SCIENTIFIC PAPER

Outcome of Patients Undergoing Laparoscopic Adrenalectomy for Primary Hyperaldosteronism

Brian K. P. Goh, MBBS, MMed(Surgery), Yeh-Hong Tan, MBBS, Sidney K. H. Yip, MBBS, Peter H. K. Eng, MBBS, Christopher W. S. Cheng, MBBS

ABSTRACT

Objectives: To study the long-term outcome of patients with primary hyperaldosteronism who underwent laparoscopic adrenalectomy and to determine the preoperative predictive factors of persistent hypertension.

Methods: Between 1996 and 2002, 47 patients with primary hyperaldosteronism underwent transperitoneal laparoscopic adrenalectomy at our institution. Their clinical and biochemical parameters were reviewed retrospectively, and the outcome of 46 patients with complete follow-up notes were determined.

Results: The study comprised 16 male and 30 female patients with a mean age of 45.6 years (range, 18 to 63 years). Almost all patients had hypertension and hypokalemia at presentation, requiring medication. The average operating time was 127 minutes (range, 70 to 240 min), and the mean postoperative stay was 2.6 days (range, 1 to 5 days). No mortalities occurred, and perioperative morbidity was minimal. Forty-two (91%) patients had adrenal cortical adenoma (including 1 with both adenoma and hyperplasia), and 4 (9%) had adrenal hyperplasia on histology. The average follow-up time was 21 months (range, 1 to 60 months), and at the end of follow-up, all patients had normal serum potassium levels without potassium supplements. Twenty-three (50%) patients were cured of hypertension, and 13 (28%) patients had better control of their hypertension as evidenced by the decrease in the number of antihypertensive medications used. On multivariate analysis, the age of the patient at surgery was shown to be an independent predictive factor of persistent hypertension after successful surgery.

Conclusion: Laparoscopic adrenalectomy is a safe and effective way to treat primary hyperaldosteronism, especially in controlling hypokalemia and in the management of hypertension. The age of a patient at surgery is an independent preoperative risk factor of persistent hypertension.

Key Words: Laparoscopy, Adrenalectomy, Hyperaldosteronism, Conn's syndrome.

INTRODUCTION

Although previously thought to be a rarity, primary hyperaldosteronism is now considered one of the most common causes of secondary hypertension. It occurs in approximately 1 in every 200 patients who are hypertensive but constitutes one of the most common causes of surgically correctable hypertension.[1] It was first described in 1955 by Jerome Conn as a syndrome characterized by hypertension, hypokalemia, and excessive urinary excretion of aldosterone in association with adrenal cortical adenoma (Conn's syndrome).[2] However, we now know that primary hyperaldosteronism may also be caused by other adrenal pathologies, such as idiopathic adrenal hyperplasia or adrenal carcinoma.[3]

Aldosterone-producing adenoma is the most common cause of primary hyperaldosteronism, and the treatment of choice is adrenalectomy.[4–8] Unilateral adrenalectomy has also been shown to be the ideal treatment for patients with unilateral sources of aldosterone secretion, such as unilateral hyperplasia and adrenal carcinoma.[8,9] For bilateral adrenocortical hyperplasia, medical therapy with aldosterone antagonists, such as spironolactone, appears to be the best treatment.[1,10]

Ever since the first laparoscopic adrenalectomy was performed in 1992 by Gagner, this procedure has become the treatment of choice and has replaced open surgery for the removal of adrenal tumors.[3,11] The transperitoneal laparoscopic approach most widely used today was pioneered by Gagner in 1994, whereby the patient is placed in the lateral decubitus position, which allows better exposure of the adrenals.[12] Laparoscopic adrenalectomy demonstrates many benefits of minimally invasive surgery including decreased postoperative pain, a shortened hospitalization, a more rapid convalescence, decrease in overall

Department of Urology, Singapore General Hospital, Singapore (Mssrs Goh, Tan, Yip, Cheng).

Department of Endocrinology, Singapore General Hospital, Singapore (Mr Eng).

Address reprint requests to: Brian K. P Goh, MD, Department of Urology, Singapore General Hospital, Outram Road, Singapore 169608. Telephone: 65 63214056, Fax: 65 62273787, E-mail: bsgkp@hotmail.com

cost and decreased morbidity with the smaller incisions and shorter postoperative recovery time.[4,7,13–19] Although it has been well demonstrated in the literature that open adrenalectomy is beneficial in patients with aldosterone producing adenoma, long-term outcome after laparoscopic adrenalectomy has not been extensively studied.

The aim of our study was to evaluate the long-term outcome of patients undergoing laparoscopic adrenalectomy for hyperaldosteronism with particular attention to the control of hypokalemia and hypertension and to determine the preoperative risk factors of persistent hypertension after successful surgery.

METHODS

From July 1996 to March 2002, 47 consecutive patients underwent laparoscopic adrenalectomy for primary hyperaldosteronism at Singapore General Hospital. Patients' medical records including the pathology and operative reports were reviewed retrospectively, and the relevant parameters were studied including the pre- and postoperative blood pressures and serum potassium levels. One patient's follow-up records were incomplete and excluded from the follow-up study. The outcome of 46 patients with complete follow-up records was determined with particular attention to the control of blood pressure and serum potassium levels.

All the patients had hypertension at presentation and 94% had hypokalemia (n=44). Patients with suspected hyperaldosteronism underwent some or all of the following laboratory investigations including random serum aldosterone and renin, 24-hour urine potassium excretion, and 24-hour urine aldosterone measured after salt loading. All our patients had a computed tomography scan to localize the adrenal adenoma. Postural studies and adrenal venous sampling were only used when the diagnosis remained uncertain after the above tests.

The surgical technique used for all our patients was the transperitoneal approach via the flank with the patient in the lateral decubitus approach as described previously.[20] Preoperative risk factors of persistent hypertension studied included age of patient at surgery, sex, duration of hypertension, systolic blood pressure, serum potassium level, and size of adenoma.

Mann-Whitney *U* tests were used to compare continuous variables, and chi-squared tests were used to compare categorical variables. A stepwise multiple logistic regression analysis was performed to assess the combined predictive effects of the clinicopathologic variables. In this analysis, outcome of hypertension was the dependent variable; and the clinical, biochemical, and pathologic variables were independent predictor variables. All statistical procedures were performed using the computer software SPSS for Windows Version 10.0.

RESULTS

Forty-six patients underwent surgery, and their demographic characteristics are summarized in **Table 1**. All the patients were hypertensive, and 44 (96%) had hypokalemia at presentation. In general, most of the patients had poorly controlled hypertension, and the mean duration of hypertension before surgery was 6.7 years (range, 0 to 20 years).

On biochemical confirmation of hyperaldosteronism, a computed tomography scan was successful in localizing all the tumors except in 1 patient whose scan was equivocal, and magnetic resonance imaging was used to localize his tumor. Laparoscopic transperitoneal adrenalectomy was performed in all the patients and no conversions were necessary. Twenty-three patients underwent left-sided and the rest had right-sided surgery. The average operating time was 127±36 minutes (range, 70 to 240 min), and the mean postoperative stay was 2.6±0.9 days (range, 1 to 5 days). No mortalities occurred, and the only morbidity was superficial wound infection in 1 patient, which settled with antibiotic treatment and wound dressing.

Histology revealed that 42 (91%) patients had cortical adenomas (including 1 with concomitant adenoma and hyperplasia) and 4 (9%) had adrenal hyperplasia. The mean size of the adenomas was 1.9 ±0.7 cm (range, 0.7 to 3.7 cm).

Postoperative Follow-up

The average follow-up time of the 46 patients was 21±19 months (range, 1 to 60 months). The functional outcome

Table 1.
Patient Demographics

No. of patients	46
Mean age (yrs)	45.6 (18–63)
Sex	16 M, 30 F
Hypertensive at presentation	46 (100%)
Hypokalemic at presentation	44 (96%)
Duration of hypt (yrs)	6.7 (0–20)

data are summarized in **Table 2**. On follow-up, all the patients had normal serum potassium levels without potassium supplements. The mean potassium level at presentation of 2.4 μmol/L (range, 1.4 to 3.5 μmol/L) was significantly lower than the mean postoperative potassium levels of 4.3 μmol/L (range, 3.7 to 5.1 μmol/L) ($P<0.05$).

At the end of follow-up, 23 patients (50%) were cured of their hypertension, not requiring any medications for blood pressure control. A further 13 (28%) had improved control of their blood pressure as evidenced by the decrease in the number of antihypertensive medications used. Of the remaining 10 patients (22%) who had persistent hypertension requiring the same number of antihypertensives, 8 (17%) had better control. This presumption was made on the fact that these patients had lower mean blood pressure after surgery, and they no longer required frequent follow-up and adjustment of their medications.

At latest follow-up, the mean blood pressure (136/83 mm Hg) was significantly lower than the preoperative measurements (166/98 mm Hg, $P<0.0005$). Patients in general also required fewer antihypertensive medications after surgery (mean, 1±1.1 antihypertensives) compared with their preoperative requirements (mean, 2.1±0.9 antihypertensives).

Table 3 summarizes the results of our analysis of the possible preoperative risk factors of persistent hypertension. Univariate analysis showed that age at surgery and duration of hypertension were statistically significant in predicting postoperative persistent hypertension. Severity of hypertension indicated by the number of antihypertensives used was also statistically significant as a risk factor of persistent hypertension. However, although a trend was present toward the higher the systolic blood pressure preoperatively, the more likely it was that the patient had persistent hypertension, this only approached statistical significance.

On multivariate analysis using stepwise logistic regression, only age at surgery was shown as an independent risk factor of postoperative persistent hypertension. A strong positive correlation existed between the duration of hypertension and age at surgery ($r=0.45$), which was evident in the logistic model.

DISCUSSION

Laparoscopic adrenal surgery is undoubtedly the most important advance in adrenal surgery over the last decade, and its impact is such that it is currently the treatment of choice for patients with various adrenal functional tumors including aldosterone-producing adenoma. It has been well documented that the laparoscopic procedure is safe with substantially less morbidity than open surgery for similar indications.[7,13,14,21] The laparoscopic approach is feasible in approximately 60% of surgically treatable adrenal disease.[7] Classically, the contraindications to the laparoscopic approach are large tumor size (>6 cm because of the high likelihood of malignancy), local tumor invasiveness or large primary adrenal malignancy.[4,14,22] However, tumor size larger than 6 cm and adrenal malignancy cannot be considered as absolute contraindications now as several authors have advocated laparoscopic removal of these tumors.[23,24] Coagulopathy and previous surgery or trauma to the region of the gland to be removed are also relative contraindications to laparoscopy.[21]

Table 2.
Comparison of Preoperative and Postoperative Patient Data*

	Preoperative	Postoperative	*P* Value†
Mean Systolic BP (mm Hg)	166±32	136±20	<.0005
Mean Diastolic BP (mm Hg)	98±19	82±14	<.0005
Serum K+ (μmol/L)	2.4±0.6	4.3±0.3	<.0005
Hypertensive	46/46 (100%)	23/46 (50%)	<.0005
Mean No. of Medications	2.1±0.9	1.0±1.1	<.0005
Hypertension Cured	NA	23/46 (50%)	NA
Hypertension Improved	NA	44/46 (95%)	NA
Normokalemia	NA	46/46	NA

*NA = Data not available.

†Wilcoxon Signed Ranks test used to determine *P* value.

Table 3.
Analysis of Possible Preoperative Risk Factors of Persistent Hypertension*

Variable	Normotensive (n = 23)	Hypertensive (n = 23)	Total	*P* Value
Mean age at surgery (yrs)	41.2±10.85	50.1±8.7	NA	0.007
Mean duration of hypertension (yrs)	4.6±4.8	8.9±6.1	NA	0.01
No. of medications before operation	1.6±0.8	2.5±0.9	NA	0.002
Mean serum K (mmol/L)	2.3±0.5	2.6±0.6	NA	0.130
Size of adenoma (cm)	1.9±0.6	1.6±0.6	NA	0.168
Systolic blood pressure (mm Hg)	156±27	173±31	NA	0.06
Sex	6M, 17F	11M, 12F	17M, 29F	0.221

*NA = Data not available.

In our series, all 46 patients underwent successful laparoscopic surgery without any conversions. The safety of the procedure was well illustrated by the absence of mortality and the minimal perioperative morbidity. However, despite the obvious success of the laparoscopic approach over the past decade, the long-term outcome of laparoscopic surgery in patients with primary hyperaldosteronism has not been extensively studied. A review of the literature revealed only a handful of outcome studies on patients who underwent laparoscopic adrenalectomy for primary hyperaldosteronism.[3,24–29] All were smaller series compared with the present report except for the recent series by Meria et al.[27] Overall, hypokalemia was cured in 96% to 100% of patients, whereas hypertension was cured in 31% to 88% of patients.[3,24–29] These results are comparable to those of outcome studies in patients who underwent open surgery whereby the cure rates of hypokalemia were also close to 100%, and the hypertensive cure rates ranged from 41% to 77%.[5,6,30] In our series, all patients were normokalemic, while 50% of patients were cured of hypertension. **Table 4** summarizes and provides a comparison between our study and 5 previous outcome studies on patients undergoing laparoscopic surgery.

Essential hypertension has been suggested as the reason behind persistent hypertension after adrenalectomy.[31] Several preoperative factors have been shown to be risk factors for the development of persistent hypertension after surgery, and these include older age of the patient at surgery, longer duration of preoperative hypertension, nonresponse of blood pressure to spironolactone, male sex, and family history of hypertension. **Table 5** summarizes some of the studies evaluating preoperative predictive factors of persistent hypertension. Although preoperative blood pressure response to spironolactone has been shown as a predictive factor, we were unable to evaluate it as most of our patients were on other concomitant antihypertensive medications preoperatively.[6,31–33]

Our univariate analysis revealed that duration of hypertension preoperatively, age of patient at surgery, and severity of preoperative hypertension were possible risk factors of persistent hypertension. However, age at sur-

Table 4.
Comparison of Current Study With Previous Outcome Studies of Patients Undergoing Laparoscopic Adrenalectomy*

Study	No. of Patients	Age (years)	Follow-up (months)	Hypertension Duration (years)	Normokalemia (%)	Hypertension Cured
Rossi[25]	30	51.2	26.1	NA	97	67
Brunt[26]	26	48	27.9	9.8	96	31
Shen[3]	42	50	NA	2.5	100	88
Bonjer[24]	26	NA	14	NA	100	64
Meria[27]	182	48	44	12	100	58
Current Study	46	45.6	21	6.7	100	50

*NA = Data not available.

Table 5.
Studies Evaluating Preoperative Predictive Factors of Persistent Hypertension*

Study	Method	n	% Cured of Hypertension	Hypertension Duration	Age	Sex	Histology	Response to Spironolactone	Family History
Obara[36]	Open	63	62	−ve	+ve	+ve	+ve	NA	−ve
Celen[32]	Open	42	60	+ve	+ve	−ve	+ve	+ve	−ve
Siren[30]	Open	29	41	+ve	NA	NA	NA	NA	NA
Proye[31]	Open	100	56	+ve	+ve	−ve	−ve	+ve	+ve
Simon[34]	Open	13	54	+ve	−ve	−ve	NA	NA	NA
Lo[6]	Open	44	77	−ve	+ve	−ve	NA	+ve	NA
Rossi[25]	Lap	30	67	+ve	−ve	−ve	NA	NA	NA

*NA = Data not available.

gery was shown as the only independent risk factor on multiple stepwise logistic regression. Several studies have shown that duration of hypertension preoperatively is a risk factor of persistent postoperative hypertension.[5,25,30,31,34] Irreversible vascular damage during longstanding hypertension despite surgical cure of metabolic derangement has been suggested as the reason why duration of hypertension is a risk factor.[35] Older age of the patient at surgery has also been shown by previous studies to be a predictive factor of postoperative hypertension.[6,31,32,36] The higher incidence of essential hypertension in older patients has been proposed as an important reason why older age is a risk factor. Furthermore, it is possible that older patients are more likely to have longstanding hypertension and are more susceptible to the irreversible hypertensive vascular changes.[32] In fact, our study suggests a strong correlation between the age of a patient and the duration of hypertension.

Identification of patients at high risk for persistent hypertension after successful surgery does not preclude them from undergoing surgery, as the majority of them will benefit from the procedure. However, identifying these patients preoperatively is important as these patients can be warned preoperatively of the slightly less favorable outcome, and they should be followed up more closely after surgery.

CONCLUSION

In summary, laparoscopic adrenalectomy is a safe and effective procedure in the treatment of patients with primary hyperaldosteronism with a good outcome in terms of hypokalemia and blood pressure control. Age of a patient at surgery is an independent predictive factor of persistent hypertension postoperatively.

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