Original Article

Management of gastrointestinal carcinoid tumours - 10 years experience at a district general hospital

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ABSTRACT

Background: There is paucity of guidelines regarding management of gastrointestinal carcinoid tumours in district hospitals.

Methods: This study was undertaken at a district hospital to analyse the management pathway of gastrointestinal carcinoid tumours.

Results: Over a period of 10 years there were 35 patients, with an estimated annual incidence of 2.5 per 100,000 population. After a median follow up of 24 months, 22 (63%) patients were alive and disease free. Only 56% patients were referred to the regional neuro-endocrine multidisciplinary team.

Conclusions: Management of patients with carcinoid tumours in district hospitals needs streamlining with increased utilisation of regional neuroendocrine multidisciplinary teams.

KEYWORDS

Gastrointestinal carcinoid tumours; neuro-endocrine tumours; district hospital

Introduction

Carcinoids are neuroendocrine tumours (NETs) arising from the diverse group of enterochromaffin cells. The common sites of carcinoid tumours include appendix, rectum, ileum, lung, bronchi and stomach (1-3). The overall incidence of carcinoid tumours has been steadily increasing and they are considered to be more aggressive with a poorer prognosis than previously thought (4-6). Gastrointestinal carcinoid tumours (GICTs) can be classified as foregut, midgut and hindgut carcinoids depending on the site of their origin. Diagnosis of GICTs can be challenging as most often they are asymptomatic and have advanced disease by the time of clinical presentation. The diagnosis of GICTs is often not made until after operative exploration for acute presentation with bowel obstruction, perforation or gastrointestinal bleeding. Although more recently staging systems for GICTs have been published, the long term prognosis is still not clear (7). Until recently there were no clear guidelines regarding diagnosis, referral, management and follow up of patients with GICTs (8).

Most published studies on GICTs originate either from large tertiary centres or are based on pooled data from multicentre studies. The current study was done to review the literature on the management of patients with GICTs and to compare our experience in managing these patients at a district general hospital catering to a stable urban population within the National Health Service (NHS) over the last decade.

Materials and methods

This single centre, retrospective study was undertaken at the South Tyneside District Hospital (STDH), South Shields, United Kingdom, between the period January 1999 to January 2009. The study was approved by the Trust audit and research committee. The hospital histopathology database was searched using the keywords 'carcinoid' and 'neuroendocrine tumour' to obtain a list of patients eligible for inclusion in the study. Only those patients with carcinoids arising from the gastrointestinal tract were included in the study. Using a pre-designed proforma, data...
including demographic information, presenting complaints, diagnostic methods, surgical procedures, histopathology and follow-up were extracted from the hospital case records and where necessary from contact with the patient's general practitioner. The data was transferred onto Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, Washington, USA) and analysed using the statistical program SPSS version 15 (SPSS, Chicago, Illinois, USA).

An important part of the study was to critically review the current evidence on the management of GICTs and thus, a systematic literature search of PubMed, Ovid and Cochrane was performed for keywords "gastrointestinal carcinoids and gastrointestinal neuro-endocrine tumours". Relevant publications were reviewed and compared with our results at STDH in order to generate conclusions and recommendations for the management of GICTs within the confines of small district hospitals.

Results

At STDH which is a small hospital providing healthcare services to a population of about 160,000, a total of 35 patients (17 males, 18 females; mean age 62±15.7 years, ranging from 20 to 92 years) were identified for inclusion in this study. This gives an estimated annual incidence of around 2.2 per 100,000 population. Patients presented with a wide spectrum of symptoms but by no means specific to carcinoid tumours. Figure 1 summarises the symptomatology in patients from the current study; the most frequently encountered symptoms being abdominal pain (66%), vomiting (31%) followed by rectal bleeding (20%). None of the patients in this series had symptoms of carcinoid syndrome.

Whilst pre-operative diagnosis of carcinoid tumour was confirmed following endoscopic biopsy of suspicious lesions in 13 (37%) patients; the remaining 22 (63%) patients had their definitive diagnosis established by immunohistopathology of the resected specimens following surgery. A total of 24 (69%) patients had a CT scan of abdomen, of which 4 (11%) had mesenteric lymph node mass and 6 (17%) had evidence of distant metastases in liver and/or lung. CT scan of one patient with midgut carcinoid demonstrating a circumscribed mesenteric mass with associated radiating mesenteric stranding is shown in Figure 2; this finding is considered to be rare but pathognomonic of small bowel carcinoid (3). Urinary 5-hydroxyindolacetic acid (5-HIAA) levels were checked in 6 (17%) patients and this was elevated in 2 patients (9); both patients had multiple liver metastases.

Figure 3 summarises the distribution of the GICTs in the current study and the majority of these tumours 21 (60%) were midgut carcinoid tumours. Of note, 16 (76%) of these patients presented acutely with abdominal pain and/or small bowel obstruction needing emergency surgery. Details of the surgical treatment of all patients are shown in Table 1. The type and the extent of the surgery varied with the site of the primary, presence of advanced disease and patient's performance status. Twenty seven (77%) patients had localized disease and were operated with a curative intent. Of the remaining 8 (23%) patients, 6 (17%) had extensive mesenteric lymph node involvement and 2 (7%) had distant visceral metastasis; surgery being either diagnostic biopsy only (n=4) or palliative resection (n=4). There were no peri-operative deaths but 2 patients who had emergency laparotomy for small bowel obstruction secondary to ileal carcinoids had to be re-operated for anastomotic leaks.

The size of the primary tumour on histology of the resected specimens ranged from 0.8 to 3.6 cm with a mean size of 2±0.9 cm. Immunohistochemistry was typical for carcinoids across all the tumours showing positive staining with Synaptophysin and Chromogranin A (Figure 4). 31 out of the 35 (89%) GICTs were well differentiated neuro-endocrine carcinomas with < 2 mitoses per high power field.

Whilst there was no fixed protocol for follow up schedule and investigations, all cases were discussed at the local GI MDTs. Referral to regional neuroendocrine multidisciplinary team (NET-MDT) services started in 2006 and of the 18 patients who were diagnosed with GICTs post 2006, 10 (56%) patients were referred to this service. In the current study, after a median follow up of 24 months (range 2-96 months), 22 patients (63%) were alive and disease free and 4 patients (11%) were alive with disease. Seven patients (20%) have died with disease and 2 patients were lost to follow up.

Discussion

GICTs account for approximately 75% of all neuroendocrine tumours and according to a recent large population based survey there has been a significant increase in the annual age adjusted incidence rates of carcinoids tumours (from 1.09/100,000 in 1973 to 5.25/100,000 in 2004) (6). Based on their embryonic origin, GICTs are classified as foregut, midgut and hindgut carcinoids. They are slow growing lesions and as a result, patients usually complain of a wide variety of non-specific abdominal pains/symptoms which eventually progress to episodes of small bowel obstruction (10) or rarely gastrointestinal bleeding. Furthermore, in a significant proportion of these patients, the diagnosis is not revealed until after emergency surgery. Table 2 summarises the distribution, characteristics and clinical manifestations of GICTs from the pooled data of
Figure 1  Presenting symptoms in patients with GICTs in the current study

Figure 2. (A and B) CT scan images (contrast enhanced) of a 67 yr lady presenting with small bowel obstruction showing an ileal carcinoid causing circumferential mural thickening of a segment of ileum with adjacent radiating mesenteric thickening and stranding (white arrow).

Figure 3. Distribution of GICTs (n=35) at STDH during the period 1999-2009.
Table 1. Surgical treatment of gastro-intestinal carcinoid tumours at South Tyneside District Hospital.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of pts (%) (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendicectomy</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Right Hemicolectomy</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Resection &amp; anastomosis of small bowel</td>
<td>8 (23)</td>
</tr>
<tr>
<td>Transanal / endoscopic excision</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Anterior Resection</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Gastrrectomy</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Whipples procedure</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Biopsy</td>
<td>4 (11)</td>
</tr>
</tbody>
</table>

Figure 4. Immunohistochemical staining of the ileal carcinoid tumour highlighted in Figure 2 with synaptophysin 10× (A) and with chromogranin immunoperoxidase, 10× (B). Note the nesting (insular) pattern of cell arrangement.

Table 2. Distribution and characteristics of gastrointestinal carcinoid tumours.

<table>
<thead>
<tr>
<th>Carcinoid site</th>
<th>Clinical presentation¹</th>
<th>Age at presentation (yr)¹</th>
<th>Percent per site²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>Anaemia, abdominal pain, haematemesis, melaena</td>
<td>60 to 70</td>
<td>6</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>Abdominal pain, small bowel obstruction</td>
<td>60 to 70</td>
<td>39</td>
</tr>
<tr>
<td>Duodenum</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Jejunum</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Ileum</td>
<td></td>
<td></td>
<td>32</td>
</tr>
<tr>
<td>Appendix</td>
<td>Appendicitis</td>
<td>40 to 50</td>
<td>18</td>
</tr>
<tr>
<td>Colon</td>
<td>Abdominal pain, anorexia, change in bowel habits</td>
<td>70</td>
<td>12</td>
</tr>
<tr>
<td>Rectum</td>
<td>Rectal bleeding, pain, change in bowel habits</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>Liver</td>
<td>Abdominal pain, anorexia, deranged liver function tests</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>Abdominal pain, deranged liver function tests</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Abdominal pain, anorexia</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Digestive tract, NOS</td>
<td></td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

¹Robertson et al. 2006 (5). ²Pooled data (n=9,421) from End Results group, Third National Cancer Survey and Surveillance, Epidemiology and End Results programme registries of National Cancer Institute (4). NOS-Not otherwise specified.
The primary lesion in MCs is usually a small (<1 cm), flat and fibrotic tumour in the submucosal plane of the ileum and is frequently not diagnosed until surgical exploration. Other operative findings usually include enlarged lymph nodes with associated mesenteric fibrosis leading to kinking of the bowel and thus obstruction. This extensive mesenteric stranding and fibrosis is probably secondary to the release of serotonin and growth factors from tumour cells and can also lead to the encasement of mesenteric vessels leading to ischemia of the bowel.

Appendiceal carcinoids are the most common malignant tumours of the appendix and are diagnosed incidentally in 0.3–0.9 per cent of patients undergoing appendicectomy (17). They are usually diagnosed in the fourth and fifth decades of life (11). Appendiceal carcinoids are more common in women (11), usually located in the distal third of the appendix where they do not cause any obstruction and thus remain asymptomatic (18). Size of the tumour is considered to be of prognostic value with more than 95 per cent of appendiceal carcinoids being less than 2 cm and rarely metastasising (19). In such patients, simple appendicectomy is curative whereas those whose tumours are greater than 2 cm, should in addition be treated with right hemicolecction (18). Treatment for lesions between 1 and 2 cm is controversial and the decision for right hemicolecction depends on factors like mesoappendiceal invasion, vascular invasion, mitotic activity, proliferation markers and patient risk factors (20,21). Goblet cell appendiceal carcinoids tend not to produce a grossly visible tumour mass but diffusely infiltrate the wall and have features of both carcinoid and adenocarcinoma (22,23). These patients should be offered hemicolecction.

Colon carcinoids account for about 12% of all carcinoid tumours but only 1% of colonic tumours. There is a slight female predominance and most patients commonly present in the seventh decade of life (24) with symptoms of pain, anorexia and weight loss (25); two thirds of colonic carcinoids being found on the right side with the majority in the caecum (25,26). Amongst all of the GICTs, colonic carcinoids are associated with a worse prognosis (27), with most of the patients presenting with advanced disease with an average tumour size of 5 cm and over two thirds having nodal and/or distant metastases (25,26). Colonic carcinoids are usually non-functional with less than 5 per cent containing cells producing serotonin and these patients can present with carcinoid syndrome (25,28,29). Clinically colonic carcinoids should be managed as colonic adenocarcinomas with radical colectomy and metastasectomy as appropriate (15,30). Also, if present, widespread metastatic disease should not preclude removal of the primary lesion (15).

Rectal carcinoids account for 2 per cent of rectal tumours and differ from other GICTs in that the neuroendocrine cells contain mostly glucagons and glicentin related peptides rather than serotonin (31). They are most common in the sixth decade of life (11), with patients presenting with pain, constipation and rectal bleeding. However, nearly half of the patients are asymptomatic and the lesions are found incidentally at routine endoscopy (32). The majority of these tumours are less than 1 cm in size and are best treated by local excision (32), whereas those lesions greater than 2 cm have traditionally been treated with anterior resection or abdomino-perineal resection. This practice has been recently questioned as there does not appear to be much survival advantage over and above that achieved by local excision (33,34).

The clinical course of patients with metastatic carcinoid tumour is highly variable, with some patients remaining symptom-free for years (19). Liver is the commonest site...
of distal spread from GICTs which also rarely metastasise to extra-abdominal organs including bone, lung, central nervous system, mediastinal and cervical lymph nodes. Carcinoid liver metastases tend to be hypervascular and thus appear isodense on conventional post-contrast CT scans (35,36). Resection of carcinoid liver metastasis is indicated in fit patients who do not have extra-hepatic metastatic disease, no tricuspid valve deficiency and have a resectable primary disease (37). Selective hepatic trans-catheter arterial embolization and trans-catheter arterial chemoembolisation can be used to treat liver metastasis in patients where major resections are not feasible. Radiofrequency ablation of liver metastases has been attempted in patients where arterial embolisation fails. Response rate of 80-95% have been reported following this treatment (38,39).

Carcinoid syndrome is typically seen in patients with liver/lung metastases with an overall incidence of 10% in GICTs but 20% in those with jejuno-ileal disease (2,4). Typical symptoms of carcinoid syndrome include flushing, diarrhoea, tachycardia, hypotension, bronchospasm and right heart failure; carcinoid heart disease is a late and potentially fatal complication presumed to be secondary to endocardial fibrosis of right side heart valves leading to pulmonary stenosis and tricuspid insufficiency. Whilst the exact chemicals responsible for the symptoms are yet to be clearly defined, the diarrhoea is probably secondary to excessive circulating levels of serotonin whereas bronchospasm is due to both serotonin and bradykinin. Prolonged high serum levels of serotonin is responsible for carcinoid heart disease (40) but valves of the left side of the heart are less affected because of the metabolism of serotonin within the lungs. Measurement of elevated levels of urinary 5-HIAA have been shown to be of value in predicting carcinoid syndrome (41). Somatostatin analogues are effective in controlling the symptoms and improve the quality of life in patients with carcinoid syndrome. They can be administered pre-operatively and continued for about 48 hours in the post-operative period to prevent a carcinoid crisis (37).

**Diagnosis**

**Biochemical tests**

Carcinoid tumour cells originate from neuroendocrine cells and are capable of synthesis, storage and release of serotonin, histamine, prostaglandin, kallikrein, bradykinin, substance P, gastrin, corticotrophin and neuron specific enolase. The most abundant of these is serotonin (5-hydroxytryptamine) which after metabolising is converted to 5-hydroxyindolacetic acid (5-HIAA), Determination of raised 5-HIAA levels in 24-hr urine samples is routinely used for diagnosis of carcinoids but it is neither specific nor sensitive as it may not be elevated in some carcinoids whereas it can be elevated in conditions like tropical sprue, coeliac disease, Whipple's disease and small bowel obstruction (5). Serum chromogranin A levels have been shown to reflect tumour load and provide evidence of persistent or recurrent carcinoid disease and is a useful parameter to monitor disease spread and recurrence (42). Presence of carcinoembryonic antigen is a poor prognostic indicator and these tumours are often classified as adenocarcinoids and treated as adenocarcinomas rather than carcinoids (43,44).

**Radiology**

Plain abdominal films may show features consistent with obstruction (dilated bowel loops with thickened walls). CT rarely demonstrate the primary lesion but the delineation of a circumscribed mesenteric mass with associated radiating mesenteric stranding is considered to be pathognomonic of a GICT [as illustrated in one of our patients (Figures 2a and 2b)]. CT is also used to identify liver metastases but as these lesions are hypervascular (vide supra), a porto-venous phase scan is considered to be more sensitive in diagnosing smaller lesions (35,36). GICT cells are rich in somatostatin receptors which have a high affinity for Octreotide and as a result, Octreoscan (a radio-labelled Octreotide scintigrapy) is currently employed to detect metastases and recurrent disease with more than 90% sensitivity (45). Similarly, positron emission tomography (PET) with 5-hydroxytryptophan (serotonin precursor) labelled with C (SHTPET) has been shown to have high specificity and is now used to monitor the effects of therapy (46).

**Histology**

Depending on the histological appearances, mitotic and proliferation indices, GICTs are classified as well differentiated neuroendocrine tumours, well differentiated endocrine carcinomas, poorly differentiated endocrine carcinomas and mixed exocrine/endocrine tumours (47). Proliferation index is assessed using immunostaining with Ki67 antibody and is usually low (<2%) in classical MCs. Whilst 85% of all MCs and their metastases react to chromogranin A and synaptophysin (Figure 3) positive immunoreactivity to serotonin on the other hand, implies that the primary tumour originates from the midgut (2,48).

**Treatment**

Surgery continues to be the main modality of treatment for GICTs with a potential to cure in early stage disease and
providing best palliation in those with advanced disease. Whilst the type and nature of surgery depends on the site and extent of the primary lesion, it is important to note that most patients with MCs are subjected to laparotomy without the awareness of a diagnosis of carcinoid tumour. Usually a wedge resection including the bowel segment containing the primary tumour and the involved lymph nodes are excised; this procedure is also indicated in those patients with synchronous liver metastases, as local disease if left untreated can lead to significant morbidity (2). Despite curative primary surgery, 80% of patients with MCs develop recurrence and these are usually evident after a median follow up of 5-10 years (3). The recurrent disease plus mesenteric fibrosis can manifest as chronic abdominal pain, intestinal obstruction and/or bowel ischaemia necessitating further surgical intervention (49,50) but earlier diagnosis of the recurrence can often be accomplished by serial estimation of serum chromogranin A levels (10).

Recently prophylactic surgery to remove mesenterico-intestinal tumour in asymptomatic patients has been advocated because patients who receive and survive medical treatment can still present with major intra-abdominal complications from the mesenteric disease (2). Pre-operative mapping of the extent of the disease within the mesentery and assessment of the involvement of the root of the major mesenteric vessels with dynamic CT scan is now considered mandatory in treatment planning. Tumour debulking in patients with advanced mesenteric metastases in the absence of liver metastases has been reported to achieve a 5-year survival of 91% (with a median survival of 12.4 years) (51). Operating on patients with carcinoid syndrome can induce carcinoid crisis (hyperthermia, shock, arrhythmia, excessive flush and bronchial spasm) and as a prophylaxis, it is important for these patients to be given intravenous octreotide (500 μg in 500 mL saline, 50 mL/hour) during surgery.

Liver metastases

The majority of carcinoid patients with liver metastases have multiple lesions widely spread in both lobes and need medical treatment including somatostatin and interferon, which are effective in symptom control as well as increasing the life expectancy (42). Less than 10% of patients have solitary or dominant lesions which are amenable for surgical resection (10). Other modalities used to treat liver metastases include radiofrequency ablation, liver embolisation, transplantation, radioactive labelled octreotide and meta-iodobenzylguanidine (MIBG) (2,42). Radiofrequency ablation which is being increasingly used, can induce necrosis of lesions up to 3-4 cm in size but, is not very effective for lesions close to major vessels. Significant and sustained symptom relief as well as reduction in tumour markers can be achieved if greater than 90% of tumour volume has been ablated or excised (52). Almost all patients who had curative liver resection will develop new metastases which typically show slow progression and are unusually tenacious; imaging even with specific methods such as octreotide scan and 5-HTP PET may fail to detect disease progression.

Medical treatment

Somatostatin is a peptide that inhibits the secretion of a number of hormones (growth hormone, insulin, glucagon and gastrin) (53) and a significant proportion of GICTs (>80%) have been shown to express somatostatin receptors on their cell surfaces. As a result, somatostatin analogues (Octreotide and Lanreotide) as well as interferons have been used to effectively palliate the symptoms of carcinoid syndrome in up to 70% of patients, to provide tumour reduction in around 5% of patients and to stabilise the disease (an average of three years) in approximately half of the patients (40,54,55). These analogues can be self-administered thrice daily (50-150 μg) through subcutaneous injections and furthermore, longer acting formulations with the convenience of once monthly injections are also available (54). The side effects of octreotide treatment are gallstone formation and pancreatic insufficiency whereas those patients receiving interferons report more adverse effects including flu-like symptoms, chronic fatigue and autoimmune reactions. Chemotherapy has yielded limited success in the treatment of GICTs and tend to be more effective in patients with aggressive variants (such as neuroendocrine carcinomas), in which a cisplatin/etoposide-based regime has been reported to achieve up to 60% response rate (56). External beam radiotherapy has been shown to have a role in the treatment of locally unresectable disease and in the effective palliation of bone and central nervous system metastases (57).

Role of multi-disciplinary team

Patients with carcinoid tumours require multiple modalities of treatment and a dedicated multi-disciplinary team (MDT) to co-ordinate the management and follow up is essential. In view of the relatively low incidence of these tumours and for optimum use of resources, these MDTs need to be centralised and based in regional tertiary centres (8). A neuro-endocrine tumour (NET) MDT should include gastroenterologists, surgeons, oncologists, endocrinologists, radiologists, nuclear medicine specialists and endocrinologists, radiologists, nuclear medicine specialists.
Prognosis and follow up

Prognosis of patients with GICTs is largely determined by age, sex and race of patients, site and size of the primary lesion, stage of the disease, histologic grade and extent of the disease (6). The incidence of nodal and distant metastasis is rare if the primary tumour size is less than 1 cm, however this increases significantly once the primary lesion is over 2 cm in size (58). As described above, patients with carcinoid tumours in appendix and rectum carry a better prognosis with a five year survival ranging from 62-100% depending on the size of the primary lesion. Patients with small intestinal and colonic carcinoids carry a poorer prognosis with a five year survival ranging from 33-75%. Large patient series from Sweden (1960-2000) and from USA (1973-1999) have reported an age adjusted 5-year survival rates of 67% for midgut carcinoids (4,59). In a series of over 300 patients median survival was 12.4 years and 5-year survival was 91% in the absence of liver metastasis and 50% in patients with inoperable liver metastases (51). Significant symptom relief and long disease free survival have been consistently been reported following liver surgery in patients with carcinoid syndrome (2,10,45). Five year survival of over 70% has been reported following radical curative liver resection but nearly all will eventually develop new metastases, often with slow progression. In fact, long term follow-up studies have identified the presence of liver metastases and carcinoid heart disease as the two most significant adverse prognostic indicators (51,59).

The current study is a small series of abdominal carcinoid tumours treated at a single institution but it does represent a modest experience of midgut carcinoids (n=21). Compared to larger published studies, the median follow up time was only 24 months with the longest follow up time being 8 years and this could be partly attributed to some patients being followed up in the regional tertiary centre following referral after initial treatment locally. As there is increasing evidence to suggest that recurrences can become clinically overt after a median of 5-10 years, clearly no concrete data about recurrence and survival can be inferred until the patients have completed a further prolonged follow up period. Furthermore, the study is also underpowered to provide information about differences in survival in those patients who were referred to the regional centre (post 2006) compared to those treated locally.

Conclusions

Currently there is still a lack of clear guidelines for referral and follow up of patients diagnosed incidentally with GICTs particularly within the setting of district general hospitals within the UK. With the recent published evidence about the staging, treatment options and prognosis of carcinoid tumours, this should be feasible and efforts should be made to align the delivery of care to these patients in tandem with the tertiary centres. The hope remains that better and / or modern treatment pathways for carcinoid tumours delivered in a regional setting would be reflected in a difference in survival. Hence, there is a need for more NET-MDTs nationwide in order to provide a co-ordinated approach in the management of this rare condition.

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