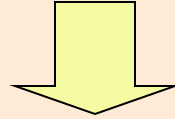


Kan Basıncı Deęişkenlięi Kalp ve Böbreęi Yorarmı?

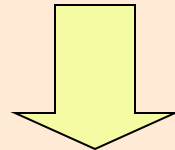
Dr Şükrü Ulusoy
KTU Nefroloji Bilim Dalı

Kan Basıncı Değişkenliği

- KBD nedir, nasıl ölçülür ?
- KBD organ hasarı oluştururmu ?



**KALP VE BÖBREĞİ NASIL ETKİLER ?
MORTALİTEYİ ETKİLERMİ**



- KBD ni değiştirebilirmiyiz ?
- Anti hipertansifler KBD ni nasıl etkiler ?

KB Deęerlendirilmesi

- **Konvansiyonel Deęerlendirme**
- **Ortalama KB**
- **KB insitabilite**
- **Pressure Variability (KB Deęiřkenlięi)**

HT –KVO Risk İlişkisi

**KB düzeyi
Komorbid durumlar**



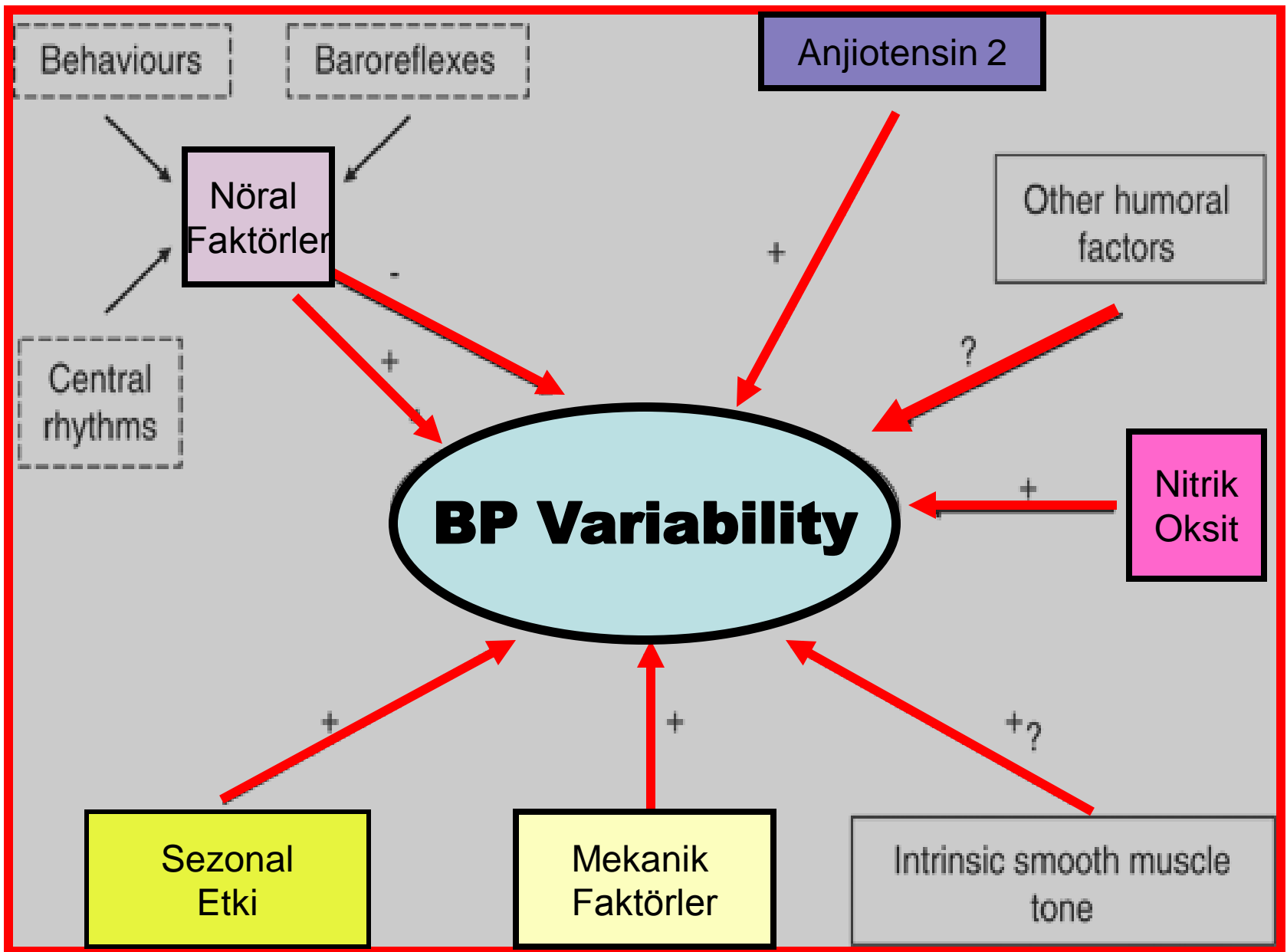
Beklenen yarar yetersiz



KB değerlendirilmesinde yeni kavramlar

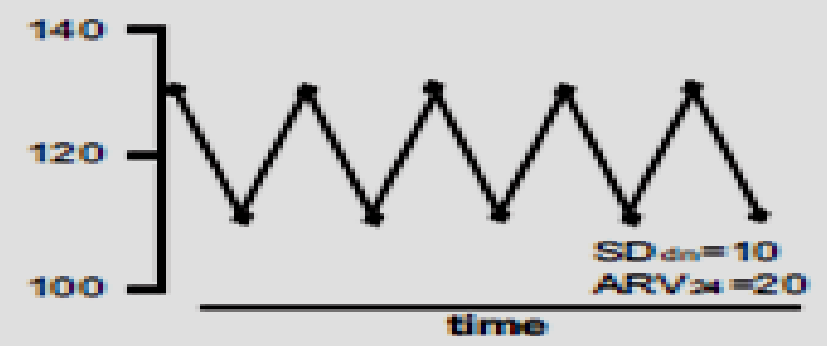
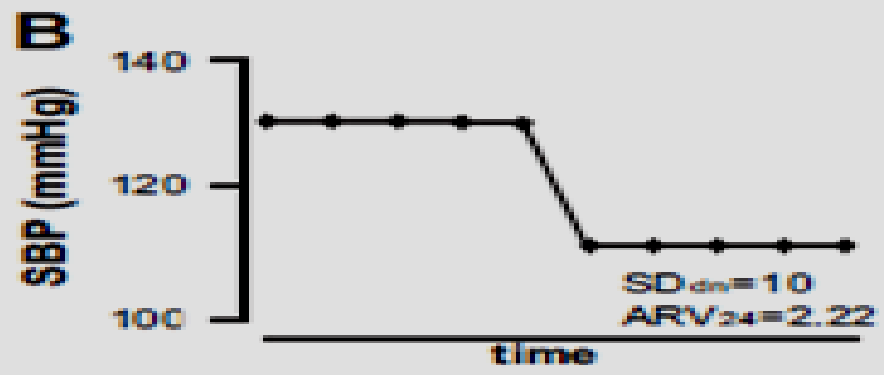
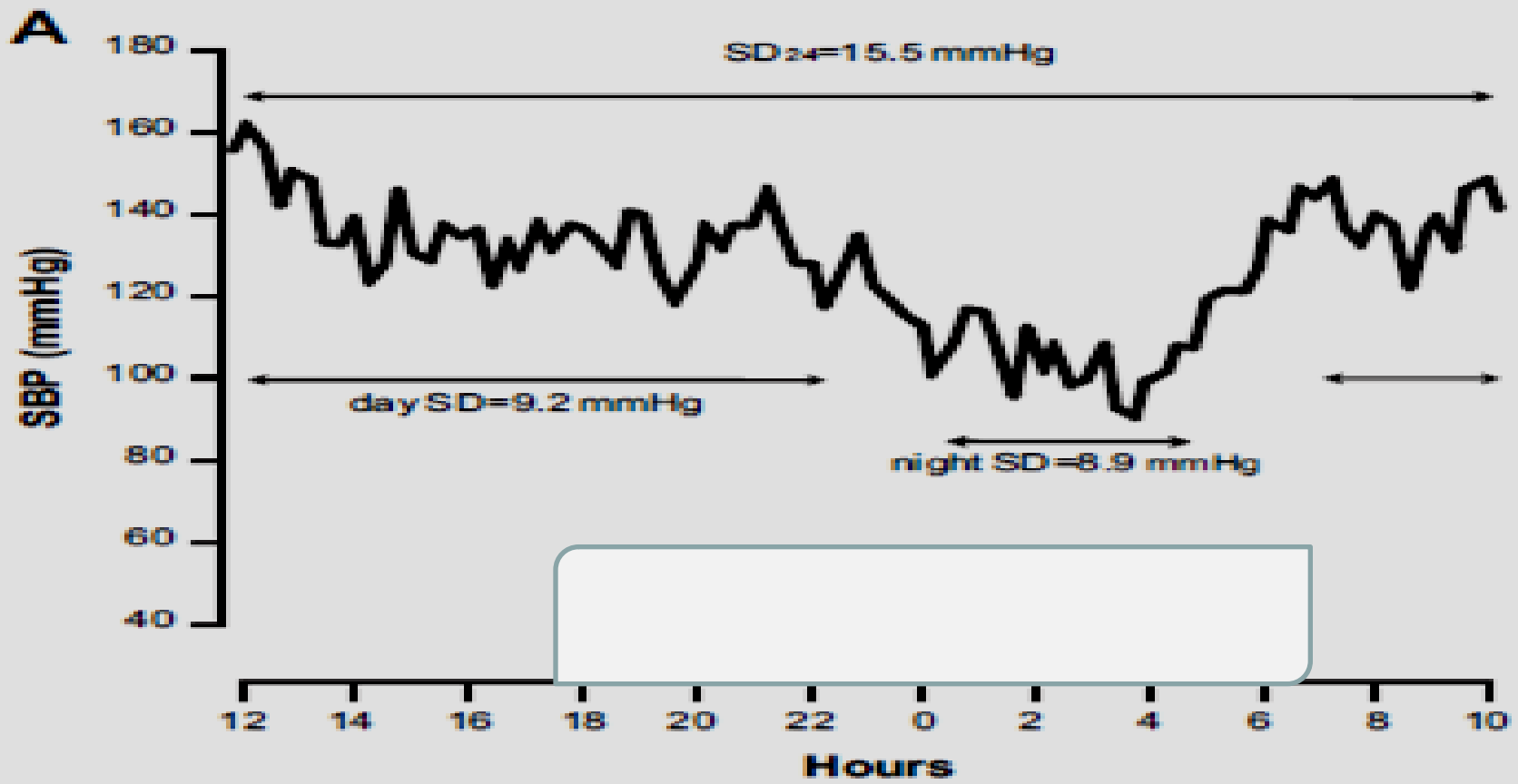
KB deęerlendirilmesi ve KBD

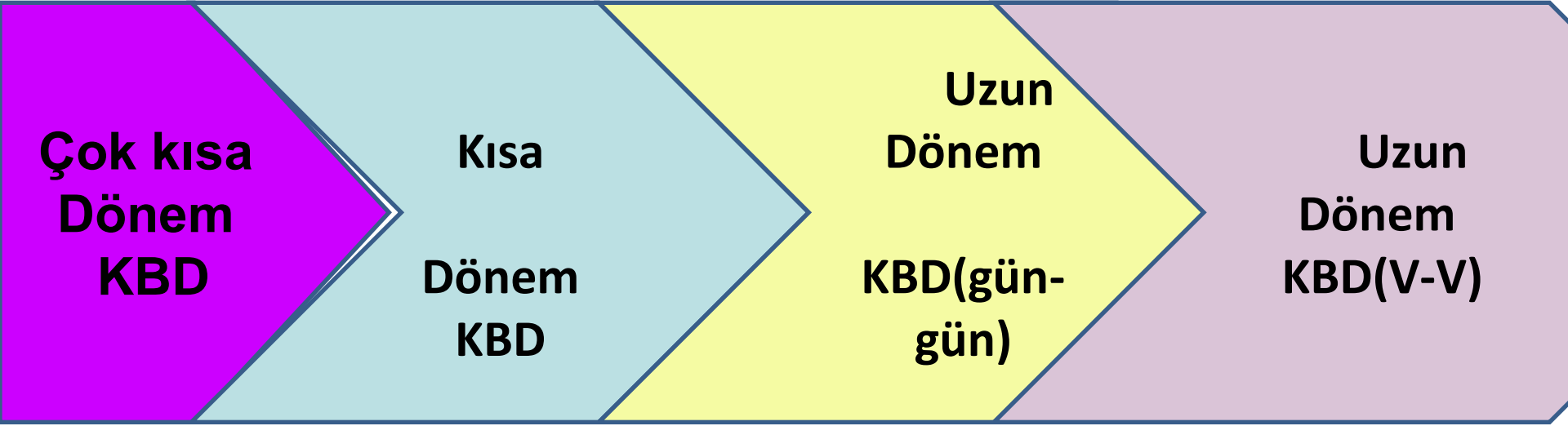
- Zaman ile kan basıncındaki deęişme olup
- Zaman periyodundaki toplam deęişkenlik(SD)
veya
- Zaman için OKB'da deęişim eğilimi(rezidüSD)
- Yakın okumalar arası farkların ortalaması



KBD ÖLÇÜLMESİ

- **SD**
- **SD_d (daytime)**
- **SD_n (nighttime)**
- **SD₂₄ (24 saatlik)**
- **SD_{dn} (daytime nighttime)**
- **ARV**
- **SI**
- **CV (coefficient variation)**
- **Range**
- **SDIM**
- **SV (successive variation)**





KBD'nin klinik önemi

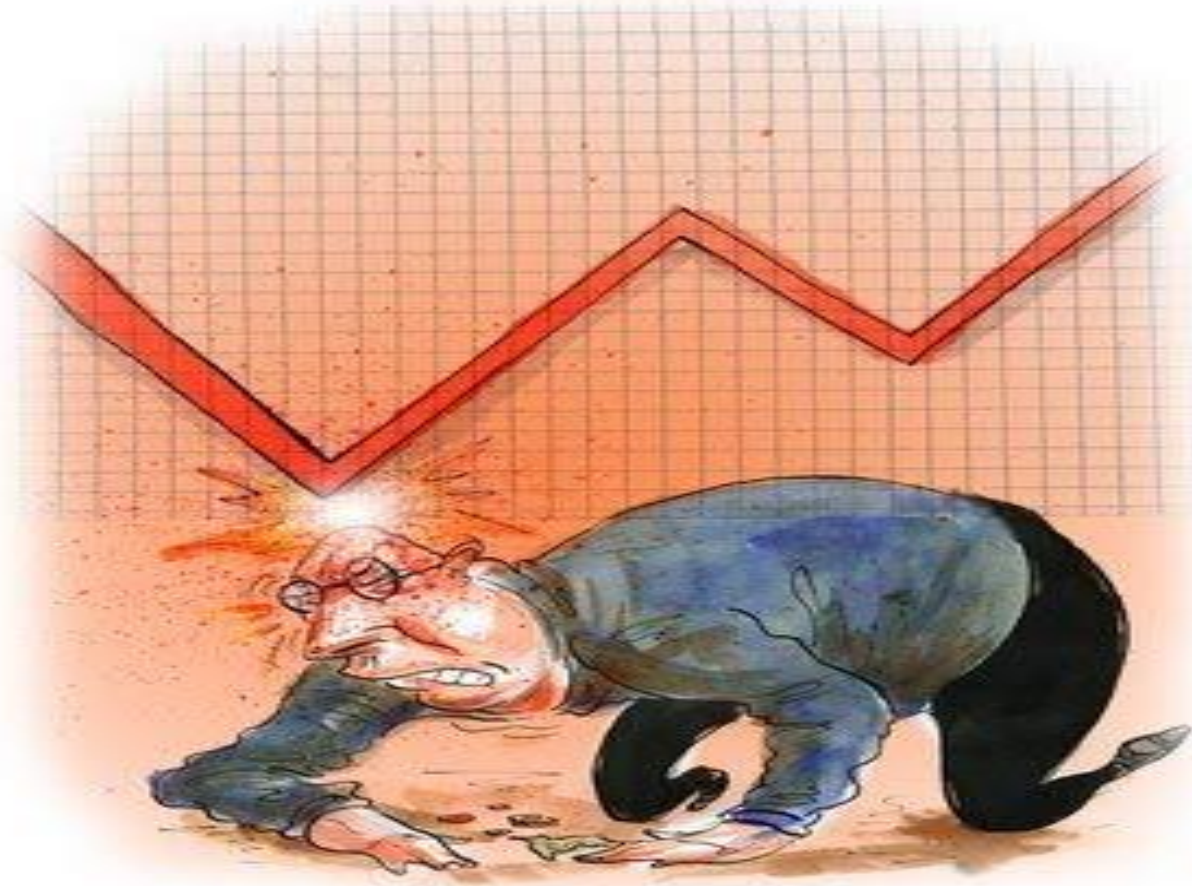
- **KB'nin sağlıklı değerlendirilmesi**
- **Yüksek riskli hastaların belirlenmesi**
- **Risk tahmini**
- **Optimum ilaç seçimi**

TABLE 1: Classification of blood pressure variability and its clinical implication.

Type of BPV	Time range	Measurement equipment or devices	Clinical implications
Ultrashort-term (very low frequency, low frequency and high frequency BPV)	Beat-to-beat variation	Direct continuous intra-arterial recordings coupled to spectral analysis	Estimation of neurohumoral systems involved in blood pressure regulation [8]
Short-term	Minutes-to-hours	Direct continuous intra-arterial recordings, ABPM	Increased variability in daytime, nighttime, and whole 24 h period associated with increased TOD [4]
Long-term	day-to-day, visit-to-visit	Office blood pressure, ABPM, home blood pressure monitoring	Large visit-to-visit BPV independently associated with increased incidence of stroke [9, 10]

ABPM: ambulatory blood pressure measurement; BPV: blood pressure variability.

Risk Faktörü Olarak KBD



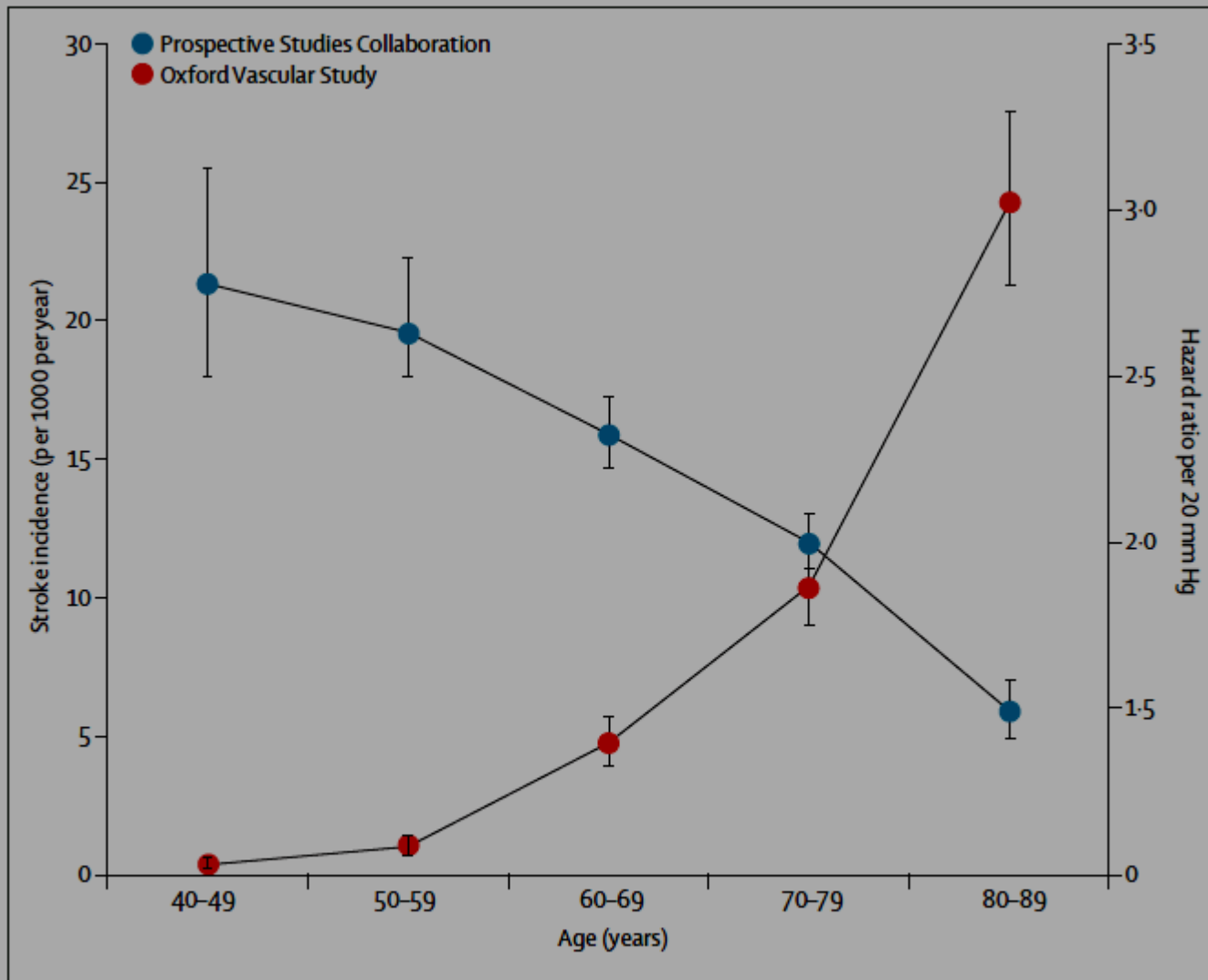
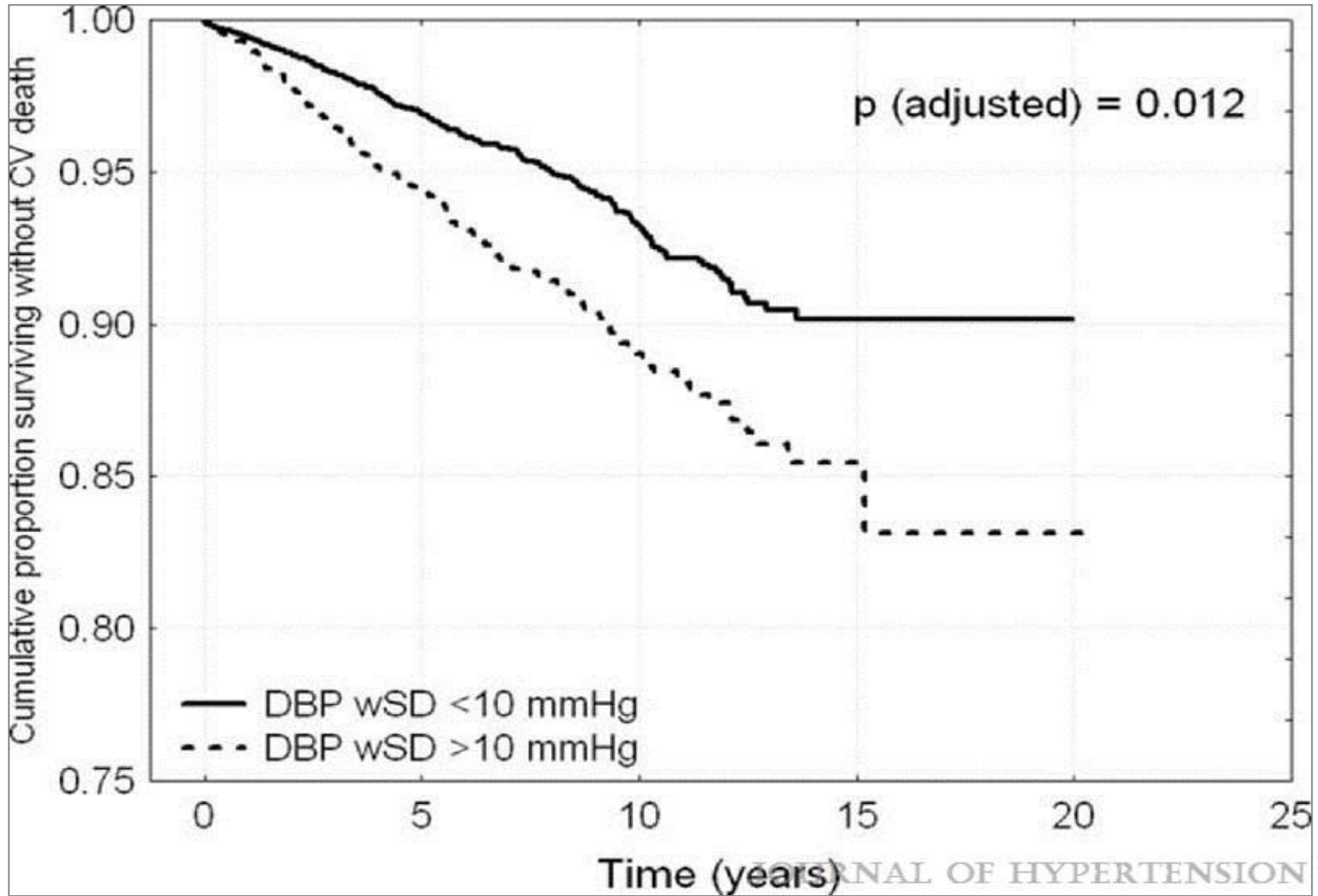


Figure 2: A comparison of age-specific incidence of stroke in the Oxford Vascular Study²⁷ and age-specific association between estimated usual systolic blood pressure and risk of stroke from the Prospective Studies Collaboration⁶

Blood Pressure Variability As A Predictor of Cardiovascular Mortality: Results of Dublin Outcome Study: 4B.01

Bilo, G; Dolan, E; o'Brien, E; Parati, G Journal of Hypertension. 28():e209, June 2010.



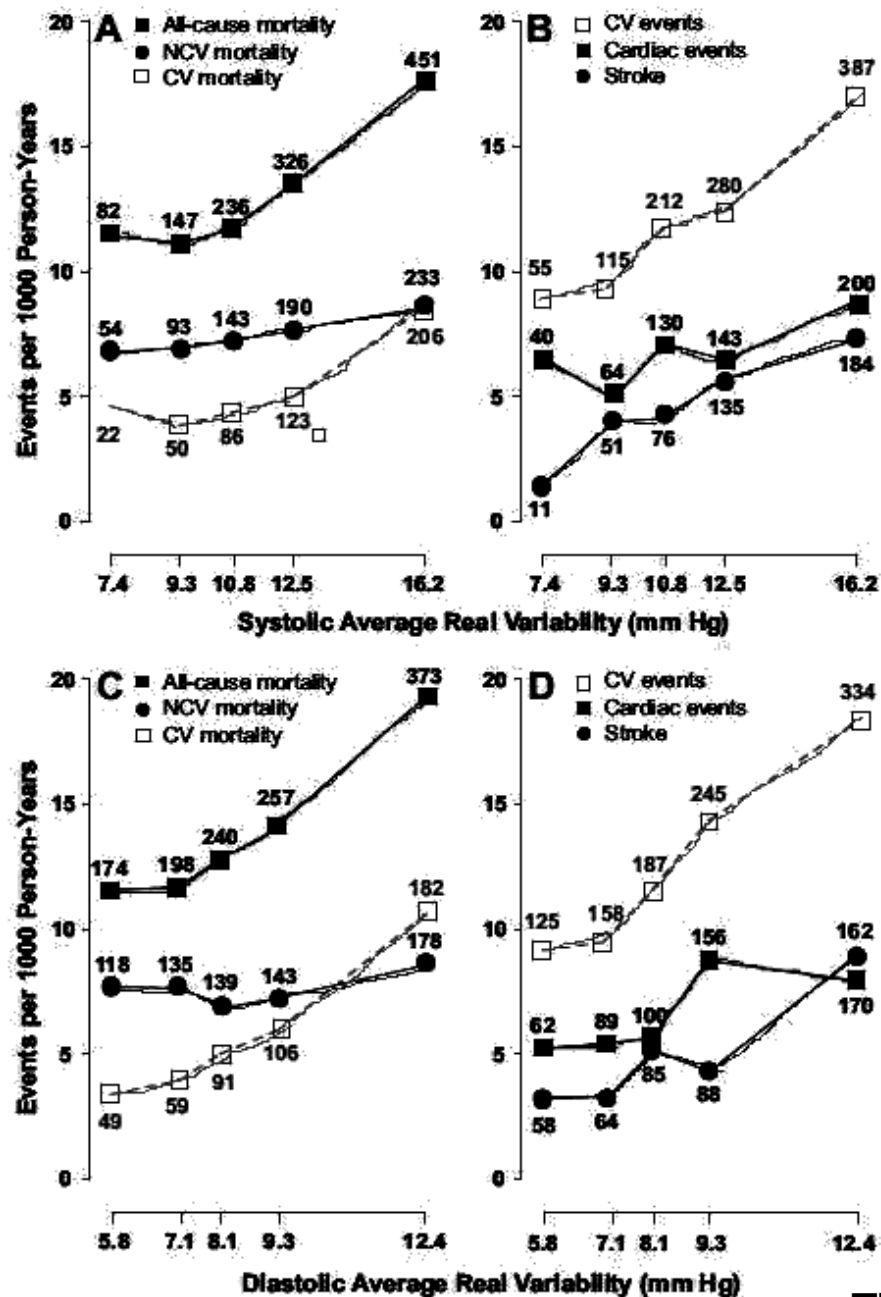


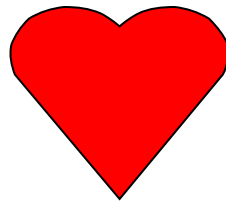
Figure 2. Incidence of mortality (A and C) and cardiovascular events (B and D) by fifths of the distributions of the systolic (A and B) and diastolic (C and D) average real variability in 8938 participants. Incidence rates were standardized for cohort, sex, and age by the direct method. The number of events contributing to the rates is presented. CV and NCV indicate cardiovascular and noncardiovascular, respectively.

Maximum home blood pressure: a novel indicator of target-organ damage in hypertension

- Blood pressure variability has recently been shown to be a strong predictor of stroke and cardiovascular events, independently of the mean systolic blood pressure level.¹
- The clinical implication of variability in blood pressure, as measured by home blood pressure monitoring, has never been reported.
- A new study has investigated the association between maximum home blood pressure and target-organ damage in 356 never-treated hypertensive subjects.

TABLE 4: Short-term blood pressure variability and target organ damage and cardiovascular events in patients.

Study	Study population	Blood pressure variability index	Outcome
Parati et al. [24]	Hospitalized subjects with essential hypertension	24 h BPV	Increase rate and severity of TOD
Palatini et al. [26]	Patients with mild to severe hypertension	Daytime systolic BPV	Higher degree of retinal abnormalities
Mancia et al. [27]	Hypertensive patients	24 h systolic BPV	Increase in carotid intima-media thickness
Sega et al. [28]	General population	Overall and residual short-term BPV	Left ventricular mass index
Sander et al. [29]	General population	Daytime systolic BPV	Progression of intima-media wall thickness
McMullan et al. [30]	Patient with chronic kidney disease	Systolic BPV	Increased overall and cardiovascular mortality
Kawai et al. [31]	Hypertensive patients	Daytime systolic BPV Nighttime systolic BPV	Increased renal vascular resistance
Iwata et al. [32]	Hypertensive patients	Nighttime systolic BPV	Increased intima-media thickness and plaque score
Schillaci et al. [33]	Hypertensive patients	24 h BPV	Large arch plaque
Cay et al. [34]	Normotensive patients	Systolic and diastolic 24 h BPV	Aortic stiffness
Schutte et al. [35]	Normotensive Africans	24 h systolic BPV	Higher risk of restenosis after percutaneous coronary intervention
Ozawa et al. [36]	Patients with type 2 diabetes	Nighttime systolic and diastolic BPV	Left ventricular hypertrophy
Sakakura et al. [37]	Elderly patients	Daytime systolic BPV	Increased risk of incident cardiovascular disease
			Cognitive dysfunction and reduction in quality of life



Nephrol Dial Transplant (2012) 27: 4404–4410

doi: 10.1093/ndt/gfs328

Advance Access publication 7 September 2012

Blood pressure variability and outcomes in chronic kidney disease

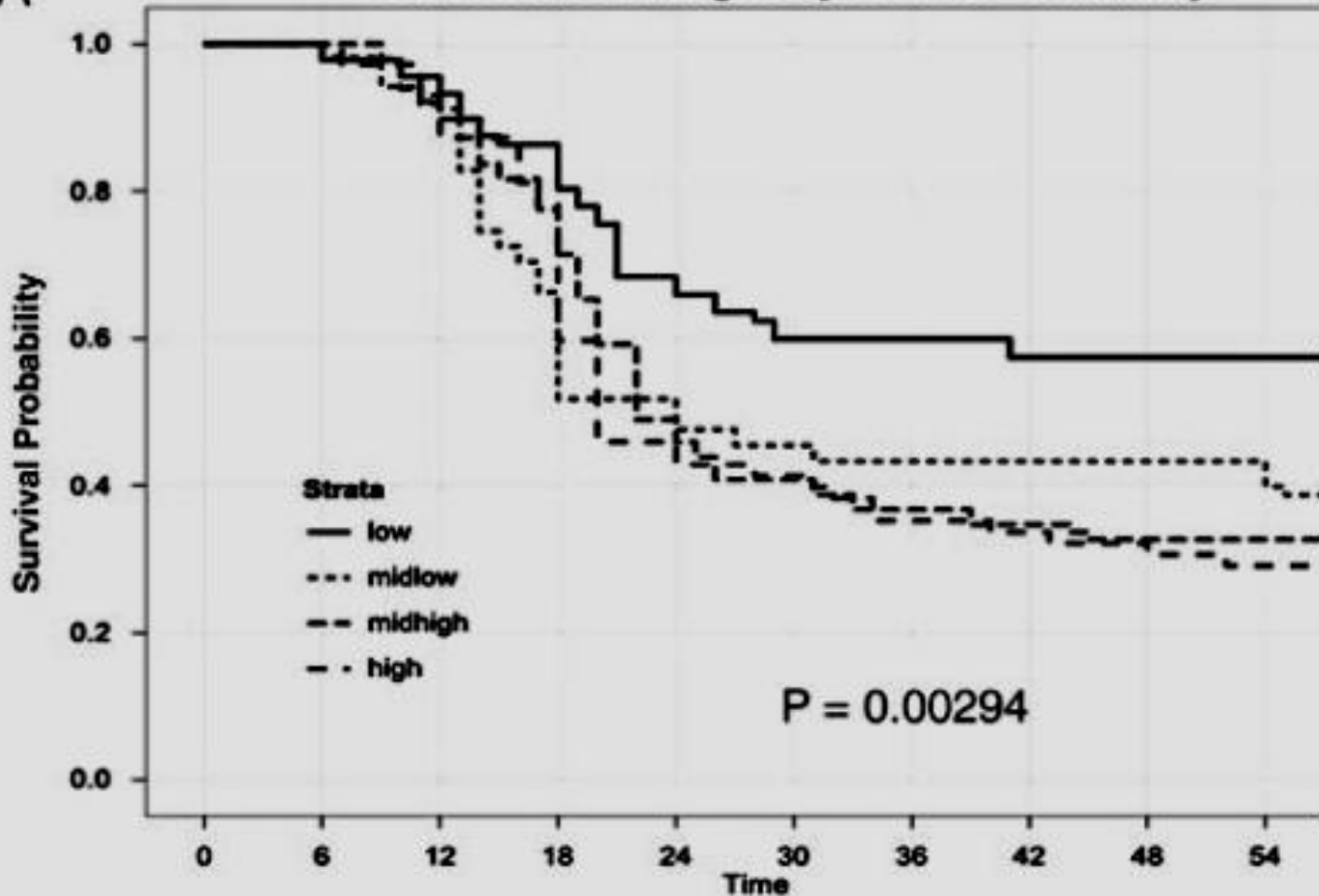
Biagio Di Iorio¹, Andrea Pota¹, Maria Luisa Sirico¹, Serena Torraca¹, Lucia Di Micco¹,
Roberto Rubino², Pasquale Guastaferrro³ and Antonio Bellasi⁴

¹Nephrology of Landolfi Hospital, Solofra AV, Italy, ²Nephrology of Sant'Ottone Hospital, Ariano, AV, Italy, ³Nephrology of Di
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Ospedaliera Sant'Anna, Como, Italy

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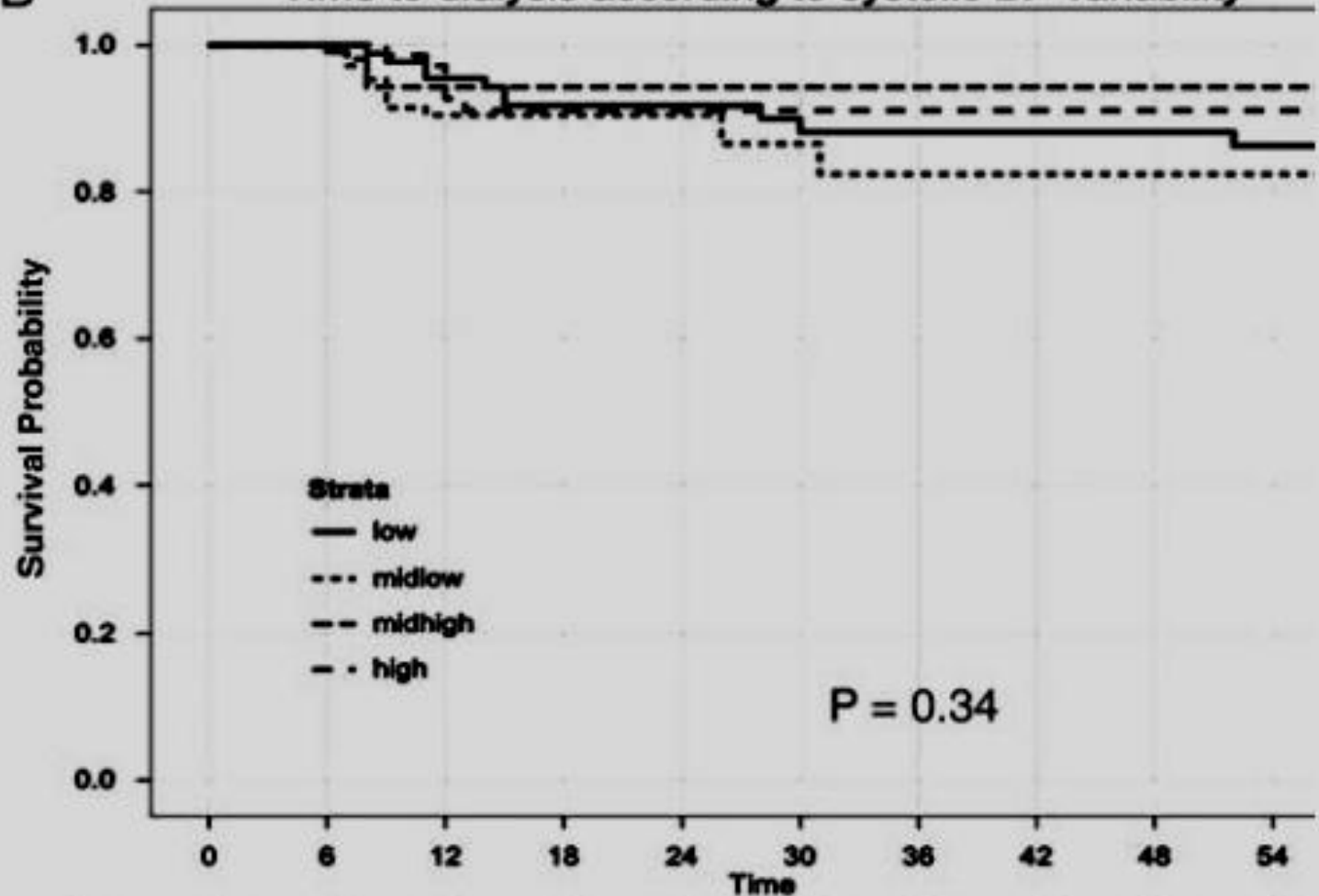
A

Survival according to systolic BP variability



	0	6	12	18	24	30	36	42	48	54
low	91	91	83	72	57	49	48	46	46	45
midlow	107	107	89	64	50	42	38	38	38	38
midhigh	104	104	90	76	48	40	36	34	32	32
high	72	72	65	51	30	27	23	22	21	19

Numbers at risk

B**Time to dialysis according to systolic BP variability**

	0	6	12	18	24	30	36	42	48	54
low	91	91	83	72	57	49	48	46	46	45
midlow	107	107	89	64	50	42	38	38	38	38
midhigh	104	104	90	76	48	40	36	34	32	32
high	72	72	65	51	30	27	23	22	21	19

Numbers at risk

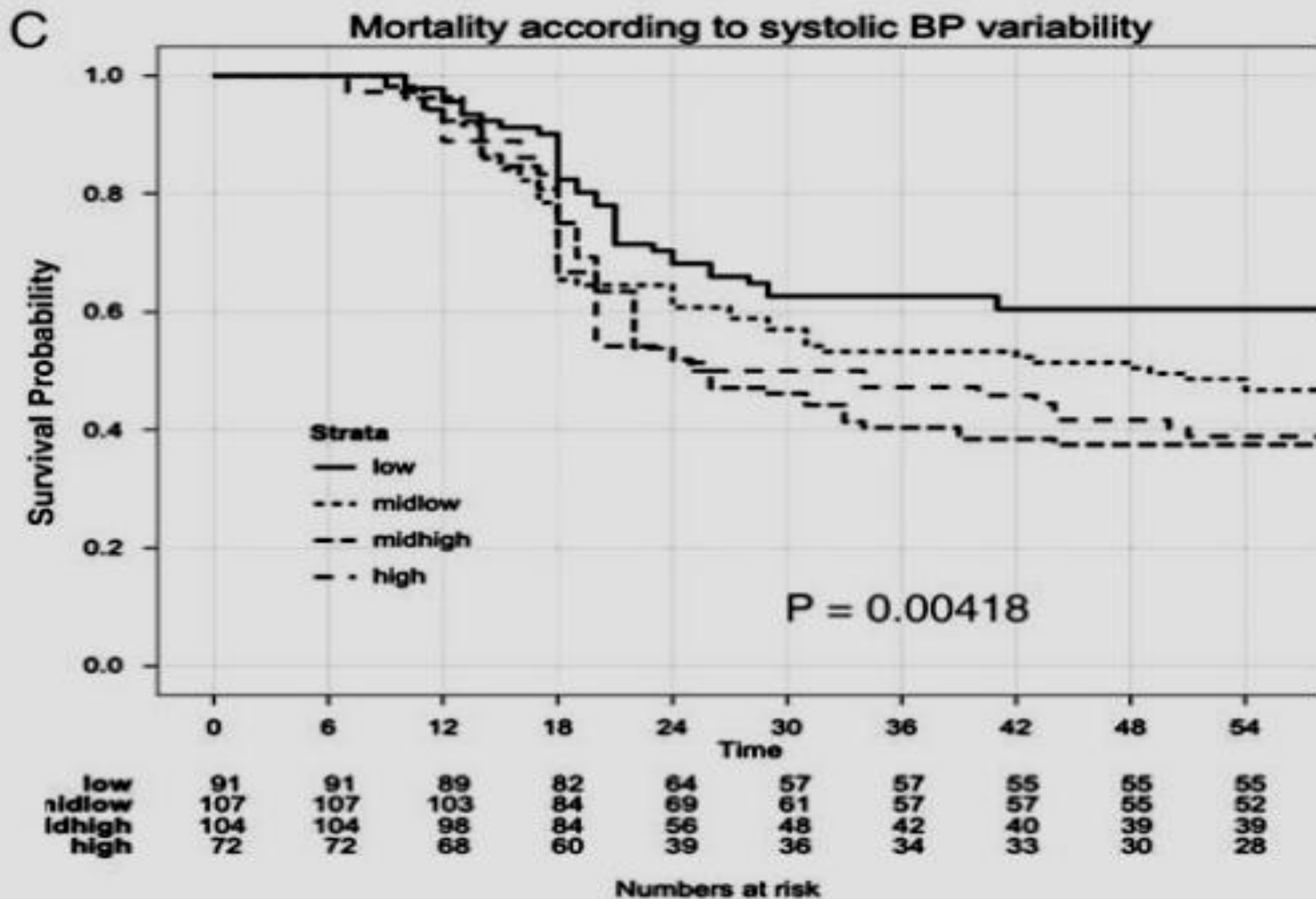


Fig. 1. Time-to-death (A), dialysis (B) and death even after dialysis (carry-over effect) initiation (C) according to the systolic BPV.

Association of BP Variability with Mortality among African Americans with CKD

Ciaran J. McMullan,^{*†} George L. Bakris,[‡] Robert A. Phillips,[§] and John P. Forman^{*†}

Summary

Background and objectives Increased systolic BP visit-to-visit variability (SBV) may be associated with higher overall mortality and cardiovascular events. However, few studies have examined these associations in patients with CKD, and the relation of SBV with CKD progression and ESRD has not been shown. This study analyzed the association of SBV with overall mortality, cardiovascular mortality, cardiovascular events, and renal events among individuals enrolled in the African American Study of Kidney Disease (AASK) trial.

Design, setting, participants, & measurements This was a prospective observational study of 908 participants during the trial phase of the AASK study, with at least 1 year of BP measurements available and followed for 3–6.4 years. SBV was calculated as the SD of the systolic pressure from five visits occurring 3–12 months after randomization. The association of SBV with risk of overall mortality, cardiovascular mortality, a composite of fatal and nonfatal cardiovascular events, and a composite of renal events was assessed using proportional hazards regression and adjusting for multiple potential confounders.

Results Greater SBV was associated with higher overall mortality. The adjusted hazard ratio (95% confidence interval) was 2.82 (1.14–6.95) comparing the highest with lowest tertile of SBV. A similar comparison revealed that greater SBV was also associated with cardiovascular mortality (adjusted hazard ratio, 4.91; 1.12–21.50). SBV was associated with both the cardiovascular renal composite endpoints in unadjusted but not adjusted analyses.

Conclusions In African Americans with CKD, SBV is strongly and independently associated with overall and cardiovascular mortality.

Clin J Am Soc Nephrol 8: 731–738, 2013. doi: 10.2215/CJN.10131012

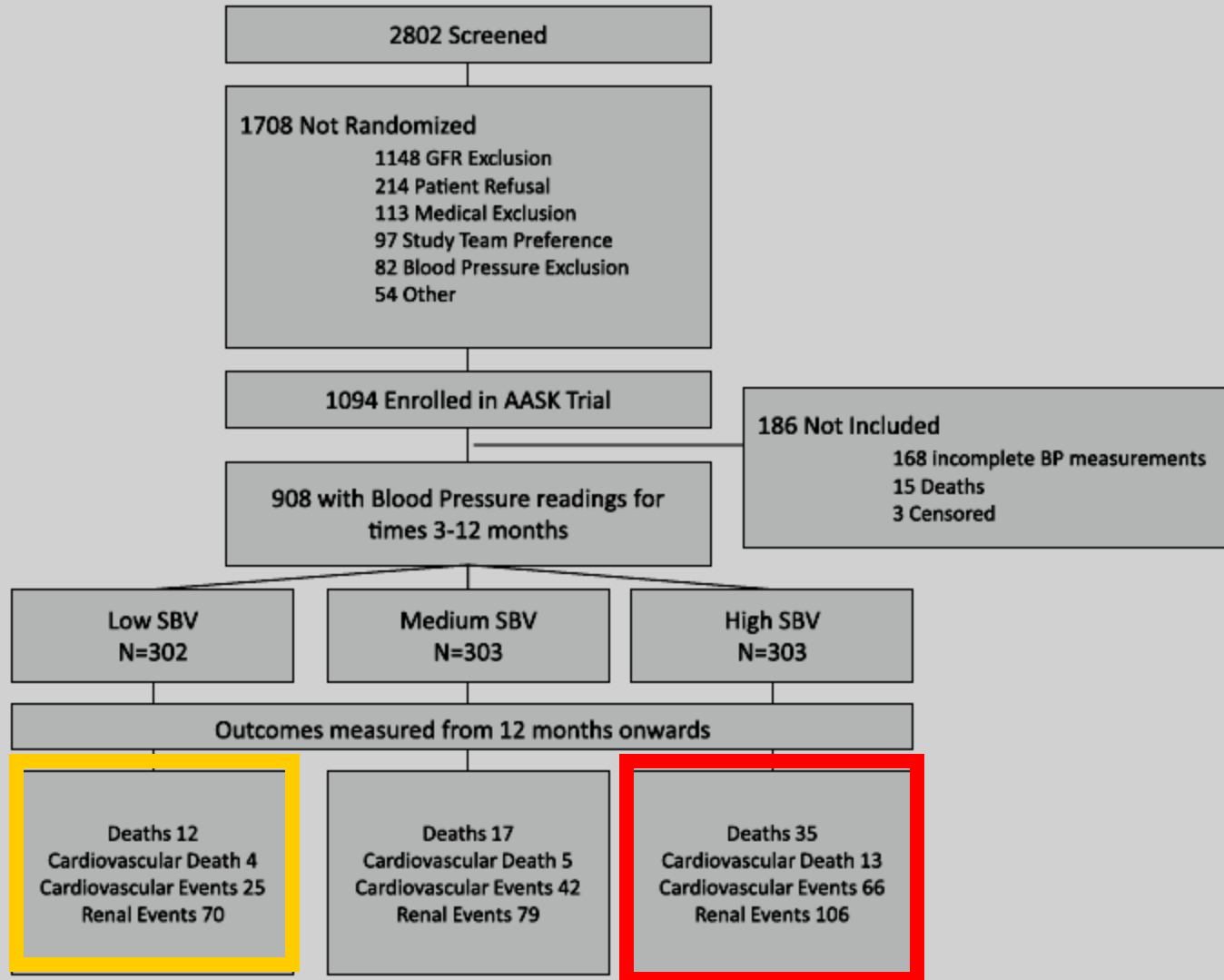
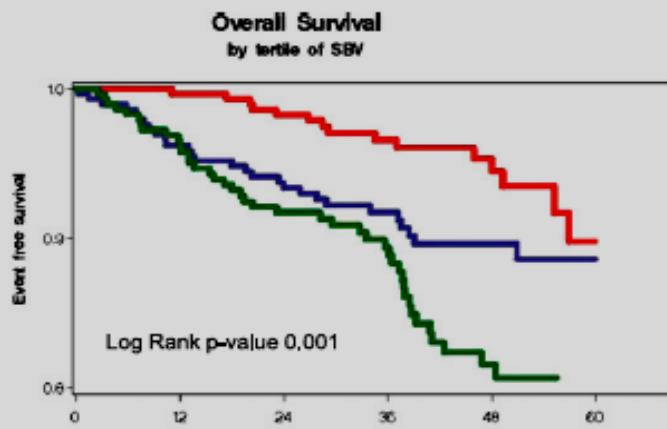
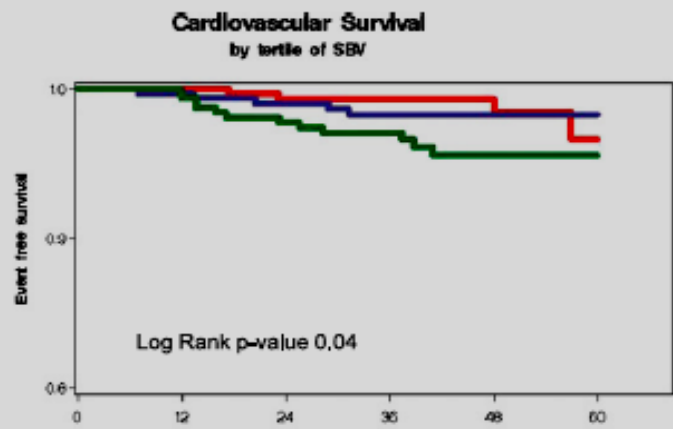


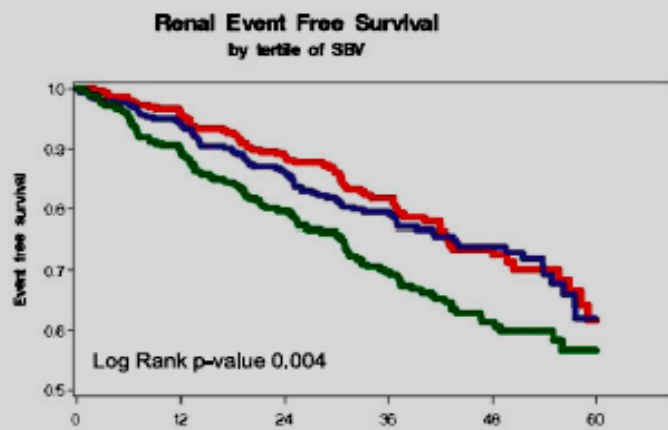
Figure 1. | Derivation of the study population and tertiles of SBV. AASK, African American Study of Kidney Disease trial; SBV, systolic BP variability.



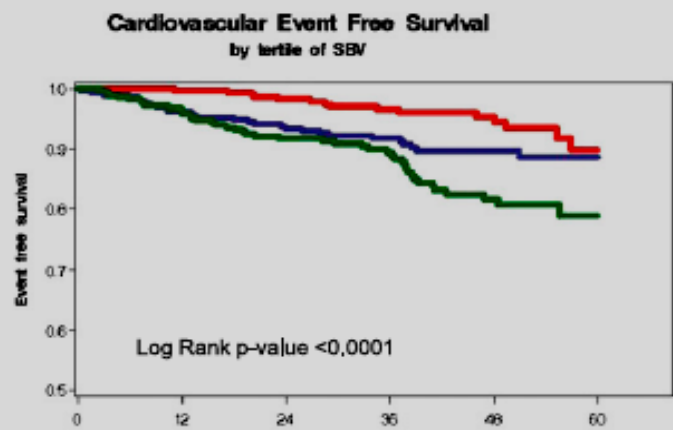
Number at Risk	0	12	24	36	48	60
Low SBV	297	289	280	191	107	29
Moderate SBV	297	275	259	193	112	24
High SBV	294	266	240	159	95	27



Number at Risk	0	12	24	36	48	60
Low SBV	302	311	295	201	111	35
Moderate SBV	306	311	297	212	125	29
High SBV	304	314	299	222	125	35



Number at Risk	0	12	24	36	48	60
Low SBV	301	299	246	156	79	30
Moderate SBV	302	294	252	176	99	22
High SBV	295	265	232	155	89	22



Number at Risk	0	12	24	36	48	60
Low SBV	297	289	280	191	107	29
Moderate SBV	297	275	259	193	112	24
High SBV	294	266	240	159	95	27

Figure 2. | Event-free survival for each tertile of SBV. SBV, systolic BP variability.

Visit-to-Visit Variability of Blood Pressure and Renal Function Decline in Patients With Diabetic Chronic Kidney Disease

Kei Yokota, MD;^{1,2,3} Masamichi Fukuda, MD, PhD;² Yoshio Matsui, MD, PhD;⁴ Kazuomi Kario, MD, PhD;¹ Kenjiro Kimura, MD, PhD³

From the Division of Cardiovascular Medicine, Department of Medicine, School of Medicine, Jichi Medical University, Tochigi;¹ Department of Nephrology, Iwakuni Medical Center, Yamaguchi;² Department of Nephrology and Hypertension, School of Medicine, St. Marianna University, Kanagawa;³ and Department of Internal Medicine, Iwakuni Medical Center, Yamaguchi, Japan⁴

The authors previously reported that the visit-to-visit variability of blood pressure is correlated with renal function decline in nondiabetic chronic kidney disease. Little is known about the association between visit-to-visit variability and renal function decline in patients with diabetic chronic kidney disease. The authors retrospectively studied 69 patients with diabetic chronic kidney disease stage 3a, 3b, or 4. The standard deviation and coefficient of variation of blood pressure in 12 consecutive visits were defined as visit-to-visit variability of blood pressure. The median observation

period was 32 months. In univariate correlation, the standard deviation and coefficient of variation of blood pressure were not significantly associated with the slope of estimated glomerular filtration rate. There was no significant association between the visit-to-visit variability of blood pressure and renal function decline in patients with diabetic chronic kidney disease, in contrast with our previous study of nondiabetic patients with chronic kidney disease. *J Clin Hypertens (Greenwich)*. 2014;16:362–366. ©2014 Wiley Periodicals, Inc.

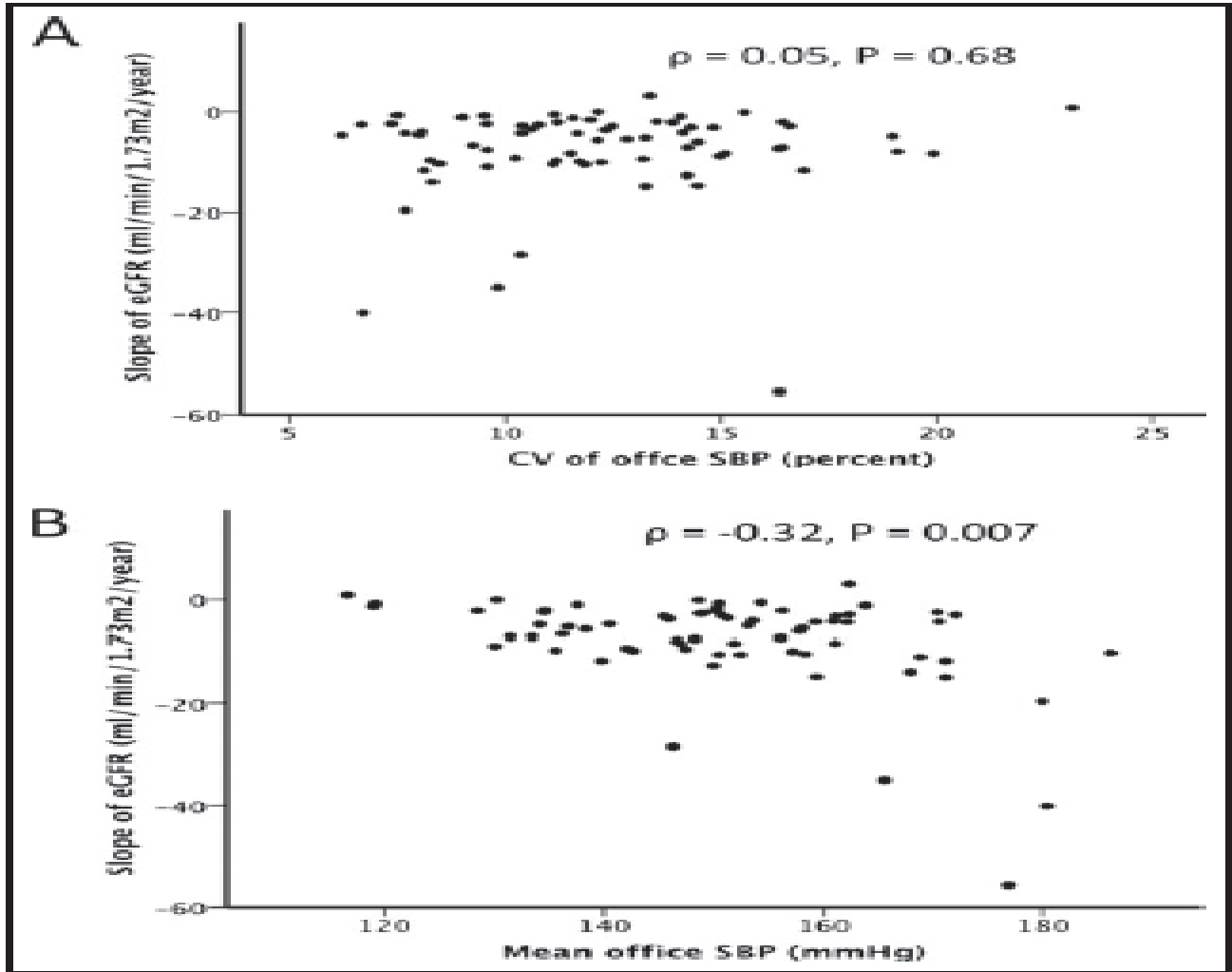


FIGURE. Simple correlations between the slope of the estimated glomerular filtration rate (eGFR) and coefficient of variation (CV) of office systolic blood pressure (SBP) (A), and mean office SBP (B) in patients with diabetic chronic kidney disease (CKD) (n=69).

Association of home blood pressure variability with progression of chronic kidney disease

Tomonari Okada, Hiroshi Matsumoto, Yume Nagaoka and Toshiyuki Nakao

Objective Home blood pressure (HBP) has been found to be a predictor of the progression of chronic kidney disease (CKD). The objective of this study is to clarify the clinical significance of day-by-day HBP variability on the progression of CKD.

Methods We recruited 135 patients with stage 3–5 CKD, who performed daily HBP measurements, every morning and evening over 7 consecutive days and recorded every 6 months, with a follow-up of 36 months. We examined the associations between the variables of blood pressure (BP) variability [SD, coefficient of variation (CV), average real variability (ARV)], and renal outcomes.

Results No significant correlations were found between the SD values, the CV values, the ARV values of each BP measurement, and the change in estimated glomerular filtration rate on multivariate regression analysis (β of SD, CV, and ARV of morning systolic BP: 0.04, 0.04, and 0.02; $P=0.69$, 0.63, and 0.20, respectively). None of these variables of each BP measurement showed a significant

risk of renal events on multivariate Cox proportional hazards analysis (hazard ratios of SD, CV, and ARV of morning systolic BP: 0.99 (95% confidence intervals: 0.80–1.23), 0.97 (0.72–1.31), and 1.01 (0.83–1.24); $P=0.94$, 0.86, and 0.92, respectively).

Conclusion Day-by-day BP variability as assessed by HBP measurements had no significant association with the progression of CKD. *Blood Press Monit* 17:1–7 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Blood Pressure Monitoring 2012, 17:1–7

Keywords: blood pressure variability, chronic kidney disease, home blood pressure measurement

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Visit-to-Visit Blood Pressure Variability Is a Strong Predictor of Cardiovascular Events in Hemodialysis: Insights From FOSIDIAL

Patrick Rossignol, Joelle Cridlig, Philippe Lehert, Michèle Kessler and Faiez Zannad

Hypertension. 2012;60:339-346; originally published online July 9, 2012;

doi: 10.1161/HYPERTENSIONAHA.111.190397

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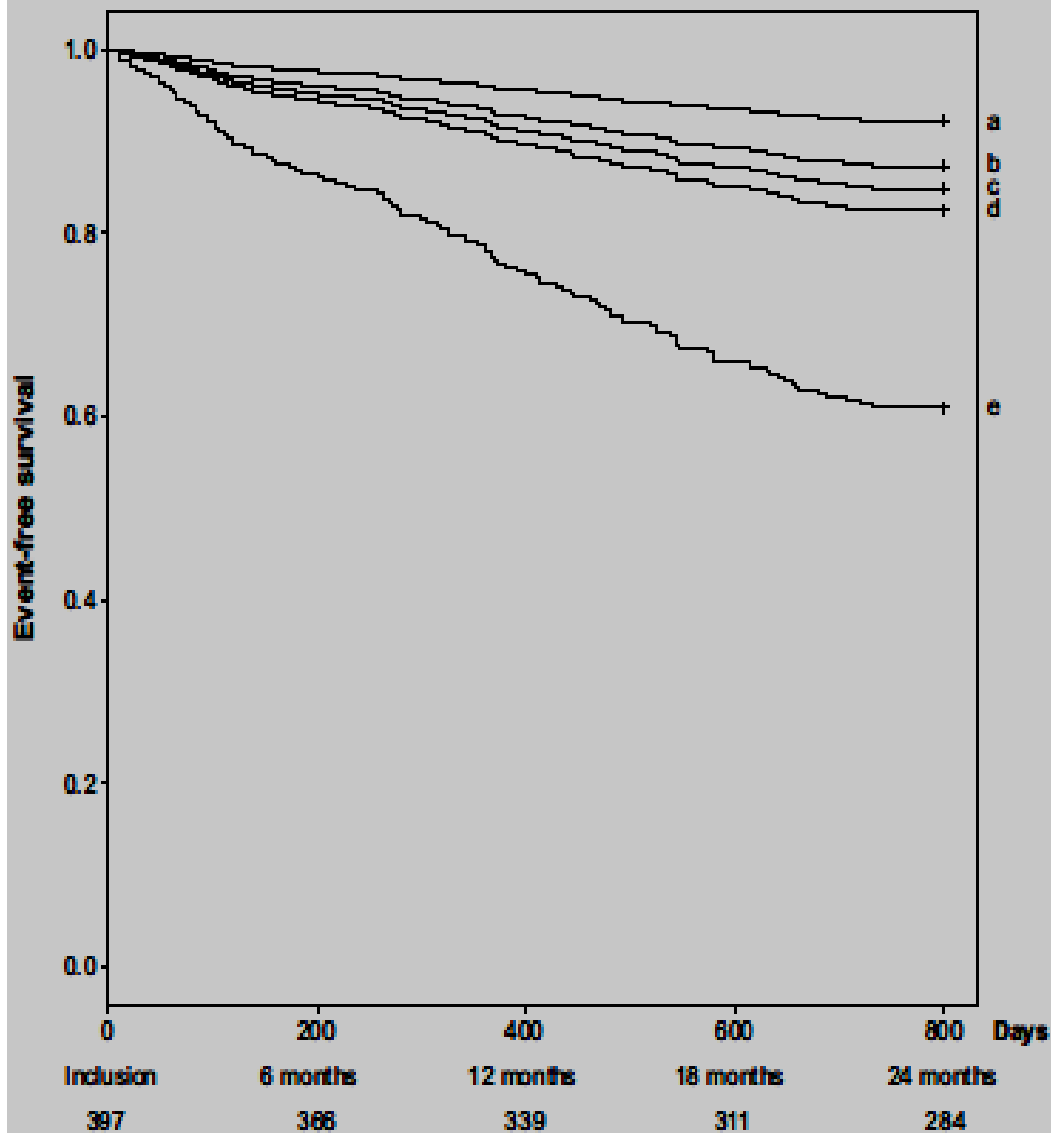


Figure. Cox prediction of cardiovascular events for (a) patients with no previous cardiovascular comorbidities; (b) patients with coronary artery disease only; (c) patients with peripheral arterial disease only; (d) patients with CVSBP=12% and no cardiovascular comorbidity; and (e) patients with CVSBP=25% and no cardiovascular comorbidity. CVSBP indicates coefficient of variation of within-patient overall variability of systolic blood pressure.

**Visit-to-visit KBD Diabetik Hastada
mikroalbumürinin bağımsız bir risk
faktörüdür**

Sistolik KBD 'i mikroalbuminüri gelişiminin belirtecidir

	Hazard ratio* (95% CI)	P value
Systolic blood pressure (mm Hg)		
SD	2.40 (1.07, 5.38)	0.033
CV	2.06 (0.95, 4.48)	0.067
Mean	1.61 (1.01, 2.57)	0.035
Peak	2.76 (1.10, 6.92)	0.023
Diastolic blood pressure (mm Hg)		
SD	1.65 (0.71, 3.83)	0.247
CV	1.35 (0.64, 2.83)	0.424
Mean	1.13 (0.41, 3.11)	0.787
Peak	1.24 (0.60, 2.53)	0.560

(SD = standard deviation; CV = coefficient of variation)

* Adjusted for age, sex, duration of diabetes, number of visits, mean pressure, baseline HbA1c, and baseline eGFR)

Systolic BP variability significantly correlated with albuminuria variability

Urinary albumin excretion variability (mg per 24 h)						
SDIM		Mean		Peak		
β^a	P value	β	P value	β	P value	
<i>Univariate models—SBP variability (mm Hg)</i>						
SDIM	0.104	0.093	0.322	<0.001	0.297	<0.001

(SBP = systolic blood pressure; SDIM = standard deviation independent of mean.)

^a Standardized β -coefficient.

^b Multivariate models are adjusted for age, sex, duration of diabetes, number of visits, mean systolic pressure, baseline HbA1c and baseline eGFR.)

TABLE 5: Long-term blood pressure variability and target organ damage and cardiovascular events in patients.

Study	Study population	Blood pressure variability index	Outcome
Kikuya et al. [50]	General population	Day-to-day systolic BPV	Increased hazard ratios for cardiovascular and stroke mortality 
Muntner et al. [51]	General population	Visit-to-visit systolic BPV	Increased all-cause mortality
Johansson et al. [52]	General population	Day-to-day morning systolic BPV	Increased rate of cardiovascular events 
Hsieh et al. [53]	Patients with type 2 diabetes	Visit-to-visit systolic and diastolic BPV	Increased all-cause mortality
Ushigome et al. [54]	Patients with type 2 diabetes	Day-to-day systolic and diastolic BPV	Development of macroalbuminuria 
Kilpatrick et al. [55]	Patients with type 1 diabetes	Annual visit-to-visit BPV	Development or progression of nephropathy 
Di Iorio et al. [56]	Subjects with chronic renal failure	Visit-to-visit systolic BPV	Elevated risk of death 
Yokota et al. [57]	Patients with nondiabetic chronic kidney disease	Visit-to-visit systolic BPV	Deterioration of renal function 
Di Iorio et al. [58]	Patients with end stage renal disease under hemodialysis	Dialysis-to-dialysis BPV	Increased cardiovascular mortality 

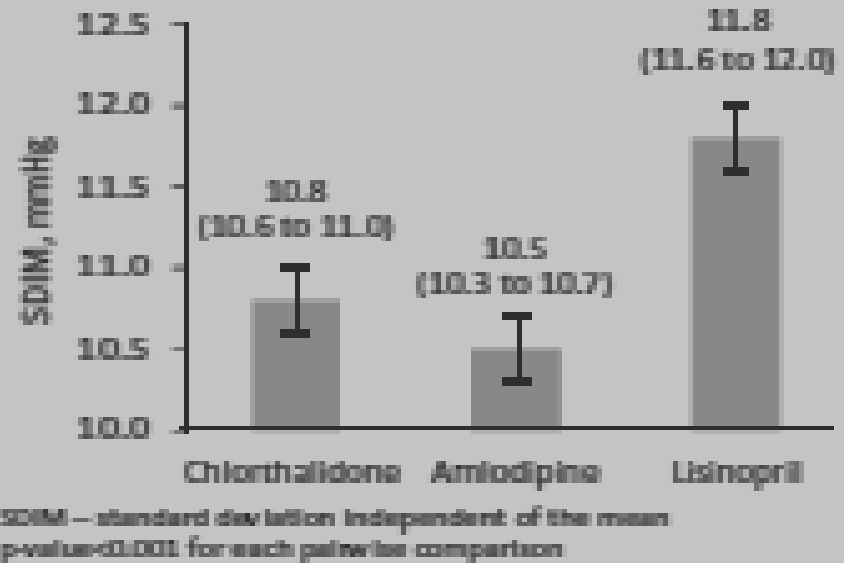
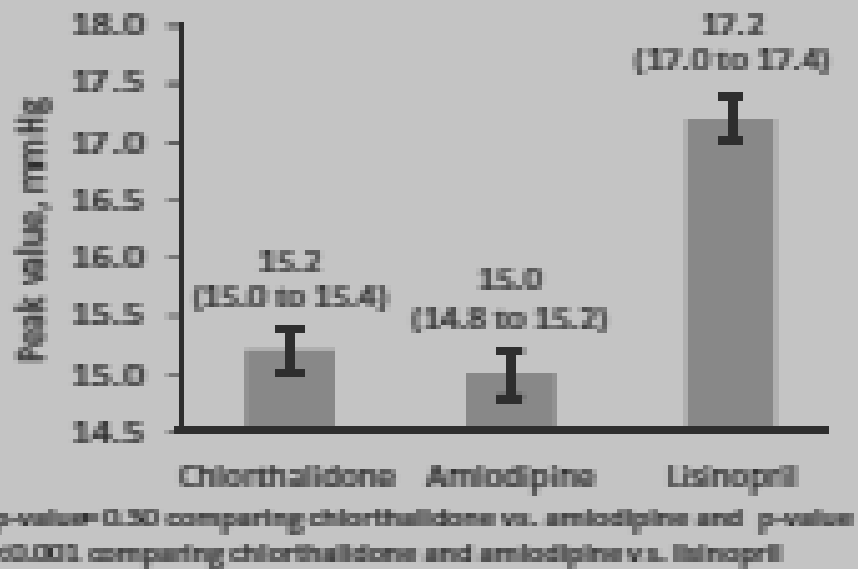
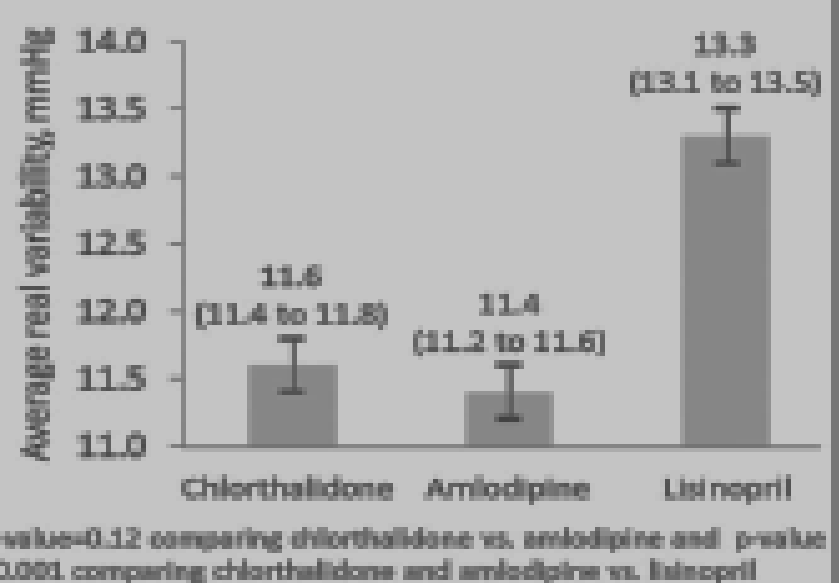
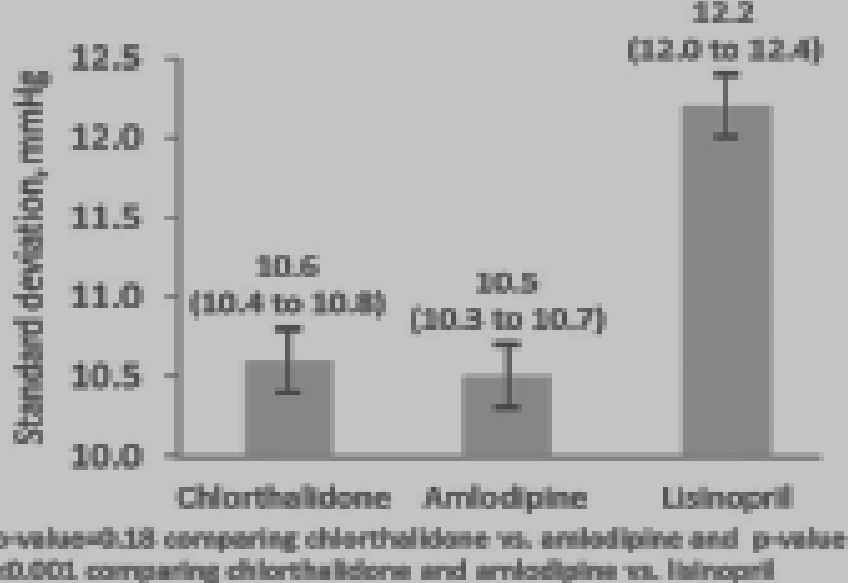
- **KBD'ni deęiřtirebilir miyiz?**
- **Antihipertansifler KBD 'ni nasıl etkiler?**

ALLHAT ve KBD Açısından Bakış

	Treatment group			p value for difference in SD SBP	
	Amlodipine	Chlorthalidone	Lisinopril	Amlodipine vs lisinopril	Chlorthalidone vs lisinopril
Baseline	146.2 (15.7)	146.2 (15.7)	146.4 (15.7)	0.5	0.5
1-year follow up	138.5 (14.9)	136.9 (15.8)	140.0 (18.5)	9×10^{-79}	7×10^{-55}
2-year follow up	137.1 (15.0)	135.9 (15.9)	138.4 (17.9)	3×10^{-48}	1×10^{-28}
3-year follow up	135.6 (15.2)	134.8 (15.4)	136.7 (17.3)	9×10^{-25}	2×10^{-25}
4-year follow up	134.8 (15.0)	133.9 (15.7)	135.5 (17.2)	1×10^{-24}	2×10^{-14}
5-year follow up	134.7 (14.9)	133.9 (15.2)	135.9 (17.9)	1×10^{-24}	8×10^{-25}

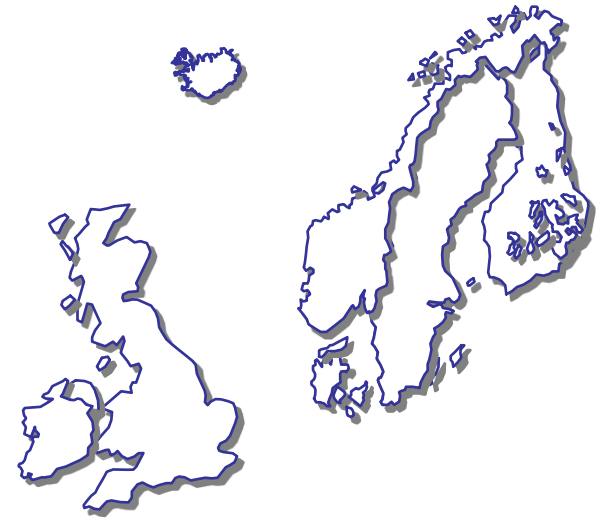
Data are mean (SD). p values for differences between treatment groups in inter-individual variation in systolic blood pressure (SBP; ie, SD SBP) are shown for every follow-up visit.

Table 2: Mean (SD) SBP at baseline and during follow-up in the ALLHAT trial,⁷⁴ stratified by randomised treatment group



Numbers are mean (95% confidence interval)

Anglo-Scandinavian
ascot
Cardiac Outcomes Trial

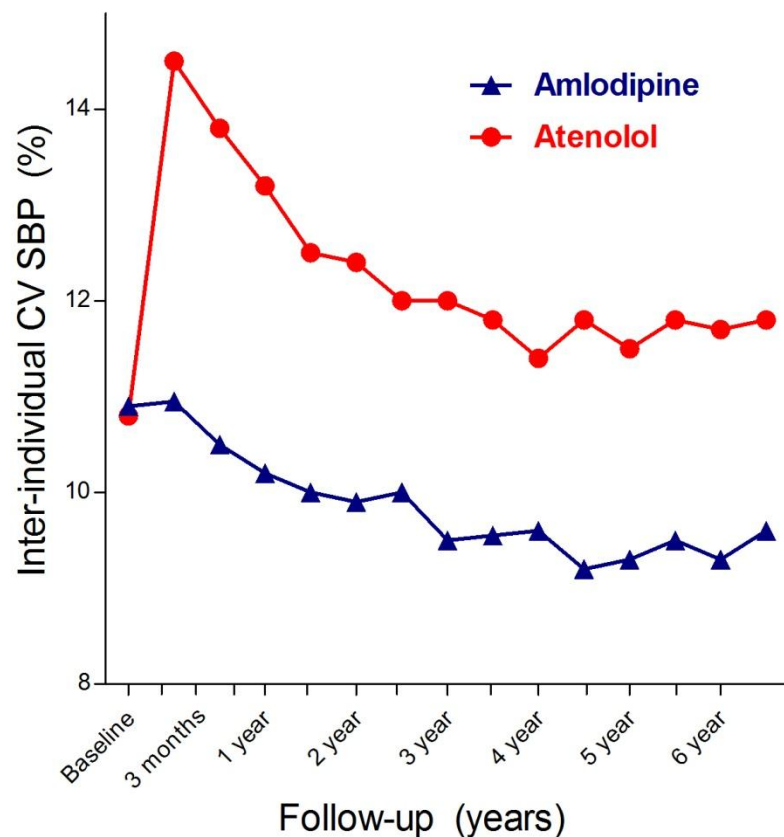
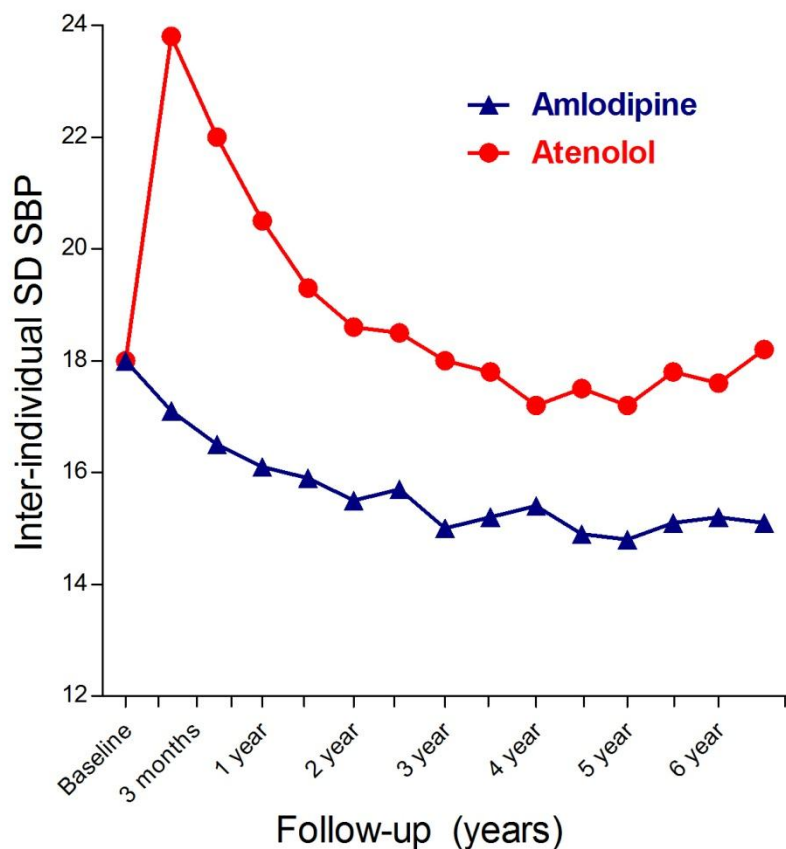


Effects of beta blockers and calcium-channel blockers on within-individual variability in blood pressure and risk of stroke

Lancet Neurol. 2010 May;9(5):469-80.

International Centre for Circulatory Health, Imperial College London

Group distribution (SD and CV) of measures of SBP at baseline and at each follow-up visit in the two treatment groups



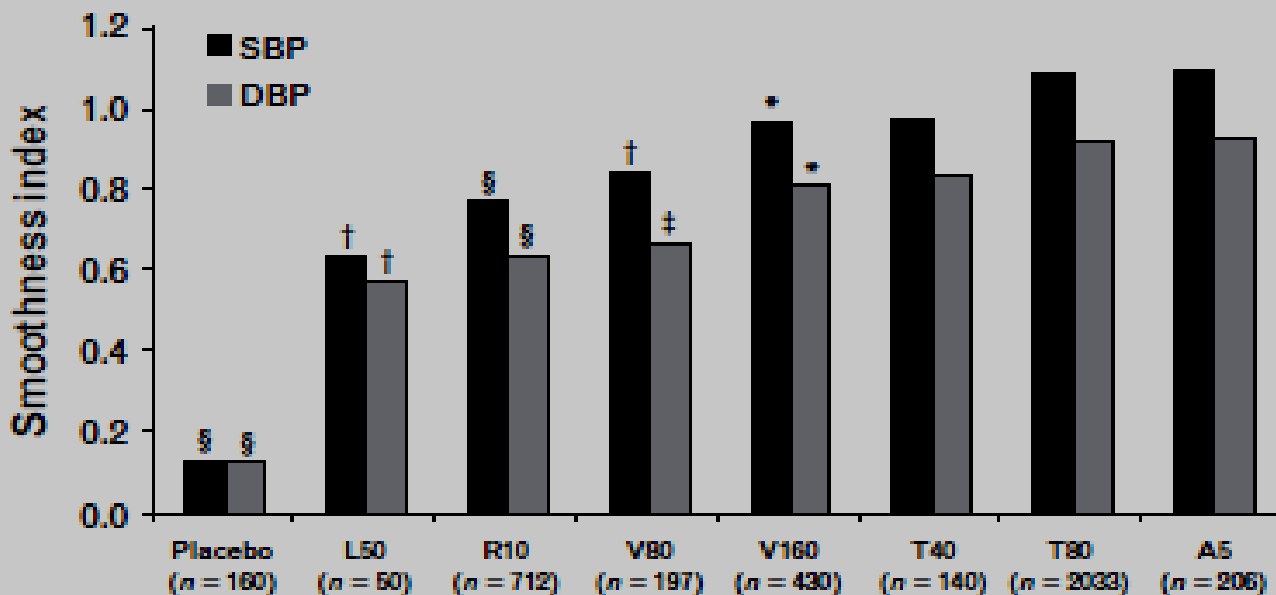
ASCOT

- **OKB strok riskini minimal etkiler KVO' a etkisi yok**
- **Vizit-vizit variabilite deęerlendirmede (SD, CV, VIM) strok ve KVH sonuęlarını etkilemekte**

ASCOT

- **Amlodipin BPV'yi atenololden daha çok azaltır**
- **Variabilite yaş ,DM, sigara vasküler hastalıkta artar**

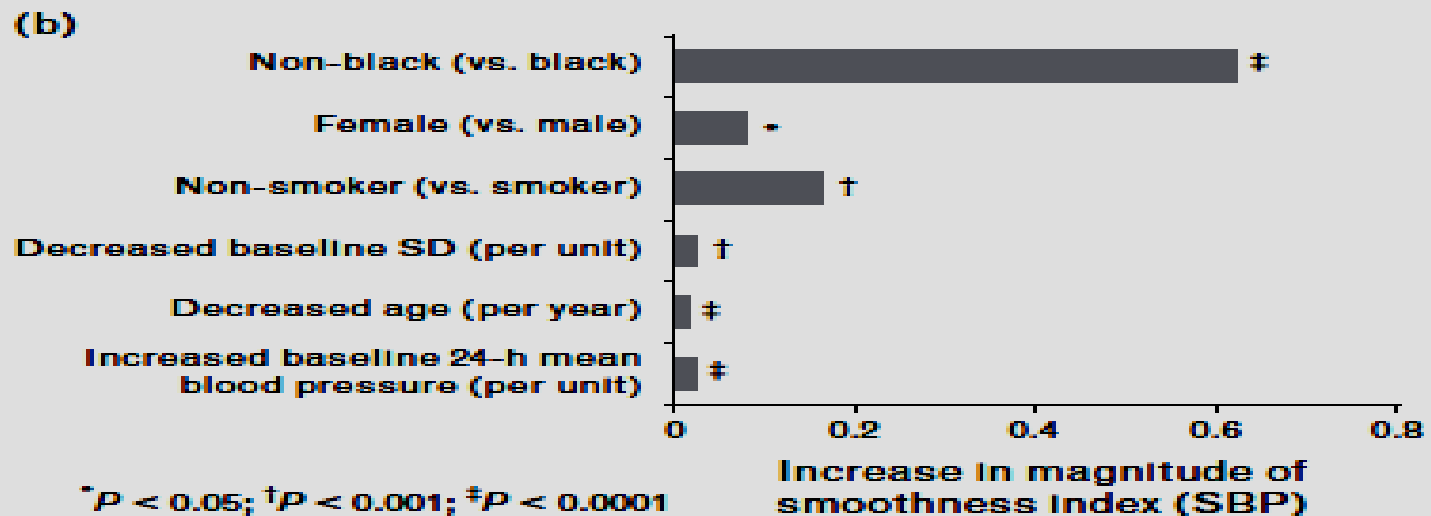
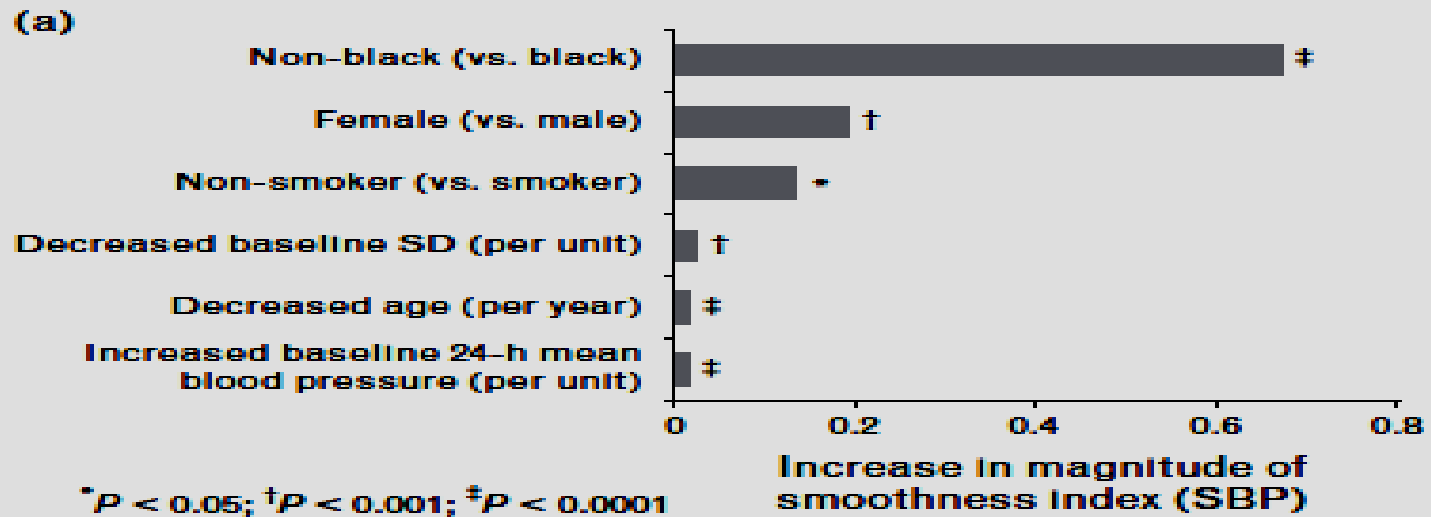
Fig. 2



* $p < 0.05$; † $p < 0.01$; ‡ $p < 0.001$; § $p < 0.0001$ vs telmisartan 80 mg

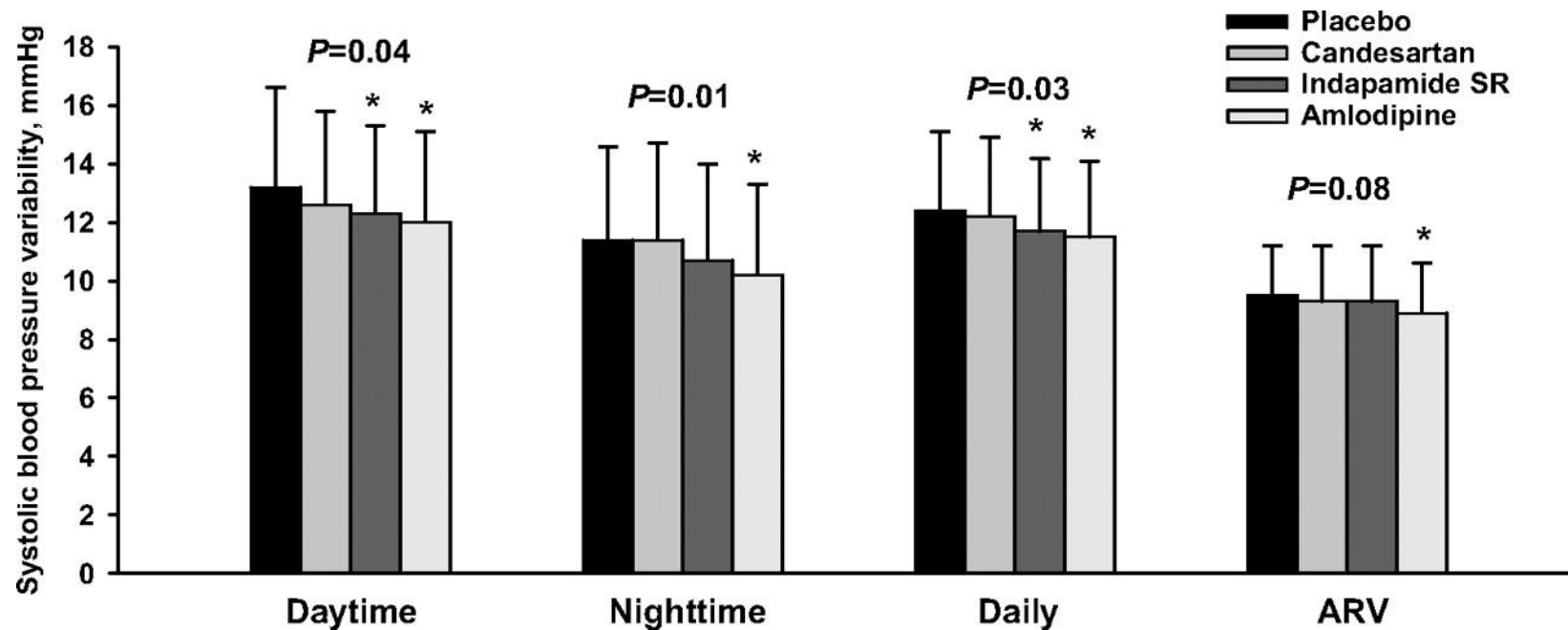
A comparison of the 24-h systolic and diastolic ambulatory blood pressure smoothness indices for seven antihypertensive monotherapies and placebo; data are based on nine trials involving 3928 monotherapy-treated patients. A5, amlodipine 5 mg; DBP, diastolic blood pressure; L50, losartan 50 mg; R10, ramipril 10 mg; SBP, systolic blood pressure; T40, telmisartan 40 mg; T80, telmisartan 80 mg; V80, valsartan 80 mg; V160, valsartan 160 mg.

Fig. 4



The impact of a number of baseline factors on the 24-h (a) systolic and (b) diastolic ambulatory blood pressure smoothness indices. DBP, diastolic blood pressure; SBP, systolic blood pressure; SD, standard deviation.

Comparisons of systolic blood pressure variability after 3-month antihypertensive treatment.



Zhang Y et al. Hypertension 2011;58:155-160

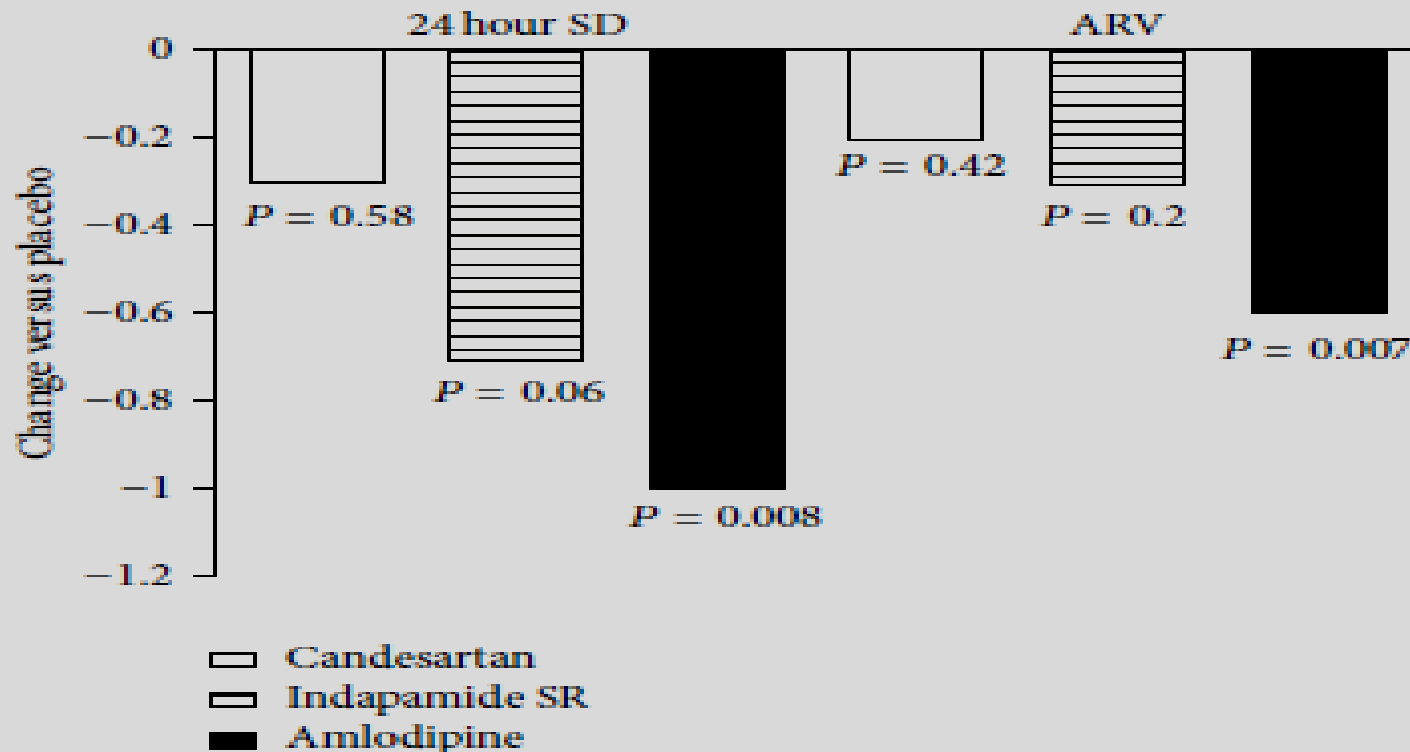


FIGURE 4: Effect of treatment with candesartan, indapamide SR, and amlodipine on short-term BPV in hypertensive patients. ARV: average real variability; SD: standard deviation. Adapted from Zhang et al. [88].

- **Amlodipin ve tiazid-tipi diüretikler VVV'yi düşürür**
- **β blokör ve ACE inhb. VVV'si daha büyük**

Webb et al. Lancet. 2010;375(9718):906-15.

Review Article

Emerging concept of anti-hypertensive therapy based on ambulatory blood pressure profile in chronic kidney disease

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Abstract: Presently hypertensive patients with chronic kidney disease (CKD) particularly diabetic nephropathy are increasing in number, and cardiovascular and renal complications are the most common cause of death in these patients. The control of blood pressure (BP) is an important issue in cardiovascular and renal protection in hypertensive patients with CKD. Although hypertension is usually diagnosed based on measurements of BP recorded during a visit to a physician, that is, office BP, several studies have shown that target organ damage and prognosis are more closely associated with ambulatory BP than with office BP. It should be important to achieve the target absolute BP levels in hypertensive patients obtained either by office or home measurements or by ambulatory recordings for the cardiovascular and renal protection. Noninvasive techniques for measuring ambulatory BP have allowed BP to be monitored during both day and night. Additionally, ambulatory BP monitoring can provide information on circadian BP variation and short-term BP variability, which is suggested to be associated with cardiovascular and renal morbidity and mortality. This review will briefly summarize the emerging concept of anti-hypertensive therapy based on ambulatory BP profile in hypertensive patients with CKD.

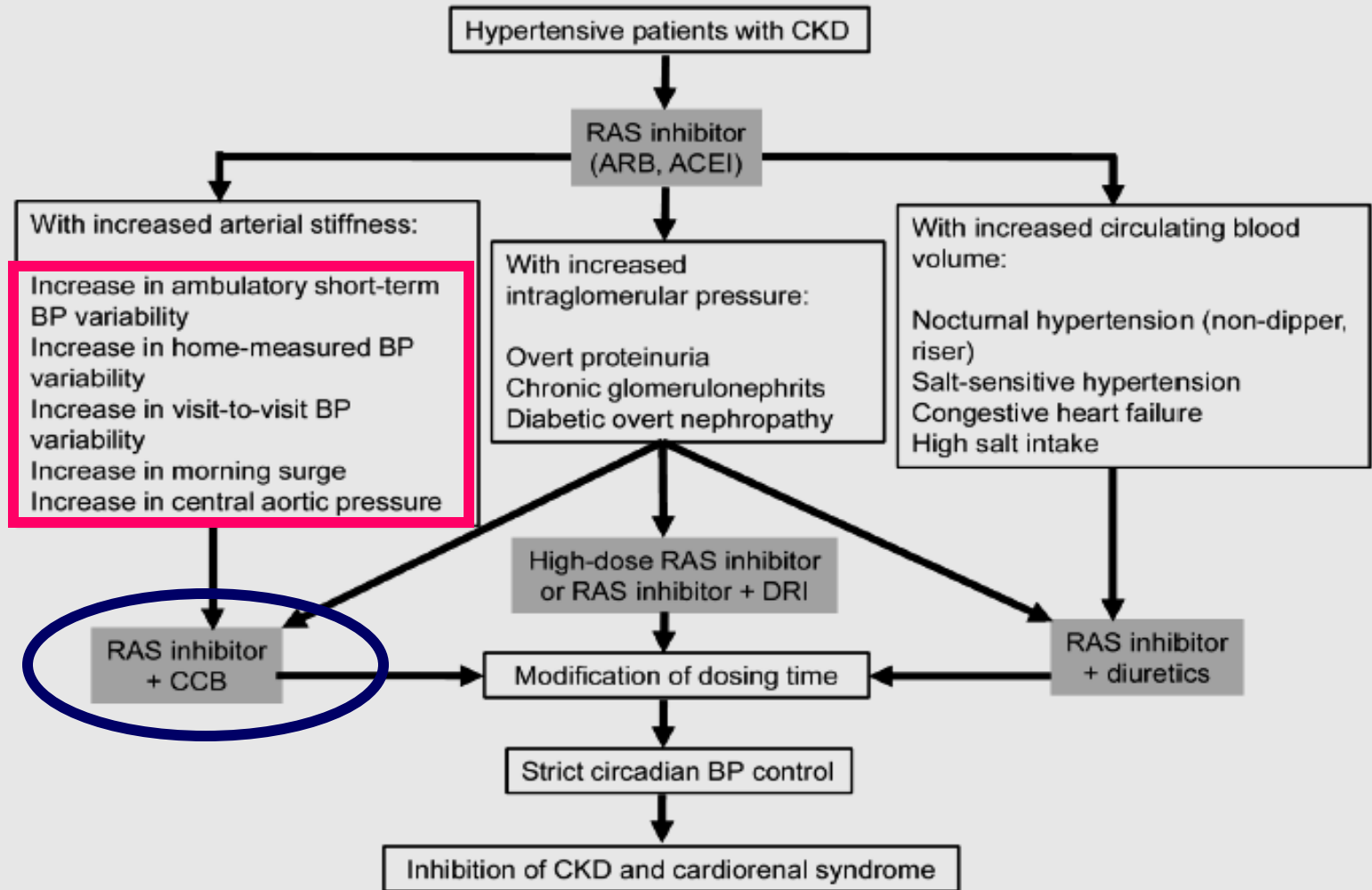


Figure 1. Schema showing the proposed strategy of RAS inhibitor-based combination therapy for hypertensive patients with CKD. ACEI, angiotensin-converting enzyme inhibitor; ARB, Ang II type 1 receptor-specific blocker; BP, blood pressure; CKD, chronic kidney disease; CCB, calcium channel blocker; DRI, direct renin inhibitor; RAS, renin-angiotensin system.

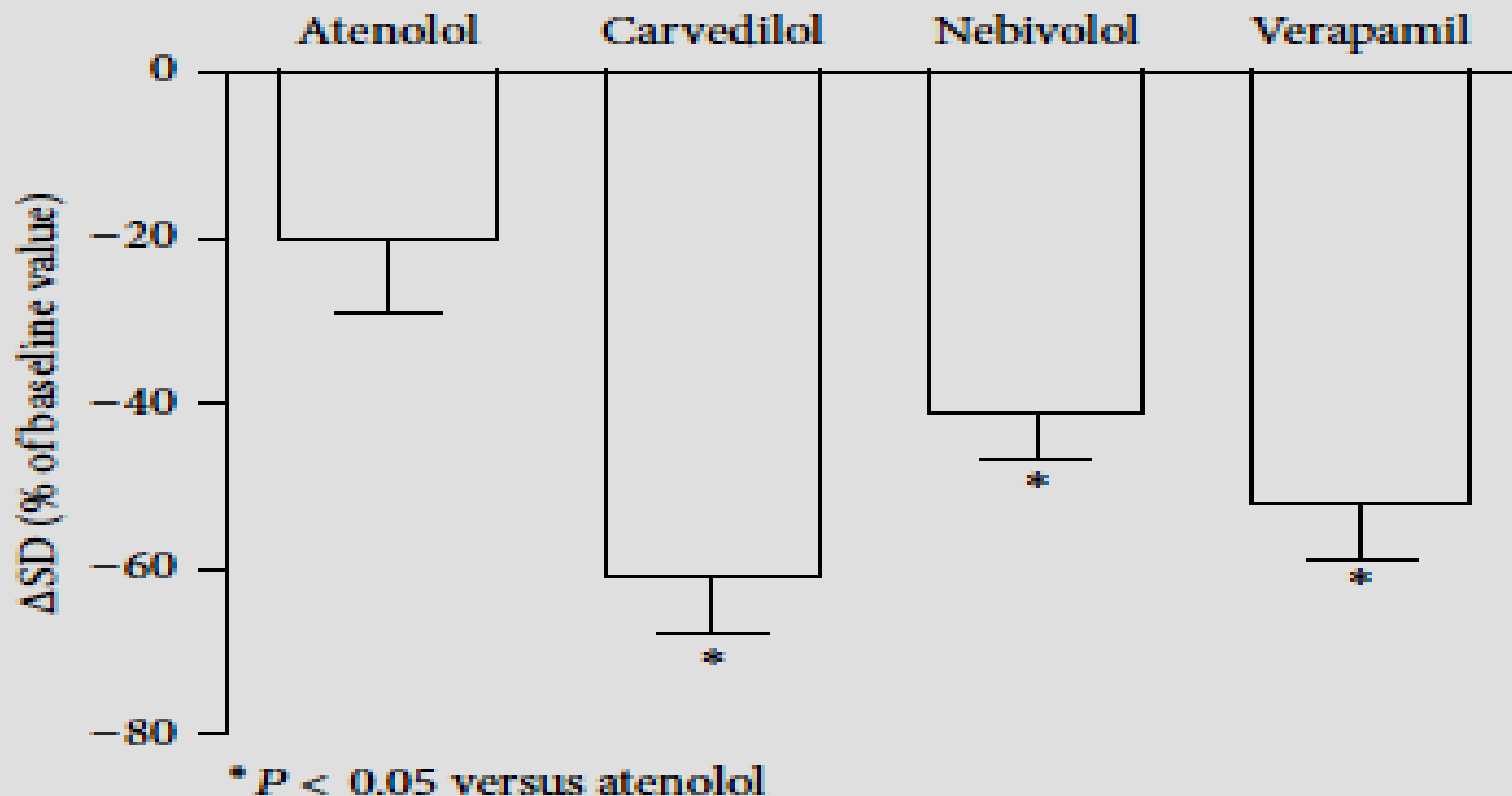


FIGURE 1: Effects of acute administration of atenolol, carvedilol, nebivolol, or verapamil on short-term BPV in SAD rats. Adapted from Bertera et al. [15].

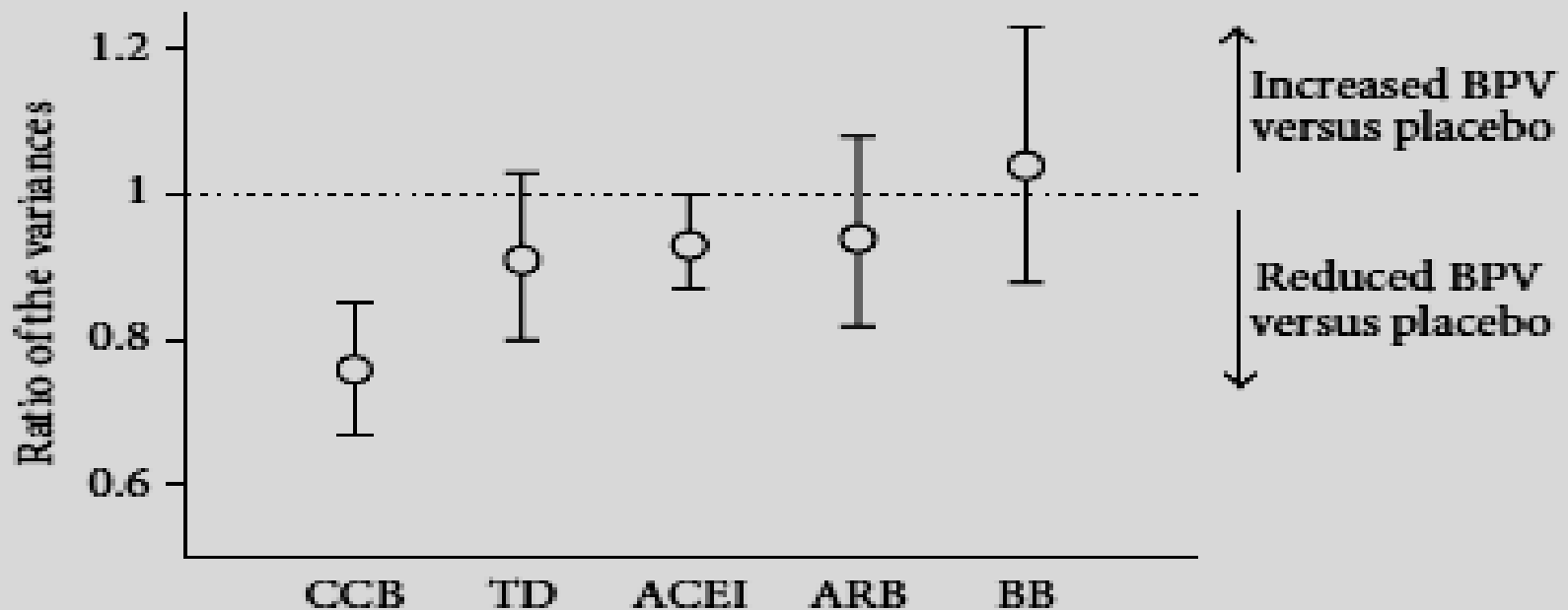
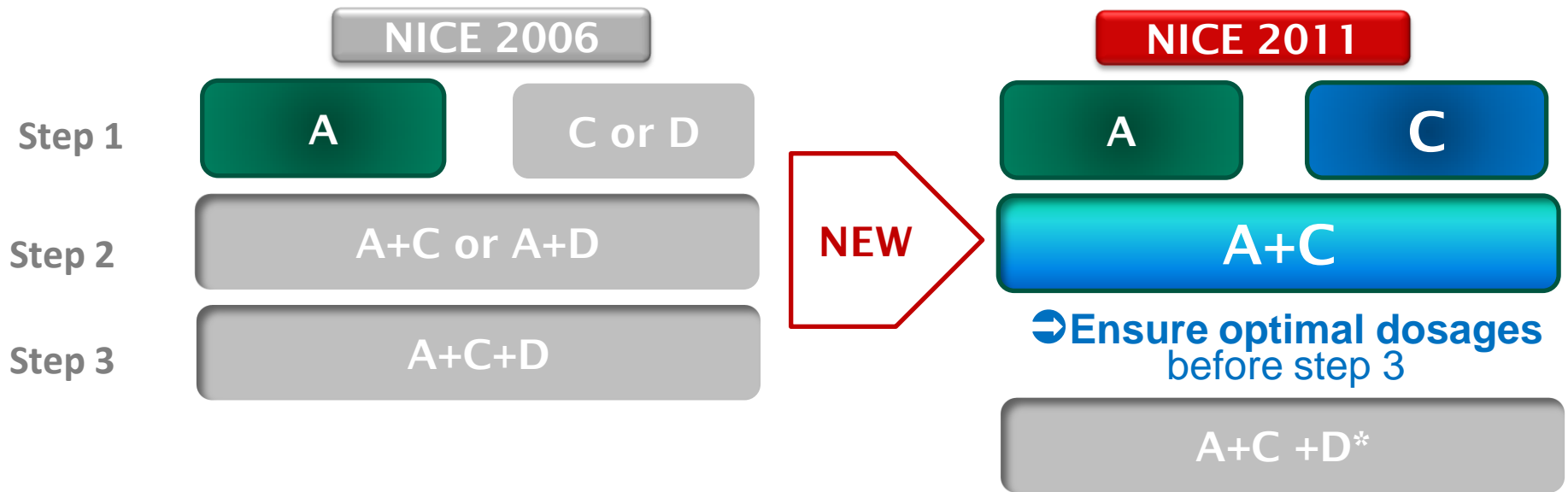


FIGURE 3: Meta-analysis of antihypertensive drug effects on long-term BPV. CCB: calcium channel blockers; TD: thiazide-like diuretics; ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin receptor blockers; BB: beta blockers. Adapted from Webb et al. [81].

Guideline recommendations about antihypertensive strategies to suppress systolic BP variability

➔ ACE inhibitor/CCB is the preferred two-drug combination



“...whatever the underlying mechanisms, **systolic blood pressure variability** appears to be an important independent predictor of clinical outcomes.”

“...the updated guidance recommends **the best available evidence-based treatment options to suppress blood pressure variability in people with hypertension.**”

TABLE 6: Ongoing clinical trials that evaluate drug effects on BPV.

Trial denomination	Objective	Endpoint	ClinicalTrials.gov Identifier
Indapamide versus hydrochlorothiazide in elderly hypertensive patients with renal insufficiency	Evaluate the effects of indapamide SR 1.5 mg on renal function, endothelial function, blood pressure variability by comparison with hydrochlorothiazide 25 mg, in patients with mild-to-moderate renal insufficiency and hypertension.	Primary outcome measures: renal function Secondary outcome measures: endothelial function, blood pressure variability	NCT01172431
Compare the effects of Lercanidipine Hydrochloride Tablet (Zanidip) and Felodipine sustained-release tablet for Hypertension	Compare felodipine sustained-release tablets to Lercanidipine hydrochloride tablets (Zanidip) for the treatment of patients with mild-to-moderate primary hypertension and to investigate the influence on patients' heart rate and blood pressure variability.	Primary outcome measures: change from baseline in mean seated diastolic BP in clinical after 6 weeks of treatment Change from baseline in mean seated systolic BP after 6 weeks of treatment	NCT01520285
ARB and CCB longest combination treatment on ambulatory and home BP in hypertension with atrial fibrillation-multicenter study on time of Dosing (ACROBAT)	Evaluate of 24-hour antihypertensive effect of long-acting ARB-CCB tablet administrated to hypertensive patients with atrial fibrillation, and comparison of 24-hour antihypertensive effect of long-acting ARB-CCB tablet between morning administration and bedtime administration.	Primary outcome measures: change in 24-hour average BP from baseline to week 12. Secondary outcome measures: Change in BP at nighttime, early-morning, and daytime from baseline to Week 12. Change in BPV from baseline to Week 12.	NCT01748253
Renal sympathetic modification in patients with metabolic syndrome	Assess the incident of composite cardiovascular events after renal sympathetic modification using THERMOCOOL catheter in patients with metabolic syndrome, and evaluate safety and efficacy of the intervention.	Primary outcome measures: composite cardiovascular events (myocardial infarction, heart failure, sudden death, cardiogenic death) Secondary outcome measures: effect on glucose and lipid metabolism and BPV	
Comparison of bisoprolol with metoprolol succinate sustained-release on heart rate and blood pressure in hypertensive patients (CREATIVE)	Demonstrate the superiority and/or noninferiority of bisoprolol on metoprolol succinate sustained-release (SR)	Primary outcome measures: change of mean diastolic ABPM in the last 4 hours after 12-week treatment from baseline. Secondary outcome measures: change of mean ambulatory 24 h, daytime and nighttime BP 24-hour variability of BP	NCT01508325

Source: www.clinicaltrials.gov.

Eve Giderken

- **KBD kalbi ve böbređi yorar**
- **KBD vasküler risk oluşturur**
- **KBD HOH ve mortaliteyi olumsuz etkiler**
- **KBD antihipertansiflerle düşürülebilir**
- **KBD'ne en olumlu etkiyi CCB(Amlodipin) sağlar**