Ελληνική Νεφρολογική Εταιρεία

20ο Πανελλήνιο Συνέδριο Νεφρολογίας

Υπέρταση στο Τελικό Στάδιο ΧΝΝ

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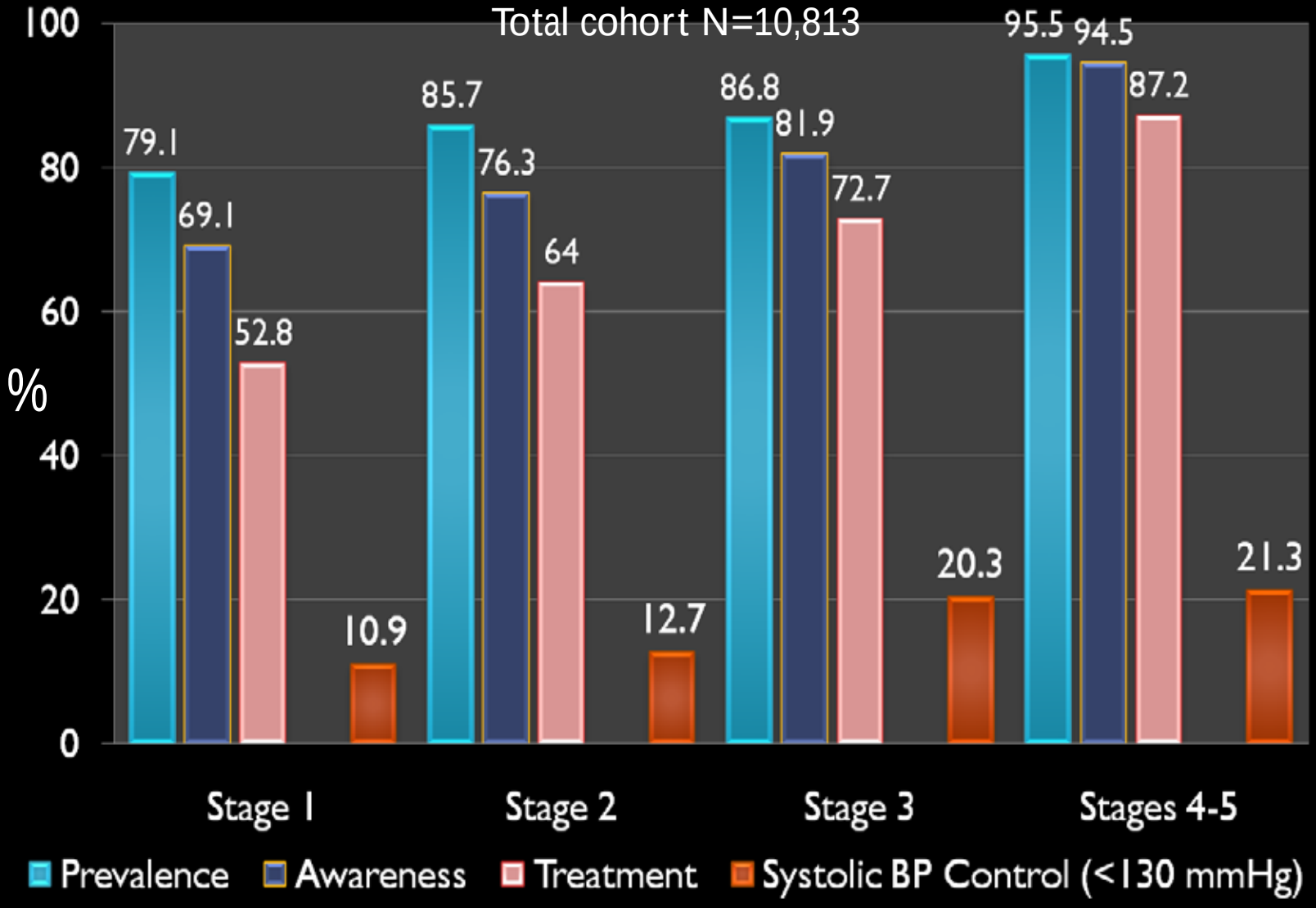
Υπέρταση στο Τελικό Στάδιο ΧΝΝ

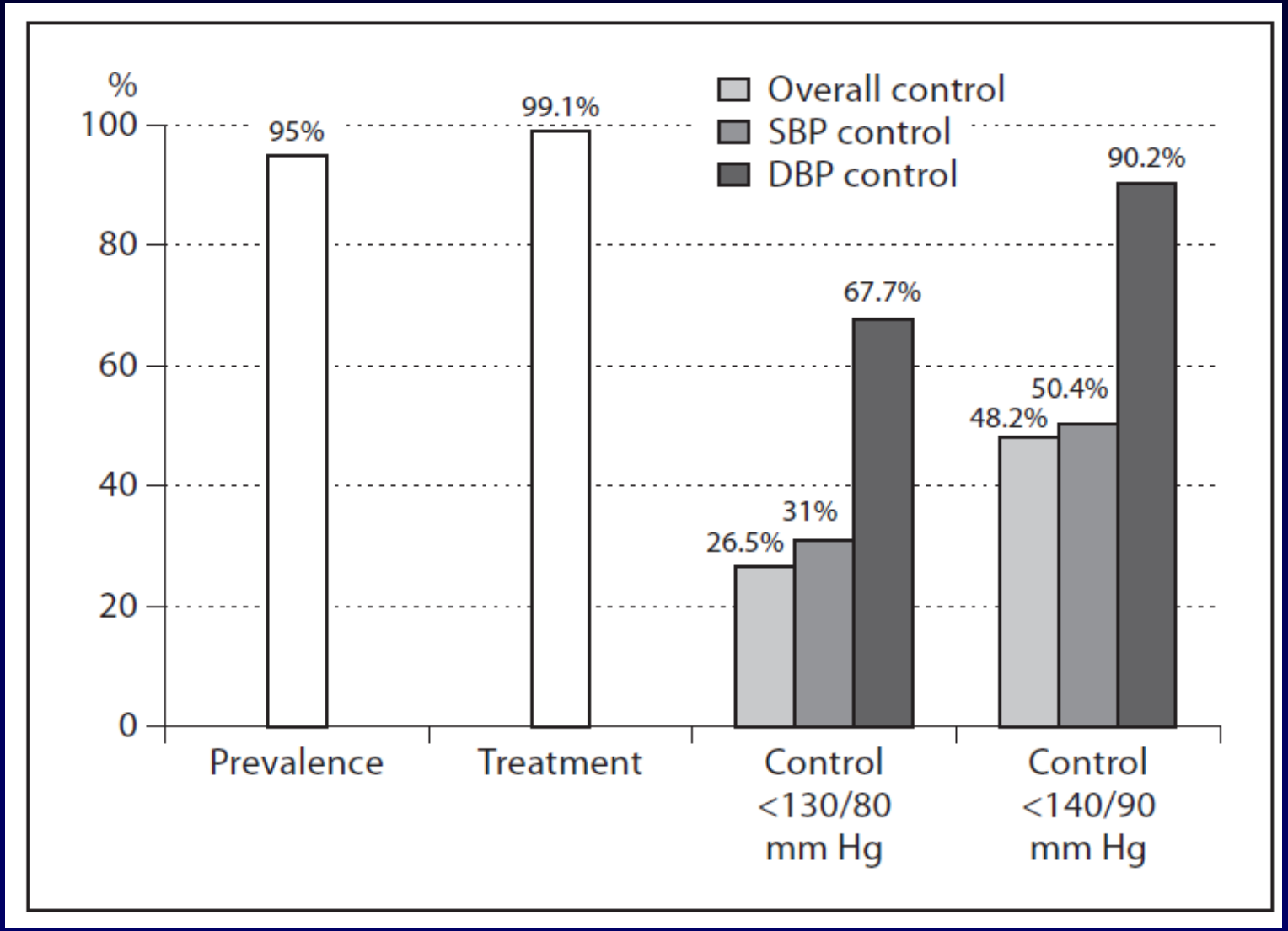
Εισαγωγή

Prevalence, Awareness, Treatment, and Control of Hypertension to Systolic Goal (<130mmHg) by CKD stage



Sarafidis P, et al. Am J Med 2008

Prevalence of hypertension in Low-Clearance patients



Sarafidis P, et al. Nephron Clin Pract 2012

Υπέρταση στο Τελικό Στάδιο ΧΝΝ

Διεθνείς Οδηγίες

Guidelines on Hypertension in ESRD (?)

K/DOQI 2005 guidelines on cardiovascular disease in dialysis patients

Predialysis and postdialysis blood pressure goals should be <140/90mmHg and <130/80mmHg respectively (C)

K/DOQI 2006 update of hemodialysis adequacy guidelines

Focus on volume control, dietary sodium restriction and avoidance of high dialysate sodium

DO NOT recommend specific blood pressure targets in hemodialysis patients

K/DOQI 2007 clinical practice guidelines for diabetes and CKD

Target blood pressure in diabetes and CKD stages 1-4 should be <130/80mmHg (B)

Targets for patients on dialysis are not recommended.

KDIGO 2009 Consensus Conference

Home BP >139/89 mmHg can only be decided by future research

KDIGO 2012. Only for CKD-ND

http://www.kidney-international.org meeting report

Blood pressure in chronic kidney disease stage 5D—report from a Kidney Disease: Improving Global Outcomes controversies conference

Nathan W. Levin[1], Peter Kotanko[1], Kai-Uwe Eckardt[2], Bertram L. Kasiske[3], Charles Chazot[4], Alfred K

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Erlangen, (
[5]Division o
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[8]CNR-IBIM,
[9]Centre Ho

http://www.kidney-international.org mini review

The lingering dilemma of arterial pressure in CKD: what do we know, where do we go?

Rajiv Agarwal[1], Alberto Martinez-Castelao[2], Andrzej Wiecek[3], Ziad Massy[4,5], Gultekin Suleymanlar[6], Alberto Ortiz[7], P
David Goldsmitl
CArdiovascular I
Transplant Asso

BRIEF REVIEW www.jasn.org

Assessment and Management of Hypertension in Patients on Dialysis

Rajiv Agarwal,* Joseph Flynn,† Velvie Pogue,‡ Mahboob Rahman,§ Efrain Reisin,‖ and Matthew R. Weir¶

The ERBP mission is to improve the outcome of patients with kidney disease in a sustainable way, through enhancing the accessibility of knowledge on patient care, in a format that stimulates its use in clinical practice.

Dear all,

Following the approval of both advisory boards of ERBP and ESH to develop a guidance document on management of hypertension in dialysis patients, I have started the necessary preliminary explorations to start this project.

As agreed, we will start from the consensus document of KDIGO 2009 on this topic (in attach).

We also agreed to restrict to two topics:

1/ does aiming at lower blood pressure targets improve outcomes (mortality, major cardiovascular events, QoL) of patients on dialysis

2/ which method of blood pressure measurement is most advisable to monitor management of blood pressure in dialysis patients?

As the impact of blood pressure on outcomes is in dialysis patients strongly associated with many interfering factors, often with opposite effects, data from observational cohorts are difficult to interpret, as was already concluded in the KDIGO 2009 consensus paper. In this regard, it seems not very useful to search for additional data, as this will not answer our questions in an appropriate manner. Therefore, we will restrict in our search to randomised clinical trials only.

Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension (ESH)*

Pantelis A. Sarafidis[a], Alexandre Persu[b,c], Rajiv Agarwal[d,e], Michel Burnier[f], Peter de Leeuw[g,h], Charles Ferro[i], Jean-Michel Halimi[j], Gunnar Heine[k], Michel Jadoul[l], Faical Jarraya[m,n], Mehmet Kanbay[o], Francesca Mallamaci[p], Patrick B. Mark[q], Alberto Ortiz[r], Gianfranco Parati[s,t], Roberto Pontremoli[u], Patrick Rossignol[v,w], Luis Ruilope[x], Patricia Van der Niepen[y], Raymond Vanholder[z], Marianne C. Verhaar[aa], Andrzej Wiecek[bb], Gregoire Wuerzner[f], Gérard M. London[cc], and Carmine Zoccali[p]

Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension (ESH)*

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21 pages

10,300 words

205 references

4 Figures, 2 Tables

6 Boxes

- INTRODUCTION
- DIAGNOSIS OF HYPERTENSION IN DIALYSIS PATIENTS
- PREVALENCE OF HYPERTENSION IN THE HEMODIALYSIS POPULATION BY THE VARIOUS METRICS AND DEFINITIONS
- BP AND THE RISK FOR CARDIOVASCULAR EVENTS AND DEATH IN HEMODIALYSIS PATIENTS
- EPIDEMIOLOGY OF HYPERTENSION IN PATIENTS TREATED WITH PERITONEAL DIALYSIS
- PATHOPHYSIOLOGY OF HYPERTENSION IN DIALYSIS PATIENTS
- HYPERTENSION TREATMENT IN DIALYSIS PATIENTS
- CONCLUSIONS

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

Υπέρταση στην Αιμοκάθαρση

Ορισμός και Συχνότητα

Prevalence, treatment and control of hypertension in dialysis patients

Author	Year	N	Definition of Hypertension	Prevalence of hypertension	BP Treatment among hypertensives	BP Control among hypertensives
Salem, M.	1995	649	Pre-hemodialysis MAP ≥114 mmHg or use of antihypertensive agents	71.9%	81.5%	48.6%
Rahman, M.	1999	489	Pre-hemodialysis SBP ≥140 mmHg and/or DBP ≥90 mm	87.7%	93.2%	71.1%
Agarwal, R.	2003	2,535	1-week average pre-hemodialysis SBP >150 mmHg and/or DBP >85 mmHg, or use of antihypertensive agents	85.8%	88.4%	30.3%
Agarwal, R.	2011	369	44-hour interdialytic ambulatory SBP≥135 mmHg and/or DBP≥85 mmHg or use of antihypertensive medications	82%	89%	38%
Cocchi, R	1999	504 PD	SBP>140 or DBP >90mmHg, or use of antihypertensive treatment	88.1%	81.5%	

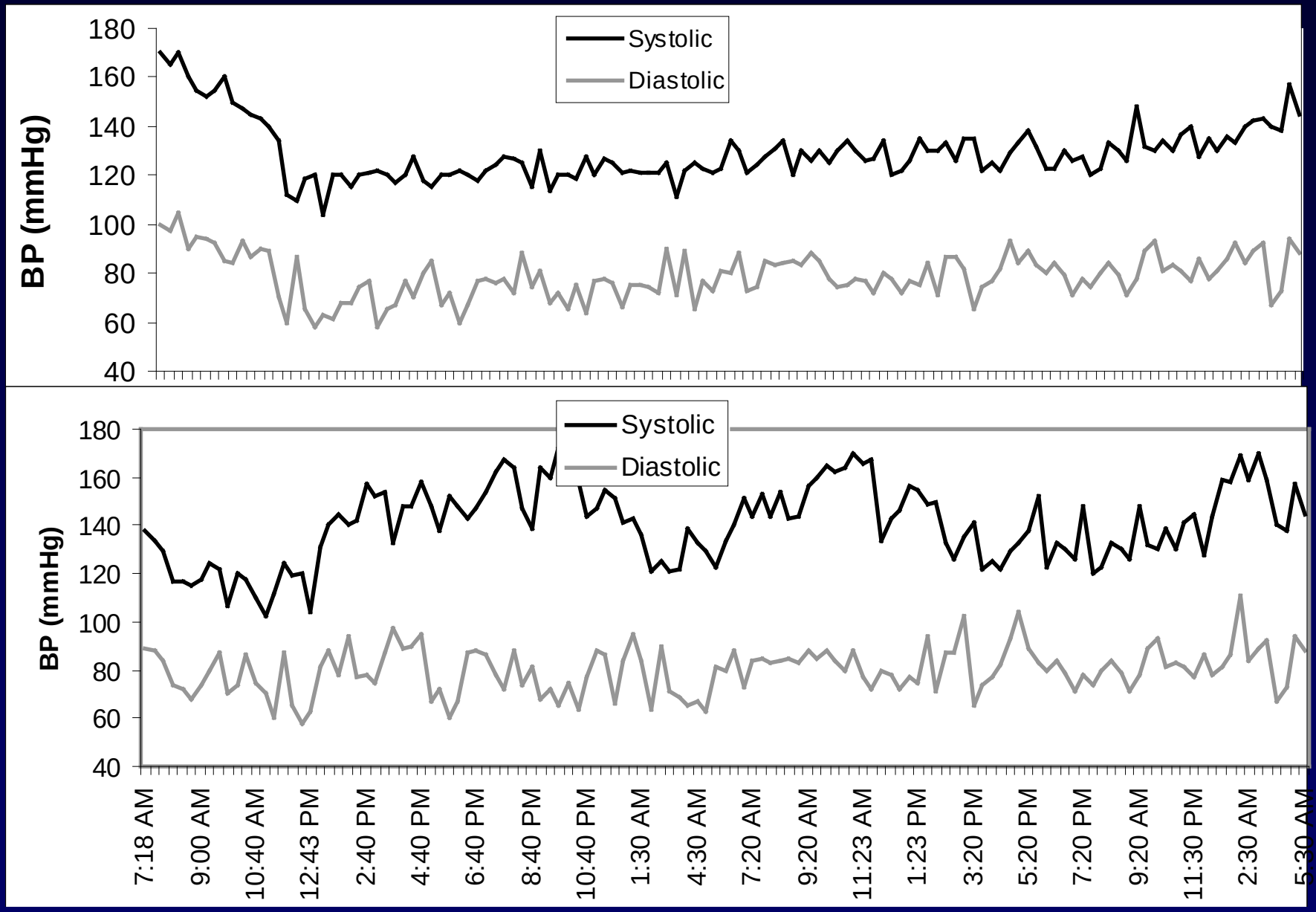
Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

Reasons of poor validity of “peridialytic” BP measurements

- Readings not made for diagnostic reasons but to exploit a major hemodynamic metric like to assess cardiovascular stability
- Office reading (white-coat effect)
- Errors in recording (wrong cuff, low number of readings)
- Invalid devices
- Inadequate “relaxation” time
- “Stress” of quick connection – disconnection / Needlephobia
- Pre = maximum, post = minumum volume overload
- Pre = maximum, post = minumum of the effect of drugs that are dialyzed

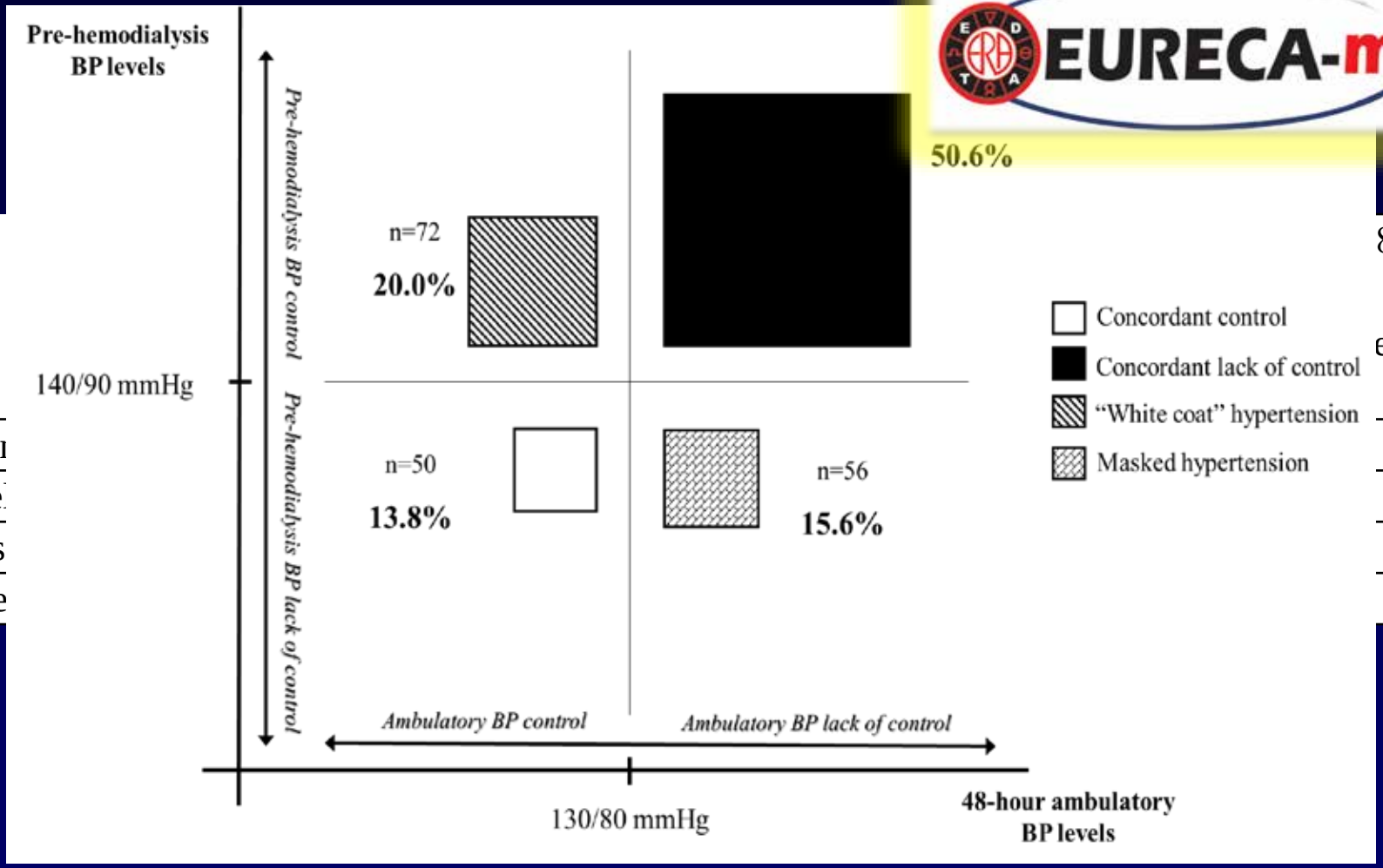
Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

ABPM in Hemodialysis



Sarafidis P. Unpublished data

Prevalence, treatment and control of hypertension in European hemodialysis patients



Sarafidis P, et al. Nephrol Dial Transplant 2018

Prevalence of hypertension in European PD patients

- WHO/ISH 1999 definition:

prevalence of hypertension 88%

- BP load >30% of values >140/90

at daytime or >120/80 at night-

time during 24-h ABPM (n=414):

prevalence of hypertension 69%

Cocchi, et al. Nephrol Dial Transplant 1999

Table 2 Ambulatory blood pressure (BP) measurements in haemodialysis and CAPD patients

	Haemodialysis (n = 22)	*CAPD* (n = 24)	*P*
44-h monitoring			
Mean			
Systolic BP (mm Hg)	133 ± 14	132 ± 17	NS
Diastolic BP (mm Hg)	85 ± 9	85 ± 14	NS
Daytime			
Systolic BP (mm Hg)	135 ± 12	142 ± 18	NS
Diastolic BP (mm Hg)	87 ± 9	91 ± 14	NS
Nightime			
Systolic BP (mm Hg)	130 ± 16	122 ± 18	NS
Diastolic BP (mm Hg)	83 ± 11	79 ± 15	NS
Hypertension *n* (%)	10 (46%)	11 (46%)	NS
First Day			
Mean			
Systolic BP (mm Hg)	125 ± 12	133 ± 17	0.06
Diastolic BP (mm Hg)	80 ± 7	83 ± 12	NS
Daytime			
Systolic BP (mm Hg)	127 ± 10	143 ± 18	<0.001
Diastolic BP (mm Hg)	81 ± 9	91 ± 14	0.006
Nightime			
Systolic BP (mm Hg)	123 ± 15	122 ± 18	NS
Diastolic BP (mm Hg)	78 ± 10	79 ± 15	NS
Hypertension *n* (%)	6 (27%)	13 (54%)	0.08
Second Day			
Mean			
Systolic BP (mm Hg)	141 ± 16	132 ± 17	0.08
Diastolic BP (mm Hg)	91 ± 11	84 ± 14	0.06
Daytime			
Systolic BP (mm Hg)	144 ± 15	141 ± 18	NS
Diastolic BP (mm Hg)	94 ± 10	91 ± 14	NS
Nightime			
Systolic BP (mm Hg)	138 ± 18	122 ± 18	0.006
Diastolic BP (mm Hg)	89 ± 12	78 ± 15	0.01
Hypertension *n* (%)	17 (77%)	10 (42%)	0.02

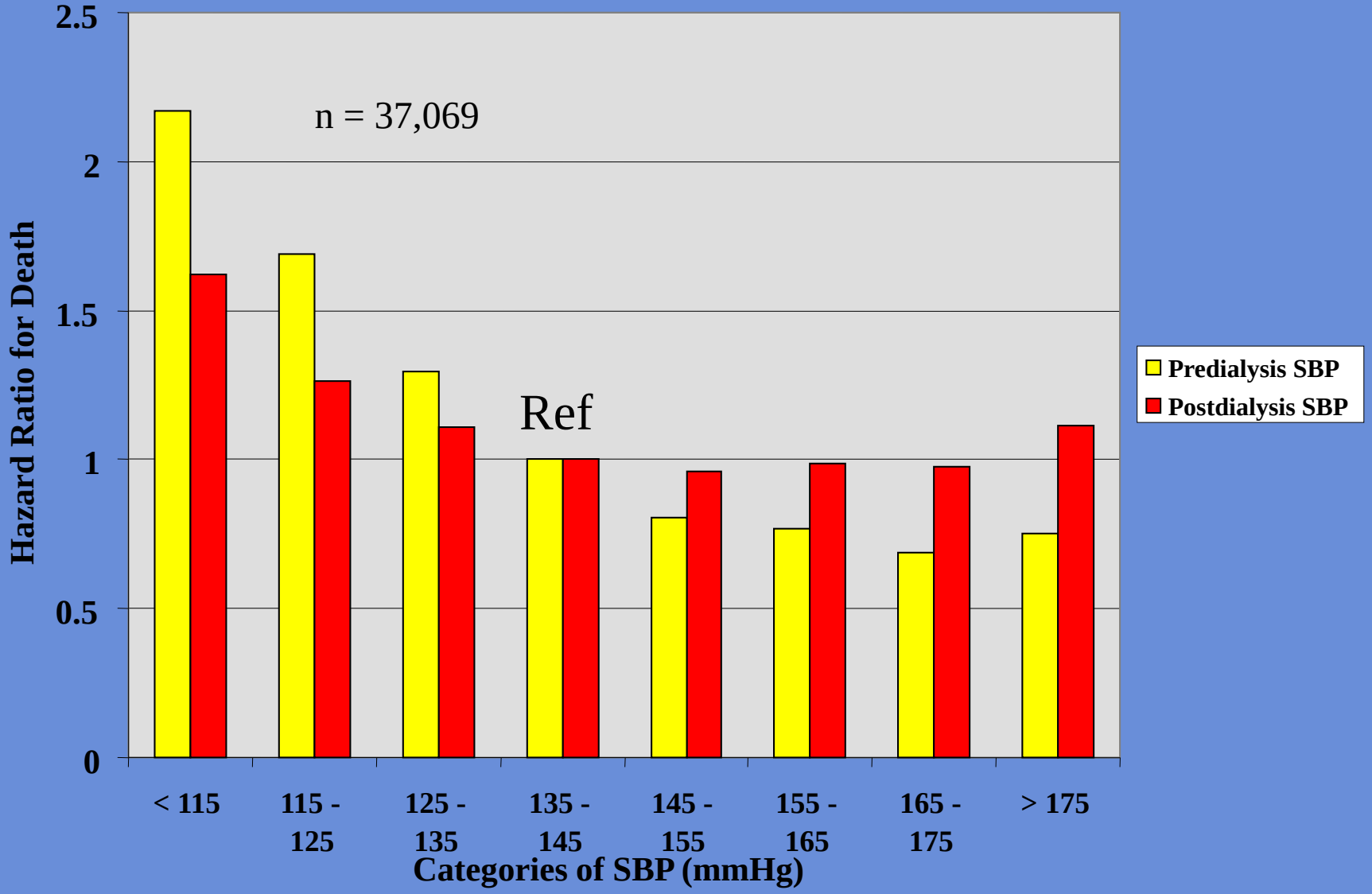
Tonbul, et al. J Hum Hypertens 2002

Υπέρταση στο Τελικό Στάδιο ΧΝΝ

Πρόγνωση Καρδιαγγειακού Κινδύνου

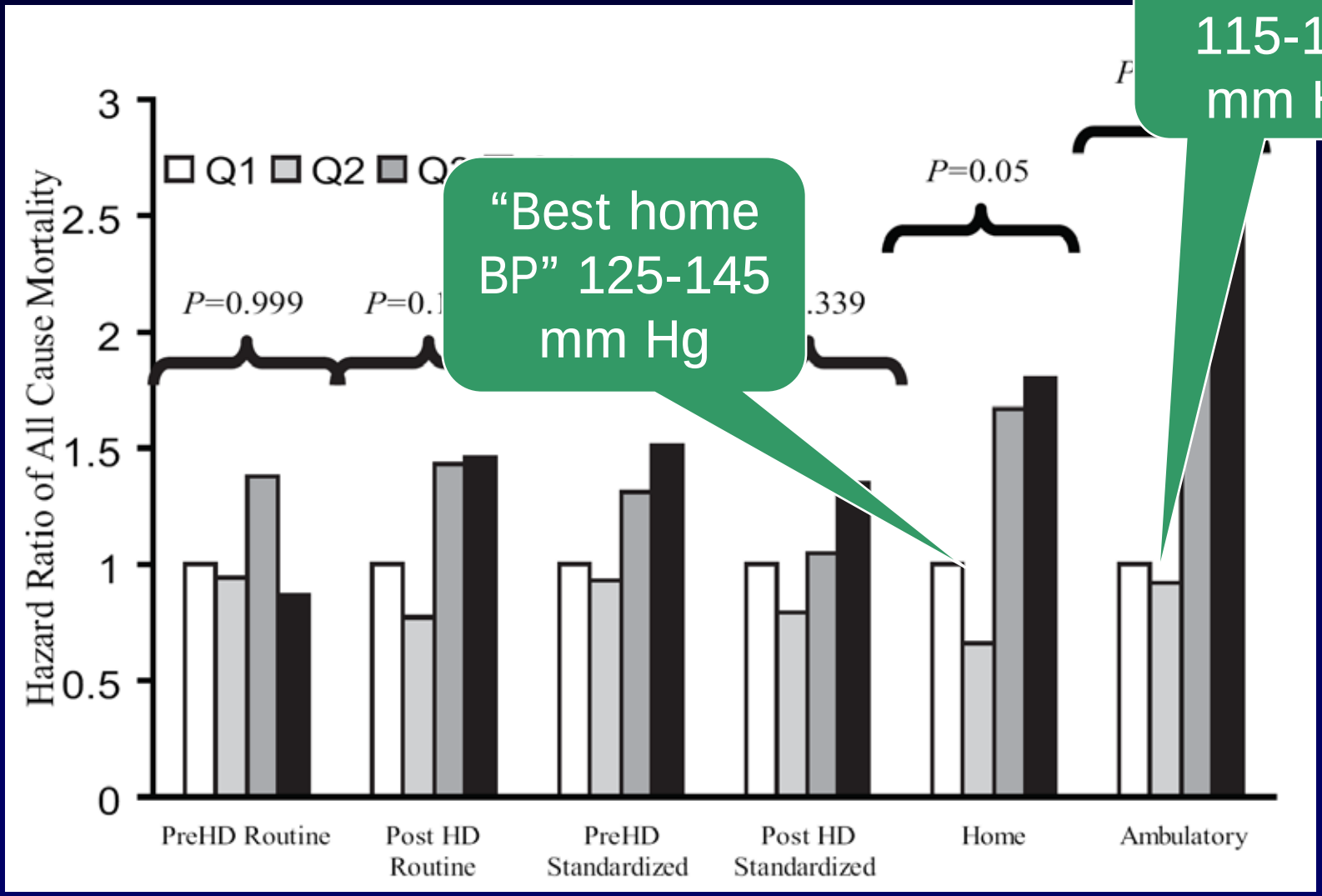
1-year Mortality predicted by SBP

Experience at 782 US dialysis facilities



Klassen et al. JAMA 2002;287:1548-1555

Home BP and ABPM monitoring is of greater prognostic value than HD units recordings



Alborzi et al. CJASN 2007;2:1228-1234

Home and ambulatory blood pressure monitoring in chronic kidney disease

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Moderator's view: Ambulatory blood pressure monitoring and home blood pressure for the prognosis, diagnosis and treatmen of hypertension in dialysis patients

Carmine Zoccali[1], Rocco Tripepi[1], Claudia Torino[1], Giovanni Tripepi[1] and Francesca Mallamaci[1,2]

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American Journal of Nephrology

Editorial Commentary Review

Am J Nephrol 2012;35:238–241
DOI: 10.1159/000336111

Published online: Feb

Ambulatory Blood Pressure Monitoring: An Invaluable Tool Comes of Age for Patients with Chronic Kidney Disease?

Pantelis A. Sarafidis Adam Rumjon Iain C. Macdougall

Hypertension in Chronic Kidney Disease Part 1

Out-of-Office Blood Pressure Monitoring: Methods, Thresholds, and Patterns

Hypertension in Chronic Kidney Disease Part 2

Role of Ambulatory and Home Blood Pressure Monitoring for Assessing Alterations in Blood Pressure Variability and Blood Pressure Profiles

Gianfranco Parati, Juan Eugenio Ochoa, Grzegorz Bilo, Rajiv Agarwal, Adrian Covic, Friedo W. Dekker, Danilo Fliser, Gunnar H. Heine, Kitty J. Jager, Luna Gargani, Mehmet Kanbay, Francesca Mallamaci, Ziad Massy, Alberto Ortiz, Eugenio Picano, Patrick Rossignol, Pantelis Sarafidis, Rosa Sicari, Raymond Vanholder, Andrzej Wiecek, Gerard London, Carmine Zoccali; on behalf of the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association-European Dialysis Transplantation Association (ERA-EDTA)

Parati G, et al. on behalf of EURECA-m Working Group. Hypertension 2016

BOX 1. Diagnosis of hypertension in dialysis patients

Hypertension in dialysis patients should be defined on the basis of home BP or ABPM measurements. Thresholds and methods proposed by the ASH/ASN [5], the EURECA-m working group of ERA-EDTA [11] and the relevant ESH Guidelines [24,41,205] can be used as follows:

- Home BP in hemodialysis: An average BP >135/85 mmHg for measurements collected in the morning and in the evening over 6 non-dialysis days (covering a period of two weeks). Measures should be performed in a quiet room, with the patient in seated position, back and arm supported, after 5 minutes of rest, and with two measurements per occasion taken 1 to 2 minutes apart.
- Home BP in peritoneal dialysis: An average BP >135/85 mmHg over 7 consecutive days with measurements collected as above.
- ABPM in hemodialysis: An average BP >130/80 mmHg over 24-hour monitoring during a mid-week day free of hemodialysis. Whenever feasible ABPM should be extended to 44-hours, i.e. covering a whole mid-week dialysis interval.
- ABPM in peritoneal dialysis: An average BP >130/80 mmHg over 24-hour monitoring

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

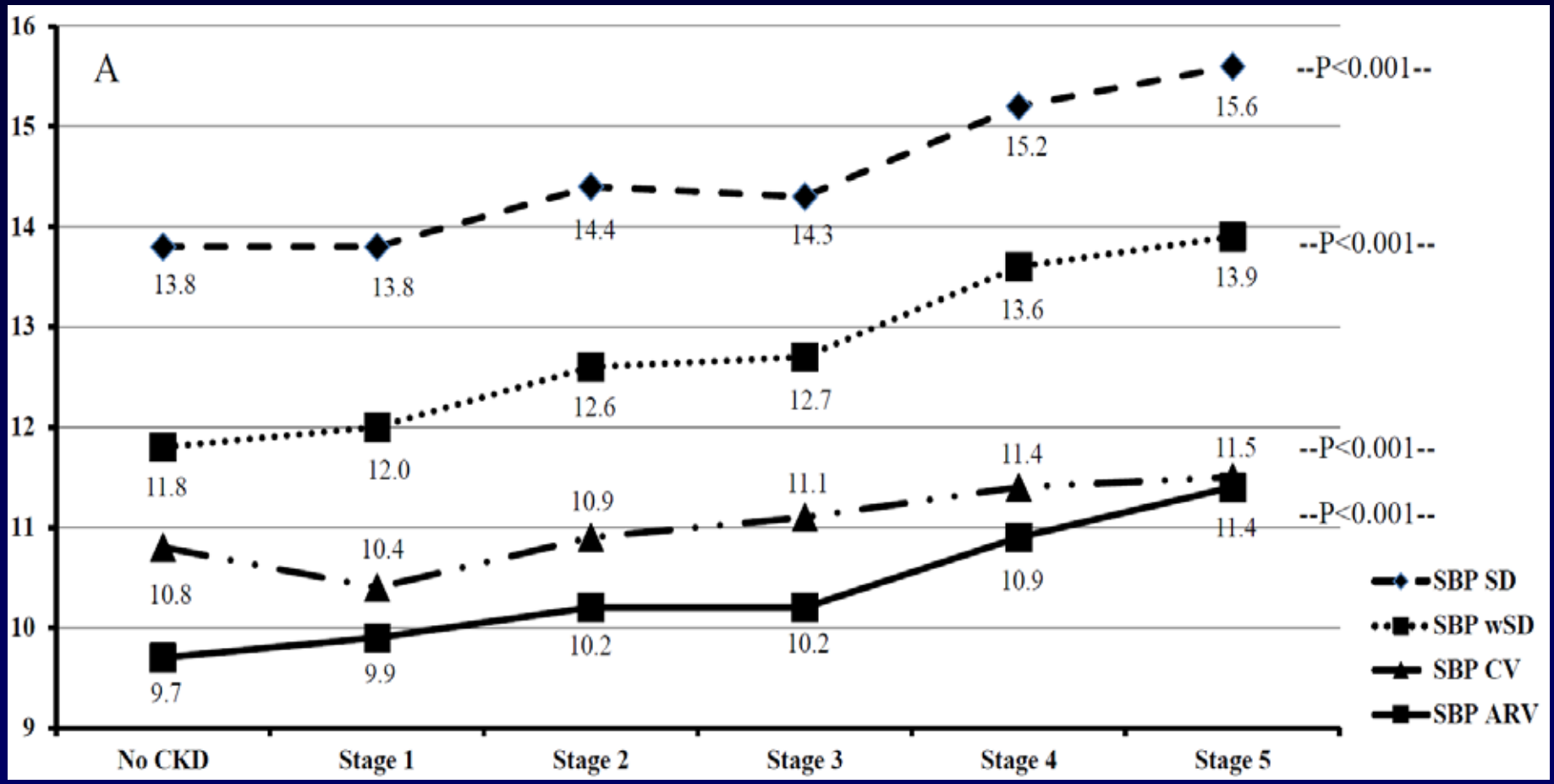
BOX 1. Diagnosis of hypertension in dialysis patients *(cont)*

- For hemodialysis patients no recommendation can be made on the basis of pre-dialysis or post-dialysis BP. When neither ABPM nor home BP measurements are available in these patients, the diagnosis can be made on the basis of office BP measurements taken during the dialysis interval, i.e. the average of three measurements with 1-2 minutes interval obtained in the sitting position by trained personnel after at least 5 minutes of quiet rest. The threshold of office BP >140/90 mmHg recommended by current guidelines for the definition of hypertension in CKD patients can be used for hemodialysis patients.
- For peritoneal dialysis patients office BP >140/90 mmHg obtained as described immediately above can be used for the diagnosis of hypertension.

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

Short-term BPV by CKD Stages: Spanish ABPM registry

24-hour Systolic BPV



Sarafidis, Ruilope, Loutradis et al. J Hypertens 2017

Blood pressure in dialysis - “conventional“ wisdom

Salt ???
Changes over time ???

Blood pressure regulation

volume-dependent
Salt/water

Heart failure

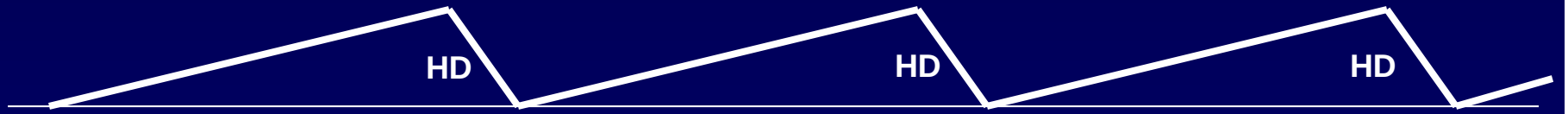
vasoconstriction

RAS, sympathetic activity, lack of NO, medullipin etc.

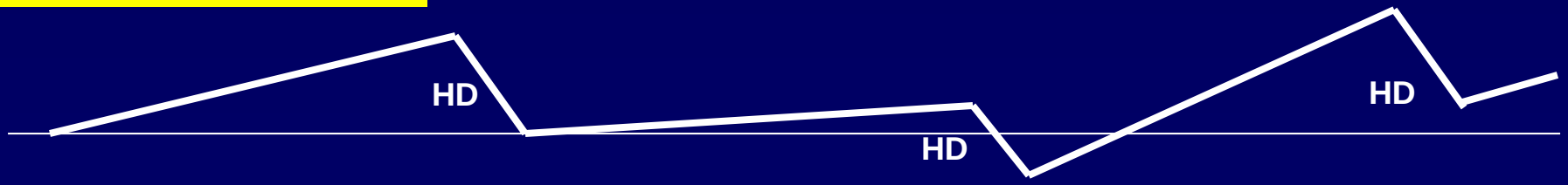
Arterial compliance

calcification

What is the “real” RR ???



Acute changes ???



48-hour BPV in Hemodialysis: Northern Greek network

TABLE 2. Blood pressure and blood pressure variability parameters of ambulatory brachial and aortic SBP and DBP in the two-days period of the 48-h period including hemodialysis and the interdialytic period and the two-days period of the 44-h interdialytic period

Variable	48-h period including hemodialysis and the interdialytic period			44-h interdialytic period		
	Day 1 (24-h period)	Day 2 (24-h period)	*P* value	Day 1 (20-h period)	Day 2 (24-h period)	*P* value
Brachial SBP (mmHg)	130.52 ± 17.40	133.51 ± 17.54	<0.001	130.22 ± 18.39	133.51 ± 17.54	<0.001
Brachial SBP SD (mmHg)	15.44 ± 4.67	15.91 ± 4.41	0.169	14.75 ± 4.38	15.91 ± 4.41	0.001
Brachial SBP wSD (mmHg)	14.40 ± 4.26	14.89 ± 3.90	0.107	13.80 ± 4.00	14.89 ± 3.90	<0.001
Brachial SBP CV (%)	11.85 ± 3.28	11.93 ± 2.94	0.747	11.34 ± 2.91	11.93 ± 2.94	0.011
Brachial SBP ARV (mmHg)	11.12 ± 3.22	12.32 ± 3.65	<0.001	11.38 ± 3.44	12.32 ± 3.65	<0.001
Brachial DBP (mmHg)	77.94 ± 11.30	78.37 ± 11.17	0.256	77.19 ± 11.59	78.37 ± 11.17	0.002
Brachial DBP SD (mmHg)	10.86 ± 2.62	11.10 ± 2.39	0.252	10.69 ± 2.66	11.10 ± 2.39	0.042
Brachial DBP wSD (mmHg)	10.12 ± 2.37	10.52 ± 2.18	0.040	10.00 ± 2.48	10.52 ± 2.18	0.008
Brachial DBP CV (%)	14.15 ± 3.65	14.37 ± 3.45	0.404	14.04 ± 3.55	14.37 ± 3.45	0.204
Brachial DBP ARV (mmHg)	8.39 ± 1.98	9.29 ± 2.12	<0.001	8.77 ± 2.20	9.29 ± 2.12	0.002
Aortic SBP (mmHg)	118.57 ± 15.35	121.72 ± 15.51	<0.001	118.50 ± 16.00	121.72 ± 15.51	<0.001
Aortic SBP SD (mmHg)	14.33 ± 4.30	14.80 ± 4.14	0.104	13.89 ± 4.19	14.80 ± 4.14	0.002
Aortic SBP wSD (mmHg)	13.50 ± 4.06	13.86 ± 3.61	0.186	13.09 ± 3.95	13.86 ± 3.61	0.006
Aortic SBP CV (%)	12.13 ± 3.43	12.19 ± 3.17	0.773	11.74 ± 3.16	12.19 ± 3.17	0.047
Aortic SBP ARV (mmHg)	10.73 ± 3.15	12.05 ± 3.33	<0.001	11.12 ± 3.37	12.05 ± 3.33	<0.001
Aortic DBP (mmHg)	79.51 ± 11.41	79.92 ± 11.37	0.301	78.79 ± 11.64	79.92 ± 11.37	0.005
Aortic DBP SD (mmHg)	10.58 ± 2.43	10.79 ± 2.30	0.276	10.46 ± 2.52	10.79 ± 2.30	0.074
Aortic DBP wSD (mmHg)	9.82 ± 2.18	10.16 ± 2.08	0.060	9.72 ± 2.30	10.16 ± 2.08	0.015
Aortic DBP CV (%)	13.49 ± 3.27	13.68 ± 3.14	0.435	13.43 ± 3.18	13.68 ± 3.14	0.285
Aortic DBP ARV (mmHg)	8.14 ± 1.81	8.99 ± 1.95	<0.001	8.53 ± 2.00	8.99 ± 1.95	0.002

Data are presented as mean ± SD. ARV, average real variability; BP, blood pressure; CV, coefficient of variation; SD, standard deviation; wSD, weighted SD.

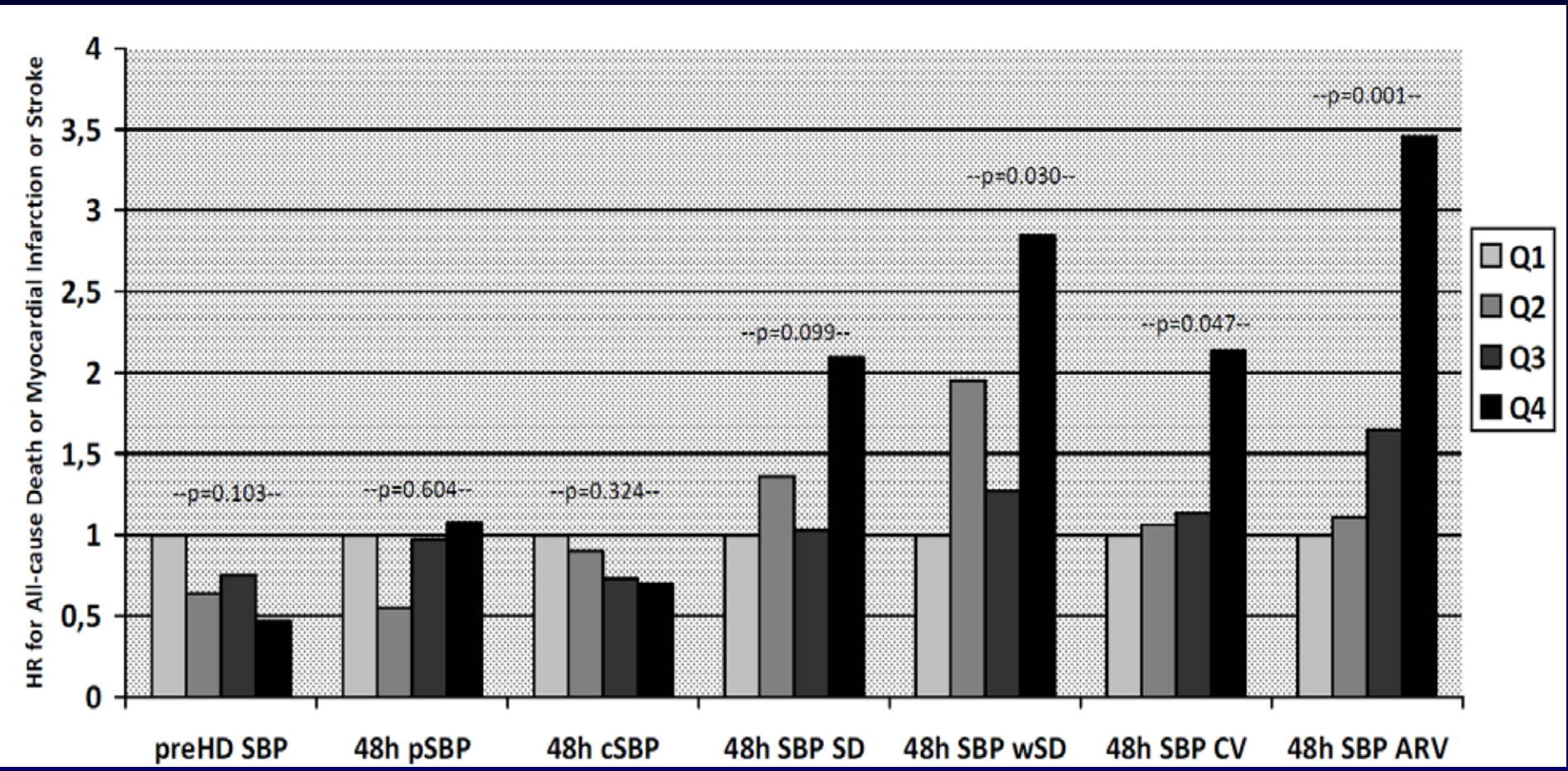
Karpetas et al. J Hypertens 2017

BPV and outcomes in hemodialysis

STUDY	POPULATION	N	BPV TYPE	DESIGN	FOLLOW-UP	MAIN RESULTS
Tozawa et al, NDT 1999	HD pts	144	Visit-to-visit pre-HD	Retrospective cohort	38 months	BPV associated with all-cause mortality
Brunelli et al, Am J Kidn Dis 2008	Incident HD pts	6,961	Visit-to-visit pre-HD	Retrospective cohort	6.1 months	BPV independently associated with all-cause mortality
Rossignol et al. Hypertension 2012	HD pts with LVH	397	Visit-to-visit pre-HD	Post-hoc RCT (FOSIDIAL)	24 months	BPV associated with composite CV outcome when added to prediction model, BP was not
Di Iorio et al, J Nephrol 2013	HD pts	1,088	Visit-to-visit pre-HD (all)	Retrospective cohort	5 years	BPV independently associated with CV- but not all-cause mortality
Flythe et al, Am J Kidn Dis 2013	HD pts	6,393	Intradialytic	Retrospective cohort		BPV independently associated with all-cause mortality, CV mortality
Kim et al. Kidn Blood Press Res 2013	HD pts	2,174	Intradialytic and Interdialytic	Retrospective cohort	5 years	BPV associated with all-cause mortality in pts<55 years
Chang et al. J Hum Hypertens 2014	HD pts	1844	Visit-to-visit pre-HD	Post-hoc RCT (HEMO)	2.5 years	BPV independently associated with all-cause but not CV mortality
Selvarajah et al. PLOS One 2014	Incident HD pts	203	Visit-to-visit pre-HD at 3-6 m	Retrospective cohort	2 years	BPV independently associated with all-cause mortality
Shafi et al. J Am Soc Nephrol 2017	HD pts	11,291	Visit-to-visit pre-HD	Prospective cohort	22 months	BPV independently associated with all-cause mortality, CV mortality, CV events
Sumida et al. J Hypertens 2017	Pre-dialysis CKD (1 year before)	17,729	Visit-to-visit	Retrospective cohort	24 months	BPV independently associated with all-cause but not CV mortality

Short-term BPV and risk in hemodialysis

170 HD patients, 28 months f-u, primary outcome: death, MI and stroke



Sarafidis et al 2018 (submitted)

Υπέρταση στο Τελικό Στάδιο ΧΝΝ

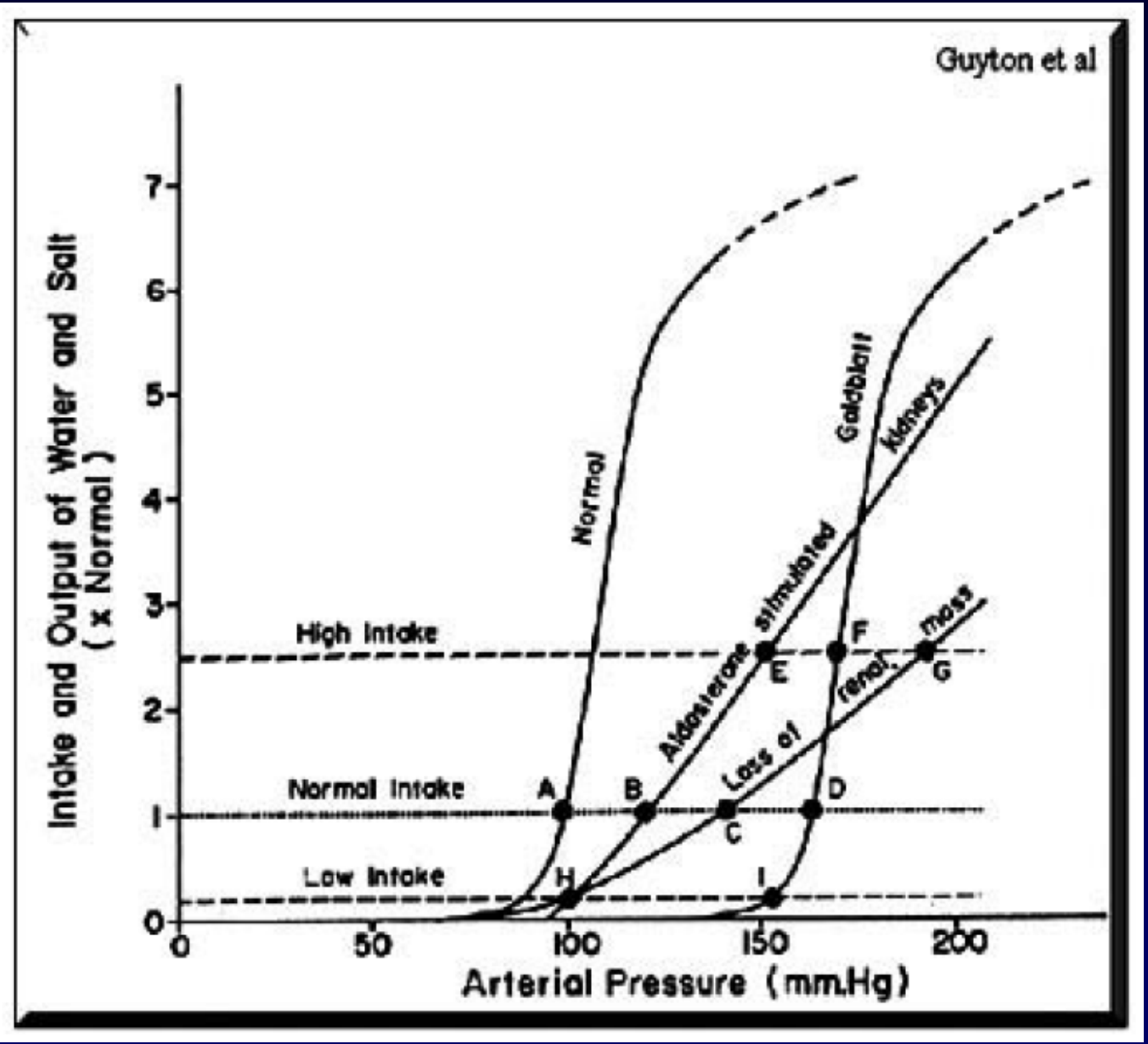
Βασική Παθοφυσιολογία

BOX 2: Main pathogenic mechanisms of hypertension in dialysis patients

- Sodium and volume overload
- Increased arterial stiffness
- Activation of the SNS
- Activation of the RAAS
- Endothelial dysfunction (i.e. imbalance between endothelium-derived vasodilators and vasoconstrictors)
- High prevalence of sleep apnea
- Use of recombinant erythropoietins (rhuEPOs)

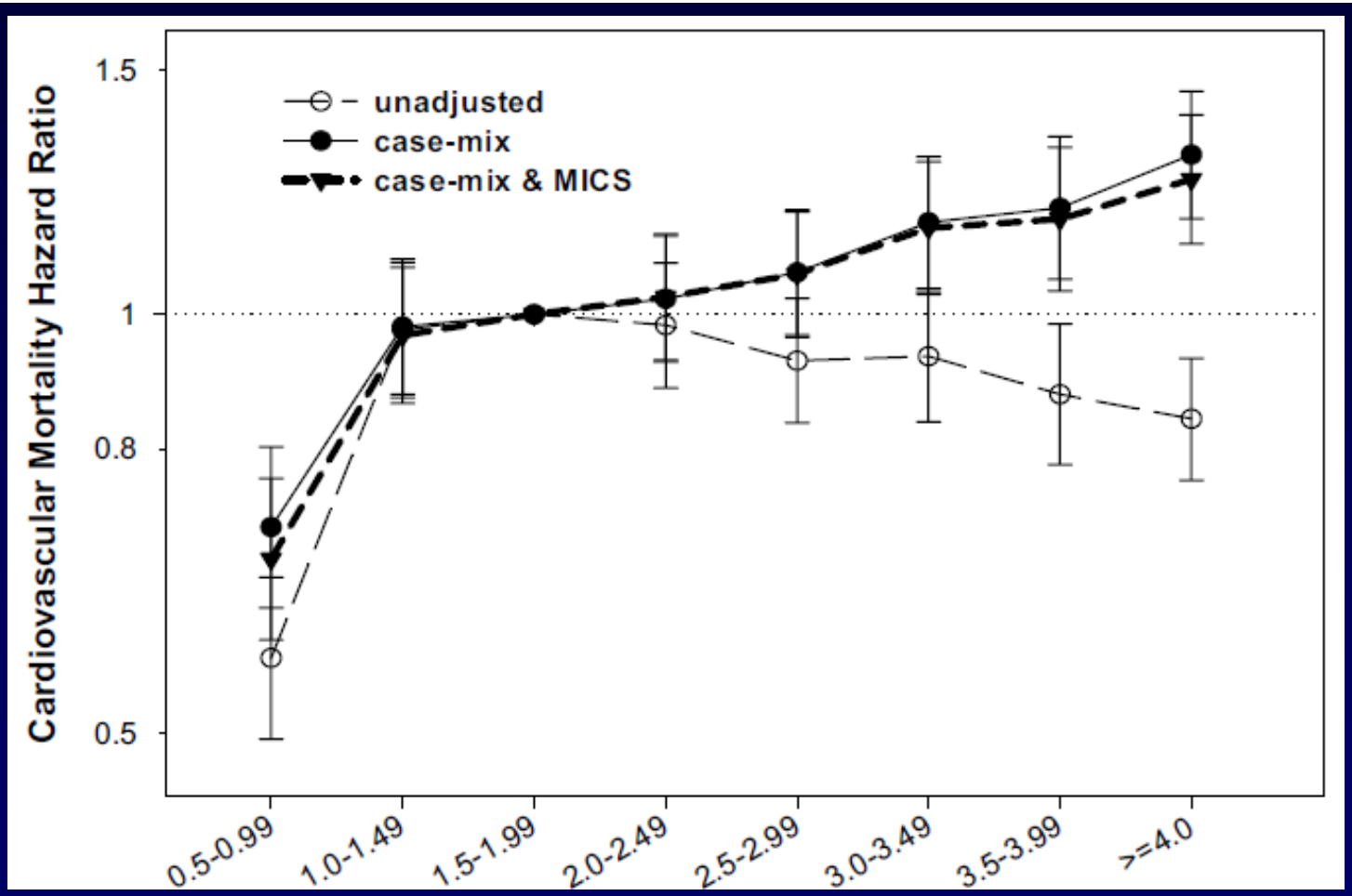
Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

Sodium Sensitivity in CKD



Fluid Retention Is Associated With Cardiovascular Mortality in Patients Undergoing Long-Term Hemodialysis

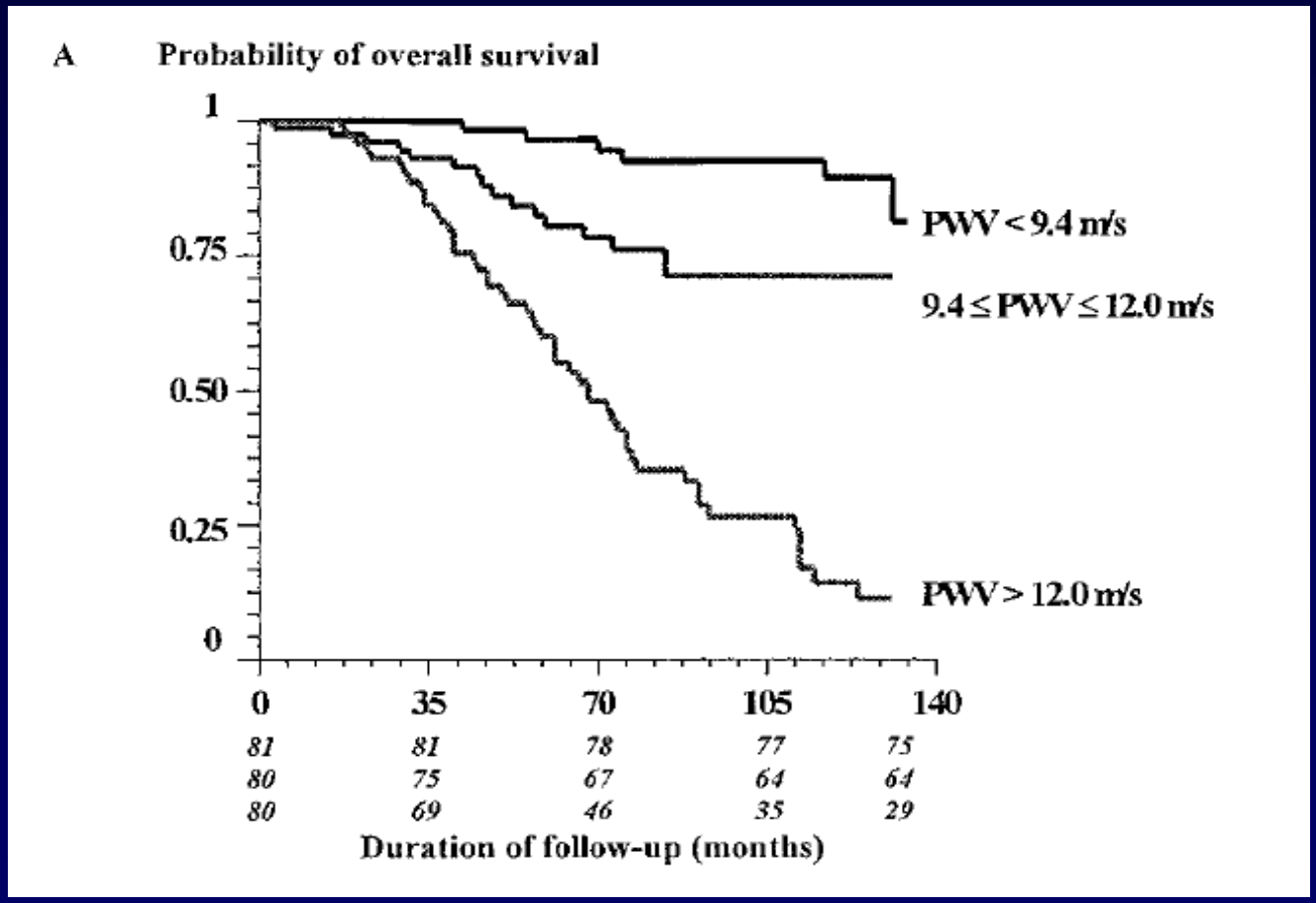
Kamyar Kalantar-Zadeh, MD, MPH, PhD; Deborah L. Regidor, MPH, PhD;
Csaba P. Kovesdy, MD; David Van Wyck, MD; Suphamai Bunnapradist, MD;
Tamara B. Horwich, MD; Gregg C. Fonarow, MD



Kalantar-Zadeh ,et al. Circulation 2009

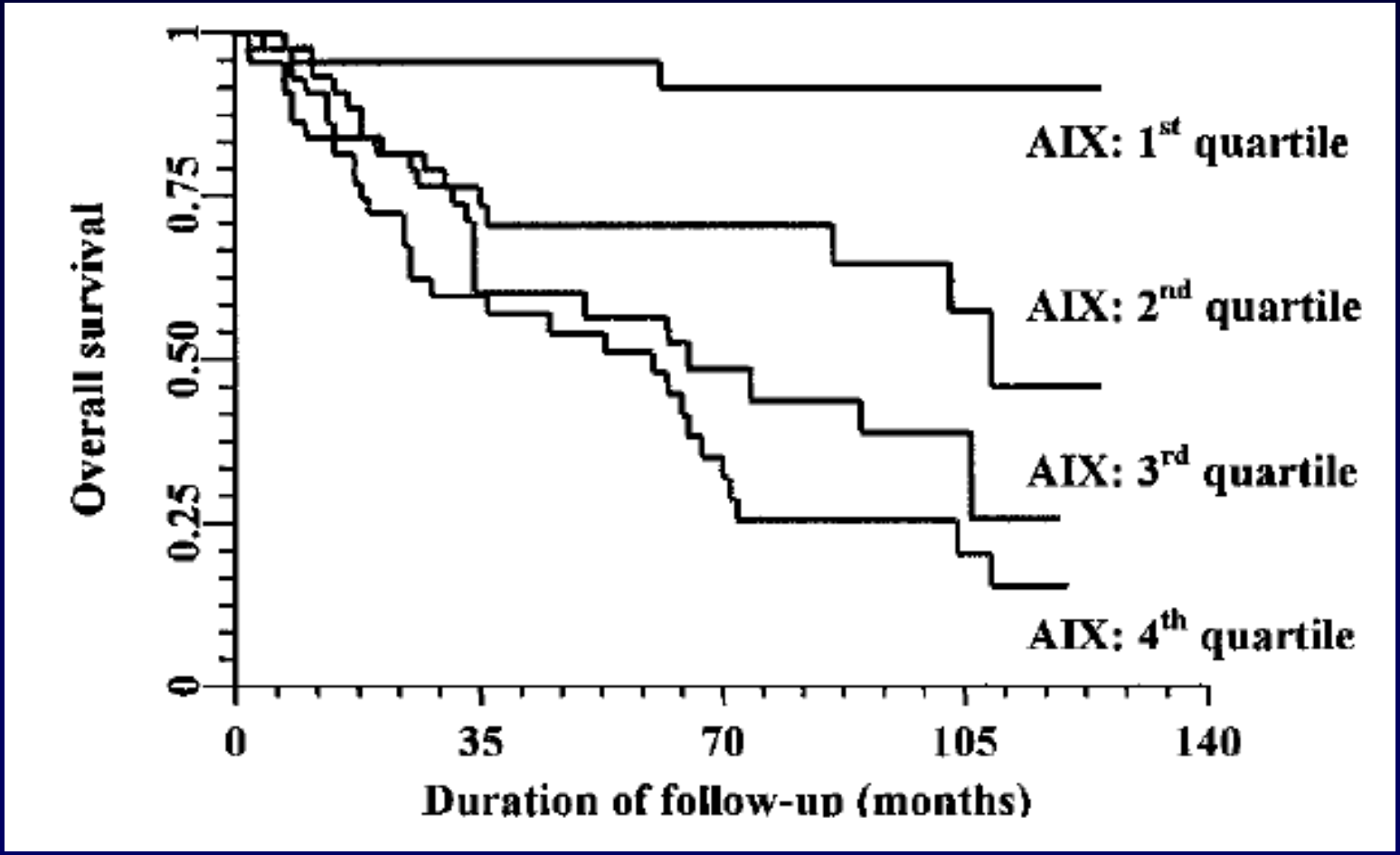
Aortic stiffness - Prognostic role of PWV

In ESRD



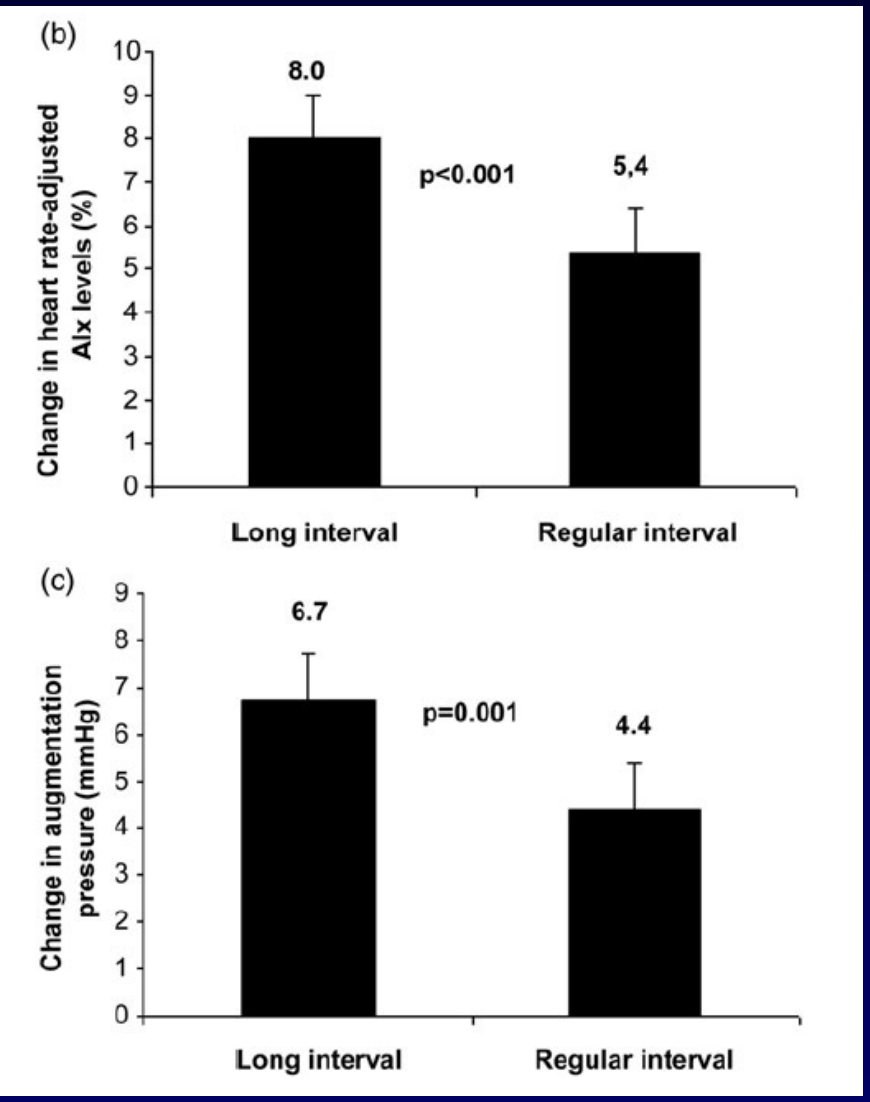
Blacher et al. Circulation 1999

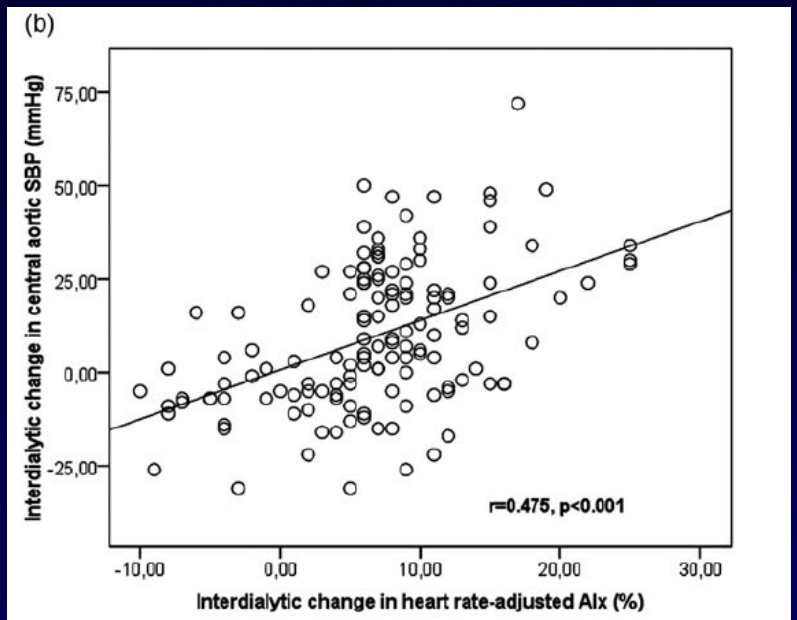
Prognostic Significance of central Augmentation Index (AIX) in ESRD patients

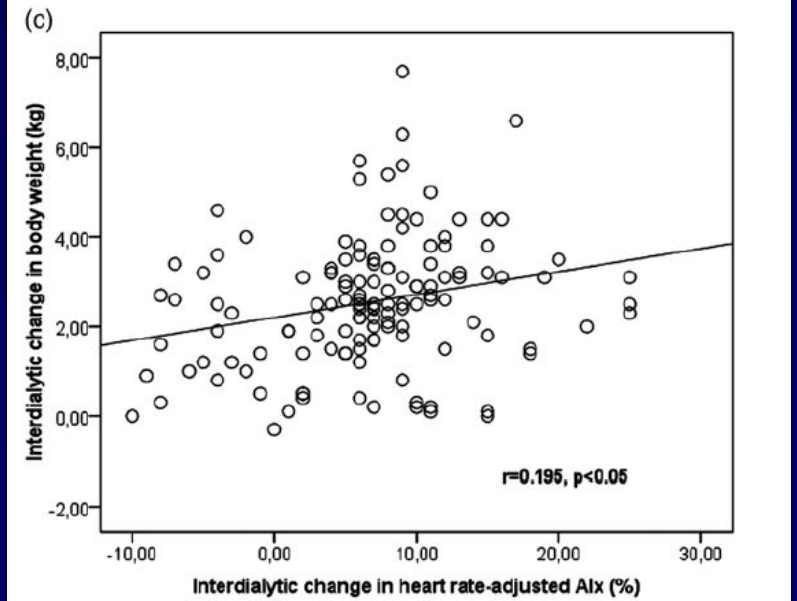


London GM et al. Hypertension, 2001, 38: 434-438.

Augmentation Index changes during long and regular intradialytic intervals

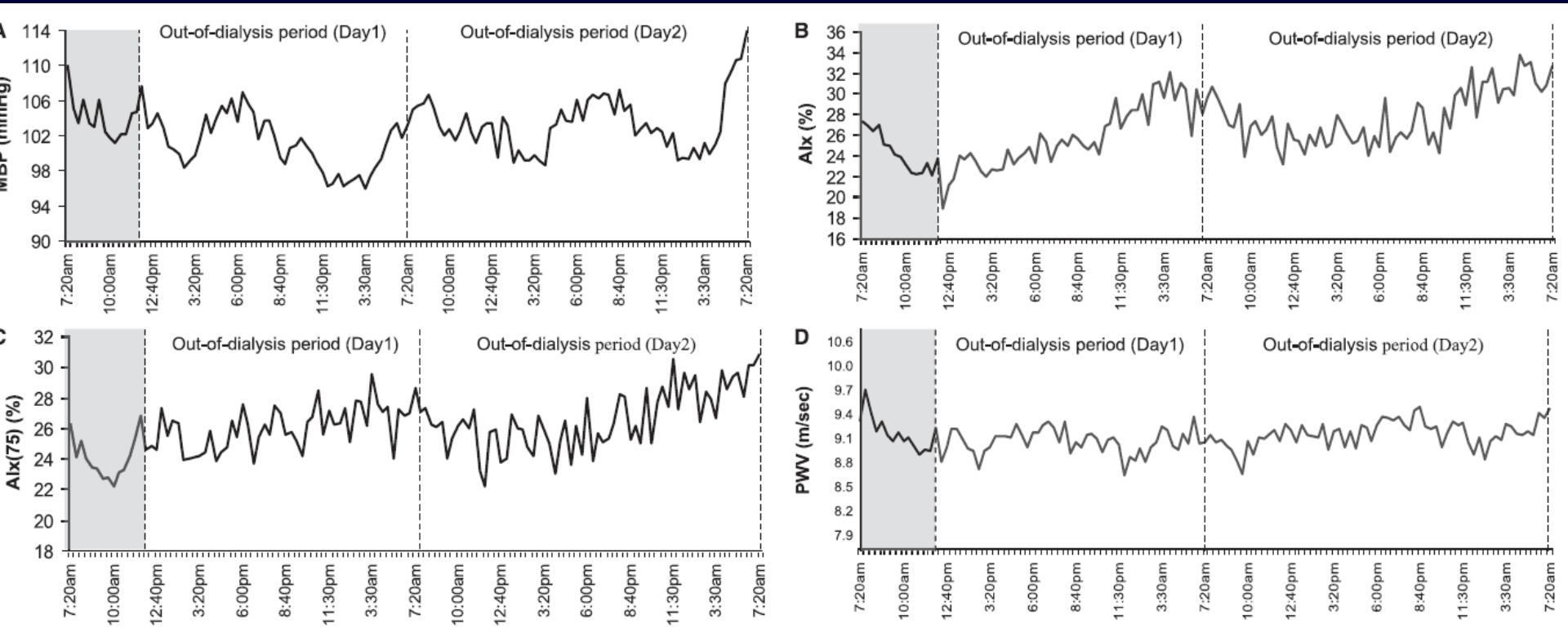






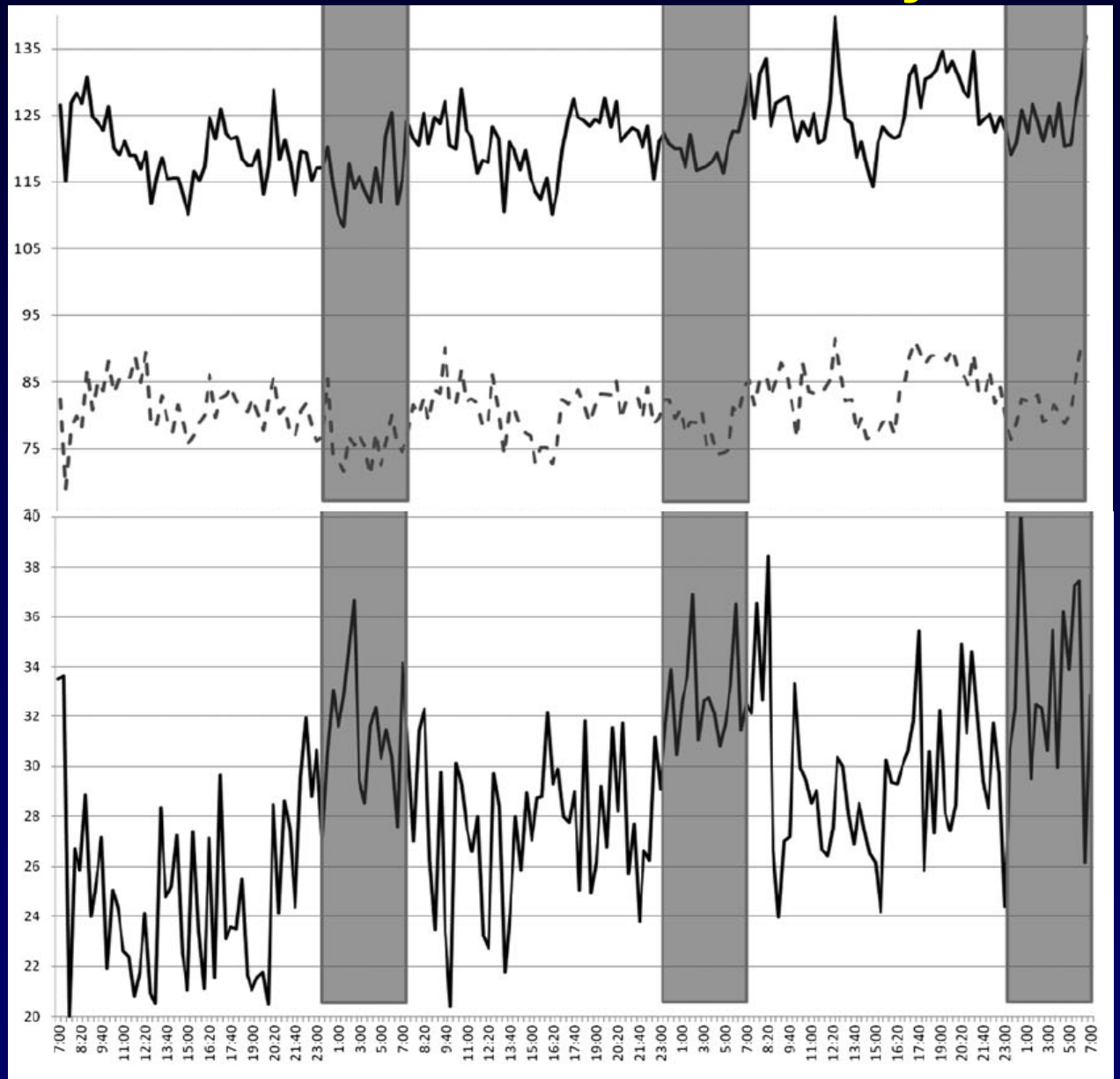
Georgianos, Sarafidis, Haidich et al,. Nephrol Dial Transplant 2013

48-hour recording of Central BP, Aix and PWV in hemodialysis



Karpetas, Sarafidis, Georgianos, et al. Clin J Am Soc Nephrol 2015

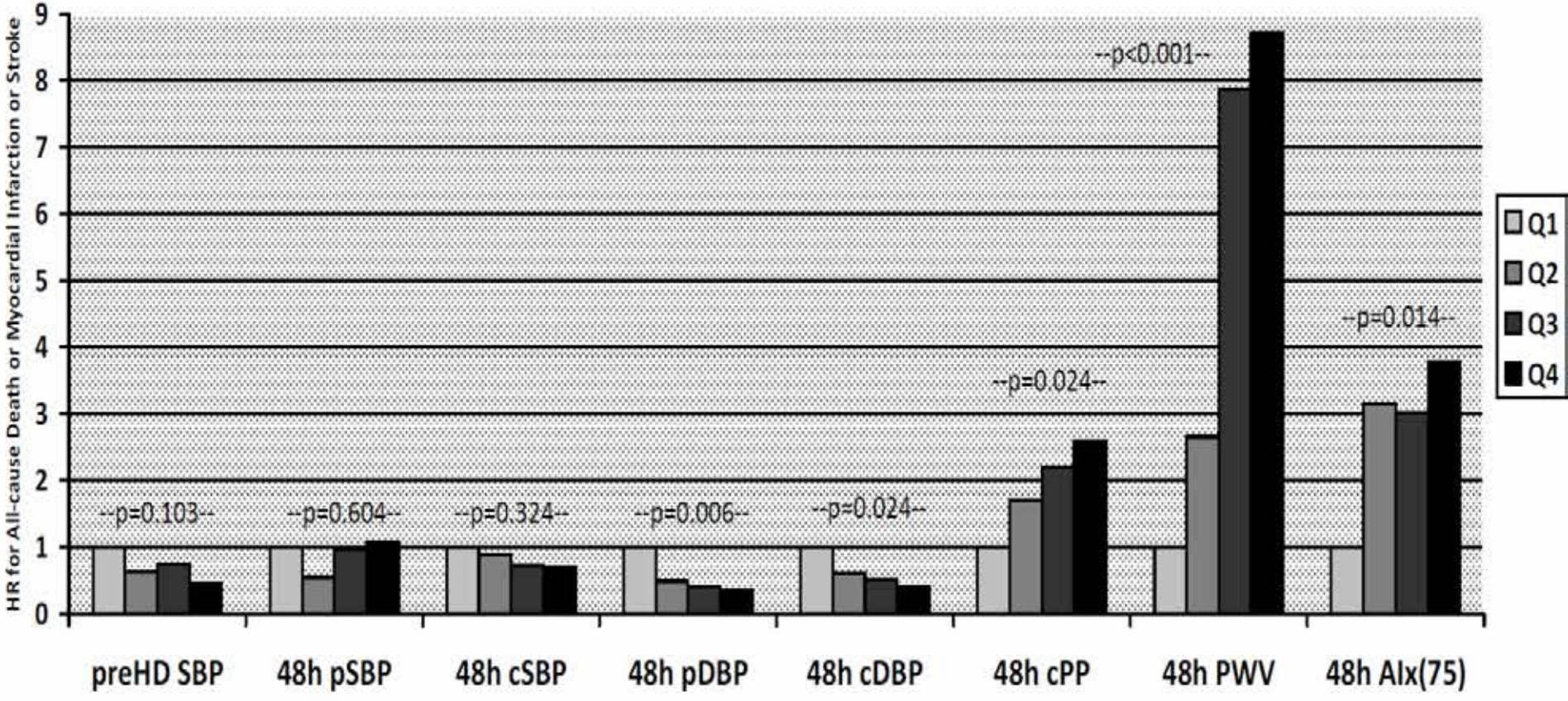
72-hour recording of Central BP, Aix and PWV in hemodialysis



Koutroumpas, Georgianos, Sarafidis, et al. Nephrol Dial Transplant 2015

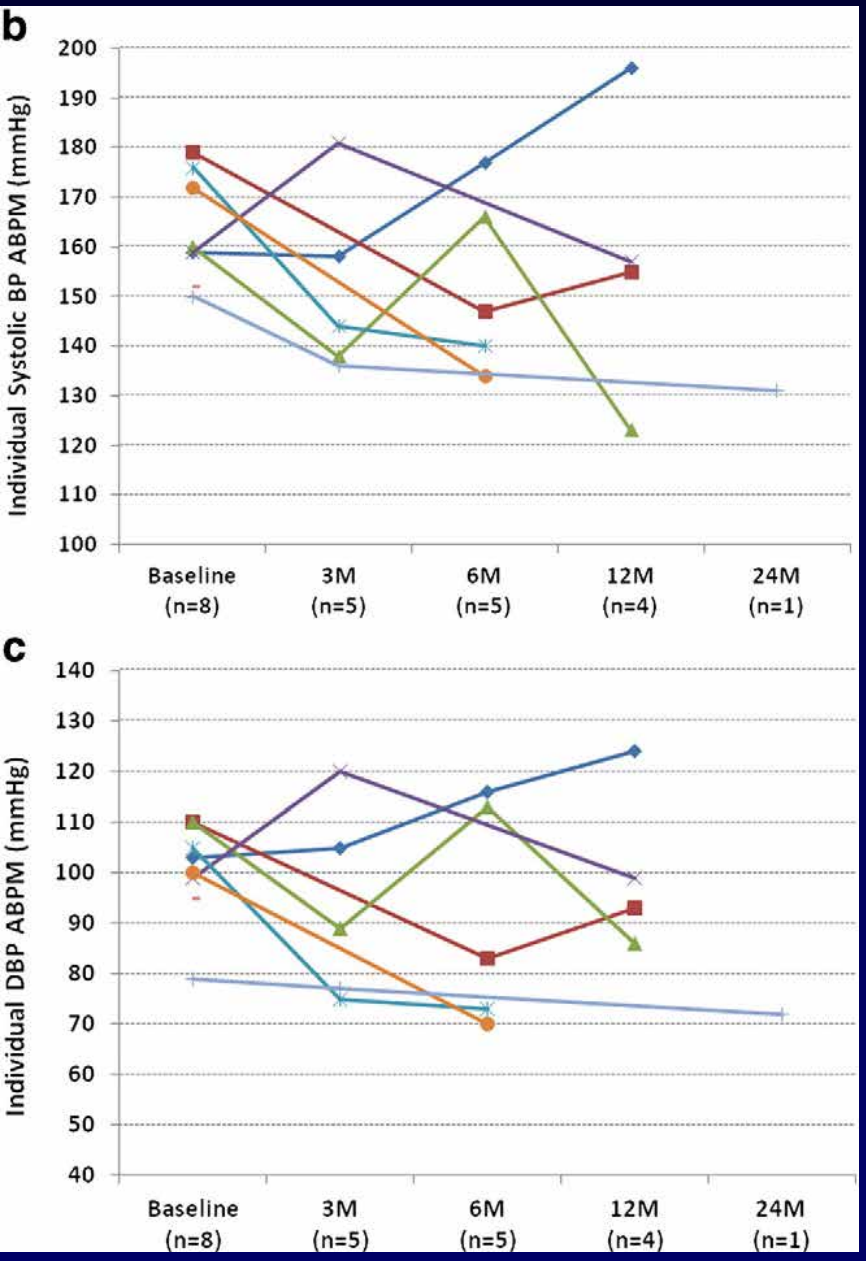
48-hour PWV and CVD risk in hemodialysis

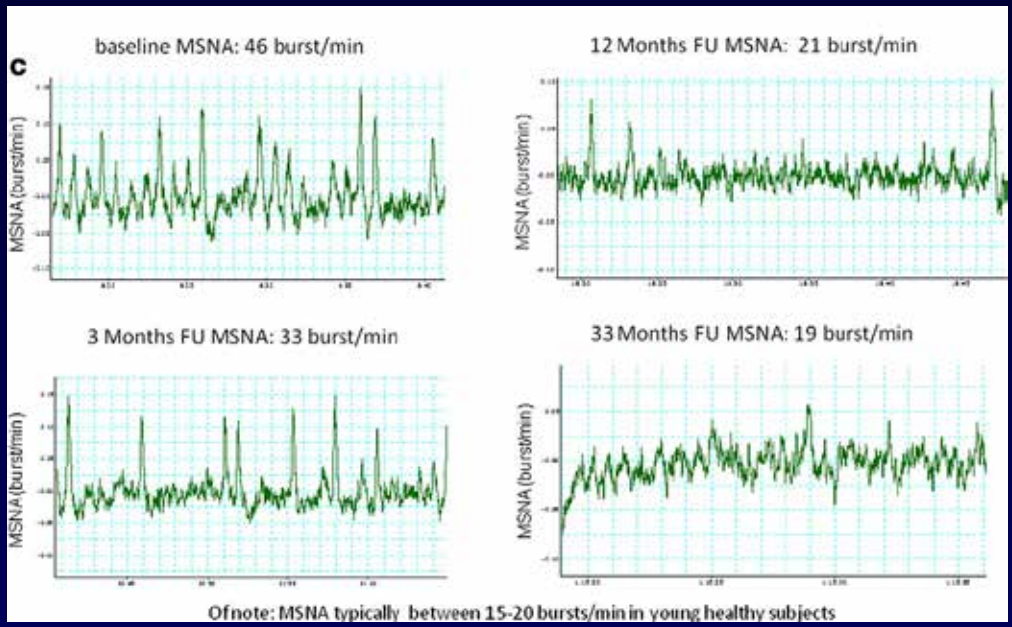
170 HD patients, 28 months f-u, primary outcome: death, MI and stroke



Sarafidis et al. Hypertension 2017

Renal Denervation in ESRD





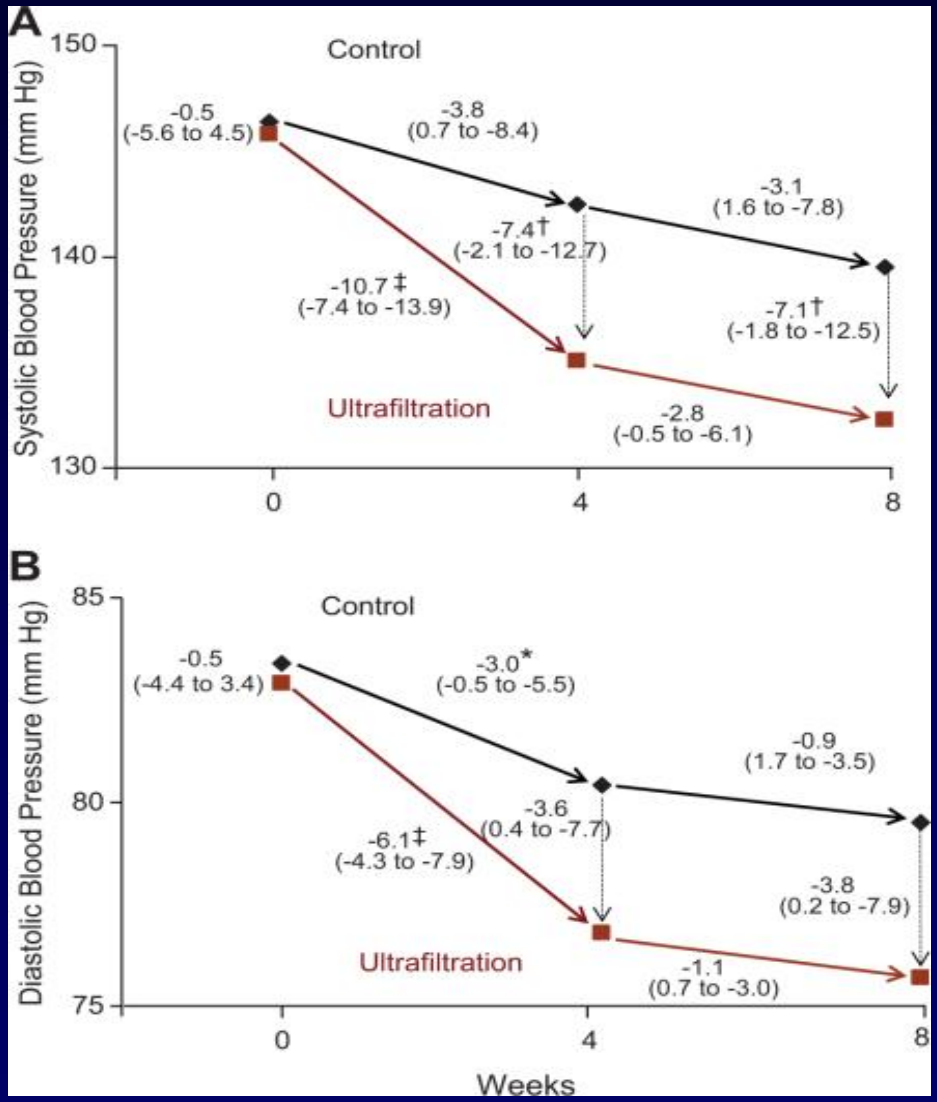
n=12,
a-h drugs from 4.2 to 2.2 at 12 months

Schlaich, et al. Int J Cardiol 2013

Υπέρταση στην Αιμοκάθαρση

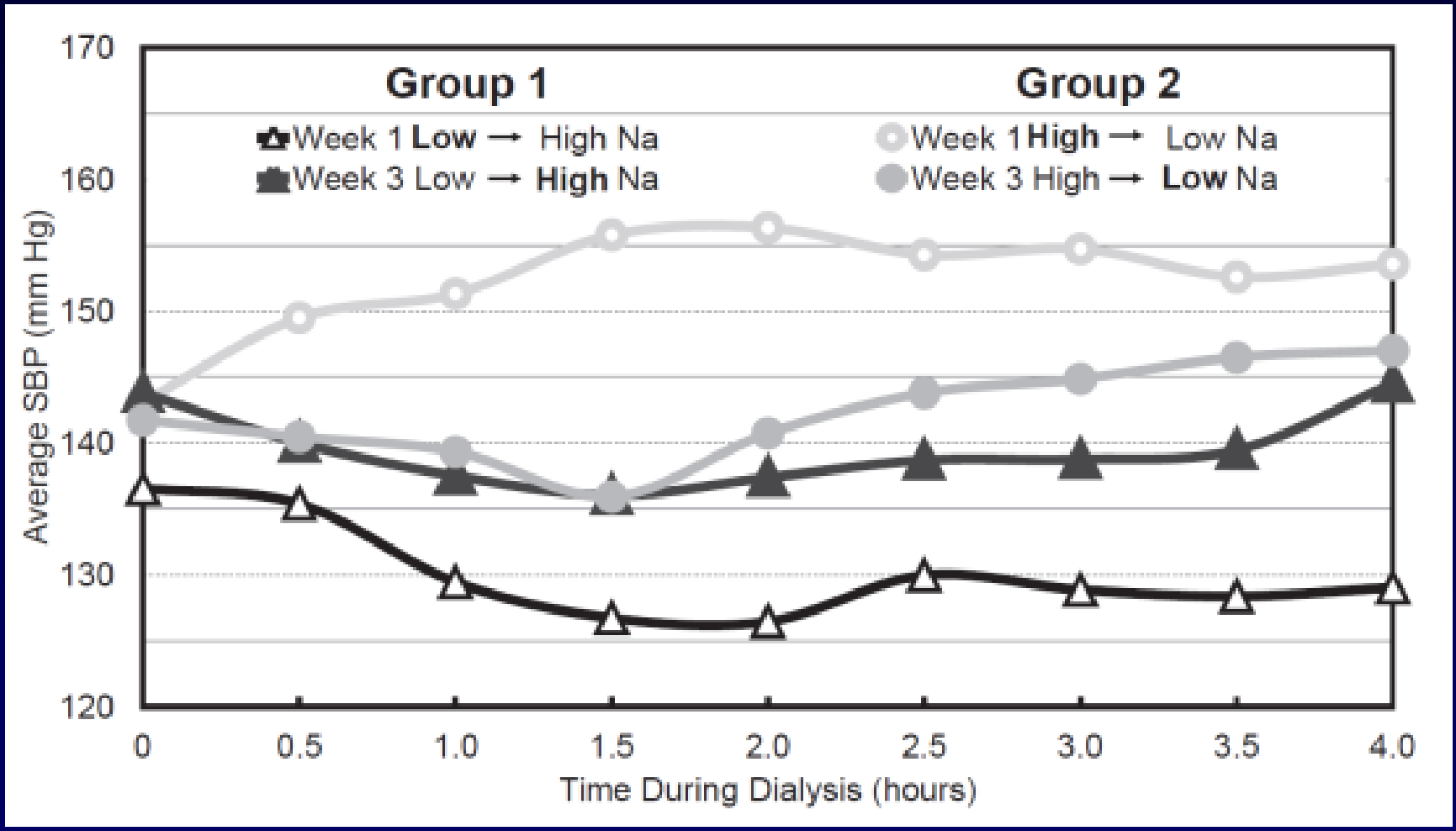
Μη-Φαρμακολογικά Μέτρα

Dry-weight reduction in hypertensive hemodialysis patients (DRIP): a randomized, controlled trial



Agarwal R, et al. Hypertension 2009; 53(3):500-7.

Dialysate [Na+] and Blood Pressure in HD



Inrig, et al. Am J Kidn Dis 2015

BOX 3. Main non-pharmacological measures to reduce sodium and volume overload in hemodialysis patients

- o Achievement of individual patient's dry-weight
- o Minimization of inter- and intradialytic sodium gain
  - • Restriction of sodium intake to less than 65 mmol (1.5 g of sodium or 4 g of sodium chloride) per day
  - • Decreasing dialysate sodium towards pre-dialysis sodium in selected individuals
  - • Avoidance of sodium-containing or sodium-exchanging drugs
- o Avoidance of short (i.e. <4 hours) dialysis duration

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

BOX 4. Barriers towards achievement of dry weight in hemodialysis patients with hypertension

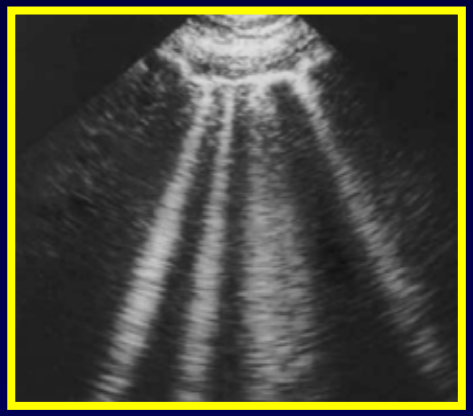
- Difficulty to objectively assess dry weight
- Fear of patient symptoms (intradialytic hypotension, muscle cramps, nausea and vomiting)
- Risk of complications (cardiovascular events, arteriovenous access loss)
- Physician and nurse inertia/ ease of prescribing a new drug versus the complex procedure of dry weight probing
- Absence of patient education on dietary sodium restriction / misguided emphasis in fluid restriction
- Low patient compliance with sodium restriction / high interdialytic weight gain
- Use of sodium containing medications
- Inappropriate dialysate sodium
- Use of high ultrafiltration rates
- Short dialysis sessions
- Concomitant diseases (heart failure, autonomic dysfunction)
- Use of high number of antihypertensive agents
- Use of “fast and easy” solutions to treat intradialytic hypotension (i.e. cessation of ultrafiltration, hypertonic sodium infusions, increasing dialysate sodium concentration, premature termination of dialysis)

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 2017

The effect of a dry-weight probing guided by lung ultrasound on ambulatory aortic blood pressure and ambulatory arterial stiffness in hemodialysis patients. A LUST sub-study.

P. Sarafidis, C. Loutradis, A. Papagianni, D. Papadopoulou, C. Zoccali, and G. London

Aim: to evaluate the outcome of a treatment strategy for dry weight probing, based on volume overload quantification with lung ultrasound, on 24-hour aortic systolic BP and arterial stiffness in hypertensive HD patients



Inclusion Criteria:

1. Patients aged >18 years
2. Patients on hemodialysis for a period of >3 months
3. Patients on a standard thrice-weekly hemodialysis schedule.
4. A history of hypertension, confirmed by valid Home BP readings (as discussed below)
5. Ability to understand and provide a written informed consent to participate in the study.

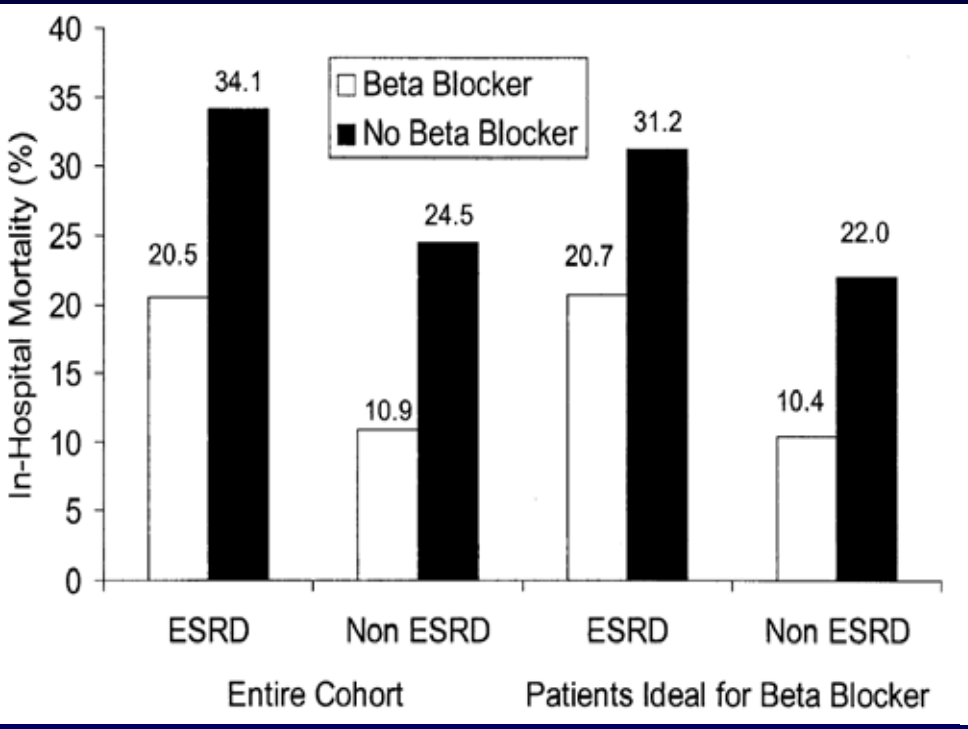
https://clinicaltrials.gov/ct2/show/NCT03058874

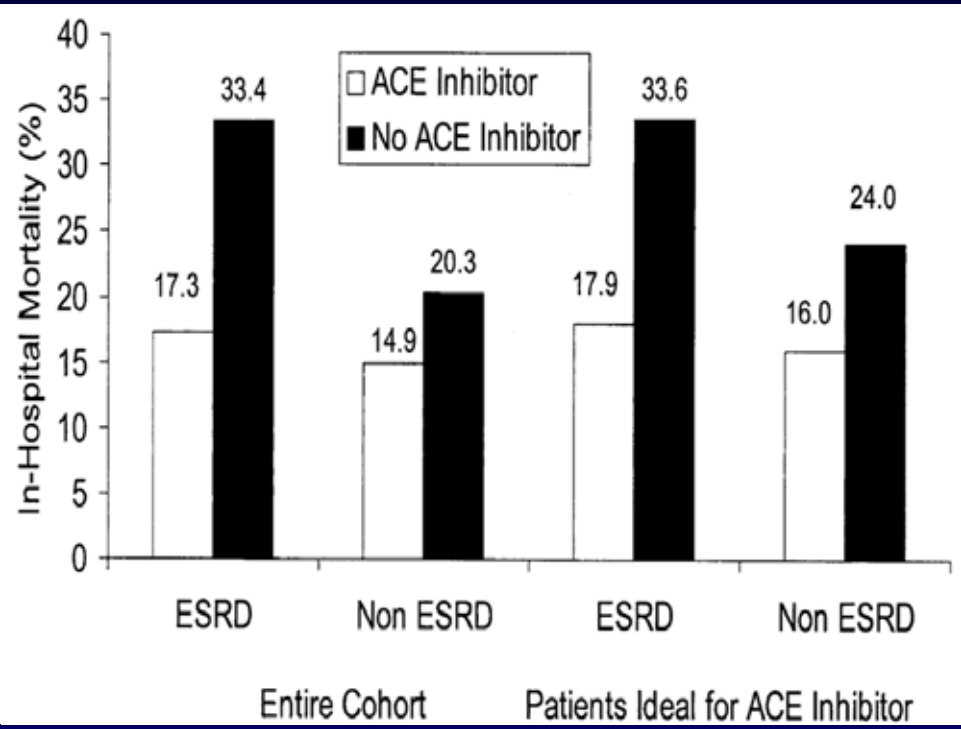
Υπέρταση στην Αιμοκάθαρση

Φαρμακολογικά Μέτρα

Observational studies of β-blockers **and ACE-Is**

ESRD Database + Cooperative Cardiovascular Project Database
Association of medication classes with 30-day mortality post-MI in ESRD





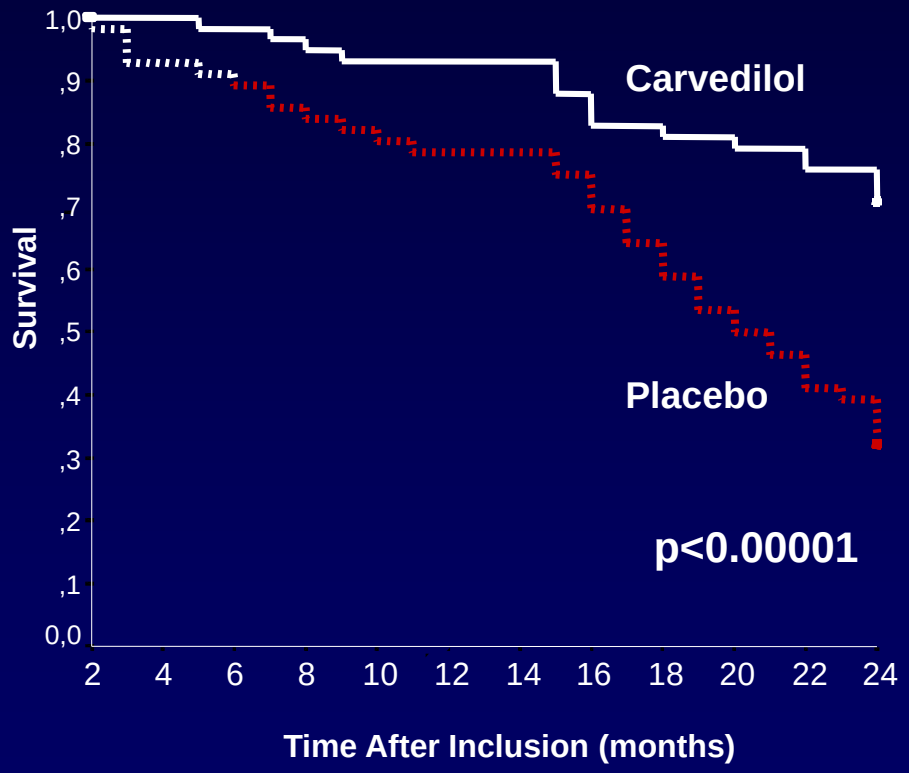
Berger et al. JACC 2003;42:201-208

Carvedilol in Hemodialysis patients with NYHA II-III HF

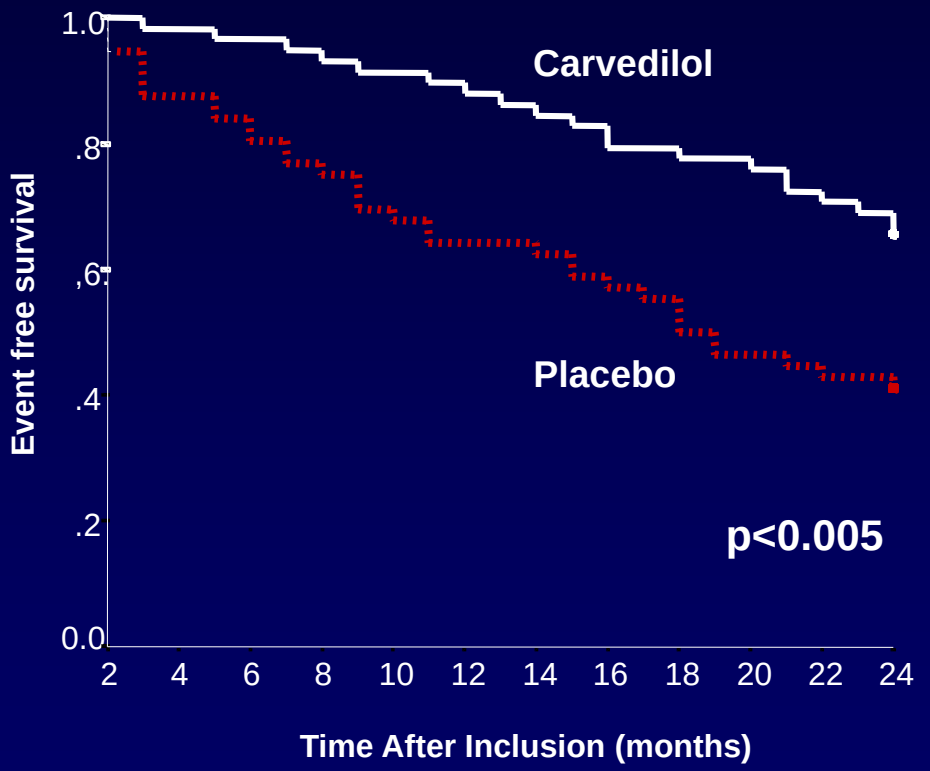
Cardiovascular mortality and all cause hospitalization

n=114

CARDIOVASCULAR SURVIVAL



EVENT-FREE SURVIVAL

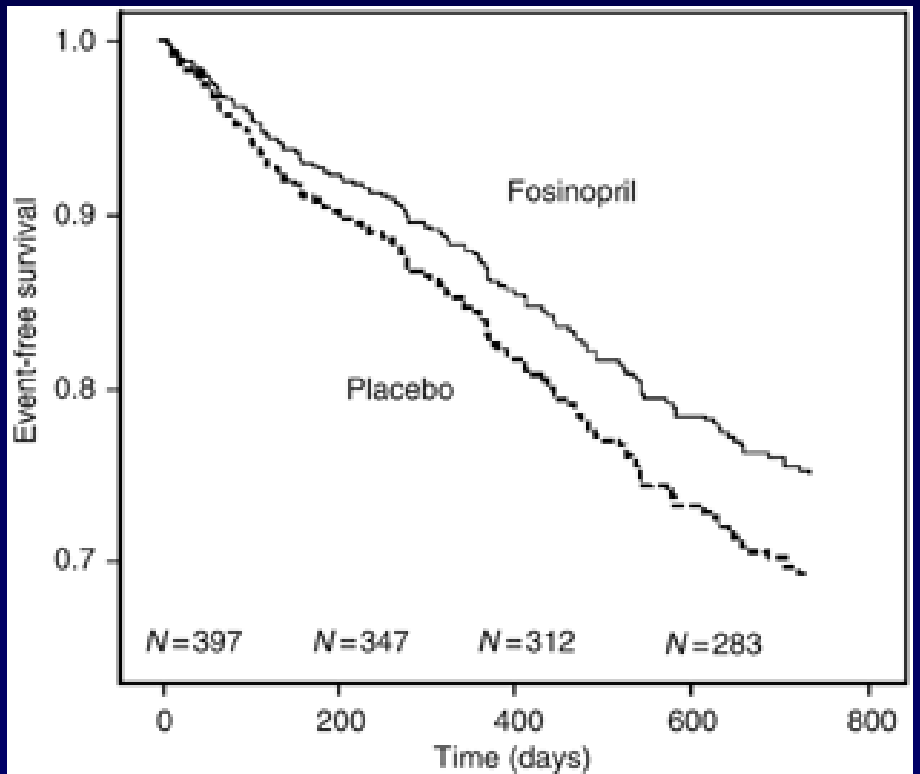


Cice et al. JACC 2003; 41:1438-1444

Fosinopril in Dialysis (FOSIDIAL) Study

	Placebo	Fosinopril	Difference (95% CI)	*P*-value (ANCOVA)
Normotensive patients (n=159)				
Change in SBP	5.3 (14.2)	5.1 (11.9)	−0.23 (−4.6, 4.1)	0.91
Change in DBP	1.2 (7.4)	1.2 (7.9)	−0.03 (−2.3, 2.2)	0.98
Hypertensive patients (n=238)				
Change in SBP	−5.4 (15.4)	−11.7 (13.4)	−6.3 (−10.3, −2.4)	0.002
Change in DBP	−2.1 (9.1)	−4.9 (9.7)	−2.8 (−5.1, −0.5)	0.01
Response proportion (<140/90 and no DBP value <50 mm Hg)				
Normotensive	65% (84)	71% (75)	RR 1.08 (0.87–1.33)	0.49
Hypertensive	19% (117)	35% (121)	RR 1.85 (1.18–2.89)	0.008

ANCOVA, analysis of covariance; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.

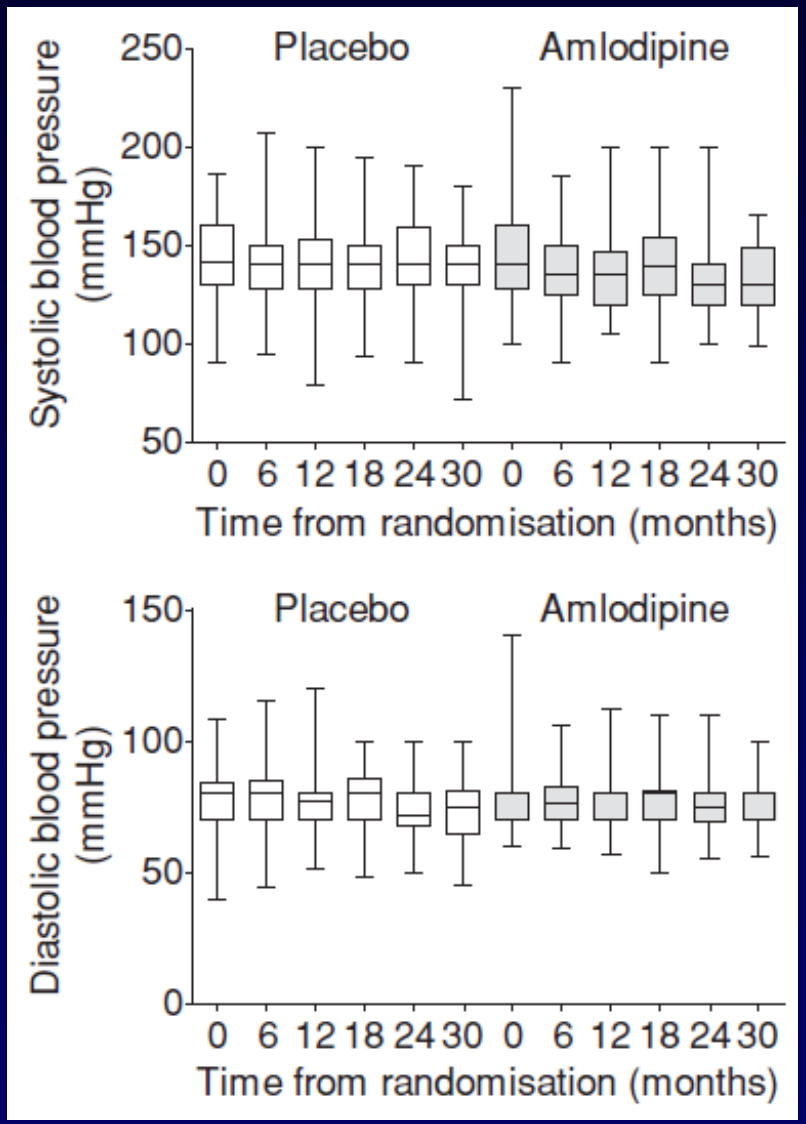


Primary end-point: cardiovascular death, resuscitated death, nonfatal stroke, heart failure, myocardial infarction, or revascularization.

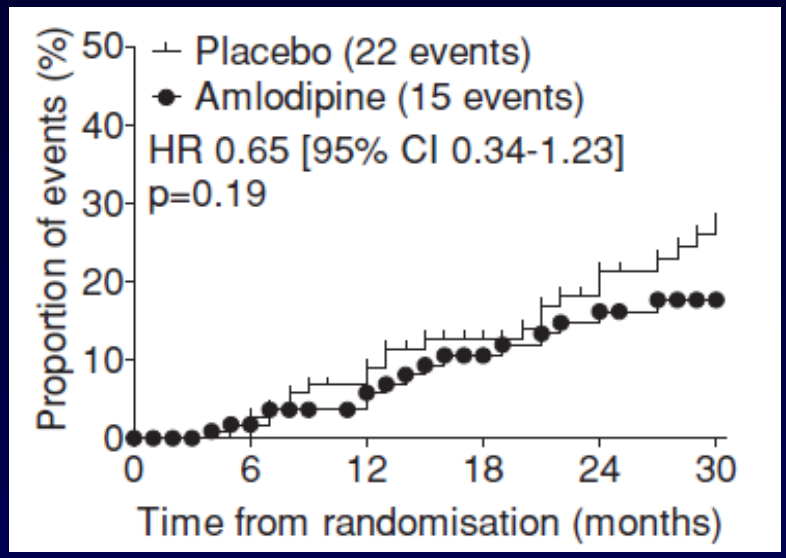
ITT: RR=0.93, 95% CI 0.68-1.26, P=0.35.

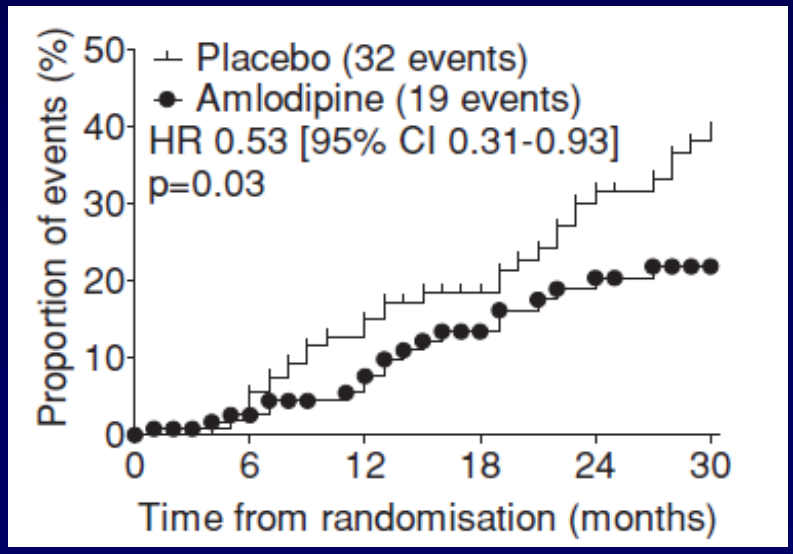
Zannad et al. Kidney Int 2006;70:1318-1324

Amlodipine in Hemodialysis Patients



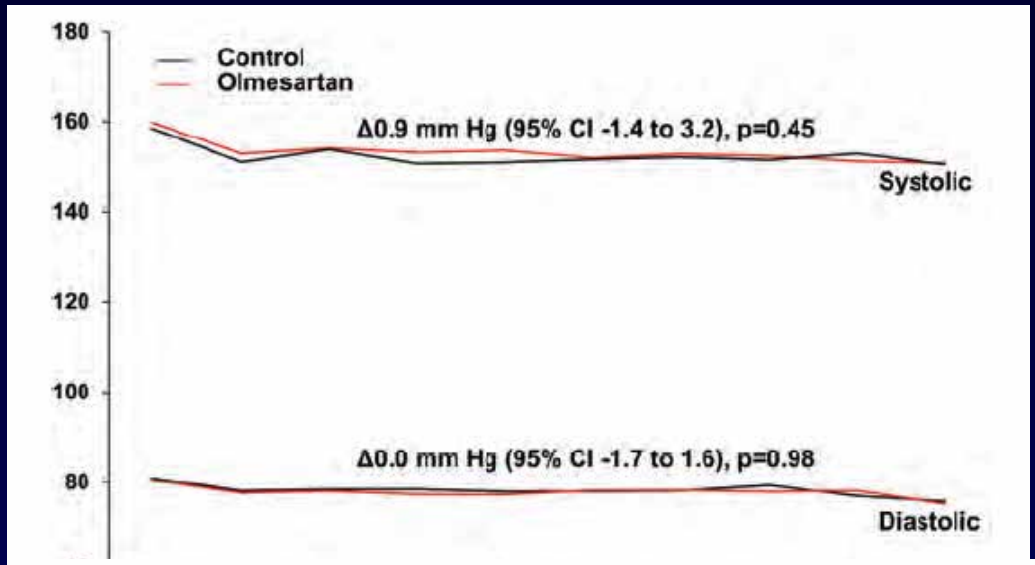
n=251





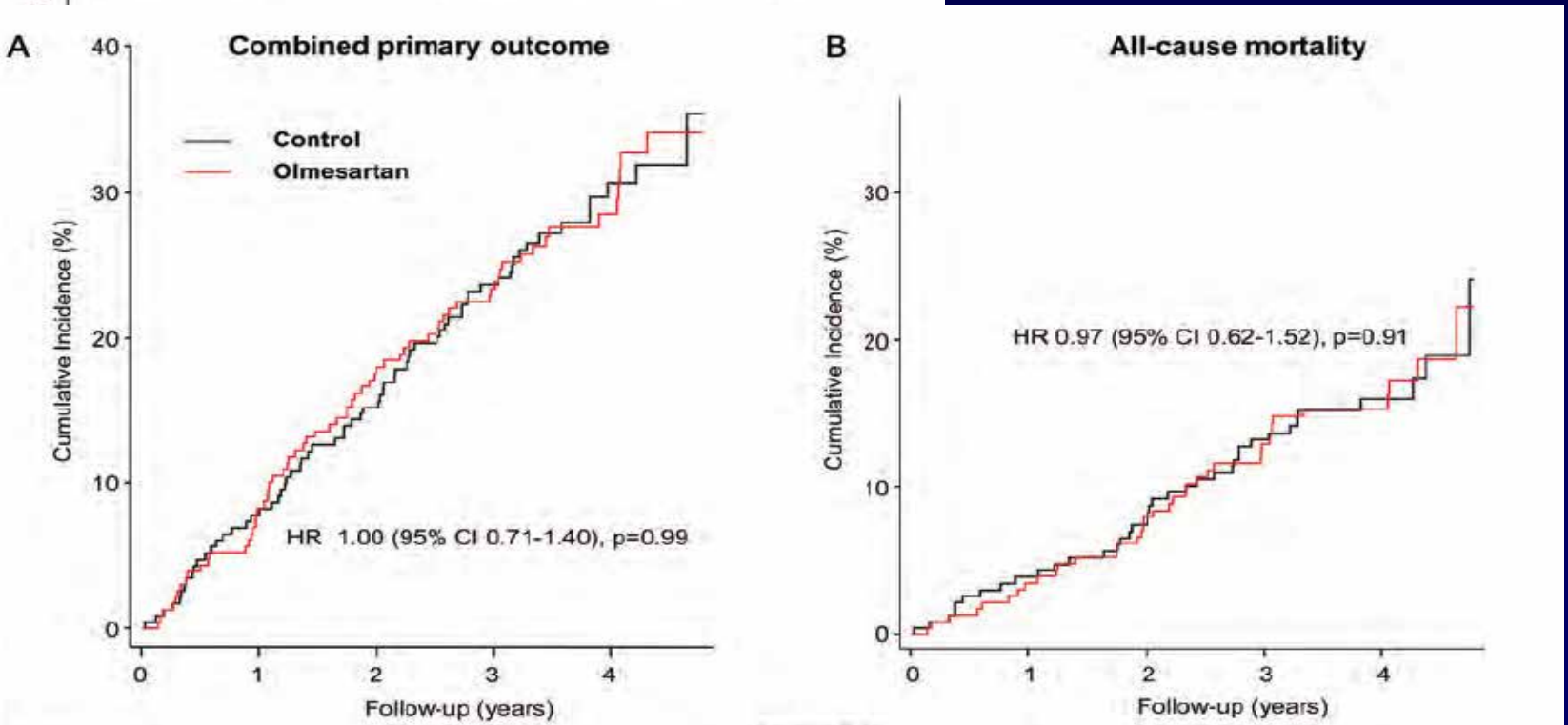
Tepel et al. Nephrol Dial Transplant 2008

Olmesartan vs active treatment in Hemodialysis



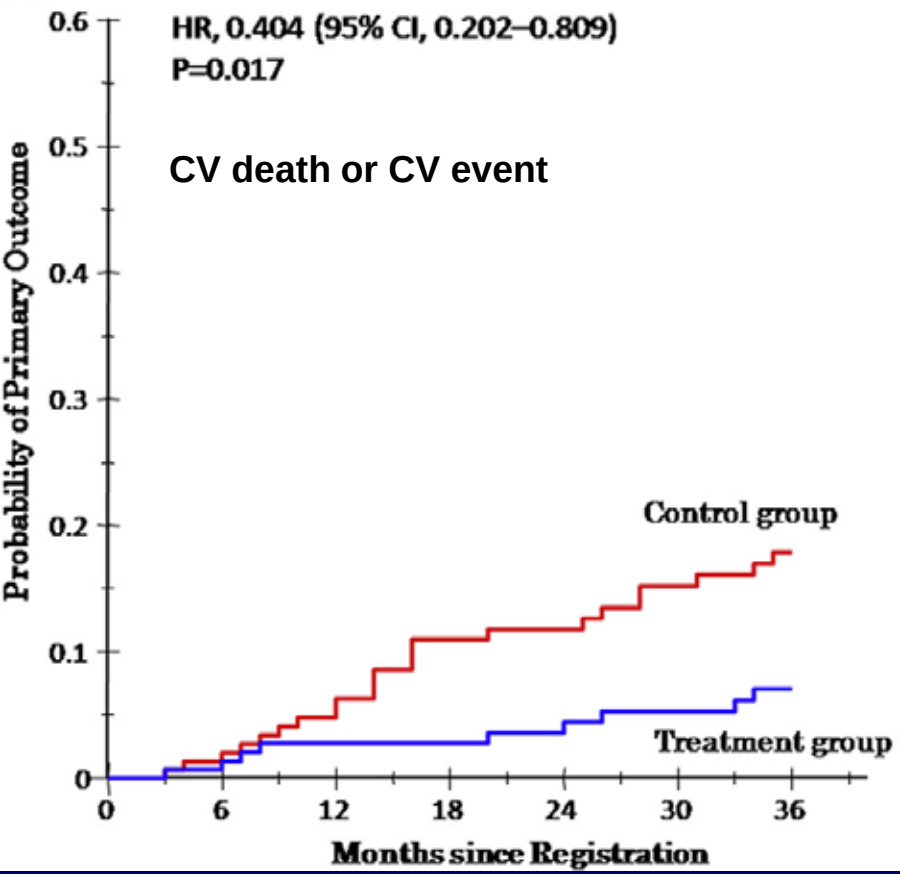
n=469

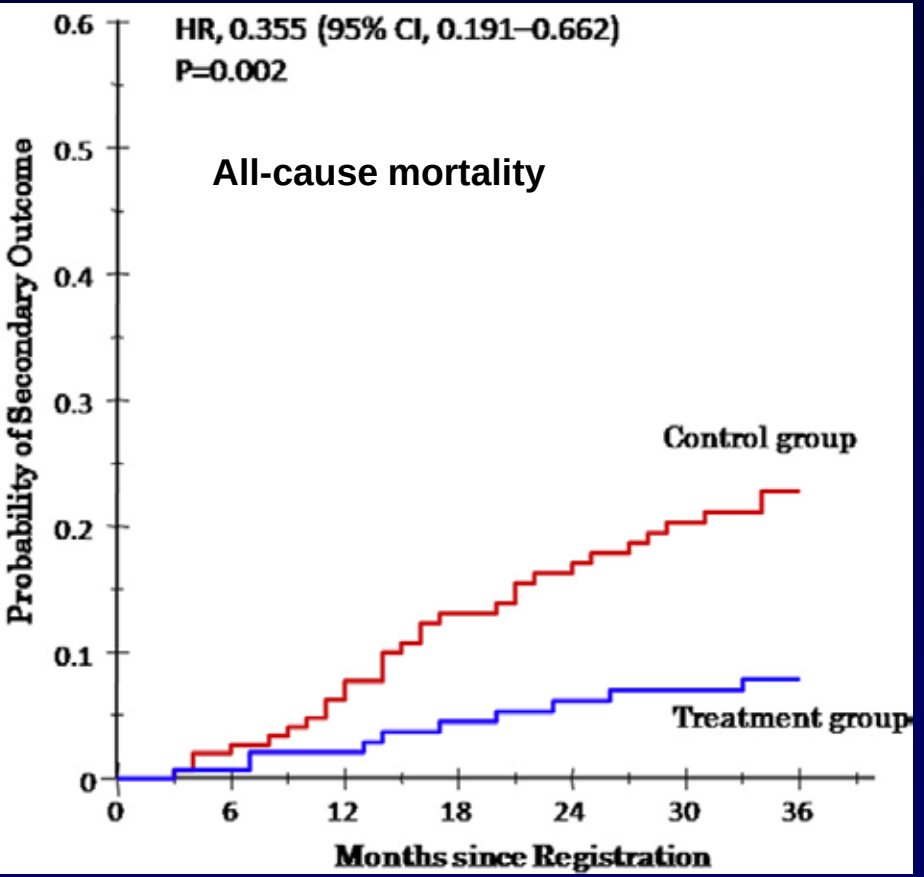
Iseki et al. Nephrol Dial Transplant 2013



Spironolactone in Hemodialysis Patients

n=309 HD patients, spironolactone 25 mg vs plb, 3 years f-u





Matsumoto et al. J Am Col Cardiol 2014

Antihypertensive Drugs in Hemodialysis

	Usual dose	Excretion	GFR <10 ml/min	Removal with dialysis		Supplement for dialysis
				Hemodialysis	Peritoneal dialysis	
Diuretics						
Acetazolamide	250 mg q6–8 h	K	Avoid	Unknown	Unknown	Not applicable
Amiloride	5–10 mg q.d.	K	Avoid	N/A	N/A	Not applicable
Bumentanide	0.5–2 mg q8–12 h	K	100%	None	None	None
Chlorthalidone	30–60 mg q.d.	K	Avoid	N/A	N/A	Not applicable
Ethacrynic acid	50–100 mg b.i.d.	L (K)	Avoid	None	None	Not applicable
Furosemide	40–80 mg b.i.d.	K (L)	100%	None	None	None
Hydrochlorothiazide	25–50 mg q.d.	K	Avoid	None	None	Not applicable
Indapamide	2.5 mg q.d.	K	Avoid	None	None	Not applicable
Metolazone	5–10 mg q.d.	K (L)	100%	None	None	None
Spironolactone	50–100 mg q.d./b.i.d.	K (L)	Avoid	N/A	N/A	Not applicable
Torsemide	5–10 mg b.i.d.	L (K)	100%	Avoid	Avoid	None
Trimaterene	25–50 mg b.i.d.	K	Avoid	N/A	N/A	Not applicable
β-blockers						
Acebutolol	400–600 mg q.d./b.i.d.	L (K)	30–50%	30%	None	150 mg
Atenolol	50–100 mg q.d.	K (L)	25–50%	50%	None	25–50 mg
Betaxolol	10–20 mg q.d.	L	50%	None	None	None
Bisoprolol	2.5–20 mg q.d.	L	100%	None	None	None
Carvedilol	25 mg b.i.d.	L (K)	50%	None	Unknown	None
Esmolol	50–150 μg/kg/min i.v.	L	100%	None	None	None
Labetalol	200–600 mg b.i.d.	K (L)	100%	None	None	None
Metoprolol	50–100 mg b.i.d.	K (L)	100%	None	None	50 mg
Nadolol	80–100 mg b.i.d.	K	25%	50%	None	80 mg
Pindolol	10–40 mg b.i.d.	K (L)	100%	None	None	None
Propanolol	80–160 mg b.i.d.	K	100%	None	None	None
Sotalol	160 mg q.d.	K	15–30%	50%	None	50 mg
Timolol	10–20 mg b.i.d.	L (K)	100%	None	None	None
CCB						
Amlodipine	2.5–10 mg q.d.	L	100%	None	None	None
Diltiazem CD	180–360 mg	L (K)	100%	None	None	None
Felodipine	5–10 mg q.d.	L	100%	None	None	None
Isradipine	2.5–10 mg b.i.d.	L	100%	None	None	None
Lacidipine	2–6 mg/day	L (K)	100%	None	None	None
Manidipine	10–20 mg/day	L	100%	None	None	None
Nicardipine	20–40 mg t.i.d.	L	100%	None	None	None
Nifedipine XL	30–90 mg q.d.	L	100%	None	None	None
Nimodipine	30 mg q8 h	K (L)	100%	None	None	None
Nisoldipine	10 mg b.i.d.	K (L)	100%	None	None	None
Nitrendipine	20 mg b.i.d.	L (K)	100%	None	None	None
Verapamil CD	180–360 mg q.d.	L	100%	None	None	None
ACEI						
Benazapril	5–40 mg q.d.	K (L)	50–75%	Negligible	None	5–10 mg
Captopril	12.5–50 mg t.i.d.	K	50%	50%	None	12.5–25 mg
Enalapril	2.5–10 mg q12 h	K (L)	50%	50%	None	2.5–5 mg
Fosinopril	10 mg q.d.	K (L)	75%	None	None	None
Lisinopril	2.5–10 mg q.d.	K	25–50%	50%	None	2.5–5 mg
Perindopril	2–8 mg/day	K (L)	25–50%	50%	None	2 mg
Quinapril	10–20 mg q.d.	K (L)	50%	25%	None	10 mg
Ramipril	5–10 mg q.d.	K (L)	25–50%	20%	None	2.5 mg
Trandolapril	0.5–4 mg/day	K (L)	25–50%	30%	None	0.5 mg
ARB						
Candesartan	8–35 mg/day	K (L)	100%	None	None	None
Eprosartan	600–1200 mg/day	L	100%	None	None	None
Ibersartan	75–300 mg/day	L	100%	None	None	None
Losartan	50–100 mg q.d.	K (L)	100%	None	None	None
Olmesartan	10–40 mg/day	K (L)	100%	None	None	None
Telmisartan	40–80 mg/day	L	100%	None	None	None
Valsartan	80–320 mg q.d.	L (K)	100%	None	None	None
DIR						
Aliskiren	150–300 mg q.d.	K	Unknown	Unknown	Unknown	Unknown

Levin N, et al. Kidney Int 2010

Intradialysis Hypertension in End-Stage Renal Disease Patients

Clinical Epidemiology, Pathogenesis, and Treatment

Panagiotis I. Georgianos, Pantelis A. Sarafidis, Carmine Zoccali

Table 1. Prevalence of Intradialytic Hypertension Among Hemodialysis Patients

Study ID	Patients	Definition	Prevalence Estimates
Inrig et al[5] *Kidney Int* 2009	438 hemodialysis patients participating in the CLIMB study	Rise in SBP ≥10 mm Hg from pre to post dialysis	13.2% of patients met the definition of intradialytic hypertension
Inrig et al[3] *AJKD* 2009	1748 hemodialysis patients participating in the USRDS Dialysis Morbidity and Mortality Wave II study	Rise in SBP >10 mm Hg from pre to post dialysis, averaged from 3 consecutive dialysis sessions	12.2% of patients were classified as intradialytic hypertensives
Van Buren et al[11] *Int J Artific Organs* 2012	362 hemodialysis patients receiving treatment in the USA	Rise in SBP >10 mm Hg from pre to post dialysis, averaged for the total number of dialysis treatments performed during 6 months of follow-up	22.3% of dialysis treatments were complicated by intradialysis hypertension. Persistent intradialytic hypertension was noted in 8% study participants

Table 2. Prospective Observational Studies Associating Intradialytic Hypertension With Increased Risk of Mortality

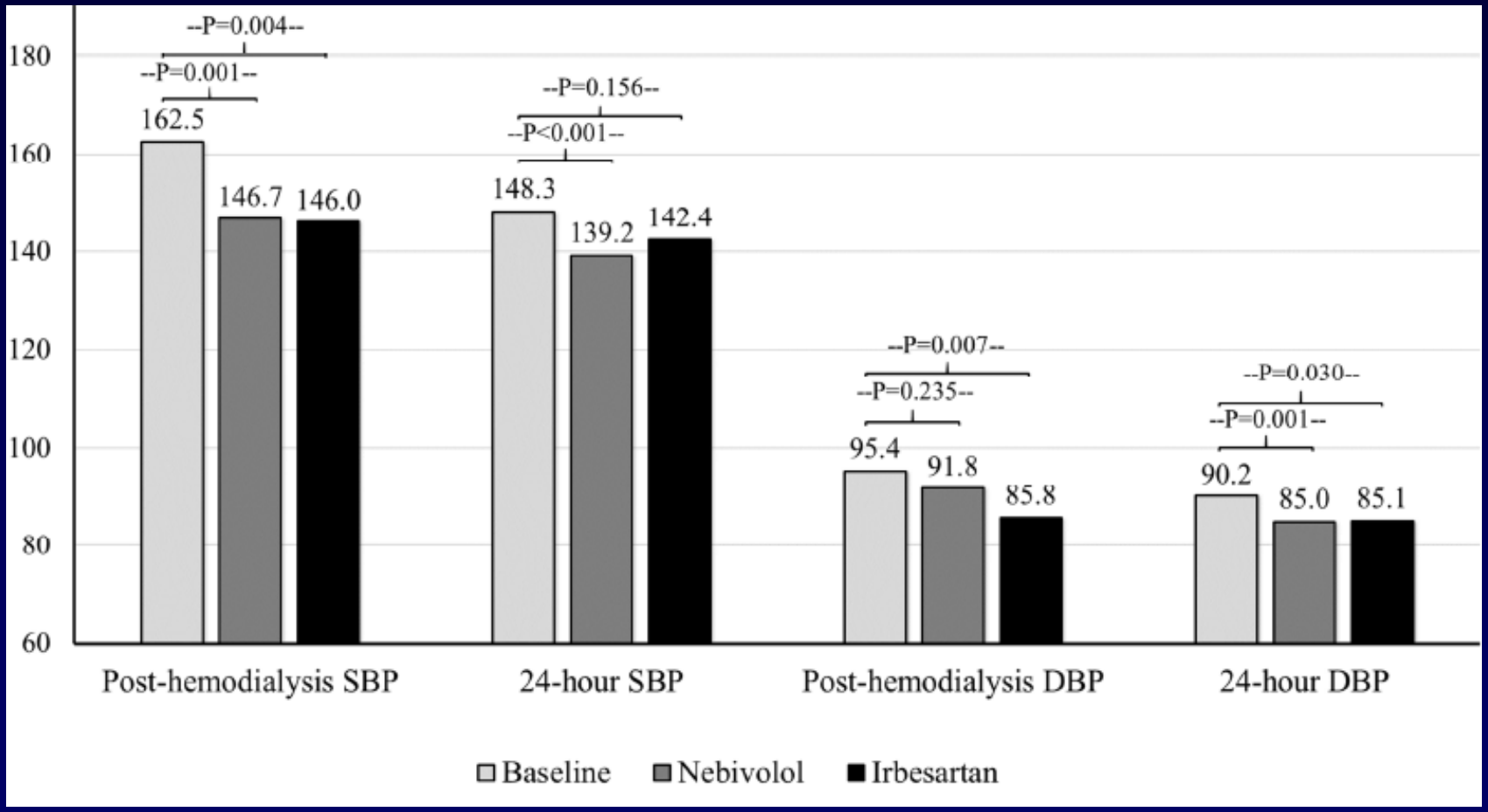
Study ID	Patients	Follow-Up	Predictor	Outcome	Risk
Inrig et al[5] *Kidney Int* 2009	438 dialysis patients participating in the CLIMB study	6 mo	ΔSBP from pre to post dialysis ≥10 mm Hg	Combined end point of non–dialysis-related hospitalization or all-cause mortality	OR, 2.17; 95% CI, 1.13–4.15
Inrig et al[3] *AJKD* 2009	1748 hemodialysis patients participating in the USRDS Dialysis Morbidity and Mortality Wave II study	2 y	ΔSBP from pre to post dialysis	All-cause mortality	HR, 1.12; 95% CI, 1.05–1.21 per 10 mm Hg increase in SBP during dialysis
Yang et al[12] *BMC Nephrol* 2012	115 prevalent dialysis patients	4 y	ΔSBP >5 mm Hg from pre to post dialysis	All-cause mortality	HR, 3.925; 95% CI, 1.410–10.846
Park et al[13] *Kidney Int* 2013	113 255 prevalent dialysis patients	2.2 yr	ΔSBP from pre to post dialysis	All cause mortality Cardiovascular mortality	Intradialytic reduction in SBP >30 mm Hg and any rise in SBP during dialysis were both associated with increased risk of all-cause and cardiovascular mortality

Georgianos, et al. Hypertension 2015

NEBIVOLOL vs IRBESARTAN IN INTRADIALYTIC HTN: A RANDOMIZED CROSS-OVER STUDY

ARISTOTLE UNIVERSITY OF THESSALONIKI

weekly intake: n=19



Bikos A, et al. 2018 (submitted)

Υπέρταση στη Μεταμόσχευση Νεφρού

Optimizing hypertension management in renal transplantation: a call to action*

Jean-Michel Halimi[a,b,c], Alexandre Persu[d,e], Pantalis A. Sarafidis[f], Michel Burnier[g], Daniel Abramowicz[h,i], Bénédicte Sautenet[a,c], Rainer Oberbauer[j], Francesca Mallamaci[k], Gérard London[c,l], Patrick Rossignol[c,m], Grégoire Wuerzner[g], Bruno Watschinger[j], Carmine Zoccali[k], on behalf of the European Renal, Cardiovascular Medicine (EURECA-m), the transplant DESCARTES working group of the European Renal Association-European Dialysis, Transplant Association (ERA-EDTA), the Working Group 'Hypertension, Kidney' of the European Society of Hypertension (ESH); the EKITA committee of the European Society of Organ Transplantation (ESOT), FCRIN INI-CRCT Cardiovascular, Renal Clinical Trialists

Optimizing hypertension management in renal transplantation: a call to action

Jean-Michel Halimi[1,2], Alexandre Persu[3,4], Pantelis A. Sarafidis[5], Michel Burnier[6], Daniel Abramowicz[7], Bénédicte Sautenet[1,2], Rainer Oberbauer[8], Francesca Mallamaci[9], Gérard London[10], Patrick Rossignol[11], Grégoire Wuerzner[6], Bruno Watschinger[8] and Carmine Zoccali[9] on behalf of the European Renal and Cardiovascular Medicine (EURECA-m) and the transplant DESCARTES working group of the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA), the Working Group 'Hypertension and Kidney' of the European Society of Hypertension (ESH), the EKITA committee of the European Society of Organ Transplantation (ESOT) and the FCRIN INI-CRCT Cardiovascular and Renal Clinical Trialists

Halimi J-M, et al. J Hypertension 2017; Halimi J-M, et al. Nephrol Dial Transplant 2017

Συμπεράσματα

- Hypertension in ESRD poses unique diagnostic, prognostic and therapeutic challenges.
- Studies with home or ABPM are needed to provide solid data on hypertension prevalence and prognostic associations and to identify objective thresholds for diagnosis and targets of treatment.
- Non-pharmacologic interventions targeting sodium and volume excess are fundamental and should be carefully implemented before pharmacological interventions.
- Use of antihypertensive agents in dialysis is associated with improvement in cardiovascular outcomes; β-blockers followed by dihydropyridine CCBs should be considered initially.
- Properly designed trials to examine the efficacy of non-pharmacologic measures and antihypertensive drugs in prevention of cardiovascular outcomes in ESRD remain a public health priority.

Sarafidis P, et al. J Hypertension 2017; Sarafidis P, et al. Nephrol Dial Transplant 201

EDUCATION

EURECA-m working group

CKD-MBD working group

CME Meeting of EURECA-m and CKD-MBD Working Groups

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September 13-15, 2018

Local Organisers and Key Speakers:
Panteleimon Sarafidis, Francesca Mallamaci, Mario Cozzolino

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Ευχαριστώ!