

Optimal follow-up strategy for resected neuroendocrine tumours: A systematic review

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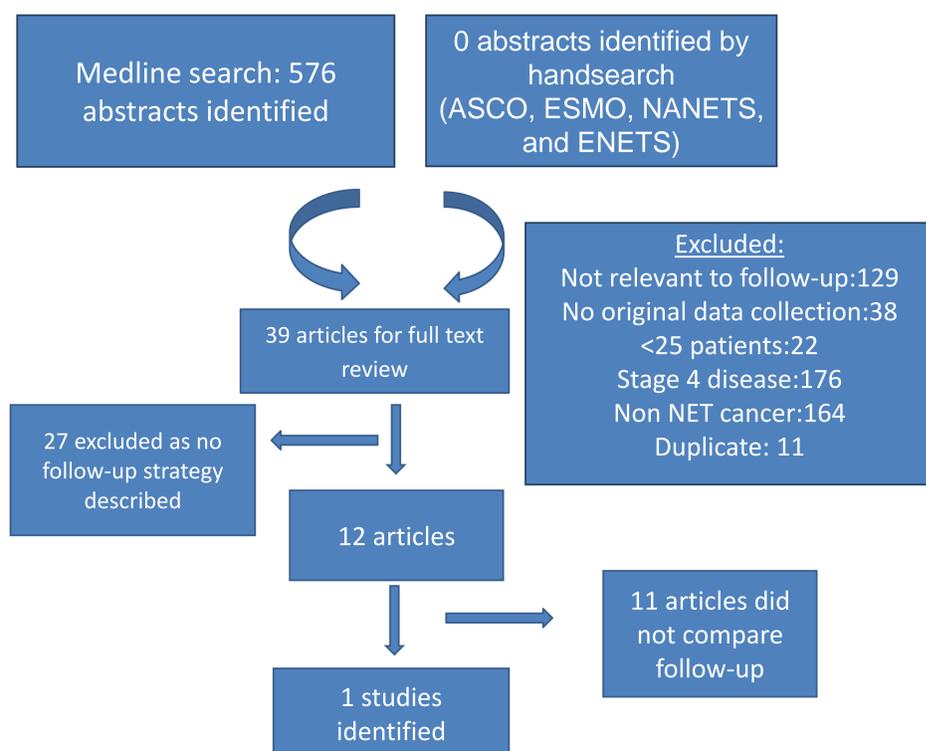
Background

- The incidence of neuroendocrine tumours (NETs) has doubled over the last 20 years with an increasing number of proven systemic treatment strategies.
- The optimal follow-up protocol for this patient population is undetermined.
- We performed a systematic review of studies describing follow-up strategy for patients with resected NETs from 1996-2016.

Methods

- A search was carried out of the MEDLINE and Cochrane Library databases as well as abstracts of major meetings (ASCO, ESMO, NANETS, and ENETS).
- Prospective studies or retrospective studies of more than 25 patients that described follow-up strategy for surgically resected non-metastatic NETs were eligible for inclusion.
- Merkel cell cancer and small cell/large cell carcinomas of the lung were excluded as they are biologically different.

Figure 1: Study flow diagram



Results

- 39 articles were subjected to full text review.
- Only one study presented a retrospective comparison between follow up strategies.
 - This study (Le Roux 2011) included 100 patients with resected ileal NET.
 - The median follow-up was 56.5 months; 42 patients relapsed.
 - “Rigorous follow-up” was defined as consultation and radiology at least yearly, and “non-rigorous” as otherwise.
 - The proportion of patients who received rigorous follow-up in the relapsed group was similar to that in the non-relapsed group.
 - Relapse was suspected based on clinical signs for 10 (23.8%). 32 other patients (76%) had relapse detected during follow-up monitoring (29 radiologically, 3 with elevated biomarkers)
- 12 studies (2920 patients) described follow-up strategies post-resection of NETs, but only one compared follow-up regimens.
- The studies reported different follow-up strategies and were marked by limitations including insufficient data, methodological bias and between-study heterogeneity.
- No formal data synthesis was possible.

Table 1: Included studies

Study	N	Primary	Follow-up	Follow-up	
				Imaging	Blood
Jung 2015 (R)	145	pNET	Variable at 3, 6 and 12 months	CT or MRI	Not specified
Birnbaum 2015 (R)	134	pNET	6 monthly for first 5 years and yearly after	CT	CgA
Kishi 2014 (R)	90	Non-functional pNET	6 monthly	CT or US	Not specified
Sato 2014 (R)	82	Type I gastric NET	Every 6-12 months	Upper GI endoscopy, CT/MRI when possible	Not specified
Zerbi 2013 (P)	140	pNET	6 monthly for 2 years	CT	Not specified
Gaujoux 2013 (P)	46	Non-functional pNET	6-12 monthly for 18 months	Not specified	Not specified
Thomas 2013 (R)	111	Type I gastric NET	6 monthly	Endoscopy, CT/MRI if biochemical recurrence	Not specified
Lopez 2011 (R)	38	pNET in MEN-1 patients	Yearly	EUS/MRI	Pancreatic polypeptide, CgA, insulin, gastrin, vasoactive polypeptide
Le Roux 2011 (R)	100	Ileal NET	Rigorous: yearly Non-rigorous: less frequent	CT/MRI/SRS/US	Not specified
Park 2011 (R)	347	Rectal NET	Not specified	Colonoscopy, CT/US	Not specified
Shields 2010 (R)	202	Rectal NET	6 monthly or yearly depending on institutional protocol	Colonoscopy/CT	Not specified
K. H. in't Hof (R)	975	Appendix NET	Not specified	CT/SRS	Not specified

R: retrospective, P: prospective, CgA: Chromogranin A. PNET: Pancreatic NET. MEN-1: Multiple Endocrine Neoplasia type I. CT: Computed tomography. MRI: Magnetic Resonance Imaging. US: Ultrasound. EUS: Endoscopic ultrasound. SRS: Somatostatin receptor scintigraphy

Discussion

- There is a significant lack of prospective (or retrospective) data to direct follow-up in resected NETs.
- Most identified studies contain heterogeneous populations and vary in their follow-up frequency, choice of modalities and length of follow-up.
- The number of patients who received specific blood tests was poorly reported by the above studies.
- In a disease where some patients have excellent recurrence-free survival (eg T1N0 appendiceal NET), there is a pressing need for evidence to minimize the amount of follow-up to minimize patient anxiety and resultant costs to the health care system.
- There is a need for validated non-invasive biomarkers for surveillance.

Conclusions

- Only one study identified which fulfilled the inclusion criteria.
- There is little reported evidence to definitively guide the optimal follow up strategy in resected NETs in terms of optimal frequency and modality.
- This systematic review has identified a gap in evidence and a need for research into different aspects of follow-up to optimize the patient journey in resected NETs.