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Clinical Research Article

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Adrenal Incidentaloma: Prevalence and Referral Patterns From Routine Practice in a Large UK University Teaching Hospital

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Abbreviations: AI, adrenal incidentaloma; CT, computerised tomography; MH, Mantel-Haenszel; MRI, magnetic resonance imaging.

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Abstract

Context: Adrenal incidentalomas (AIs) are increasingly being identified during unrelated imaging. Unlike AI clinical management, data on referral patterns in routine practice are lacking.

Objective: This work aimed to identify factors associated with AI referral.

Methods: We linked data from imaging reports and outpatient bookings from a large UK teaching hospital. We examined (i) AI prevalence and (ii) pattern of referral to endocrinology, stratified by age, imaging modality, scan anatomical site, requesting clinical specialty, and temporal trends. Using key radiology phrases to identify scans reporting potential AI, we identified 4097 individuals from 479 945 scan reports (2015-2019). Main outcome measures included prevalence of AI and referral rates.

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Results: Overall, AI lesions were identified in 1.2% of scans. They were more prevalent in abdomen computed tomography and magnetic resonance imaging scans (3.0% and 0.6%, respectively). Scans performed increased 7.7% year-on-year from 2015 to 2019, with a more pronounced increase in the number with AI lesions (14.7% per year).
Only 394 of 4097 patients (9.6%) had a documented endocrinology referral code within 90 days, with medical (11.8%) more likely to refer than surgical (7.2%) specialties ($P < .001$). Despite prevalence increasing with age, older patients were less likely to be referred ($P < .001$).
Conclusion: While overall AI prevalence appeared low, scan numbers are large and rising; the number with identified AI are increasing still further. The poor AI referral rates, even in centers such as ours where dedicated AI multidisciplinary team meetings and digital management systems are used, highlights the need for new streamlined, clinically effective systems and processes to appropriately manage the AI workload.

Key Words: adrenal incidentaloma, prevalence, referral pattern, radiology, computerized tomography, magnetic resonance imaging

Adrenal incidentalomas (AIs) are increasingly being identified in the course of imaging investigations. The estimated prevalence of AI at abdominal computed tomography (CT) scan was reported at 4.4% in a prospective study of 520 patients reported in 2006 [1]. This was markedly higher than earlier imaging series [2]. More recent epidemiological evidence indicates a rising incidence of AI (up to 7.3% in 2017-2018 according to Reimondo et al [3]). This was confirmed by Ebbehoj et al [4], who showed, in a study of adrenal tumor incidence as a proportion of all patients with tumors, that AI incidence increased 10-fold between 1995 and 2017. The increase could reflect the higher resolution of modern scanning technology and that that the 2006 study included only patients older than 55 years (the earlier study included patients aged 41-73 years), a population with a greater prevalence of AIs [3, 5]. It has been reported that the prevalence of AI increases with age: from approximately 3% in those aged 50 years, rising to 10% in those 70 years or older [6], though Reimondo et al [3] suggested that this increase with age may peak around 70 years.

Given the aging population, together with increasing use of cross-sectional imaging in modern medicine (eg, CT urogram, magnetic resonance angiogram), it is likely that a significant proportion of AIs detected will be in those older than 50. This has been substantiated by autopsy series, with a large study (n = 321 847 cases) from Japan reporting that 75% of the identified adenomas were in patients older than 50 [7].

While the clinical investigation and management of AI have been extensively explored and reported, the process (pattern of detection, referral and approach) has received much less attention by comparison. For example, we have noticed that AIs have been referred from other imaging modalities (eg, magnetic resonance imaging; MRI) and when other anatomical sites (eg, thorax, spine) have been scanned. In addition, little is known about the determinants of subsequent endocrine referral (eg, according to clinical specialty and in relation to the age of the patient).

Therefore, the aim of this study was to use linkage of data from the hospital records of imaging and outpatient bookings in a real-world clinical setting from a large UK teaching hospital/trauma center to explore the following:

1. the proportion of patients with AI by age based on current imaging trends;
2. the change in prevalence rates over time and relationship to imaging modality;
3. the pattern of referral of potential lesions to specialist endocrinology teams; and
4. the range of clinical specialties that were responsible for requesting CT and MRI scans that led to reporting potential adrenal lesions, and specialty-specific referral rates.

Materials and Methods

We extracted data for all body CT and MRI scans from April 2015 to December 2019 from the Computerised Radiology Information System at the University Hospitals of North Midlands NHS Trust. This identified 479 945 scans.

We searched radiology reports of these scans using predefined key phrases ("adrenal adenoma," "adrenal lesion," "adrenal mass," "adrenal nodule," "adrenal incidentaloma," "incidental adrenal," and "indeterminate adrenal") to identify scans reporting potential adrenal lesions. Where possible, we excluded false hits (eg, "no adrenal lesion"). A limitation of this approach are variants on these phrases

that may have resulted in false positives and negatives (eg, "No large adrenal mass" would result in a false-positive inclusion in the data set, while typographical errors such as "adronal mass" would have resulted in a false negative). To avoid underestimates and overestimates, when patients underwent more than 1 cross-sectional imaging event in the 5-year period, only 1 event was included. This also included those instances where subsequent dedicated adrenal scans were performed following initial detection. When patients were referred from endocrinology for suspected adrenal lesion (eg, Conn syndrome or adrenal-dependent Cushing), these were excluded because, by definition, these would not constitute an incidentaloma.

We also determined the number of patients where potential AI lesions were reported, along with the number of positive scans referred to the endocrinology service for further follow-up and management. When matching data to what were likely to be endocrine outpatient referrals, we used outpatient activity where the specialty was indicated as: Endocrinology Specialty (clinic code 302), including the codes for individual endocrinology consultants.

In addition, we extracted data on the date of scan, patient age, scan modality (CT or MRI), anatomical area scanned, source of original scan request, and date of subsequent referrals as identified by a logged referral or an attendance (new or follow-up) to the endocrine clinic 90 days post index scan. In our experience, this 90-day period is more than adequate to capture almost all referrals. Rather than individual nonendocrinologists requesting further testing, the prevailing practice in our center is to refer patients directly to endocrinology to decide if further hormone investigations or imaging are warranted and/or appropriate. Additionally, we attempted to identify the source of referral to endocrinology (and whether this matched the specialty that originally requested the scan) specifically in response to the AI lesion.

These data were used to assess changes in patterns of AI detection and referral over time, by imaging modality and site, by age, and by specialty requesting the scan. In terms of changes with time, unique patients were counted based on the year of their first scan. Hence, some patients had scans over multiple years, but were represented only once in the data. Accordingly, those counted in 2015, for example, may have had scans in earlier years.

Statistical Analysis

The Pearson chi-square test was used for comparison of proportions. The Mantel-Haenszel (MH) chi-square test for linear trend was used to assess referral pattern over time, stratified by year, and by age, stratified by 10-year age groups. Differences in continuous numerical variables (eg, differences in mean ages) were assessed using the *t* test. Probability values less than or equal to .05 (2-tailed) were considered statistically significant. All statistical analyses were performed using Stata version 14, with the exception of the MH test, for which OpenEpi (version 3.01) was used.

Results

Prevalence of Adrenal Incidentaloma

Overall, AI lesions were identified in 5832 of the 479 945 (1.22%) CT and MRI scans (Table 1). This equated to AI being detected in 4097 unique patients over the 5 years of data collection. When adrenal scans were excluded, AI was reported in 1.54% of all remaining CT scans and 0.17% of MRI scans. During the study period, AIs were identified most commonly on CT and MRI scans of the abdomen (together accounting for 1793 of the reported 5832 AI lesions; 30.7%), which reported an AI prevalence of 3.02% and 0.64%, respectively (see Table 1).

Effect of Age

We also examined the link between age and AI prevalence. The mean (± SD) age of patients with AIs was 69.2 ± 13.3 years. Of the total case group, 74.1% of scans were in patients aged 50 years or older (median age 70.0 years). Overall prevalence in all scans increased with age to a peak prevalence of 1.7% in the 61- to 70-year age group (Fig. 1). For abdominal CT scans alone, prevalence increased linearly with age, rising to 4.2% in the 90-year and older age group. The median age at detection of AI remained constant across the period studied (data not shown).

Changes Over Time

Over the 5-year study period, the total number of scans performed increased, year on year, from 83 234 in 2015 to 111 981 in 2019 (34.5% increase, with a mean increase of 7.7% per year; Fig. 2A). The number of abdominal CT scans also increased by 55.2% from 7449 to 11 564 (mean increase 11.7% per year; see Fig. 2A). During this period, the number of scans with AI lesions reported increased from 848 to 1443 (70.2%, with a mean increase of 14.7% per year; Fig. 2B). Increases were similar for CT (70.3%) and MRI scans (68.8%).

CT/MRI abdomen scans, with AI reported, increased by 133% (from 147 to 343) over the same period. In proportion to total scans reporting AIs, this increased year on year from 2015 to 2019 (MH $\chi^2_1 = 14.2$, $P < .001$).

Referral Patterns

Of the 4097 unique patients, only 394 (9.6%) had an allocated endocrine referral code within the subsequent 90 days. Annual referral rates increased over the study period (Fig. 3A; MH $\chi^2_1 = 11.9$, $P < .001$).

Age was also linked to referral pattern. The numbers of identified lesions gradually increased with age to a peak in the 61- to 70-year age group. However, the proportion referred was higher in those aged 50 and younger (60/384, 15.6%) than those older than 50 years (334/3713, 9.0%; $\chi^2_1 = 17.6$, $P < .001$). Indeed, there was a statistically significant trend toward decreasing referral with age group (see Fig. 3B; MH $\chi^2_1 = 38.1$, $P < .001$).

Table 1. Total number of scans, scans with adrenal incidentaloma, and the proportion referred to endocrinology

	Total scans	No. of scans with AI (%)	No. referred (%)
Total	479 945	5832 (1.22)	394 (6.76)
CT	332 078	5545 (1.67)	367 (6.62)
MRI	147 867	287 (0.19)	27 (9.41)
Total nonadrenal	479 053	5492 (1.15)	319 (5.81)
Nonadrenal CT	341 882	5254 (1.54)	292 (5.56)
Nonadrenal MRI	137 171	238 (0.17)	27 (11.34)
Total CT/MRI abdomen	60 519	1793 (2.96)	113 (6.30)
CT abdomen	58 954	1783 (3.02)	113 (6.34)
MRI abdomen	1565	10 (0.64)	0 (0.00)

Abbreviations: AI, adrenal incidentaloma; CT, computed tomography; MRI, magnetic resonance imaging.

Only 367 of 3924 (9.35%) and 27 of 173 (15.61%) patients with reported potential lesions, detected by CT and MRI, respectively, were referred for endocrine review. Hence, patients who had undergone MRI were more likely to be referred than those with CT scans ($\chi^2_1 = 19.3$, $P < .001$). Patients who had MRI scans were generally younger (median age 62; interquartile range, 43-73 y) than those who had a CT scan (median 71; interquartile range, 63-79 y) with a significantly larger proportion younger than 50 years (32.6% vs 6.0%; $\chi^2_1 = 288.7$, $P < .001$).

The average time from detection by imaging to referral receipt did not differ between those aged < 60 years (mean ± SD = 39.1 ± 26.0 d) and those older than 60 years (mean ± SD = 36.7 ± 25.0 d; *t* test $P = .386$).

Pattern of Referral to Endocrinology According to Clinical Specialty

The 4097 imaging requests in people with AI lesions came from 105 different clinical specialties (medical and surgical), though the 394 cases who were subsequently referred to endocrinology were derived from 53 of these specialties. The top 12 of these referring specialties accounted for 352 of 394 (89.3%) of these requests. Of these top 12 specialties, medical specialties (general practice, respiratory medicine, accident and emergency, nephrology, acute medicine, cardiology, clinical hematology, general medicine, gastroenterology) accounted for 232 of 394 (58.9%) requests, while surgical specialties (general

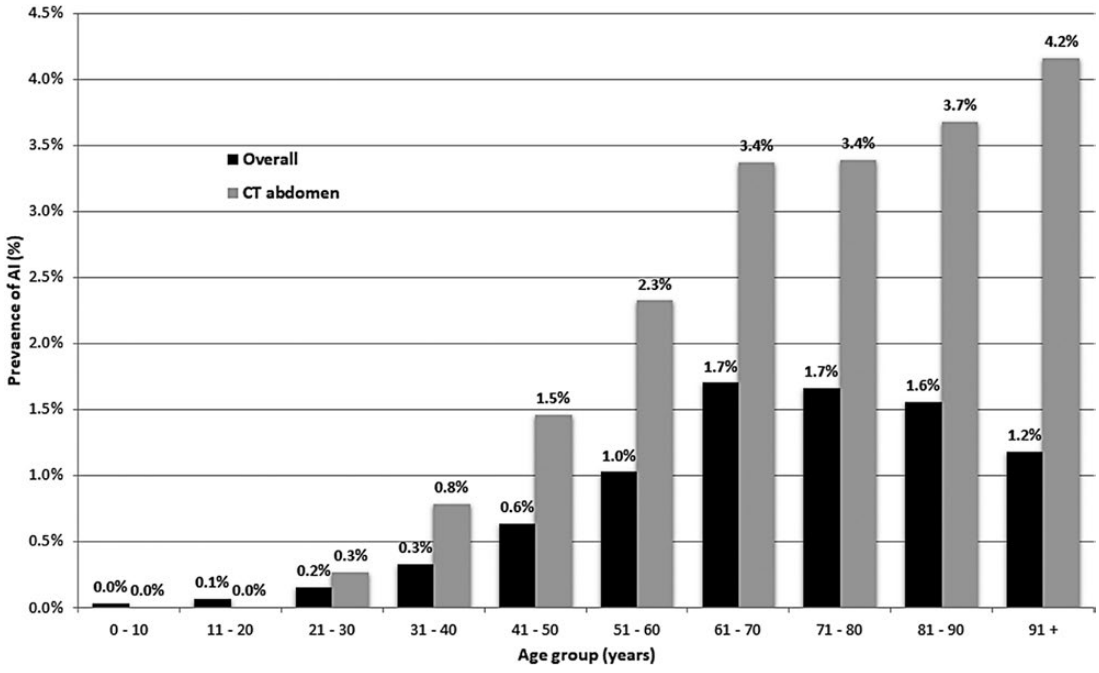

Figure 1. Prevalence of adrenal incidentaloma (AI) in the total group and computed tomography (CT) abdominal scans, stratified by age group.

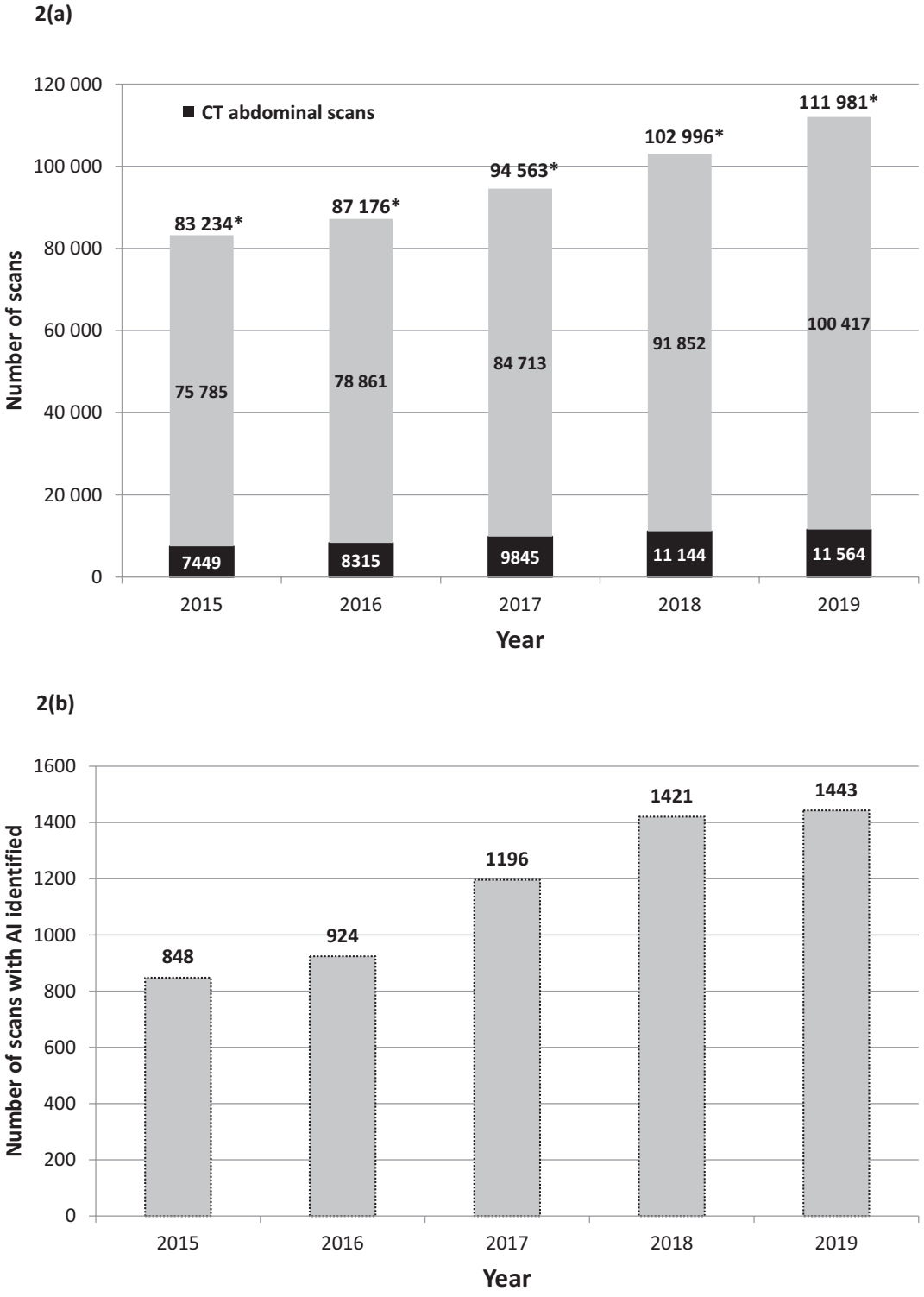

Figure 2. Temporal changes in number of A, total scans, and B, scans with adrenal incidentaloma (AI) identified.

surgery, urology, colorectal surgery) accounted for 120 of 394 (30.5%). The overall proportion of cases referred was 9.6%, with medical specialties more likely to refer to endocrinology (11.8%) than surgical (7.2%) specialties ($\chi^2_1 = 25.1$, $P < .001$).

We noted that some specialties had very low referral rates. For example, clinical oncology referred only 0.7% of AI cases, while care of the elderly referred just 4.0%.

Discussion

Overall, the prevalence of reported AIs in our cohort was 1.22% of all CT and MRI scans. This is lower than

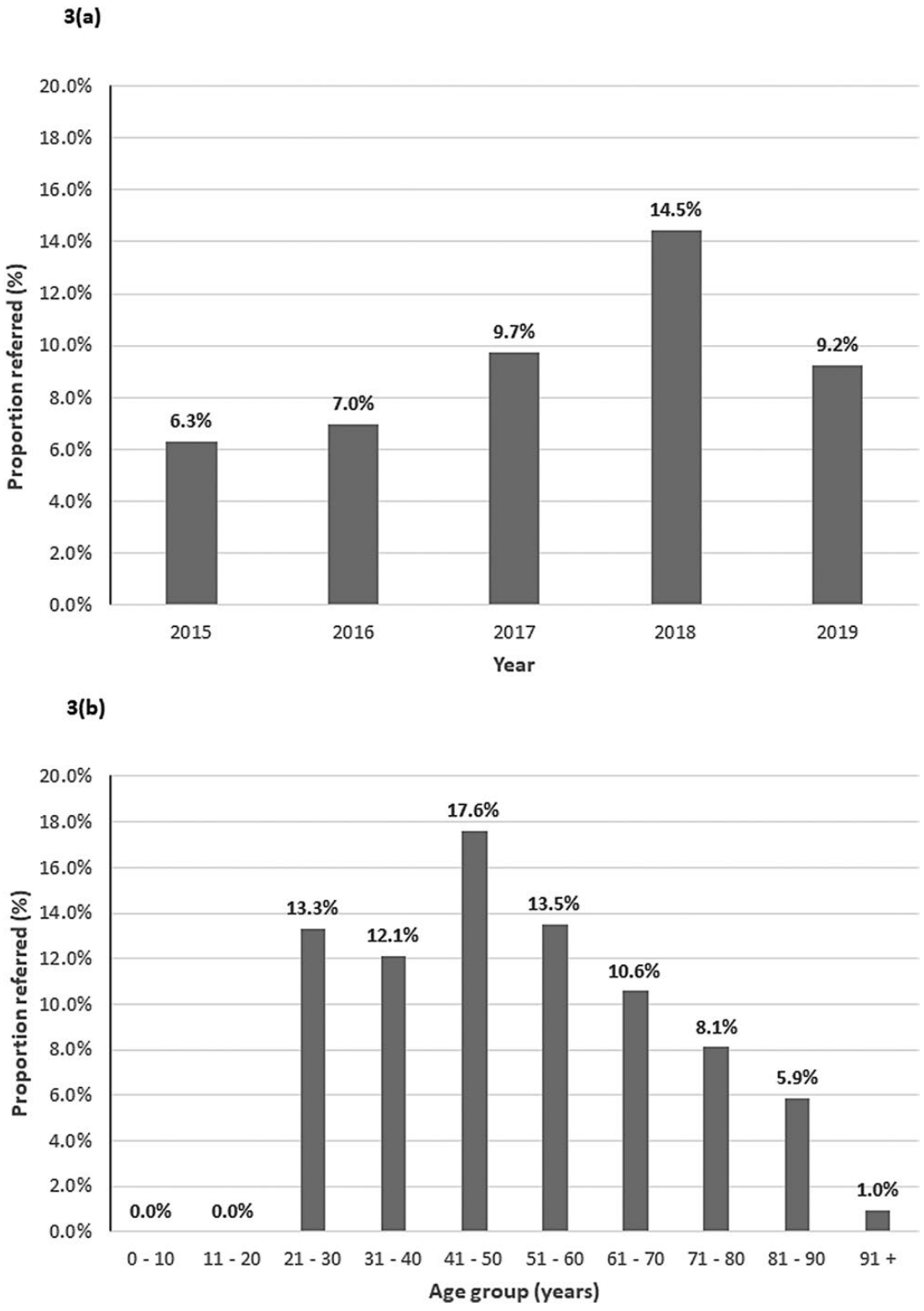

Figure 3. Referral pattern: A, over time, and B, with age.

previously reported [1]. However, unlike previous literature, this included all body scans irrespective of site (eg, CT thorax, CT angiogram). Focusing on CT of the abdomen alone, across all ages, the prevalence rose to 2.7% in our cohort. Furthermore, published data often include a dedicated review of adrenal imaging in a significant proportion of cases, with a likelihood of diagnosing more AIs than would have been reported in routine radiological practice

[8, 9]. The latter work confirms that 43% of the AI cases detected using dedicated radiological review had been omitted from the original radiology report, highlighting the potential missed cases possible in the absence of experienced abdominal radiologist review [9]. Our data represent routine practice in a large major trauma center and university teaching hospital. In keeping with a previous finding [3, 5], the majority of AIs were identified in those aged 50 years and older. In our cohort, 90.2% of AIs were identified in those older than 50 years, reflecting the increasing role of cross-sectional imaging in modern medicine [10], in addition to the more proactive management of people in this group. This is illustrated by our finding of a 7.7% year-on-year increase in the total number of scans performed. The year-on-year increase in AIs reported was almost double this (14.7%). This is consistent with previous work [3, 4] and reflects the local innovation program targeting AI management, as exemplified by our previous work [11].

Of concern, despite our innovation program, the recorded referral rates to endocrinology remained low, with more than 90% of cases seemingly not referred. However, referral rates rose from 6.7% in 2015 to 2016 to 11.4% from 2017 onward. While encouraging, further work is required to address this. There is no reason to suggest that other centers, at least in the United Kingdom, will be any different. While the proportion of patients with AI rises in older age groups, the referral rates decrease (from 15.6% in those aged ≤ 50 years to 9.0% in those older than 50 years).

We did identify that overall referral rates were higher in medical than in surgical specialties. The reason for this is unclear, but may represent the observation that intramedical specialty interaction tends to be greater than between surgical and medical specialties. The low referral rate in clinical oncology may reflect the seriousness of the primary condition, with an incidental finding treated as a lower priority. Low referral rates in the care of the elderly patients may reflect the multiple comorbidities and frailty of many of these patients, and hence possible high surgical risk.

Managing all identified AI cases would overwhelm current capacity. In our center, if all AI cases were to be referred, this would constitute 30% of all commissioned endocrine referrals. This raises operational and logistical challenges to be addressed by all stakeholders. Streamlined processes promise to reduce the clinical and administrative hands-on time significantly, especially if supported by initiatives such as implementing an AI management algorithm for nonendocrine specialties, use of digital management systems [11], and an agreed on protocol for laboratory investigations. These approaches could support the safe management of people with AI without overwhelming the endocrinology service.

Strengths and Limitations

As a result of how outpatient activity is coded, our cohort may have resulted in a slight overestimation of number of cases referred to endocrinology in some referral data, including activity for departments such as diabetes. In contrast, the fact that some of the CT/MRI reports may not have commented on an incidentaloma will inevitably result in underestimating the true prevalence. This is especially true in scans conducted for acute cases during emergency admissions. However, this is unlikely to detract from the overall findings as most diabetes clinicians are also specialists in endocrinology and therefore would tend to investigate the AI parallel to their diabetes management. Indeed, this could potentially strengthen the core message that a significant proportion are not referred appropriately.

We also recognize that the use of predefined key phrases, per se, do not necessarily exclude cases in which CT and MRI might have been performed for clinical suspicions of Cushing, hyperaldosteronism, etc. However, our data indicated that only 64 of 4097 patients were labeled as being under the care of an endocrinologist with only 5 being subsequently followed up in endocrine outpatient clinics. Most likely, these were scans booked in their names for which the endocrinologist was the admitting physician rather than triggered by outpatient activity to investigate adrenal dysfunction.

While our retrospective data are collected from a single center, based on coding of information in radiology reports, this study represents a large number of patients scanned over a 4.5-year period in a large university teaching hospital, with almost all clinical disciplines represented. Furthermore, given the fact that key phrases were used for searching AI cases, it reflects real-life clinical care, as opposed to studies allocating dedicated radiology review, which may overestimate the prevalence of AI (see earlier).

We noted a marked difference in reported AI prevalence between MRI and CT scans. The literature does not provide a clear explanation for this. We explored 2 possible reasons: First, this may be related to age because the younger than 50 group comprised 40.0% of MRI scans, but only 19.6% of CT scans. However, even in those older than 50 years, prevalence of AI was much higher in those with CT scans (1.93%) than in those with MRI scans (0.21%). Second, the use of phrase codes may underestimate AI prevalence, especially in MRIs. MRI is often a more focused and organ-specific (eg, MRI liver) examination, and therefore radiologists may look less widely for any abnormalities. In contrast, CT scans tend

to be used in more acute/emergency situations where the radiologists are likely to review images more widely. However, this will not fully explain the magnitude of the difference in reported prevalence, especially as radiologists are duty bound to report any abnormality both on MRI and CT scans.

We also observed that the prevalence of AI was higher in abdominal scans than in the total scans (see Table 1). While the incidence should be the same, the "total scans" group included scans dedicated for specific areas (eg, CT spine, CT angiogram), where there may be less focus on the visceral organs during reporting. Abdominal scans, by default, tend to focus on the visceral organs of the abdomen, including the kidneys and therefore adrenals. Our report aims to highlight current routine practice.

We recognize that other centers may have different local arrangements for AI services. In the absence of agreed-on criteria for reporting adrenal abnormalities, together with the variability in reporting and referral arrangements, this will remain a challenge for any health system. We have previously published our own attempts to enhance referrals within our center [11].

As far as we are aware, there is very little information on the true prevalence of AIs and the referral pattern based on real-life clinical practice data. Most of the published data are from case series, based on dedicated radiological support, with potential overestimation of the prevalence [8].

While the use of ultrasound scanning as a first-line test is not standard practice in the United Kingdom, we are aware that ultrasonography is relatively inexpensive and accessible for any abdominal disorder (eg, where the patients present with relatively vague abdominal symptoms, and hence where CT or MRI would not generally be performed initially), especially in emergency departments. In these cases, ultrasound could identify a proportion of cases of incidentalomas if of adequate size, though a CT or MRI scan would be required to confirm the morphological picture.

It is possible, depending on the setting, that some clinicians may request hormone tests without referral to a specialist endocrinologist, thereby accounting for low referral rates. In our unit, patients are referred to the endocrine team to decide on the relevant investigations and their subsequent interpretation.

Notwithstanding the aforementioned, the practical applications derived from our findings indicate that there remains a huge unmet caseload of AIs. The majority of these will require a more streamlined approach to reassure patients with benign and nonfunctioning lesions without delay. The few with abnormalities could be fast-tracked for more prompt management.

Conclusions

In summary, we demonstrated that the majority of AI cases are in those older than 50 years, as previously shown. However, while onward referral rates to endocrinology were extremely low, the younger patients were more likely to be referred.

Our findings emphasize the importance of translating the available evidence and published guidance into a clear pathway for local implementation, including standardized reporting and referral patterns.

This work also acutely highlights the need to address the poor referral rates for AIs. Detection of adrenal abnormalities within radiology is essential, as is providing guidance to the requesters, who are often nonspecialists, regarding onward referral to endocrinology. Further discussions with commissioners and service providers are also needed to ensure streamlined, clinically effective processes to cope with the additional workload within the finite resources of the health system, with optimization of technology solutions to support timely and proportionate clinical decision-making.

Additional Information

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Disclosures: The authors have nothing to disclose.

Data Availability: Some or all data sets generated during and/or analyzed during the present study are not publicly available but are available from the corresponding author on reasonable request.

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