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# Unique Features of Hypertension in ADPKD

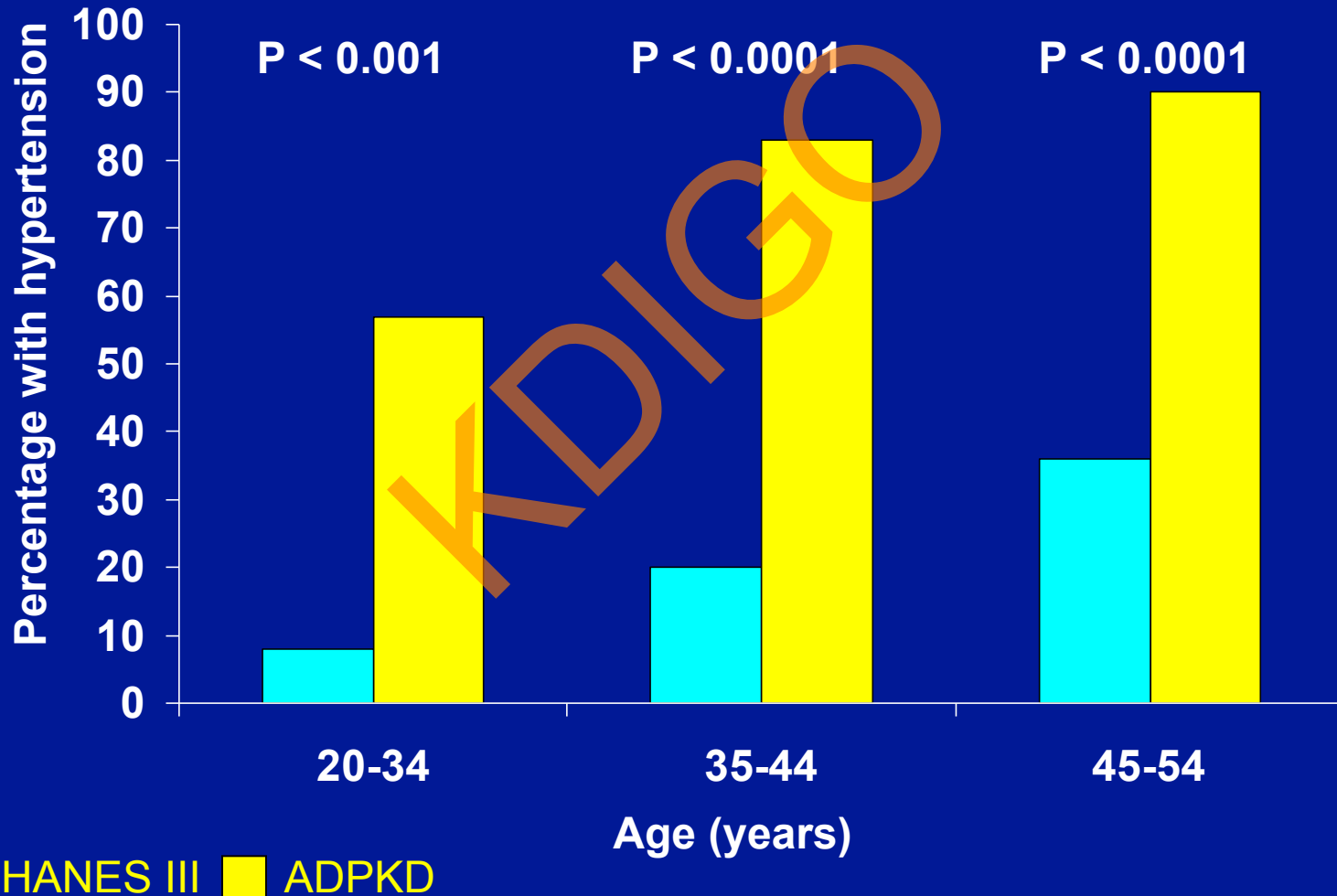
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**School of Medicine**

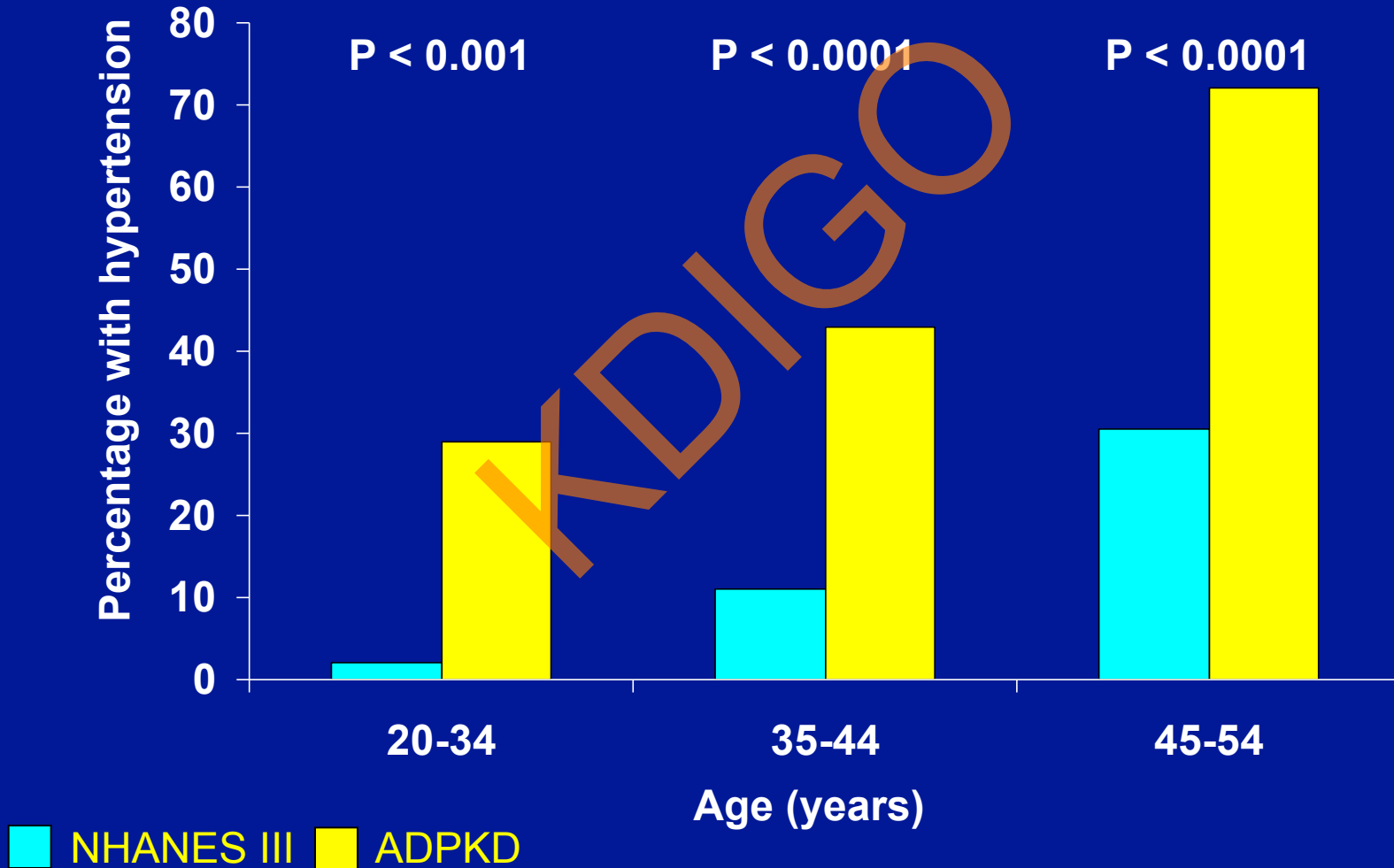
## Disclosures

Dr. Robert W. Schrier serves as an Advisor to Novartis, Janssen, Ikaria, and Otsuka Pharmaceuticals.

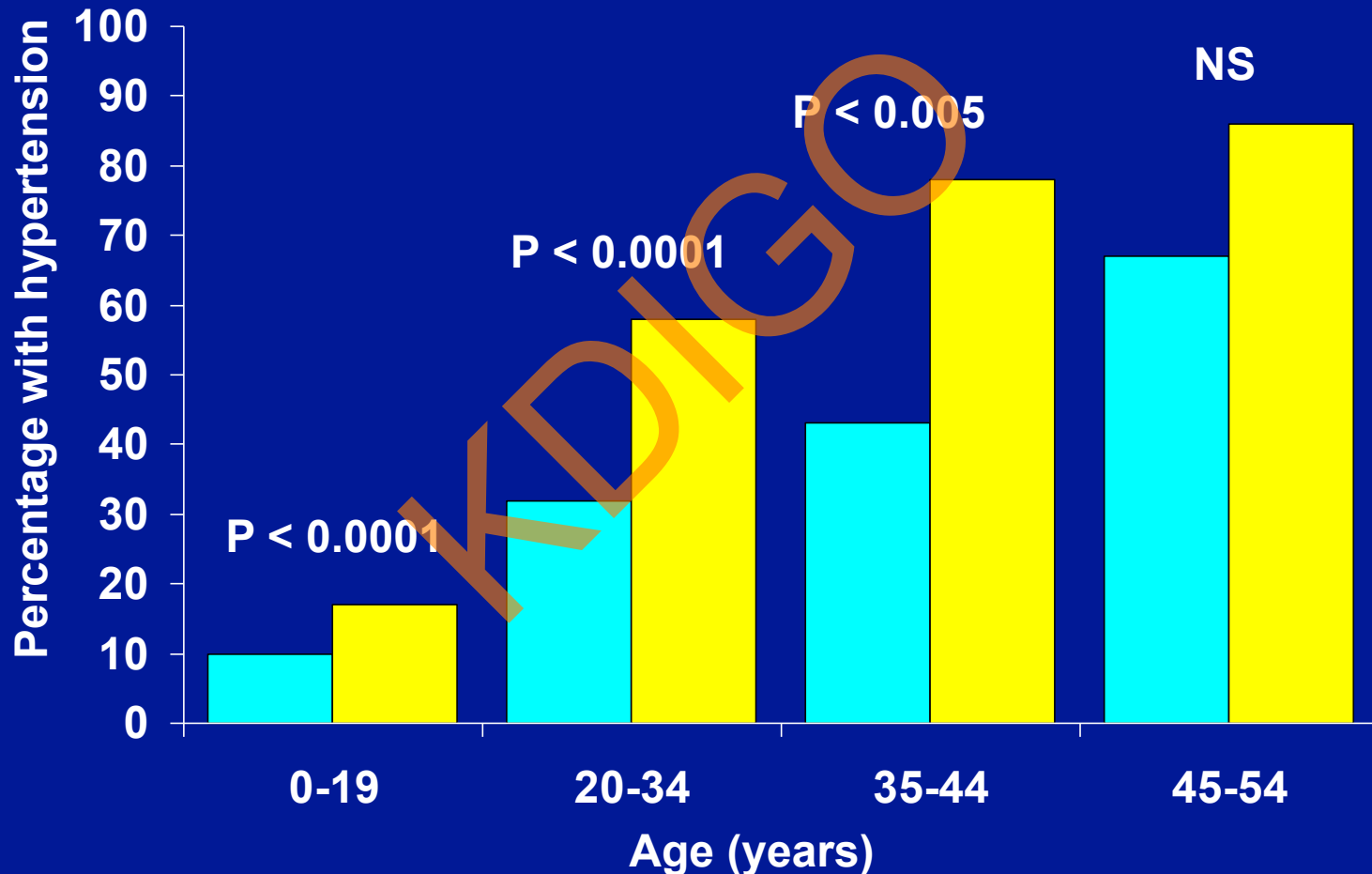
# Prevalence of Hypertension in ADPKD Males, 1985-1994 versus NHANES III, 1988-1994



# Prevalence of Hypertension in ADPKD Females, 1985-1994 versus NHANES III, 1988-1994

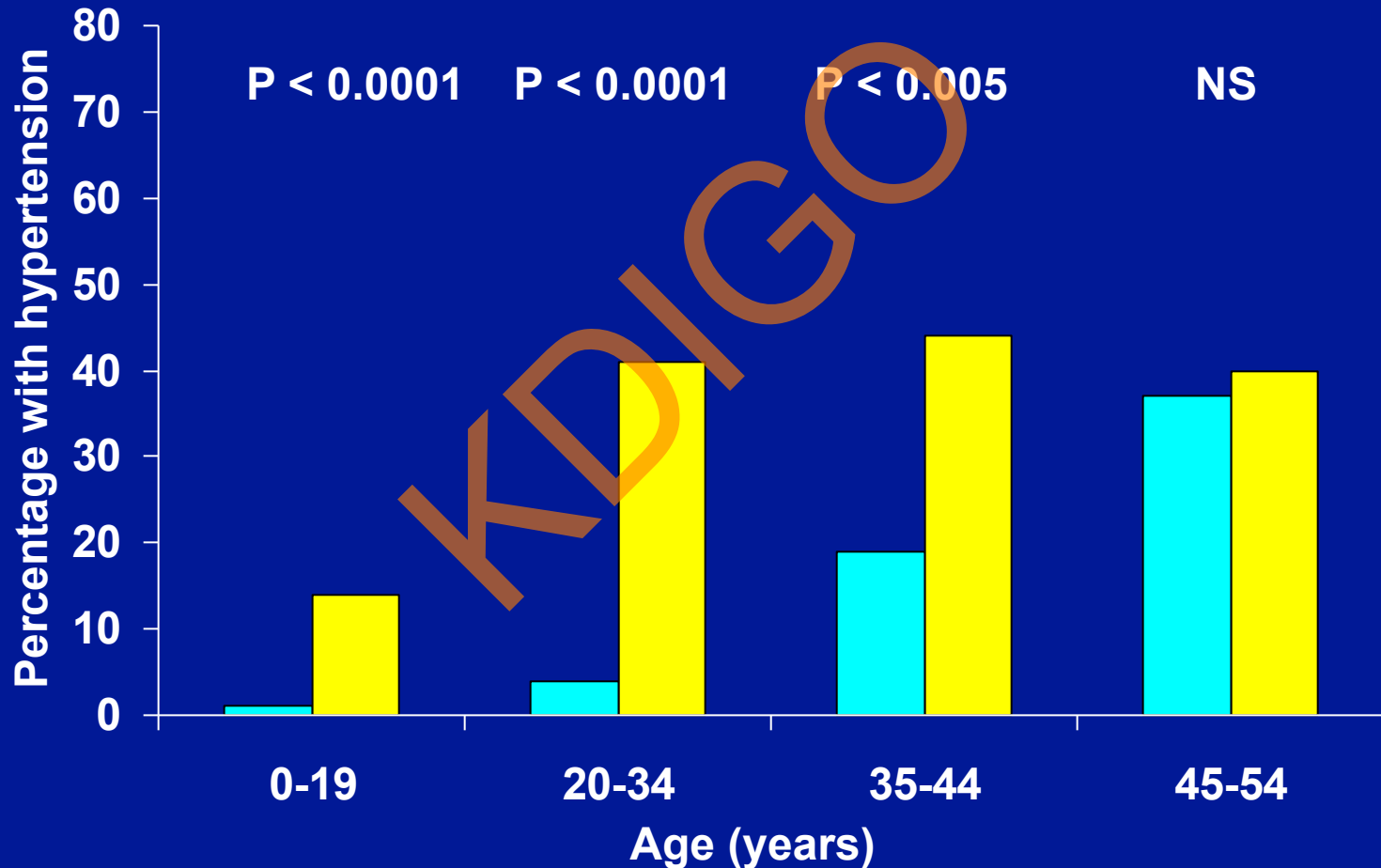


# Prevalence of Hypertension in ADPKD Males 1995-2000 versus NHANES IV 1999-2000



■ NHANES IV ■ ADPKD

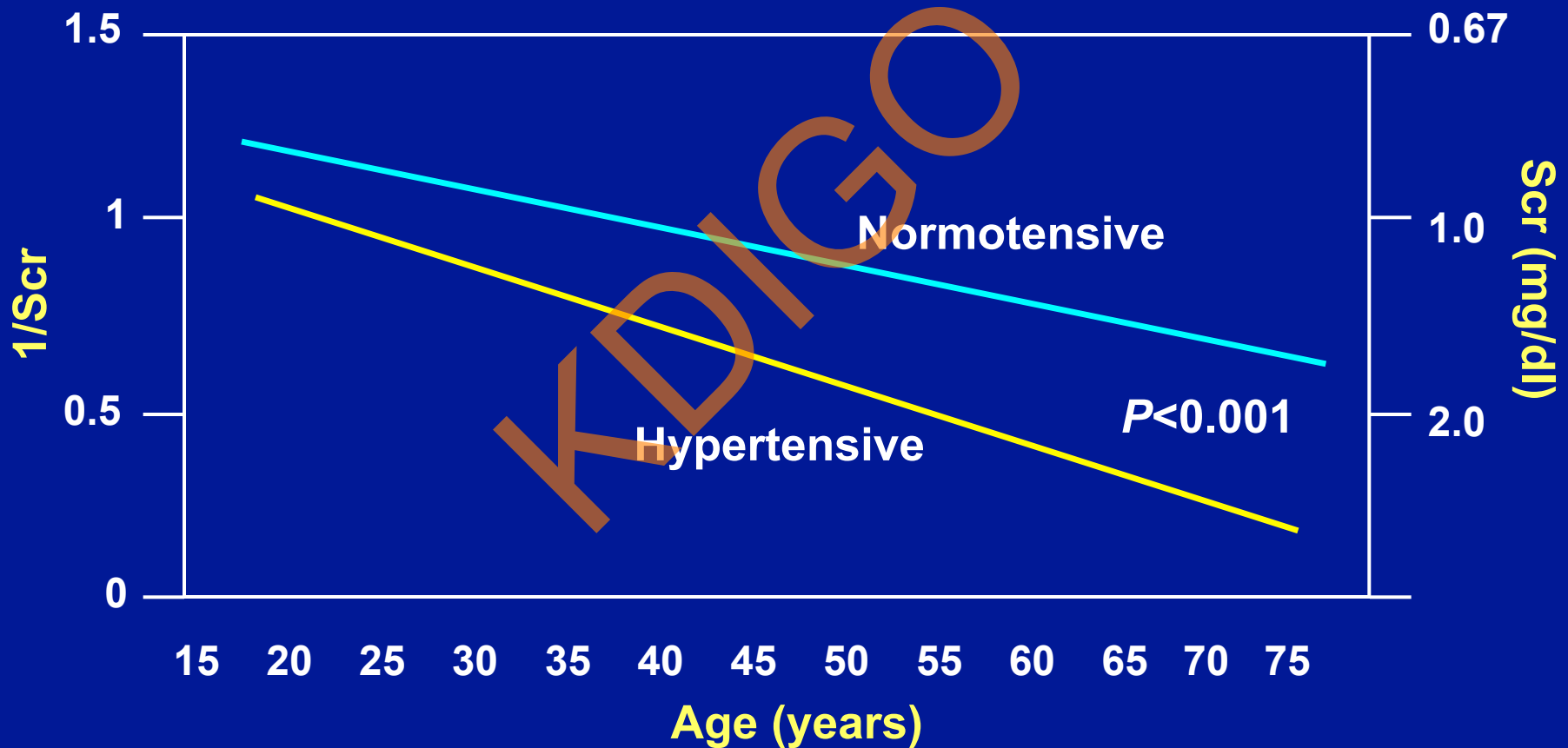
# Prevalence of Hypertension in ADPKD Females 1995-2000 versus NHANES IV 1999-2000



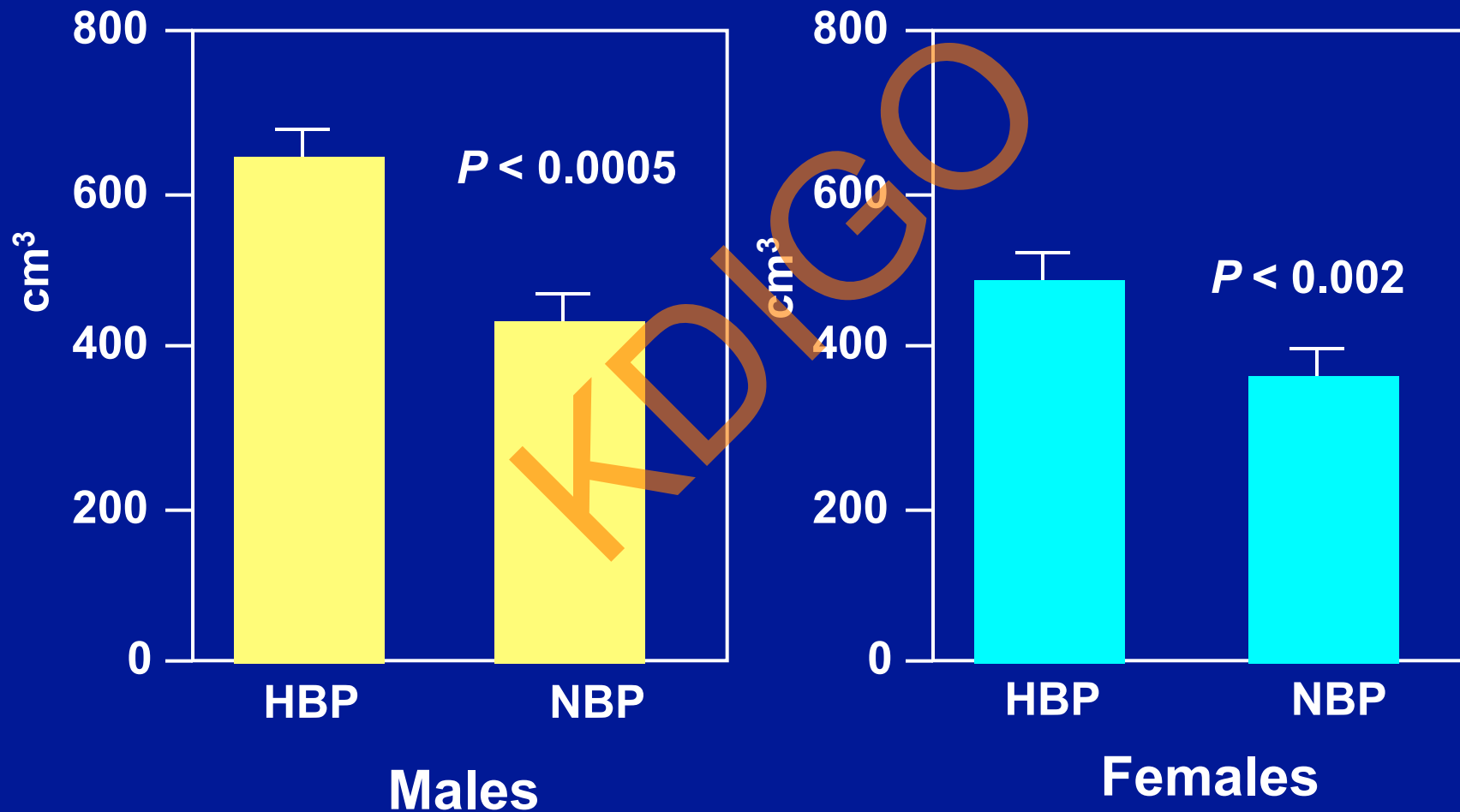
■ NHANES IV ■ ADPKD

*Kelleher, Schrier, et al., Am J Hypertension, 17:1029-34, 2004.*

# The Progression of Renal Disease in Hypertensive and Normotensive ADPKD Patients

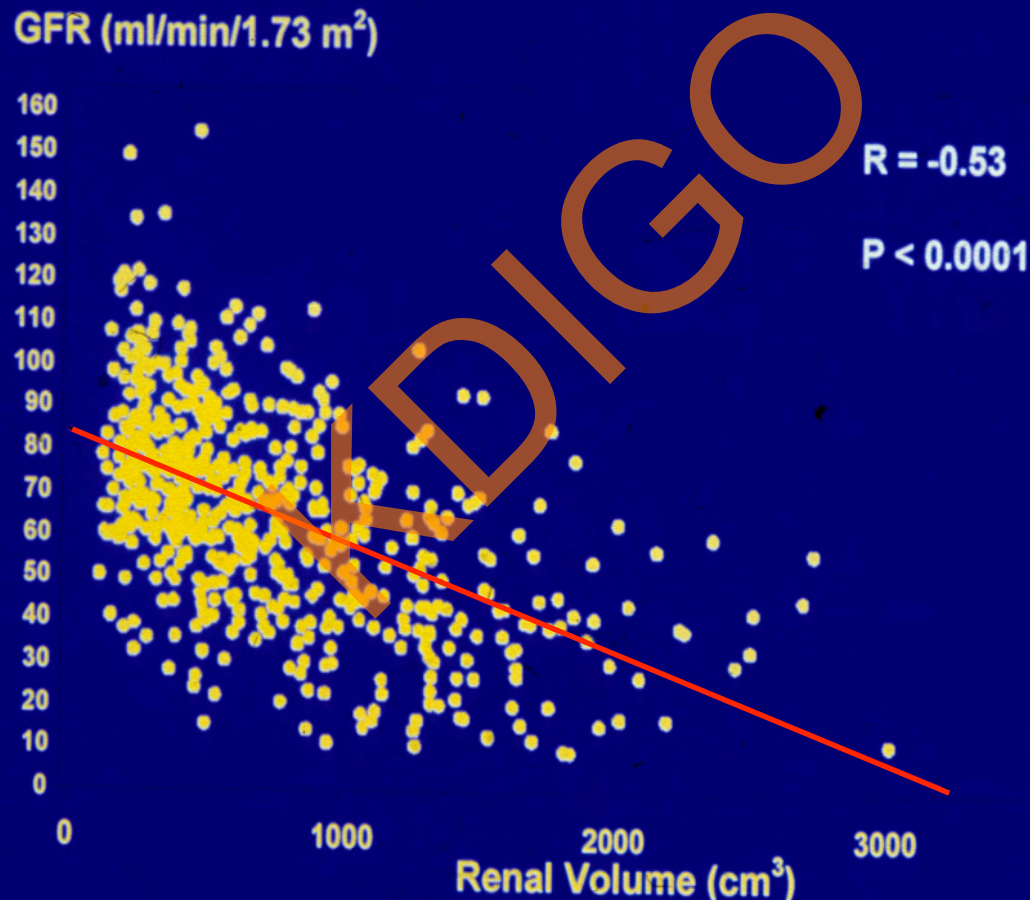


# Mean Renal Volume is Significantly Higher in Hypertensive versus Normotensive ADPKD Patients





# Relationship between GFR and Renal Volume in 229 ADPKD Subjects

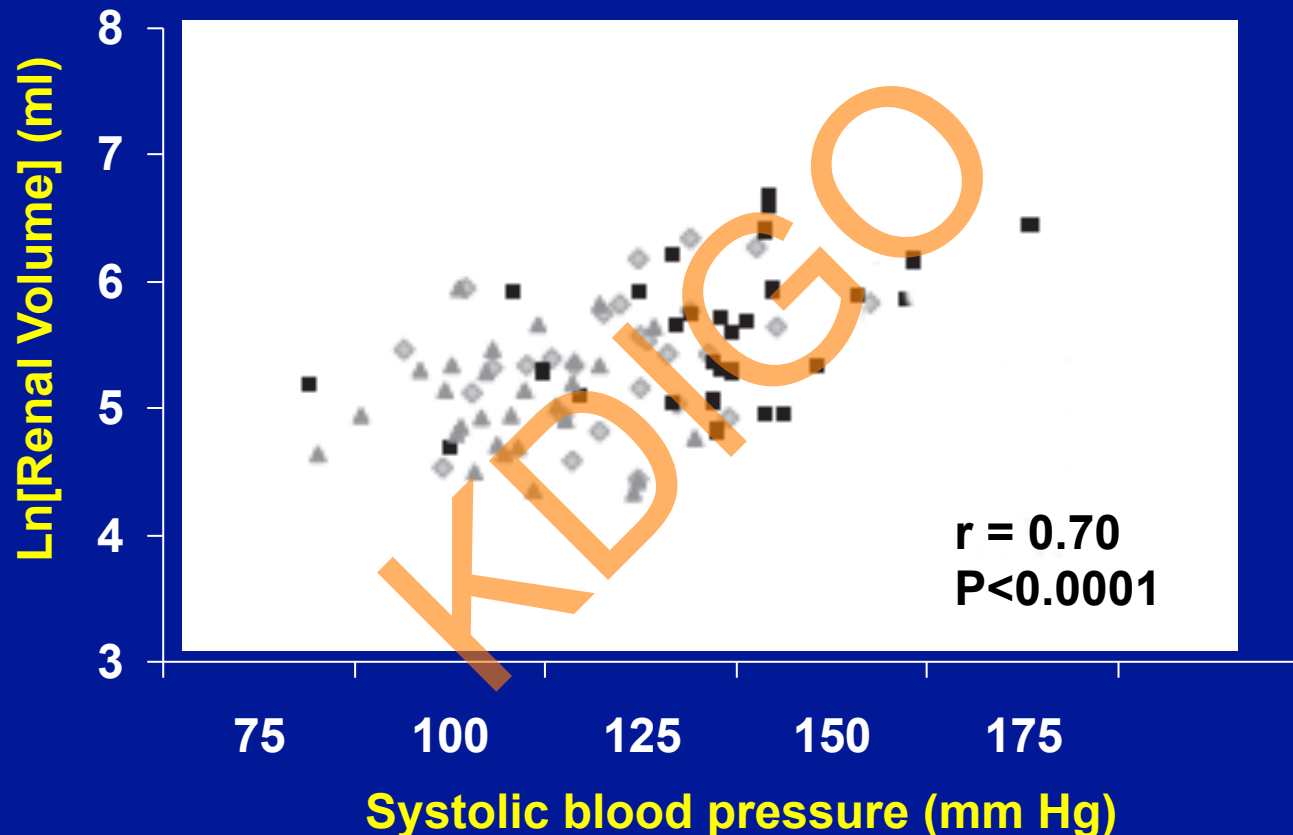


## Normotensive (NBP), borderline hypertensive (BBP), and hypertensive (HBP) subjects

Parameter	NBP (N=30)	BBP (N=27)	HBP (N=28)	P-value for ANOVA
Male/female	13/17	15/12	17/11	NS
Age (years)	12.0 ± 0.8	11.8 ± 0.8	13.6 ± 0.8	NS
Height (cm)	151 ± 5	151 ± 5	160 ± 4	NS
Serum creatinine (mg/100 ml)	0.66 (0.57–0.70)	0.69 (0.62–0.77)	0.74 (0.68–0.81)	NS
24-h creatinine clearance (ml/min/1.73 m <sup>2</sup> )	135 (127–145)	127 (117–138)	130 (120–141)	NS
Urine microalbumin excretion (mg/day)	31 (19–51)	22 (14–35)	23 (16–33)	NS
Systolic blood pressure (mm Hg)	109 ± 2	119 ± 2	130 ± 3	<0.0001
Diastolic blood pressure (mm Hg)	64 ± 1	68 ± 1	72 ± 2	0.0005

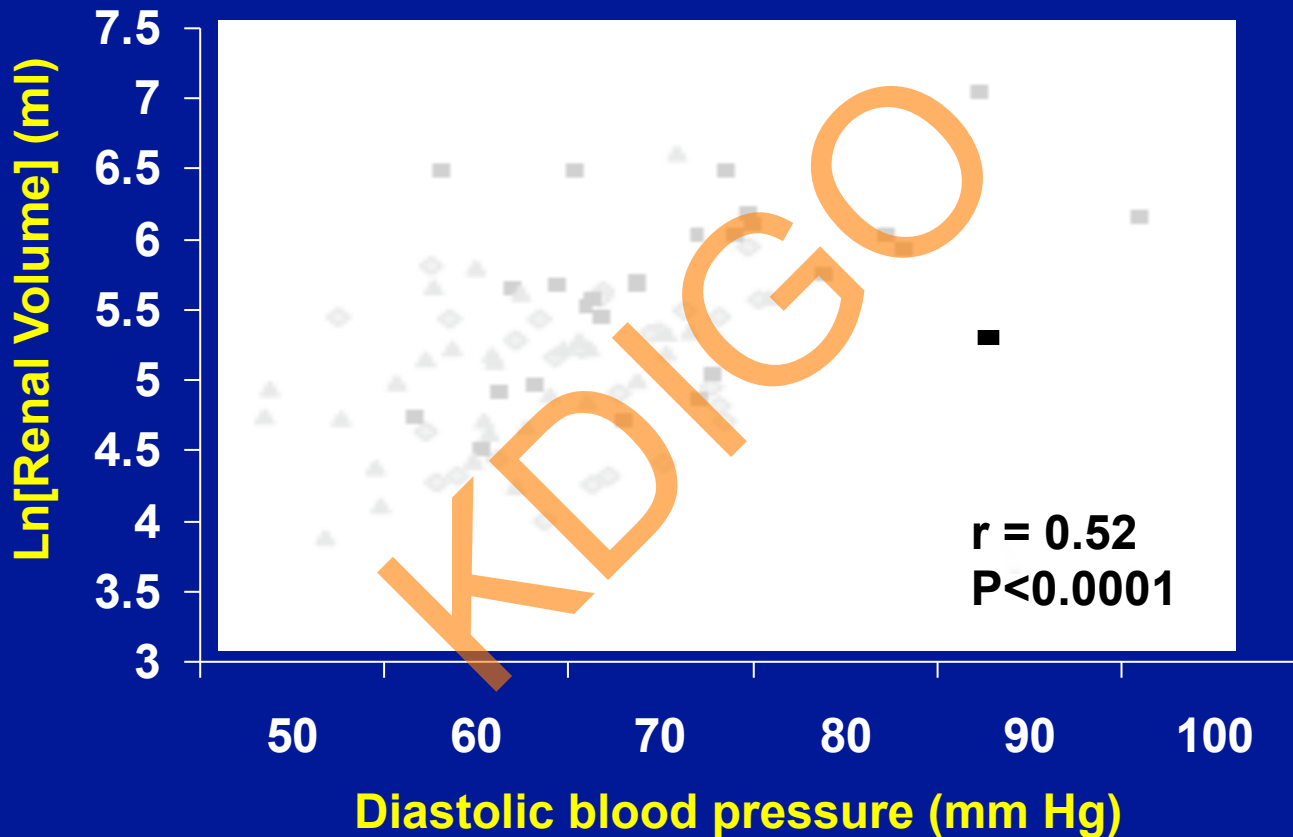
Note. SBP: NBP vs BBP ( $P=0.0122$ ), NBP vs HBP ( $P<0.0001$ ), BBP vs HBP ( $P=0.0022$ ); DBP: NBP vs BBP ( $P=NS$ ), NBP vs HBP ( $P=0.0003$ ), BBP vs HBP ( $P=NS$ ). Data presented as mean ± s.e. or geometric mean (95% CI).

# Correlation between systolic blood pressure and renal volume in 85 ADPKD children



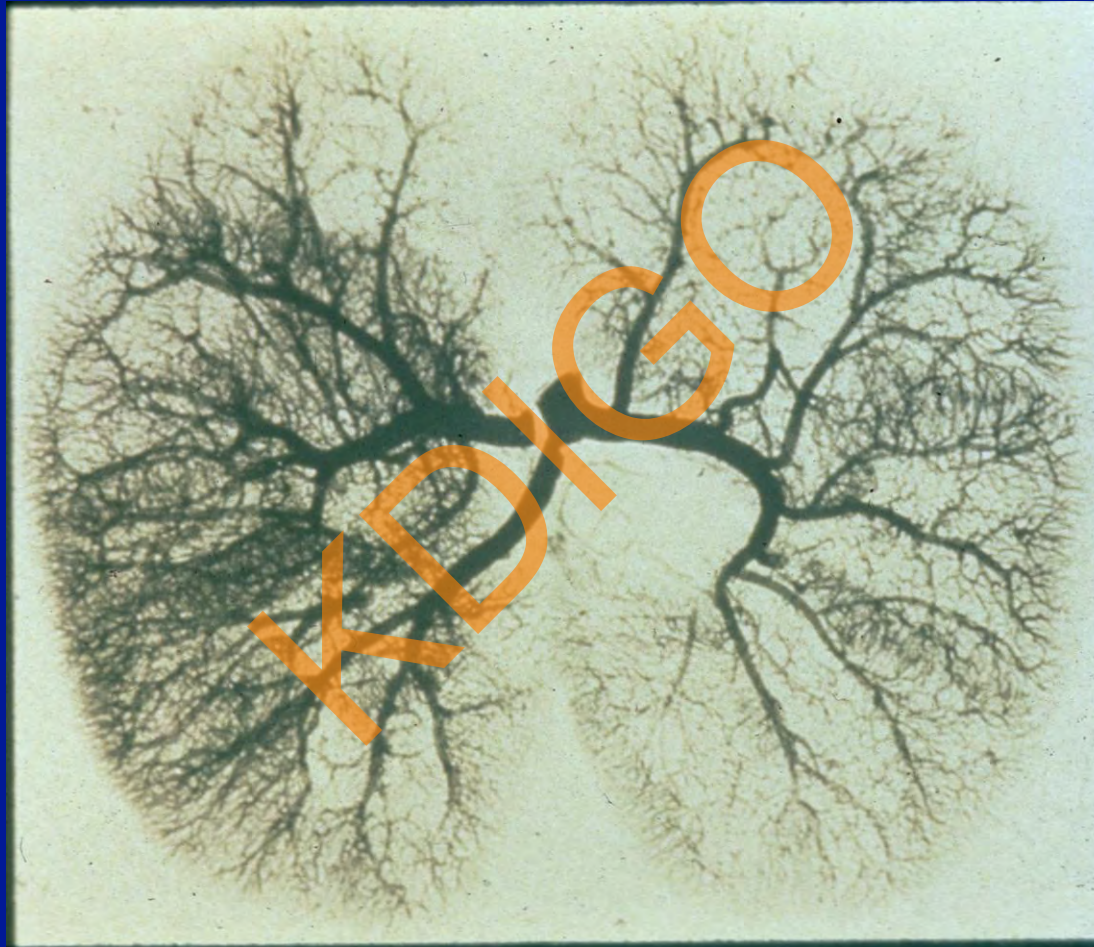
◆ Borderline    ■ Hypertensive    ▲ Normotensive

# Correlation between diastolic blood pressure and renal volume in 85 ADPKD children



◆ Borderline    ■ Hypertensive    ▲ Normotensive

# NORMAL RENAL VASCULATURE



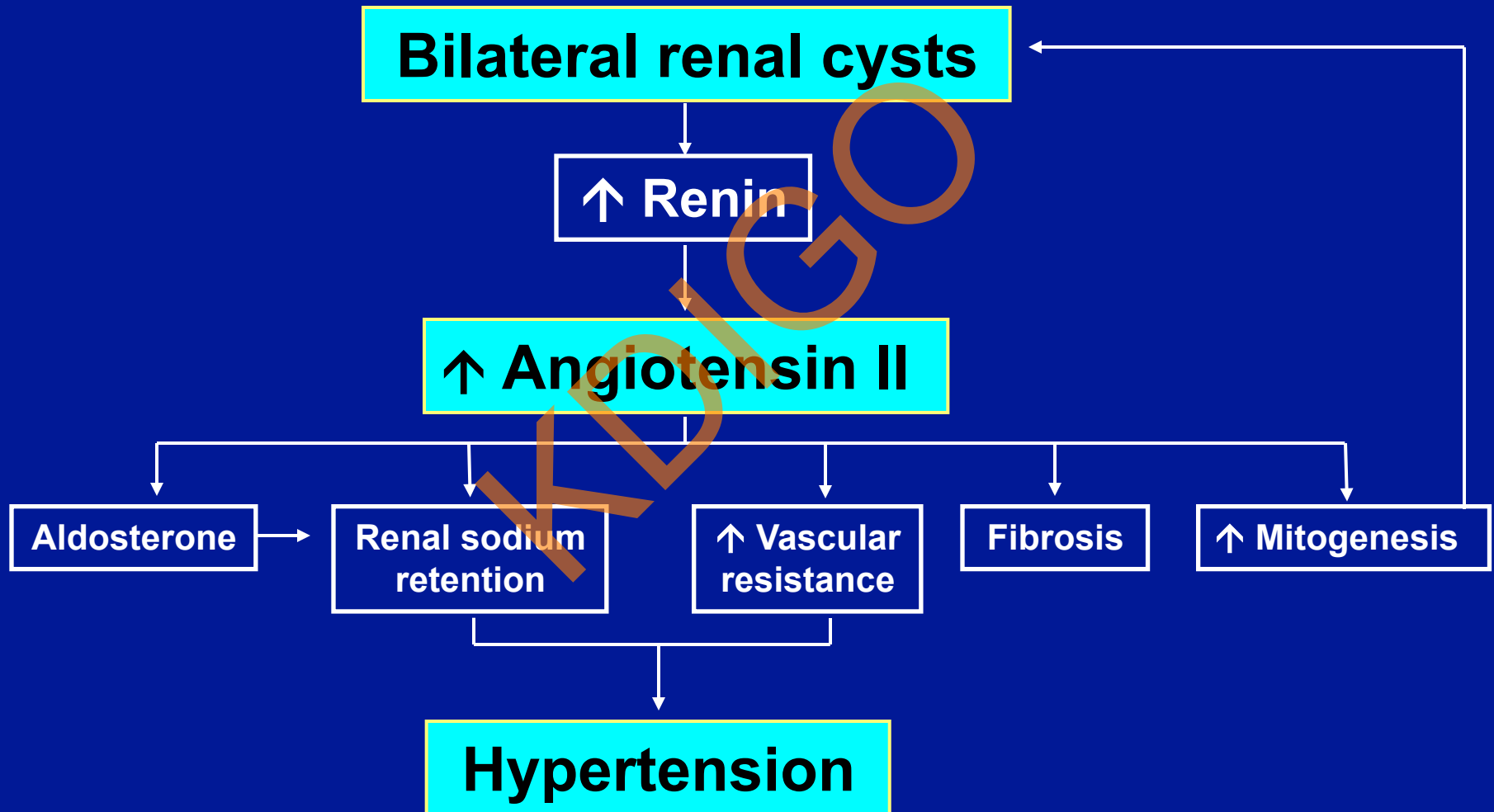
# RENAL VASCULATURE IN ADPKD



# Hypothesis

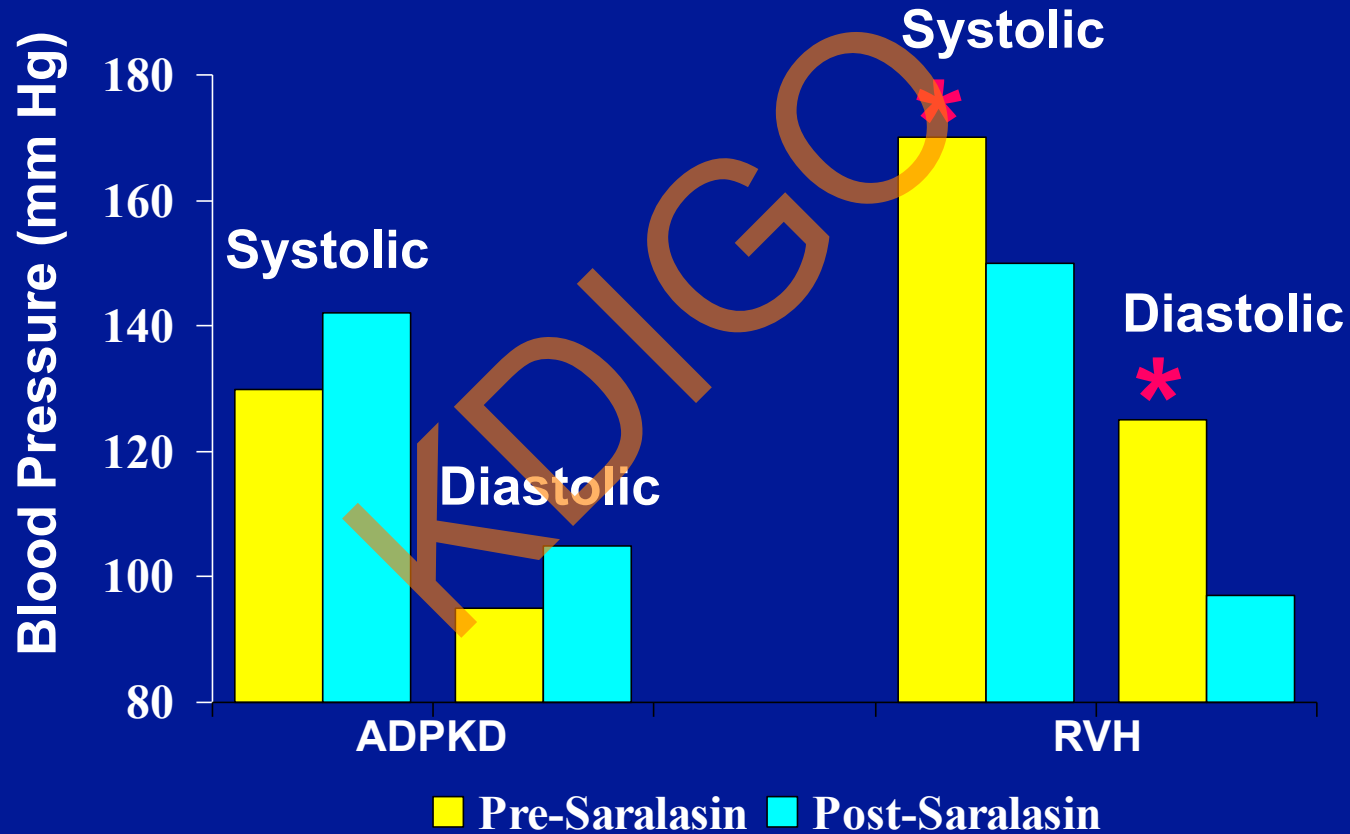
- ▶ Bilateral cyst enlargement causes compression of adjacent parenchyma and stretch of arterioles lining cyst cavities, leading to intrarenal ischemia and activation of the renin-angiotensin-aldosterone system.

# The Effect of the RAAS in the Development of Hypertension and Progression of ADPKD





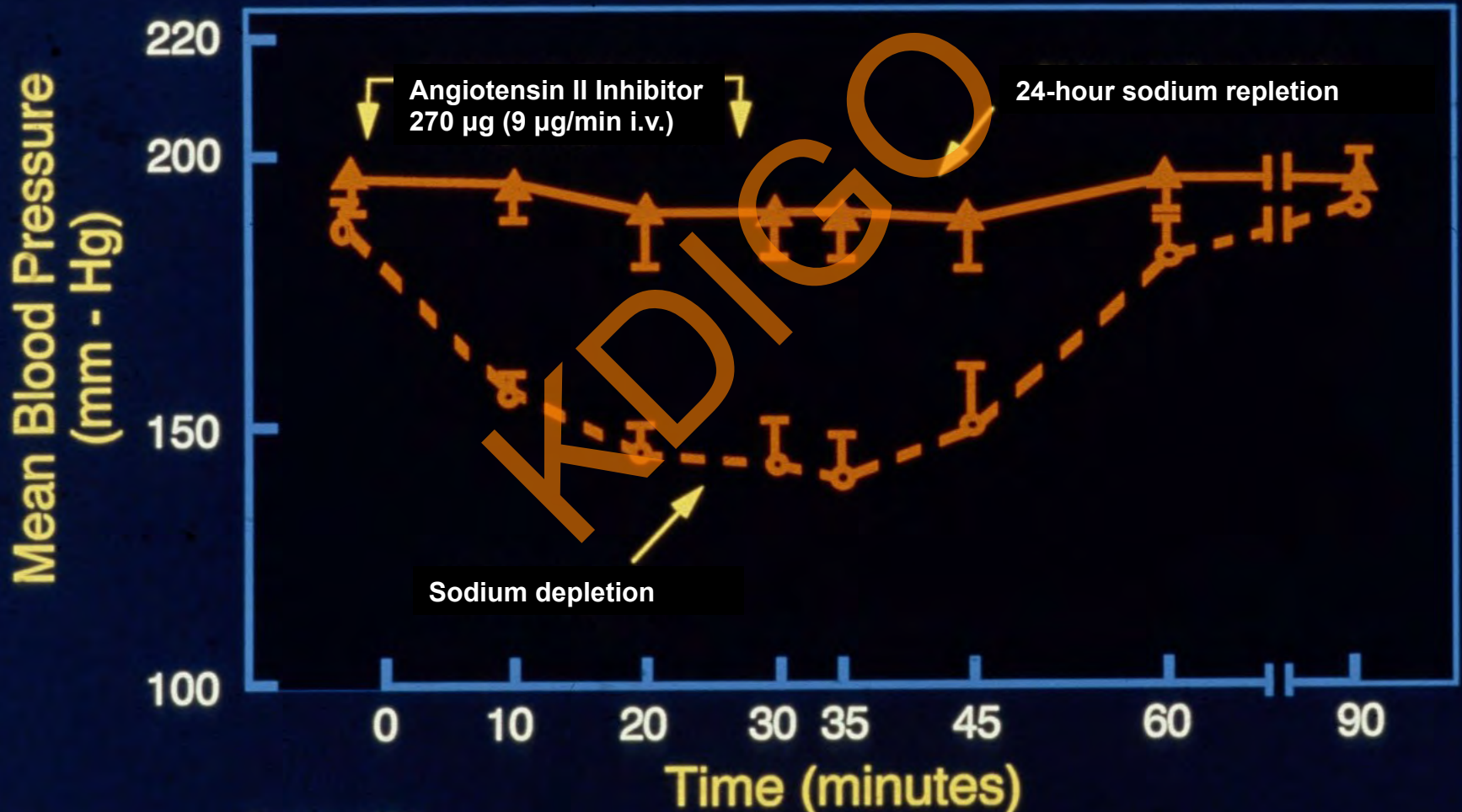
# Blood Pressure Responses to Saralasin in Hypertensive patients with PKD and Renal Vascular Hypertension (mean $\pm$ SEM)



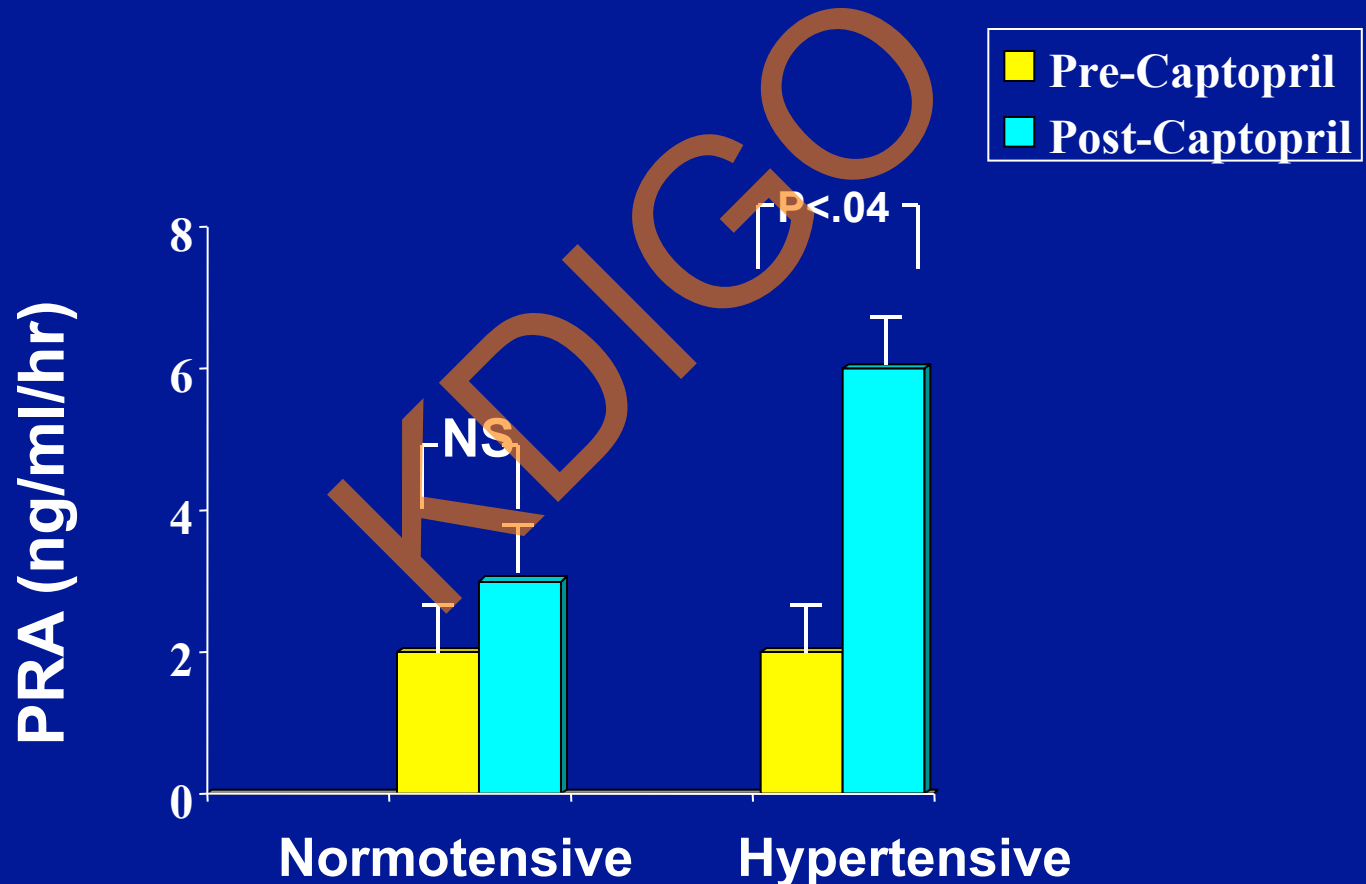
\* P < 0.05 Pre- vs Post- Saralasin

*Anderson et al. (1979).*

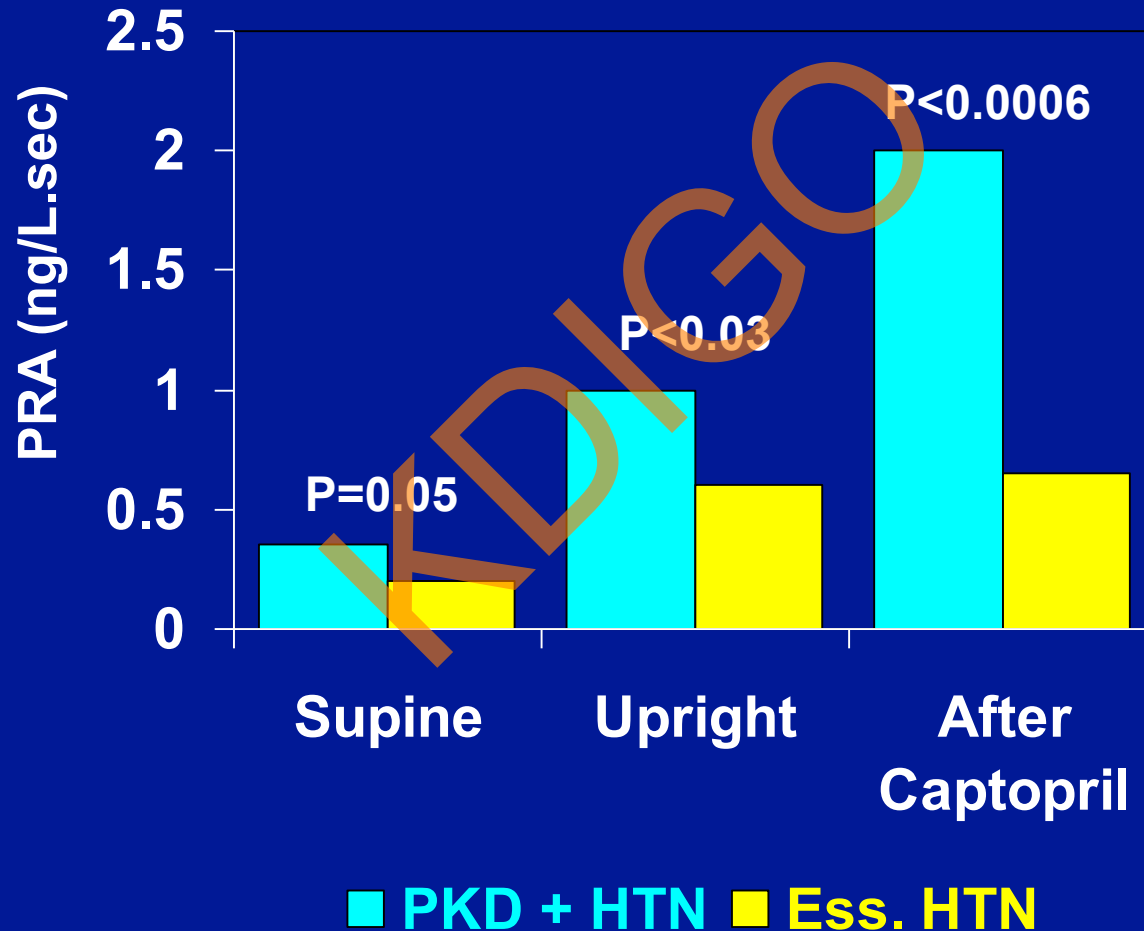
# MAP response to All Inhibitor in 1K1C HBP Rats



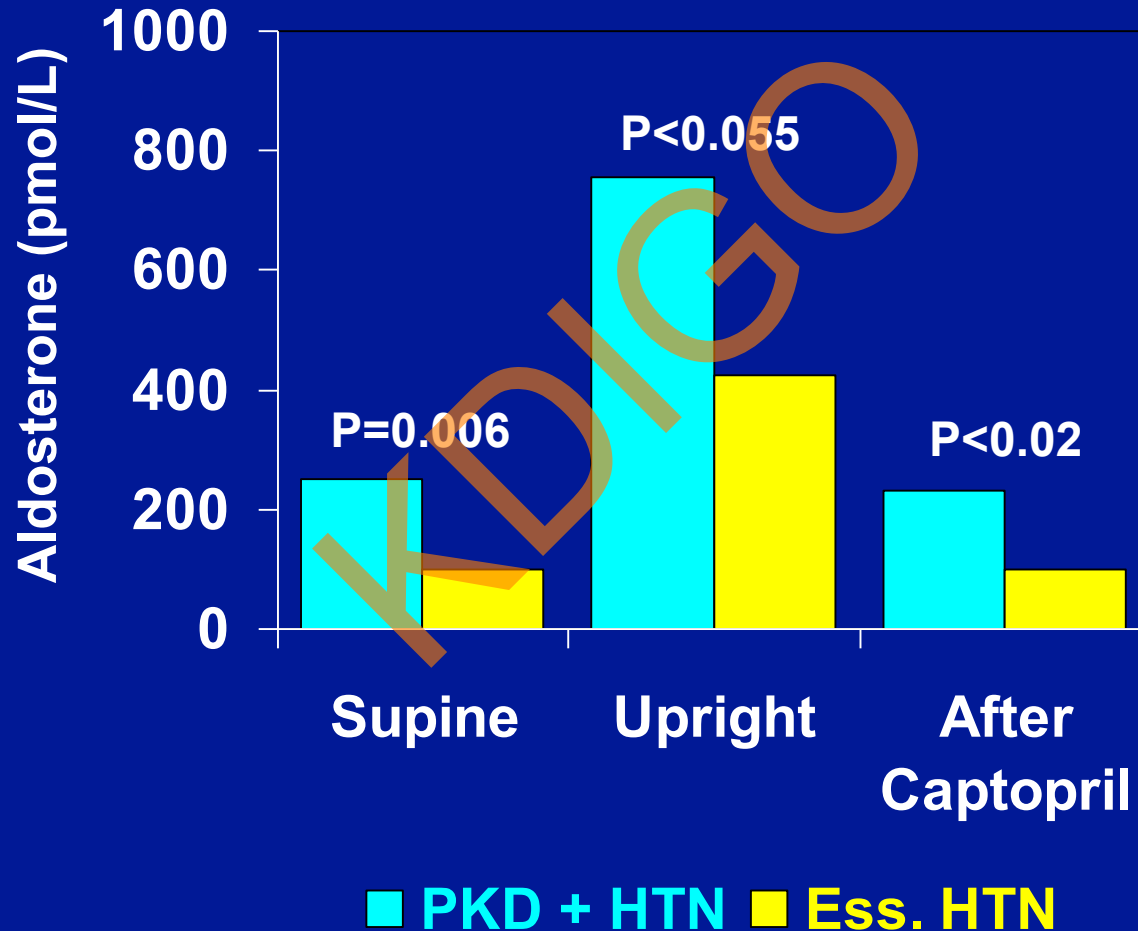
# Plasma Renin Activity (PRA) Response to Captopril During High Sodium Diet in ADPKD (300 mEq/day)



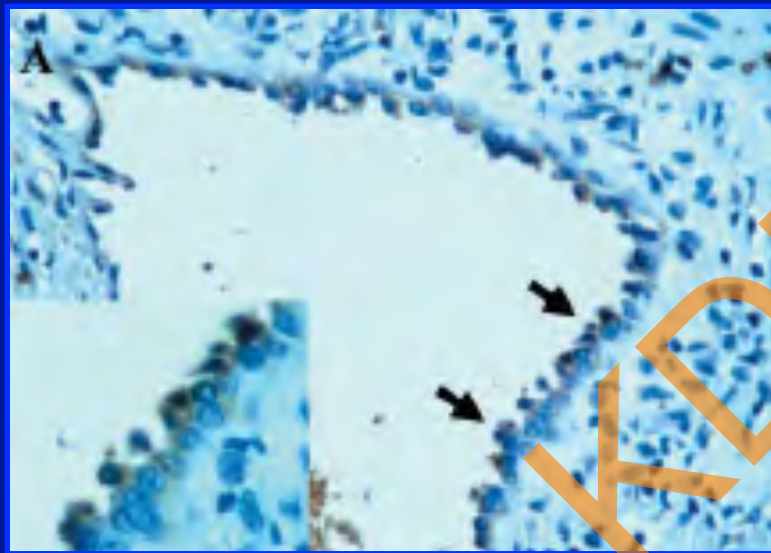
# The Renin-Angiotensin-Aldosterone System is Stimulated in ADPKD as Compared to Essential Hypertension



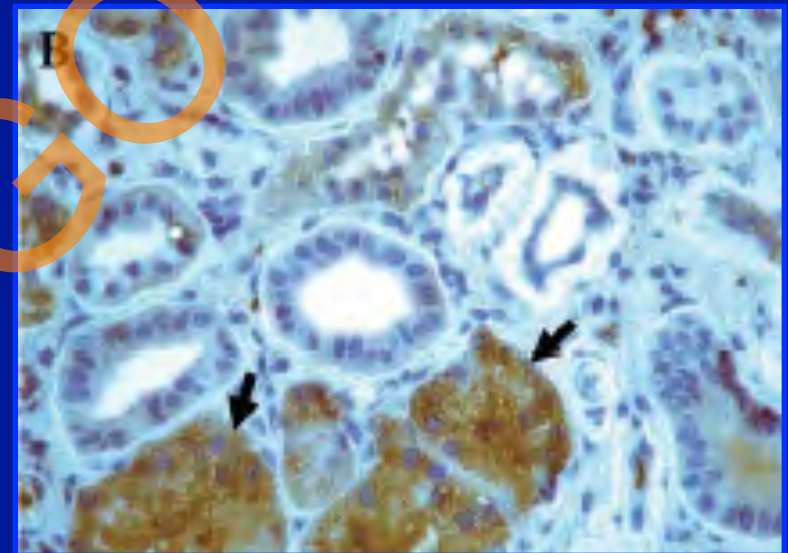
# The Renin-Angiotensin-Aldosterone System is Stimulated in ADPKD as Compared to Essential Hypertension



# ANGIOTENSINOGEN (AGT) EXPRESSION BY ADPKD KIDNEY

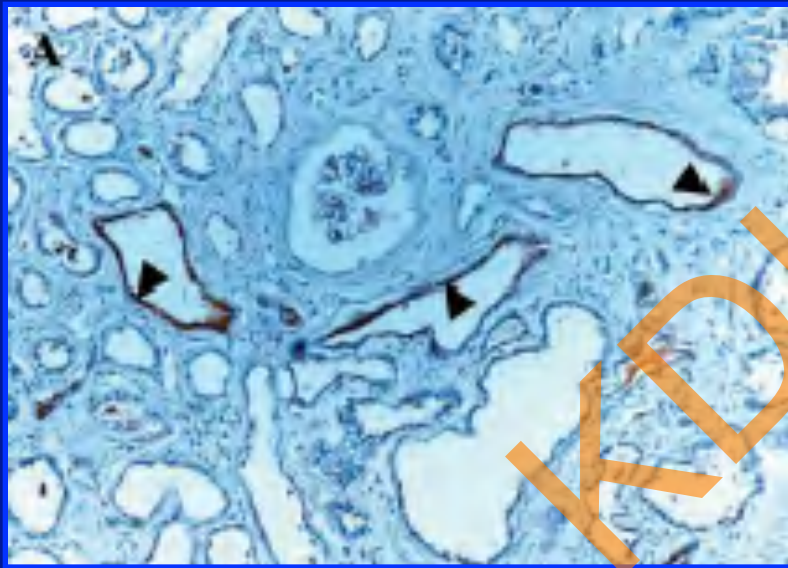


**Renal Cyst**

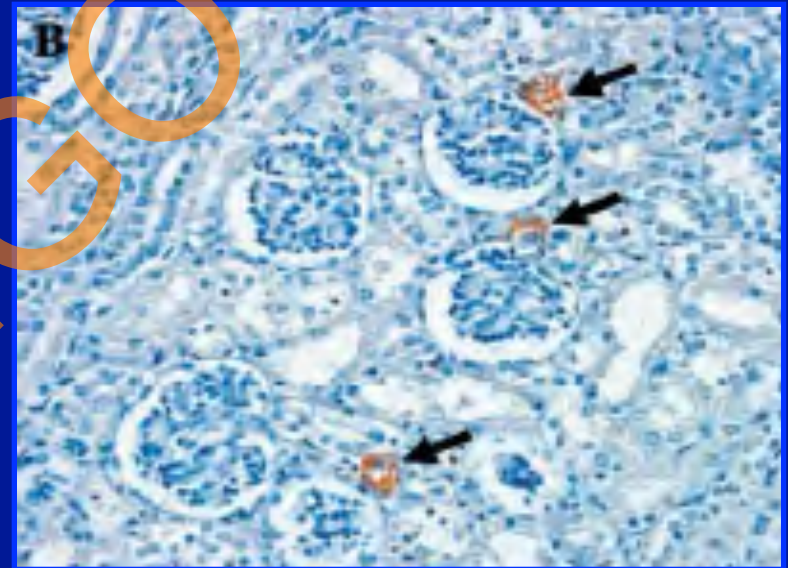


**Renal Tubules**

# RENIN EXPRESSION BY ADPKD KIDNEY

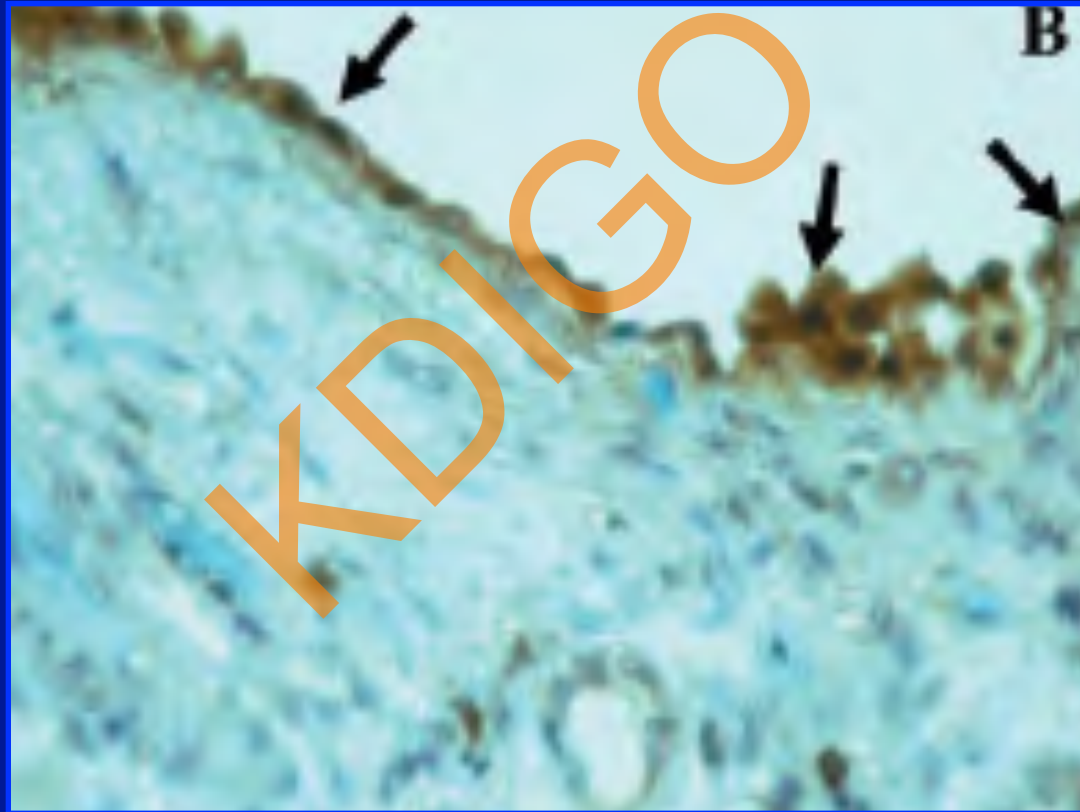


**ADPKD Kidney**



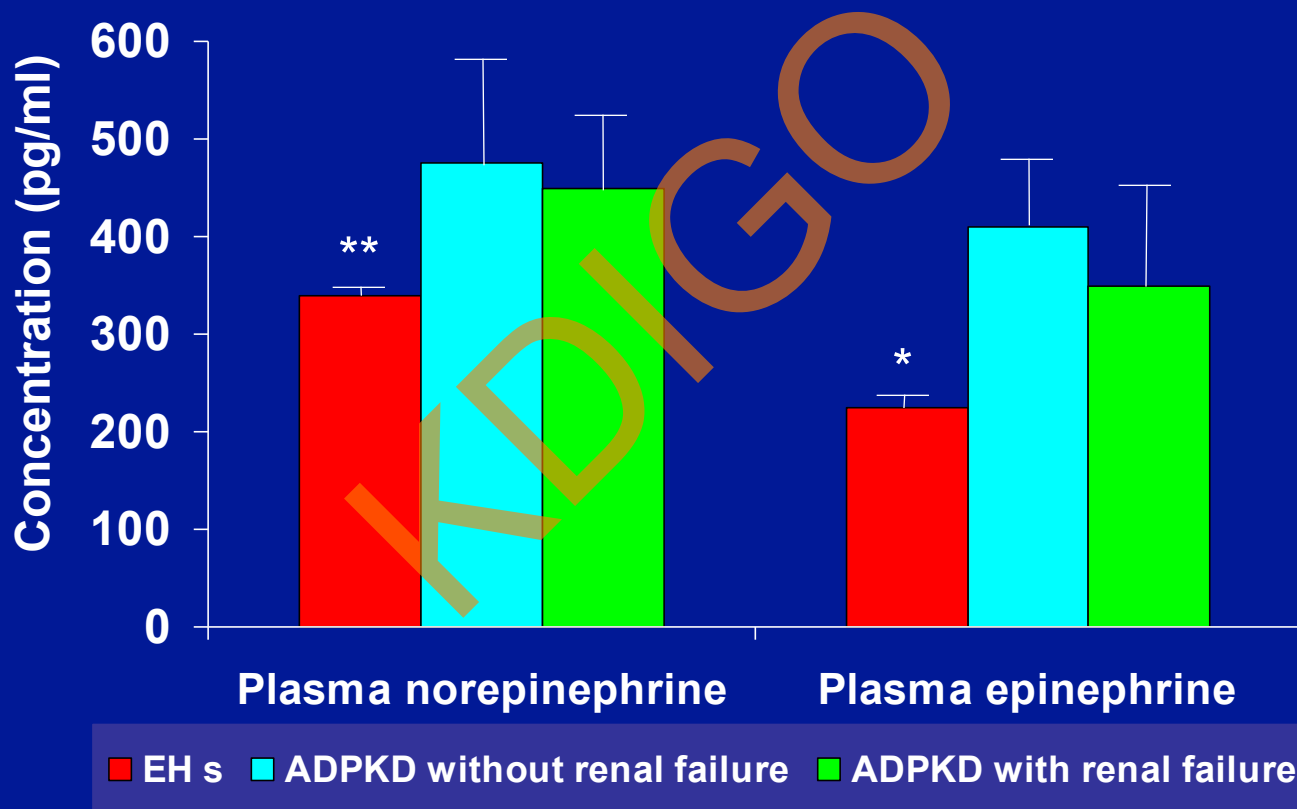
**Normal Kidney**

# ANGIOTENSIN II EXPRESSION BY ADPKD KIDNEY

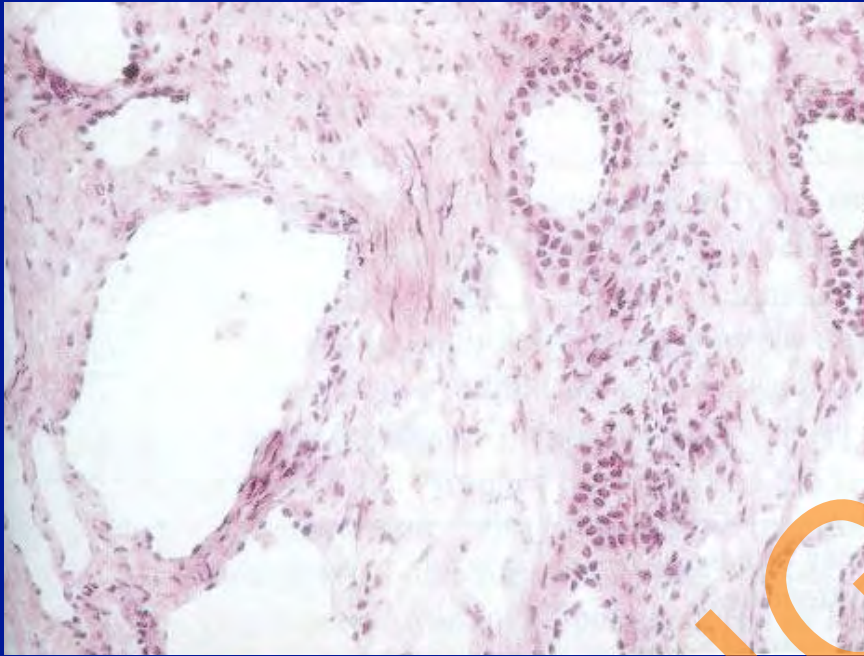




# PLASMA CATECHOLAMINES IN ESSENTIAL HYPERTENSIVES (EH) AND IN HYPERTENSIVES WITH ADPKD DIVIDED IN TWO GROUPS ACCORDING TO RENAL FUNCTION



\* $p < 0.001$  and \*\* $p < 0.01$  vs. ADPKD



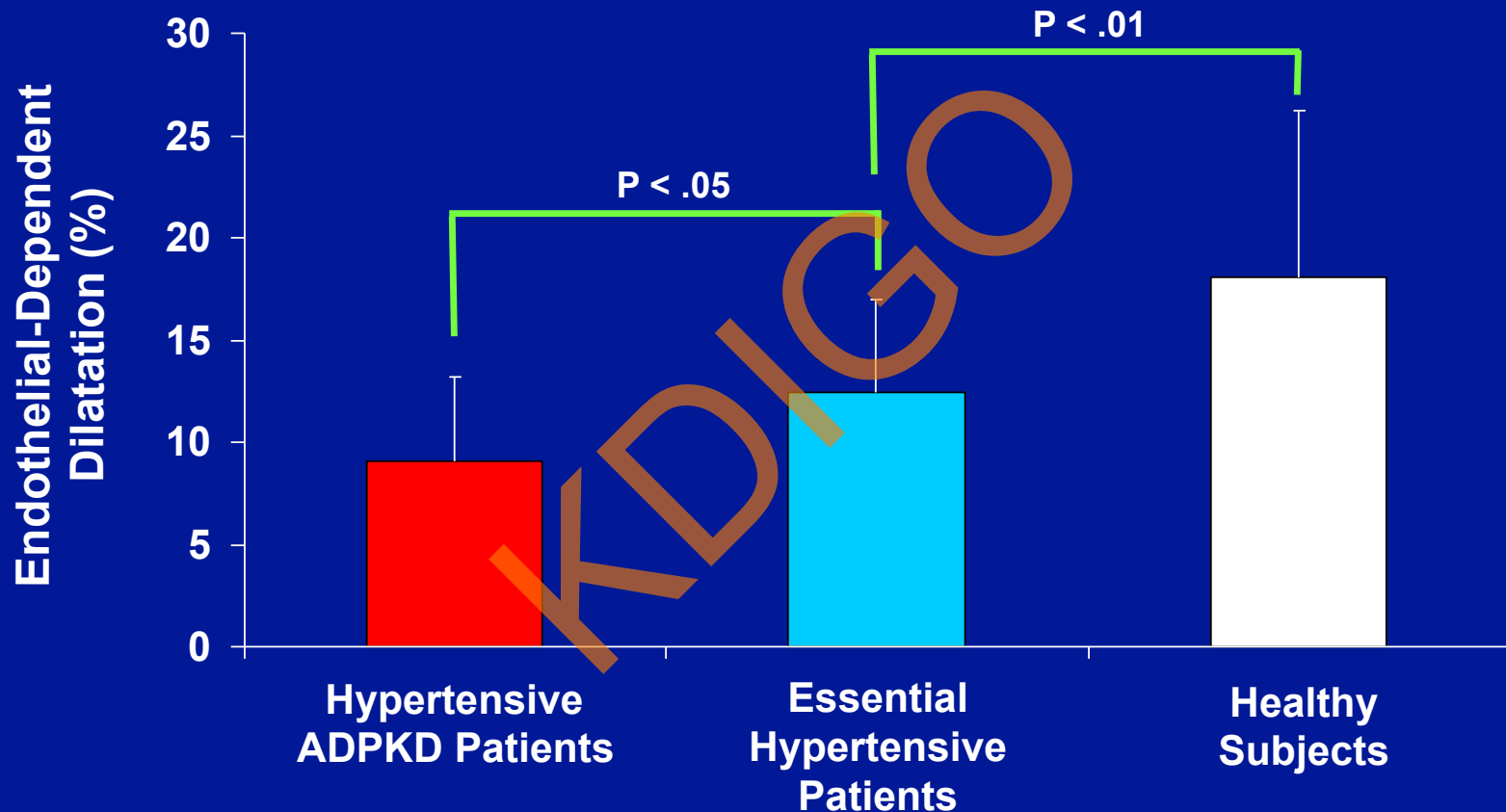
**Kidney section from  
a 39-yr-old patient with  
typical ADPKD (H and E  
stain)**



**Immunohistochemical  
staining using an ET-1  
antibody**

*Hocher et al. J Am Soc Nephrol 9:  
1169-77, 1998.*

# EVIDENCE FOR IMPAIRED ENDOTHELIAL FUNCTION IN ADPKD

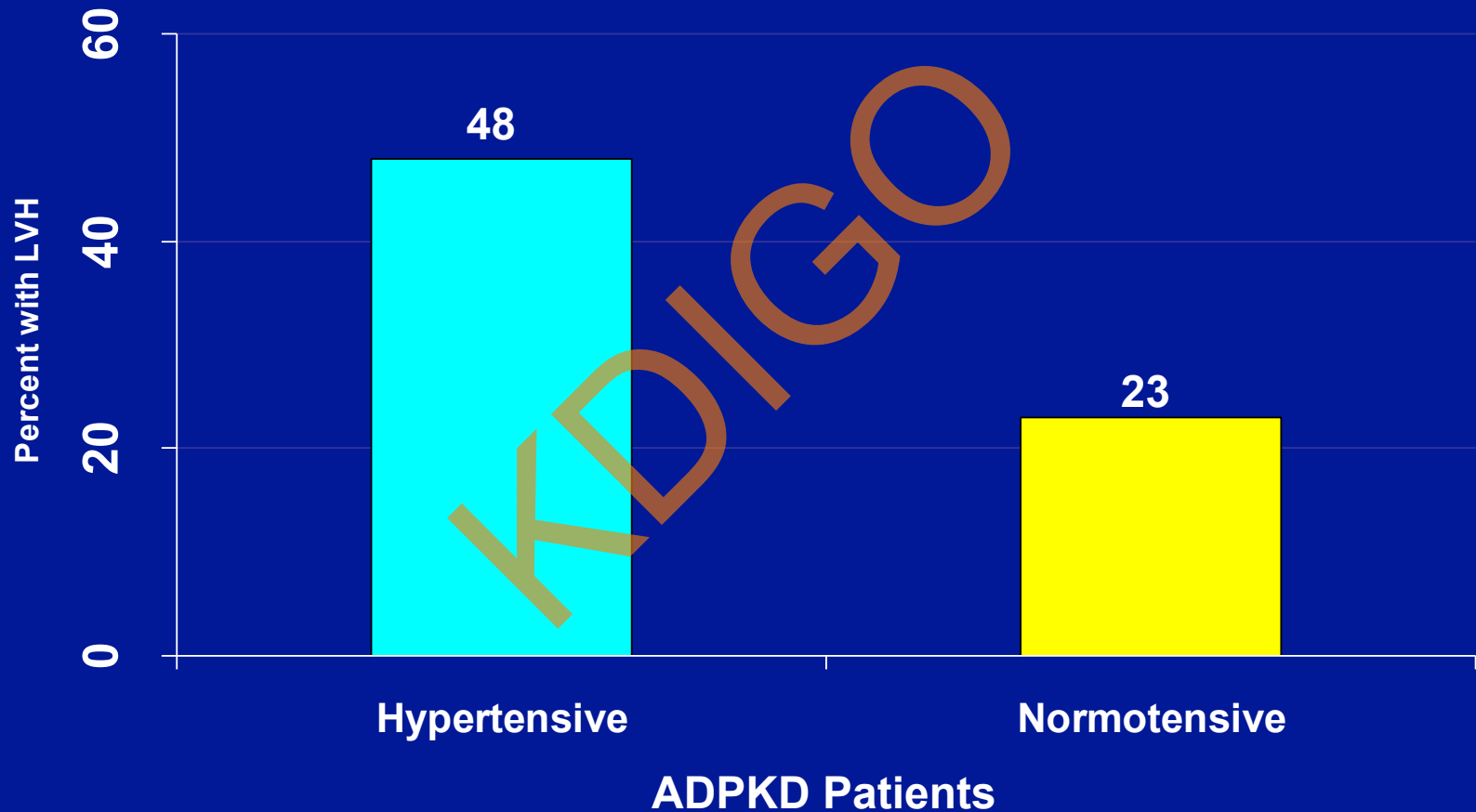


# PATIENT CHARACTERISTICS

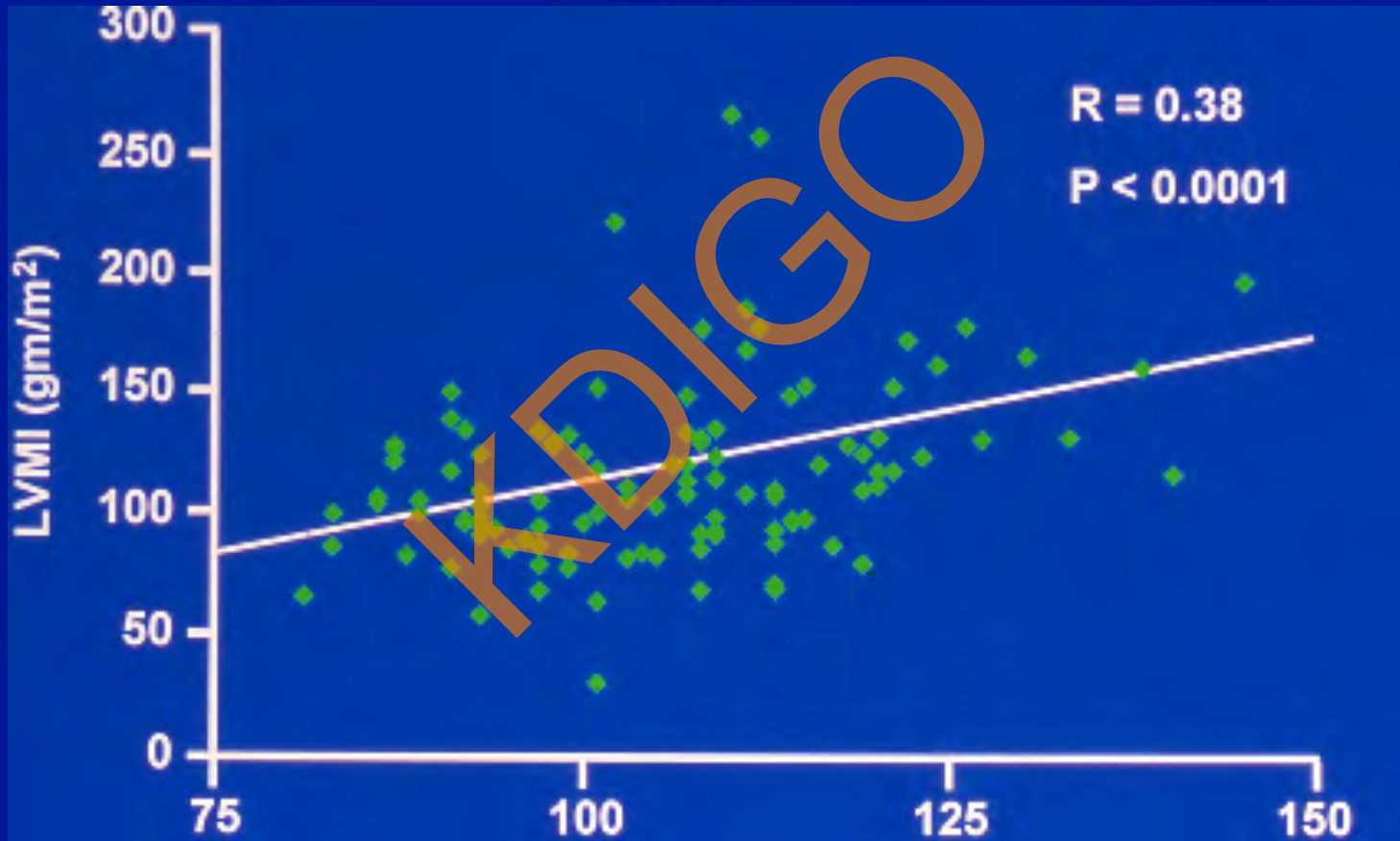
	Hypertensive ADPKD Patients (n = 15)	Essential Hypertensive Patients (n = 16)	Healthy Subjects (n = 24)
Age (y)	39.6 ± 7.2	40.8 ± 4.8	38.1 ± 8.8
Sex (M/F)	4/11	7/9	8/16
BMI (kg/m <sup>2</sup> )	25.5 ± 3.5	26.0 ± 3.2	24.7 ± 3.5
Smokers (n)	2	4	3
Systolic BP (mm Hg)	138 ± 18 *	134 ± 14 *	119 ± 14
Diastolic BP (mm Hg)	85 ± 11 **	77 ± 13	75 ± 9
CrCl (ml/min/1.73 m <sup>2</sup> )	91 ± 29	112 ± 14	105 ± 12
Total cholesterol (mg/ dl)	195 ± 23	179 ± 29	180 ± 30
Triglycerides (mg/dl)	121 ± 37	115 ± 35	114 ± 37
LVMI (g/m <sup>2</sup> )	132 ± 23 ***	111 ± 16 ****	95 ± 17

\*  $P < 0.01$  vs. healthy subjects; \*\*  $P < 0.005$  vs. healthy subjects; \*\*\*  $P = 0.02$  vs. essential hypertensive patients,  $P < 0.0001$  vs. healthy subjects; \*\*\*\*  $P < 0.005$  vs. healthy subjects

# Percentage of LVH in ADPKD Patients



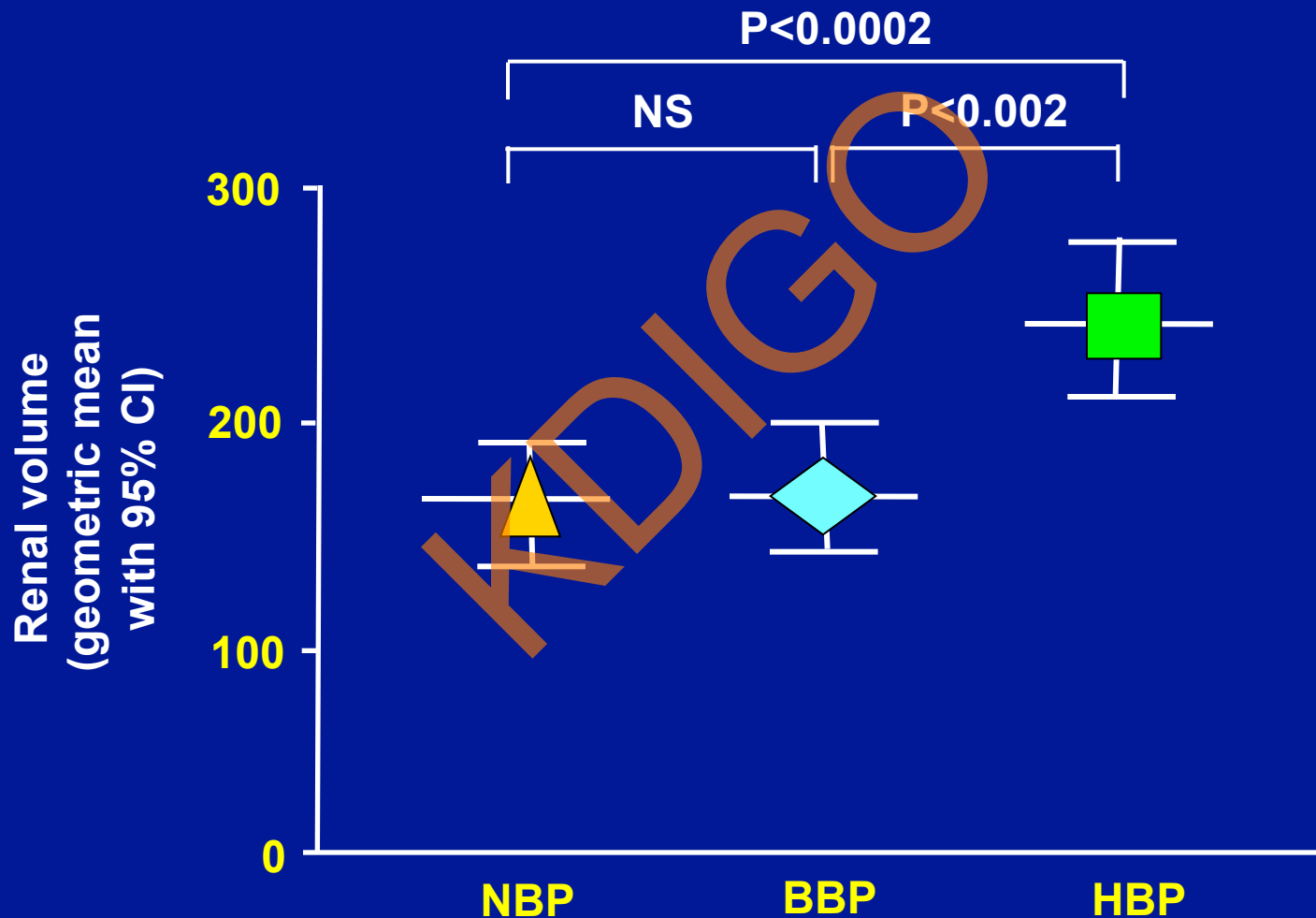
# Correlation Between Blood Pressure and Left Ventricular Hypertrophy in Polycystic Kidney Disease



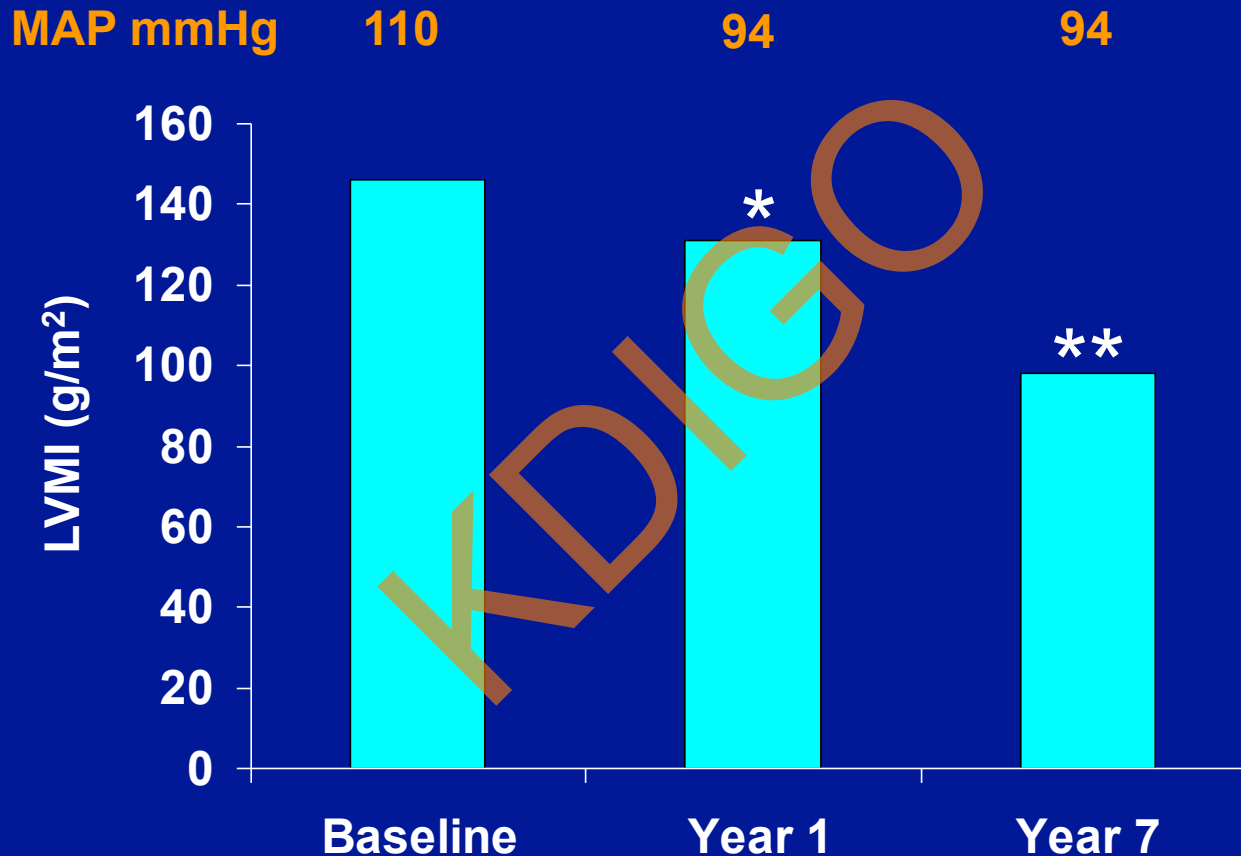
Mean Arterial Pressure (mm Hg)

*Chapman, Schrier, et al. JASN,8(8):1292-7,1997.*

# Renal volume was markedly increased in hypertensive (HBP) as compared to borderline hypertensive (BBP) and normotensive (NBP) children with ADPKD



# Effect of ACE Inhibitors on Left Ventricular Hypertrophy in ADPKD



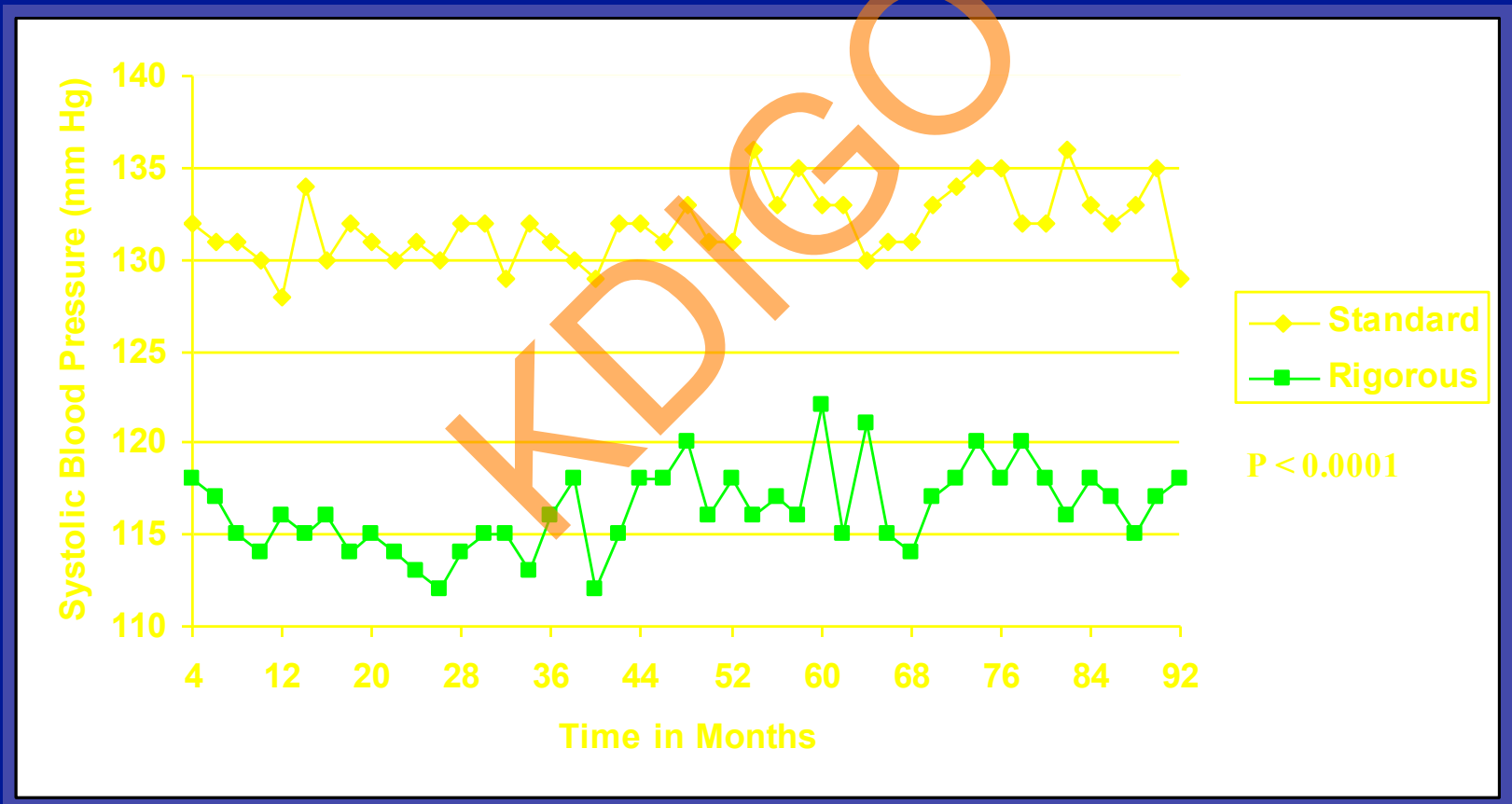
\* P < 0.05 versus baseline; \*\* P < 0.01 versus year 1 and baseline



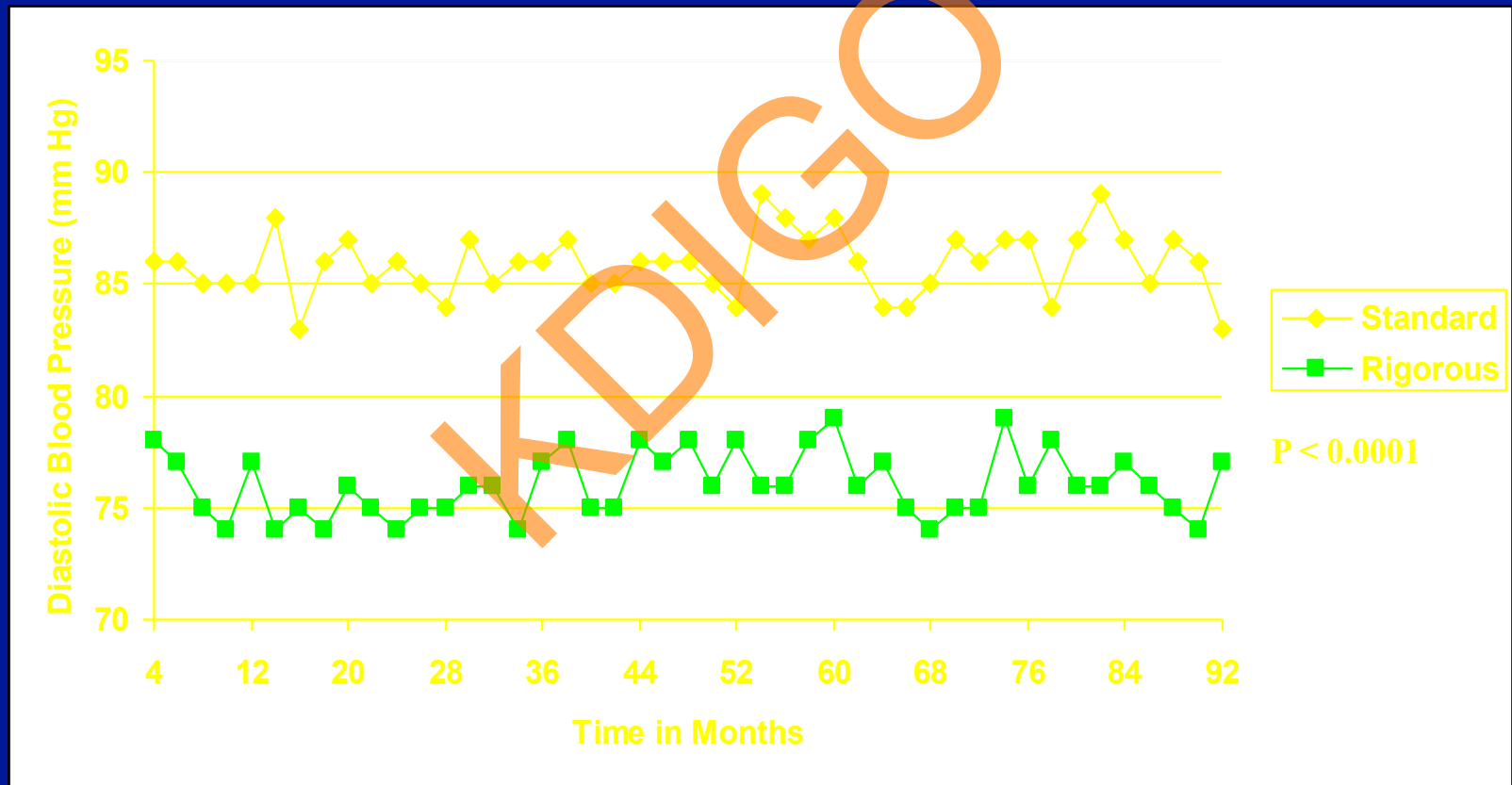
# Introduction

- ▶ In a 7-year prospective randomized study, 79 hypertensive ADPKD patients with left ventricular hypertrophy (LVH) were randomized to standard blood pressure control (135-140/85-90 mm Hg) or rigorous blood pressure control (< 120/80 mm Hg).
- ▶ With angiotensin converting enzyme inhibitor or calcium channel blocker, amlodipine

# Mean Sitting Systolic BPs from the 4<sup>th</sup> month through year 7 of ADPKD Patients Randomized to Rigorous (<120/80 mm Hg) or Standard 135-140/85-90 mm Hg) BP Control



# Mean Sitting Diastolic BPs from the 4<sup>th</sup> month through year 7 of ADPKD Patients Randomized to Rigorous (<120/80 mm Hg) or Standard 135-140/85-90 mm Hg) BP Control



# Effect of Rigorous versus Standard BP Control on Left Ventricular Mass Index in ADPKD Patients Over 7 years



# Effect of BP Control with Amlodipine versus Enalapril on Left Ventricular Mass Index in ADPKD Patients Over 7 Years

