Resection of liver metastases from colorectal cancer: prognostic factors influencing recurrence and survival rates.

RESECTION OF LIVER METASTASES FROM COLORECTAL CANCER: PROGNOSTIC FACTORS INFLUENCING RECURRENCE AND SURVIVAL RATES

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Summary. The Authors reviewed the result of 107 patients who underwent a total of 135 hepatic resection for colorectal carcinoma (CCR). The following prognostic factors which may influence the recurrence and survival rate were analized: primary tumor localization, Dukes stage, presence of single or multiple metastases and their presence in a single lobe or both, number of metastases (less than 3 and more than 3), synchronous or metachronous, type of resection (minor or major and anatomical or non anatomical).

Perioperative morbidity and mortality rate were 1,9% and 6,5%. Overall survival and disease-free survival rate were 41,2% and 31,5% at 5 years. Survival was significantly better for metachronous than for synchronous lesions (60,9% vs 28,1%; p<0,05) and for <3 or >3 lesions (42% vs 05; p=0,054).

Liver resection remain the "gold standard" for the treatment of liver metastases from colorectal cancer. Metachronous lesions and less then 3 nodules appared to be significant prognostic factors.

Introduction

Approximately 50% of colorectal primaries are complicated by liver metastases. Unfortunately, only 10% to 20% of these patients have a resectable disease at the time of presentation [1]. Liver resection represents the best curative treatment and should be always considered as the first therapeutic option in case of hepatic metastases because of the reporter rates of 25% to 58% of survival [2]. A lot has been written about many prognostic factors who may influence the prognosis after liver resection, but the debate is still opened and, for the majority of them, a definitive agreement is still not reached.

We reviewed retrospectively our series of patient resected for liver metastases from colorectal cancer (CRC) and the aim is to evaluate retrospectively surgical results as well as to point out some prognostic factors which may affect the long term results.

Patients and methods

Between May 1989 and May 2004, 107 patients underwent liver resection for metastases from CRC, 43 were women and 64 were men (median age 59aa, range 31-79). Globally were performed 135 hepatectomies. The following parameters were evaluated as possible prognostic factors: primary tumor localization, Dukes stage, presence of single or multiple metastases and their presence in a single lobe or both, number of metastases (less than 3 and more than 3), synchronous or metachronous, type of resection (minor or major and anatomical or non anatomical). Primary tumor was localized in the colon in 62 pts (58.75%) and in the rectum in 45 pts (41.25%). Dukes stage was A in only two patient, B in 31 pts and C in 74 pts. Synchronous lesions were 70 (65.5%) while metachronous were 37 (34.5%). A major resection was performed in 33 pts (30.8%) while a minor in 74 pts (69.1%).

Among synchronous liver metastases 41 (58.2%) of them were resected simultaneously with the primary tumor while 29 (41.8%) underwent a delayed hepatic resection. According to Couinaud classification of liver segments, 13 (14.9%) out of 70 hepatic resections performed for synchronous lesions were major (at least 3 segments) but only one was simultaneous, in comparison with 28 (57.9%) out of 37 performed in the metachronous setting. Liver metastases were single in 53 pts (49.5%) and multiple in 54 pts (50.5%). Among multiple lesions, liver metastases were 3 or less than 3 in 80 pts (75%) and more than 3 in 27 pts (25%). Bilobar metastases were present in 25 pts (23.5.%) while in 82 (76.5%) they were unilobar.

Results

A total of 56 patients eventually died, and the death was due to cancer in 53 patients (94%). In hospital mortality rate (within 30 days) was 1.9 % (2 out of 107 pts). Major complications occurred in seven patients (6.5%): we observed four right pleural effusions and three peri-hepatic collections due to a biliary leakage which spontaneously healed.

Overall survival at 3, 5 and 10 years, according to Kaplan - Meier curves, was 51,4%, 41.2% and 36.8% respectively, and median survival was 44 months (range 3-168 months) (Fig. 1). The percentage of disease free survival at 3, 5 and 10 years was 41,4%, 31,5% and 27% respectively (Fig. 2). Overall survival at 3, 5 and 10 years for synchronous and metachronous metastases was respectively 46,8%, 34,3% and 28,1% for synchronous and 73,4%, 60,9% and 60,9% for metachronous (Fig. 3). Survival rates were better for metachronous lesions than for synchronous, with significant effect on the prognosis (p<0,05). There were not significant difference in term of long term survival between synchronous simultaneous and delayed metasteses.

Concerning the number of the lesions and their localizations, there were not significant differences beetwen unilobar or bilobar metastases and between singles or multiples metastases, while there was a better survival for patients resected for three or less than three lesions compared to those resected for more than three lesions, with an overall survival at five years of 42% vs. 0% respectively (Fig. 4), even if this difference was on the limits of statistical significativity (p=0.054). The type of hepatic resection (typical or atypical and major or minor), had no significant effect on the prognosis.

Concerning the primary tumour, the localization in the colon or in the rectum had no significant effect on the prognosis, while the Dukes stage was correlated with the overall survival, whit a percentage of overall survival at five years equal to 57,8% for dukes A and B and 34,3% for dukes C.

Conclusions

Since liver metastases develop in 40 to 70% of patients with a colorectal cancer at same stage of the disease, the epidemiologic impact of this secondary hepatic disease is clearly evident. The frequency of synchronous lesions is between 15 and 40% while metachronous metastases develop in a similar percentage of patients over a period of 3 years.

Interestingly, there is almost no spontaneous long-term survivors (1-3% at 5 years) in untreated patients; mean survival time is infact 9 months and there is no doubt at present that liver resection represents the best option and probably the only curative option for patients with colorectal liver metastases, with percentage of overall survival ranging from 25% to 45%, mortality rate between 0% and 2% and very low morbidity rate.

Concerning the localization of the primary tumour, some authors has observed a better survival in resected patients for metastases from colon cancer versus rectum cancer, but in our results this difference is not significant.

In our series patients resected for metachronous metastases showed a better long term survival if compared with patients resected for synchronous ones. Most of authors also observed a lower survival in synchronous versus metachrounous metastases which was probably due also to a poorer selection of candidates in the synchronous setting [3-4].

Simultaneous and delayed resection of synchronous liver metastases from CRC showed similar results in terms of 5 year survival; therefore, it seems that the timing of liver resection is not crucial for the oncological outcome even if performed as a delayed procedure.

The number of metastatics nodules is considered an important prognostic factor. In the past, in fact, the indication for surgery was limited to patients with less than three metastatics nodules possibly localized in one lobe. Our results seems to confirm these data but, because of the fact that liver resection offer the only hope for cure with low morbidity and mortality rate approaching 0%, there are increasing reports about the efficacy in the long term of multiple liver resection (mostly wedge) performed for more than four nodules [5], also performed as a staged resection [6]. Wedge resection in fact yields the same results of typical resection, in term of long term survival.

Fig 1 - Overall survival of resected patients

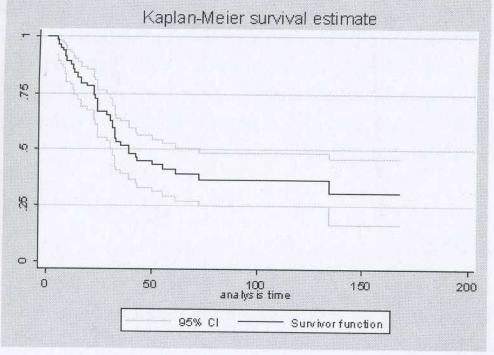


Fig 2 - Disease free survival of resected patients

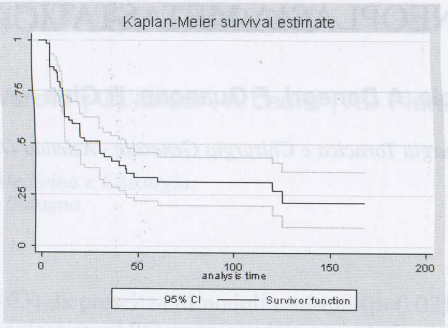


Fig 3 - Survival rate of patients resected for synchronous and matachronous metastases from colon rectal cancer

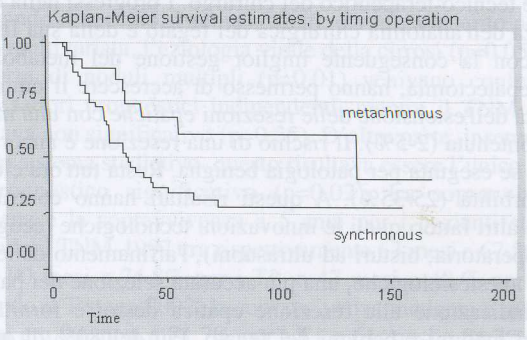
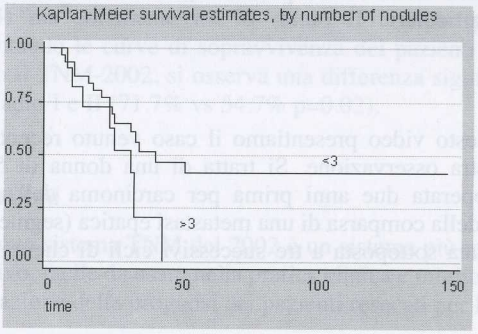


Fig. 4 - Survival rates of resected patients with more than three or less than three metastases



References

1. Doci R, Gennari L, et al.: One hundred patients with hepatic metastases from colorectal cancer treated by resection: analysis of prognostic determinants. Br J Surg, 78: 797-801, 1991.
2. Adams R, Pascal G, et al.: Liver Resection for Colorectal metastases. Ann Surg, 238: 871-884, 2003.
3. Altendorf-Hofmann A, Scheele J: A critical review of the major indicators of prognosis after resection of hepatic metastases from colorectal carcinoma. Surg Oncol Clin N Am, 12: 165-192, 2003.
4. chlag P, Hohenberger P, et al: Resection of liver metastases in colorectal cancer- competitive analysis of treatment results in synchronous versus metachronous metastases. Eur J Surg Onc, 16: 360-365, 1990.
5. Kokudo N, Imamura H, et al.: Surgery for multiple hepatic colorectal metastases. J Hepatobiliary Pancreas Surg , 11: 84-91, 2004.
6. Adam R, Laurent A, et al.: Two-Stage Hepatectomy: A planned strategy to treat irresecable liver tumors. Ann Surg, 232: 777-785, 2000.