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## Abstract

A number of cardiovascular disease have been shown to be characterized by a marked increase in sympathetic drive to the heart and peripheral circulation as in essential hypertension, and chronic kidney disease (CKD) and Hemodialysis (HD). CKD patients show sympathetic hyperactivity, with aggravation of arterial hypertension. Hypertension in CKD and HD patients is difficult to control, and need multiple drugs use. Here we report our first experience on renal sympathetic nerve ablation for treatment of severe resistant hypertension in CKD patients. Our results demonstrate the high efficacy of this procedure for treatment of resistant hypertensive in CKD.

**Introduction:** Hypertension is highly prevalent and one of the most frequent chronic disease worldwide. Despite the availability of many safe and effective antihypertensive drugs, control rates to target blood pressure remain low. 10% of the patients are resistant to treatment. In CKD patient's resistant hypertension is defined as > 130/80 mmHg in the presence of three or more classes. Today catheter based renal artery denervation (RAD) offers a new approach targeting the renal sympathetic nerve activity.

**Methods:** 33 patients- aged average between 40-79 years old were treated with renal denervation. 22 Patients with follow up to 3 months (Range 1-12 months): 9 patients with CKD ( Two of them were on hemodialysis and two with RAS). All patients were with systolic BP $\geq$ 160 mmHg under three drugs. Mean number of antihypertensive drugs per patient were 4.5. Patients with CKD: Plasma Creatinine range was 2-3.6 mg/dl.

**Results:** At Baseline: Mean systolic blood pressure of the whole group = 179 $\pm$ 19 mmHg and Mean diastolic blood pressure = 83 $\pm$ 17 mmHg. Three months after RAD: Mean systolic BP = 142 $\pm$ 16 mmHg and Mean diastolic blood pressure = 77 $\pm$ 11 mmHg. There was significant reduction of the systolic blood pressure in the whole group by an average of 36 mmHg with (P <0.0001). Significant reduction in the diastolic BP by an average of 6 mmHg (P= 0.038). Baseline (Subgroup analysis of patients with CKD): Mean SBP: 183 $\pm$ 20 mmHg and Mean DBP: 79 $\pm$ 12 mmHg. Three months after RAD: Mean SBP = 147 $\pm$ 17 mmHg and Mean DBP = 75 $\pm$ 10 mmHg. CKD patients had significant reduction of 36 mmHg in the systolic blood pressure (P- 0.005). There was no significant reduction in the diastolic blood pressure. During follow-up, Renal function estimated by eGFR was unchanged.

## Conclusions:

1. Bilateral renal arteries denervation is associated with significant reduction in systolic and diastolic blood pressure in hypertensive patients resistant to multiple drug therapy.
2. CRF patients had significant reduction in systolic BP but no significant reduction in diastolic BP and without any short term kidney injury.

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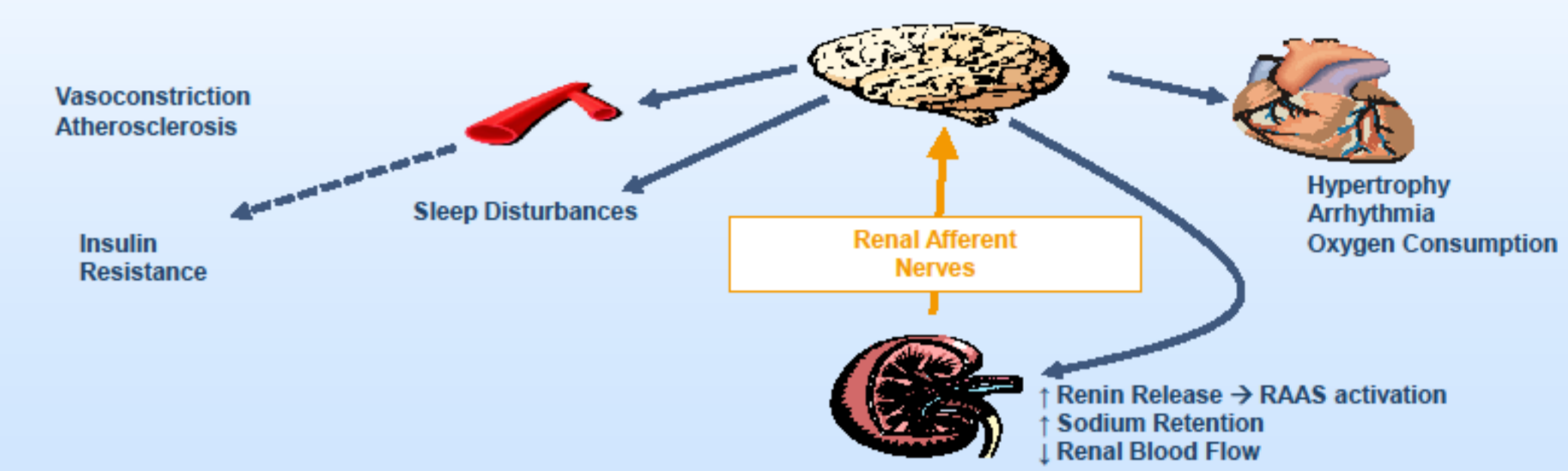
## Background

- > Sympathetic nervous system (SNS) activation  $\rightarrow$  development and progression of systemic hypertension.
- > The degree of SNS activation correlates with the severity of BP elevation.
- > The response of the kidneys to SNS signaling increases blood pressure by:
  - $\uparrow$  Rennin secretion
  - $\downarrow$  NA excretion
  - Induction of renal vasoconstriction.
- > Activation of the renal somatic afferent nerves leads to elevated central sympathetic drive.

## INTRODUCTION

A marked increase in sympathetic neural discharge, has been shown to occur in the predialytic stage of chronic kidney disease. Recent data published showed that hypersympathetic activity is involved in the progression of renal disease and aggravation of arterial blood pressure. Hypertension is frequent and difficult to control in the dialysis population, with high mortality rate, high prevalence of cerebrovascular complication, cardiac failure, coronary heart disease. Subset of dialytic patients exhibiting intradialytic hypertension prone to development of malignant hypertension. Sympathetic hyperactivity, rennin-angiotensin system activation, vascular resistance are lying in the base of these condition. Recent reports of a novel catheter - based technique for renal sympathetic denervation offer a promising therapeutic option for patients with resistant hypertension. This technique is proved to be safe in the patients with chronic renal disease suffering from resistant hypertension.

## Renal Sympathetic Afferent Nerves: Kidney as Origin of Central Sympathetic Drive



2.

## Methods

**Patients** with resistant hypertension to at least three drugs, randomly assigned to undergo renal denervation, the femoral artery was accessed with the standard endovascular technique and the Simplicity catheter (Fig.1) was advanced into the renal artery and connected to a radiofrequency generator. 11 four-to-six discrete, low-power radio frequency treatments were applied along the length of both main renal arteries. Participants were given heparin to achieve an activated clotting time of more than 250 s.

33 patients- aged average between 40-79 years old were treated with renal denervation by endovascular catheter technology. 22 Patients with follow up to 3 months (Range 1-12 months): 9 patients with CKD (Two of them were on hemodialysis and two with RAS). All patients were with systolic BP $\geq$ 160 mmHg treated with three drugs. Mean number of antihypertensive drugs per patient were 4.5. Patients with CKD: Plasma Creatinine range was 1.2-3.6 mg/dl. All patients with systolic BP $\geq$ 160 mmHg.

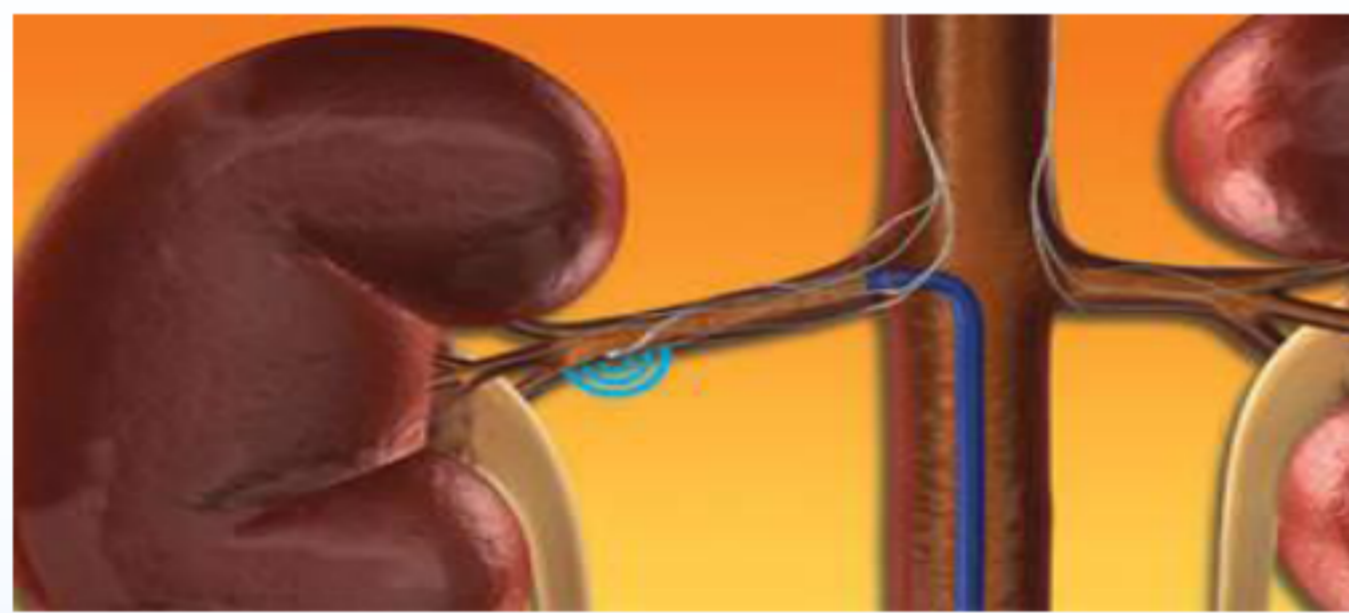


Fig.1: Simplicity Catheter in the renal artery

## Patients Characteristics

	Number	Percent (%)
DM	15	68
HLP	17	77
CAD	16	72
PVD	5	22
Stroke	4	18
Mean LVEF	0.52	
LVEF<45%	4	18
LVH	14	64
Diastolic Dysfunction(Grade I)	10	46

3.

## Results

At Baseline: Mean systolic blood pressure of the whole group = 179 $\pm$ 19 mmHg and Mean diastolic blood pressure = 83 $\pm$ 17 mmHg. Three months after RAD: Mean systolic BP = 142 $\pm$ 16 mmHg and Mean diastolic blood pressure = 77 $\pm$ 11 mmHg. There was significant reduction of the systolic blood pressure in the whole group by an average of 36 mmHg with (P <0.0001). Significant reduction in the diastolic BP by an average of 6 mmHg (P= 0.038). Baseline (Subgroup analysis of patients with CKD): Mean SBP: 183 $\pm$ 20 mmHg and Mean DBP: 79 $\pm$ 12 mmHg. Three months after RAD: Mean SBP = 147 $\pm$ 17 mmHg and Mean DBP = 75 $\pm$ 10 mmHg. CKD patients had significant reduction of 36 mmHg in the systolic blood pressure (P- 0.005). There was no significant reduction in the diastolic blood pressure. During follow-up, Renal function estimated by eGFR was unchanged.

## Mean follow up 3 months (range 1-12 months) Baseline:

- Mean systolic blood pressure of the whole group  $\rightarrow$  179 $\pm$ 19 mmHg
- Mean diastolic blood pressure  $\rightarrow$  83 $\pm$ 17 mmHg.

## Three months after RAD:

- Mean systolic Blood pressure  $\rightarrow$  142 $\pm$ 16 mmHg
- Mean diastolic blood pressure  $\rightarrow$  77 $\pm$ 11 mmHg.

## Patients with CRF

Baseline (Subgroup analysis of patients with CRF):

- Mean SBP: 183 $\pm$ 20 mmhg
- Mean DBP: 79 $\pm$ 12 mmhg

Three months after RAD:

- Mean SBP: 147 $\pm$ 17 mmhg
- Mean DBP: 75 $\pm$ 10 mmhg

CRF patients had significant reduction of 36 mmHg in the systolic blood pressure (P- 0.005)

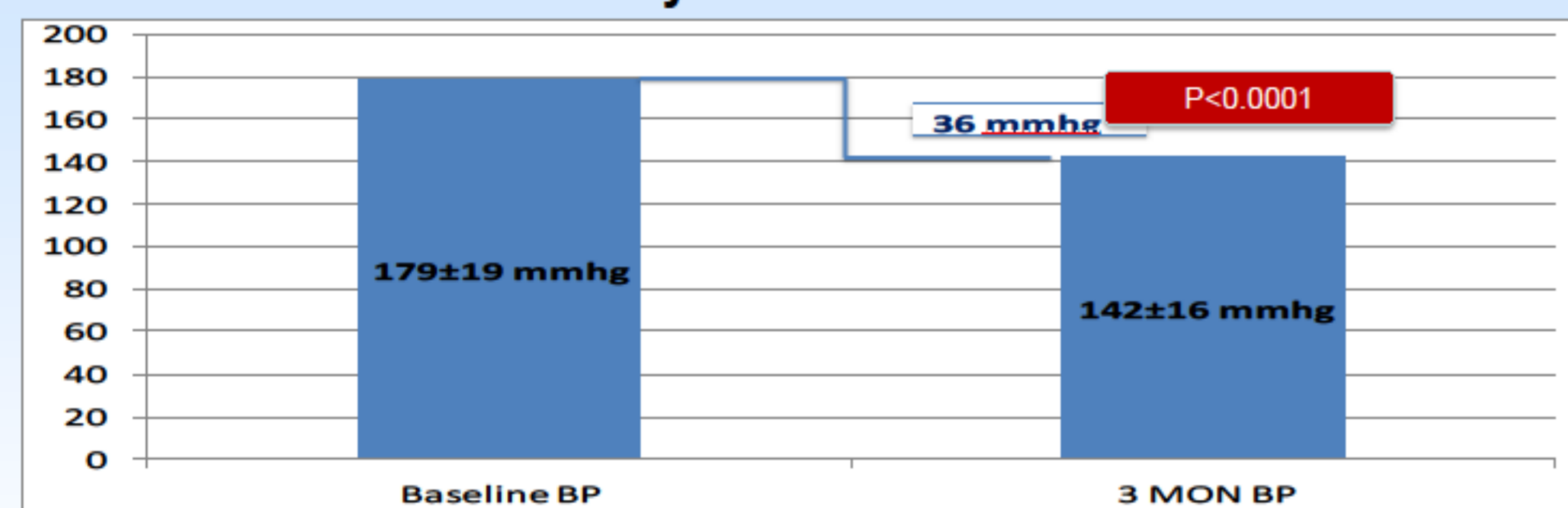
There was no significant reduction in the diastolic blood pressure.

Renal denervation had no adverse affect on the renal function.

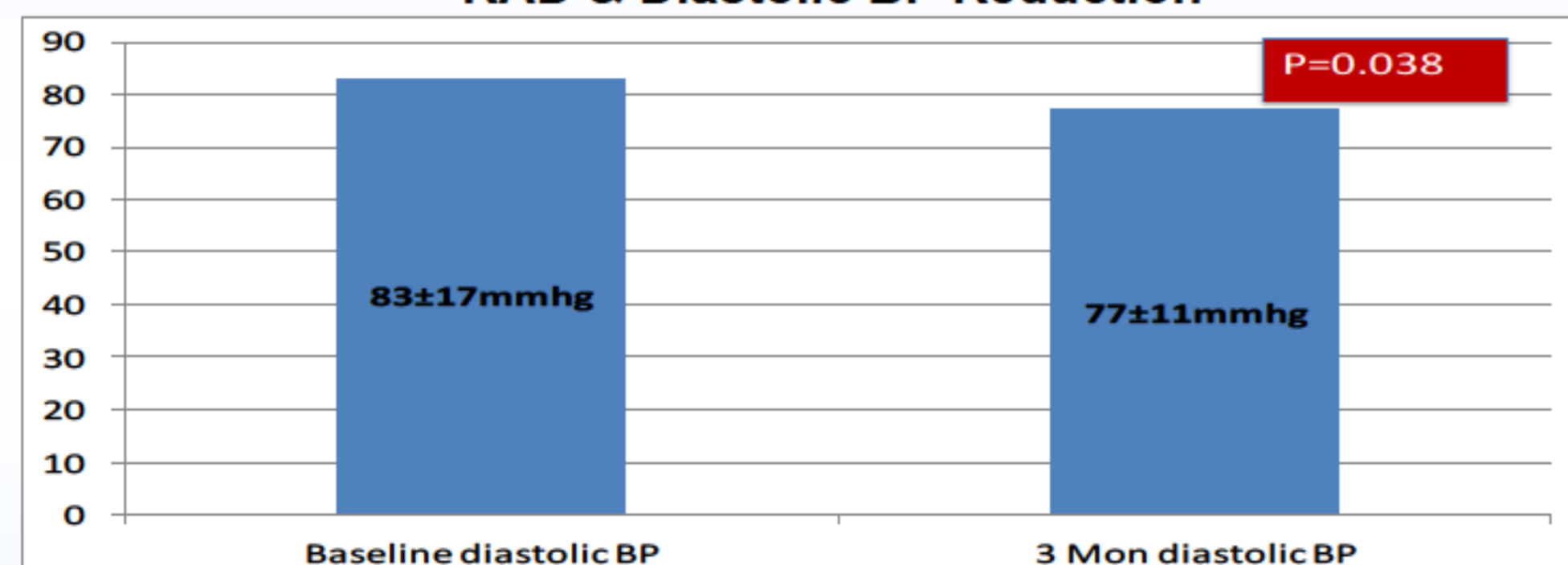
4.

## Results

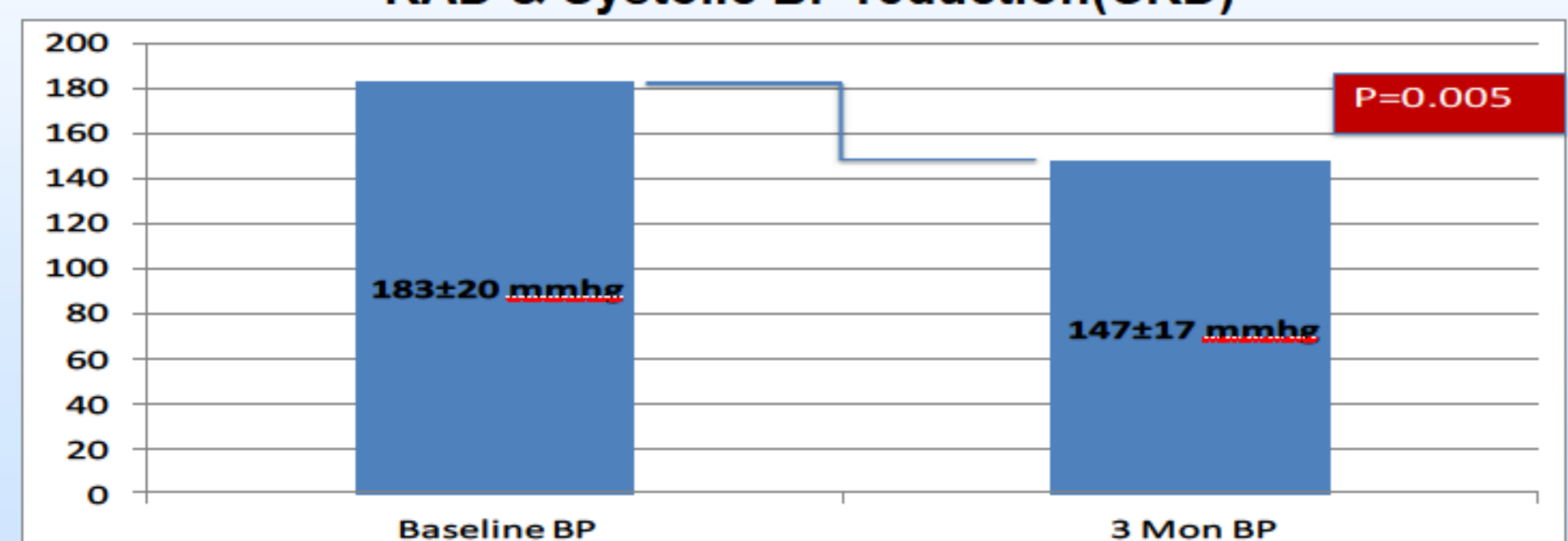
### RAD & Systolic BP Reduction



### RAD & Diastolic BP Reduction



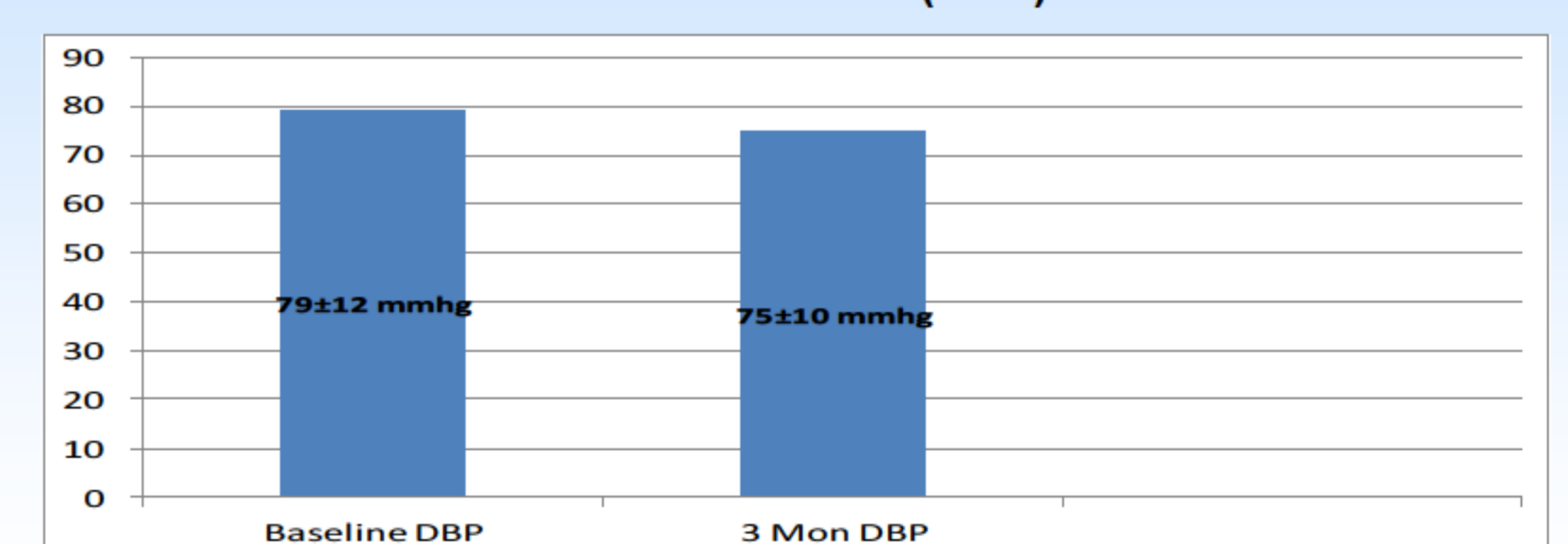
### RAD & Systolic BP reduction(CKD)



5.

## Results

### RAD & Diastolic BP Reduction(CKD)



## Conclusion

Bilateral renal arteries denervation (RAD) is associated with significant reduction in systolic and diastolic blood pressure in hypertensive patients resistant to multiple drug therapy.

Chronic Kidney Disease (CKD) patients had significant reduction in systolic BP but without significant reduction in diastolic BP. There was no change GFR, and without any short term kidney injury.

RAD is a safe procedure, and long period of observation needs to see benefit.

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