Surgical approaches of resectable synchronous colorectal liver metastases: Timing considerations

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Abstract

AIM: To compare the safety and efficacy of simultaneous versus two stage resection of primary colorectal tumors and liver metastases.

METHODS: From January 1996 to May 2004, 103 colorectal tumor patients presented with synchronous liver metastases. Twenty five underwent simultaneous colorectal and liver surgery and 78 underwent liver surgery 1-3 mo after primary colorectal tumor resection. Data were retrospectively analyzed to assess and compare the morbidity and mortality between the surgical strategies. The two groups were comparable regarding the age and sex distribution, the types of liver resection and stage of primary tumors, as well as the number and size of liver metastases.

RESULTS: In two-stage procedures more transfusions were required (4 ± 1.5 vs 2 ± 1.8, pRBCs, $P < 0.05$). Chest infection was increased after the two-stage approach (26% vs 17%, $P < 0.05$). The two-stage procedure was also associated with longer hospitalization (20 ± 8 vs 12 ± 6 d, $P < 0.05$). Five year survival in both groups was similar (28% vs 31%). No hospital mortality occurred in our series.

CONCLUSION: Synchronous colorectal liver metastases can be safely treated simultaneously with the primary tumor. Liver resection should be prioritized over colon resection. It is advisable that complex liver resections with marginal liver residual volume should be dealt with at a later stage.

INTRODUCTION

Colorectal metastases to the liver either synchronous or metachronous can be excised resulting in a 5-year survival of 25%-40%[1-6], provided that the extrahepatic disease has been controlled and the remaining liver harbors no cancer. Even re-resections of liver metastases are rewarded with a 5 year-survival of 20%-30% and should be carried out in selected patients[6-9]. Many aspects of surgical strategies for the management of colorectal liver metastases have been extensively analyzed[10-15] and patient selection has been elucidated[1,3,7,15-17]. However, the question of when is the most favorable time to operate on synchronous liver metastases in relation to the primary colorectal tumor remains a controversial and debatable issue[10,12,14,16,18]. Several authors assume that combined liver and colon resection has higher morbidity and mortality rates[9,19,20] and favor a staged approach resecting the liver metastases 2 to 3 mo after treating the primary tumors.

However, recent advances in anesthesiology and surgical techniques prompted some surgeons to resect simultaneously colon lesions and liver metastases with mortality rates varying from 0% to 24%[10,12,14,18,21]. The conclusion is that in selected patients, one-stage approach is comparable to the two-stage procedure in mortality, morbidity and long-term survival[3,10,12,14,18].

Our retrospective study aimed to determine whether the one-stage surgical strategy for synchronous colorectal

liver metastases grants an optimal outcome to the patients compared to the two-stage procedure.

MATERIALS AND METHODS

From January 1996 to May 2004 one hundred and three patients with resectable synchronous colorectal liver metastases underwent surgical treatment. Both endoscopies and biopsies confirmed the diagnosis of the primary tumors. The resectability of the liver metastases was assessed by ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI) and intraoperative ultrasonography (IUS), only in cases where there was no extrahepatic tumor spreading and the number of lesions was ≤ 3. The decision for the type of surgical treatment was based on whether both liver lesions could be managed through one subcostal or midline incision. When trisegmentectomy or biliary reconstruction was anticipated the two-stage procedure was adopted.

Based on the timing of surgical excision of the liver secondaries, the patients were assigned to two groups. The one-stage group (n = 25) underwent simultaneous colorectal and liver surgery and the two-stage group (n = 78) underwent liver surgery 1 to 3 mo after excision of the primary lesion. The patients suitable for combined colorectal and liver surgery were operated through either a bilateral subcostal (n = 19, 75%) or a midline (n = 6, 25%) incision. Two patients (8%) had bilobar metastases. Patients of the two-stage group (n = 78) were operated via a midline incision for the control of the primary tumors and 1 to 3 mo later via a bilateral subcostal incision for the resection of liver metastases. The bilateral subcostal incision provided adequate surgical field suitable for any liver resection and was a safe approach for primary tumors located in the cecum to the descending colon. In contrast, the midline incision offered an access to the whole colorectal tract but only to the left hepatic lobe and segments V and VI of the right lobe. Twelve patients (16%) had bilobar resectable liver diseases. Patient characteristics, histological features, location of the primary lesions and the liver metastases are illustrated in Table 1.

The Pringle maneuver[22] was used in minor liver resections, while in major hepatic resections additional occlusion of the hepatic veins was opted. Liver transection was conducted by the clamp crushing technique with Kelly clamp or by the sharp liver transection technique. Details of the liver transection have been described elsewhere[10,23].

The factors analyzed to compare the two surgical strategies were: intraoperative blood loss, transfusion requirements to keep hematocrit above 29%, postoperative complications, hospital stay, 30-day mortality rate and cumulative survival. Oncological validity of each procedure was assessed by the narrowest tumor-free margin determined by painting the cut surface of the resected specimen with Sinic ink.

Statistical analysis

Statistical analyses of the data were performed with chi-square test for qualitative variables and Student's t-test for quantitative variables. Cumulative long-term survival was calculated by the Kaplan-Meier method and differences

Table 1 Epidemiological and pathological data of patients with synchronous colorectal metastases to the liver, operated on in one stage (Group A) and two stages (Group B) n (%)

Characteristics	Group A (n = 25)	Group B (n = 78)	P
Gender			NS
Male	15 (58)	47 (61)	
Female	10 (42)	31 (39)	
Age (yr, mean ± SD)	63 ± 12	61 ± 14	NS
Tumor differentiation			NS
Well	6 (21)	17 (21)	
Moderate	9 (37)	28 (36)	
Poor	10 (42)	24 (32)	
Astler-Coller staging[27]			NS
B2	5 (21)	8 (11)	
C1	11 (42)	37 (47)	
C2	9 (37)	33 (42)	
Size of liver disease (cm)			NS
1-3 cm	6 (21)	25 (32)	
4-6 cm	12 (50)	33 (42)	
> 7 cm	7 (29)	20 (26)	
Colon location			
Right colon	17 (67)	15 (18)	P < 0.005
Left colon	5 (21)	55 (71)	P < 0.005
Rectum	3 (12)	8 (11)	
Liver location			NS
Right lobe	20 (83)	61 (79)	
Left lobe	5 (17)	17 (21)	

NS: Not significant.

were analyzed by the log rank test. P < 0.05 was significant.

RESULTS

The age, gender and pathological features of the primary tumor did not differ between the two groups except that in the one-stage approach right-sided colon tumors dominated, 17 out of 25 vs 15 out of 78 (P < 0.05). In contrast, in the two-stage approach, left-sided colon tumors were more frequent, 63 out of 78 vs 8 out of 25 (P < 0.05) (Table 2). The size and location of liver metastases were equally distributed between the two groups (Table 1). The extent of liver resection and warm ischemia time were not different between the two groups. By contrast, operative time, blood loss and transfusion requirement to keep the hematocrit above 29% were significantly lower in the one-stage group compared to the two-stage group (Table 2). The rate of postoperative complications between the two groups was not different and no re-operation was needed to treat any of the complications. Subhepatic collections were treated with CT-guided aspiration (Table 3). The tumor-free margin was not different between the two groups (9 ± 1.4 mm in one-stage group vs 11 ± 1.2 mm in two-stage group). Hospital stay was shorter in the one-stage group compared to the two-stage group (12 ± 6 d vs 20 ± 8 d, P < 0.05). Overall survival was 90%, 40% and 28% at 1, 3 and 5 years, respectively after one-stage resections and 93%, 44% and 31% at 1, 3 and 5 years, respectively after two-stage resections.

DISCUSSION

Hepatic tumor resection constitutes the only therapeutic

Table 2 Intraoperative data of patients with synchronous colorectal metastases to the liver, operated on in one stage (Group A) and two stages (Group B) n (%)			
Intraoperative data	Group A (n = 25)	Group B (n = 78)	P
Major liver resections (⩾ 3 segments)	7 (25)	23 (29)	NS
Minor liver resections (⩽ 2 segments)	18 (67)	55 (71)	NS
Warm ischemic time (min)	27 ± 9	32 ± 11	NS
Operative time (min)	260 ± 30	340 ± 60	$P < 0.05$
Transfusions (RBCs)	2 ± 1.8	4 ± 1.5	$P < 0.05$
Right hemicolectomies	67%	18%	$P < 0.05$
Left hemicolectomies	21%	71%	$P < 0.05$
Abdominoperineal resections	12%	11%	NS

NS: Not significant.

Table 3 Complications and hospital stay of patients with synchronous colorectal metastases to the liver, operated on in one stage (Group A) and two stage (Group B) n (%)			
Postoperative data	One-stage group (n = 25)	Two-stage group (n = 78)	P
Hospital mortality	-	-	-
Wound infection	2 (8)	3 (4)	$P < 0.05$
Chest infection	4 (17)	20 (26)	$P < 0.05$
Pleural effusion	5 (21)	18 (24)	NS
Bile leak	2 (8)	7 (9)	NS
Subphrenic collections[1]	3 (12)	8 (11)	NS
Splenic rupture	-	1 (1)	NS
Anastomotic leak	-	1 (1)	NS
Rectovaginal fistula	1 (4)	-	NS
Hemorrhage	1 (4)	1 (1)	NS
Hospital stay (d)	12 ± 6	20 ± 8	$P < 0.05$

[1]Resolved with aspiration under CT guidance. NS: Not significant.

option with curative intent for patients with colorectal liver metastases[5,6,16]. All efforts should be made to eliminate the hepatic lesions after controlling the loco-regional disease and ruling out extrahepatic tumor spread. In such cases there are well documented reports demonstrating a 5-year survival of 20%-40%[1-6], and 20%-30% when a re-resection has been executed in highly selected individuals[6-9].

The indications and criteria of patient selection for liver surgery due to metachronous colorectal metastases have been clarified in numerous excellent papers[14-16]. In contrast, for synchronous metastases the prevailing issue is the timing of liver resection in relation to the treatment of the primary tumor[18,20,21]. The strategy of the two-stage surgical approach gained popularity over the years and has been established as the standard surgical practice[3-7]. However, the fact that two-stage surgery requires two separate operations and accumulating evidence of the negligible morbidity and mortality of modern liver surgery prompted some surgeons to attempt simultaneous resections of primary tumors and liver metastases[10,12,14,18,21]. This approach was awarded with a mortality of 0%-24%[10,12,14,18,24]. Nordlinger *et al*[15] reported a 7% mortality for one-stage surgery and 2% for two-stage. Bolton and Fuhrman showed a 12% mortality for synchronous liver resections, which increased to 25% when a major hepatectomy (resected segments ⩾ 3) was performed[24]. Martin *et al*[10] demonstrated a 4% mortality and comparable morbidity between the two surgical approaches[12]. Our study, with the inherent limitations of a retrospective analysis, indicates that one-stage approach is equally safe to the two-stage regarding the morbidity, mortality and long-term survival and is consistent with other studies[12-14,18].

The majority of studies addressing the issue of one-stage over two-stage surgical treatment of synchronous colorectal liver metastases are retrospective and thus some biases are unavoidable and should be taken into consideration[6,10,11,18,19]. However, helpful conclusions have been drawn concerning the criteria for patient selection for either strategy (one-stage and two-stage) and valuable lessons have been learned[2,10,11,16,17]. It has been shown that patients who underwent a single operation had invariably smaller and fewer hepatic metastases and were treated with less extensive liver resections[10,12,18,19]. The above mentioned variables are negatively associated with postoperative complications and should be taken into consideration when simultaneous liver resections are anticipated[6,7,16]. Bolton *et al*[24] proposed that complex hepatic resections should be delayed for at least 3 mo.

Expertise in liver resections is an important factor in determining patient outcome, since the majority of postoperative morbidity and mortality are mainly related to liver surgery, a point that has been established by many studies[4,10,18,24-26]. Bleeding during hepatectomy is a poor prognostic factor and all efforts should be centered at minimizing blood loss by meticulous techniques and liver vascular control[1-3,10,23]. It appears that application of the Pringle maneuver in an intermittent manner should be preferred because it causes less liver reperfusion injury and intestinal edema, which might compromise the safety of gut anastomoses[4,10,21]. Some bleeding from the area of gut resection can be easily controlled by careful ligation of the divided mesentery and is not a major problem as has been illustrated by Martin *et al*[10] and Weber *et al*[12], who reported that intraoperative blood loss was less in the one-stage approach, a fact confirmed by our findings. However, in complex hepatectomies when protracted vascular occlusion is anticipated, the two-stage procedure seems more prudent.

In our series, complications related to sepsis around the liver appeared to be equally distributed in both groups, a finding possibly related to the precautions taken during surgery to eliminate spillage of intestinal contents (one-stage, 12%; two-stage, 11%). However, it is advisable to avoid one-stage procedure when bowel obstruction or a perforated tumor is found. Vascular occlusion of the liver does not jeopardize the safety of gut anastomoses and we think the protective ileostomy recommended by Elias *et al*[21] unnecessary. Nevertheless, we agree with these authors that gut resection should precede liver resection and intermittent vascular control should be applied. Cardio-respiratory status and complexity of liver surgery should be always taken into account when a combined

liver and colon resection is planned[10,12,25]. Biliary fistula, subphrenic abscess, liver failure and chest infection are cited as the leading causes of postoperative morbidity in the majority of studies[10-13]. Laurent *et al*[25] demonstrated a clear connection of postoperative morbidity with long-term survival. Therefore, in order to optimize the surgical outcome when dealing with colorectal liver metastases, the liver surgical technique should be prioritized over the colectomy, because as mentioned before, liver surgery is related to the majority of postoperative complications and long-term survival[5,10,24,26]. Adequate exposure of the liver should be the primary concern of the surgeon in order to achieve a safe hepatectomy fulfilling the oncological principles of liver resection with a sufficient tumor-free margin[13,16,21,24,26]. In that respect, our study did not show any difference in the oncological validity between the two techniques. Martin *et al*[10] observed increased positive margin rate in wedge excisions and advocate anatomic hepatectomies. This view is shared by Tanaka *et al*[26]. Bilateral subcostal incision provides excellent liver exposure and facilitates colon resection from the cecum up to the descending colon. In contrast, malignancies located in the sigmoid colon downward necessitate a midline incision and an extension to the right (Rio-Branco incision)[21].

In conclusion, simultaneous resections of the liver and primary colon malignancies are equally safe and efficient with the two-stage procedure. The overall complication, postoperative mortality and long-term survival rates are similar to those of two-stage procedures, but hospital stay was significantly shorter with the one-stage approach. Simultaneous liver and colon surgery should be preferred for most of the right colon lesions and for small liver lesions that can be approached from a midline incision, regardless of the colonic tumor location. It is advisable that complex liver resections should be postponed for a later stage, especially for patients having potential cardio-respiratory and liver impairment.

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