



Factors Affecting Periprocedural Morbidity and Mortality and Long-term Patient Survival after Arterial Embolization of Hepatic Neuroendocrine Metastases

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ABSTRACT

Purpose: To identify factors affecting periprocedural morbidity and mortality and long-term survival following hepatic artery embolization (HAE) of hepatic neuroendocrine tumor (NET) metastases.

Materials and Methods: This single-center, institutional review board–approved retrospective review included 320 consecutive HAEs for NET metastases performed in 137 patients between September 1996 and September 2007. Forty-seven HAEs (15%) were performed urgently to manage refractory symptoms in inpatients (urgent group), and 273 HAEs (85%) were elective (elective group). Overall survival (OS) was estimated by Kaplan–Meier methodology. Complications were categorized per Common Terminology Criteria for Adverse Events, version 4.0. Univariate and multivariate analyses were performed to determine independent predictors for OS, complications, and 30-day mortality. The independent factors were combined to develop clinical risk score groups.

Results: Urgent HAE ($P = .007$), greater than 50% liver replacement by tumor ($P < .0001$), and extrahepatic metastasis ($P = .007$) were independent predictors for shorter OS. Patients with all three risk factors had decreased OS versus those with none (median, 8.5 vs 86 mo; $P < .001$). Thirty-day mortality was significantly lower in the elective (1%) versus the urgent group (8.5%; $P = .0009$). There were eight complications (3%) in the elective group and five (10.6%) in the urgent group ($P = .03$). Male sex and urgent group were independent factors for higher 30-day mortality rate ($P = .023$ and $P = .016$, respectively) and complications ($P = .012$ and $P = .001$, respectively).

Conclusions: Urgent HAE, replacement of more than 50% of liver by tumor, and extrahepatic metastasis are strong independent predictors of shorter OS. Male sex and urgent HAE carry higher 30-day mortality and periprocedural morbidity risks.

ABBREVIATIONS

CI = confidence interval, HAE = hepatic artery embolization, NET = neuroendocrine tumor, OS = overall survival

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Because of their indolent nature, neuroendocrine tumors (NETs) have been described as “cancers in slow motion” (1). Nevertheless, most patients will die from this disease, predominantly as a result of liver metastases (1). Approximately 50% of NETs secrete hormones that may lead to clinical symptoms (2). Arterially directed therapies including transcatheter arterial chemoembolization (3–6), radioembolization (7), and hepatic artery embolization (HAE) (8–10) have been used for the management of NET hepatic metastases. Common indications for arterially directed therapies for NET hepatic metastases include management of hormonal

symptoms refractory to somatostatin analogues, radiologic evidence of disease progression, and large tumors causing pain or other bulk symptoms (11). Many reports have shown that HAE and chemoembolization are beneficial to patients with metastatic NETs by reducing hormone levels and tumor size (1,3,10,12–18). However, the literature that focuses on patient selection, procedural circumstances, and clinical factors that may influence the immediate and long-term outcomes of HAE in this patient population is fairly scarce.

The purpose of the present study was to identify factors affecting long-term overall patient survival as well as periprocedural morbidity and mortality related to HAE in patients with NET hepatic metastases.

MATERIALS AND METHODS

Patients treated with HAE for NET hepatic metastases and with at least 5 years of follow-up were eligible for the present review. Patients were included in this study at the time of their very first embolization session. All patients who underwent previous hepatic embolization were excluded. A total of 137 patients who underwent a total of 320 consecutive HAEs between August 1996 and September 2007 comprise this cohort. All patients signed informed consent for HAE. Institutional review board waiver was obtained for this Health Insurance Portability and Accountability Act–compliant retrospective chart review study.

Patients Demographics

Table 1 depicts patient and tumor characteristics. Patients underwent HAE within a median time of 13.3 months (range, 0–201 mo) from the initial diagnosis of liver metastasis. Chart review was performed to identify the referral pattern for HAE. Two distinct referral patterns were identified:

The urgent group includes patients who were urgently admitted with symptoms attributed to NET hepatic metastases and received inpatient medical care (somatostatin infusion, intravenous hydration and electrolyte management, patient-controlled analgesic pump) for at least 24 hours without symptom improvement. This urgent group included 47 HAEs performed in 30 patients. In these cases, HAE was undertaken as a salvage therapy to control symptoms refractory to medical management. Symptoms at presentation in the urgent group included severe fluid and electrolyte disorders, hypoglycemia with or without seizure activity, and acute abdominal pain.

The elective group included 273 of 320 HAEs (85%) performed electively in 107 patients at a previously scheduled date. These patients came to the hospital only for the embolization and did not require any earlier admission for symptom control. Other than the need for hospitalization for refractory symptomatology, there

Table 1. Patient Characteristics

Characteristic	Carcinoid (n = 78)	Islet Cell (n = 59)
Sex		
Male	26 (33)	36 (61)
Female	52 (67)	23 (39)
Age (y)		
Median	60	55
Range	32–85	28–83
Race		
White	67 (86)	54 (92)
Black	7 (9)	2 (3)
Asian	1 (1)	1 (2)
Other/Unknown	3 (4)	2 (3)
Primary origin/tumor type		
Foregut	23 (30)	–
Midgut	31 (40)	–
Hindgut	7 (9)	–
Unknown	17 (21)	–
Insulinoma	–	2 (3)
Glucagonoma	–	4 (7)
Vipoma	–	4 (7)
Gastrinoma	–	4 (7)
Somatostatinoma	–	1 (2)
Islet cell multiple	–	13 (22)
Islet cell nonfunctional	–	31 (52)
Primary histologic grade		
High	8 (10)	2 (3)
Intermediate	7 (9)	6 (10)
Low	33 (42)	31 (53)
Unknown	30 (39)	20 (34)
Previous octreotide treatment	55 (71)	47 (80)
Previous liver surgery	27 (35)	12 (20)
Primary resected	43 (55)	28 (47)
Extrahepatic metastasis*	32 (41)	25 (42)
Metastatic liver involvement*		
< 50%	45 (58)	30 (51)
> 50%	32 (41)	26 (44)
Unknown	1 (1)	3 (5)
No. of embolizations	162	156
Median per patient	2	2
Range per patient	1–10	1–9

Values in parentheses are percentages.

*At presentation.

was no significant difference in baseline characteristic between the elective and the urgent groups (**Table 2**).

Preprocedure Evaluation

All patients were determined to have unresectable disease by a multidisciplinary team including a hepatobiliary surgeon and a gastrointestinal and hepatobiliary oncologist. Patients with liver-dominant (ie, limited extrahepatic metastases) or liver-only (ie, no extrahepatic metastases) disease were eligible for HAE. Patients

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