Original Article

Pre-operative renal function and selective renal vein rennin levels as markers of favourable outcome in renovascular hypertension

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Abstract

Objective: To evaluate factors that affect outcome following revascularization in patients with renovascular hypertension.

Methods: This study was conducted at the Aga Khan University Hospital. It included all the patients diagnosed to have Renovascular hypertension confirmed by renal angiography between July 1996 to September 2000. Using ANOVA (Analysis of variance) and paired-sample t-test, several preoperative factors were evaluated for their ability to predict postoperative improvement of blood pressure and renal function. For descriptive purpose patients were divided into cured, improved and failure groups.

Results: Of the total 15 patients, 9 were males and 6 were females. Before the surgical procedure, 13 patients were on 3 or more antihypertensive drugs. Eleven patients received vein grafts, three patients had PTFE (polytetraflouroethyline) grafts while one patient underwent angioplasty and stenting. The patients had a median follow-up period of nine months with a range of 2 to 84 months. Five were completely cured, as they became normotensive without antihypertensive therapy after operation, whereas four showed marked improvement in BP control postoperatively, requiring two antihypertensive drugs. Six patients showed no improvement requiring 3 or more drugs. Extended cure or improvement of renovascular hypertension was achieved in nine patients. Normal preoperative serum creatinine level, high preoperative unstimulated peripheral renin levels and renal vein renin ratio of at least 1.75:1 were the most significant predictive factors for favorable outcome.

Conclusion: This study confirms the long term effectiveness and safety of renovascular reconstruction in the relief of severe hypertension. The results further suggest that normal preoperative renal function, high renal vein renin ratio and high preoperative unstimulated peripheral renin levels are associated with the most favourable postoperative outcome ($p < 0.01$). Preoperative severity and duration of hypertension and degree of disparity in kidney sizes do not affect the overall results in terms of postoperative improvement in renal function and blood pressure control ($p=0.734$) (JPMA 57:178;2007).

Introduction

Renovascular hypertension is one of the most common potentially curable types of secondary hypertension.[1] The exact prevalence of renovascular hypertension in the general population is not known and diagnosis is missed in many patients.[2] It is important to diagnose it at an early stage since it is the most common curable form of hypertension and is one of the few potentially reversible causes of chronic renal failure.[1] Preponderance of experimental data suggests that the mechanism of hypertension in renovascular disease is produced by stimulation of renin-angiotensin system.

About 80% of patients require less medication for hypertension after angioplasty or operation[3] whereas about 30% of all patients require no antihypertensive therapy after the procedure.[4] Approximately two-thirds of patients have arterial changes due to atherosclerosis and almost one third have changes due to fibromuscular dysplasia. Untreated cases of renovascular disease indefinitely progress to worsening of renal function and high cardiovascular morbidity and mortality.[5,6] Medical therapy in general does not inhibit progressive loss of renal function.[6-8] Once renal artery is stenosed more than 70%, revascularization is indefinitely required. Renal revascularization performed in such cases not only prevents or reverses renal failure but also results in adequate blood pressure control[5] and significantly improved survival in these patients compared with a comparable-age matched population.[5,9] There has never been a prospective randomized comparison of PTA and reconstructive procedures. However all retrospective comparisons have found surgical results to be superior to PTA for patients with atherosclerotic disease, whereas patients with fibrodysplastic lesions responded well to either therapy. Surgical revascular procedures are not without risk. Overall mortality is about 5%, and major complication rate is approximately 10%.[10] We conducted this study to evaluate factors that affect common following revascularization in patients with renovascular hypertension. In order to define which patients will get benefit from revascularization procedure and hence to avoid un-necessary risks associated with surgery.

Patients and Methods

This study was conducted at the Aga Khan University Hospital. It included all the patients diagnosed to have renovascular hypertension confirmed by renal angiography between 1997 to 2000. Record files were reviewed in terms of age, sex, clinical presentation, laboratory investigations including S.Creatinine, electrolytes, Ultrasound kidneys, duplex scan, captopril DTPA scan and conventional angiography. Pre and post operative blood pressure recordings, renal function and renal and peripheral venous samples for renin estimation were also assessed. All the data was analyzed using SPSS version (Release 8.0, standard version, copyright SPSS; 1989-97). Using ANOVA (Analysis of variance) and paired-sample t-tests, several preoperative factors including duration of hypertension at the time of presentation, renal vein renin ratio (affected versus non-affected kidney), disparity in kidney sizes, renal function at the time of presentation and unstimulated peripheral renin levels were analyzed for their ability to predict postoperative improvement of blood pressure and renal functions.

For descriptive purpose patients were divided into cured, improved and failure groups. Cure was defined as normalization of renal function and blood pressure without any anti-hypertensive therapy.

Improvement was defined as > 20 % decrease in post operative S. Creatinine and post-operative blood pressure of < 160/100 mmHg, but greater than 140/90 mm of Hg.

Failure was defined as rise in S. Creatinine of >20% as compared to preoperative levels and blood pressure of >160/100 mmHg in the postoperative phase.

Patients with extrinsic compression of renal arteries or stenosis of renal grafts were excluded.

Results

Summarized in Table 1 are clinical and biochemical data from 15 patients with Renovascular hypertension who were subsequently operated upon and followed up for a period of 9 months (median) with the range from 2 to 84 months. Among 15 patients, 9 were males and 6 were females. Eleven patients received vein grafts, three received PTFE (polytetraflouroethyline) grafts while one patient underwent angioplasty and stenting. According to the criteria set before starting the study, 5 patients were cured, 4 showed marked improvement while 6 patients showed no improvement. Mean age in the cured group was 45 years (range 15-64 years), in improved group, 30 years (range 22-38) and in failure group it was 35 years (Range 27-52 years).

In the cured group renal function was normal in 3 patients at the time of presentation and impaired in 2 patients. After surgical intervention renal function normalized in one while in the others it showed marked improvement over a period of 9 months.

In the improved group, Serum Creatinine (S. Cr) was high in three patients (range 1.7-3.9) and normal in one patient at the time of presentation. Of the three patients with high S.Cr at presentation two showed marked improvement while in third patient renal function became normal postoperatively.

Table 1. Pre and postoperative features of Renovascular Hypertension.

Sr. No.	Age (Years)	Sex	Pre-operative		Post-operative		Disparity in kidney size cm	Peripheral renin level ng/ml/hr	Renal vein renin ratio (RVRV)	Duration of HTN Years	Mean FU (Months)	Site of lesion	Outcome
			BP mmHg	S.Cr mg/dl	BP mmHg	S.Cr mg/dl							
1	54	F	246/130	1.2	120/80	1.1	2.0	8.6	2.73:1	7	84	L	Cure
2	50	M	160/110	1.1	125/70	1.1	3.0	10.0	2.50:1	6	9	R	Cure
3	64	M	165/105	2.7	110/80	2.5	4.0	11.3	2.60:1	4	9	R	Cure
4	43	F	180/100	1.5	135/65	1.0	2.3	8.2	2.80:1	5	24	R	Cure
5	15	M	160/110	0.7	110/65	0.7	3.2	15.5	5.50:1	2.6	6	L	Cure
6	28	F	270/140	3.9	150/85	3.6	2.8	14.40	2.20:1	6	12	L	Improved
7	38	M	230/130	1.0	145/90	1.0	2.6	15.9	1.90:1	16	24	L	Improved
8	22	M	220/140	1.7	140/95	1.0	2.2	19.7	2.00:1	2	32	R	Improved
9	31	M	160/105	1.8	150/80	1.7	2.5	10.0	1.75:1	0.8	2	R	Improved
10	27	F	190/110	2.1	230/130	2.2	3.0	5.1	0.78:1	0.4	51	L	Failure
11	41	M	235/130	2.8	220/140	2.8	2.8	5.3	0.83:1	8	5	R	Failure
12	52	F	180/110	2.5	180/100	4.0	0.0	4.8	1.10:1	12	12	R+L	Failure
13	30	F	180/100	0.8	140/98	1.8	2.2	4.1	0.51:1	0.8	0	L	Failure
14	27	M	170/110	1.6	170/80	2.9	2.1	6.0	0.68:1	2	0	R	Failure
15	40	M	170/80	0.9	160/110	2.7	4.1	5.2	1.1: 88	30	6	R+L	Failure

Four patients in the failure group had high S.Cr inicially (mean 2.5 mg, range 1.6-2.5 mg) and these four patients showed further worsening over an average period of 17 months. In the remaining two patients in whom renal function was normal at the time of presentation, it deteriorated over an average period of four months. The blood pressure remained uncontrolled in one patient who refused to undergo surgery and showed deterioration of renal function over a period of six months.

The mean preoperative BP was 183/111mm Hg in the cured group, 220/128 mmHg in improved group and 188/106 mmHg in the failure group. Mean duration of hypertension was 60 months, 74 months and 106 months in the groups respectively.

The mean postoperative BP in the cured group was 120/70 mmHg, 145/88 mmHg in the improved group and 183/110 mmHg in the failure group.

The mean disparity in kidney size was 2.9 cm (Range 2-4) in the cured group, 2.5 cm in improved group, and 2.33 cm (Range 0.0 - 4.10) in the failure group.

The mean renal vein rennin ratio (affected versus non affected kidney) was 3.23:1 (range 2.50-5.50: 1) in the cured group, 1.96:1 (range 1.75-2.2: 1) in the improved group and 0.83:1 (range 0.51-1.1: 1) in the failure group.

The mean peripheral rennin level was 10.72 ng/ml/hr / (Range 8.2-15.5) in the cured group, 15.2 ng/ml/hr (range 10.0-19.7) in the improved group and 5.13 ng/ml/hr (range 4.1-6) in the failure group.

Discussion

Renovascular hypertension is the most common curable form of high blood pressure. Several new concepts have emerged in recent years relative to atherosclerotic renal artery stenosis. Most notably, the indications for intervention have changed.[5,6] The enhanced efficacy of medical anti-hypertensive therapy has decreased the number of patients who require intervention solely to treat renovascular hypertension. On the other hand, recent studies of the natural history of atherosclerotic renal artery stenosis have shown that progressive vascular obstruction occurs commonly in patients treated medically and in most of cases leads to deterioration of renal function.[7] This information has reinforced the importance of relieving renal arterial obstruction to preserve renal function in these patients.[7] However, in some patients with atherosclerotic renovascular disease, it is difficult to determine whether the hypertension is truly renovascular or the progression of atherosclerosis due to long standing hypertension caused the renal artery stenosis. Thus, more extensive investigations, particularly in elderly patients, may be necessary to confirm the renovascular mechanism of hypertension before surgical treatment is recommended. While patients with atherosclerotic renal artery stenosis were formerly considered high risk candidates for operative therapy[8], it has been demonstrated that surgical revascularization can now be done safely and successfully even in older patients with extensive extrarenal vascular disease.[9-11] This has been accomplished predominately through vigorous preliminary screening and correction of existing coronary or cerebrovascular occlusive disease. In addition, the development of more effective techniques for surgical revascularization has made possible operating even on a badly diseased abdominal aorta.[12] In our study, the long-term clinical outcome following surgical revascularization in terms of blood pressure response and post-operative renal function was evaluated. Extended cure or improvement of RVH was achieved in 60% of patients with low pre-operative S.Cr level, renal vein renin ratio of at least 1.75:1 and high unstimulated peripheral renin levels, all of which constituted significant predictive factors for the outcome ($p < 0.012$).

Of the 15 patients in the series, 33% were completely cured, as they became normotensive after operation without anti-hypertensive therapy, while 27% showed marked improvement in blood pressure control post-operatively needing fewer medications. These results compare favourably to those of Laurie et al who noted a favorable blood pressure response to surgical revascularization in 82% of 919 patients, followed-up for a period of six years.[13] However, when both kidneys are involved the situation becomes more complex as there is no normal kidney to excrete the retained sodium and water. In such patients, the renin and aldosterone levels may become normal but hypertension persists because of the increased plasma volume. In a compilation of 58 different series of patients, Rudnik et al calculated a sensitivity of 80% and specificity of 62% for renal vein renin ratio.[14] Our study has shown that individuals with renal vein renin ratio of at least 1.75:1 have either marked improvement or complete cure. Disparity in kidney sizes as well as severity and duration of hypertension did not affect the overall post-operative results.

Conclusion

Our study confirmed that long term safety and efficacy of renovascular reconstruction for the treatment of severe hypertension. Most favourable results were obtained in cases with normal pre-operative renal function, high renal vein rennin ratio and high preoperative unstimulated peripheral rennin levels.

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