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Perioperative Morbidity Affects Long-Term Survival in Patients Following Liver Resection for Colorectal Metastases

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Abstract

Background Hepatic resection is the treatment of choice in patients with colorectal liver metastases. Perioperative morbidity is associated with decreased long-term survival in several cancers. The aim of this study was to assess the impact of perioperative morbidity and other prognostic factors on the outcome of patients undergoing liver resection for colorectal metastases.

Methods One hundred ninety seven patients undergoing liver resection with curative intent were investigated. The influence of prognostic factors, such as complications, tumor stage, margins, age, sex, number of lesions, transfusion, portal inflow obstruction, and era and type of resection, was assessed using univariate and multivariate analysis. Complications were graded using an objective surgical complication classification.

Results The 5-year survival rate was 38%, with a median follow up of 4.5 years. The disease-free survival rate at 5 years was 23%. The perioperative morbidity and mortality rates were 30 and 2.5%, respectively. The median survival of patients with perioperative complications was 3.2 years, compared to 4.4 years in those patients without complications ($p<0.01$). For patients with positive resection margins, the median survival was 2.1 years, compared 4.4 years in patients with a margin ($p=0.019$).

Conclusion Perioperative morbidity and a positive resection margin had a negative impact on long-term survival in patients following liver resection for colorectal metastases.

Keywords Perioperative complications · Colorectal metastases · Liver resection · Prognostic factors · Hepatectomy

Introduction

Hepatic resection with curative intent is considered the treatment of choice in patients with colorectal metastases confined to the liver. Advances in surgical techniques, staging, and perioperative care have contributed to improved results. Major centers have reported perioperative mortality rates of less than 5% in series including major resections.[1–4] Numerous uncontrolled studies have assessed long-term survival and disease-free survival and reported 5-year survival following hepatic resection with curative intent ranging from 25 to 37%.[1,2,4,5] In the more recent series, improved 5-year actuarial survival rates up to 58% are reported.[6,7]

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There are well known risk factors for survival in patients undergoing liver resection for colorectal metastasis. More advanced stage of the primary and positive resection margins of the liver resection are consistently associated with a reduced overall survival,[1,2,8] whereas synchronous metastases and number of lesions have been reported as both significant and nonsignificant for the long-term prognosis.[9–12]

However, very little information exists about the impact of perioperative morbidity on the outcome in patients following liver resection for colorectal metastases. A single study has reported reduced long-term survival in patients with perioperative morbidity.[13] The concept of perioperative morbidity as a risk factor for survival is well known in other cancer surgery, such as esophageal, pancreas, and colorectal cancer.[14–16]

The lack of standardized definitions for perioperative complications is one confounding factor contributing to the limited evidence in this field. To address this issue, we used an objective surgical complication classification, which has been developed recently and has been proven to be very reliable.[17]

The aim of this study was to assess the impact of prognostic factors, in particular perioperative morbidity, ranked by a quantitative surgical complication classification, on the long-term survival in patients undergoing liver resection for colorectal metastases.

Methods

Patients and Data Collection

Patients who underwent liver resection for colorectal metastases from February 1992 until June 2005 at Flinders Medical Centre, Ashford Community Hospital, and Queen Elizabeth Hospital in Adelaide were included in a prospective database. Data about the operation, transfusion, tumor characteristics, and postoperative complications were recorded prospectively by the responsible surgeons. Data about resection margins, tumor number and size, staging of the primary, chemotherapy, recurrence, and follow-up period were obtained from patients' charts and direct follow-up with the respective general practitioners, referring physicians, oncologists and surgeons. Mortality was cross-checked with the state (South Australian) cancer registry.

Preoperative tumor staging was performed using contrast-enhanced computer tomography or magnetic resonance imaging. In addition, chest x-ray or computer tomography of the chest and colonoscopy were performed. Positron emission tomography was used selectively, in the latter part of the series, to rule out extrahepatic disease.

Surgical Therapy

Laparotomy and abdominal exploration including intraoperative ultrasound was performed routinely in each case to confirm and assess the intrahepatic tumors. Only patients undergoing single-stage surgery with curative intent were included. Resections were classified as nonanatomical wedge resections, segmentectomy, sectionectomy, hepatectomy, or extended hepatectomy according to the classification of the International Hepato-Pancreatico-Biliary Association.[18] All resections were performed or supervised by three hepatobiliary surgeons (GM, JC, and RP). The parenchymal dissection was achieved using a combination of clip dissection, cavitron ultrasonic aspirator, waterjet dissector, argon beam, and ultrasonic shears. Portal inflow occlusion was applied at the discretion of the operating surgeon. Hepatic resection was not combined with colorectal resection in this study.

Prognostic Factors

Potential prognostic factors were identified from previous reports[6,19] and were used for univariate and multivariate analysis: sex, age (under or over 70 years[20]), tumor stage (Dukes classification), tumor number (single or multiple), resection margin, perioperative complications, blood transfusions, period of operation (before and after 2001), portal inflow occlusion (applied or not applied), extent of resection (hemihepatectomy and extended hemihepatectomy were considered extensive resections, other resections were considered as less extensive resections), and type of resection (anatomic and nonanatomic). The resection margins were defined as involved if the margin was microscopically less than 1 mm. The period of operation was chosen such as to achieve a balance of sufficient patient number and adequate follow-up in both groups. Data about carcinoembryonic antigen levels were incomplete and not included in the analysis.

Assessment of Complications

Complications that occurred within 28 days of the operation were defined as "perioperative." A recently published standardized complication classification system was used to grade postoperative complications.[17] The grading of the severity of a complication is based on the therapy used to correct it. This grading eliminates the inconsistencies of different complication definitions. Briefly, grade 1 complication includes minor deviation from the normal postoperative course without the need for any specific treatment. Grade 2 complications can be treated solely by drugs, blood transfusion, physiotherapy, and nutritional support. Grade 3 complications require interventional or surgical treatment. Grade 4 complications are life-threatening complications requiring ICU management. Grade 5 is defined as death of the patient. If a patient had more than one complication, only the highest-ranked complication was used for the analysis. In-hospital mortality was defined as a perioperative complication.

Statistics

All statistical analysis was performed using SPSS® (version 12.0.1). Overall survival rates and disease-free survival were analyzed using Kaplan–Meier survival statistics. Univariate analysis was performed to calculate the impact of different prognostic determinants. Differences in survival rates were computed using the log rank test. Differences were considered significant if p was less than 0.05. Multivariate analysis of all prognostic factors was performed using Cox regression analysis to adjust for confounding factors.

Results

Demographics

We investigated a total of 197 consecutive patients with metastatic colorectal cancer who underwent liver resection with curative intent at Flinders Medical Centre, Ashford Community Hospital, and Queen Elizabeth Hospital. The median follow-up was 4.5 years, and there were 124 men (63%) and 73 women (37%). The median age was 64 years (range 22 to 92 years). Sixty-seven patients (34%) were older than 70 years, 106 (54%) were between 50 and 70 years, and 24 (12%) were younger than 50 years.

Tumor Characteristics

The primary tumor was in the colon in 127 cases (65%) and in the rectum in 70 cases (35%). One hundred twenty five (63%) of the colorectal tumors had involved regional lymph nodes and were classified as Dukes C. Thirty-five (18%) patients presented with synchronous liver metastasis at the diagnosis of the primary. One hundred twenty three (62%) patients underwent resection for a single metastasis, whereas the remaining 74 (38%) had two or more lesions. Sixty-seven (34%) patients had preoperative chemotherapy. Different chemotherapy regimens were used, and the number of administered cycles was variable. Therefore, we did not include the use of chemotherapy in the analysis.

Surgical Therapy

An anatomical resection was performed in 108 patients (55%); the remaining 89 underwent a nonanatomical resection. Ninety-two operations were performed before 2001. In 63 patients (32%), the interval between the resection of the primary and the liver resection was less than 6 months. In 79 patients (40%), the interval was 6 to 24 months, and in 54 patients (28%), it was more than 24 months. The resection margin was clear in 173 patients (88%). In 24 patients, the resection margin was involved. A Pringle maneuver was applied in 76 patients. In 27 patients, information about the Pringle maneuver was not available. One hundred three out of 197 patients did not receive any blood transfusion during or after the procedure. In 12 patients, no information about the use of blood transfusions was recorded.

Complications

Fifty-nine patients (30%) experienced perioperative complications. Complications were graded into five categories according to their severity.[17] Details are given in Table 1. Fourteen patients suffered from biloma or biliary leakage. Five patients experienced cardiac complications. Three patients developed postoperative liver failure with encephalopathy and increased international normalized ratio and decreased factor V, which required prolonged ICU stay. Twenty-six patients had pulmonary complications, including pneumonia, atelectasis, pleural effusion, and pneumothorax. Eleven patients had other complications including urinary infection, wound infection, hematoma, unexplained fever, deep venous thrombosis, and delirium. Five patients died during the hospitalization within 5 to 48 days after the operation. The overall in hospital mortality was, therefore, 2.5%. Two patients died as a result of postoperative sepsis and multiorgan failure. Two died from a myocardial infarction and one patient due to postoperative liver failure. Two of these five patients died within 28 days after the operation. The complication rate in patients over 70 years of age was 34% (23 out of 67), compared to 28% (36 out of

Table 1 Incidence and Severity of Postoperative Complications

Complication Grade	Patients (n)	Percent
1	4	2.0
2	28	14.2
3	12	6.1
4	10	5.1
5	5	2.5

Incidence and severity of complications according to a standardized complication classification.[17] Grade 1: Minor deviation from the normal postoperative course without the need for any specific treatment. Grade 2: Complications that can be treated solely by drugs, blood transfusion, physiotherapy, or nutritional support. Grade 3: Complications that require interventional or surgical treatment. Grade 4: Complications that are life-threatening and require ICU management. Grade 5 is defined as death of the patient

130) in patients under 70 years. This observation was statistically not significant (chi square test). The extent of the hepatic resection on the other hand was associated with a higher perioperative complication rate. Thirty five percent (44 out of 126) of patients with a hemihepatectomy or an extended hemihepatectomy experienced a complication, vs. 21% (15 out of 71) of patients undergoing less extensive hepatic resection ($p=0.042$). The prevalence of complications in the 82 patients who received blood transfusions was significantly higher than in patients not receiving blood transfusions ($p<0.01$).

Long-Term Outcomes

The actuarial survival at 5 years was 38%, with a median survival of 4.1 years. The 1- and 3-year survival rates were 88 and 62%, respectively. Using univariate analysis, survival was not influenced by tumor number, stage of the primary, transfusion requirement, resection type (anatomical vs. nonanatomical), extent of resection, period of operation, and occlusion of hepatic inflow. In contrast, positive resection margins, perioperative complications, female sex, and age over 70 years were significant predictors of overall survival (Table 2). Even when we excluded the patients that died in the perioperative period, we found the same results. To analyze the impact of the severity of the complications on survival, we compared severity grades 3, 4, and 5 vs. grade 1 and 2 complications. There was a significantly reduced median survival in patients with more severe complications of 2.1 years, compared to 4.1 years in patients with no or minor complications ($p<0.012$). Complications were more likely to occur in the extensive resections, but the effect of morbidity on outcome was independent of this.

In the multivariate analysis, age and sex were no longer predictive factors for reduced survival. However, the presence of complications or positive resection margins were still significant predictors of reduced survival (Table 3). The Kaplan–Meier curves for survival stratified by resection margins and complications are given in Figs. 1 and 2.

Disease-Free Survival

A total of 103 patients developed a recurrence during the follow-up period. Seventy had a local recurrence in the liver, whereas the others developed recurrence in the lung, bone, or elsewhere. Twenty-one patients with recurrence confined to the liver underwent repeat hepatectomy; the remaining patients received palliative chemotherapy or supportive care. The overall disease-free survival at 5 years was 23%, with a median disease-free survival of 1.7 years. Patients with a positive resection margin had a significantly lower disease-free survival of 0.7 vs. 1.8 years, as expected ($p<0.01$) (Table 4). Twenty-one patients out of 24 with involved margins developed a local recurrence or died within the follow-up period. Twenty-eight out of 59 patients who suffered from a perioperative complication developed recurrent disease. The disease-free survival in patients with perioperative complications was significantly shorter ($p=0.04$) (Table 4). These results were confirmed in the multivariate analysis. All other prognostic factors did not reach statistical significance in the multivariate analysis (Table 5).

Discussion

The major finding of this study is that patients suffering from postoperative complications after liver resec-

Table 2 Predictors of Overall Survival: Univariate Analysis

	Patients (*n*)	Median Survival	CI 95%	*p* Value
Resection margins				
Clear	173	4.4	3.6–5.2	0.019
Involved	24	2.1	1.8–2.5	
Tumor number				
Solitary	123	3.6	3.0–4.3	0.272
Multiple	74	4.7	3.4–6.0	
Complications				
Absent	138	4.4	3.2–5.7	<0.01
Present	59	3.2	2.1–4.4	
Transfusion				
Yes	82	4.4	2.8–6.0	0.934
No	103	4.1	3.2–5.0	
Extent of resection				
Extensive	126	4.3	3.5–5.1	0.928
Less extensive	71	3.6	2.7–4.5	
Resection type				
Anatomic	108	3.9	2.9–4.8	0.490
Nonanatomic	89	4.1	2.8–5.4	
Period of operation				
Before 2001	92	4.1	3.2–5.0	0.670
After 2001	105	3.6	3.1–4.8	
Sex				
Female	73	2.5	1.1–3.8	0.015
Male	124	4.5	3.9–5.2	
Age				
<70 years	130	4.7	3.5–5.9	0.012
≥70 years	67	3.0	2.0–4.1	
Nodal status				
Positive	125	3.4	2.5–4.3	0.062
Negative	71	4.9	3.6–6.2	
Pringle				
Applied	76	4.3	2.9–5.7	0.629
Not applied	94	3.6	2.4–4.8	

Median survival in years. Differences in survival rates were computed using log rank test

CI 95% = 95% confidence interval

Table 3 Predictors of Survival: Multivariate Analysis

Risk Factor	HR (95% CI)	*p* Value
Margin involved	2.1 (1.1–4.1)	0.028
Complications present	2.2 (1.3–3.7)	0.003
Age (>70 years)	1.3 (0.7–2.2)	0.376
Female	1.5 (0.9–2.5)	0.142
Multiple lesions	0.9 (0.5–1.5)	0.670
Extensive resection	0.8 (0.5–1.3)	0.325
Nonanatomical	1.1 (0.6–1.8)	0.816
Nodal positive	1.5 (0.9–2.6)	0.153
Era before 2001	1.4 (0.8–2.4)	0.198
Pringle applied	0.9 (0.5–1.5)	0.652

Cox regression analysis of patient survival
HR = hazard ratio, 95% CI = 95% confidence interval

tion for colorectal metastases had a reduced survival rate. This study clearly showed that the incidence and the severity of complications were a prognostic factor for survival. Furthermore, advanced age was not a risk factor for reduced survival or development of complications. It should also be emphasized that, although the extent of resection influenced morbidity, the impact of morbidity on long-term survival was independent of the extent of resection.

The correlation of perioperative morbidity and long-term survival is a well recognized concept in cancer surgery. Infections, anastomotic leakage, and multiorgan failure have been shown to be associated with decreased survival after tumor resection in previous studies.[14–16,21] In patients undergoing liver resection for colorectal metastasis, there has been only one other group that investigated the impact of perioperative morbidity on long-term survival.[13] Their survival rates were almost identical compared to the outcomes in the current study, but the follow-up period was considerably shorter.

While mortality is an objective parameter, morbidity is only poorly defined, and this shortcoming has severely hampered conclusive analysis of its impact on outcome.[22–24] Therefore, we used an objective surgical complication classification, which grades the complications according to their therapeutic relevance.[17] For the first time, we correlated the findings of this classification to the outcome in patients undergoing liver resection for colorectal metastasis.

The rationale behind the observation that complications affect the long-term outcome is unclear. It has been postulated that severe complications like septicemia lead to an extended period of immunosuppression, which allows residual tumor cells to further proliferate and survive in the host.[25] This could explain the reduced disease-free survival rate in some patients with complications.

Positive resection margins were identified as an independent risk factor for survival. The influence of positive resection margins on disease-free survival and overall

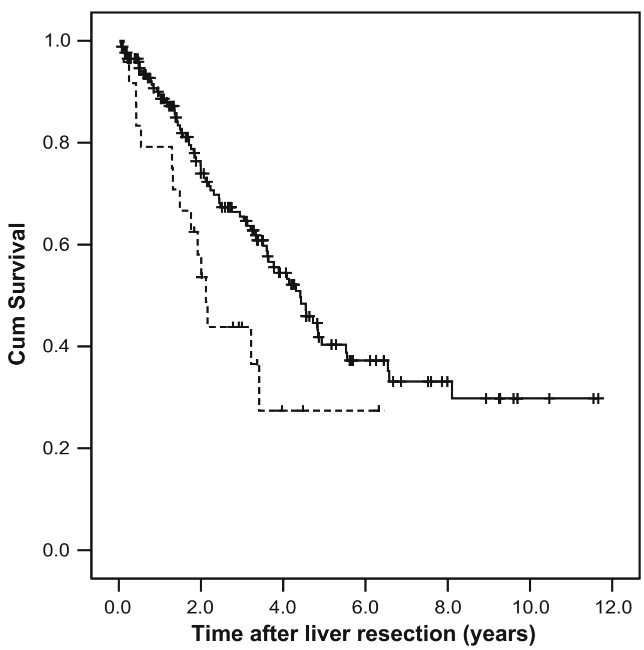

Figure 1 Overall survival according to resection margins. Kaplan–Meier curve of patients undergoing hepatectomy for colorectal metastasis. *Dotted line*: For patients with positive resection margins (n=24), the median survival was 2.1 years. *Continuous line*: Patients with clear resection margins (n=173) had a median survival of 4.4 years. Differences of survival were assessed using log rank test (p=0.019).

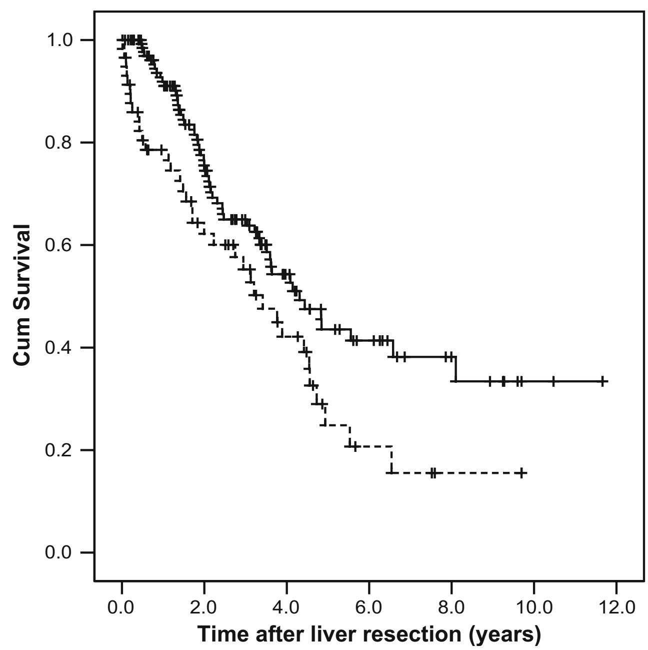

Figure 2 Overall survival according to perioperative complications. Kaplan–Meier curve of patients undergoing hepatectomy for colorectal metastasis. *Dotted line*: Patients with complications (n=59) had a median survival of 3.2 years. *Continuous line*: Patients without perioperative complications (n=138) had a median survival of 4.4 years. Differences of survival were assessed using log rank test (p<0.01).

Table 4 Predictors of Disease Free Survival: Univariate Analysis

	Patients (*n*)	Median Survival	CI 95%	*p* Value
Resection margins				
Clear	173	1.8	1.4–2.3	<0.01
Involved	24	0.7	0.3–1.0	
Tumor number				
Solitary	123	1.8	1.4–2.3	0.718
Multiple	74	1.4	0.8–2.1	
Complications				
Absent	138	1.8	1.3–2.3	0.041
Present	59	1.4	0.8–2.1	
Transfusion				
Yes	82	2.0	1.2–2.8	0.542
No	103	1.5	1.3–1.8	
Extent of resection				
Extensive	126	1.6	1.2–2.0	0.975
Less extensive	71	1.8	1.2–1.4	
Resection type				
Anatomic	108	1.7	1.3–2.2	0.703
Nonanatomic	89	1.7	1.1–2.3	
Period of operation				
Before 2001	92	1.8	1.2–2.3	0.599
After 2001	105	1.5	1.1–2.0	
Sex				
Female	73	1.6	1.0–2.2	0.626
Male	124	1.7	1.2–2.2	
Age				
<70 years	130	1.5	1.2–2.9	0.411
≥70 years	67	1.9	1.3–2.5	
Nodal status				
Positive	125	1.5	1.0–2.0	0.084
Negative	72	2.4	1.5–3.2	
Pringle				
Applied	76	1.4	1.0–1.9	0.919
Not applied	94	1.8	1.3–2.4	

Median survival in years. Differences in survival rates were computed using log rank test
CI 95% = 95% confidence interval

survival has been confirmed by other groups in many reports.[8,10] Remaining tumor cells predispose to a local recurrence, and early recurrence translates to a decreased overall survival. In patients with positive margins, the reduced overall survival and disease-free survival rates in our study are in accordance with other reports.[2,5,6,11] Therefore, clear resection margins should be achieved whenever they are possible, although repeated resections are feasible and show favorable results in selected patients.[26,27]

In contrast to the study of Choti et al.,[6] we could not confirm any difference of survival according to the era of resection. Most studies report survival rates between 25 and 37%. Two recent publications achieved remarkable 5-year survival rates over 50%.[6,7] However, the median follow-up periods of these cohorts were only 22 and 31 months. Reasons for the better results are thought to be improved staging, patient selection, and increased use of new chemotherapy regimens. Whether survival following resection in more recent times is really associated with an improved survival will need to be confirmed with longer follow up of the reported cohorts.

Advanced age has been a risk factor for long-term survival in our univariate analysis in accordance to the recently published results of Nagano et al.[28] However, we could not confirm these findings in the multivariate analysis. The study of Nagano showed no difference in perioperative morbidity and mortality in aged and young patients, and the aged group still achieved a remarkable long-term outcome of 34%. These findings are in accordance with our results. Therefore, advanced age cannot be regarded as a contraindication to hepatic resection for colorectal liver metastasis.

Although we collected data about chemotherapy, the chemotherapy regimens and the administered cycles of chemotherapy pre- and post-liver surgery were very heterogeneous. Therefore, we were not able to make any meaningful analysis regarding the influence of chemotherapy on mortality or complications.

In conclusion, postoperative morbidity and positive resection margins have an impact on long-term survival and disease-free survival in patients following resection for colorectal metastases. Advanced age is not an independent risk factor for either survival or perioperative morbidity. The results of this study are consistent with many others on the decreased survival associated with positive resection margins. Of greater interest is the finding of decreased survival associated with the incidence and severity of perioperative complications. This does indicate that there are potential benefits in performing the surgery with meticulous technique to minimize complications such as subphrenic abscess, perioperative bleeding, and biliary

Table 5 Predictors of Disease Free Survival: Multivariate Analysis

Risk Factor	HR (95% CI)	*p* Value
Involved margins	2.2 (1.3–3.8)	0.005
Complications present	1.8 (1.2–2.8)	0.006
Age (>70 years)	0.9 (0.6–1.3)	0.502
Female	1.1 (0.7–1.7)	0.669
Multiple lesions	1.0 (0.7–1.6)	0.864
Extensive Resection	0.8 (0.4–1.6)	0.471
Nonanatomical	0.9 (0.6–1.4)	0.673
Nodal positive	1.3 (0.9–2.1)	0.214
Era before 2001	1.1 (0.7–1.6)	0.750
Pringle applied	0.9 (0.6–1.3)	0.494

Cox regression analysis of disease free survival
HR = hazard ratio, 95% CI = 95% confidence interval

leakage. Careful postoperative care to avoid pulmonary and other complications could be beneficial.

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References

1. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg 1999;230(3):309–318; discussion 318–321.
2. Nordlinger B, Guiguet M, Vaillant JC, Balladur P, Boudjema K, Bachellier P, et al. Surgical resection of colorectal carcinoma metastases to the liver. A prognostic scoring system to improve case selection, based on 1568 patients. Association Francaise de Chirurgie. Cancer 1996;77(7):1254–1262.
3. Rosen CB, Nagorney DM, Taswell HF, Helgeson SL, Ilstrup DM, van Heerden JA, et al. Perioperative blood transfusion and determinants of survival after liver resection for metastatic colorectal carcinoma. Ann Surg 1992;216(4):493–504; discussion 504–505.
4. Scheele J, Stang R, Altendorf-Hofmann A, Paul M. Resection of colorectal liver metastases. World J Surg 1995;19(1):59–71.
5. Jenkins LT, Millikan KW, Bines SD, Staren ED, Doolas A. Hepatic resection for metastatic colorectal cancer. Am Surg 1997;63(7):605–610.
6. Choti MA, Sitzmann JV, Tiburi MF, Sumetchotimetha W, Rangsin R, Schulick RD, et al. Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg 2002;235 (6):759–766.
7. Fernandez FG, Drebin JA, Linehan DC, Dehdashti F, Siegel BA, Strasberg SM. Five-year survival after resection of hepatic metastases from colorectal cancer in patients screened by positron emission tomography with F-18 fluorodeoxyglucose (FDG-PET). Ann Surg 2004;240(3):438–447; discussion 447–450.
8. Jaeck D, Bachellier P, Guiguet M, Boudjema K, Vaillant JC, Balladur P, et al. Long-term survival following resection of colorectal hepatic metastases. Association Francaise de Chirurgie. Br J Surg 1997;84(7):977–980.
9. Kokudo N, Tada K, Seki M, Ohta H, Azekura K, Ueno M, et al. Anatomical major resection versus nonanatomical limited resection for liver metastases from colorectal carcinoma. Am J Surg 2001;181(2):153–159.
10. Cady B, Jenkins RL, Steele GD Jr, Lewis WD, Stone MD, McDermott WV, et al. Surgical margin in hepatic resection for colorectal metastasis: a critical and improvable determinant of outcome. Ann Surg 1998;227(4):566–571.
11. Elias D, Cavalcanti A, Sabourin JC, Pignon JP, Ducreux M, Lasser P. Results of 136 curative hepatectomies with a safety margin of less than 10 mm for colorectal metastases. J Surg Oncol 1998;69(2):88–93.
12. Minagawa M, Makuuchi M, Torzilli G, Takayama T, Kawasaki S, Kosuge T, et al. Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer: long-term results. Ann Surg 2000;231(4):487–499.
13. Laurent C, Sa Cunha A, Couderc P, Rullier E, Saric J. Influence of postoperative morbidity on long-term survival following liver resection for colorectal metastases. Br J Surg 2003; 90(9):1131–1136.
14. Fujita S, Teramoto T, Watanabe M, Kodaira S, Kitajima M. Anastomotic leakage after colorectal cancer surgery: a risk factor for recurrence and poor prognosis. Jpn J Clin Oncol 1993;23(5): 299–302.
15. Hirai T, Yamashita Y, Mukaida H, Kuwahara M, Inoue H, Toge T. Poor prognosis in esophageal cancer patients with postoperative complications. Surg Today 1998;28(6):576–579.
16. Howard TJ, Krug JE, Yu J, Zyromski NJ, Schmidt CM, Jacobson LE, et al. A margin-negative R0 resection accomplished with minimal postoperative complications is the surgeon's contribution to long-term survival in pancreatic cancer. J Gastrointest Surg 2006;10(10):1338–1345; discussion 1345–1346.
17. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240(2):205–213.
18. IHPBA TCot. Terminology of liver anatomy and resections. HPB Surg 2000;2:333–339.
19. Minagawa M, Makuuchi M, Takayama T, Kokudo N. Selection criteria for repeat hepatectomy in patients with recurrent hepatocellular carcinoma. Ann Surg 2003;238(5):703–710.
20. Nagano Y, Tanaka K, Togo S, Matsuo K, Kunisaki C, Sugita M, et al. Efficacy of hepatic resection for hepatocellular carcinomas larger than 10 cm. World J Surg 2005;29(1):66–71.
21. Mynster T, Christensen IJ, Moesgaard F, Nielsen HJ. Effects of the combination of blood transfusion and postoperative infectious complications on prognosis after surgery for colorectal cancer. Danish RANX05 Colorectal Cancer Study Group. Br J Surg 2000;87(11):1553–1562.
22. Clavien PA, Camargo CA Jr, Croxford R, Langer B, Levy GA, Greig PD. Definition and classification of negative outcomes in solid organ transplantation. Application in liver transplantation. Ann Surg 1994;220(2):109–120.
23. DeOliveira ML, Winter JM, Schafer M, Cunningham SC, Cameron JL, Yeo CJ, et al. Assessment of complications after pancreatic surgery: A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. Ann Surg 2006;244(6):931–937; discussion 937–939.
24. Martin RC 2nd, Brennan MF, Jaques DP. Quality of complication reporting in the surgical literature. Ann Surg 2002;235 (6):803–813.
25. Panis Y, Ribeiro J, Chretien Y, Nordlinger B. Dormant liver metastases: An experimental study. Br J Surg 1992;79 (3):221–223.
26. Morise Z, Sugioka A, Fujita J, Hoshimoto S, Kato T, Hasumi A, et al. Does repeated surgery improve the prognosis of colorectal liver metastases? J Gastrointest Surg 2006;10(1):6–11.
27. Petrowsky H, Gonen M, Jarnagin W, Lorenz M, DeMatteo R, Heinrich S, et al. Second liver resections are safe and effective treatment for recurrent hepatic metastases from colorectal cancer: A bi-institutional analysis. Ann Surg 2002;235(6):863–871.
28. Nagano Y, Nojiri K, Matsuo K, Tanaka K, Togo S, Ike H, et al. The impact of advanced age on hepatic resection of colorectal liver metastases. J Am Coll Surg 2005;201(4):511–516.