

Austrian Consensus on the surgical treatment of colorectal liver metastases

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Received 3 January 2009; accepted 9 February 2009

An Austrian expert panel comprising surgeons and medical oncologists from tertiary care centres in Austria was convened in Vienna in 2008 to assess the current strategies of the management of liver metastasis in colorectal cancer with special focus on the surgical approach. Following topics were discussed based on the current literature: liver surgery, role of systemic therapy, resection margins, role of the application of ablation techniques or laparoscopic liver resection. The results were summarized and are now presented as the Austrian consensus report.

Keywords: Colorectal cancer, liver metastasis, liver resection, chemotherapy, consensus

Report

Colorectal cancer (CRC) is one of the most commonly diagnosed malignancies in Austria with approximately 5,000 newly diagnosed cases per year [1]. 30 to 50% of patients either present with or develop hepatic metastases. The liver is the exclusive site of secondary tumours in up to half of these patients [2]. Liver resection is the treatment of choice in patients with resectable colorectal hepatic metastases [3] and is repeatedly demonstrated to be safe with postoperative mortality rates of less than 5% [4]. Safety of liver resection was additionally shown in synchronous liver metastases, when resection of the primary colorectal tumour was accompanied with synchronous minor liver resection (less than or equal to 2 segments) [5]. Besides safety, the efficacy of hepatectomy was repeatedly demonstrated. 5-year survival rates in the range from 40 to 50% are consistently reported. Nevertheless, in the past only a relatively small proportion of patients (15 to 20%) was considered for hepatectomy [6] and indication was based on several clinico-pathological features that were used

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to determine the suitability for a surgical approach [7]. These comprised size [3], number [8] and site of hepatic lesions, additionally extra-hepatic disease and the general rule of at least 1 cm tumour free resection margin [9]. Sustaining on currently available data [10, 11] a shift of paradigm focusing on how resectability is delineated took place in the last years. Instead of defining the appropriateness of the surgical approach by what has been removed, it now concentrates on what will remain left after resection with the intention to gain both macroscopic and microscopic complete resection (R0) and to preserve an adequate volume and consecutive function of the future liver remnant. Furthermore, advanced surgical procedures (e.g., extended hepatectomy [12], two-stage hepatectomy [13]) and the availability of adjunctive techniques like radio frequency ablation [14] and portal vein embolisation [12] broadened the cycle of patients that are resectable. The expansion of criteria for resectability of colorectal liver metastases was accompanied with the development of new effective cytotoxic agents (e.g., irinotecan or oxaliplatin) and monoclonal antibodies (e.g., cetuximab or bevacizumab), leading to secondary resectability of primarily unresectable or potentially resectable liver metastases [15–19]. Moreover, even in primarily resectable patients preoperative chemotherapy seems to be beneficial [18]. This resulted even in the recently adopted trend of a reversed sequence of local and systemic therapy, with systemic chemotherapy in patients with synchronous liver metastases in asymptomatic colorectal cancer, i.e. to apply systemic therapy prior to surgery [20], even in primarily resectable liver metastases.

Today, indication for liver resection of colorectal metastases has become a much more nuanced and sophisticated approach, which includes all aspects of multidisciplinary. Selection of patients is crucial and the complex clinical decision-making is best performed in the setting of an interdisciplinary team comprising surgeons experienced in liver surgery. An Austrian expert panel comprising surgeons and medical oncologists from tertiary care centres in Austria was convened in Vienna, Austria, in 2008 to assess the current situation with a focus on the surgical approach. After a series of presentations and consecutive discussions – all presentations were based on recently published studies or data presented at relevant congresses – the members of the panel were asked to contribute to a consensus statement. A consensus on the medical treatment of colon cancer was published recently in this journal [21].

Consensus and position statement

- Patients with hepatic metastases should be routinely discussed at a multidisciplinary tumour board which has experience in the management of liver metastases. In particular, this interdisciplinary team has to include surgeons with experience in liver surgery.
- Liver resection is safe and should be performed with a post-operative mortality rate of less than 5%.
- Advanced liver surgery and adjunctive techniques (i.e. extended liver resection, two-stage hepatectomy, portal vein embolisation, ablative procedures) should be considered as long as a R0 situation can be achieved.
- Repeated liver resection for recurrent disease is safe and associated with a survival benefit.
- The ultimate goal in the treatment of metastatic colorectal cancer is to administer adequate systemic therapy as soon as possible.
- Extra-hepatic disease (predominantly lymph node metastases at the hepatoduodenal ligament or lung metastases) does not represent a contraindication for surgery “per se” when a R0 resection seems feasible.
- Tumour-free resection margins of only few millimetres yield the same cure rate when compared with the “old” rule requiring 1 centimetre. In special anatomical situations (e.g. adjacency to major vessels), tumour very close to or at the resection margin is acceptable, when ultrasonic dissection devices are used.
- Minor liver resection can be carried out effectively after preoperative down-sizing of the tumour.
- Patients with progressive disease while on chemotherapy should probably not be considered for hepatic resection.
- Application of ablation techniques, in particular of radio frequency or thermoablation and stereo-tactic radio-surgery, as a stand-alone procedure is still considered to be an experimental approach. Liver resection is the therapy of choice.
- Laparoscopic liver resection represents an experimental approach.
- In the case of synchronous metastases to the liver, systemic adequate chemotherapy can be administered before resection of the primary tumour. Upfront surgery should be carried out for patients with symptomatic primaries.
- Liver resection along with resection of the primary tumour should be performed only when liver resection does not exceed more than 2 segments of the liver.

Acknowledgements

The authors would like to acknowledge financial support from Merck-Serono for the meeting. Merck-Serono had no input into the content of the manuscript.

Authors' disclosures of potential conflicts of interest

The author(s) indicated no potential conflicts of interest.

References

- [1] http://www.aco-asso.at/manual/aktuell/kolorekt/kap_01.html
- [2] Zitt M, Mühlmann G, Weiss H, et al. Assessment of risk-independent follow-up to detect asymptomatic recurrence after curative resection of colorectal cancer. *Langenbecks Arch Surg*, 391: 369–375, 2006.
- [3] Fong Y, Fortner J, Sun RL, et al. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg*, 230: 309–318, 1999.
- [4] Simmonds PC, Primrose JN, Colquitt JL, et al. Surgical resection of hepatic metastases from colorectal cancer: a systematic review of published studies. *Br J Cancer*, 94: 982–999, 2006.
- [5] Reddy SK, Pawlik TM, Zorzi D, et al. Simultaneous resections of colorectal cancer and synchronous liver metastases: a multi-institutional analysis. *Ann Surg Oncol*, 14: 3481–3491, 2007.
- [6] Nordlinger B, Van Cutsem E, Rougier P, et al. Does chemotherapy prior to liver resection increase the potential for cure in patients with metastatic colorectal cancer? A report from the European Colorectal Metastases Treatment Group. *Eur J Cancer*, 43: 2037–2045, 2007.
- [7] Ekberg H, Tranberg KG, Andersson R, et al. Determinants of survival in liver resection for colorectal secondaries. *Br J Surg*, 73: 727–731, 1986.

- [8] Hughes KS, Simon R, Songhorabodi S, et al. Resection of the liver for colorectal carcinoma metastases: a multi-institutional study of patterns of recurrence. *Surgery*, 100: 278–284, 1986.
- [9] Cady B, Jenkins RL, Steele GD, et al. Surgical margin in hepatic resection for colorectal metastasis: a critical and improvable determinant of outcome. *Ann Surg*, 227: 566–571, 1998.
- [10] 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, xi, 2003.
- [11] Pawlik TM, Scoggins CR, Zorzi D, et al. Effect of surgical margin status on survival and site of recurrence after hepatic resection for colorectal metastases. *Ann Surg*, 241: 715–722, 2005.
- [12] Abdalla EK, Barnett CC, Doherty D, et al. Extended hepatectomy in patients with hepatobiliary malignancies with and without preoperative portal vein embolization. *Arch Surg*, 137: 675–680, 2002.
- [13] Adam R, Laurent A, Azoulay D, et al. Two-stage hepatectomy: A planned strategy to treat irresectable liver tumors. *Ann Surg*, 232: 777–785, 2000.
- [14] Elias D, Goharin A, El Otmány A, et al. Usefulness of intraoperative radiofrequency thermoablation of liver tumours associated or not with hepatectomy. *Eur J Surg Oncol*, 26: 763–769, 2000.
- [15] Bokemeyer C, Bondarenko I, Makhson A, et al. Cetuximab plus 5-FU/FA/oxaliplatin (FOLFOX-4) versus FOLFOX-4 in the first-line treatment of metastatic colorectal cancer (mCRC): OPUS, a randomized phase II study. *J Clin Oncol*, ASCO Annual Meeting Proceedings, #4035, 2007.
- [16] Cunningham D, Kretschmar A, Berry S, et al. Efficacy and safety of surgery with curative intent in patients treated with first-line bevacizumab for mCRC: First BEAT. *J Clin Oncol*, ASCO Gastrointestinal Cancers Symposium, #445, 2008.
- [17] Giacchetti S, Itzhaki M, Gruia G, et al. Long-term survival of patients with unresectable colorectal cancer liver metastases following infusional chemotherapy with 5-fluorouracil, leucovorin, oxaliplatin and surgery. *Ann Oncol*, 10: 663–669, 1999.
- [18] Nordlinger B, Sorbye H, Glimelius B, et al. Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. *Lancet*, 371: 1007–1016, 2008.
- [19] Van Cutsem E, Nowacki M, Lang I, et al. Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial. *J Clin Oncol*, ASCO Annual Meeting Proceedings, #4000, 2007.
- [20] Mentha G, Majno P, Terraz S, et al. Treatment strategies for the management of advanced colorectal liver metastases detected synchronously with the primary tumour. *Eur J Surg Oncol*, 33(Suppl 2): S76–S83, 2007.
- [21] Kornek G, Scheithauer W, Anghel R, et al. Consensus on the medical treatment of colon cancer. *Memo*, 1: 79–90, 2008.