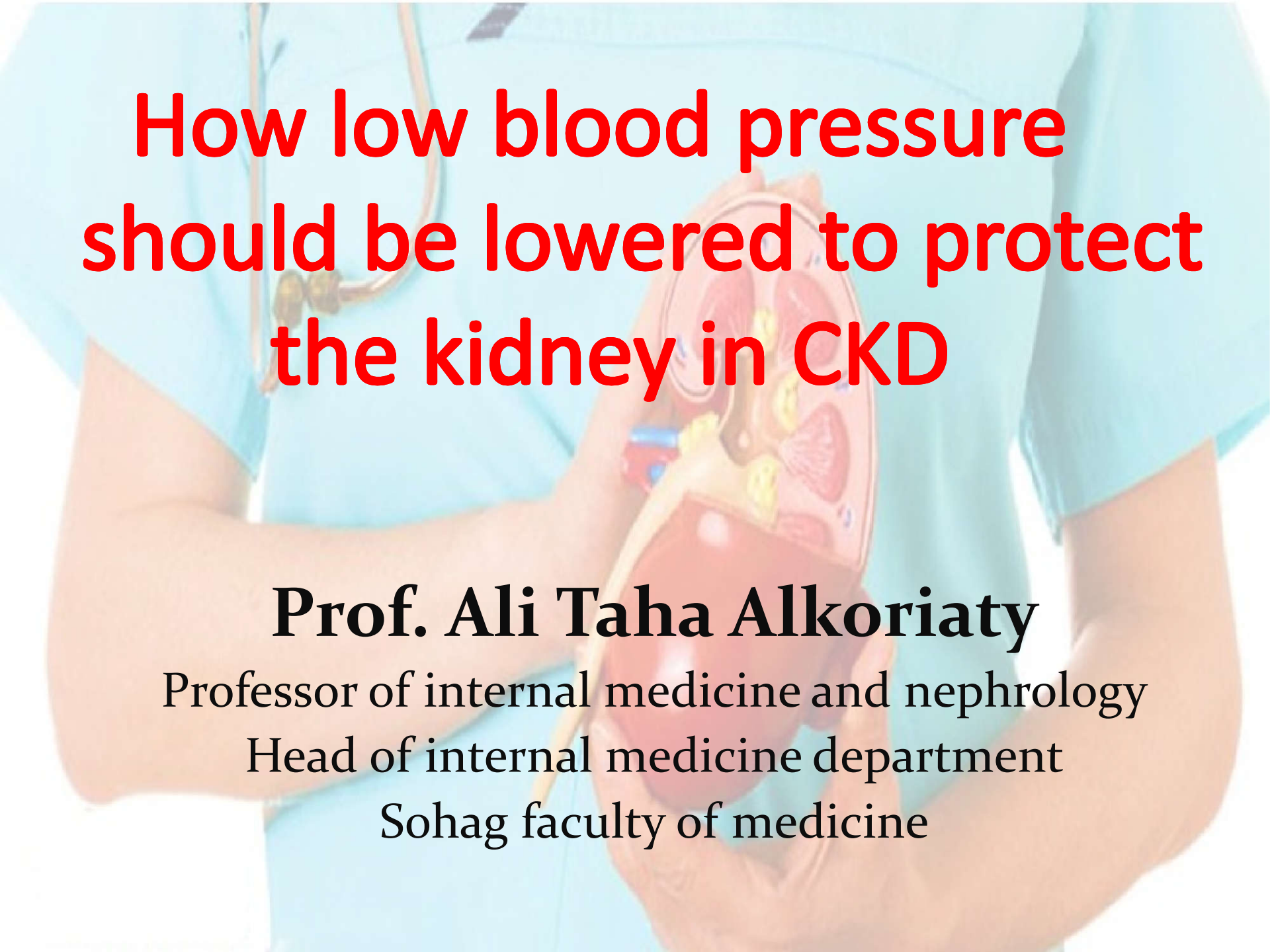

How low blood pressure should be lowered to protect the kidney in CKD

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Prevalence of HTN

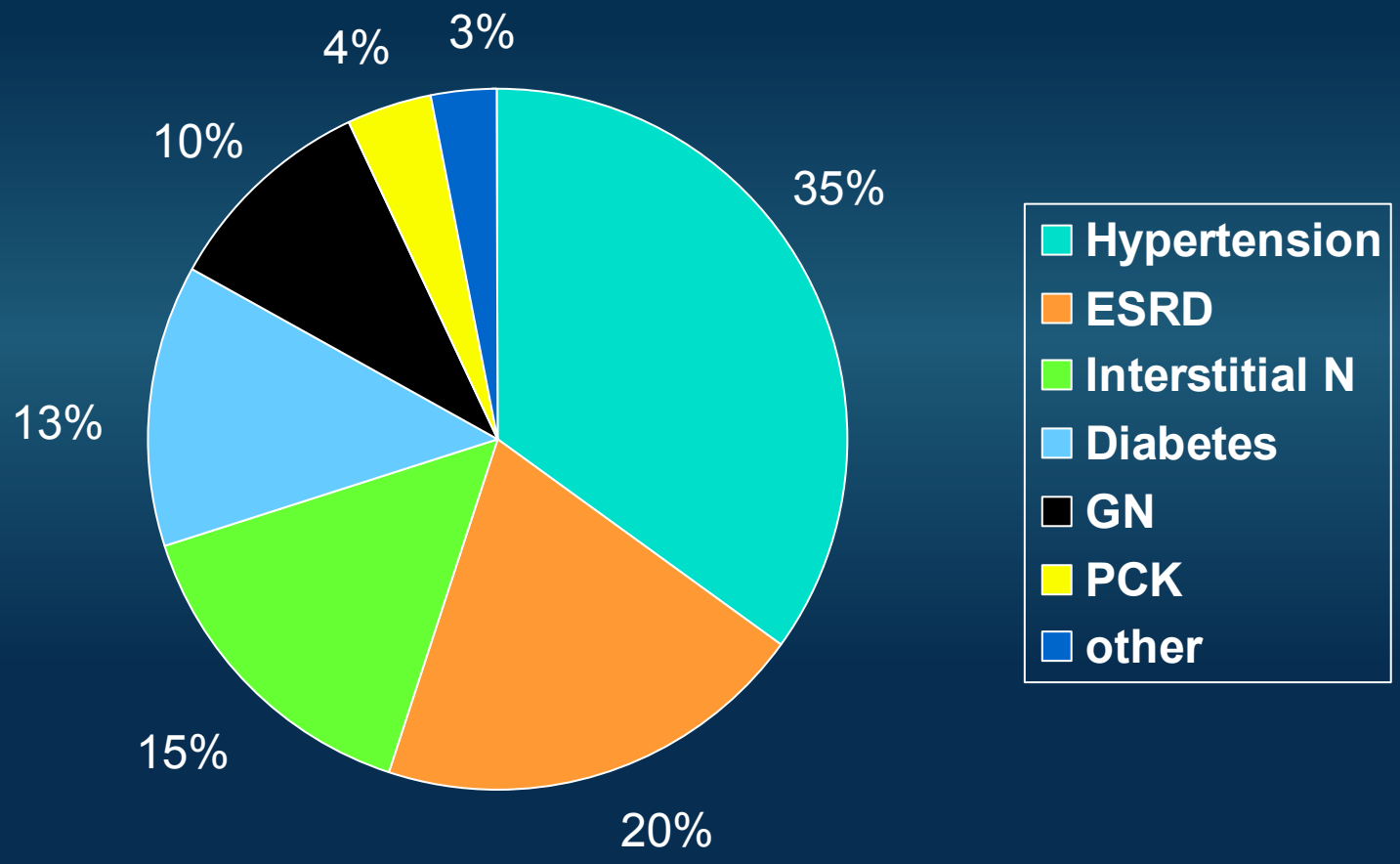
- Uncontrolled HTN is a risk factor for developing CKD , and is the second leading cause of ESRD in the U.S (1st cause in Egypt)
- HTN is associated with a more rapid progression of CKD.

Botdorf J, et al, *Cardiorenal Med*. 2011;1:183–192.
Segura J, et al, *Adv Chronic Kidney Dis*. 2011;18:23–27

- HTN has been reported to occur in 85% to 95% of patients with CKD (stages 3–5)

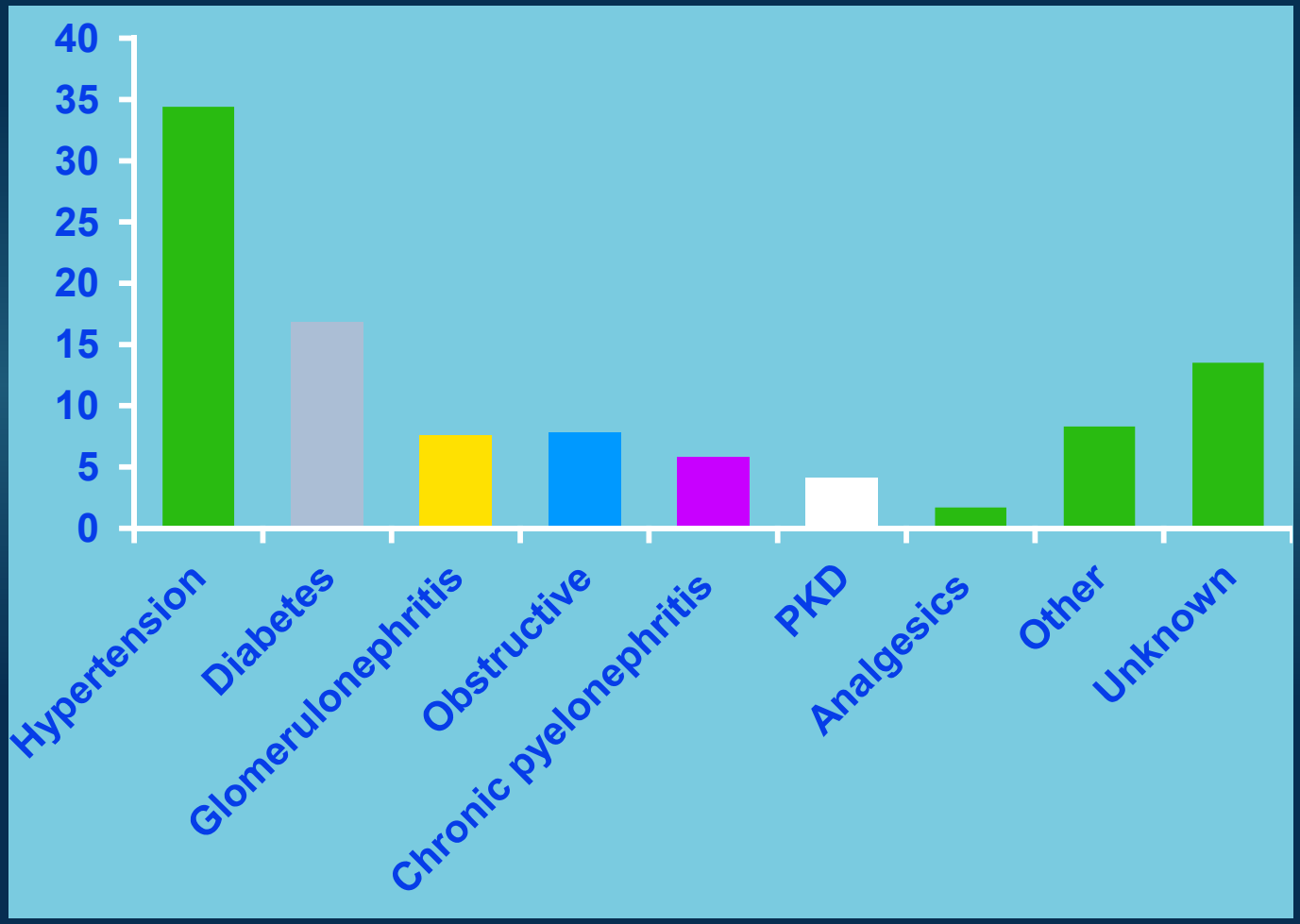
Rao MV, et al, *AJKD* 2008;51(suppl 2):S30-S37.

Aetiology of CKD in Egypt



Barsoum RS, Kidney International Supplements (2013) 3, 164–166

Etiology of chronic kidney disease in HD patients in Egypt (n=22,070)



PKD, polycystic kidney disease

Sarhan I, et al. Ain Shams University, 2014

PATHPHYSIOLOGY

Mechanisms of CKD & its progression

1. Reduction in kidney mass: Glomerulosclerosis & Fibrosis
2. Glomerular hypertension : Adaptive haemodynamic changes
3. Intratubular proteinuria: increased glomerular BP and Endothelial injury

How Does Blood Pressure Relate To Progression of CKD?

In a sick kidney,

Increased in BP Lead to increased Glomerular Hypertension that causes

PROGRESSION OF CKD (INCREASED FIBROSIS)

Effect Proteinuria

- **Studies demonstrate presence of proteins in renal tubules activates tubular cells**

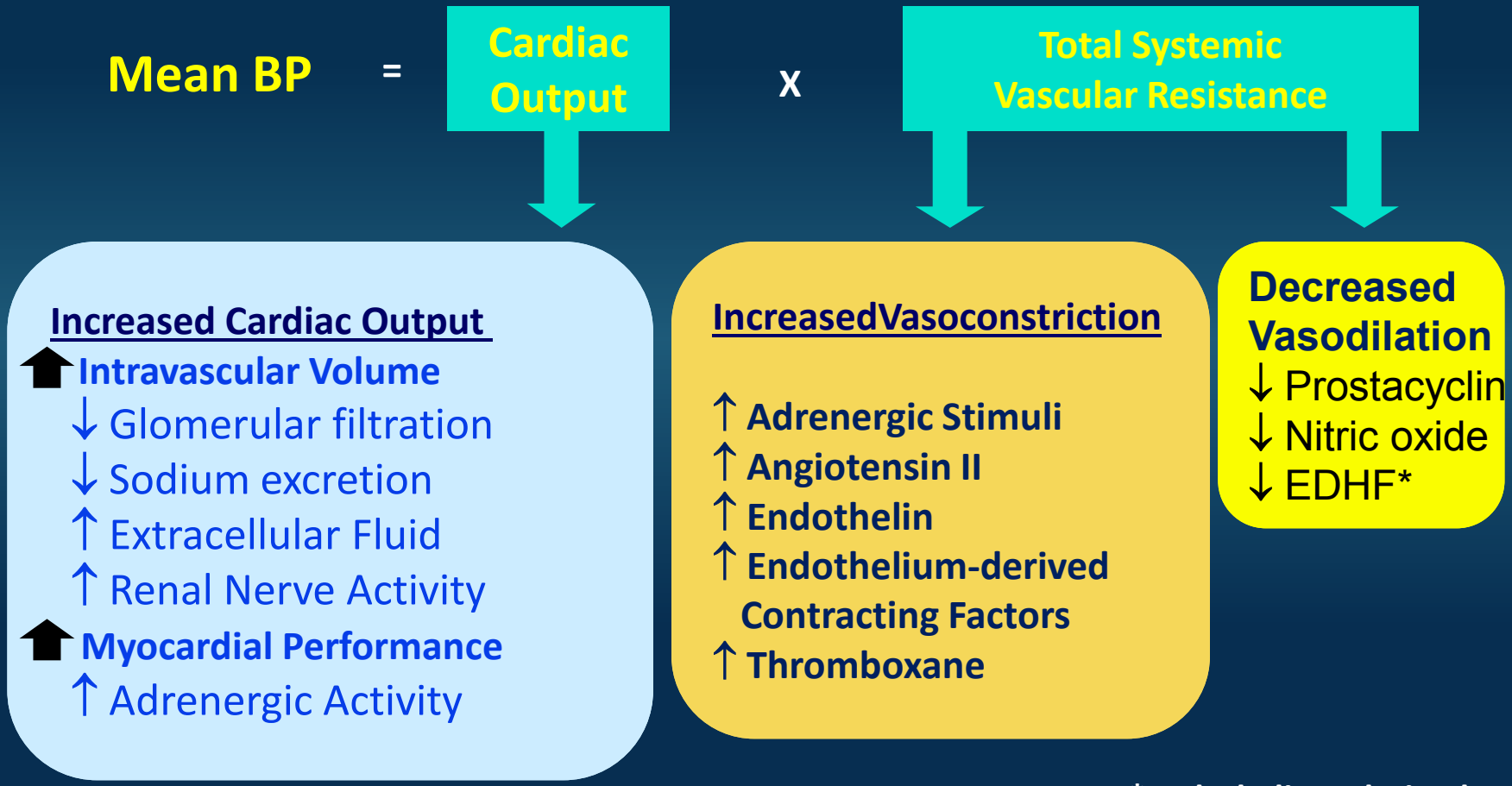
  – **upregulated inflammatory/vasoactive cytokines**

  -- associated with complement component activation on proximal tubule apical membranes

- **Intratubular complement activation** may be key mechanism

  progressive damage that lead to interstitial fibrosis & scarring

Hypertension and Chronic Renal Disease: Hemodynamic Abnormalities



*Endothelium-derived Hyperpolarizing Factors

Textor SC. Atlas of Diseases of the Kidney, 2001.

Pathogenetic Mechanisms of High Blood Pressure in CKD

- Pre-existing essential hypertension
- Extracellular fluid volume expansion
- Renin-agniotensin aldosterone system stimulation
- Increased sympathetic activity
- Alteration in endothelium-derived factors (NO/endothelin)
- Increased body weight
- Erythropoietin administration
- PTH secretion/hypercalcemia
- calcified arterial tree
- renal vascular disease and renal artery sten

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Therapeutic Strategies to protect the kidney in HTN and CKD

What Are The Targets Of Treatment

KIDNEY DISEASES OUTCOME INITIATIVE

Antihypertensive therapy should be used in CKD to:

1. Lower blood pressure

2. Reduce the risk of CVD, in patients with or without hypertension

3. Slow progression of kidney disease, in patients with or without hypertension

4. The early you control BP (s.creatinine <3mg), the greater the chance to bring s.creatinine to normal.

Treatment Guideline

KIDNEY DISEASES OUTCOME INITIATIVE (K/DIGO)

- Antihypertensive therapy should be coordinated with other therapies for CKD as part of a multi-intervention strategy .

- Modifications to antihypertensive therapy should be considered based on the level of proteinuria during treatment

- Target blood pressure for CVD risk reduction in CKD should be <130/80 mm Hg (kdigo 2012)

Recommendations for BP and RAS Management in CKD

Patient Group	Goal BP (mm Hg)	First Line	Adjunctive
+ Diabetes	<130/80	ACE-I or ARB	Diuretics then CCB or BB
– Diabetes + Proteinuria	<130/80	ACE-I or ARB	Diuretics then CCB or BB
– Diabetes – Proteinuria	<130/80	No specific preference: Diuretics then ACE-I, ARB, CCB, or BB	

EXPECT TO NEED TO USE 3+ AGENTS TO ACHIEVE GOALS

Recommendations largely consistent across JNC 7, ADA, and K/DOQI

BP = blood pressure; RAS = renin angiotensin system; CCB = calcium channel blocker; BB = β-blocker; JNC 7 = The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

ADA. *Diabetes Care*. 2005;28(suppl 1); Chobanian et al. *JAMA.* 2003;289:2560-2572; Kidney Disease Outcomes Quality Initiatives (K/DOQI). *Am J Kidney Dis.* 2004;43(5 suppl 1):S1-S290.

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Recommendations for Controlling HTN in Non-Diabetic CKD

Population	BP Goal	Nondrug Rx	Drug RX
CKD + >200mg/g Prot/Cr Ratio	<130/80	Reduce salt BMI≤25 kg/m2 Mod EtOH Stop Smoking Exercise	ACEI/ARB Then diuretic Then BB or CCB
CKD + no proteinuria	<130/80	Same	Thiazide/Loop Then ACEI/ARB Then BB or CCB

KDOQI Table 118, Guideline 9

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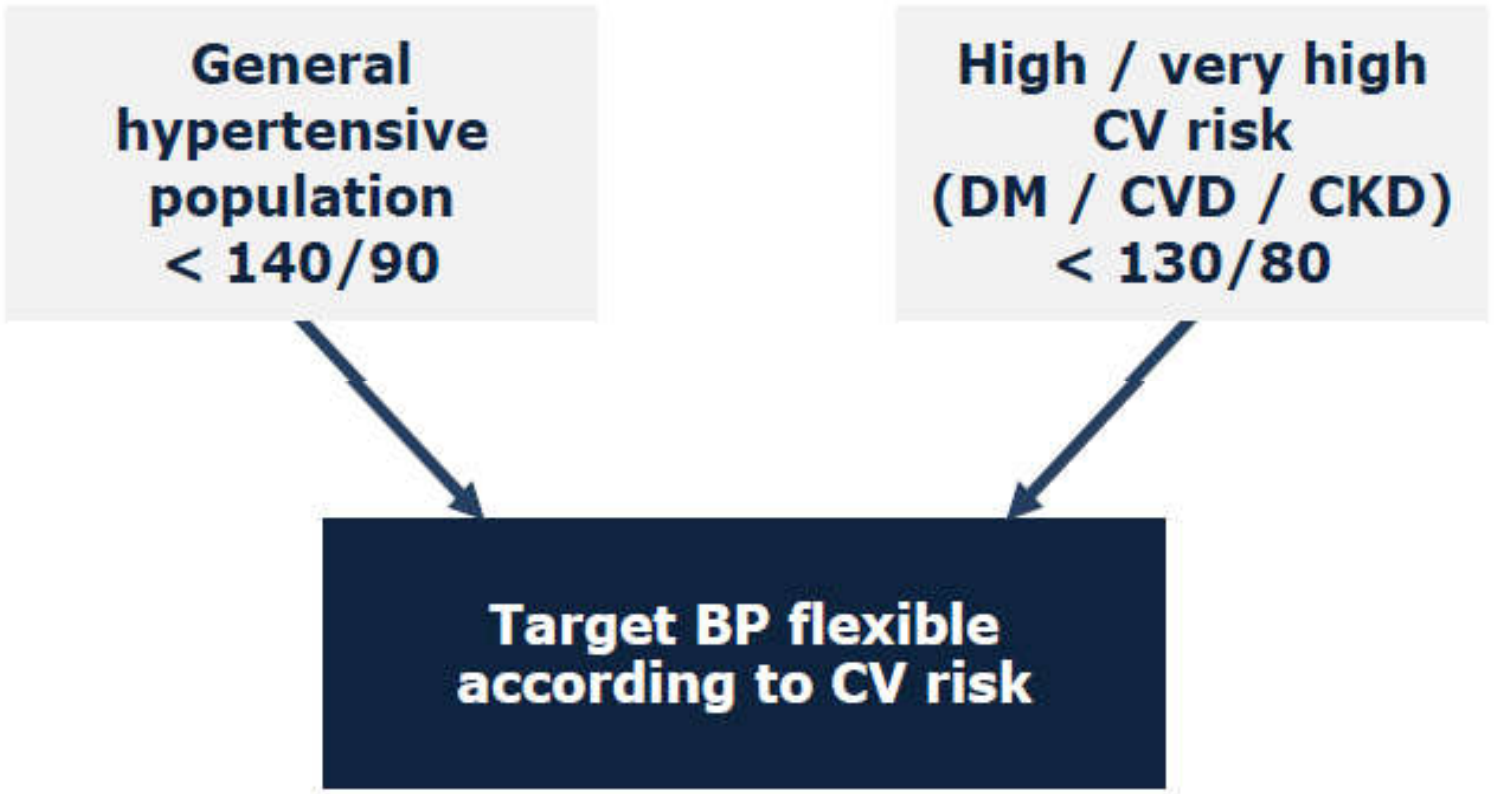
2007 ESC/ESH hypertension guidelines



Target BP in recent guidelines

Guideline	Population	Goal BP, mm Hg
2014 Hypertension guideline	General ≥60 y	<150/90
	General <60 y	<140/90
	Diabetes	<140/90
	CKD	<140/90
ESH/ESC 2013[37]	General nonelderly	<140/90
	General elderly <80 y	<150/90
	General ≥80 y	<150/90
	Diabetes	<140/85
	CKD no proteinuria	<140/90
	CKD + proteinuria	<130/90
CHEP 2013[38]	General <80 y	<140/90
	General ≥80 y	<150/90
	Diabetes	<130/80
	CKD	<140/90
ADA 2013[39]	Diabetes	<140/80

A single SBP target for almost all patients

- **JNC VIII (BP target)**
  - In patients with CKD, initiate treatment at SBP ≥140 mmHg or DBP ≥90 mmHg, and treat to achieve SBP <140 mmHg and DBP <90 mmHg.

ESC/ESH 2013 BP Goals,

Recommendations	Class[a]	Level[b]
A SBP goal <140 mmHg:		
a) is recommended in patients at low–moderate CV risk;	I	B
b) is recommended in patients with diabetes;	I	A
c) should be considered in patients with previous stroke or TIA;	IIa	B
d) should be considered in patients with CHD;	IIa	B
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

2013 ESH/ESC Guidelines for the management of arterial hypertension

Treatment of Hypertension in association with Diabetic Nephropathy

If Creatinine over 150 µmol/L or creatinine clearance below 30 ml/min (0.5 ml/sec), a loop diuretic should be substituted for a thiazide diuretic if control of volume is desired

DIABETES with Nephropathy

→ **ACE Inhibitor or ARB**

→ **Addition of one or more of** Long-acting CCB or Thiazide diuretic

IF ACEI and ARB are contraindicated or not tolerated, SUBSTITUTE
- **Long-acting CCB or**
- **Thiazide diuretic**

3 - 4 drugs combination may be needed

Monitor serum potassium and creatinine carefully in patients with CKD prescribed an ACEI or ARB


KIDNEY DISEASE
IMPROVING GLOBAL OUTCOMES
KDIGO

BP and RAAS interruption

- Individualize BP targets and agents.
- Inquire about postural dizziness and check for postural hypotension regularly when treating CKD patients with BP-lowering drugs.
- We recommend that in both diabetic and non-diabetic adults with CKD and urine albumin excretion ≥30 mg/ 24 hours whose office BP is consistently >140/90mm Hg be treated with BP-lowering drugs to maintain a BP that is consistently ≤140/90mm Hg

KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3:136-150.
http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf Accessed February 26, 2013

BP and RAAS interruption

- We suggest that an ARB or ACE-I be used in diabetic adults with CKD and urine albumin excretion 30–300 mg/ 24 hours.
- We recommend that an ARB or ACE-I be used in both diabetic and non-diabetic adults with CKD and urine albumin excretion >300 mg/24 hours even with normal BP
- There is insufficient evidence to recommend combining an ACE-I with ARBs to prevent progression of CKD.
- We suggest that an ARB or ACE-I be used in children with CKD in whom treatment with BP-lowering drugs is indicated, irrespective of the level of proteinuria.

KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3:136-150.
http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf Accessed February 26, 2013

RAAS System Blockers in DKD

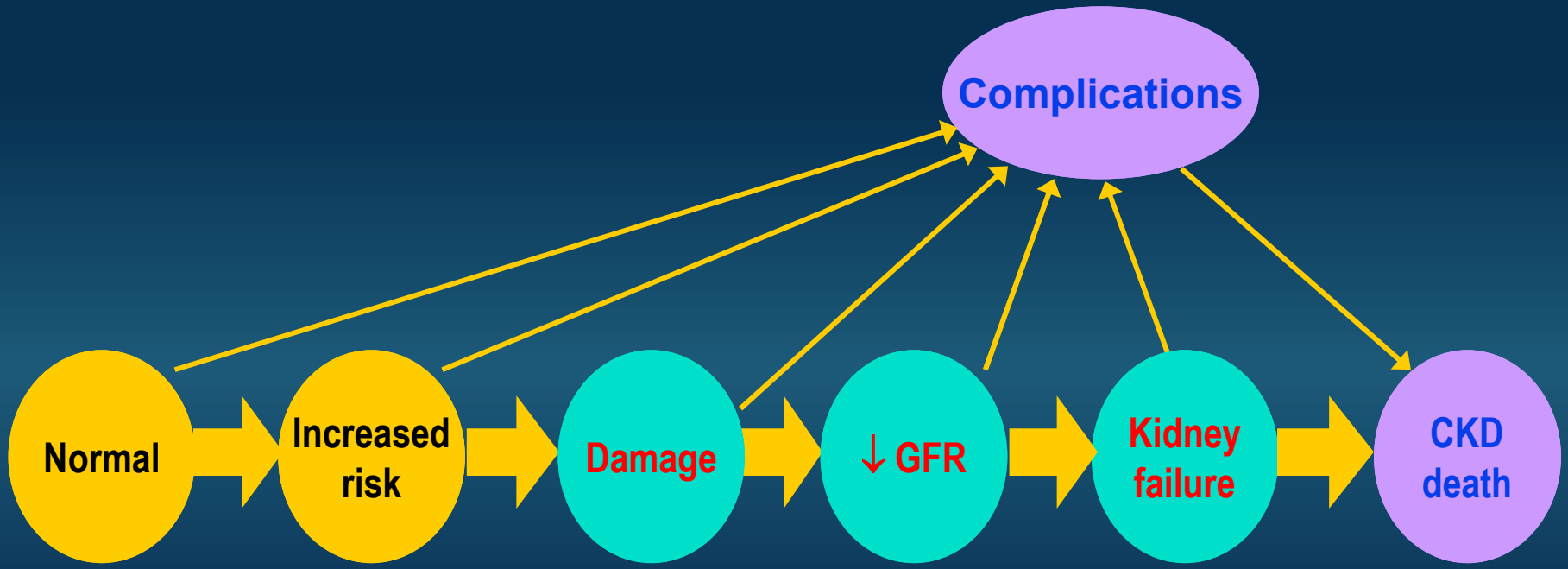
6.1: We recommend not using an angiotensin-converting enzyme inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) for the primary prevention of DKD in normotensive normoalbuminuric patients with diabetes. (*1A*)

6.2: We suggest using an ACE-I or an ARB in normotensive patients with diabetes and albuminuria levels ≥30 mg/g who are at high risk of DKD or its progression. (*2C*)

National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. *Am J Kidney Dis*. 2012;60(5):850-886.

National Kidney Foundation®
KDOQI

Therapeutic Strategies in different stages Progression of Chronic Kidney Disease and



Lesley Stevens, Clinical Practice Guidelines for Management of **Hypertension** in **CKD** Oct 2004

How can people prevent or slow the progression of kidney disease from high blood pressure?

The best way to slow or prevent kidney disease from high blood pressure is to take steps to lower blood pressure. These steps include a combination of medication and lifestyle changes, such as

- healthy eating
- physical activity
- maintaining a healthy weight
- quitting smoking
- managing stress

No matter what the cause of the kidney disease, high blood pressure can increase damage to the kidneys. People with kidney disease should keep their blood pressure below 140/90.[4]

Conclusion

- Hypertension is the leading cause of CKD in Egypt
- There are still many debates on the “optimal” BP target and the “optimal” antihypertensive agents in patients with CKD.
- In the absence of significant proteinuria or non-diabetes, it might be appropriate to consider a BP target <140/90 mm Hg.
- No definite benefit of tight BP control (i.e., <130/80 mm Hg) on any clinical outcomes. But still it may be helpful in diabetic with proteinuria.


Thank You