



KDIGO BLOOD PRESSURE IN CKD GUIDELINE

37th Meeting of the Turkish Society of Nephrology
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@CharlieTomson

Retired Consultant Nephrologist, Newcastle upon Tyne, UK

DISCLOSURES

- No conflicts of interest to declare

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KDIGO BP GUIDELINE UPDATE WORK GROUP



Co-Chairs

Alfred K. Cheung and Johannes Mann

Members

*Tara Chang, William Cushman, Susan Furth, Fan Fan Hou,
Joe Ix, Greg Knoll, Paul Muntner, Roberto Pecoits-Filho,
Mark Sarnak, Sheldon Tobe, Charlie Tomson*

Evidence Review Team

*Martin Howell and David Tunnicliffe
Cochrane Kidney and Transplant*

GROUP EVIDENCE REVIEW



- Evidence Review Team - Cochrane Kidney Transplant
- Existing (2012 KDIGO Guideline) PICO questions and new PICO questions
- Critical and important outcomes identified
- Focus on RCTs

Critical outcomes	Important outcomes
All-cause mortality	Doubling serum creatinine
End-stage kidney disease	Acute kidney injury
Cardiovascular outcomes (myocardial infarction, stroke, heart failure)	Falls
Dementia or cognitive impairment	Fatigue

PICO QUESTIONS

Population	Intervention	Comparator	Outcome
Patients with CKD General population	Automated BP measurement Ambulatory BP measurement	Office-based BP measurement	Differences, sensitivity, specificity
Adults, children , and elderly with CKD Transplant recipients	Lower BP target (<120/80 mm Hg; <130/90 mm Hg, etc.)	Standard BP target	Critical and important outcomes
Adults, children, and elderly with CKD Transplant recipients	Antihypertensive medication	Placebo or active control	Critical and important outcomes
Adults and children with CKD Transplant recipients	Diet (salt intake, dietary patterns)	Placebo or normal diet	Critical and important outcomes
Adults and children with CKD Transplant recipients	Exercise	Placebo or no exercise	Critical and important outcomes

GROUP MAGICAPP (MAKING GRADE THE IRRESISTIBLE CHOICE)

Electronic guideline software

KDIGO is piloting this online publishing platform to:

- directly link evidence to recommendations
- increase transparency of guideline process
- improve accessibility of guidelines through digital publishing
- create “living guidelines” that ease update process
- Allow generation of patient decision aids



NOMENCLATURE AND GRADING OF STATEMENTS

Within each recommendation, the strength of recommendation is indicated as **Level 1** or **Level 2**, and the quality of the supporting evidence is shown as **A, B, C, or D**.

Grade	Implications		
	Patients	Clinicians	Policy
Level 1 “We recommend”	Most people in your situation would want the recommended course of action and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 “We suggest”	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

GRADING STRENGTH OF EVIDENCE

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect lies close to the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of effect is very uncertain and often will be far from the truth.

TIMELINE

- Work Group formed April-May 2016
- Controversies conference September 2017, Edinburgh, UK
 - Cheung AK et al: Kidney International 2019; 95: 1027-1036
- Face-to-face meeting January 2019, New Orleans, USA
 - All subsequent work done by videoconference
- Draft guideline for public review issued 31/01/2020
- Full guideline submitted to Kidney International Supplements 25/09/2020: Executive Summary submitted to Kidney International 09/10/2020
- Guideline will also be published on www.magicapp.org

HEADLINE RECOMMENDATIONS

- All treatment decisions relating to BP-lowering should be based on “office” standardized, resting BP measurements (1B)
 - ABPM and HBPM may be used to complement standardized office BP (2B)
- Aim for dietary NaCl < 90 mmol/day (2C), exercise for > 150 min/week (2C)
- Aim for SBP < 120 in CKD (2B), < 130 < 80 in KTR (*practice point*); daytime mean Amb BP < 50th percentile in children (2C)
- Use ACEI/ARB in CKD G1-4, A2-3 (1B-2C depending on diabetes/non-diabetes and degree of albuminuria)
- Use a dihydropyridine CCB or ARB in KTR (1C)
- Avoid any combination of ACEI, ARB and DRA (1B)

WHY LOWER BP IN PATIENTS WITH CKD?

- Reduce all-cause mortality and significant morbidity
 - Largely via reduction in risk of cardiovascular disease
- Reduce risk of progression to ESKD
- We don't know which outcomes matter more to patients with CKD – but it is reasonable to expect that most patients with early CKD would worry more about all-cause or cardiovascular mortality than ESKD
 - e.g. in 5% Medicare sample of CKD, risk of death was 45.7 times higher than risk of RRT (6.4 vs 0.14 per 100 pt-years)*

*Foley RN. J Am Soc Nephrol 2005;16: 489-495

STANDARDISED OFFICE BP MEASUREMENT

- Patient preparation
 - 5 minutes relaxation, seated (feet on floor, back supported), no caffeine/exercise/nicotine in preceding 30min, empty bladder, no clothing under the cuff, no conversation during measurement
- Proper technique for BP measurement
 - Validated, calibrated device; arm supported at heart level; correct size cuff
- Proper measurements
 - Check in both arms: use arm that gives higher reading. Separate repeated measurements by 1-2min. For auscultatory readings, inflate to 30mmHg above radial pulse obliteration pressure; deflate at 2 mmHg/sec; use 1st and 5th Korotkoff sounds (nearest even number)
- Average the readings

RATIONALE FOR STANDARDISED 'OFFICE' BP

- All outcome trials of BP targets have used standardized BP measurement
- Average HBPM or ABPM values are lower (e.g. 10/5 mmHg) lower than standardized office values in most populations, but this does not predict the difference in an individual
- 'Casual' office BP (e.g. without 5 min rest, while talking to the patient) are highly variable: use of such measurements to decide on prescription of BP-lowering therapy is indefensible and risks serious over-treatment

STANDARDISED VS. CASUAL VS. APBM

275 patients, 98% men, 17% black, 32%>75y, 65% diabetic

Table 2. Agreement Assessed With the Bland–Altman Method Using the 3 Blood Pressure Measurement Techniques

Variable	Bias (95% CI)	Limits of Agreement
Research grade, routine SBP	−12.7 (−14.7 to −10.7)	−46.1 to 20.7
Research grade, routine DBP	−12.0 (−13.4 to −10.7)	−34.2 to 10.1
Research grade, day ABPM SBP	−7.9 (−9.4 to −6.4)	−33.2 to 17.4
Research grade, day ABPM DBP	−11.7 (−12.7 to −10.8)	−27.8 to 4.3
Routine clinic, day ABPM SBP	4.8 (2.9–6.7)	−26.9 to 36.5
Routine clinic, day ABPM DBP	0.3 (−0.9 to 1.5)	−19.5 to 20.1

ABPM indicates ambulatory blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

- Great variability between standardized and casual clinic BP, even when measured on the same day; standardized SBP on average 7.9 mmHg lower than daytime Amb SBP; routine SBP 4.8 mmHg higher.
- Strength of association between standardized and daytime ambulatory SBP and LVH similar, and both stronger than routine SBP

STANDARDISED BP IS MORE TIME-CONSUMING THAN CASUAL BP, BUT ASK YOURSELF:

- Would you accept this degree of bias and inaccuracy for measurements of
 - Creatinine?
 - Potassium?
 - Body weight?
 - Age?

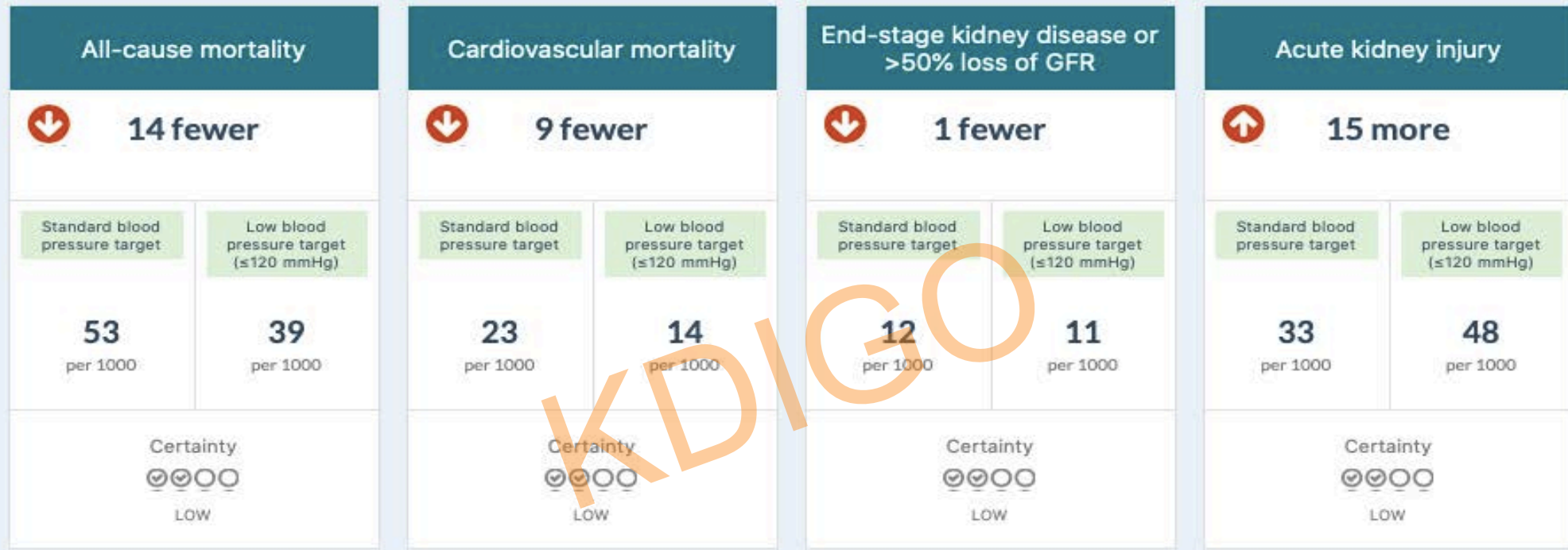
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RATIONALE FOR TARGET SBP<120 IN CKD

- For most patients with CKD, Cardiovascular Disease is a more important outcome for many patients than ESKD (1)
- SPRINT confirmed benefit in non-diabetic CKD (2)
- ACCORD showed marked reduction in stroke in diabetes, but only included 401 patients with eGFR<60; benefits of SBP<120 in the standard glycaemia arm similar to those seen in SPRINT (3,4)
- Meta-analyses demonstrate reduction of CV risk proportional to BP lowering, though some show lower proportional risk reduction in the presence of CKD and of DM (5,6,7)


1:O'Hare J Am Soc Nephrol 2007;18: 2758. 2:Cheung JASN 2017; 28: 2812. 3: Papademetriou Am J Nephrol 2016; 43: 271. 4:Tsujiimoto Hypertension 2018;72;323. 5: BPLTC BMJ 2013;347:f5680; 6:Ettehad Lancet 2016;387:435; 7: Malhotra JAMA Int Med 2017;177:1498

Among a 1000 patients like you, on average with Low blood pressure target (≤ 120 mmHg)




- Hypokalemia
- >30% loss in eGFR
- >40% loss in eGFR
- Mild cognitive impairment
- Cardiovascular events
- Myocardial infarction
- Stroke
- Heart failure
- Probable dementia
- Falls
- Fatigue
- Serious adverse events
- Hyperkalemia
- Practical issues

All-cause mortality

 **14 fewer**

Standard blood pressure target	Low blood pressure target (≤ 120 mmHg)
53 per 1000	39 per 1000

Certainty



LOW

Among a 1000 patients like you, with Low blood pressure target (≤ 120 mmHg)



947 with no event

MALHOTRA: META-ANALYSIS OF TRIALS OF INTENSIVE VS. LESS INTENSIVE BP-LOWERING IN CKD

RESULTS This study identified 30 RCTs that potentially met the inclusion criteria. The CKD subset mortality data were extracted in 18 trials, among which there were 1293 deaths in 15 924 participants with CKD. The mean (SD) baseline systolic BP (SBP) was 148 (16) mm Hg in both the more intensive and less intensive arms. The mean SBP dropped by 16 mm Hg to 132 mm Hg in the more intensive arm and by 8 mm Hg to 140 mm Hg in the less intensive arm. More intensive vs less intensive BP control resulted in 14.0% lower risk of all-cause mortality (odds ratio, 0.86; 95% CI, 0.76-0.97; $P = .01$), a finding that was without significant heterogeneity and appeared consistent across multiple subgroups.

CONCLUSIONS AND RELEVANCE Randomization to more intensive BP control is associated with lower mortality risk among trial participants with hypertension and CKD. Further studies are required to define absolute BP targets for maximal benefit and minimal harm.

RATIONALE FOR KIDNEY TRANSPLANT PRACTICE POINT

- No informative RCT evidence for optimal BP target in Kidney Transplant Recipients (KTRs)
- KTRs value graft survival highly, and many would value death with a functioning graft more highly than avoidance of return to dialysis*
- Intensive BP control associated with a (slightly) higher rate of loss of GFR over time in SPRINT and a higher risk of “AKI”
 - Single, denervated kidneys may be at higher risk

* Tong A. Transplantation 2017; 101: 1887-1896

RISK OF PROGRESSION WITH INTENSIVE BPLT



- Intensive BP control causes initial drop in GFR, without increase in tubular injury markers, and with reduction in albuminuria – probably due to altered intrarenal haemodynamics
- However, overall rate of decline in eGFR higher in SPRINT (in both CKD and non-CKD cohorts), ACCORD, SPS
- Difference in rate of decline after initial 6 months in SPRINT: 0.47 vs 0.32 ml/min/1.73m²/year in intensive vs standard: if sustained over 20y, this would cause a 3 ml/min difference

RATIONALE FOR RECOMMENDATION IN CHILDREN

Recommendation 5.1: We suggest that in children with CKD, 24-hour mean arterial pressure (MAP) by ABPM should be lowered to less than or equal to the 50th percentile for age, sex, and height (2C).


- Rests heavily on ESCAPE: probable benefit in slowing progression, and reducing LVH, with no increased risk of adverse events. Children with proteinuria may benefit more; risks may be higher in those with salt-wasting disease

CHALLENGES FOR IMPLEMENTATION



- Conflicts with other national and international guidelines
- Resource implications
 - Standardised office BP measurement, augmented by ABPM and HBPM
 - Costs of intensive BP control
 - Direct costs of drug therapy
 - Indirect costs – e.g. electrolyte monitoring

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FOR MORE INFORMATION



KDIGO CLINICAL PRACTICE GUIDELINE ON THE
MANAGEMENT OF BLOOD PRESSURE IN CKD
(**ND**)



KDIGO Guideline Co-Chairs:
Alfred K. Cheung, MD
Johannes F.E. Mann, MD

- Recorded ISN Webinar

THANK YOU FOR YOUR ATTENTION

