

# Recovery of Renal Function in Malignant Hypertension Patients on Dialysis

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## Citation

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## Abstract

We present four patients who suffered from malignant hypertension and recovered sufficient renal function to be withdrawn from dialysis. All of them were on continuous ambulatory peritoneal dialysis (CAPD) for varying periods of time, from four to 15 months, before dialysis could be suspended. Kidney size was relatively preserved except in one patient. Renal biopsy was performed in three patients: all showed some degree of acute tubular necrosis and hyperplastic arteriolitis, two showed fibrinoid necrosis; four to 20 % of glomeruli were sclerosed, there was no evidence of tubular atrophy or interstitial fibrosis. Blood Pressure (BP) control was achieved in all patients. Up to the last follow-up visit none of them had to come back for dialysis. We conclude that patients diagnosed as end-stage renal disease due to malignant hypertension should undergo a prudent period of strict BP control before being considered for transplantation because there is always the possibility of recovery of dialysis-independent renal function.

## INTRODUCTION

Chronic Renal Failure patients, who are started on dialysis, either hemodialysis (HD) or peritoneal dialysis (PD), are considered to need dialysis forever, unless a renal transplant is performed. Although not of common occurrence, it is well documented that between 1% to 6% of patients with end-stage renal disease recover some degree of renal function to the point of allowing the discontinuation of the renal replacement therapy for a varying period of time and, in a few, even permanently.<sup>1</sup> Some studies suggest that recovery of dialysis-independent renal function is more common in patients treated with PD than in those treated with HD<sup>2-4</sup> although not all researchers agree on this.<sup>1</sup>

Several hypotheses try to explain this recovery: some acute component can co-exist at the time of commencing dialysis, like acute tubular necrosis (ATN) or renal hypoperfusion aggravated by the use of diuretics and antihypertensive medication; likewise, some reversibility can be expected after blood pressure control and improvement of cardiac function is achieved.

Certain causes of renal failure are more likely to show some recovery in renal function (for example autoimmune renal disease, hemolytic uremic syndrome, interstitial nephritis, obstructive uropathy, paraproteinemia and renovascular nephrosclerosis); while recovery is less likely to happen in

polycystic kidney disease or diabetic nephropathy.<sup>1</sup> There is limited data in the literature but some authors have found that malignant hypertension, either primary or secondary, is the condition more often associated with withdrawal from dialysis of patients previously considered dialysis-dependent end-stage renal disease.<sup>5</sup>

Other factors associated with the potential for recovery are normal size kidney, oliguric presentation and evidence of glomerular preservation on histology.

The time needed for recovery can vary from weeks to a few years, but most patients recover during the first year on dialysis.<sup>1</sup>

We present four cases of chronic renal failure and malignant hypertension in which renal function recovered significantly and in which the patients have been able to survive off dialysis for a long period of time. We would like to contribute to the better understanding of this phenomenon with this study of a small number of patients from the rural areas within an African country.

## PATIENTS AND METHOD

Polokwane Renal Unit is the only dialysis centre available within the public health sector in Limpopo Province. It serves a population of about six million. Most of our patients come from rural areas with some of them living up to 300

Km from the dialysis unit. Those patients on HD travel to the centre three times a week but a few of them only manage the journey twice a week because of the distance. Therefore we initially try CAPD in all patients if there is no contraindication or refusal from the patient.

A program for chronic renal failure patients started on a regular basis in January 2004. All primary data were collected in an electronic database designed ad hoc. From its opening until July 2010, 204 patients had entered chronic dialysis in both modalities, HD and CAPD. Six patients came as transfers from other provinces after varying periods of time on dialysis. They are not included in the study.

The diagnosis of malignant hypertension was based on the presence of hypertensive retinopathy grade III or IV.

Recovery of renal function was defined as the ability to discontinue dialysis for more than three months in a patient who had been on dialysis for at least the same period of time.

The time to recover renal function was considered as the time from the date of the first dialysis session until the date of the last one.

Glomerular filtration rate was estimated according to the Cockcroft-Gault formula. Kidney size and the presence of left ventricular hypertrophy (LVH) were assessed by abdominal ultrasonography and echocardiography respectively.

The clinical history, physical signs and histology, if performed, for those four patients with malignant hypertension who recovered renal function were reviewed and will be presented in detail.

### **RESULTS**

Malignant hypertension was diagnosed in 46 patients from a total of 198; 34 were considered primary and 12 secondary to various types of glomerulopathies.

Five patients (2.5%) recovered renal function to such an extent that dialysis could be suspended. Four of them had malignant hypertension and one was a diabetic nephropathy patient but the last-mentioned patient will not be included in the analysis since he absconded and was lost to follow-up.

#### **PATIENT 1**

She was a 31 year-old woman who had been suffering from severe hypertension for five years. She presented with a history of leg edema which she had suffered for “a couple of

months”, she had been vomiting for a week and she complained of weakness. On examination she looked very ill, pale and edematous and was bedridden. Her blood pressure was 210/122 mmHg. Fundoscopy showed retinopathy grade III. A pericardial friction rub, a fourth heart sound and a systolic apical murmur were heard. She had a mild proteinuria and hematuria. See Table 1 and 2.

Kidney sizes were small, although corticomedullary differentiation was not totally lost. A biopsy was not performed.

She was initially non-reactive for HIV but two months after initiation of dialysis she proved to be to be reactive.

She was started on HD for the first three weeks then shifted to PD. Blood pressure was controlled with furosemide, perindopril and nifedipine. After fifteen months on PD her renal function recovered and dialysis was discontinued. Her blood pressure remained under control with the same treatment mentioned above. She was seen alive for the last time a year after discontinuation of dialysis. She was working as a teacher and was not yet on anti-retroviral therapy. Since then we have lost contact with her.

#### **PATIENT 2**

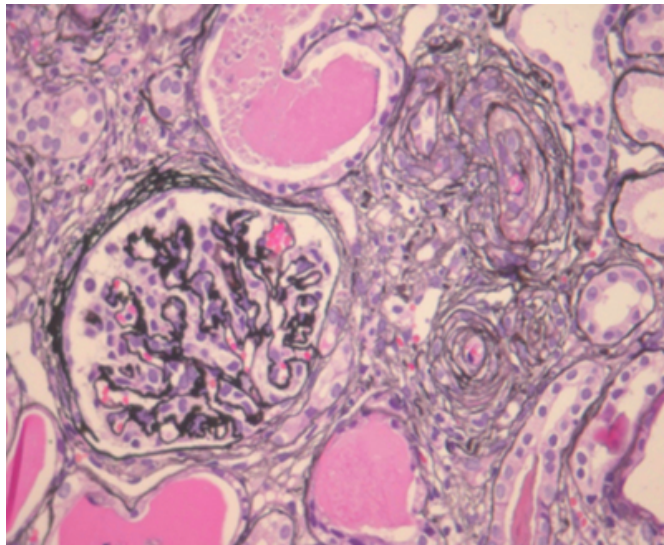
This 32 year-old female patient presented to her referring hospital with impaired consciousness (stupor). She was found to be anemic, with a blood pressure of 167/112 mmHg. There was not a previous history of hypertension. Fundoscopy: grade IV retinopathy. Other results can be seen in Tables 1 and 2.

After resuscitation she was started on PD. Good BP control was obtained only after using four antihypertensive drugs: perindopril, nifedipine, atenolol and hydralazine at maximal doses plus diuretics. A biopsy confirmed the diagnosis of malignant hypertension but only three sclerosed glomeruli out of 15 were found. Figure 1.

She eventually recovered renal function significantly after just four months on PD. Currently she is alive and well. Her blood pressure is just above target, she is on perindopril, nifedipine and furosemide.

**Figure 1**

Fig 1. Hyperplastic arteriolitis, “onion skin” lesion



### PATIENT 3

This 39-year-old woman had no history of hypertension but presented with leg edema, oliguria and BP of 214/142 mmHg. She was very weak. Fundoscopy: grade III hypertensive retinopathy. She had anemia of 6.3 g/dL and normal size kidneys. Her urine showed mild proteinuria and severe hematuria. Histology confirmed malignant hypertension. Only one glomerulus out of 23 was found sclerosed.

Her renal function recovered to a considerable extent and PD was stopped after seven months. Currently she remains asymptomatic, although with poor BP control despite being treated with three antihypertensive drugs: perindopril, nifedipine, atenolol, and diuretics. Poor compliance is suspected.

### PATIENT 4

A 25-year-old male patient who had no previous history of hypertension, presented with oliguria, chest pain, anemia and a BP of 260/150 mmHg, pericardial friction rub and grade IV retinopathy, including a macular star. He also had nephrotic range proteinuria and severe hematuria (Table 1). His kidneys were normal in size. A biopsy was performed which showed histological evidence of malignant hypertension (hyperplastic arteriolitis and fibrinoid necrosis). Thirteen percent of glomeruli were sclerosed however interstitial fibrosis and tubular atrophy were not found. PD was commenced after a short period on HD. Strict BP control was achieved and a significant recovery was obtained after seven months.

He remains well, asymptomatic, with a BP just above target. He is currently on perindopril, nifedipine and furosemide.

**Figure 2**

Table 1. Characteristics of patients

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
Gender	f	f	f	m
Age	31	32	39	25
Hx of HPT	yes	no	no	no
Presentation	vomiting, edema	stupor	edema	chest pain, edema
Oliguria (<400 ml/24h)	no	yes	yes	yes
BP (mmHg)	210/122	167/112	214/142	260/150
Retinopathy	III	IV	III	IV+ macular star
Hb (g/dL)	8.2	6.7	6.3	6.6
Na/K (mmol/L)	128/6.9	129/3.1	126/5.3	123/3.7
Creatinine (μg/L)	1104	505	1422	1145
Kidneys size, mm (Rt/Lt)	8.9/8.8	10.2/9.8	9.3/9.6	10.2/10.0
Ventricular septum, mm	16	11	14	18
Protein/blood in urine	1+/2+	0.6g/Nil	1+/3+	4.7 g/4+
Biopsy	no	yes	yes	yes
Glomeruli/sclerosed (%)		15/3 (20)	23/1 (4.3)	23/3 (13)
Fibrinoid necrosis		no	yes	yes
Hyperplastic arteriolitis		yes	yes	yes
ATN		yes	yes	yes
Interstitial fibrosis		no	no	no
Tubular atrophy		no	no	no
Recovery time (months)	15	4	7	7

**Figure 3**

Table 2. Patient characteristics at the time of discontinuation of dialysis and current status

Patient	Hb	BP	Creatinine/GFR	Current status
1	14.1	113/88	219/34.2	Alive twelve month after discontinuation of PD. Currently?
2	12.1	150/97	169/44.9	Alive, well 53 months after.
3	13.3	182/104	147/29.9	Alive, well 35 months after.
4	11.4	154/96	309/20.5	Alive, well 34 months after.

## DISCUSSION

Five percent of our patients recovered renal function a rate that falls within the range of from one to six percent reported in the literature<sup>1</sup>. All our patients who recovered renal

function were on PD which is the modality more often associated with the recovery of the renal function because there is more preservation of residual renal function and more physiologic control of BP without the wide fluctuation and potential endothelial damage that characterizes HD.<sup>2•</sup> However not all authors find the same utility of PD with some of them considering that there is no difference between PD and HD.<sup>11</sup> We believe that the evidence is in favor of PD use, although we accept that there could be a bias in favor of including patients with better residual renal function on PD which is, on its own, a factor associated with recovery of renal function regardless of the etiology or dialysis modality employed. □

Youth, female gender and good BP control are factors that have been associated with the recovery of renal function in African patients<sup>12</sup> as is the case in our study. Although the group is small and there is only one male patient, all subjects were below forty years of age and BP control was achieved in all of them, with values of less than 150/100 mmHg, soon after dialysis commenced. (Data not shown in the table).

Three of our patients presented with oliguria, a sign that has been associated with recovery. This presentation, although severe, is considered to have a higher chance of improvement since it might represent some degree of acute tubular injury caused by fibrinoid necrosis and renal ischemia and therefore have the potential for recovery.<sup>12</sup> However others have found good urinary output as a sign associated with recovery; although in this study none of the patients had malignant hypertension.<sup>13</sup>

All of our cases who were biopsied showed hyperplastic arteriolitis and some component of ATN. In two of them fibrinoid necrosis was also seen but there was no evidence of advanced chronic renal failure as indicated by the relatively few sclerosed glomeruli and the absence of interstitial fibrosis or tubular atrophy.

Most patients recover renal function during the first year and more than half are back on dialysis soon after that. □ Only one of our cases recovered renal function after a year; the rest took from four to seven months. Coincidentally the patient with the smallest kidneys was the one that took 15 months to recover. Most of the cases in this small study showed normal or just mildly reduced kidney size. None of our cases has had to come back for dialysis so far and all of them remain alive and non-anemic with varying degrees of BP control. Most of the reviewed literature reports that more than 50 % of cases are back into dialysis during the first twelve months

after discontinuation of renal replacement therapy.<sup>1•</sup> □

We conclude that patients diagnosed as end-stage renal disease due to malignant hypertension should undergo a prudent period of strict BP control before being contemplated for transplantation because there is a possibility of recovery of renal function to such a degree that dialysis might be suspended. Renal biopsy, although reported hazardous in the past, might provide evidence of the potential for reversibility and should be tried if not contraindicated. Normal, or slightly reduced, kidney size is also a favorable sign of the potential for recovery.

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