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PILOT STUDY

Chemo-embolization of inoperable liver tumors

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Abstract: A small percentage of patients suitable for radical surgery require us to introduce alternative palliative methods prolonging the good quality of life in patients with malignant liver tumors. Apart from thermo-ablation or cryo-ablation, one of the alternative methods with palliative influence on tumors is the chemo-embolization of tumors.
A group of 18 patients, who underwent chemo-embolization at the Surgical Clinic and Radiodiagnostic Clinic, Medical Faculty, Charles University in Pilsen from 2007 to 2008, were assessed from the point of view of complications, overall survival and the patients' life quality. The most common complication was temperature and pain in the right infracostal area in connection with the performed procedure. The patients' quality of life after chemo-embolization was very good and the time of hospitalization was only 3.5 days on average. We had to perform the procedure repeatedly in 30 % of cases. The chemo-embolization was done on inoperable liver metastases of colorectal carcinoma and on inoperable hepatocellular carcinoma *(Tab. 1, Fig. 2, Ref. 5)*. Full Text in free PDF *www.bmj.sk.*
Key words: liver tumor chemoembolisation.

In spite of the high incidence of colorectal carcinoma liver metastases, only about one quarter of patients in our population are suitable for radical surgery. The remaining patients depend on palliative methods and palliative chemotherapy. Although the median survival rate of patients dependent on chemotherapy alone is prolonging mainly owing to new biological therapeutic means, the average survival rate is short, namely 20 months when compared to patients who have undergone radical resection of liver metastases where a five-year survival occurs in 30–40 % of cases. In order to increase the survival rate in patients with large, radically inoperable metastases, we use (in accordance with findings) palliative destruction through radiofrequency ablation RFA, which provides an improvement in the 5-year survival rate in up to 23–30 % of our patients. RFA is used more in multiple focuses, whereas in large solitary focuses (beyond the possibilities of RFA – i.e. over 6 cm), chemo-embolization is used more often. We use thrombo-spheres filled with up to 100 mg of Irrinotecan in a single application, since they are the almost ideal embolization material.

Through chemo-embolization we achieve ischemia at the focus, prolongation of the chemotherapeutic effect at the site of the tumor and a reduction in the overall adverse effects of chemotherapy. The advantage is that we can choose the optimal size of the thrombo-spheres in accordance with vascular supply of the metastatic focus, followed by a slow and gradual release of the chemotherapeutic drug into the tumor. The same embolization material is used in inoperable hepatocellular carcinoma but here it is filled with up to 100 mg of Doxorubicin. Although RFA in small focuses of hepatocellular carcinoma provides good results comparable with liver resection, chemo-embolization is used in large solitary inoperable focuses. Liver transplantation provides excellent results in smaller hepatocellular carcinomas in cases of cirrhosis meeting the Milan criteria.

Group of patients and methods

The group of patients includes 18 patients, 9 of whom have inoperable colorectal carcinoma metastases and 9 have an inoperable finding of hepatocellular carcinoma. All these patients (6 men and 12 women) were treated with chemo-embolization at the Surgical Clinic and Radiodiagnostic clinic, Medical Faculty and Faculty Hospital in Pilsen from 2007 to 2008. A total of 26 chemo-embolizations were performed by intervention radiologists. The patients were included in the group based on histological diagnosis and multiphase liver examination by computer tomography. Extrahepatic affliction was excluded either by positron emission tomography – PET CT – or through examining the chest and abdomen by computer tomography and control endoscopy. The indication for chemo-embolization was given by a liver surgeon after considering the overall patient's condition and by the fact that the local finding did not allow radical tumor resection or its destruction with RFA.

The Seldinger technique was used for embolization through the inguinal region while arteries leading to the focus were se-

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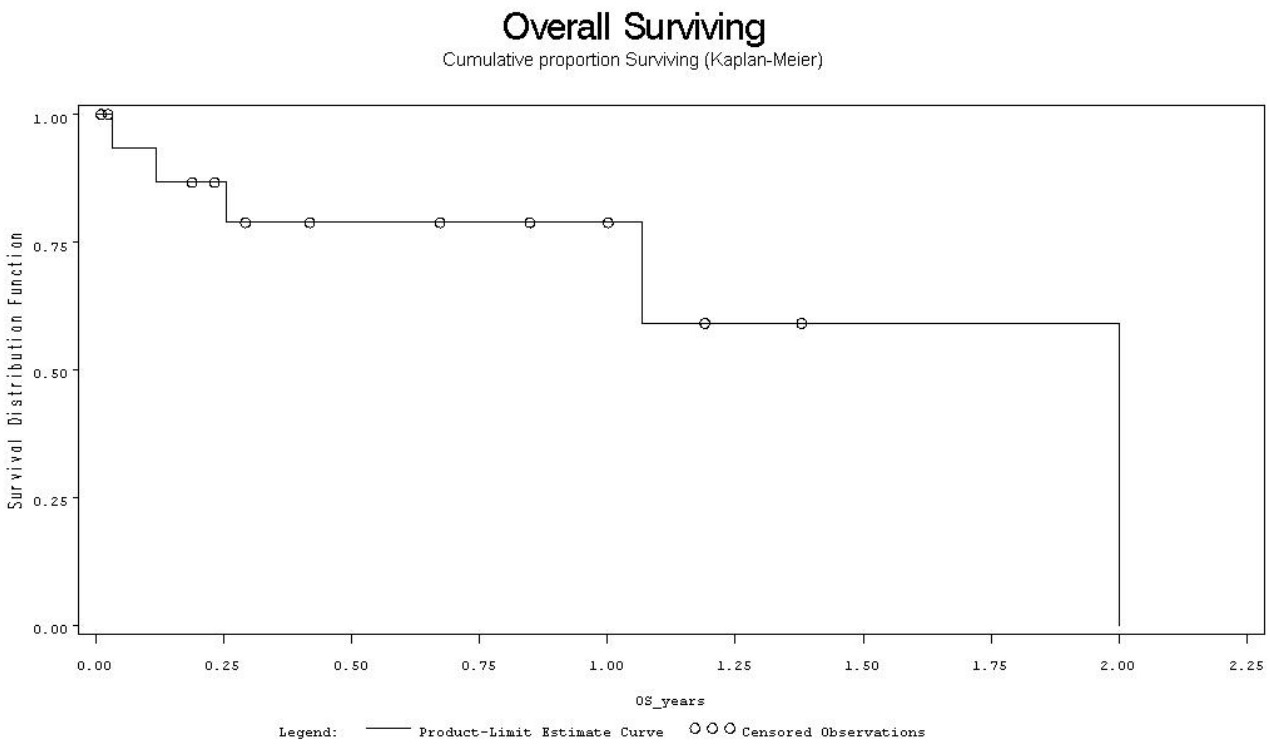

Fig. 1. Overall survival of patients after chemo-embolization of inoperable tumor liver metastases at the Faculty Hospital in Pilsen.

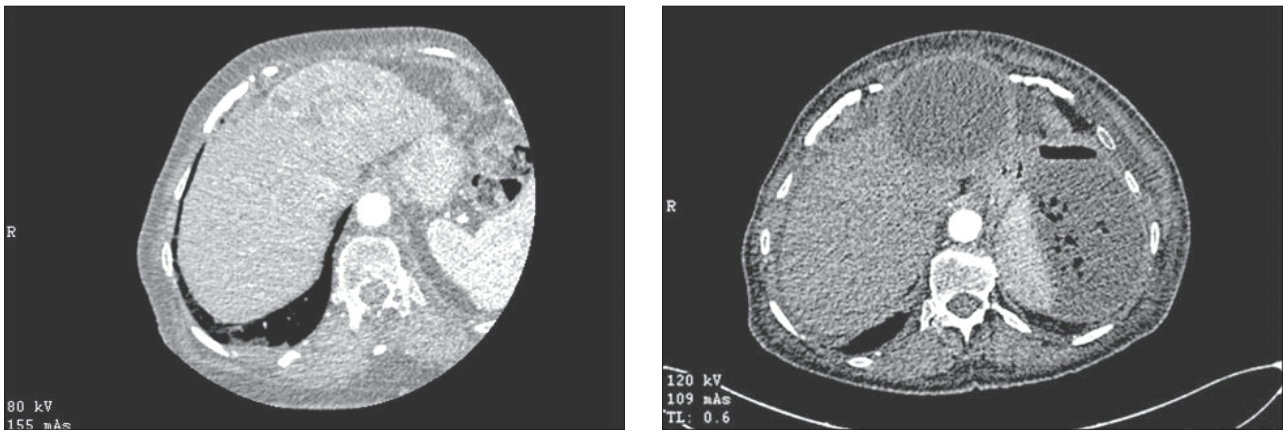

Fig. 2. Condition a. before and b. after chemo-embolization of primary hepato-cellular liver carcinoma in an 80-year-old female patient with a heart disorder.

lectively occluded. The DC head thrombo-spheres sized 100 – 300, 300 – 500 and 500–700 microns from Vamex Company were applied. The liver surgeon was always consulted in order to decide whether to exclude radical performance either because of unsuitable localization of tumor or due to inability of the patient to undergo surgery owing to his/her poor health condition. The average number of chemo-embolizations in the focus was 1.5 in our group (from 1 to 3). The time between individual chemo-embolizations was three to four weeks and the repeated performance was indicated based on CT liver examination when the signs of tumor vitality were present in the arterial phase. Patients with severe liver function disorder were excluded as well as patients with Child B or C liver cirrhosis. Moreover, patients with simultaneous portal thrombosis were not included in the group. Loco-regional embolization treatment was supplemented in all patients with complete systemic therapy in accordance with the schemes of the Czech Oncological Society. In embolization of colorectal carcinoma liver metastases, Irinotekan was used as a chemotherapeutic drug in a dose of 100 mg for one embolization, while in primary hepatocellular carcinoma, Doxorubicin was used in a dose of 50 – 100 mg for single embolization. As a main complication in almost all patients, we registered the so-

called post-embolization syndrome expressed by pain of varying intensity in the right infracostal area, raised body temperature, and nausea lasting from one to five days. This syndrome is accompanied by laboratory results of increased AST and ALT and in about 10 % of patients there are higher levels of bilirubin and alkaline phosphatase.In our patients we did not register any other complications described in literature (1, 4, 5), such as acute stomach ulcer, acute cholecystitis and others.

Statistical analysis of the monitored group of patients was performed by S.A.S. statistical software, version 6.12 (Statistical Analysis Software, Inc.). The analysis was performed with regard to the overall survival (OS) of patients in view of the palliative character of the procedure, which excluded the disease-free interval (DFI).

Results

One year after the procedure, the overall survival of the patients was 79 %. Two-year survival was influenced by a high number of patients who were monitored for only a short follow-up period (59 % of patients). Still, this result can be considered promising (Figs 1 and 2). Statistical analysis comparing the overall survival between the groups of patients with colorectal carcinoma liver metastases and hepatocellular carcinoma was not performed because of the small number of patients in the groups. In two patients, there was HCC regression while the second resection of the tumor was possible.

Discussion

The only hope in treating the liver metastases and primary liver tumors is surgery. That is why we must offer this treatment to all patients with operable findings. For other patients, apart from palliative chemotherapy, various procedures have been developed in order to prolong the good quality life in patients with liver tumors while their combination is sometimes designated as a multimodal approach. Among the common methods of treating inoperable hepato-cellular carcinoma is the so-called TACE, i.e. trans-arterial chemo-emboliozation, which uses the application of chemotherapeutic drugs and is followed by embolization of the arterial bed of the liver, for example by lipiodol, glues or coils. The new methods using thrombo-spheres with an active surface and the ability to bind and gradually release the drug shift the chemo-embolization to a higher level. The drug is effective in higher concentrations for a longer period targeted at the tumor, together with ischemia at the focus (2, 3).

The complications after chemo-embolization are of various types and degrees of severity and they are almost always present (Tab. 1). Post-embolization syndrome may disappear within 24 – 48 hours, but it may also persist for 4–5 days. When medium-strength analgesic drugs and antipyretic drugs are administered, temperature and pain can be well managed. It is more difficult to deal with nausea resulting possibly in limited peroral food intake in spite of antiemetic treatment. The inception of a stomach ulcer is connected rather with the development of a stress ulcer, and this complication can be influenced positively by prophylactic administration of anti-ulcerous therapy. On the other hand, in cases when the embolization is performed in the proximity of the gallbladder, the development of chemical cholecystitis can be influenced less, while in rare cases, it may lead to organ perforation and necessity of surgical treatment of this complication. If the focuses are in dorsal positions, a reactive right-side fluidothorax occurs, but again this requires no intervention. In our group of patients, we recorded a development of ascites in two patients, probably as a reaction to the worsening of the portal vein flow under the pressure at the focus, due to development of aseptic inflammation, or because of worsened liver functions.

Tab. 1. Complications of Chemo-embolizations at the Faculty Hospital in Plisen.

Total	18		
	1st day	2nd–3rd day	3rd–5th day
Post-emboliz. Syndrome	17		0 0
Fluidothorax right	8 (44%)	11 (61%)	3 (17%)
Ascites	3 (17%)	0	0
Other	1 (5%) hematoma in the inguinal region		

Long-term monitoring of patients after chemo-embolization performed by multiphase CT should be accompanied by sonographic examination with an administration of contrast medium where such a combination increases the sensitivity during the diagnosis of relapse. An alternative is offered in form of an examination with magnetic resonance imaging. On the other hand, examination with PET CT, which often provides partially false positive results because of the occurrence of inflammatory reaction around the necrotic tissue, is not beneficial. Monitoring the dynamics of onco-markers represents an inseparable part of the monitoring of patients. After successful chemo-embolization it is good to consider whether the tumor might be secondarily operable. In the group of patients who had undergone chemo-embolization of a large primary liver tumor, we have two patients in whom the embolization brought about downstaging and it was possible to perform a secondary radical resection of the tumor.

Conclusion

Fairly promising results in patients who have undergone chemo-embolization of the liver does not constitute a reason for great optimism since the groups (as well as groups in literature) are still small and from the long-term point of view, surgery is the only treatment for liver tumors with a potentially curative effect. Therefore, chemo-embolization has its role in the treatment of inoperable liver tumors, both primary and secondary. It can also be used in large tumors with a minimum burden on the patients and repeated several times. The use of chemo-embolization in downstaging the inoperable hepatocellular carcinoma is also of potential value.

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