Safety of Transarterial Liver Directed Therapy for Metastatic Neuroendocrine Tumors for Patients with Carcinoid Heart Disease

Jason Kim, MD[1]; Nicholas Fidelman, MD[1]; Parmede Vakil, MD, PhD[2]; Emily Bergsland, MD[1]; Kirsten Tolstrup, MD[1]; Etay Ziv, MD, PhD[3]; Erica Alexander, MD[3]; Adrian Gonzalez Aguirre, MD[3]

1. University of California San Francisco; 2. Oregon Health Sciences University; 3. Memorial Sloan Kettering Cancer Center

INTRODUCTION

- Transarterial liver directed therapies such as bland embolization, transarterial chemoembolization, and Yttrium-90 radioembolization help control tumor burden for patients with neuroendocrine tumor liver metastases
- Functional neuroendocrine tumors secrete vasoactive substances that can lead to carcinoid heart disease

Purpose

To evaluate safety of liver embolotherapy and risk of cardiac adverse events in the setting of carcinoid heart disease

MATERIALS AND METHODS

- Retrospective analysis at two institutions (UCSF and MSKCC)
- Adults with well-differentiated neuroendocrine tumor liver metastases and evidence of carcinoid heart disease on transthoracic echocardiography who underwent embolotherapy from 2000 to 2023
- Evaluate the prevalence of cardiac adverse events
- Cardiac adverse event defined by:
  - New onset symptoms (edema, ascites, dyspnea, pleural effusion) within 6 weeks after embolotherapy
  - Severity graded by NCI CTCAE v5.0
- Association between cardiac adverse events and ECOG performance status (PS), severe tricuspid regurgitation, type of embolotherapy, and NET grade tested with generalized estimating equation method

RESULTS

Clinicodemographic Features

Total patients, n	29
Age (y), median (range)	63 (36-75)
Gender, n (%)	
Male	15 (51.7)
Female	14 (48.3)
ECOG PS, n (%)	
ECOG 0	19 (65.5)
ECOG 1	8 (27.6)
ECOG 2	0
ECOG 3	2 (6.9)

NET WHO Grade, n (%) Ki-67 Index, median % (range)	
Grade 1 Ki-67 Index	16 (55.2) 1 (0.1-2.4)
Grade 2 Ki-67 Index	12 (41.3) 10.5 (3.2-18.8)
Grade 3 Ki-67 Index	1 (3.44) 40
Primary NET site, n (%)	
Small bowel	23 (79.3)
Large bowel	3 (10.3)
Pancreas	3 (10.3)

Baseline Cardiac Data

Tricuspid Regurgitation, n (%)	
None	3 (10.3)
Mild	4 (13.8)
Mild to Moderate	2 (6.9)
Moderate	3 (10.3)
Moderate to Severe	1 (3.4)
Severe	16 (55.2)
Pulmonic Regurgitation, n (%)	
None	6 (20.7)
Mild	2 (6.9)
Mild to Moderate	5 (17.2)
Moderate	4 (13.8)
Moderate-severe	3 (10.3)
Severe	4 (13.8)
Prior valve replacement, n (%)	
Tricuspid only	2 (6.9)
Pulmonic only	0
Tricuspid/Pulmonic	5 (17.2)

Procedural Data

Total transarterial embolizations (n)	79
Bland embolization, n (%)	37 (46.8)
TACE, n (%)	31 (39.2)
Y90, n (%)	11 (13.9)
Total embolization procedures per patient, median (range)	2 (1-11)
Postprocedure length of hospital stay, median days (range)	1 (0-68)
Procedures with length of hospital stay ≥4 days, n (%)	9 (11.4)
Follow up duration (months), median months (range)	36.6 (1.1-142.1)

Cardiac Adverse Events

Prevalence of cardiac adverse events (patients), n (%)	7 (24%)
Prevalence of cardiac adverse events (procedures), n (%)	7 (8.9%)
Bland embolization	3
TACE	4
Y90	0
Cardiac adverse events requiring re-admission postprocedure, n	5
Time of onset post procedure, median days (range)	17 (1-39)
Length of hospital stay, median days (range)	4 (2-14)

- 5 severe cardiac adverse events in 5 patients: decompensated heart failure requiring hospitalization (CTCAE Grade 3-4)
  - 1 hospitalization required ICU admission (CTCAE Grade 4)
  - 4 hospitalizations managed with non-ICU level care (CTCAE Grade 3)
  - All hospitalized patients were medically managed and discharged
- 2 cardiac adverse events in 2 patients: lower extremity edema that were managed in the outpatient setting (CTCAE Grade 2)
- Correlation between cardiac AE and grade 3 NET (p=0.009)
- No statistically significant association between cardiac AE with the following:
  - ECOG PS
  - Severe tricuspid regurgitation
  - Embolotherapy type
- Median follow up for these patients: 23.9 months (range 4.3-50.7)
- Overall survival following embolotherapy in this population
  - 1 year: 85.7%
  - 3 years: 70.4%
  - 5 years: 43%

CONCLUSION

Transarterial liver directed therapies for patients with carcinoid heart disease was associated with 8.9% prevalence of cardiac adverse events, which all improved with medical management.

1. Chen JX, et al. Cardiovasc Intervent Radiol. 2017;40(1):69-80; 2. Currie BM, et al. J Vasc Interv Radiol. 2019;30(12):1915-1923; 3. Eads JR, et al. Endocr Relat Cancer. 2023;30(8):e220206; 4. Lehrman ED, et al. Semin Intervent Radiol. 2020;37(5):499-507