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Parotid incidentalomas: a systematic review

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Abstract

Objective. Parotid incidentalomas on fluorodeoxyglucose positron emission tomography/computed tomography imaging are rare. A systematic review was performed to assess their aetiology and association with scanning indication, and to develop an evidence-based algorithm for their management.

Methods. A literature search was performed on 25 August 2020 using the keywords 'incidentaloma', 'incidental finding', 'parotid', 'parotid gland', 'salivary gland' and 'head and neck'. Articles were reviewed by two authors before their inclusion.

Results. Forty articles were included, totalling 558 incidentalomas. The mean incidence was 0.74 per cent. Lung cancer was the most common imaging indication. The most common aetiologies were cystadenolymphoma, pleomorphic salivary adenoma and metastases. Only cystadenolymphoma ($p = 0.015$) and pleomorphic salivary adenoma ($p = 0.011$) were significantly associated with a primary malignancy (lung). The most common further investigations were aspiration cytology, ultrasound imaging and core biopsy, usually prior to parotidectomy.

Conclusion. If appropriate, parotid incidentalomas should be followed up with flexible endoscopy, skin examinations, and head and neck examinations. Ultrasound-guided core biopsy provides higher accuracy, avoiding repeat sampling and excision biopsy.

Review Article

Mr C Thompson takes responsibility for the integrity of the content of the paper

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Introduction

The use of radiolabelled fluorodeoxyglucose (FDG) with positron emission tomography (PET) and computed tomography (CT) is well-established in: staging certain cancers, assessing for distant metastases, identifying occult primary malignancies and examining disease response following treatment. Additional indications for use include localising sources of infection and pyrexia of unknown origin. A proportion of FDG-PET/CT scans consistently detect increased uptake in regions of the body. Such findings are termed incidentalomas, defined as 'unexpected, asymptomatic tumours discovered serendipitously during an unrelated procedure'.[1]

Increased use of PET-CT imaging has resulted in an increase in the discovery of incidentalomas, with an overall detection rate of up to 2 per cent.[2] Common sites for incidental increased FDG uptake include the thyroid, gastrointestinal tract, lung, breast, and adrenal and prostate glands.[2–4] Incidentalomas pose a challenge for the clinician because of the uncertainties that exist regarding their ideal management, the possible requirements for further investigation, and the potential for unnecessary or excessive treatment.[5] Patient anxiety as a result of incidentaloma detection is a well-recognised feature, and recommendations have been made to discuss the implications of their detection prior to imaging.[6]

Increased uptake within the parotid glands is particularly uncommon given their low tissue volume and reduced avidity for radiolabelled glucose analogues.[7,8] However, a number of case reports have been published reporting this finding, as well as series assessing the prevalence. We performed a systematic review of parotid incidentalomas detected on FDG-PET/CT to assess the overall incidence and aetiologies, and to develop an evidence-based investigation and management guideline to aid surgeons and multidisciplinary team members in the care of patients with these findings.

Materials and methods

A systematic review was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis ('PRISMA') guidelines, on the 25 August 2020.[9] The key words used were: 'incidentaloma', 'incidental finding', 'parotid', 'parotid gland', 'salivary gland' and 'head and neck'. No restrictions were placed on date of publication or language. Articles were reviewed independently by two authors (CT and MB) to determine whether they should be included in the analysis.

Results

The results of the Preferred Reporting Items for Systematic Review and Meta-Analysis are shown in Figure 1. Forty articles were included, discussing 558 parotid incidentalomas.[10–50] Aetiology was recorded in 377 incidentaloma cases (67.6 per cent). The aetiology of the parotid incidentalomas included in the review are described in Table 1.

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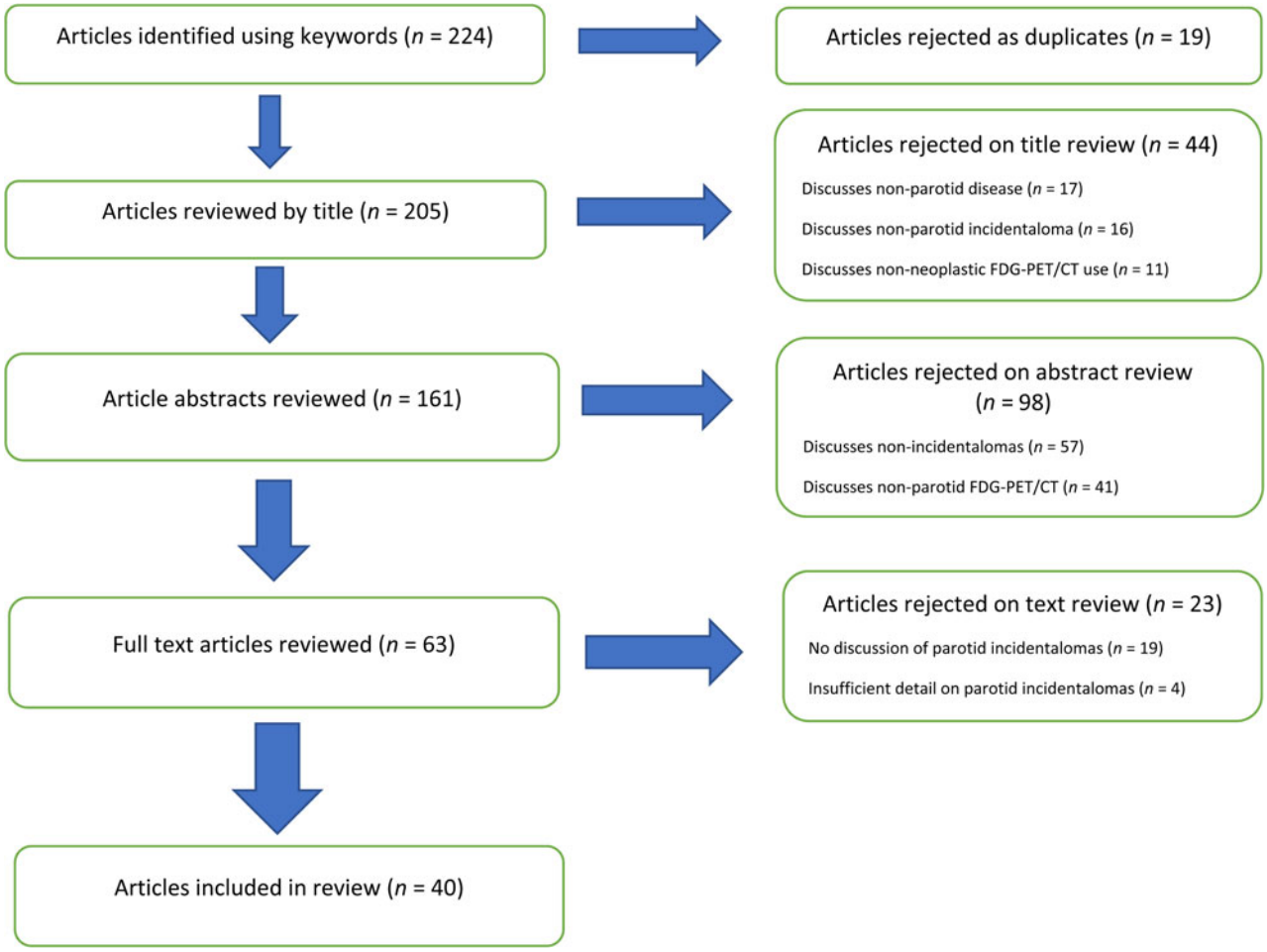


Fig. 1. Preferred Reporting Items for Systematic Review and Meta-Analysis ('PRISMA') flowchart. FDG = fluorodeoxyglucose; PET = positron emission tomography; CT = computed tomography

Benign aetiology was reported in 256 incidentaloma cases (69.6 per cent) and malignant aetiology in 112 (30.4 per cent) ($p = 0.21$; two-tailed *t*-test); the aetiology could not be identified in 9 incidentaloma cases. The commonest aetiology was cystadenolymphoma or Warthin's tumour (30.8 per cent), followed by metastatic disease to the gland (15.1 per cent).

The aetiology of metastatic disease was reported in 23 cases (40.6 per cent). Metastatic melanoma was the most common aetiology (43.5 per cent) ($p = 0.01$; two-tailed *t*-test), which demonstrated 100 per cent metastasis in this review. Metastatic disease corresponded with the primary malignancy being investigated using FDG-PET/CT in all cases ($p = 1$; two-tailed *t*-test). Incidentaloma incidence within a larger series of imaging was reported in 12 articles. The mean overall incidence was 0.74 per cent (range, 0.21–1.55 per cent).

The indication for imaging was reported in 202 cases (36.2 per cent), with no indication stated in the remaining 356 cases (63.8 per cent). The commonest indication for FDG-PET/CT imaging was lung cancer staging; other indications are reported in Table 2. The only imaging indication significantly associated with an incidentaloma aetiology was primary lung cancer, which was associated with both cystadenolymphoma ($p = 0.015$; two-tailed *t*-test) and pleomorphic salivary adenoma ($p = 0.011$; two-tailed *t*-test).

Patient gender was identified in 131 cases, and included 92 males (70 per cent) and 39 females (30 per cent) ($p = 0.65$; two-tailed *t*-test). The side of increased uptake was described in 78 patients, with unilateral involvement demonstrated in 70 patients (90 per cent). There was no statistical difference in the side of involvement ($p = 0.78$; two-tailed *t*-test). The majority of incidentalomas were not investigated further because of the poor prognosis of the primary malignancy or the otherwise reassuring nature of the FDG-PET/CT finding.

Further investigations performed in the assessment of parotid incidentalomas are identified in Table 3. The most common investigation was fine needle aspiration cytology (FNAC) with or without ultrasound imaging, for either guidance or purely for imaging. However, this changed to core biopsy in more recent cases. The accuracy of core biopsy sampling (sensitivity = 100 per cent; positive predictive value = 100 per cent) was higher than that for FNAC (sensitivity = 67 per cent; positive predictive value = 67 per cent), in line with recent literature.

Ultrasound was the most commonly performed radiological investigation following incidentaloma detection. When further management was undertaken, partial or superficial parotidectomy was performed, with total parotidectomy reserved for proven cases of primary parotid malignancy.

Discussion

The overall incidentaloma detection rate on FDG-PET/CT imaging in the literature is reported as 6.7–12 per cent.[51,52] The low mean parotid incidentaloma incidence reported in this review corresponds with the lower incidence of neoplastic and non-neoplastic disease in these glands. Whilst only a small

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Table 1. Aetiology of parotid incidentalomas

Aetiology	Cases (*n*)
Cystadenolymphoma	116
Metastatic lymph node	57
Pleomorphic salivary adenoma	53
Unspecified benign	31
Lymphoma	17
Reactive lymph node	16
Inflammation	11
Mucoepidermoid cancer	11
Sialadenitis	9
Unidentified	9
Unspecified malignant	9
Acinic cell carcinoma	5
Normal	5
Oncocytoma	4
Parotid adenocarcinoma	4
Salivary ductal carcinoma	3
Adenoid cystic carcinoma	2
Basal cell adenoma	2
Granuloma	2
Lymphoepithelial cyst	2
Mikulicz syndrome	2
Mixed malignant parotid carcinoma	2
Carcinoma ex pleomorphic adenoma	1
Myoepithelioma	1
Parotid cyst	1
Sarcoid	1
Undifferentiated parotid carcinoma	1

Table 2. Indications for FDG-PET/CT imaging

Indication	Cases (*n*)
Lung cancer	48
Lymphoma	35
Upper aero-digestive tract cancer (unspecified)	16
Melanoma	10
Oesophageal cancer	9
Colorectal cancer	7
Screening imaging	6
Thyroid cancer	6
Gastric cancer	5
Laryngeal cancer	4
Oral cavity cancer	4
Sarcoma	4
Skin cancer	4
Breast cancer	3
Oropharyngeal cancer	3
Primary malignancy of unknown origin	3
Prolonged fever	3
Pulmonary nodule	3
Biliary cancer	2
Muscle tumour	2
Osteomalacia	2
Pancreatic cancer	2
Sinonasal cancer	2
Bladder cancer	1
Brain cancer	1
Cavernous sinus cancer	1
Fibrous histiocytoma	1
Generalised lymphadenopathy	1
Horton disease	1
Hypopharyngeal cancer	1
Liver cancer	1
Mandible cancer	1
Mesothelioma	1
Monoclonal gammopathy	1
Ovarian cancer	1
Peritoneal carcinomatosis	1
Petrous apex cancer	1
Post-infection	1
Prostate cancer	1
Testicular cancer	1
Thrombocytopaenia	1
Weight loss	1

FDG = fluorodeoxyglucose; PET = positron emission tomography; CT = computed tomography

proportion of incidentaloma aetiology was non-neoplastic (6.3 per cent), this review alerts both clinicians and radiologists to this possibility and particularly systemic disease in cases of bilateral involvement.

The high incidence of cystadenolymphomas amongst parotid incidentalomas is of interest, and Treglia *et al.* observed a similar finding when assessing focal uptake levels in different types of parotid incidentaloma.[53] Cystadenolymphomas account for approximately 30 per cent of benign parotid masses and 24 per cent of all tumours within the gland, though the incidence over a 25-year study period has demonstrated this to be rising.[54,55] A number of theories have been proposed regarding increased FDG accumulation in cystadenolymphomas. These include increased propensities for accumulation within lymphoid tissue and active lymphocytes, but also the higher incidence of cystadenolymphomas in smokers, who are at greater risk of developing lung malignancy and thereby undergo imaging.[56]

The high rate of solid malignant incidentalomas (25.6 per cent) differs from previous studies.[57–60] Rates of primary parotid malignancy are generally quoted at 20 per cent or less, and Britt *et al.* have previously reported a 6 per cent malignancy rate in incidentalomas.[60] The reporting of mucoepidermoid cancer as the most common solid primary malignancy corresponds to its global increase in incidence over time.[60–63]

In addition to follow up with clinical and flexible nasoendoscopy examination, the recommendation for core biopsy in the assessment of incidentaloma mass is based on the higher sensitivity and positive predictive values that we have

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Table 3. Further investigations performed

Investigation	Cases (*n*)
FNAC only	60
FNAC + ultrasound of parotid	26
Core biopsy only	7
MRI of neck + ultrasound of parotid	5
Core biopsy + ultrasound of parotid	4
MRI of neck only	4
CT of neck only	2
CT of neck + FNAC	2
Open biopsy	2
Ultrasound of parotid only	2
CT of neck + MRI of neck	1
CT of neck + ultrasound of parotid	1
Core biopsy + FNAC	1
Core biopsy + FNAC + ultrasound of parotid	1
Core biopsy + CT of neck	1

FNAC = fine needle aspiration cytology; CT = computed tomography; MRI = magnetic resonance imaging

calculated. The power for these calculations is low, but the conclusion confirms the findings of previous work assessing the accuracy of core biopsy in parotid neoplasia assessment.[64] This more definite result achieved from histological analysis rather than from a cytological sample can assist in developing a more suitable course of management for the incidentaloma, and delays from repeat sampling can also be avoided. The addition of ultrasound to guide sampling also improves 'hit rate', with core biopsy suggested as superior to fine needle aspiration.[64–66]

Competing interests. None declared

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