LIVER TRANSPLANTATION (FOR COLORECTAL LIVER METASTASES)

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Liver transplantation (Lt) for malignant diseases is feasible and induces excellent outcome in selected patients. Lt for malignant tumors comprises 14% of all Lts in the European Liver Transplant Registry (ELTR). Types of primary liver carcinomas eligible for transplantation include hepatocellular carcinoma (HCC), cholangiocarcinoma (CCA), hepatoblastoma, and hemangioendothelioma. The most common secondary carcinomas that are considered for Lt include metastases from carcinoid tumors, neuroendocrine tumors and gastrinomas.

Lt for HCC within Milan- and the Up to Seven criteria show excellent short- and long term patient survival. In recent studies of Lt for HCC even better results can be obtained in patients receiving immunosuppression containing the antiproliferative agent sirolimus. In patients transplanted for cholangiocarcinoma using a multimodal approach with neoadjuvant radiation and chemotherapy a 5 year survival above 80% can be achieved in selected patients.

Colorectal carcinoma (CRC) is one of the most frequent cancers in western societies. The incidence is 700 per million people. About half of the patients develop metastases from the primary tumor and liver and lung are primary metastatic sites. The prognosis of the disease is poor and only 10% of patients with unresectable CRC survive beyond five years.

Prior to 1995 several Lts for CRC liver mets (CRLM) were performed. In ELTR 58 secondary liver tumors of CRC origin have been registered as the primary indication for Lt and reported 1- and 5-year survival was 62% and 18%, respectively. In 44% of these cases, graft loss was not related to tumor recurrence. Still, the outcome of these Lts was considered as poor and consequently, Lt for tumors of colorectal origin was abandoned.

Over the last 20 years the survival following Lt has improved by 20% - 30%. Thus, merely based on the previous data and current outcome of Lt, a 5 year survival of approximately 50% could be anticipated in patients transplanted for liver only CRC mets. Due to this argumentation and a fortunate donor situation in Norway we acquired an ethical approval (S-05409) for a clinical study to investigate Lt as for treatment in selected CRC patients with liver metastases (SECA1-study). Major inclusion criteria were: non-resectable liver mets, no extra hepatic disease or local relapse determined by PET/CT scan, CT- or MRI scan and colonoscopy. No
mets. on frozen section biopsies at time of surgery, ECOG 0-1, at least one line of chemotherapy for metastatic disease. The mTOR inhibitor Rapamune® was included in the standard immunosuppression from postoperative day 1. Thirteen men and 8 women with non-resectable CRLM received Lt in the period of Nov 2006 to March 2011. Median age was 56 years (range 45-65 years). Thirteen patients had colon cancer and 8 patients had rectal cancer. The T-stage of the primary tumor was T2,T3 and T4 in 2, 16 and 3 patients, respectively. N status of the primary tumor was pN0 - pN2. Nine patients had received 1.line chemotherapy and 12 patients had received 2. or 3.line therapy. The median number of liver mets was 8 (range 2-40) and the median size of the largest lesion was 4.5cm (range 2.8-13cm).

At follow up the patients had good, stable or increased Global Health Score and Physical Function after Lt. Kaplan-Meier estimate of survival at 1-, 3 and 5 year was 96%, 70% and 60%, respectively. Recurrent disease was common, only 7 patients (33%) had no evidence of disease and two of the patients were resected for lung metastases. Importantly, retrospective analyzes of CT scans obtained immediately prior to transplantation showed that 7 of the patients had lung metastases at the time of Lt. In these patients, the 5 year survival was above 80%, indicating that liver mets (and not lung mets) are the main cause of death in metastatic CRC patients. Further studies on Lt for CRLM have been initiated (SECA2 trial).

While long term survival after first Lt for ordinary diagnoses is very good, the 5-year survival after repeat Lt is 50% - 60% and for hepatitis C patients it is even less. In the study all patients had advanced metastatic CRC at the time of Lt, still the long term outcome is comparable to repeat Lt for other indications. These data could make it difficult to discriminate selected patients with CRC liver mets in liver allocation systems, especially when compared to patients listed for repeat Lt.

References

