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Medical Policy Manual

Topic: Liver Transplant

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Recipients

Liver transplantation is now routinely performed as a treatment of last resort for patients with end-stage liver disease. Liver transplantation may be performed with liver donation after brain, circulatory or cardiac death or with a liver segment donation from a living donor. Patients are prioritized for transplant according to length of time on the waiting list, mortality risk and severity of illness criteria developed by the Organ Procurement and Transplantation Network (OPTN) and the United Network of Organ Sharing (UNOS).

In June 2013, OPTN and UNOS published its most recent allocation system.[1] Status 1A patients have acute liver failure with a life expectancy of less than 7 days without a liver transplant. Status 1A patients also include primary graft non-function, hepatic artery thrombosis and acute Wilson's disease. Status 1A patients must be recertified as Status 1A every 7 days. Status 1B patients are defined as pediatric patients, (ages 0-17 years) with chronic liver disease listed as: fulminant liver failure, primary non function, hepatic artery thrombosis, acute decompensated Wilson's disease, chronic liver disease; and non-metastatic hepatoblastoma. Pediatric patients move to Status 1A upon age18 but still qualify for pediatric indications.

Following Status 1, donor livers will be prioritized to those with the highest scores on MELD (model for end-stage liver disease) or PELD (pediatric end-stage liver disease). MELD and PELD are a continuous

disease severity scale based entirely on objective laboratory values. These scales have been found to be highly predictive of the risk of dying from liver disease for patients waiting on the transplant list. The MELD score incorporates bilirubin, prothrombin time (i.e., INR) and creatinine into an equation, producing a number that ranges from 6 to 40. The PELD score incorporates albumin, bilirubin, INR growth failure, and age at listing. Aside from Status 1, donor livers are prioritized to those with the highest MELD or PELD number; waiting time is only used to break ties among patients with the same MELD or PELD score and blood type compatibility. In the previous system, waiting time was often a key determinant of liver allocation, and yet waiting time was found to be a poor predictor of the urgency of liver transplant, since some patients were listed early in the course of their disease, while others were listed only when they became sicker. In the revised allocation system, patients with a higher mortality risk and higher MELD/PELD scores will always be considered before those with lower scores, even if some patients with lower scores have waited longer.[2] Status 7 describes patients who are temporarily inactive on the transplant waiting list due to being temporarily unsuitable for transplantation.

Donors

Due to the scarcity of donor livers, a variety of strategies have been developed to expand the donor pool. For example, split grafts refers to dividing a donor liver into two segments that can be used for two recipients. Living donor transplantation (LDLT) is now commonly performed for adults and children from a related or unrelated donor. Depending on the graft size needed for the recipient, either the right lobe, left lobe or the left lateral segment can be used for LDLT. In addition to addressing the problem of donor organ scarcity, LDLT allows the procedure to be scheduled electively, shortens the preservation time for the donor liver, decreases disease transmission and allows time to optimize the recipient's condition pretransplant.

MEDICAL POLICY CRITERIA

I. A liver transplant, using a cadaver or living donor, may be **medically necessary** for patients with irreversible, end-stage liver failure due to conditions that include, but are not limited to, the following:

   A. Cholestatic Liver Diseases

      1. Biliary atresia
      2. Familial cholestatic syndromes
      3. Primary biliary cirrhosis
      4. Secondary biliary cirrhosis
      5. Primary sclerosing cholangitis
      6. Secondary sclerosing cholangitis when the primary etiology is resolved
      7. Alagille syndrome
      8. Nonsyndromic paucity of the intrahepatic bile ducts
      9. Cystic fibrosis

B. Hepatocellular disease

1. Alcoholic cirrhosis
2. Viral hepatitis (including A,B, C, or non-A, non-B)
3. Autoimmune hepatitis
4. Cryptogenic cirrhosis
5. Alpha-1 antitrypsin deficiency
6. Hemochromatosis
7. Protoporphyria
8. Wilson's disease
9. Non-alcoholic steatohepatitis

C. Malignancies such as the following:

1. Primary hepatocellular carcinoma confined to the liver
2. Rare, non-hepatocellular malignancies originating in the liver such as hemangioepitheliomas in young adults and hepatoblastomas in children, and hemangioendotheliomas
3. Fibrolamellar hepatocellular carcinoma
4. Unresectable hilar cholangiocarcinoma

D. Vascular disease

1. Budd-Chiari syndrome (congenital hepatic vein thrombosis)
2. Veno-occlusive disease

E. Inborn errors of metabolism

F. Trauma and toxic reactions

G. Miscellaneous

1. Polycystic disease of the liver in patients who have massive hepatomegaly causing obstruction or functional impairment.
2. Familial amyloid polyneuropathy (Corino de Andrade's disease, paramyloidosis)
3. Amyloidosis
4. Disorders of branch chain amino acids (e.g., Maple syrup urine disease (MSUD), branched chain a-ketoacid dehydrogenase (BCKD)

5. Fulminant hepatitic failure
6. Glycogen storage disease type IV
7. Hyperoxaluria
8. Steatohepatitis
9. Tyrosinemia
10. Urea cycle defects

II. Liver transplantation is considered **not medically necessary** in the following patients:

A. Patients with hepatocellular carcinoma that has extended beyond the liver.

B. Patients with active alcohol and/or substance abuse. (Evidence for abstinence may vary among liver transplant programs, but generally a minimum of three months is required.)

III Liver transplantation is considered **investigational** in the following patients:

A. Intrahepatic cholangiocarcinoma

B. Patients with an extrahepatic malignancy, other than those noted above

C. Patients with neuroendocrine tumors metastatic to the liver

IV. Liver retransplantation may be considered **medically necessary** in patients with one or more of the following diagnoses:

A. Primary graft non-function

B. Hepatic artery thrombosis

C. Chronic rejection

D. Ischemic type biliary lesions after donation after cardiac death

E. Recurrent non-neoplastic disease causing late graft failure

SCIENTIFIC EVIDENCE

Relevant outcomes for studies on liver transplantation include waiting time duration, dropout rates, survival time, and recurrence. As experience with liver transplantation has matured, patient selection criteria have broadened to include a wide variety of etiologies. The most controversial etiologies include viral hepatitis and primary hepatocellular cancer. In particular, the presence of hepatitis B virus (HBV) and hepatitis C virus (HCV) has been a controversial indication for liver transplantation because of the high potential for recurrence of the virus and subsequent recurrence of liver disease. However, registry data indicate a long-term survival rate (7 years) of 47% in HBV+ transplant recipients, which is lower than that seen in other primary liver diseases such as primary biliary cirrhosis (71%) or alcoholic liver disease (57%).[2] Recurrence of HCV infection in transplant recipients has been nearly universal and 10-

20% of patients will develop cirrhosis within 5 years.[3] Although these statistics raise questions about the most appropriate use of a scarce resource (donor livers), the long-term survival rates are significant in a group of patients who have no other treatment options. In the past, the long-term outcomes in patients with primary hepatocellular malignancies (19%) were poor compared to the overall survival of liver transplant recipients. However, recent use of standardized patient selection criteria, such as the Milan criteria (a solitary tumor with a maximum tumor diameter of 5 cm or less, or up to 3 tumors 3 cm or smaller and without extrahepatic spread or macrovascular invasion), has dramatically improved overall survival rates. In a systematic review of liver transplant for hepatocellular carcinoma (HCC) in 2012, Maggs et al. found 5-year overall survival rates ranged from 65-94.7% in reported studies.[4] Nevertheless, transplant represents the only curative approach for many of these patients who present with unresectable organ-confined disease and expansion of patient selection criteria, bridging to transplant or down-staging of disease to qualify for liver transplantation is frequently being studied. Liver transplant cannot be considered curative in patients with locally extensive or metastatic liver cancer, or in patients with isolated liver metastases with extrahepatic primaries.[2]

Living Donor Liver Transplantation: Donor Outcomes

Due to the scarcity of donor organs and the success of living donation living-donor liver transplantation has become accepted practice. The living donor undergoes hepatectomy of the right lobe, left lobe, or left lateral segment, which is then transplanted into the recipient. Since right hepatectomy involves the resection of 60%-70% of the total volume of the donor liver, the safety of the donor has been the major concern. For example, the surgical literature suggests that right hepatectomy of diseased or injured livers is associated with mortality rates of about 5%. However, initial reports suggest that right hepatectomy in healthy donors has a lower morbidity and mortality. The Medical College of Virginia appears to have the most extensive experience and has reported the results of their first 40 adult-to-adult living donor liver transplantations, performed between June 1998 and October 1999.[5] There were an equal number of related and unrelated donors. Minor complications occurred in 7 donors. The outcomes among recipients were similar to those associated with cadaveric donor livers performed during the same period of time. However, in the initial series of 20 patients, 4 of 5 deaths occurred in recipients who were classified as 2A. In the subsequent 20 patients, recipients classified as 2A were not considered candidates for living donor transplant. Other case series have reported similar success rates.[6-8]

In 2003, Brown and colleagues reported on the results of a survey focusing on adult living-related recipients in the United States.[9] The following statistics were reported:

- The survey encompassed 449 adult-to-adult transplantations
- Half of the responding programs already had performed at least 1 adult-to-adult living donor liver transplantation, and 32 of the remaining 41 centers were planning to initiate such surgery
- 14 centers had performed more than 10 such transplantations, and these centers accounted for 80% of these transplants
- A total of 45% of those evaluated for living donation subsequently donated a liver lobe; 99% were genetically or emotionally related to the recipient
- Complications in the donor were more frequent in the centers that performed the fewest living-related donor transplantations

- There was 1 death among the donors, but complications were relatively common, i.e., biliary complications in 6% and reoperation in 4.5%

Reports of several donor deaths re-emphasize the importance of careful patient selection based in part on a comprehensive consent process and an experienced surgical team.[10-12] In December 2000, the National Institutes of Health convened a workshop on living donor liver transplantation. A summary of this workshop was published in 2002.[13] According to this document, the risk of mortality to the donor undergoing right hepatectomy was estimated to be approximately 0.2%-0.5%. Based on survey results, the workshop reported that donor morbidity was common: 7% required re-exploration, 10% had to be re-hospitalized, and biliary tract complications occurred in 7%. The median complication rate reported by responding transplant centers was 21%. The summary report concluded that the incidence and type of complications encountered and mortality associated with living donor liver transplant in both donors and recipients needs to be determined and compared with that for patients undergoing cadaveric transplantation.

Due to the potential morbidity and mortality experienced by the donor, the workshop also noted that donor consent for hepatectomy must be voluntary and free of coercion; therefore, it was preferable that the donor have a significant long-term and established relationship with the recipient. According to the workshop summary, "At the present time, nearly all centers strive to identify donors who are entirely healthy and at minimal risk during right hepatectomy. As a result, only approximately one third of persons originally interested in becoming a living liver donor complete the evaluation process and are accepted as candidates for this procedure."

Criteria for a recipient of a living-related liver are also controversial, with some groups advocating that living-related donor livers be used only in those most critically ill, while others state that the risk to the donor is unacceptable in critically ill recipients due to the increased risk of postoperative mortality of the recipient. According to this line of thought, living-related livers are best used in stable recipients who have a higher likelihood of achieving long-term survival.[13]

In 2000 the American Society of Transplant Surgeons issued the following statement:[14]

"Living donor transplantation in children has proven to be safe and effective for both donors and recipients and has helped to make death on the waiting list a less common event. Since its introduction in 1990, many of the technical and ethical issues have been addressed and the procedure is generally applied.

The development of left or right hepatectomy for adult-to-adult living donor liver transplantation has been slower. Because of the ongoing shortage of cadaver livers suitable for transplantation, adult-to-adult living donor liver transplantation has been undertaken at a number of centers. While early results appear encouraging, sufficient data is not available to ascertain donor morbidity and mortality rates. There is general consensus that the health and safety of the donor is and must remain central to living organ donation."

Living Donor versus Deceased Donor Liver Transplant: Recipient Outcomes

Few high quality studies are available regarding recipient outcomes based upon direct comparison of living vs. deceased donor. In 2013, Grant et al. reported on a systematic review and meta-analysis of 16 studies to compare recipient outcomes between living donor liver transplants and deceased donor liver transplants for HCC.[15] For disease-free survival after living donor liver transplantation, the combined

hazard ratio (HR) was 1.59 (95% confidence interval [CI]: 1.02-2.49) compared to deceased donor liver transplantation. For overall survival, the combined HR was 0.97 (95% CI: 0.73-1.27). The studies included in the review were mostly retrospective and considered to be of low quality. Further study is needed to determine any differences between living and deceased liver transplantation outcomes for various etiologies.

Malignancies

The following two issues were the focus of the literature review regarding liver transplant for malignancy: 1) whether selection criteria for hepatocellular carcinoma should be expanded and 2) whether extrahepatic cholangiocarcinoma should be considered an acceptable indication for liver transplantation.

Hepatocellular Carcinoma

Selection Criteria for Hepatocellular Carcinoma

On the first issue, patient selection criteria for liver transplantation for hepatocellular carcinoma (HCC) have focused mainly on the number and size of tumors. An editorial by Llovett noted that the Milan criteria are considered the gold standard. The Milan criteria specify that patients may either have a solitary tumor with a maximum tumor diameter of 5 cm or less, or up to three tumors 3 cm or smaller.[16] Patients with extrahepatic spread or macrovascular invasion have a poor prognosis. UNOS adopted the Milan criteria, combined with one additional criteria (no evidence of extrahepatic spread or macrovascular invasion), as its liver transplantation criteria. A 2001 paper from the University of California, San Francisco (UCSF), proposed expanded criteria to include patients with a single tumor up to 6.5 cm in diameter, 3 or fewer tumors with maximum size 4.5 cm and a total tumor size of ≤ 8 cm or less.[17] It should be noted that either set of criteria can be applied preoperatively with imaging or with pathology of the explanted liver at the time of intended transplant. Preoperative staging often underestimates what is seen on surgical pathology. To apply pathologic criteria a backup candidate must be available in case preoperative staging is inaccurate. Given donor organ scarcity, any expansion of liver transplant selection criteria has the potential to prolong waiting times for all candidates. Important outcomes in assessing expanded criteria include waiting time duration, death or deselection due to disease progression while waiting (dropout), survival time, and time to recurrence or related outcomes such as disease-free survival. Survival time can be estimated beginning when the patient is placed on the waiting list using the intention-to-treat principal or at the time of transplantation. Llovet stated that 1-year dropout rates for patients meeting Milan criteria are 15%–30% and 5-year survival rates not reported by intention-to-treat should be adjusted down by 10%–15%.

A limited body of evidence is available for outcomes among patients exceeding Milan criteria but meeting UCSF criteria (see table below). The largest series was conducted in 14 centers in France including an intention-to-treat total of 44 patients based on preoperative imaging at the time of listing, and a subset of 39 patients meeting pathologic UCSF criteria.[18] The median waiting time was 4.5 months, shorter than the typical 6–12 months in North America. Dropouts composed 11.4%. The post-transplant overall patient 5-year survival of 63.6% was more favorable than the intention-to-treat probability of 45.5% but less favorable than among larger numbers of patients meeting Milan criteria. Similar findings were seen for disease-free survival and cumulative incidence of recurrence. Three centers in Massachusetts included ten patients beyond pathologic Milan criteria but within UCSF criteria.[19] Two-year survival post-transplant was 77.1%, with two patients dying and eight alive after a median of 32 months. A group of 74 patients meeting preoperative Milan criteria had a 2-year survival

probability of about 73%, but it is inadvisable to compare different preoperative and pathologic staging criteria.

From the series of patients from which the expanded UCSF criteria was developed, 14 satisfied those criteria on pathology but exceeded the Milan criteria.[20] UCSF investigators did not provide survival duration data for this subgroup but noted that two patients died. Although the French series suggested that outcomes among patients exceeding Milan criteria and meeting UCSF criteria are worse than for patients meeting Milan criteria, it is unclear if the latter group still achieves acceptable results. A benchmark of 50% 5-year survival has been established in the liver transplant community. The French study met this by post-transplant pathologic staging results (63.6%) and fell short by preoperative intention-to-treat results (45.5%). United States centers have published data for only 24 patients exceeding Milan criteria and meeting UCSF criteria; survival and recurrence data are very sparse. Overall, the evidence base is insufficient to permit conclusions about health outcomes after liver transplantation among patients exceeding Milan criteria and meeting expanded UCSF criteria.

In their 2008 review, Schwartz and colleagues argue that selection based exclusively on the Milan criteria risks prognostic inaccuracy due to the diagnostic limitations of imaging procedures and the surrogate nature of size and number of tumors.[21] They predict that evolution of allocation policy will involve the following:

1. The development of a reliable prognostic staging system to help with allocation of therapeutic alternatives;
2. New molecular markers that might improve prognostic accuracy;
3. Aggressive multimodality neoadjuvant therapy to downstage and limit tumor progression before transplant and possibly provide information about tumor biology based on response to therapy; and,
4. Prioritization for transplantation should consider response to neoadjuvant therapy, time on waiting list, suitability of alternative donor sources.

Two papers describe work on identifying predictors of survival and recurrence of disease. Ioannou and colleagues analyzed UNOS data pre- and post-adoption of the MELD allocation system finding a 6-fold increase in recipients with hepatocellular carcinoma and that survival in the MELD era was similar to survival to patients without hepatocellular carcinoma (HCC).[22] The subgroup of patients with larger (3-5 cm) tumors, serum alpha-fetoprotein level equal to or greater than 455 mg/mL, or a MELD score equal to or greater than 20, however, had poor transplantation survival. A predicting cancer recurrence scoring system was developed by Chan et al. based on a retrospective review and analysis of liver transplants at 2 centers to determine factors associated with recurrence of hepatocellular carcinoma.[23] Of 116 patients with findings of hepatocellular carcinoma in their explanted livers, 12 developed recurrent hepatocellular carcinoma. Four independent significant explant factors were identified by stepwise logistic regression: size of 1 tumor greater than 4.5 cm, macroinvasion, and bilobar tumor were positive predictors of recurrence, and the presence of only well-differentiated HCC was a negative predictor. Points were assigned to each factor in relation to its odds ratio. The accuracy of the method was confirmed in 2 validation cohorts.

In 2010, Guiteau and colleagues reported on 445 patients transplanted for HCC in a multicenter, prospective study in UNOS Region 4.[24] On preoperative imaging, 363 patients met Milan criteria, and 82 patients were under expanded Milan criteria consisting of 1 lesion less than 6 cm, equal to or less than 3 lesions, none greater than 5 cm and total diameter less than 9 cm. Patient, allograft and recurrence-free survival at 3 years did not differ significantly between patients meeting Milan criteria

versus patients under the expanded criteria (72.9% and 77.1%, 71% and 70.2% and 90.5% and 86.9%, respectively). While preliminary results showed similar outcomes when using expanded Milan criteria, the authors noted their results were influenced by waiting times in Region 4 and that similar outcomes may be different in other regions with different waiting times. Additionally, the authors noted that an HCC consensus conference report on liver allocation in HCC patients does not recommend expanding Milan criteria nationally and encourages regional agreement.[25] The report addressed the need to better characterize the long-term outcomes of liver transplantation for patients with HCC and to assess whether it is justified to continue the policy of assigning increased priority for candidates with early stage HCC on the transplant waiting list in the U.S. Overall, the evidence base is insufficient to permit conclusions about health outcomes after liver transplantation among patients exceeding Milan criteria and meeting expanded UCSF or other criteria.

Outcomes Among Patients with Hepatocellular Carcinoma Exceeding Milan Selection Criteria and Meeting UCSF Criteria

Study	Outcome	Group	Probability (%)			
			n	1yr	2yr	5yr
Decaens et al., 2006[18] 14 centers in France, Meeting Milan criteria (Milan+). Exceeding Milan criteria, meeting UCSF criteria (Milan-/UCSF+)	Intention-to-treat, preoperative					
	Overall patient survival	Milan+	279			60.1
		Milan-/UCSF+	44			45.5
	Cumulative incidence of recurrence	Milan+				20.2
		Milan-/UCSF+				27.1
	Disease-free survival	Milan+				60.4
		Milan-/UCSF+				47.8
	Post-transplant, pathologic (p)					
	Overall patient survival	pMilan+	184			70.4
		pMilan-/pUCSF+	39			63.6
	Cumulative incidence of recurrence	pMilan+				9.4
		pMilan-/pUCSF+				16.5
	Disease-free survival	pMilan+				7.02
		pMilan-/pUCSF+				62.7
	Milan-/UCSF+ median waiting time 4.5 mo (0.1-20.4); 5/44 dropouts (11.4%)					
Leung et al., 2004[19] 3 centers in Massachusetts, Meeting preoperative Milan criteria (Milan+)	Post-transplant overall patient survival	Milan+	74	85.9	~73	50.9
		pMilan-/pUCSF+	10		77.1	
	2 patients died at 3 and 22 months, 8 patients alive after median 32 mo follow-up (6.6-73.5)					
Yao et al., 2002[20] University of California, San Francisco	Post-transplant overall patient survival	pMilan+	46	91	81	72
	pMilan-/pUCSF+, n=14, 2 patients died, 8 alive but no information on survival duration, 1 patient retransplanted 5 mo after initial transplant					
Sotiropoulos et al., 2006[26]	Milan-/UCSF+, n=4, 1 patient died at 20 mo, 3 patients alive at median					

Essen, Germany. Unclear if criteria preoperative or pathologic.	follow-up 57 mo.

Liver Transplantation versus Liver Resection for Hepatocellular Carcinoma

Liver transplantation is the gold standard treatment for HCC meeting Milan criteria in decompensated livers such as Child-Pugh class B or C (moderate to severe cirrhosis). Liver resection is generally used for early HCC in livers classified as Child-Pugh class A.[27] Additionally, current UNOS criteria indicate a liver transplant candidate must not be eligible for resection. [1] However, the best treatment approach for early HCC in well-compensated livers is controversial.

In 2013, Zheng et al. reported on a meta-analysis of 62 cohort studies (n=10,170 total patients) comparing liver transplantation to liver resection for HCC.[28] Overall 1-year survival was similar between procedures (OR 1.08; 95% CI, 0.81 - 1.43; p=0.61). However, overall 3- and 5-year survival significantly favored liver transplantation over resection (odds ratio 1.47; 95% CI, 1.18 - 1.84; p<0.001, and odds ratio 1.77; 95% CI, 1.45 - 2.16; p<0.001, respectively). Disease-free survival in liver transplant patients was 13%, 29%, and 39% higher than liver resection patients at 1-, 3-, and 5-years, respectively (p<0.001). Recurrence rates were also 30% lower in liver transplantation than resection (OR 0.20; CI, 0.15 - 0.28; p<0.001). While liver transplantation outcomes appear favorable compared to liver resection, a shortage of donor organs may necessitate liver resection as an alternative to liver transplantation.

Salvage Liver Transplantation after Liver Resection for Hepatocellular Carcinoma

In patients who have a recurrence of HCC after primary liver resection, salvage liver transplantation has been considered a treatment alternative to repeat hepatic resection, chemotherapy or other local therapies such as radiofrequency ablation, transarterial chemoembolization percutaneous ethanol ablation or cryoablation. Several systematic reviews have evaluated the evidence on outcomes of salvage transplant compared to primary transplant.

A 2013 meta-analysis of 14 non-randomized comparative studies by Zhu et al, (n=1272 for primary transplant and n=236 for salvage).[29] Overall survival at 1-, 3- and 5-years and disease-free survival at 1- and 3-years was not significantly different between groups. Disease-free survival, however, was significantly lower at 5-years in salvage liver transplantation compared to primary transplantation (OR 0.62; 95% CI 0.42-0.92; p=0.02). There was insufficient data to evaluate outcomes in patients exceeding Milan criteria but in patients meeting Milan criteria, survival outcomes were not significantly different suggesting salvage liver transplantation may be a viable option in these patients.

In a 2012 meta-analysis, Li and colleagues compared primary liver transplantation to salvage liver transplantation (liver transplantation after liver resection) for HCC.[30] Included in the meta-analysis were 11 case-controlled or cohort studies totaling 872 primary liver transplants and 141 salvage liver transplants. Survival rates of patients who exceeded the Milan criteria at 1, 3 and 5 years were not significantly different between the 2 groups (1-year odds ratio [OR]: 0.26, 95% CI: 0.01-4.94, p=0.37; 3-year OR: 0.41, 95% CI: 0.01-24.54, p=0.67; and 5-year OR: 0.55, 95% CI: 0.07-4.48, p=0.57).

In 2013, Chan et al. systematically reviewed 16 non-randomized studies (n=319) on salvage liver transplantation after primary hepatic resection for HCC[31] The authors found overall and disease-free survival outcomes with salvage liver transplantation were similar to reported primary liver

transplantation outcomes. The median overall survival for salvage liver transplantation patients was 89%, 80% and 62% at 1-, 3- and 5-years, respectively. Disease-free survival was 86%, 68% and 67% at 1-, 3- and 5-years, respectively. Salvage liver transplantation studies had median overall survival rates of 62% (range 41- 89%) compared to a range of 61-80% in the literature for primary liver transplantation. Median disease-free survival rates for salvage liver transplantation were 67% (range 29-100%) compared to a range of 58-89% for primary liver transplantation. Given a limited donor pool and increased surgical difficulty with salvage liver transplantation, further studies are needed. UNOS criteria indicate liver transplant candidates with HCC who subsequently undergo tumor resection must be prospectively reviewed by a regional review board for the extension application.

Cholangiocarcinoma

Reports on liver transplantation for cholangiocarcinoma or bile duct carcinoma generally distinguish between intrahepatic and extrahepatic tumors, the latter including hilar or perihilar tumors. Recent efforts have focused on pretransplant downstaging of disease with neoadjuvant radiochemotherapy. Relevant outcomes included waiting time duration; dropout rates, survival time, and recurrence.

In 2012, Gu and colleagues reported on a systematic review and meta-analysis of 14 clinical trials on liver transplantation for cholangiocarcinoma.[32] Overall 1-, 3- and 5-year pooled survival rates from 605 study patients were 0.73 (95% CI: 0.65-0.80), 0.42 (95% CI: 0.33-0.51), and 0.39 (95% CI: 0.28-0.51), respectively. When patients received adjuvant therapies preoperatively, 1-, 3- and 5-year pooled survival rates improved and were 0.83 (95% CI: 0.57-0.98), 0.57 (95% CI: 0.18-0.92), and 0.65 (95% CI: 0.40-0.87), respectively.

In 2012, Darwish Murad et al. reported on 287 patients from 12 transplant centers treated with neoadjuvant therapy for perihilar cholangiocarcinoma followed by liver transplantation.[33] Intent-to-treat survival (after a loss of 71 patients before liver transplantation) was 68% at 2 years and 53% at 5 years, and recurrence-free survival rates post-transplant were 78% at 2 years and 65% at 5 years. Survival time was significantly shorter for patients who had a previous malignancy or did not meet UNOS criteria by having a tumor size greater than 3 cm, metastatic disease, or transperitoneal tumor biopsy. ($p<0.001$).

Among the various publications, the Mayo Clinic in Minnesota had the most favorable results.[34,35] Between 1993 and 2006, 65 patients underwent liver transplantation for unresectable perihilar cholangiocarcinoma or had perihilar tumor due to primary sclerosing cholangitis. Unresectable patients underwent neoadjuvant radiochemotherapy. One-year survival was 91% and 5-year survival was 76%. In a series of 38 patients from the Mayo Clinic, cumulative recurrence was 0% at 1 year, 5% at 3 years, and 13% at 5 years.

The University of California, Los Angeles (UCLA)/Cedars-Sinai reported on 25 cases of both intrahepatic and extrahepatic cholangiocarcinoma.[36] One-year survival was 71% and 3-year survival was 35%. The University of Pittsburgh found 1-year survival of 70% and 18% 5-year survival among 20 patients with intrahepatic cholangiocarcinoma.[37] A German study of 24 patients reported the poorest results.[38]

The European Liver Transplant Registry reported that, among 186 patients with intrahepatic cholangiocarcinoma, 1-year survival was 58% and 5-year survival was 29%.[39] In 169 patients with extrahepatic cholangiocarcinoma, the probabilities were 63% and 29%. The Cincinnati Transplant Registry reported on 207 patients with either intrahepatic or extrahepatic cholangiocarcinoma, finding a

1-year survival of 72% and a 5-year rate of 23%.[40] The multicenter report included 36 patients with hilar tumors and 23 with peripheral intrahepatic disease.[41] One-year survival was 82% and 77%, while 5-year survival was 30% and 23%, respectively. Crude recurrence rates were 53% and 36% for extrahepatic and intrahepatic cholangiocarcinoma, respectively. The German center at Hannover found a crude recurrence rate of 63%.[38]

Outcomes Among Patients with Cholangiocarcinoma							
Study	Outcome	Group	n	Probability (%)			
				1yr	2yr	3yr	5yr
Pascher et al. 2003 (review,[19]) European Liver Transplant Registry	Overall patient survival	IH-CCA	186	58		38	29
		EH-CCA	169	63		38	29
Meyer et al. 2000[20] Cincinnati Transplant Registry unresectable CCA, cholangiohepatoma, incidental median follow-up 23 mo (<1-96)	Overall patient survival	IH/EH-CCA	207	72	48		23
Robles et al. 2004[26] Multiple Centers in Spain 03/88-09/01; hilar or peripheral CCA; unresectable, postoperative recurrent, or incidental	Overall patient survival	Hilar CCA	36	82		53	30
		Peripheral CCA	23	77		65	23
	Crude recurrence rate: EH-CCA: 19/36 (53%); IH-CCA: 8/23 (35%)						
Heimbach et al. 2006[34]; Rea et al. 2006[35] Mayo Clinic, Rochester MN, USA 01/93-01/06, aggressive neoadjuvant radiochemotherapy, unresectable perihilar CCA or perihilar CCA from primary sclerosing cholangitis mean follow-up 32 mo (2 d – 13 yr)	Overall patient survival	Perihilar CCA	65	91			76
	Cumulative recurrence		38	0		5	13
	Crude recurrence rate: 11/65 (17%) median onset 22 mo (7-65)						
Shimoda et al. 2001[36] UCLA/Cedars-Sinai, Los Angeles, CA, USA 1984-2000; IH or EH CCA median follow-up 22.3 mo	Overall patient survival	All	25	71		35	
		IH-CCA	16	62		39	
		EH-CCA	9	86		31	
	Disease-free survival	All	25	67		42	
		IH-CCA	16	70		35	
		EH-CCA	9	57		57	
Casavilla et al., 1997[37] University of Pittsburgh, PA, USA 1981-1994	Overall patient survival	IH-CCA	20	70		29	18
	Tumor-free		20	67		31	31

	survival						
Weimann et al. 2000[38] Hannover, GER 07/78-12/96; unresectable CCA	Overall patient survival	IH-CCA	24	21	8	4	0
	Crude recurrence rate: 15/24 (63%)						
CCA: cholangiocarcinoma; EH: extrahepatic; IH: intrahepatic							

In a 2008 review, Heimbach considers the published outcomes of the combined protocol in the context of data on outcomes for surgical resection and concludes that outcomes of neoadjuvant chemoradiotherapy with subsequent liver transplantation for patients with early-stage hilar cholangiocarcinoma, which is unresectable, or arising in the setting of primary sclerosing cholangitis are comparable to transplantation for patients with hepatocellular carcinoma and other chronic liver diseases and superior to resection.[42] The author describes intraoperative challenges attributable to the neoadjuvant therapy including severe inflammatory changes and dense fibrosis and suggests that key principles to be considered by centers considering use of the combined protocol include a multidisciplinary approach, pretransplant staging, inclusion of only patients without lymph node metastasis, replacement of irradiated vessels (when possible), and monitoring for postoperative vascular complications.

Wu et al. describe an extensive surgical procedure combined with radiotherapy.[43] They retrospectively review their experience with surveillance and early detection of cholangiocarcinoma and en bloc total hepatectomy-pancreaticoduodenectomy-orthotopic liver transplantation (OLT-Whipple) in a small series of patients with early-stage cholangiocarcinoma complicating primary sclerosing cholangitis. Surveillance involved endoscopic ultrasound and endoscopic retrograde cholangiopancreatography and cytological evaluation. Patients diagnosed with cholangiocarcinoma were treated with combined extra-beam radiotherapy, lesion-focused brachytherapy, and OLT-Whipple. Cholangiocarcinoma was detected in 8 of the 42 patients followed up according the surveillance protocol between 1988 and 2001, and 6 patients underwent OLT-Whipple. One died at 55 months after transplant of an unrelated cause without tumor recurrence, and 5 are without recurrence at 5.7–10.1 years.

Panjala and colleagues report on a small case series of 22 patients with cholangiocarcinoma treated with neoadjuvant chemoradiotherapy and subsequent liver transplantation.[44] Estimated rates of 1, 2, and 3 year survival, were 90%, 70%, and 63%, respectively, calculated based upon survival after a median follow-up of 601 days. Smaller tumors and those in the earliest stages of disease were associated with the most promising outcomes. However, long-term (post-3 year transplant) data is not available.

Conclusion

Treatment benefit of liver transplant has been demonstrated for select patients with cholangiocarcinoma and evidence on patients with perihilar cholangiocarcinoma have shown reasonable survival rates at 5 years. However, current evidence regarding 5 year survival rates for intrahepatic cholangiocarcinoma are less certain as a majority of studies which demonstrated lower overall survival rates, reported on a combined intra- and extrahepatic patient population.

Pediatric Hepatoblastoma

Hepatoblastoma is a rare malignant primary solid tumor of the liver that occurs in children. Treatment consists of chemotherapy and resection; however, tumors aren't often discovered until they are

unresectable. In cases of unresectable tumors, liver transplantation with pre- and/or post-chemotherapy is a treatment option with reports of good outcomes and high rates of survival.[45] UNOS guidelines list non-metastatic hepatoblastoma as a condition eligible for pediatric liver transplantation.[1]

In 2011, Barrena et al. reported on 15 children with hepatoblastoma requiring liver transplantation.[46] Overall survival after liver transplant was 93.3 ± 6.4% at 1-, 5- and 10-years. In 2010, Malek et al. reported on liver transplantation results for 27 patients with primary liver tumor identified from a retrospective review of patients treated between 1990 and 2007.[47] Tumor recurrence occurred in 1 patient after liver transplantation and overall survival was 93%. In 2008 Browne et al. reported on 14 hepatoblastoma patients treated with liver transplantation. Mean follow-up was 46 months with overall survival in 10 of 14 patients (71%).[48] Tumor recurrence caused all 4 deaths. In the 10 patients receiving primary liver transplantation, 9 survived while only 1 of 4 patients transplanted after primary resection survived (90% vs. 25%, p=0.02).

Metastatic Neuroendocrine Tumors

Neuroendocrine tumors (NETs) are relatively rare neoplasms that are generally slow growing but rarely cured when metastatic to the liver. Treatment options to control or downstage the disease include chemotherapy and debulking procedures, including hepatic resection. In select patients with non-resectable, hormonally active liver metastases refractory to medical therapy, liver transplantation has been considered as an option to extend survival and minimize endocrine symptoms.

In 2011, Mathe and colleagues conducted a systematic review of the literature to evaluate patient survival after liver transplant for pancreatic NETs.[49] Data from 89 transplanted patients from 20 clinical studies were included in the review. Sixty-nine patients had primary endocrine pancreatic tumors, 9 patients were carcinoids, and 11 patients were not further classified. Survival rates at 1-, 3-, and 5-years were 71%, 55%, and 44%, respectively. The mean calculated survival rate was 54.45 ± 6.31 months, and the median calculated survival rate was 41 months (95% CI: 22–76 months).

Gedaly and colleagues reported on a retrospective analysis of liver transplants conducted on 150 patients with metastatic NETs.[50] Survival rates at 1-, 3-, and 5-years were similar to those reported in the systematic analysis above: 81%, 65%, and 49%, respectively. No significant differences were seen in rates of patient survival between patients with metastatic NETs compared with those with hepatocellular carcinoma. Because longer wait times were associated with improved health outcomes, the researchers suggest allowing for disease stabilization before attempting transplantation.

In 2007, Mazzaferro and colleagues conducted a literature review to establish transplant selection criteria for patients with metastatic neuroendocrine tumors.[51] Eight studies were reviewed between 1970-2006 and all but one study reported either poor or limited 5 year survival outcomes. Suboptimal patient selection was considered to be the cause for the lower rates of long-term survival. However, Mazzaferro's group reported outcomes on 24 patients who were selected for transplant using strict patient selection criterion known as the Milan criteria[52], and reported a high 5 year survival rate of 77%. Although, the utilization of these criteria to select optimal transplantation candidates in patients with non-resectable metastatic neuroendocrine tumors is promising, the data is limited to a small sample (n=24), from a single study. Larger, long-term studies are required to validate the usefulness of the Milan criteria in improving 5 year survival rates for this unique patient population.

<u>Conclusion</u>

While there may be centers that perform liver transplantation on select patients with NETs, further studies are needed to determine appropriate selection criteria. Few studies are available and the quality is limited by their retrospective nature and heterogeneous populations.

HIV Positive Recipients

The subgroup of HIV positive liver transplant recipients has been controversial due to the long term prognosis for HIV positivity, the impact of immunosuppression on HIV disease, and the interactions of immunosuppressive therapy with antiretroviral therapy in the setting of a transplanted liver. For example, most antiretroviral agents are metabolized through the liver and can cause varying degrees of hepatotoxicity. HIV candidates for liver transplantation are frequently co-infected with hepatitis B or C, and viral co-infection can further exacerbate drug related hepatotoxicities. Although HIV positive transplant recipients may be a research interest of some transplant centers (e.g., the University of Pittsburgh, University of Miami and the University of California at San Francisco), the minimal data regarding long term outcomes in these patients consists primarily of case reports, a small case series and abstract presentations.[53-58] Nevertheless, some liver transplant surgeons would argue that HIV positivity is no longer an absolute contraindication to liver transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease, and the increasing experience with liver transplant in HIV positive patients. The most recent recommendations from the United Network for Organ Sharing (UNOS) agree that HIV status is no longer an absolute contraindication, stating, "A potential candidate for organ transplantation whose test for HIV is positive should not be excluded from candidacy for organ transplantation unless there is a documented contraindication to transplantation based on local policy.[59] In 2001, the Clinical Practice Committee of the American Society of Transplantation proposed that the presence of AIDS could be considered a contraindication to kidney transplant unless the following criteria were present.[60] These criteria may be extrapolated to other organs:

- CD4 count >200 cells/mm-3 for >6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy >3 months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidioses mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
- Meeting all other criteria for transplantation

It is likely that each individual transplant center will have explicit patient selection criteria for HIV+ patients.

In 2011, Cooper and colleagues conducted a systematic review to evaluate liver transplantation in patients co-infected with HIV and hepatitis.[61] The review included 15 cohort studies and 49 case series with individual patient data. The survival rate of patients was 84.4% (95% confidence interval [CI]: 81.1-87.8%) at 12 months. Patients were 2.89 (95% CI: 1.41-5.91) times more likely to survive when HIV viral load at the time of transplantation was undetectable compared to those with detectable HIV viremia.

Terrault and colleagues reported on a prospective, multicenter study to compare liver transplantation outcomes in 3 groups: patients with both hepatitis C virus (HCV) and HIV (n=89), patients with only HCV (n=235), and all transplant patients age 65 or older.[62] Patient and graft survival reductions were significantly associated with only one factor: HIV infection. At 3 years, in the HCV only group, patient and graft survival rates were significantly better at 79% (95% CI:72-84%) and 74% (95% CI: 66-79%), respectively, than the group with both HIV and HCV infection at 60% (95% CI: 47-71%) and 53% (95% CI: 40-64%).

Conclusion

While HIV infection reduced 3-year survival rates after liver transplantation in patients also infected with HCV, there were still a majority of patients experiencing long-term survival. Overall, survival rates are relatively high for patients with viral loads are low at the time of transplantation.

Nonalcoholic Steatohepatitis

Nonalcoholic steatohepatitis (NASH) is a condition where fat build up in the liver causes inflammation of the liver. Liver transplantation is a treatment option for patients with NASH who progress to liver cirrhosis and failure. In a 2013 systematic review and meta-analysis, Wang et al. evaluated 9 studies comparing liver transplantation outcomes in patients with and without NASH.[63] Patients with NASH had similar 1-, 3- and 5-year survival outcomes after liver transplantation as patients without NASH. Patients with NASH also had lower graft failure risk than those without NASH (OR, 0.21; 95% CI, 0.05-0.89; p=0.03). However, NASH liver transplant patients had a greater risk of death related to cardiovascular disease (OR, 1.65; 95% CI, 1.01-2.70; p=0.05) and sepsis (OR, 1.71; 95% CI, 1.17-2.50; p=0.006) than non-NASH liver transplant patients. Given the relatively equivocal survival rates compared to transplant patients without NASH, transplant in patients with NASH appear to be of benefit.

Conclusion

Long-term 5 year survival rates appear to well exceed the 50% benchmark indicating liver transplant is of benefit in children with unresectable NASH.

Retransplantation

In 2012, Bellido and colleagues reported on a retrospective cohort study of 68 consecutive adult liver retransplantations using registry data.[64] Survival probability using Kaplan-Meier curves with log-rank tests to compare 21 urgent versus 47 elective retransplantations were calculated. Overall survival rates were significantly better in patients undergoing urgent procedures (87%), which were mostly due to vascular complications than elective procedures (76.5%) related to chronic rejection.

In 2011, Remiszewski et al. examined factors influencing survival outcomes in 43 liver retransplantation patients.[65] When compared to primary liver transplantation patients, retransplantation patients had significantly lower 6-year survival rates (80% vs. 58%, respectively; p=0.0001). The authors also reported low negative correlations between survival time and time from original transplantation until retransplantation and between survival time and patient age. Survival time and cold ischemia time showed a low positive correlation.

Hong and colleagues, in 2011, reported on a prospective study of 466 adults to identify risk factors for survival after liver retransplantation.[66] Eight risk factors were identified as predictive of graft failure, including age of recipient, MELD score greater than 27, more than 1 prior liver transplant, need for mechanical ventilation, serum albumin of less than 2.5 g/dL, donor age greater than 45 years, need for more than 30 units of packed red blood cells transfused intraoperatively, and time between prior transplantation and retransplantation between 15 and 180 days. The authors propose this risk-stratification model can be highly predictive of long-term outcomes after adult liver retransplantation and can be useful in patient selection.

Conclusion

Recent data regarding liver retransplantation suggest survival rates are not as good as with initial transplantation; however, overall survival rates appear to meet the benchmark of 50% 5-year survival.

Clinical Practice Guidelines

In December 2010, 10 international liver diseases or transplantation societies held an international consensus conference on liver transplantation for hepatocellular carcinoma (HCC).[67] Consensus criteria for selecting candidates for liver transplantation were developed at the conference. Milan criteria were recommended for use as the benchmark for patient selection and as the basis for comparison with other suggested criteria for selecting non-HCC patients. The Milan criteria set limits on the size and quantity of tumors and have been shown to be an independent prognostic factor for outcomes after liver transplantation.[67,68] Panel members did refer to several studies which indicated that in some circumstances, the Milan criteria may be modestly expanded for patients who do not have HCC. It was warned, however, that expanding Milan criteria could result in a variety of outcomes and that patients, "…would need to achieve 5-year survival of 60% or higher to prevent a substantial decrement to the life-years available to the entire population of candidates for liver transplantation."[67] In addition, candidates for liver transplantation should also have a predicted survival of 5 years or more. The consensus criteria indicate alpha-fetoprotein concentrations may be used with imaging to assist in determining patient prognosis.

With respect to liver retransplantation, the consensus criteria issued a weak recommendation indicating retransplantation after graft failure of a living donor transplant for HCC is acceptable in patients meeting regional criteria for a deceased donor liver transplant. A strong recommendation was issued indicating liver retransplantation with a deceased donor for graft failure for patients exceeding regional criteria is not recommended. And the consensus criteria issued a strong recommendation that liver retransplantation for recurrent HCC is not appropriate. However, a de-novo HCC may be treated as a new tumor and retransplantation may be considered even though data to support this are limited.

American Association for the Study of Liver Diseases (AASLD)

In 2005, the AASLD issued guidelines on evaluating patients for liver transplant.[69] These guidelines state liver transplantation is indicated for acute or chronic liver failure from any cause after all effective medical treatments have been attempted. Furthermore, the AASLD guidelines indicate patients should be assessed by a transplantation center to determine whether liver transplantation is appropriate. While the AASLD guidelines indicate liver transplant may be appropriate in patients with cholangiocarcinoma and metastatic neuroendocrine tumors, these recommendations and many of the recommendations in the AASLD guidelines are based on opinion.

National Comprehensive Cancer Network (NCCN)[27]

The NCCN guidelines on hepatobiliary cancers recommends referral to a liver transplant center or bridge therapy in patients with hepatocellular carcinoma (HCC) meeting UNOS criteria of a single tumor equal to or less than 5 cm, or 2-3 lesions equal to or less than 3 cm when there is no macrovascular involvement or extrahepatic disease.

The NCCN guidelines also recommend that patients should be referred to the transplant center before biopsy. The NCCN states that patients meeting UNOS criteria who are ineligible for transplant and in select patients with Child-Pugh Class A or B liver function with tumors that are resectable and meet who UNOS criteria, resection is the preferred treatment option or locoregional therapy or transplant may be considered. The guidelines indicate that patients with unresectable HCC should be evaluated for liver transplantation and if the patient is a transplant candidate, then referral to a transplant center should be given or bridge therapy should be considered.

The NCCN guidelines on hepatobiliary cancers also indicate liver transplant is appropriate in select patients with extrahepatic cholangiocarcinoma which is unresectable, but biliary and hepatic function is otherwise normal or when underlying chronic liver disease precludes surgery. These are level 2A recommendations based on lower-level evidence and uniform consensus.

Summary

Liver transplant is an accepted treatment of end-stage liver disease that provides a survival benefit in appropriately selected patients and thus may be considered medically necessary for indications such as cholestatic liver diseases, hepatocellular diseases, certain types of malignancies and in those otherwise meeting the Organ Procurement and Transplantation Network (OPTN) and the United Network of Organ Sharing (UNOS) criteria. Liver transplantation is investigational in patients in whom the procedure is expected to be futile due to comorbid disease or in whom post-transplantation care is expected to significantly worsen comorbid conditions.

HIV-Positive Patients

Case series and case-control data indicate that HIV-infection is not an absolute contraindication to liver transplant; for patients who meet selection criteria, these studies have demonstrated patient and graft survival rates are similar to those in the general population of transplant recipients.

Malignancies

Recent literature continues to address expanded criteria for transplantation for hepatocellular carcinoma, predictors of recurrence, the role of neoadjuvant therapy in patients with hepatocellular carcinoma, expanded donor criteria, transplantation and retransplantation for hepatitis C, and living donor transplantation. Further study is needed before liver transplant selection criteria can be expanded for hepatocellular carcinoma. Additionally, further study is needed to address salvage liver transplantation for HCC recurrence after primary liver resection.

Liver transplantation for hilar cholangiocarcinoma is performed at some transplant centers and long-term survival has been reported in select patients with unresectable disease. For metastatic neuroendocrine tumors, cure of disease is not achieved and 5-year survival is generally not high. However, there have been reports of survival benefit in patients receiving liver transplantation for

unresectable neuroendocrine tumor metastasis confined to the liver. Based on this survival data, transplantation in patients with hilar cholangiocarcinoma who meet strict eligibility criteria may be considered medically necessary. Transplantation for neuroendocrine tumors metastatic to the liver is considered investigational.

Liver transplant in patients with hepatocellular carcinoma extending beyond the liver and in patients with active alcohol and/or substance abuse is considered not medically necessary.

Retransplantation

Case series have demonstrated favorable outcomes with liver retransplantation in certain populations, such as when criteria for an original liver transplantation are met for retransplantation. While some evidence suggests outcomes after retransplantation may be less favorable than for initial transplantation, long-term survival benefits have been demonstrated. Benefit from retransplantation in carefully selected patients has been demonstrated following:

- primary graft non-function
- hepatic artery thrombosis
- ischemic biliary injury after donation after cardiac death
- chronic rejection
- and in certain recurrent non-neoplastic diseases resulting in end- stage liver failure in a primary transplant.

As a result, retransplantation after initial failed liver transplant may be considered medically necessary in these situations.

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CROSS REFERENCES

Small Bowel/Liver and Multivisceral Transplant, Transplant, Policy No. 18

CODES	NUMBER	DESCRIPTION
CPT	47133	Donor hepatectomy (including cold preservation) from cadaver donor
	47135	Liver allotransplantation; orthotopic; partial or whole, from cadaver or living donor, any age
	47136	Liver allotransplantation; heterotopic, partial or whole, from cadaver or living donor, any age
	47140	Donor hepatectomy (including cold preservation), from living donor; left lateral segment only (segments II and III)
	47141	Donor hepatectomy (including cold preservation), from living donor; total left lobectomy (segments II, III and IV)
	47142	Donor hepatectomy (including cold preservation), from living donor; total right lobectomy (segments V, VI, VII and VIII)
	47143	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the

CODES	NUMBER	DESCRIPTION
		vena cava, portal vein, hepatic artery, and common bile duct for implantation; without trisegment or lobe split
	47144	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with trisegment split of whole liver graft into two partial liver grafts (i.e., left lateral segment (segments II and III) and right trisegment (segments I and IV through VIII))
	47145	Backbench standard preparation of cadaver donor whole liver graft prior to allotransplantation, including cholecystectomy, if necessary, and dissection and removal of surrounding soft tissues to prepare the vena cava, portal vein, hepatic artery, and common bile duct for implantation; with lobe split of whole liver graft into two partial liver grafts (i.e., left lobe (segment II, III, and IV) and right lobe (segments I and V through VIII)
	47146	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; venous anastomosis, each
	47147	Backbench reconstruction of cadaver or living donor liver graft prior to allotransplantation; arterial anastomosis, each
HCPCS	None	