

INTRODUCTION

- Carcinoid crisis (CC) is a life-threatening event caused by release of vasoactive substances from neuroendocrine tumors (NETs), which can be triggered by medical interventions including anesthesia, embolotherapy, and surgery.
- Octreotide, a somatostatin analog (SSA), is commonly used in the peri-procedural setting as prophylaxis against CC.
- In this retrospective study, we aimed to describe peri-procedural management and outcomes of patients with metastatic NETs who underwent liver-directed procedures at UCSF.

METHODS

- **Population:** We identified 79 patients with NETs with hepatic metastases who underwent liver resection/ablation (n=39) or liver embolotherapy (n=40) at UCSF during 2012-2016.
- **Data:** Anesthesia and clinical data were abstracted from electronic medical records.
- **Outcome:** Primary outcome was occurrence of either CC or hemodynamic instability (HDI). CC was identified based on clinical documentation. HDI was defined as ≥ 10 min of SBP < 80 or > 180 mmHg or pulse > 120 BPM in anesthesia records.¹
- **Analysis:** Pearson chi-square tests were used to test associations with the outcome (CC or HDI). A multivariate logistic regression was performed to calculate adjusted odds ratio of the outcome for variables chosen based on factors found significant in prior studies.¹⁻³

RESULTS

Table 1a. Patient characteristics & HDI or CC

Characteristic	Value	No Event N (%)	HDI or CC N (%)	P-value ^a
Total		55 (70)	24 (30)	NA
Age at procedure	25-39	4 (67)	2 (33)	0.58
	40-49	6 (55)	5 (45)	
	50-59	15 (79)	4 (21)	
	60-79	30 (70)	13 (30)	
Gender	Male	29 (74)	10 (26)	0.37
	Female	26 (65)	14 (35)	
ECOG	0	27 (77)	8 (23)	0.35
	1	21 (62)	13 (38)	
	2	2 (100)	0 (0)	
	3	1 (100)	0 (0)	
	Unknown	4	3	
Primary tumor location	Small Bowel	28 (67)	14 (33)	0.57
	Other ^b	7 (64)	4 (36)	
	Pancreas	15 (79)	4 (21)	
	Unknown	5	2	
Tumor grade	G1	23 (74)	8 (26)	0.24
	G2	20 (63)	12 (38)	
	G3	4 (100)	0 (0)	
	Unknown	8	4	
Hepatic involvement on imaging	< 25%	25 (66)	13 (34)	0.50
	25-50%	16 (70)	7 (30)	
	50-75%	9 (82)	2 (18)	
	>75%	3 (100)	0 (0)	
	Unknown	2	2	
History of carcinoid syndrome	Yes	22 (63)	13 (37)	0.27
	No	32 (74)	11 (26)	
	Unknown	1	0	
CGA greater than 2x ULN	Yes	29 (73)	11 (28)	0.61
	No	18 (67)	9 (33)	
	Unknown	8	4	

^aThree renal and four bronchus tumors.

Table 1b. Urine 5-HIAA & HDI or CC

Characteristic	Value	No Event median [range]	HDI or CC median [range]	P-value ^a
5-HIAA % of ULN		185 [27, 17500]	243 [30, 3850]	0.85
	Unknown	16	3	

^aKruskal-Wallis one-way analysis of variance test.

Occurrence of HDI and CC

- CC was documented in 3 patients (4%), and HDI was identified in 24 (30%).
- Among only patients with small bowel NETs, 3 (7%) experienced CC and 11 (26%) experienced HDI.
- Thirty-day mortality was 0.

Table 2. Procedural factors & HDI or CC

Procedural factor	Value	No Event N (%)	HDI or CC N (%)	P-value ^a
Surgery	Yes	23 (59)	16 (41)	0.04
	No	32 (80)	8 (20)	
Long-acting SSA use prior month	Yes	31 (69)	14 (31)	0.87
	No	24 (71)	10 (29)	
Octreotide use pre-procedure	Yes	22 (73)	8 (27)	0.57
	No	33 (67)	16 (33)	
Octreotide use intra-procedure	Yes	34 (69)	15 (31)	0.95
	No	21 (70)	9 (30)	
Any pre or intra-procedure octreotide	Yes	36 (71)	15 (29)	0.80
	No	19 (68)	9 (32)	

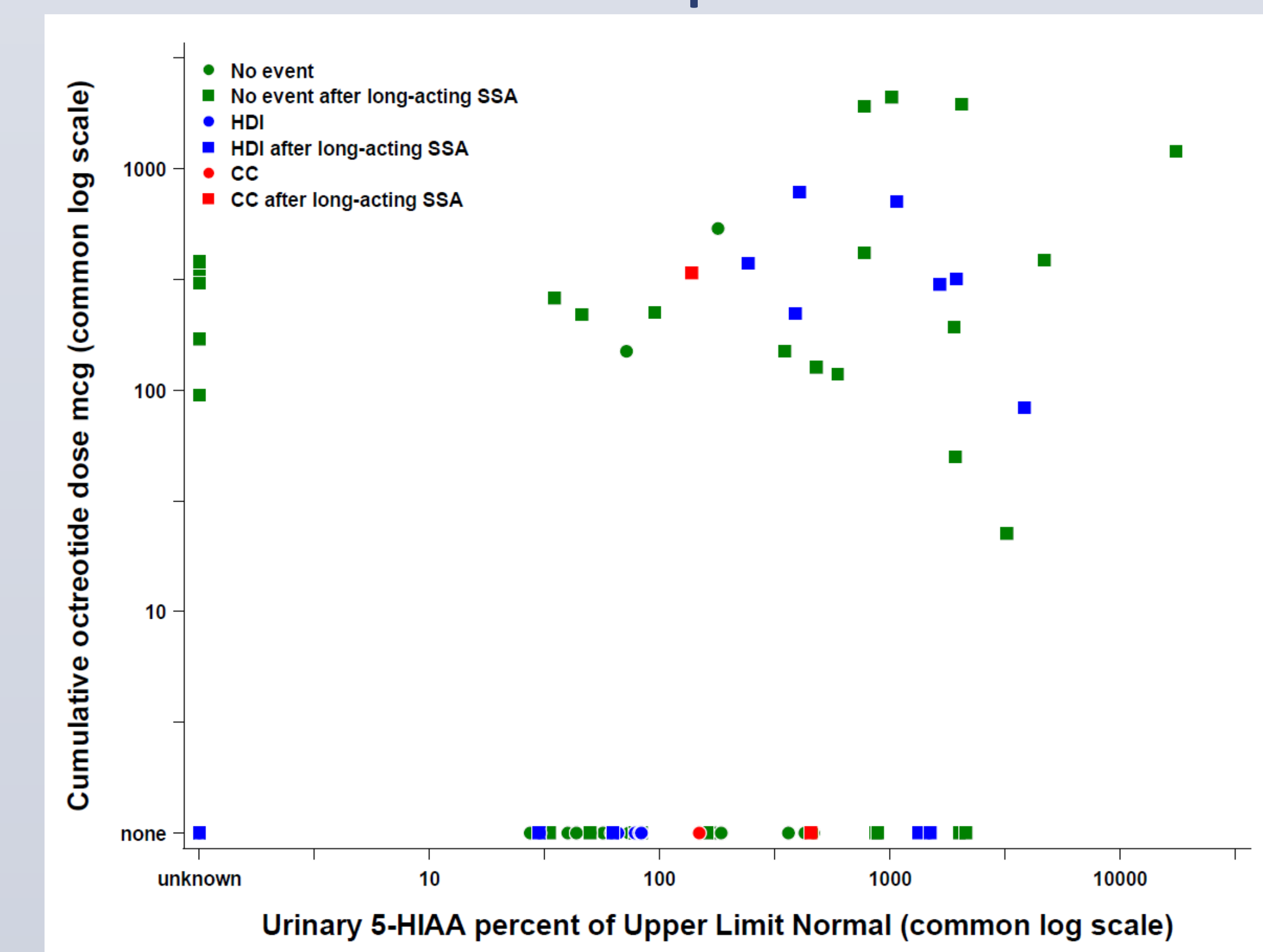
^aPearson chi-square tests do not include counts of characteristics of value unknown.

Table 3. Multivariate analysis of clinical determinants of HDI or CC

Clinical factor	Odds Ratio	95% CI	P-value
Age at procedure	1.00 ^a	[0.95, 1.05]	0.92
Hepatic involvement on imaging	0.51 ^b	[0.19, 1.38]	0.19
Surgery	1.53 ^c	[0.33, 7.20]	0.59
Urine 5-HIAA >2x ULN	1.45 ^c	[0.39, 5.33]	0.58
Any pre-procedure octreotide	1.41 ^c	[0.33, 6.02]	0.64

Note: results unchanged with removal of patients with pancreatic NETs, removal of patients with urine 5-HIAA < 2x ULN, or removal of pre-procedure octreotide variable.
^aContinuous variable, estimated OR of event (HDI or CC) for each 1 year increase in age.
^bOrdinal variable, estimated OR of event (HDI or CC) for each 25% increase in tumor involvement.
^cCategorical variable, estimated OR of event (HDI or CC) for a value of Yes compared to No.

Figure 1. Relationship of urine 5-HIAA and pre-proc. octreotide dose to development of HDI & CC



Note: neither urine 5-HIAA nor pre-procedure octreotide associated with HDI or CC (Tables 1a and 2)

CONCLUSIONS

- CC occurred infrequently; however, a significant portion of patients developed HDI that was revealed only by review of anesthesia records. Peri-procedural CC may in fact be a spectrum diagnosis and clinically under-recognized.
- Only surgery was associated with HDI or CC, but this association was not statistically significant after controlling for extent of hepatic involvement.
- Pre-procedural octreotide was not associated with a reduced rate of HDI or CC, and its removal from the multivariate model did not change surgery's effect on HDI or CC, suggesting it is not a modifier.
- Given its safety profile, octreotide should continue to be used peri-procedurally until more studies show lack of benefit.

LIMITATIONS

- A single-center, retrospective study.
- Lack of standardization in peri-procedural octreotide administration.
- Inclusion of pancreatic NETs and cases with normal urine 5-HIAA may have decreased the frequency of both independent and outcome variables.
- Under-recording of HDI in anesthesia records may have occurred since low/high SBPs are likely to be treated promptly.

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