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## INTRODUCTION

### Background:

- Delayed diagnoses are reportedly common in patients with neuroendocrine tumor.
- Few studies have prospectively characterized the type and duration of presenting symptoms in this patient population.

### Objective:

- We aimed to characterize the presenting symptoms of neuroendocrine tumor patients and to estimate the duration of symptoms prior to diagnosis.

## METHODS

### Patient population

- Case recruitment at the Dana-Farber Cancer Institute (DFCI) from 2003-2010 for a prospective study
- 937 NET patients enrolled
- 717 patients completed questionnaires regarding type of symptoms prior to diagnosis.
- 393 symptomatic patients completed questionnaires regarding duration of symptoms prior to diagnosis

### Statistics

- Symptom type and duration summarized in the cohort overall and in subgroups of patients with small bowel carcinoid (SBC), pancreatic NET (panNET), or other NET.
- Variables associated with symptom duration prior to diagnosis were evaluated by a multivariate Cox proportional hazards regression analysis adjusting for age and stage at diagnosis, gender, tumor origin, and grade of differentiation

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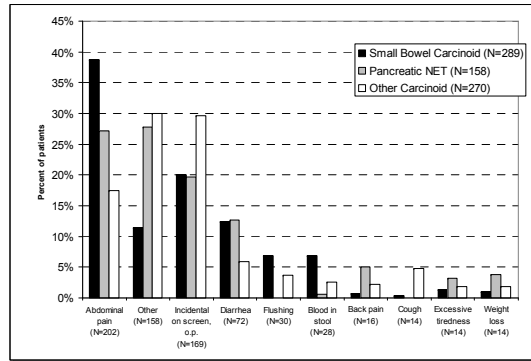
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## I. Population Characteristics

**Table 1: Baseline Characteristics of the Patient Population (N=717)**

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Median Age at Diagnosis (range)</b>  | 54 yrs (13-85)             |
| <b>Gender (M,F)</b>                     | 325 (45%)<br>392 (55%)     |
| <b>Well differentiated</b>              | 624 (87.0%)                |
| <b>Moderately differentiated</b>        | 45 (6.3%)                  |
| <b>Poorly differentiated</b>            | 27 (3.8%)                  |
| <b>Unknown</b>                          | 21 (2.9%)                  |
| <b>Metastatic at Diagnosis (no/yes)</b> | 317 (44.2%)<br>400 (55.8%) |
| <b>Small Bowel Carcinoid</b>            | 289 (40.3%)                |
| <b>Pancreatic NET</b>                   | 158 (22.0%)                |
| <b>Other NET</b>                        | 270 (37.7%)                |
| <b>Symptoms prior to diagnosis</b>      | 548 (76%)                  |
| <b>Incidental diagnosis</b>             | 169 (24%)                  |

## II. Patient-reported symptoms by tumor subgroup



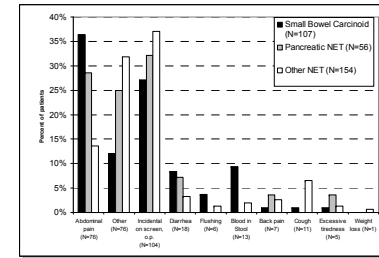
**Figure 1.** Patient-reported symptoms, entire cohort (N=717)

Other symptoms include: bone pain, chest pain, constipation, difficulty swallowing, enlarged lymph nodes, fever/night sweats, jaundice, shortness of breath, shoulder pain, vomiting blood

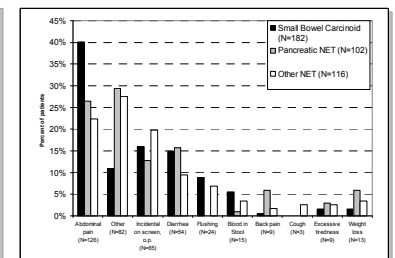
- Abdominal pain was the most common single complaint with gastrointestinal NET**
- Diarrhea was reported in 12% of SBC and 13% of panNET**
- Flushing was reported in 7% of SBC and 0% of panNET**
- Incidental diagnoses were common, reported in 24% of the cohort overall (20% SBC, 20% panNET, 30% other NET)**

## RESULTS

## III. Patient-reported symptoms by stage and tumor subgroup



**Figure 2.** Symptoms reported by patients with localized disease (N=317)



**Figure 3.** Symptoms reported by patients with metastatic disease (N=400)

- Incidental diagnosis was more common in patients with localized disease (33%) than in those metastatic at diagnosis (16%)**
- Symptoms of flushing or diarrhea were less common in patients with localized disease than in those metastatic at diagnosis**
  - Flushing: 2% in localized and 4% in metastatic
  - Diarrhea: 6% in localized and 14% in metastatic

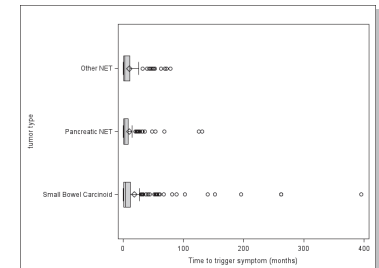
## IV. Time from Onset of Symptoms to Diagnosis

**Table 2.** Patient-reported Time from Initial Onset of Symptoms to Diagnosis (N=393)

|                  | N   | Median (months) | Mean (months) |
|------------------|-----|-----------------|---------------|
| <b>Overall</b>   | 393 | 3.4             | 13.9          |
| <b>SBC</b>       | 174 | 4.3             | 18.5          |
| <b>panNET</b>    | 104 | 2.9             | 10.2          |
| <b>Other NET</b> | 115 | 2.9             | 10.2          |

**Table 3.** Variable association with shorter duration of symptom prior to diagnosis (N=393)

| Variable                         | aHR (95%CI), p-value   |
|----------------------------------|------------------------|
| <b>Age at diagnosis</b>          | 1.0 (0.9, 1.0) p=0.89  |
| <b>Stage at diagnosis</b>        | 0.9 (0.7, 1.2) p=0.53  |
| <b>Gender (F=ref)</b>            | 1.1 (0.9, 1.3) p=0.42  |
| <b>panNET</b>                    | 1.1 (0.8, 1.5) p=0.47  |
| <b>SBC</b>                       | 0.9 (0.7, 1.2) p=0.62  |
| <b>Moderately differentiated</b> | 1.4 (0.9, 2.1) p=0.1   |
| <b>Poorly differentiated</b>     | 2.5 (1.6, 4.0) p<0.001 |
| <b>Unknown diff.</b>             | 1.4 (0.7, 2.7) p=0.3   |



**Figure 4.** Patient-reported Time from Initial Onset of Symptoms to Diagnosis (N=393)

- The median time from symptom onset to diagnosis was 3.4 months and mean was 13.9 months for NET overall**
- There are large differences between medians and means for each tumor subgroup, due to extreme outliers, particularly for SBC**
- Only poor grade of differentiation was significantly associated with a shorter symptom duration prior to diagnosis**

## Discussion and Conclusion

- Our study suggests that abdominal pain is the most common symptom leading to diagnosis of gastrointestinal NET.**
- Symptoms of hormone hypersecretion are relatively uncommon, and when they do occur, patients are more likely to already have metastatic disease**
- The majority of NET patients appear to be diagnosed less than 4 months after symptom onset, yet prolonged symptom duration prior to diagnosis remains a prominent feature of this disease**
- Further effort is needed to facilitate an earlier diagnosis for patients with NET**