Characterizing the Epidemiology and Treatment Patterns of Carcinoid Syndrome Among Neuroendocrine Neoplasms in a Large Population-Based Database

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BACKGROUND

- Neuroendocrine neoplasms (NENs) are a group of rare malignancies arising from neuroendocrine cells throughout the body; their prevalence has been increasing over the past several decades due to improved detection of early-stage disease[1,2]
- A subset of NENs secrete hormones and vasoactive substances that enter the systemic circulation and result in clinical consequences for the patient, such as carcinoid syndrome (CS)[1,3]
- CS is the most common functional syndrome associated with NENs (predominantly extrapancreatic NENs) and is characterized by the hallmark symptoms of diarrhea and flushing, along with reduced survival and impaired quality of life[3,4]

OBJECTIVE

- To determine the frequency of CS among older adults with extrapancreatic NENs in the United States and to compare common disease characteristics and treatment patterns in patients with and without CS

METHODS

Design: Retrospective, claims-based analysis

Data Source: SEER-Medicare database

Study Period: April 2017 to December 2021

Study Population

✓ Adults aged ≥65 years
✓ Primary diagnosis of NEN
✓ Continuous Medicare coverage
✓ No pancreatic NENs, NSCLC, or SCLC

Definition of CS

≥1 claim for CS (E43.0) or CHD (I36.0, I36.8) **OR** ≥2 claims for diarrhea (K59.1, R19.7) and/or flushing (R23.2)

within the predefined study window (ie, 3 months prior to diagnosis and up to 6 months after)

Key Outcomes

✓ Frequency of CS over the study period
✓ Disease characteristics (eg, tumor stage, grade)
✓ Use of common treatments (eg, SRLs, PRRT)

} In patients with vs without CS

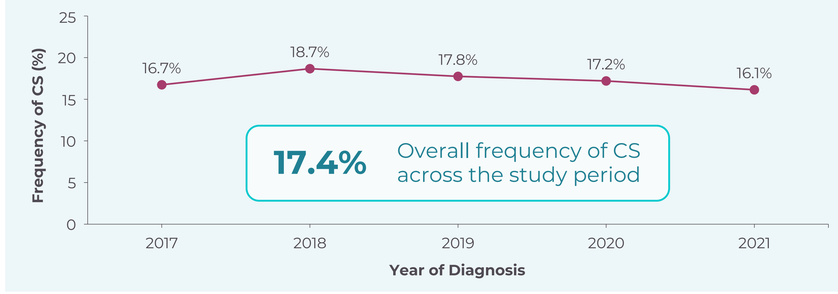
Statistical Analysis: Chi-square tests, multivariable logistic regression

Diagnostic codes for the definition of CS per ICD-10.
CHD = carcinoid heart disease; CS = carcinoid syndrome; ICD-10 = International Classification of Diseases, 10th Revision; NEN = neuroendocrine neoplasm; NSCLC = non–small cell lung cancer; PRRT = peptide receptor radionuclide therapy; SCLC = small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results; SRL = somatostatin receptor ligand.

RESULTS

- Of 8966 patients diagnosed with extrapancreatic NENs between April 2017 and December 2021, an estimated 1558 (17.4%) had claims supporting a diagnosis of CS
  - Patients with CS were more likely to be female than patients without CS (62.5% vs 58.0%; *P*=0.001)
  - The frequency of CS was largely stable over the study period

Frequency of CS Among Older Adults With Extrapancreatic NENs (2017-2021)

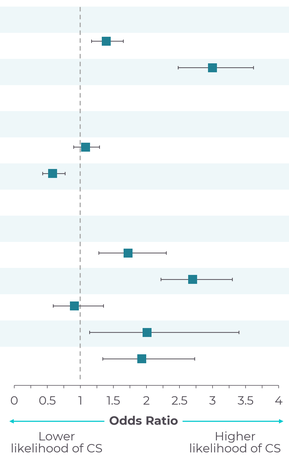


CS = carcinoid syndrome; NEN = neuroendocrine neoplasm.

- According to multivariate logistic regression analyses, patients with midgut tumors and regional or distant disease were more likely to have CS, and patients with grade 3 tumors were less likely to have CS (*P*<0.001 for all)

Effect of Tumor Stage, Grade, and Primary Site on the Likelihood of CS

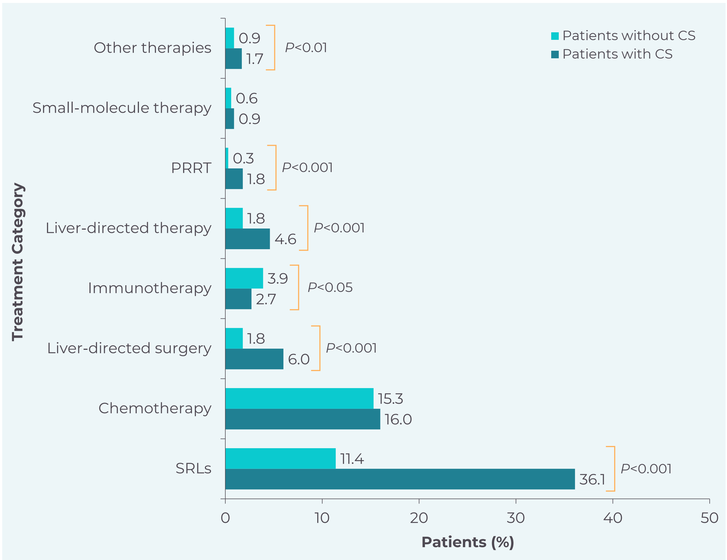
Patients, n (%)	With CS (n=1558)	Without CS (n=7408)	Odds Ratio	95% CI	*P*
Tumor Stage					
Localized	534 (34.3)	3855 (52.0)	*Reference category*		
Regional	390 (25.0)	1642 (22.2)	1.39	1.17-1.65	**<0.001**
Distant	436 (28.0)	1062 (14.3)	3.00	2.48-3.62	**<0.001**
Tumor Grade					
Grade 1	822 (52.8)	3914 (52.8)	*Reference category*		
Grade 2	222 (14.2)	794 (10.7)	1.08	0.90-1.29	0.395
Grade 3	73 (4.7)	473 (6.4)	0.58	0.43-0.77	**<0.001**
Primary Site					
Lung and bronchus	284 (18.2)	2607 (35.2)	*Reference category*		
Stomach	123 (7.9)	712 (9.6)	1.72	1.28-2.30	**<0.001**
Midgut	860 (55.2)	2662 (35.9)	2.70	2.22-3.30	**<0.001**
Rectum	47 (3.0)	491 (6.6)	0.91	0.59-1.35	0.640
Colon	29 (1.9)	130 (1.8)	2.01	1.14-3.40	**0.012**
Other sites	215 (13.8)	806 (10.9)	1.93	1.34-2.73	**<0.001**



Data based on multivariate logistic regression analyses. Midgut includes small intestine, cecum, and appendix.
CI = confidence interval; CS = carcinoid syndrome.

- Across all tumor grades, patients with CS received more treatments than those without CS
  - Somatostatin receptor ligands (SRLs; octreotide, lanreotide) were the most common treatment overall

Treatment Use in Patients With and Without CS in the First Year Post–NEN Diagnosis



Small-molecule therapy refers to belzutifan, cabozantinib, everolimus, lenvatinib, pazopanib, and sunitinib; PRRT refers to lutetium ^{177}Lu-DOTATATE; and other therapies refers to cyproheptadine, ketoconazole, and telotristat. *P* values comparing treatment rates across patients with and without CS calculated using chi-square tests.
CS = carcinoid syndrome; NEN = neuroendocrine neoplasm; PRRT = peptide receptor radionuclide therapy; SRL = somatostatin receptor ligand.

CONCLUSIONS

- Analysis of a large population database of older adults found the frequency of CS at the time of NEN diagnosis (ie, 3 months prior to and up to 6 months after) is approximately 17% and has remained relatively steady over time
- In the year following a NEN diagnosis, the use of SRLs was lower than anticipated, suggesting potential barriers to uptake and/or inaccurate coding of patients with CS
- Standardized approaches for diagnosing CS, along with studies with a wider age range and/or longer follow-up period, are warranted

References
1. Sultana Q, et al. *J Clin Med*. 2023;12(15):5138. **2.** Dasari A, et al. *JAMA Netw Open*. 2025;8(6):e2515798. **3.** Grozinsky-Glasberg S, et al. *J Neuroendocrinol*. 2022;34(7):e13146. **4.** Halperin DM, et al. *Lancet Oncol*. 2017;18(4):525-534.

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