Outcomes of simultaneous and delayed resections of synchronous colorectal liver metastases

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Background: The optimal strategy for the treatment of synchronous colorectal liver metastases has not been established yet. In this study, we present the outcomes and survival rates of the patients who underwent simultaneous or delayed resections.

Methods: We performed a retrospective analysis of liver resections in our institution between 1997 and 2006.

Results: Among the 89 patients presenting with synchronous colorectal liver metastases, 28 underwent simultaneous and 61 underwent delayed resection. Age, sex and localization of the primary tumour were similar in the 2 groups. Duration of surgery and hospital stay were longer in the simultaneous resection group, and blood loss was also greater in this group. However, these factors did not influence the frequency of complications, which did not differ between the groups. When we included data from initial colectomy, these differences were either not significant or in favour of synchronous resection. In the delayed resection group, colon resection was performed in different hospitals. The 1-, 3- and 5-year survival rates were 78%, 70% and 45%, respectively, in the simultaneous and 88%, 55% and 38%, respectively, in the delayed resection groups.

Conclusion: In select patients, the risk of simultaneous resection of synchronous colorectal liver metastases is comparable to delayed resection, and increases in blood loss and operating time associated with simultaneous resections do not have a negative influence on long-term outcome. Positive outcomes of simultaneous liver resections in our study could be a result of good patient selection or experience with oncological liver surgery.

Contexte : La stratégie optimale pour traiter des métastases hépatiques et colorectales simultanées n'est pas encore définie. Dans cette étude, nous présentons les résultats et les taux de survie des patients qui ont subi une résection simultanée ou décalée.

Méthodes : Nous avons procédé à une analyse rétrospective des résections du foie pratiquées dans notre établissement entre 1997 et 2006.

Résultats : Chez les 89 patients qui avaient des métastases hépatiques et colorectales simultanées, 28 ont subi une résection simultanée et 61, une résection décalée. L'âge, le sexe et l'emplacement de la tumeur primitive étaient semblables chez les participants des 2 groupes. L'intervention chirurgicale et l'hospitalisation ont duré plus longtemps chez les patients qui ont subi la résection simultanée, et ils ont aussi perdu plus de sang. Ces facteurs n'ont toutefois pas influencé la fréquence des complications, qui n'était pas différente entre les groupes. Lorsque nous avons inclus les données découlant de la colectomie initiale, les différences étaient non significatives ou favorables à la résection simultanée. Chez les patients qui ont subi la résection décalée, on a pratiqué la résection du côlon dans des hôpitaux différents. Les taux de survie à 1, 3 et 5 ans s'établissaient à 78 %, 70 % et 45 % respectivement chez les patients qui ont subi la résection simultanée et à 88 %, 55 % et 38 % respectivement chez ceux qui ont subi une intervention décalée.

Conclusion : Chez certains patients, le risque que présente la résection simultanée de métastases hépatiques et colorectales est comparable à celui que présente la résection décalée et les augmentations de la perte de sang et de la durée de l'intervention associées aux résections simultanées n'ont pas d'effet négatif sur le résultat à long terme. Les résultats positifs des résections simultanées du foie révélés par notre étude pourraient découler d'une bonne sélection des patients ou de l'expérience de la chirurgie oncologique du foie.

Colorectal cancer remains one of the most frequent malignancies and is a common cause of cancer-related death.[1,2,3] The liver is the most common site for colorectal cancer metastases; they occur in about 50% of patients with colorectal cancer, and the presence of liver metastases has an important influence on survival prognosis.[1,2] The median survival is 9–18 months for patients in whom the cancer is nonresected.[3] Liver resection is the only treatment that offers long-term survival (5-yr survival in 25%–50% of patients) and the only potentially curative treatment.[2,4–7]

Survival rates can be influenced by many factors: patient age and overall condition, biology and advancement grade of the neoplasm, number and localization of metastases and resection margin.[4]

Despite increasing interest in performing colorectal resections combined with liver resections, both simultaneous and delayed, and despite the acceptance that the simultaneous resection approach has gained over the last few years, the optimal approach has not yet been determined.[7–10] We reviewed and analyzed the surgical outcomes and overall survival rates following simultaneous and delayed resections of synchronous colorectal cancer liver metastases at our institution.

Methods

We performed a retrospective analysis of data for patients with synchronous colorectal cancer liver metastases who underwent liver resection our institution between 1997 and 2006. Before surgery, all patients were investigated to exclude extrahepatic metastases. Every patient underwent ultrasonography, abdominal computed tomography (CT) and chest radiography or chest CT, and in certain cases additional pelvis magnetic resonance and positron emission tomography (PET) were also performed.

We estimated resection margin status macroscopically and verified it histopathologically. In all resections, tumour-free margins of at least 1 cm were obtained, and patients underwent intraoperative ultrosonography to reduce the risk of overlooking smaller lesions. All patients received leucovorine and adjuvant chemotherapy with 5-fluorouracil (5-FU). All patients had hepatic metastases at the time of colorectal cancer diagnosis. We considered liver resection to be "minor" if fewer than 3 segments were resected and "major" if more than 3 were resected.

The data we analyzed comprised information from medical records and follow-up data gathered using questionnaires. We performed statistical analyses using the Statistica 6.0 program. We compared quantitative variables using Student t tests and qualitative variables using χ^2 tests. We calculated cumulative survival using the Kaplan–Meier method and analyzed the differences using log-rank tests. We considered results to be significant at $p < 0.05$.

Results

We included 89 patients (37 women and 52 men) with a mean age of 59.9 years in our study. We divided patients were divided into 2 groups: group A comprised 28 patients who underwent simultaneous resection, and group B comprised 61 patients in whom colorectal resection preceded liver resection. There was no significant difference in age or sex between the groups. Primary tumour localization was also similar; however, in group A the rectum was more frequent and the left colon less frequent than in group B. There was a difference in tumour histopathological differentiation: 43% in group A were poorly differentiated compared with 20% in group B ($p = 0.026$). The percentage of minor resections was greater in group A than in group B. The TNM classification of primary tumour and size of metastases did not differ significantly between the groups; however, there was a difference in the average number of metastases (2.9 in group A v. 3.8 in group B; $p = 0.037$). Details about resections are presented in Table 1.

Seven patients from group A and 5 from group B underwent abdominoperineal resection of the rectum. In all patients from group B, colorectal cancer and liver metastases were diagnosed in other hospitals and the first operations (colorectal resection) were performed at those hospitals. Liver resection took place 8–11 weeks later in our hospital.

The percentage of postoperative complications was similar in both groups (Table 1). The most frequent postoperative complications were pleural effusion requiring drainage, fluid in the resection site requiring puncture and wound infection.

The duration of surgery and hospital stay were longer in group A than group B; intraoperative blood loss was also greater in group A than group B (Table 2). These differences became less evident when we included data from initial colectomy in group B (Table 3).

Cumulative survival rates at 1, 3 and 5 years were 78%, 70% and 45%, respectively, in group A and 88%, 55% and 38%, respectively, in group B ($p = 0.006$). The median survival was 51.2 months in group A and 37.6 months in group B (Fig. 1). Early death (within 30 days of surgery) occurred in 1 patient from group B because of prolonged hepatic failure.

Eight patients in group A experienced a recurrence; 6 rehepatectomies and 2 thermal ablations were performed. In group B 15 patients experienced a recurrence and qualified for rehepatectomy; 3 of them underwent a third hepatectomy.

A disseminated neoplasmatic process was diagnosed in 4 patients from group A (14%) and 14 from group B (23%); 4 from group B experienced a colorectal recurrence.

Discussion

We present the results of simultaneous and delayed liver

metastases resections performed in our hospital. We found that simultaneous resections did not increase the risk for postoperative complications or have a negative influence on patients' long-term outcomes compared with delayed resections. Furthermore, even simultaneous major liver resection and rectum cancer resection is possible: 3 of 10 patients in group A who underwent rectum resection also underwent major liver resection. These results support the conclusion that resection of synchronous colorectal cancer liver metastases is a safe procedure, and the number of complications does not depend on the extent of the procedure.[9,11] The only differences we observed between the groups were duration of surgery, blood loss and hospital stay. Interestingly, when we included data from colectomy in group B and compared cumulative scores, both duration of surgery (p = 0.06) and hospital stay (p = 0.017) were longer in group B; blood loss was also greater in this group, but the difference was not significant (p = 0.42). Despite the extent of simultaneous operations, no early deaths occurred in group A and only 1 occurred in group B. The overall 5-year survival rate was 40%, which is comparable to the results presented by other authors.[2,5–7,10,12–15]

Because of the advance in associated treatment, extensive anatomic liver resections are less frequently necessary, and often a tissue-saving nonanatomic resection can be performed, especially in the case of simultaneous resection. That was partially the cause of the lower percentage of

Table 1. Characteristics of patients, primary tumours, metastases and resections

Characteristic	Group, no. (%) of patients* Group A, n = 28	Group B, n = 61	p value
Sex			0.48
Female	10 (36)	27 (44)	—
Male	18 (64)	34 (56)	—
Mean age, yr	59.4	60.2	0.71
Tumour differentiation			0.026
Well and moderately differentiated	16 (57)	49 (80)	—
Poorly differentiated	12 (43)	12 (20)	—
Primary site			0.49
Right colon	6 (21)	13 (21)	1.00
Left colon	12 (43)	34 (56)	0.26
Rectum	10 (36)	14 (23)	0.49
Liver resection extent			0.09
Major	8 (28)	29 (48)	—
Minor	20 (72)	32 (52)	—
Type of hepatectomy			0.08
Right lobe	4 (14)	13 (22)	0.38
Extended right	0	2 (3)	0.36
Extended left	4 (14)	12 (20)	0.50
Trisegmentectomy	1 (4)	2 (3)	0.81
Bisegmentectomy	2 (7)	15 (24)	0.05
Segmentectomy	6 (21)	9 (15)	0.48
Nonanatomic resection	11 (39)	8 (13)	0.006
Metastases, mean (range)			—
Size, cm	3.5 (1–7)	4.1 (1.5–8)	0.32
No.	2.9 (1–5)	3.8 (1–7)	0.037
CEA level	74.2 (8–750)	87.3 (5–810)	0.28
TNM staging			
T1/T2	4 (14)	7 (11)	0.69
T3/T4	24 (86)	54 (89)	—
N0	10 (36)	14 (23)	0.20
N+	18 (64)	47 (77)	—
Colorectal resection margin < 3 cm	0	13 (21)	0.010
Complications	4 (14)	8 (13)	0.90

CEA = carcinoembryonic antigen; TNM = tumour–node–metastasis.
*Unless otherwise indicated.

Table 2. Surgical data for liver resections

Variable	Group, mean (95% CI) Group A	Group B	p value
Duration of surgery, min	250 (160–360)	200 (140–260)	0.003
Blood loss, mL	950 (0–3000)	620 (0–1170)	0.014
Hospital stay, d	12 (10–26)	9 (7–19)	0.06
Warm ischemia time, min	27 (10–75)	34 (12–74)	0.06

CI = confidence interval.

Table 3. Surgical data for initial colectomy in group B

Variable	Mean (95% CI)
Duration of surgery, min	90 (50–190)
Blood loss, mL	420 (0–1200)
Hospital stay, d	6 (5–14)

CI = confidence interval.

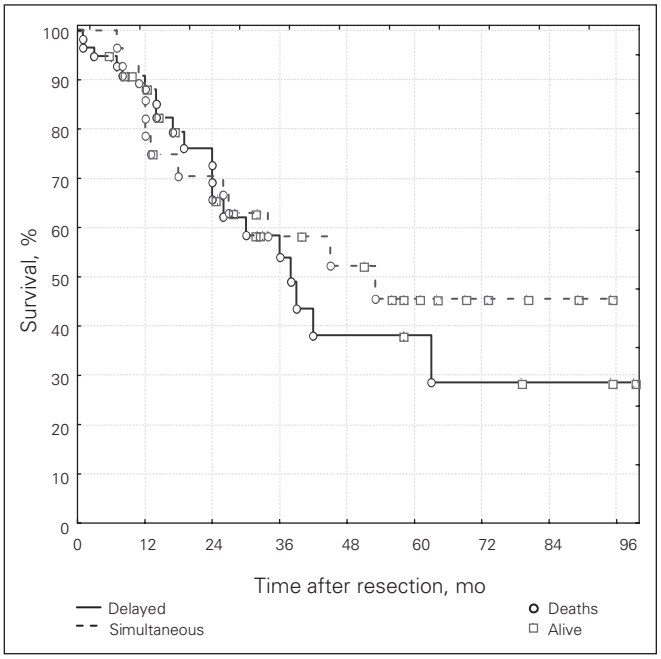

Fig. 1. Cumulative Kaplan–Meier survival curves in simultaneous and delayed resection groups.

major resections compared with nonanatomic ones in group A than in group B. The better outcome in the simultaneous resection group could have been influenced by colorectal resection margin (in group A the margin was > 3 cm in all patients, whereas in group B it was < 3 cm in 21% of patients). In addition 4 patients experienced colorectal recurrence in group B (v. none in group A), whereas TNM staging of the primary tumour did not differ between groups. There were more poorly differentiated tumours in group A than in group B; however, this did not appear to have a significant influence on patient outcomes.

One study has indicated that colorectal cancer metastases spread through portal vein branches or even bile ducts.[16] This could mean that hepatic metastases resection performed as early as possible may influence survival.[17] The fact that colorectal resections in the delayed resection group were performed in different hospitals with different experience levels in oncological surgery, which is connected with insufficient resection margins in some patients, could also influence the outcome.

Our study has several limitations, partially owing to the fact that it was not a prospective, randomized trial. The groups differ in 2 aspects, the extent of liver resection (although this difference was not significant) and the number of liver metastases, which could explain the lower risk for recurrence in the simultaneous resection group. Such differences, however, are not uncommon in studies on this topic. In fact, the extent of hepatectomy and the number of liver metastases are often significantly larger in patients undergoing simultaneous resection.[7] In addition, the policy at our hospital to perform simultaneous resections in all patients who present with colorectal cancer with synchronous liver metastases and are suitable for operative treatment (group A) could have contributed to the bias. It must, however, be stressed that to our knowledge no large, prospective, randomized trial comparing simultaneous and delayed resections has been performed.[7] Despite these limitations, our study showed that simultaneous resection can be safely performed in select patients with colorectal cancer and liver metastases without increased risk of complications and can result in good long-term survival rates.

Conclusion

The risk of simultaneous resection of synchronous colorectal liver metastases in select patients is comparable to that of delayed resection. Neither early mortality nor the number of complications is increased by simultaneous resection. Increase in blood loss and duration of surgery associated with simultaneous resections does not have a negative influence on long-term outcome. There may be a connection between the removal of all neoplasmatic tissue in simultaneous resection and higher 5-year survival rates.

Competing interests: None declared.

Contributors: Drs. Slupski, Wlodarczyk and Jasinski designed the study. Drs. Slupski, Jasinski, Masztalerz and Tujakowski acquired the data, which Drs. Slupski and Jasinski analyzed. Drs. Slupski and Jasinski wrote the article, which all other authors reviewed. All authors provided approval for publication.

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