

## Chapter 12

### **MALIGNANT LIVER TUMORS; LIVER TRANSPLANTATION AS A SURGICAL TREATMENT**

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#### **MALIGNANT LIVER TUMORS**

Malignant tumors in the liver can be classified as primary (cancers that originate in the liver) or metastatic (cancers that spread to the liver from an extrahepatic primary site). Primary cancers in the liver that originate from hepatocytes are known as hepatocellular carcinomas (HCCs or hepatomas), whereas cancers arising in the bile ducts are known as cholangiocarcinomas.

#### **HEPATOCELLULAR CARCINOMA AND LIVER TRANSPLANTATION**

The treatment of HCC is complex and is best managed by a multidisciplinary liver transplant team. A complete algorithm for the evaluation and management of HCC is shown (Figure). For patients without cirrhosis who develop HCC, resection is the treatment of choice. For patients with Child's class A cirrhosis with preserved liver function and no portal hypertension, resection also is considered. If resection is not possible because of poor liver function and the HCC meets transplant criteria, liver transplantation is the treatment of choice (Schwartz M, Roayaie S, Uva P 2007), (Zarrinpar A, Kaldas F, Busuttil RW 2011).

The Barcelona-Clinic Liver Cancer Group has refined its HCC management strategy and has developed the American Association for the Study of Liver Diseases Practice Guidelines (Bruix J, Sherman M, 2011), management guidelines vary slightly in Asia, Europe, the United States, and other countries based in part on availability of organ donors for liver transplantation. Living donor liver transplantation also is an alternative for patients with HCC awaiting transplantation to avoid dropout as a candidate for cadaveric donor liver transplantation due to tumor progression (Zarrinpar A, Kaldas F, Busuttil RW 2011). The rationale supporting Orthotopic liver transplantation (OLT) for HCC includes the fact that most HCCs (>80%) arise in the setting of cirrhosis (Marsh JW et al. 2004),

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ter neoadjuvant therapy. Transplantation may prolong survival by delaying death from tumor replacement of the liver for NEC. Even more controversial is the role of LT in the treatment of metastatic colorectal cancer. Liver transplantation achieves results comparable to resection for patients with HEHE. The long-term survival rate after transplant for hepatoblastoma is, a quite promising.

Additional experience is necessary to confirm reports that transplantation is beneficial for patients with limited extrahepatic disease.

## REFERENCES

- Alessiani M, et al: Assessment of ve-year experience with abdominal organ cluster transplantation, *J Am Coll Surg* 180:1–9, 1995.
- Brandsaeter B, et al: Liver transplantation for primary sclerosing cholangitis; predictors and consequences of hepatobiliary malignancy, *J Hepatol* 40:815–822, 2004.
- Bruix J, Sherman M, American Association for the Study of Liver Disease. Management of hepatocellular carcinoma: an update. *Hepatology*. 2011;53(3):1020.
- Castaldo ET, Pinson CW. Liver transplantation for non-hepatocellular carcinoma malignancy. *HPB (Oxford)*. 2007;9(2):98-103.
- Chapman WC, Majella Doyle MB, Stuart JE, et al. Outcomes of neoadjuvant transarterial chemoembolization to downstage hepatocellular carcinoma before liver transplantation. *Ann Surg*. 2008;248(4):617.
- Chapman WC. Liver transplantation for unresectable metastases to the liver: a new era in transplantation or a time for caution? *Ann Surg*. 2013;257(5):816-817.
- Cholongitas E, et al: Mammalian target of rapamycin inhibitors are associated with lower rates of hepatocellular carcinoma recurrence after liver transplantation: a systematic review, *Transpl Int* 27(10):1039–1049, 2014.
- De Villa V, Lo CM. Liver transplantation for hepatocellular carcinoma in Asia. *Oncologist*. 2007;12(11):1321.
- Duffy JP, Vardanian A, Benjamin E, et al. Liver transplantation criteria for hepatocellular carcinoma should be expanded: a 22-year experience with 467 patients at UCLA. *Ann Surg*. 2007;246(3):502.
- Fan ST, et al: Liver transplantation for neuroendocrine tumour liver metastases, *HPB (Oxford)* 17:23–28, 2015.
- Foss A, Adam R, Dueland S. Liver transplantation for colorectal liver metastases: revisiting the concept. *Transpl Int*. 2010;23(7):679- 685.
- Frilling A, et al: Recommendations for management of patients with neuroendocrine liver metastases, *Lancet Oncol* 15:e8–e21, 2014.
- Garrett Richard Roll, John Paul Roberts (2016). Liver transplantation for hepatocellular carcinoma. In William R. Jarnagin. (2016), *Blumgart’s Surgery of the Liver, Biliary Tract, and Pancreas* (6th ed., Chapter 115A, pp. 1781-1790, 1790 e1-e4).
- Geller DA, Tsung A, Marsh JW, Dvorchik I, Gamblin TC, Carr BI. Outcome of 1000 liver cancer patients evaluated at the UPMC Liver Cancer Center. *J Gastrointest Surg*. 2006;10(1):63.
- Ghali P, et al: Liver transplantation for incidental cholangiocarcinoma: analysis of the Canadian experience, *Liver Transpl* 11:1412–1416, 2005.
- Groeschl RT, Turaga KK, Gamblin TC. Transplantation versus resection for patients with combined hepatocellular carcinoma- cholangiocarcinoma. *J Surg Oncol*. 2013;107(6):608-612.

- Grotz TE, et al: Hepatic epithelioid hemangioendothelioma: is trans-plant the only treatment option? *HPB (Oxford)* 12:546–553, 2010.
- Gu J, Bai J, Shi X, et al. Efficacy and safety of liver transplantation in patients with cholangiocarcinoma: a systematic review and meta-analysis. *Int J Cancer*. 2012;130(9):2155-2163.
- Haberal M, Akdur A, Moray G, Arslan G, Özçay F, Selçuk H, Özdemir H. Expanded Criteria for Hepatocellular Carcinoma in Liver Transplant. *Exp Clin Transplant*. 2017 Mar;15(Suppl 2):55-58.
- Hackl C, Gerken M, Loss M, Klinkhammer-Schalke M, Piso P, Schlitt HJ. A population-based analysis on the rate and surgical management of colorectal liver metastases in Southern Germany. *Int J Colorectal Dis*. 2011;26(11):1475-1481.
- Hackl C, Schlitt HJ, Kirchner GI, Knoppke B, Loss M. Liver transplantation for malignancy: current treatment strategies and future perspectives. *World J Gastroenterol*. 2014;20(18):5331-5344.
- Hagness M, Foss A, Line PD, et al. Liver transplantation for nonresectable liver metastases from colorectal cancer. *Ann Surg*. 2013;257(5):800-806.
- Hayashi PH, et al: Impact of pretransplant diagnosis of hepatocellular carcinoma on cadaveric liver allocation in the era of MELD, *Liver Transpl* 10(1):42–48, 2004b.
- Hertl M, Cosimi AB. Liver transplantation for malignancy. *Oncologist*. 2005;10(4):269-281.
- Hibi T, Itano O, Shinoda M, Kitagawa Y. Liver transplantation for hepatobiliary malignancies: a new era of “Transplant Oncology” has begun. *Surg Today*. April 29, 2016.
- Hoshida Y, et al: Gene expression in xenograft tissues and outcome in hepatocellular carcinoma, *N Engl J Med* 359(19):1995–2004, 2008.
- International Agency for Research on Cancer. GLOBOCAN 2008. Available at: <http://globocan.iarc.fr/>. Accessed June 7, 2013.
- Jonas S, et al: Vascular invasion and histopathologic grading determine outcome after liver transplantation for hepatocellular carcinoma in cirrhosis, *Hepatology* 33(5):1080–1086, 2001.
- Justin M. Burns, Charles B. Rosen, Julie K. Heimbach, and Gregory J. Gores (2016). Liver transplantation for nonhepatocellular malignant disease In William R. Jarnagin. (2016), Blumgart’s Surgery of the Liver, Biliary Tract, and Pancreas (6th ed., Chapter 115B, pp. 1791-1800).
- Kayaalp C, Ince V, Ersan V, Karakas S, Kahraman AS, Yilmaz S. Liver Transplantation for Hepatocellular Carcinoma at Inonu University. *J Gastrointest Cancer*. 2017 Jul 3.
- Le Treut YP, et al: Liver transplantation for neuroendocrine tumors in Europe—results and trends in patient selection, *Ann Surg* 257:807–815, 2013.
- Llovet JM, et al: Intention-to-treat analysis of surgical treatment for early hepatocellular carcinoma: resection versus transplantation, *Hepatology* 30(6):1434–1440, 1999.
- Llovet JM, et al: Liver transplantation for small hepatocellular carcinoma: the tumor-node-metastasis classification does not have prognostic power, *Hepatology* 27(6):1572–1577, 1998.
- Makhlouf HR, Ishak KG, Goodman ZD. Epithelioid hemangio-endothelioma of the liver: a clinicopathologic study of 137 cases. *Cancer*. 1999;85(3):562-582.
- Marsh JW, Geller DA, Finkelstein SD, Donaldson JB, Dvorchik I. Role of liver transplantation for hepatobiliary malignant disorders. *Lancet Oncol*. 2004;5(8):480.
- Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med*. 1996;334(11):693.

- Mehrabi A, Kashfi A, Fonouni H, et al. Primary malignant hepatic epithelioid hemangioendothelioma: a comprehensive review of the literature with emphasis on the surgical therapy. *Cancer*. 2006;107(9):2108-2121.
- Meyer CG, et al: Liver transplantation for cholangiocarcinoma: results in 207 patients, *Transplantation* 69:1633–1637, 2000.
- Na GH, Kim EY, Hong TH, You YK, Kim DG. Effects of loco regional treatments before living donor liver transplantation on overall survival and recurrence-free survival in South Korean patients with hepatocellular carcinoma. *HPB (Oxford)*. 2016 Jan;18(1):98-106.
- Neuhaus P, et al: Extended resections for hilar cholangiocarcinoma, *Ann Surg* 230:808–818, discussion 819, 1999.
- Organ Procurement and Transplantation Network. Available at: <http://www.optn.org>. Accessed June 4, 2013.
- Otto G, et al: Response to transarterial chemoembolization as a biological selection criterion for liver transplantation in hepatocellular carcinoma, *Liver Transpl* 12(8):1260–1267, 2006.
- Rana A, Hong JC. Orthotopic liver transplantation in combination with neoadjuvant therapy: a new paradigm in the treatment of unresectable intrahepatic cholangiocarcinoma. *Curr Opin Gastroenterol*. 2012;28(3):258-265.
- Robles R, et al: Spanish experience in liver transplantation for hilar and peripheral cholangiocarcinoma, *Ann Surg* 239:265–271, 2004.
- Rodriguez JA, Becker NS, O'Mahony CA, Goss JA, Aloia TA. Long-term outcomes following liver transplantation for hepatic hemangioendothelioma: the UNOS experience from 1987 to 2005. *J Gastrointest Surg*. 2008;12(1):110-116.
- Rodriguez-Peralvarez M, et al: Reduced exposure to calcineurin inhibitors early after transplantation prevents recurrence of hepatocellular carcinoma, *J Hepatol* 59(6):1193–1199, 2013.
- Sala MJ, et al: High pathological risk of recurrence after surgical resection for hepatocellular carcinoma: an indication for salvage liver transplantation, *Liver Transpl* 10(10):1294–1300, 2004.
- Schwartz M, Roayaie S, Konstadoulakis M. Strategies for the management of hepatocellular carcinoma. *Nat Clin Pract Oncol*. 2007;4(7):424.
- Schwartz M, Roayaie S, Uva P. Treatment of HCC in patients awaiting liver transplantation. *Am J Transplant*. 2007;7(8):1875.
- Van Vilsteren FG, et al: Liver transplantation for gastroenteropancreatic neuroendocrine cancers: defining selection criteria to improve survival, *Liver Transpl* 12:448–456, 2006.
- Volk ML, et al: A novel model measuring the harm of transplanting hepatocellular carcinoma exceeding Milan criteria, *Am J Transplant* 8(4):839–846, 2008.
- Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. *Cancer*. 1982;50(5):970-981.
- Wiesner RH, Freeman RB, Mulligan DC. Liver transplantation for hepatocellular cancer: the impact of the MELD allocation policy. *Gastroenterology*. 2004;127(5 Suppl 1):S261.
- Yao FY, et al: Excellent outcome following down-staging of hepatocellular carcinoma prior to liver transplantation: an intention-to-treat analysis, *Hepatology* 48(3):819–827, 2008.
- Zarrinpar A, Kaldas F, Busuttil RW. Liver transplantation for hepatocellular carcinoma: an update. *Hepatobiliary Pancreat Dis Int*. 2011;10(3):234.