PAPERS AND ORIGINALS

Comparative study of ultrasound, ¹³¹I-19-iodocholesterol scintigraphy, and aortography in localising adrenal lesions

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Summary

Twenty-seven consecutive patients with endocrinological disease necessitating adrenal surgery underwent blind preoperative investigation with ultrasound, renal aortography, and adrenocortical scintigraphy for an adrenal lesion. Nine patients had pituitary-dependent Cushing's syndrome, five had pituitary-independent Cushing's syndrome, four had an adrenocortical androgenic excess, and nine had a preoperative diagnosis of pheochromocytoma. The predictive value of preoperative ultrasound was 100% for a positive finding and 79% for a negative result. Preoperative aortography had a predictive value of 83% for a positive finding and 64% for a negative result; and the predictive value of adrenocortical scintigraphy was 100% for a positive finding and 85% for a negative finding.

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In localising biochemically suspected adrenal lesions ultrasound should be the first choice, since it is rapid, noninvasive, cheap, and reasonably accurate. Adrenocortical scintigraphy has a similar diagnostic value, especially in Cushing's syndrome, but it is time consuming. Nevertheless, it may be preferable for diagnosing small glucocorticoid-secreting adenomas. Aortography should be reserved for cases with inconclusive diagnoses and suspected extra-adrenal pheochromocytomas.

Introduction

Adrenal arteriography,^{1,2} adrenal venography,^{3,4} and, more recently, ultrasound⁵⁻⁷ and ¹³¹I-19-iodocholesterol scintigraphy⁸⁻¹⁰ have all been used to show adrenal lesions in patients scheduled for adrenal surgery. But no systematic studies have been performed comparing the diagnostic values of these techniques in localising adrenal lesions.

In the present prospective study of 27 consecutive patients undergoing adrenal surgery the diagnostic value of ultrasound, iodocholesterol scintigraphy, and renal aortography was examined.

Patients and methods

We studied prospectively 27 consecutive patients undergoing adrenal surgery from October 1973 to January 1976. The indication for surgery was based solely on clinical history and biochemical findings suggesting an adrenal disorder.

Nine patients (cases 1-9) had pituitary-dependent Cushing's syndrome; five (cases 10-14) had pituitary-independent Cushing's syndrome; four (cases 15-18) had an adrenocortical androgenic excess, and the remaining nine (cases 19-27) had a preoperative diagnosis of pheochromocytoma (table I).

Ultrasound investigation was performed in all 27 patients. A conventional (bistable) compound scanning technique was used. With the patient prone, the long axis of the kidneys was established from transverse scans through their upper and lower poles. Scans, spaced

TABLE I—Clinical data on 27 consecutive patients scheduled for adrenal surgery and studied preoperatively with ultrasound, renal aortography, and adrenal scintiscan

Case No	Age and sex	Preoperative clinical and biochemical diagnosis	Preoperative ultrasound diagnosis	Preoperative adrenal scintigraphy: visualisation of adrenal cortex		Preoperative aortographic diagnosis	Findings during surgery	Adrenal histology
				Right	Left			
1	36 F	Pituitary-dependent Cushing's syndrome	Normal	+	+	Normal	Bilateral normal or hyperplastic adrenal glands	Bilateral adrenocortical hyperplasia
2	21 F	"	"	+	+	"	"	"
3	46 F	"	"	+	+	"	"	"
4	17 F	"	"	+	+	"	"	"
5	44 F	"	"	+	+	"	"	"
6	24 F	"	"	+	+	"	"	"
7	30 F	"	"	+	+	"	"	"
8	57 F	"	"	+	+	"	"	"
9	58 F	"	"	+	+	Tumour (3 × 5 cm) in left adrenal (suspected)	"	"
10	57 F	Pituitary-independent Cushing's syndrome	Tumour (8 × 8 cm) in left adrenal	0	+	Tumour (9 × 10 cm) in left adrenal	Tumour (8 × 10 cm) in left adrenal	Adrenocortical adenoma
11	58 F	"	Tumour (4 × 4 cm) in right adrenal	+	0	Tumour (4 × 4 cm) in right adrenal	Tumour (4 × 5 cm) in right adrenal	"
12	36 F	"	Tumour (3 × 5 cm) in right adrenal	0	+	Normal	Tumour (3 × 3 cm) in left adrenal	"
13	26 F	"	Tumour (3 × 3 cm) in right adrenal	+	0	"	Tumour (5 × 3 cm) in right adrenal	"
14	52 F	"	Normal	+	0	"	Tumour (3 × 3 cm) in right adrenal	"
15	27 F	Adrenocortical androgen-excess	Tumour (6 × 8 cm) in right adrenal			Tumour (10 × 10 cm) in right adrenal	Tumour (6 × 8 cm) in right adrenal	"
16	27 M	"	Tumour (8 × 8 cm) in left adrenal	+	0	Tumour (10 × 10 cm) in left adrenal	Tumour (10 × 10 cm) in left adrenal	"
17	35 F	"	Tumour (5 × 7 cm) in left adrenal	+	+	"	Tumour (9 × 6 cm) in left adrenal	"
18	21 F	"	Tumour (4 × 4 cm) in left adrenal	+	+	Normal	Left adrenal enlarged (6.5 × 12 cm) right normal	Adrenocortical hyperplasia (left adrenal)
19	41 F	Phaeochromocytoma	Tumour (6 × 6 cm) in left adrenal			Tumour (5 × 7 cm) in left adrenal	Tumour (6 × 7 cm) in left adrenal	Phaeochromocytoma
20	36 M	"	Tumour (5 × 5 cm) in left adrenal			Tumour (5 × 5 cm) in left adrenal	Tumour (6 × 6 cm) in left adrenal	"
21	24 F	"	Tumour (5 × 5 cm) in right adrenal			Tumour (6 × 5 cm) in right adrenal	Tumour (6 × 5 cm) in right adrenal	"
22	52 F	"	Tumour (5 × 5 cm) in right adrenal	+	+	Tumour (6 × 6 cm) in right adrenal	Tumour (6 × 6 cm) in right adrenal	"
23	41 M	"	No tumour but right kidney displaced	+	+	Tumour (7 × 7 cm) in right adrenal	Tumour (8 × 8 cm) in right adrenal	"
24	57 M	"	Normal	+	+	Normal	Tumour (4 × 3 cm) in left adrenal	"
25	28 F	"	Tumour (7 × 7 cm) in left adrenal	+	+	Tumour (9 × 9 cm) in left adrenal	Tumour (8 × 8 cm) in left adrenal	Adrenal carcinoma
26	49 M	"	Normal	+	+	Normal	Left adrenal slightly indurated	Normal left adrenal
27	17 M	"	"	+	+	Tumour (7 × 5 cm) in right adrenal	Normal adrenals	No histology

*Impaired visualisation.

at 1 cm were then taken through the adrenal regions parallel as well as perpendicular to the long axis of the kidneys.⁵ All examinations were supplemented by transverse and longitudinal scans of the adrenal regions with the patient supine. With this technique it was not considered possible to visualise the normal adrenals.

Renal aortography was performed in 26 patients. With the Seldinger technique a teflon 7F catheter (US CI No 7445) was inserted via a femoral artery. The tip of the catheter was placed just above the origin of the uppermost renal artery and a tip occluder was inserted. At a rate of 15–20 ml/sec 40 ml of 76% Urografin was injected. Radiographs were taken using two x-ray tubes 12° apart as a sort of stereo technique in 15 cases and an ordinary anterior-posterior technique in seven cases. In the remaining four patients midstream aortograms from other hospitals were used.

Adrenocortical scintigraphy was carried out in 23 patients using an Ohio Nuclear rectilinear scanner and ¹³¹I-19-iodocholesterol.¹⁰ The radiopharmaceutical was obtained from the University of Michigan, Ann Arbor, USA or from the Institute of Atomic Energy, Kjeller, Norway. Four patients (table I) were not examined with adrenal scintigraphy since this technique was not in use when the study began. Scintigraphy was performed seven to 10 days after the injection of 2.0–2.5 mCi of the radiopharmaceutical and, if necessary, repeated after an enema had been given.

The ultrasound and aortography investigations were performed and the results evaluated before surgery without knowledge of the endocrinological diagnosis. The scintiscans were all reviewed blindly.

In 25 of the patients the interval between ultrasound and surgery was on an average 16 days (range 5–43 days), between adrenal scintigraphy and surgery 20 days (range 7–44 days), and between aortography and surgery 21 days (range 4–66 days). In case 26 the interval between investigation and surgery was four months, and in case 3 it was 10 months.

In all patients an operative diagnosis (table I) was made by scrupulous dissection and palpation of both adrenal glands through an anterior transabdominal approach. The surgeon was always aware

of the results of all the preoperative investigations. Finally a histological diagnosis was made from the specimens removed.

Fisher's exact probability test was used for significance testing.

Results and comment

The results are summarised in table II.

TABLE II—Results of preoperative investigations compared with diagnosis made at surgery

	Diagnosis at surgery		Total	Predictive value of diagnosis (%) (95% confidence limits)
	Unilateral adrenal lesion	Bilateral normal or hyperplastic adrenals		
<i>Diagnosis on ultrasound</i>				
Unilateral adrenal lesion	13	0	13	100 (79–100)
Normal	3	11	14	79 (49–95)
Total	16	11	27	
<i>Diagnosis on aortography</i>				
Unilateral adrenal lesion	10	2	12	83 (52–98)
Normal	5	9	14	64 (35–87)
Total	15	11	26	
<i>Diagnosis on scintigraphy</i>				
Unilateral adrenal lesion	10	0	10	100 (69–100)
Normal	2	11	13	85 (55–98)
Total	12	11	23	

UNILATERAL ADRENAL LESIONS VERIFIED BY SURGERY

Sixteen patients (cases 10-25) had a unilateral adrenal lesion.

Preoperative ultrasound examination correctly identified 13 of these lesions but gave false-negative results in the remaining three patients. Preoperative aortographic examination showed a true-positive result in 10 patients and a false-negative result in the remaining five of the 15 patients studied. Preoperative scintigraphy was carried out in 12 of the 16 patients with a unilateral adrenal lesion. The adrenal lesion was correctly localised in 10 patients. In the remaining two patients (cases 18 and 24) a normal bilateral scintiscan was obtained.

BILATERAL NORMAL OR HYPERPLASTIC ADRENALS VERIFIED BY SURGERY

Eleven patients had bilateral normal or hyperplastic adrenals. Nine of these patients (cases 1-9) had pituitary-dependent Cushing's syndrome and the remaining two patients (cases 26-27) had a pre-operative diagnosis of pheochromocytoma.

Preoperative ultrasound examination was normal in all 11 patients. Preoperative aortographic examination showed no evidence of unilateral adrenal lesions in nine of these 11 patients but gave false-positive results in cases 9 and 27. However, the tumour was only suspected.

Preoperative scintigraphy showed normal bilateral visualisation of the adrenals in all 11 patients.

PREDICTIVE VALUES OF FINDINGS

The results showed (table II) that the predictive value of a positive finding at preoperative ultrasound examination for unilateral adrenal lesion was 100% (95% confidence limits 79-100%) and the corresponding predictive value of a negative finding during preoperative ultrasound was 79% (95% confidence limits 49-95%).

The predictive value of a positive finding at preoperative aortographic examination for a unilateral adrenal lesion was 83% (95% confidence limits 52-98%) and of a negative finding 64% (confidence limits 35-87%). There was no difference ($P > 0.1$) between the efficacy of ultrasound and aortography in diagnosing adrenal lesions.

The predictive value of a positive finding at preoperative scintigraphy for a unilateral adrenal lesion was 100% (95% confidence limits 69-100%) and of a negative finding 85% (95% confidence limits 55-98%). But in determining the predictive value of a positive or negative finding by adrenocortical scintigraphy the ability of the lesion to take up ^{131}I -19-iodocholesterol should also be taken into consideration. Thus, the glucocorticoid-secreting adrenal tumours can be localised by showing abolished uptake and visualisation of the contralateral gland. In contrast, androgen-secreting tumours and pheochromocytomas may be localised by showing defects on the scintigrams. Our results showed a correct scintigraphic diagnosis in all 14 patients with Cushing's syndrome, five of whom had a glucocorticoid-secreting adenoma. Among the seven patients with androgen excess or pheochromocytoma examined the adrenal scintigraphic diagnosis was correct in five. The difference between the value of adrenal scintigraphy in diagnosing adrenal lesions in Cushing's syndrome and its value in patients with androgen-secreting adenomas and pheochromocytomas was not significant ($P > 0.1$). Nevertheless, adrenal scintigraphy was more valuable in obtaining the correct adrenal diagnosis in patients with Cushing's syndrome than aortography ($P = 0.1$) but no more valuable than ultrasound ($P > 0.1$). There was no difference ($P > 0.1$) between the value of the three techniques in diagnosing androgen-secreting tumours and pheochromocytomas.

Discussion

Preoperative localisation of unilateral adrenal lesions is of considerable help to the surgeon operating on patients in whom an adrenal disorder has been shown by biochemical and endocrinological investigations.²⁻¹¹ The diagnostic tools available for showing adrenal lesions are renal aortography or selective adrenal angiography, adrenal venography, ultrasound imaging, and adrenal scintigraphy with ^{131}I -cholesterol. The relative

diagnostic value of these techniques is difficult to evaluate since there have been no studies in which consecutive patients have been submitted to several of these investigations. Much experience, however, has recently been gained with arteriography and adrenal venography; they have a diagnostic accuracy of about 80-95%.^{1-3, 4, 11-13} Selective adrenal arteriography seems to be slightly more accurate than renal aortography.^{12, 13} Adrenal venography seems to be especially valuable in localising adrenal lesions in Conn's syndrome,^{3, 4} but its apparently greater sensitivity must be weighed against a potentially higher complication rate than in other angiographic techniques.⁴ We found that non-selective adrenal angiography missed a unilateral adrenal lesion in five out of 15 cases (table II). Four of these patients had small tumours about 3 cm in diameter, but a higher diagnostic success rate might have been obtained by selective adrenal catheterisation.

The value of ultrasound in diagnosing adrenal lesions has already been suggested.⁴⁻⁷ We found that the diagnostic accuracy of adrenal ultrasound imaging was similar to that of renal aortography and adrenocortical scintigraphy. Furthermore, our data support earlier suggestions that adrenal lesions measuring less than 3 cm will be difficult to outline.^{4, 5, 7} It must be emphasised that we had no cases of Conn's syndrome, a disorder in which ultrasound would probably be less valuable because of the smaller adrenal lesion⁴; adrenal venography⁴ or adrenocortical scintigraphy¹⁴ would probably be the method of choice.

The value of ^{131}I -19-iodocholesterol adrenocortical scintigraphy in diagnosing adrenal lesions in Cushing's syndrome^{8-10, 15} and pheochromocytomas¹⁶ has been reported. Our results confirm its high diagnostic accuracy in Cushing's syndrome,¹⁵ since all 14 patients with Cushing's syndrome were correctly diagnosed as having adrenocortical adenomas or adrenocortical hyperplasia (table I). Although our data do not permit a conclusion, scintigraphy may be expected to be more accurate in diagnosing small (under 3 cm) glucocorticoid-secreting adenomas than either ultrasound or aortography.

Although here were no significant differences between the techniques in the whole series of patients, adrenocortical scintigraphy was more accurate than angiography in diagnosing tumours in patients with Cushing's syndrome ($P = 0.1$) but no more accurate than ultrasound ($P > 0.1$). On the basis of these results we suggest that in the preoperative localisation of adrenal lesions ultrasound should be the first choice since it is accurate, rapid, noninvasive, and cheap. Adrenocortical scintigraphy is just as accurate but is time consuming, although it may be preferable for diagnosing small glucocorticoid-secreting adenomas. Aortography should be reserved for inconclusive cases and suspected extra-adrenal pheochromocytomas.

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