

ORIGINAL ARTICLE

Comprehensive analysis on 559 cases of adrenal incidentalomas in the elderly Chinese

Tuo Li¹  | Weiqin Li² | Xiao Fang³ | Qian Lv¹ | Yan Song¹ | Yongquan Shi¹

¹Department of Endocrinology, the Second Hospital of Navy Medical University, Shanghai, China

²Department of Pathology, the Second Hospital of Navy Medical University, Shanghai, China

³Department of Urology, the Second Hospital of Navy Medical University, Shanghai, China

Correspondence

Yongquan Shi, Department of Endocrinology, the Second Hospital of Navy Medical University, Shanghai, China.
Email: young.stone@smmu.edu.cn

Abstract

Objective: This study was conducted to describe the incidence, classifications and characteristics of adrenal incidentalomas (AIs) in the elderly Chinese.

Methods: Primary clinical records in Shanghai Changzheng Hospital (n = 559) were collected for incident cases of AI between January 1, 2002 and December 1, 2016. We examined demographics, endocrine functions, treatment, etiology, and prognoses.

Results: We identified 559 new diagnoses of elderly onset AIs, of which 41.25% were male and were diagnosed at a mean age of 74.39 ± 9.03 years. About 61% showed no typical symptoms. Upon systematic review, 41.34% showed dysglycemia, high blood pressure, kaliopenia, and so on. 24.15% (n = 135) received complete or partial endocrine function assessments. A total of 281 cases underwent surgical treatment, and 278 cases went through regular follow-ups without any operation. Preoperative evaluation was basically consistent with postoperative pathology ($P > .05$). During the follow-up, the presence of new subclinical hypercortisolism was 8.99%, and the tumor grew up 3.92% per year (1.96 ± 0.09 mm). 51 cases (9.12%) eventually received further invasive examinations or surgical treatments.

Conclusion: The detection of AI in the elderly Chinese is increasing annually. The imaging method and endocrine function tests have great roles in distinguishing between benignancy and malignancy. The diagnosis and treatment of the elderly Chinese with AI should receive multidisciplinary assessment. Biochemical and morphological follow-up of aged patients with AI should be conducted every 5 years at least.

KEYWORDS

adrenal mass, incidentaloma, elderly

1 | INTRODUCTION

Adrenal incidentaloma (AI) is the term given to an adrenal mass discovered incidentally, often during an imaging procedure. The incidence of AI has been rising sharply due to the increased use of radiographic imaging, becoming the leading diagnosis of adrenal

disease.¹ Less commonly, AI is also discovered as part of the clinical workup for suspected adrenal disease, e.g. Cushing syndrome.

The current diagnostic criteria of AI are based on the 2016 guidelines set by the American Association of Clinical Endocrinologists (AACE) and the American Association of Endocrine Surgeons (AAES). The adrenal tumor and its malignancy must have been

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2018 The Authors. *Aging Medicine* published by Beijing Hospital and John Wiley & Sons Australia, Ltd.

discovered incidentally from an imaging method performed for nonadrenal-related reasons before any operation.²

The detection of AI is 4%-6%, and the rate of autopsy is about 8% (1%-32%).³ According to Bovio's research, the detection of AI by high-resolution computed tomography (CT) scan was about 4.4%.⁴ AI increases with aging. The detection of AI in adolescents was only 0.2% compared to 3%-5% in adults and 7%-10% in the elderly.⁵ Among those who suffered from malignancies, about half of AIs were metastatic.³

In this study, we examined 559 AI patients who were diagnosed and treated in Shanghai Changzheng Hospital from January 2002 to December 2016. 41.25% were identified during routine imaging procedures. The diagnosis and treatment process of AI will be discussed using current reports in combination with existing clinical data.

2 | MATERIALS AND METHODS

2.1 | Patients

A total of 559 AI patients above 65 years of age were received in our hospital from January 2002 to December 2016. The medical records of these patients were collected and collated for the research objects. In all objects, 281 patients underwent surgery and the specimens were sent to the pathological laboratory. The remaining 278 patients went through regular follow-ups in our hospital without any operation.

All 559 patients were retrospectively analyzed, examining gender, age, race, reasons for seeking medical treatment, laboratory examinations, complications, operation methods, postoperative pathological diagnoses, and follow-up observations.

2.2 | Methods

Some patients agreed to receive an endocrine function assessment. The following tests could also be conducted to diagnose Cushing syndrome: (i) 24-hour urinary free cortisol (UFC); (ii) adrenocorticotropic hormone (ACTH); (iii) midnight 1 mg dexamethasone suppression test (1 mg DST); (iv) low-dose dexamethasone suppression test (LDDST). 1 mg DST and LDDST were used to inhibit the post-serum cortisol >50 nmol/L as a diagnostic point.³ According to the ACTH level and high-dose dexamethasone suppression test (HDDST), we can identify ACTH-dependent and non-ACTH-dependent Cushing disease. Primary aldosteronism was screened for using the plasma aldosterone-to-renin ratio (ARR; >30), and was performed at the same time as a vertical decubitus test. Pheochromocytoma was diagnosed by image evaluation and other methods, and the patients were diagnosed by postoperative pathology. The malignant nature was diagnosed by postoperative etiology.

2.3 | Statistics

SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for data processing. The measurement data were indicated by the

mean \pm standard deviation (mean \pm SD), and *F* test was used for comparison between groups. The count data were expressed in terms of number and proportion (n, %), and chi-squared test was used for comparison between groups. The difference of *P* < .05 was statistically significant.

3 | RESULTS

3.1 | First clinic visit

Of the 559 patients, about 61.00% (n = 341) were diagnosed during routine medical examinations without having displayed any subjective symptoms or signs. The highest reason for the patients' first visit was for endocrinology (42.01%), followed by urology (28.65%), general surgery (17.43%), and thoracic surgery (11.90%). The remaining 218 patients showed dysglycemia, thyroid dysfunction, electrolyte disorder or dizziness, fatigue, anorexia, and edema, among other complaints (Table 1).

3.2 | Examinations and etiological characteristics

All patients underwent adrenal CT or magnetic resonance imaging scanning. 135 cases (24.15%) completed an endocrine function assessment, and 141 cases (25.22%) showed suspicious positive symptoms or signs, including weight gain (25.57%), dysglycemia or insulin resistance (21.28%), and hypertension (30.92%).

Of the 281 patients who received adrenal surgeries, adrenal adenoma is the most common pathological type, accounting for nearly 90%. Functional AI accounts for 15.93% in all AI surgeries, of which 2.32% are pheochromocytoma, 8.38% are aldosterone adenomas, and 4.53% are autonomic cortisol secretion. The etiology in 52 cases with bilateral AIs showed metastatic carcinoma, congenital adrenocortical hyperplasia, adrenal adenoma, lymphoma, infection, bleeding, and so on. The summary and comparison of various pathological types are described in Table 2.

TABLE 1 Adrenal incidentaloma patients' first reason for hospital visit (n = 559)

Chief complaint ^a	N (%)
Asymptomatic	341 (61.00)
Lumbago	64 (11.44)
Urination discomfort	25 (4.47)
Abdominal discomfort	26 (4.65)
Cardiovascular	19 (3.39)
Pulmonary	17 (3.04)
Others ^b	67 (11.99)

^aSome patients with existing complaints.

^bIncluding dysglycemia, thyroid dysfunction, electrolyte disturbances, dizziness, and fatigue.

TABLE 2 The nature of adrenal incidentaloma and comparison of literature reports^{3,6-10}

All subjects ^a	Study (%)	Literature ⁶⁻⁸ (%)	Etiology ^a	Study (%)	Literature ^{3,6-10} (%)
Adenoma	79.81	33-96	Nonfunctional benignancy	88.92	52-88
Nonfunctional ^b	66.17	71-84	Pheochromocytoma	2.32	11-23
Primary aldosteronism	2.81	1.6-3.3	Autonomic cortisol secretion	4.53	1.0-15
Autonomic cortisol secretion	11.32	1.0-29	Primary aldosteronism	8.38	2.0-7.0
Pheochromocytoma	0.13	1.5-14	Carcinoma	3.02	1.2-12
Carcinoma	4.12	1.2-11	Metastatic carcinoma	1.66	0-21
Metastatic carcinoma	5.81	0-18	Others ^c	4.26	0-13

^aFive hundred fifty-nine aged patients in our hospital, 281 cases received surgical treatments.

^bIncluding adenoma, cyst.

^cIncluding adrenal schwannoma, adrenal lymphoma, adrenal teratoma, and ganglion cell neurofibroma.

3.3 | FOLLOW-UP

Of the 281 aged patients, 82.21% (n = 231) were frequently followed up postoperatively. 61.49% of cases with preoperative hypokalemia showed the normal level postoperatively. 38.02% of hypertensive patients showed better blood pressure control, while 119 patients still needed oral antihypertensive therapy. In the latest follow-ups, 51 patients were found to have suffered recurrences (3.55%), with malignancy-related mortality at 68.62%.

During the observation of the 278 patients who did not undergo any operation, 8.99% revealed new positive endocrine function, and the mean size of adrenal masses increased annually (1.96 ± 0.09 mm, 3.92% per year). 9.12% (n = 51) eventually received invasive or surgical treatments.

4 | DISCUSSION

In recent decades, the incidence of AI has been increasing sharply, while related mortality has had no obvious relative change.³ We have reasons to believe that the high detection rate is due to the rapid development and wide application of imaging technology.

Adrenal incidentaloma patients usually show no specific signs of hormonal excess or obvious underlying malignancy. In our study, adrenal masses were incidentally discovered in routine examinations of more than half of the patients, who mostly complained of lumbago (11.44%) or urinary symptoms (4.47%; Table 1). Besides, more than 40% of the patients (n = 141) were found to display suspicious positive symptoms such as high blood pressure, abnormal blood glucose, weight gain, or obesity during the systematic review. The main reason is that abdominal imaging examination is the optimal method for finding chronic diseases in China, and there exists a lack of self-health awareness as well.^{1,11}

In addition, the measurement on diagnosis still lacks in certain workups. The majority of patients' first visits are to the surgical departments, such as urology (28.65%), general surgery (17.43%), and cardiothoracic surgery (11.90%). All patients underwent preoperative imaging to distinguish between benignancy and malignancy, while endocrine function tests are more likely to be overlooked (24.15%).

There are still differences in opinion and controversies about the operation time and style for elderly patients with AI.^{1,12-14} Basically, we can reach a unified consensus on a few important factors: functional AI,¹⁵ malignancy,¹⁶ life expectancy,^{1,2} and good physical condition, among others. Most studies suggest that the size of the tumor is one of the most important clinical predictors of benignancy or malignancy of the index.¹⁷ However, our study found no significant differences between benignancy and malignancy (31.16 ± 10.33 mm vs 42.28 ± 23.70 mm, $P = .0327$).

Meanwhile, it is particularly important to re-examine related indicators during the follow-up. In our study, 24 cases of AI patients who were suspected of autonomic cortisol secretion function during the follow-up period showed dysglycemia (n = 22), hypertension (n = 8), and other complications. There is no clear evidence by large-scale study of screening for negative or suspicious positive symptoms in patients without follow-up assessments of the endocrine function. In particular, more comparative and cohort studies revealed an increasing propensity of subclinical hypercortisolism.¹⁸⁻²⁴ A study by Lopez et al. found that the risk of incident diabetes in some patients with nonfunctional, benign AI increases year by year.²⁵ Considering that there is still a certain misdiagnosis rate in 1 mg DST, it is recommended to complete imaging and endocrine function examinations in at least 5 years of follow-up, and further set up 1 mg DST cut-off points that are in line with the Chinese population.

5 | CONCLUSION

Adrenal masses are one of the most common tumors in the elderly Chinese. In the first diagnosis of AI, the nature of the tumor should be determined preoperatively. CT scan is the most valuable image screening method to determine its nature. At the same time, functional properties of endocrine function tests to evaluate AI should exclude autocortisol secretion independent, pheochromocytoma, primary aldosteronism, and other functional lesions. Most benign nonfunctional adenomas do not need further diagnosis and treatment, while treatment of functional ones depends on complications. The adrenal malignancy must be treated by a combined multidisciplinary treatment once an operation is considered, and the follow-up procedure will be greatly simplified.

ACKNOWLEDGMENTS

The authors acknowledge the patients in the Changzheng Research and Surveillance Center (CZRSC) who formed the basis for this analysis.

AUTHOR CONTRIBUTIONS

L.T. contributed to the literature search and data analysis. L.T., F.X., L.W.Q., L.Q., S.Y., and S.Y.Q. contributed to background research and data interpretation. L.T., F.X., and L.W.Q. contributed to conception of the study. L.T. and S.Y. contributed to statistical analysis. S.Y.Q. contributed to study design and planning of data analysis. All authors contributed to data collection and substantially to writing of the manuscript. S.Y.Q. is the guarantor of this work and, as such, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

CONFLICT OF INTEREST

No potential conflicts of interest relevant to this article were reported.

ORCID

Tuo Li  <http://orcid.org/0000-0002-6691-7423>

REFERENCES

- Fassnacht M, Arlt W, Bancos I, et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. *Eur J Endocrinol*. 2016;175:1-34.
- Zeiger MA, Thompson GB, Duh QY, et al. American Association of Clinical Endocrinologists (AACE) and American Association of Endocrine Surgeons (AAES) Adrenal Incidentaloma guidelines. *Endocr Pract*. 2009;15(Suppl):1.
- Benitah N, Yeh BM, Qayyum A, Williams G, Breiman RS, Coakley FV. Minor morphologic abnormalities of adrenal glands at CT: prognostic importance in patients with lung cancer. *Radiology*. 2005;235:517-522.
- Bovio S, Cataldi A, Reimondo G, et al. Prevalence of adrenal incidentaloma in a contemporary computerized tomography series. *J Endocrinol Invest*. 2006;29:298-302.
- Li LL, Dou JT, Gu W, et al. Etiologies of 1,173 hospitalized cases with adrenal incidentaloma. *Natl Med J China*. 2014;94:587-590.
- Barzon L, Sonino N, Fallo F, Palu G, Boscaro M. Prevalence and natural history of adrenal incidentalomas. *Eur J Endocrinol*. 2003;149:273-285.
- Kloos RT, Gross MD, Francis IR, Korobkin M, Shapiro B. Incidentally discovered adrenal masses. *Endocr Rev*. 1995;16:460-484.
- Mantero F, Terzolo M, Arnaldi G, et al. A survey on adrenal incidentaloma in Italy. Study Group on Adrenal Tumors of the Italian Society of Endocrinology. *J Clin Endocrinol Metab*. 2000;85:637-644.
- Cawood TJ, Hunt PJ, O'Shea D, Cole D, Soule S. Recommended evaluation of adrenal incidentalomas is costly, has high false-positive rates and confers a risk of fatal cancer that is similar to the risk of the adrenal lesion becoming malignant; time for a rethink? *Eur J Endocrinol*. 2009;161:513-527.
- Young WF Jr. Clinical practice. The incidentally discovered adrenal mass. *N Engl J Med*. 2007;356:601-610.
- Li T, Shi YQ. Advance in diagnosis and treatment of adrenal incidentalomas. *Chin J Pract Int Med*. 2017;37:12-17.
- Kanagarajah P, Ayyathurai R, Manoharan M, Narayanan G, Kava BR. Current concepts in the management of adrenal incidentalomas. *Urol Ann*. 2012;4:137-144.
- Bednarczuk T, Bolanowski M, Sworcak K, et al. Adrenal incidentaloma in adults—management recommendations by the Polish Society of Endocrinology. *Endokrynol Pol*. 2016;67:234-258.
- Kapoor A, Morris T, Rebello R. Guidelines for the management of the incidentally discovered adrenal mass. *Can Urol Assoc J*. 2011;5:241-247.
- Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. *Lancet*. 2015;386:913-927.
- Farrugia FA, Martikos G, Surgeon C, et al. Radiology of the adrenal incidentalomas. Review of the literature. *Endocr Regul*. 2017;51:35-51.
- Boland GW, Lee MJ, Gazelle GS, Halpern EF, McNicholas MM, Mueller PR. Characterization of adrenal masses using unenhanced CT: an analysis of the CT literature. *Am J Roentgenol*. 1998;171:201-204.
- Barzon L, Scaroni C, Sonino N, Fallo F, Paoletta A, Boscaro M. Risk factors and long-term follow-up of adrenal incidentalomas. *J Clin Endocrinol Metab*. 1999;84:520-526.
- Morelli V, Reimondo G, Giordano R, et al. Long-term follow-up in adrenal incidentalomas: an Italian multicenter study. *J Clin Endocrinol Metab*. 2010;99:827-834.
- Di Dalmazi G, Vicennati V, Garelli S, et al. Cardiovascular events and mortality in patients with adrenal incidentalomas that are either non-secreting or associated with intermediate phenotype or subclinical Cushing's syndrome: a 15-year retrospective study. *Lancet Diabetes Endocrinol*. 2014;2:396-405.
- Fagour C, Bardet S, Rohmer V, et al. Usefulness of adrenal scintigraphy in the follow-up of adrenocortical incidentalomas: a prospective multicenter study. *Eur J Endocrinol*. 2009;160:257-264.
- Cho YY, Suh S, Joung JY, et al. Clinical characteristics and follow-up of Korean patients with adrenal incidentalomas. *Korean J Intern Med*. 2013;28:557-564.
- Comlekci A, Yener S, Ertilav S, et al. Adrenal incidentaloma, clinical, metabolic, follow-up aspects: single centre experience. *Endocrine*. 2010;37:40-46.
- Yener S, Ertilav S, Secil M, et al. Prospective evaluation of tumor size and hormonal status in adrenal incidentalomas. *J Endocrinol Invest*. 2011;33:32-33.
- Lopez D, Luque-Fernandez MA, Steele A, Adler GK, Turchin A, Vaidya A. "Nonfunctional" adrenal tumors and the risk for incident diabetes and cardiovascular outcomes: a cohort study. *Ann Intern Med*. 2016;165:533-542.

How to cite this article: Li T, Li W, Fang X, Lv Q, Song Y, Shi Y. Comprehensive analysis on 559 cases of adrenal incidentalomas in the elderly Chinese. *Aging Med*. 2018;1:35-38. <https://doi.org/10.1002/agm2.12006>