

THE IMPORTANCE OF EARLY DIAGNOSIS OF NEUROENDOCRINE TUMOURS

How early diagnosis can help to ease the disease burden of neuroendocrine tumours

Introduction

Neuroendocrine tumours (NETs) are a heterogeneous group of neoplasms that originate from endocrine cells.¹

NETs are a rare cancer with an estimated prevalence of 35 cases per 100,000 people² and can be divided into two groups: functional and non-functional.³ Functional tumours are typically characterised by the hormones they secrete.³ Carcinoid syndrome, the most common hormonal disorder, is characterised by flushing, diarrhoea and bronchospasm.⁴ Non-functional tumours are free of hormone-related symptoms.³ Approximately two-thirds of NETs derive from the gastrointestinal system and represent the group of gastroenteropancreatic neuroendocrine tumours (GEP-NETs).⁵ Most GEP-NETs are non-functional; therefore, patients with GEP-NETs may lack the symptoms associated with hormone hypersecretion, which may lead to delays in diagnosis.^{1,3,6}

The burden of GEP-NETs on patients

NET-related symptoms, such as abdominal pain, bowel obstruction and diarrhoea are common symptoms of NETs and can persist for long periods of time before a diagnosis is made, thus placing a large burden on the patient and their quality of life (QoL).^{3,4} Multiple studies have shown that patients with NETs have a lower health-related QoL compared with the general population.⁷⁻⁹ One survey-based study involving 1,928 patients with NETs reported that a NET diagnosis had a significant negative impact on patients' personal and work lives.³ Patients reported that they experienced multiple NET-related symptoms such as fatigue, diarrhoea and abdominal pain on a daily basis and that the diagnosis had a negative impact on their day-to-day lives, including overall energy levels (70%), finances (50%) and the ability to perform everyday household tasks (45%) or care for family (39%).³ In addition, almost two-thirds of patients stated that living with NETs substantially affected their emotional health.³ Nearly three-quarters of patients reported that NETs had at least a moderate negative impact on their lives.¹⁰

Diagnostic delay in NETs

The delay in the diagnosis of NETs may also contribute to the burden on patients.³ Due to the non-specific nature of NET symptoms, there is no clear pathway of care for these patients.³ Patients may see multiple specialists and undergo extensive and repetitive testing, leading to inaccurate diagnoses and varying, potentially conflicting, treatments.³ Survey-based studies have shown that patients saw a mean of 5.7–6.2 healthcare professionals (HCPs) across a mean of 11.8–12.7 doctor visits from symptom onset to receiving a diagnosis of NETs.^{3,10} Patients would like to see improvements in NET care, such as clearer information on the long-term impact of NETs (66%), increased access to NET specialist HCPs (63%) and more knowledgeable HCPs (58%).¹⁰ The survey results demonstrate several unmet needs contributing to diagnostic delay, including a lack of specialist NET centres, as well as low access to medical teams with knowledge of NETs.¹⁰

In a survey-based study in the USA, approximately 50% of patients reported being incorrectly diagnosed with another condition before receiving a diagnosis of NETs.¹⁰ In 34% of these patients, a diagnosis took five years or more.¹⁰ Patients with NETs were most commonly misdiagnosed as having irritable bowel syndrome (n=182/368; 49%), gastritis or another gastric disorder (n=169/368; 46%), or anxiety or a psychosomatic-type condition (n=97/368; 26%) (**Figure 1**).¹⁰

A global survey of patients (n=1,670) found similar results: 44% of patients with GEP-NETs were misdiagnosed.¹¹ The most common misdiagnoses were gastritis (n=254/582; 44%), irritable bowel syndrome (n=254/582; 44%) and anxiety (n=131/582; 23%).¹¹ At the time of diagnosis, it was estimated that 38% of patients had stage IV NETs or metastases.¹¹ In addition, a prospective database study (N=900 patients) showed that 44% and 56%

Figure 1: Diagnoses received before a NET diagnosis. Question: Which of the following conditions were you initially diagnosed with before receiving a NET diagnosis? NET = neuroendocrine tumour.

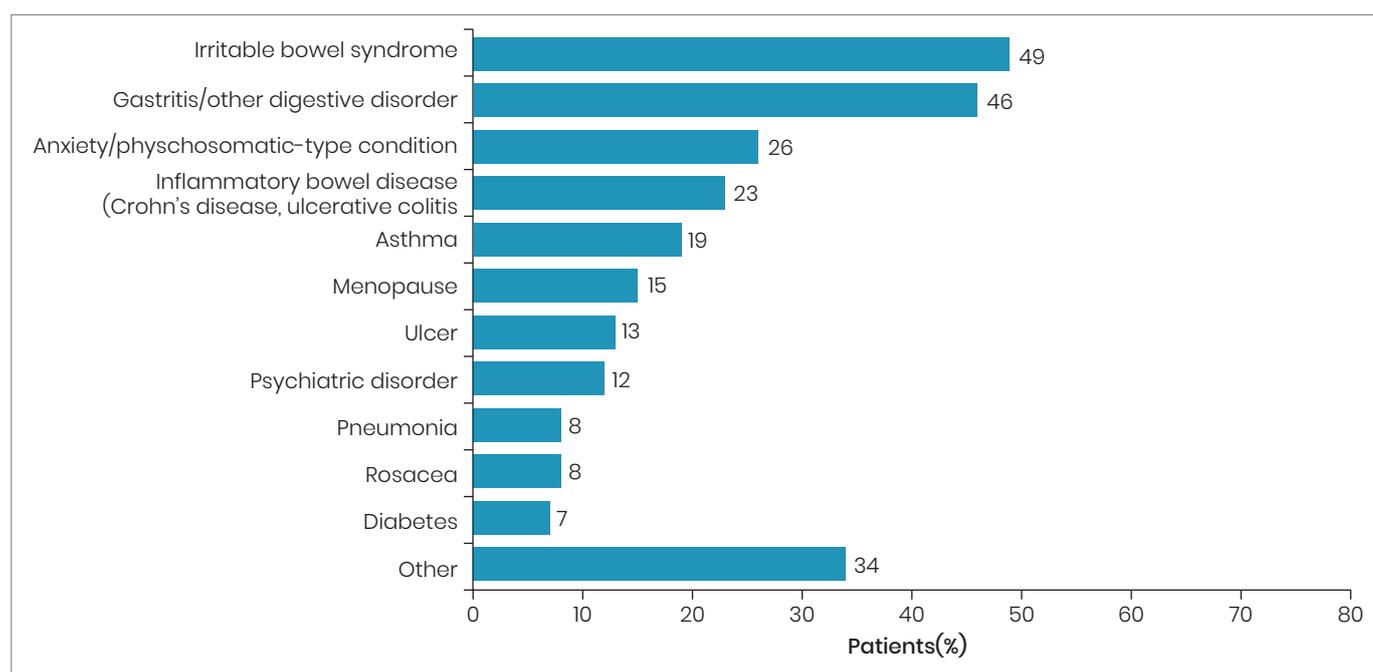


Figure sourced from: Wolin, et al. 2017¹⁰

of patients with NETs had localised disease and distant metastases, respectively, at the time of their initial diagnosis.¹² Therefore, delays in diagnosis may increase the probability of patients progressing to advanced or metastatic disease.¹³

Early diagnosis of GEP-NETs

Clinical signs and symptoms in patients with non-functional tumours are usually due to the local invasion of the tumour mass and the formation of distant metastases.¹ For example, in patients with GEP-NETs, common non-specific symptoms are abdominal pain and change in bowel habit.^{14,15} Therefore, the diagnosis of NETs requires careful investigation of these vague non-specific symptoms.² Earlier diagnosis of NETs may improve QoL and survival as well as reduce healthcare costs.¹⁵

The prognosis of patients with NETs is associated with the primary location, stage and grade of the disease.¹⁶ It is estimated that the five-year survival of patients with a grade 1 GEP-NET is 96%, and 73% for patients with a grade 2 tumour.¹⁶ In terms of disease stages, the five-year survival is estimated to be 95% in localised disease, 85% in cases with regional lymph node involvement and 45% in metastatic disease.¹⁶ The stage and grade of a tumour will also affect what treatments are available to patients.¹⁷ For instance, surgery, which may be potentially curative, is the first-line treatment for local or locoregional grade 1 or grade 2 NETs.^{18,19} However, in patients with advanced or metastatic disease, curative surgery is mostly not an option.^{18,19} In these patients, systemic treatments, such as peptide receptor radionuclide therapy (PRRT), somatostatin analogues, mammalian target of rapamycin (mTOR) inhibitors, tyrosine kinase inhibitors and others may be used to reduce tumour growth.^{18,20}

Conclusion

NET-related symptoms can persist for long periods of time before a diagnosis is made, thus potentially placing a large burden on the patient.³ Multiple studies have shown that patients with NETs have a lower health-related QoL compared with the general population.⁷⁻⁹ Most GEP-NETs do not secrete biologically active substances; therefore, these patients typically lack symptoms, which can lead to a delay in diagnosis.¹⁸ The stage and grade of a tumour will affect what treatments are available to patients and those with metastatic disease may not be eligible for potentially curative surgery.^{18,20} Systemic therapies may be viable treatment options in these patients.^{18,21}

This report was developed as part of the touchFEATURE activity, 'The importance of early diagnosis in NETs'. To view the full touchFEATURE activity, which also includes engaging videos, please visit: <http://www.touchoncologytmc.com/neuroendocrine-tumours/learning-zone/results-from-NETTER-1-trial/>.

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Abbreviations: GEP-NET, gastroenteropancreatic neuroendocrine tumour; HCP, health care professional; PRRT, peptide receptor radionuclide therapy; mTOR, mammalian target of rapamycin; NET, neuroendocrine tumour; QoL, quality of life.