terminal illness, and profound hypoglycemia may occur, although the cause is unclear. Erythrocytosis occurs in 3–12% of patients and hypercholesterolemia in 10–40%. A high percentage of patients have thrombocytopenia associated with their fibrosis or leukopenia, resulting from portal hypertension, and not from cancer infiltration of bone marrow, as in other tumor types. Furthermore, large HCCs have normal or high platelet levels (thrombocytosis), as in ovarian and other gastrointestinal cancers, probably related to elevated interleukin 6 (IL-6) levels.

STAGING

Multiple clinical staging systems for HCC have been described. A widely used one has been the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) classification. However, the Cancer of the Liver Italian Program (CLIP) system is now popular because it takes cirrhosis into account, based on the original Okuda system (Table 111-4). Patients with Okuda stage III disease have a dire prognosis because they usually cannot be curatively resected, and the condition of their liver typically precludes chemotherapy. Other staging systems have been proposed, and a consensus is needed. They are all based on combining the prognostic features of liver damage with those of tumor aggressiveness and include the Barcelona Clinic Liver Cancer (BCLC) system from Spain (Fig. 111-1), which is externally validated and incorporates baseline survival estimates; the Chinese University Prognostic Index (CUPI); the important and simple Japan Integrated Staging Score (JIS); and SLiDe, which stands for *s* tage, *li* ver damage, and *de* s-γ-carboxy prothrombin. CLIP and BCLC appear most popular in the West, whereas JIS is favored in Japan. Each system has its champions. The best prognosis is for stage I, solitary tumors less than 2 cm in diameter without vascular invasion. Adverse prognostic features include ascites, jaundice, vascular invasion, and elevated α fetoprotein (AFP). Vascular invasion in particular has profound effects

TABLE 111-4 CLIP AND OKUDA STAGING SYSTEMS FOR HEPATOCELLULAR CARCINOMA

CLIP Classification

	Points		
Variables	**0**	**1**	**2**
i. Tumor number	Single	Multiple	–
Hepatic replacement by tumor (%)	<50	<50	>50
ii. Child-Pugh score	A	B	C
iii. α Fetoprotein level (ng/mL)	<400	≥400	–
iv. Portal vein thrombosis (CT)	No	Yes	–

CLIP stages (score = sum of points): CLIP 0, 0 points; CLIP 1, 1 point; CLIP 2, 2 points; CLIP 3, 3 points.

Okuda Classification

Tumor Extent[a]		Ascites		Albumin (g/L)		Bilirubin (mg/dL)	
≥50%	<50	+	–	≤3	>3	≥ 3	<3
(+)	(–)	(+)	(–)	(+)	(–)	(+)	(–)

Okuda stages: stage 1, all (–); stage 2, 1 or 2 (+); stage 3, 3 or 4 (+).

[a]Extent of liver occupied by tumor.

Abbreviation: CLIP, Cancer of the Liver Italian Program.

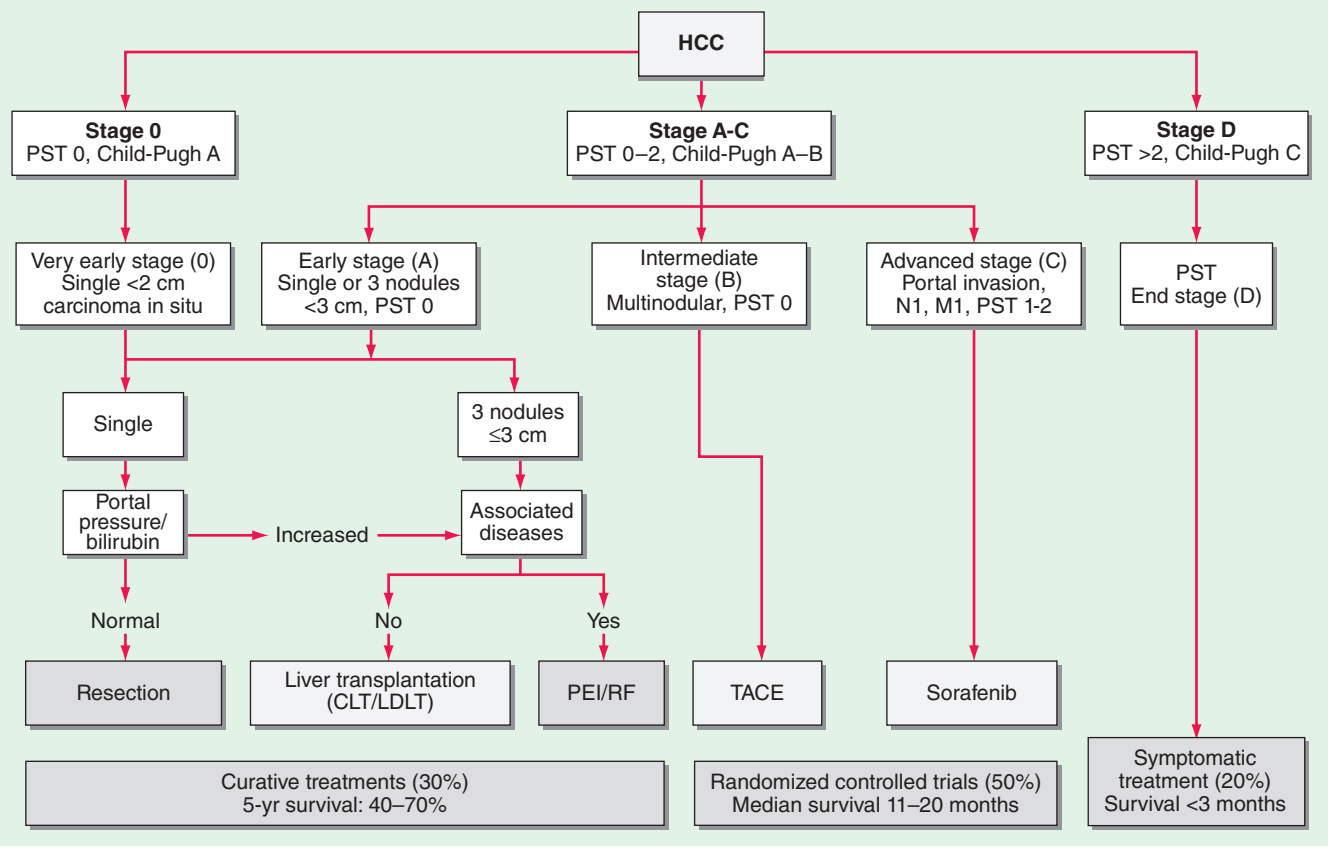

FIGURE 111-1 Barcelona Clinic Liver Cancer (BCLC) staging classification and treatment schedule. Patients with very early hepatocellular carcinoma (HCC) (stage 0) are optimal candidates for resection. Patients with early HCC (stage A) are candidates for radical therapy (resection, liver transplantation [LT], or local ablation via percutaneous ethanol injection [PEI] or radiofrequency [RF] ablation). Patients with intermediate HCC (stage B) benefit from transcatheter arterial chemoembolization (TACE). Patients with advanced HCC, defined as presence of macroscopic vascular invasion, extrahepatic spread, or cancer-related symptoms (Eastern Cooperative Oncology Group performance status 1 or 2) (stage C), benefit from sorafenib. Patients with end-stage disease (stage D) will receive symptomatic treatment. Treatment strategy will transition from one stage to another on treatment failure or contraindications for the procedures. CLT, cadaveric liver transplantation; LDLT, living donor liver transplantation; PST, Performance Status Test. *(Modified from JM Llovet et al: JNCI 100:698, 2008.)*