I will not restate your results as I would rather listen to you expound on the implications of your findings. Ultimately your experience complements the existing literature that suggests we can perform simultaneous resections in selected patients with a degree of morbidity comparable to those performed in a staged manner.

I don't know that your comments on patients requiring major hepatectomy are biased, as you know, and partially pointed out in your introductory comments, is to be very selective in those patients, although I think we would also agree from our experience authored by Reddy that in patients requiring minor hepatectomy it is likely acceptable.

The simultaneous approach appears to have advantages with respect to patient convenience and possible cost-associated measures including length of stay, operative time, et cetera. I think it would be a mistake, though, to simply leave it as that, as there are broader implications of your findings.

Aside from what systemic therapy should be given to patients, the appropriate timing of the modes of therapy, I think, is fundamental as the most important question in these patients. If in fact a simultaneous approach is equivalent in morbidity and offers other advantages, it clearly necessitates even more an integrated approach with medical oncologists, hepatic surgeons, and colorectal surgeons. For the rectal cancer patient population you would also include the radiation oncologist.

I have a few questions. One of the criticisms of performing simultaneous hepatic resections is that early recurrences are theoretically more likely; these patients have not been selected by time and/or