HİPERTANSİF HASTALARDA ENDOTEL DİSFONKSİYONUNU NASIL ARAŞTIRALIM?

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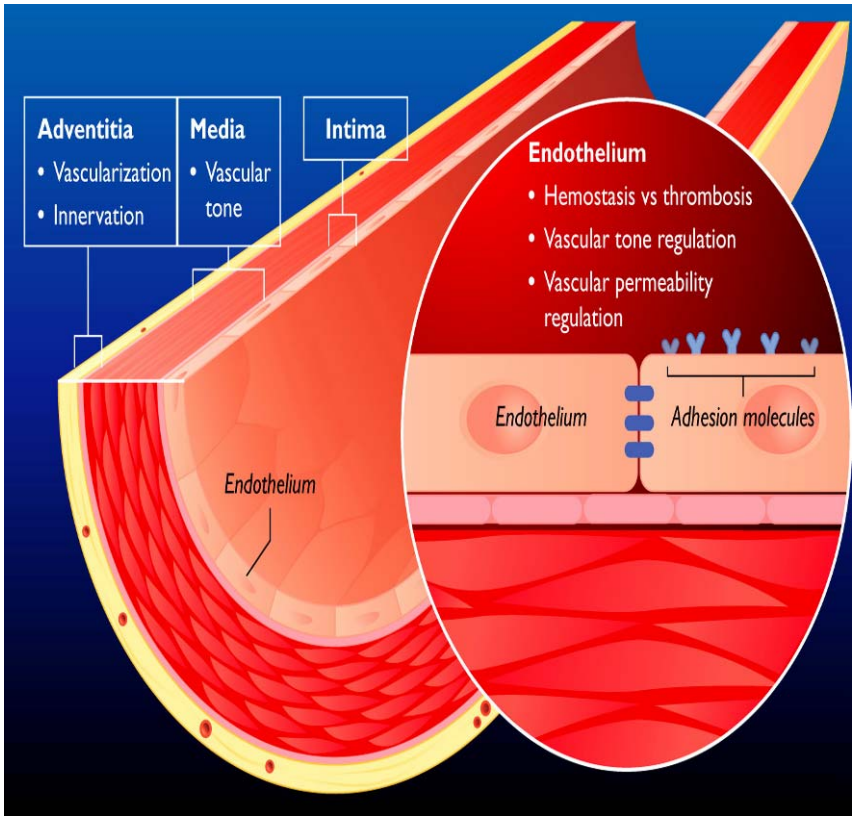
24 Mayıs 2008 Antalya

EN BÜYÜK ENDOKRİN ORGANDIR



ENDOTEL

- **Endotel,** vasküler fonksiyonların normal bir şekilde yürüyebilmesinde son derece önemli görevlere sahip bir organdır.
- **Endotel disfonksiyonu** kardiyovasküler sistemi ilgilendiren birçok hastalığın en önemli parçasıdır.
- Endotel fonksiyonlarının düzenlenmesinde en önemli aracı moleküllerden biri **nitrik oksittir.**
- **Nitrik oksit eksikliği** *endotel disfonksiyonuna* yol açarak, kardiyovasküler sistemi hedef alan birçok hastalığa zemin hazırlayabilir.

1- Vasokonstriktörler
- Angiotensin converting enzim (ACE)
- Endotelinler (ET-1, ET-2, ET-3)
- Angiotensin II
- Tromboksan A_2
- Asetil kolin, araşidonik asit, PGH_2, trombin, nikotin

2- Vasodilatatörler
- Nitrikoksit (NO=EDRF)
- Adrenomedullin
- Endotelium derived hiperpolarizing faktörler
- Prostasiklin (PGI_2)
- Bradikinin, asetilkolin, serotonin, histamin, substance P

3- Antitrombotik (homeostaz) maddeler
- Trombomodülin
- Doku plazminojen aktivatör (t-PA)
- Plazminojen aktivatör inhibitör tip I (PAI-1)

4- Büyüme modülatör / mediatörleri

a) Büyüme promotörleri
- PDGF
- Basic FGF
- IGF-1
- IL-1
- Endotelin
- AII

b) Büyüme inhibitörleri
- Heparin sülfat
- TGF-β
- NO
- Bradikinin
- Prostasiklin

5- İnflamatuar mediatörler

Adezyon molekülleri;
- Endotelyal Lökosit Adezyon Molekülü (ELAM)
- İntraselüler Adezyon Molekülü (ICAM)
- Vasküler Hücre Adezyon Molekülleri (VCAM)

Antijenler ;
- Major histokompatibilite kompleks 2 (MHCII)

6- Redoxitite

ENDOTELDE DENGE

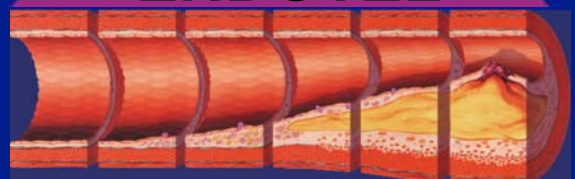
Dilatasyon
Büyüme inhibisyonu
Antitrombotik
Anti-inflamatuar
Antioksidan

Endotel

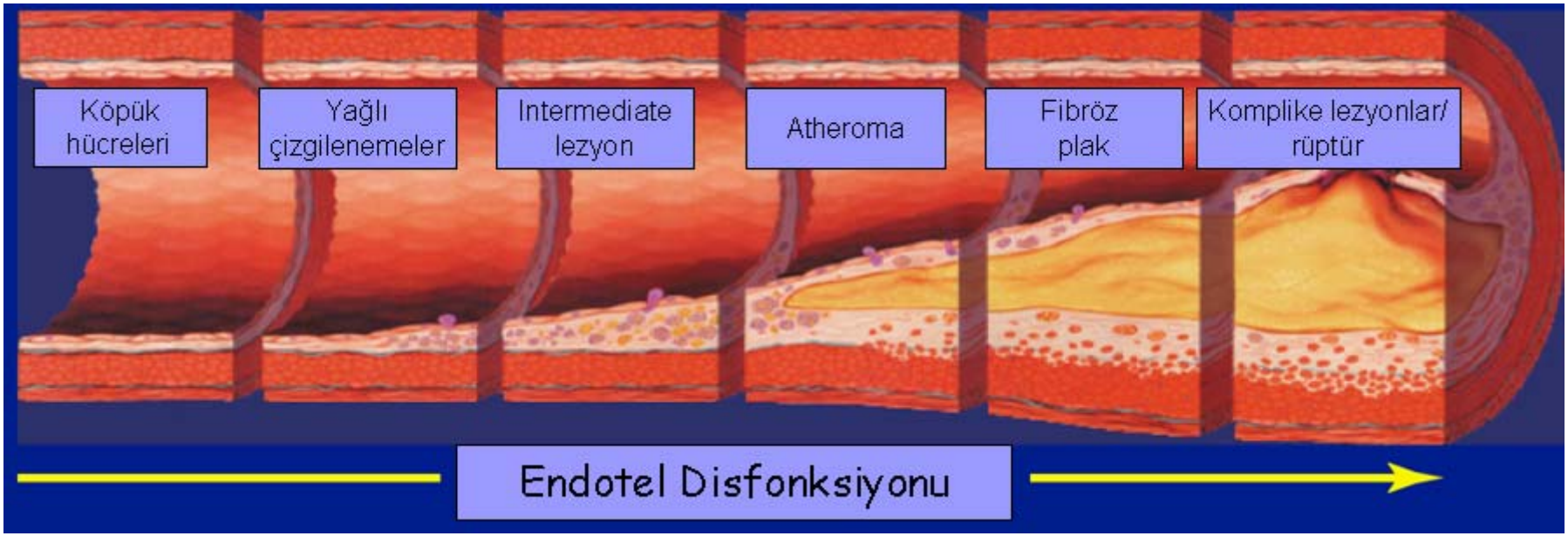
Disfonksiyonu

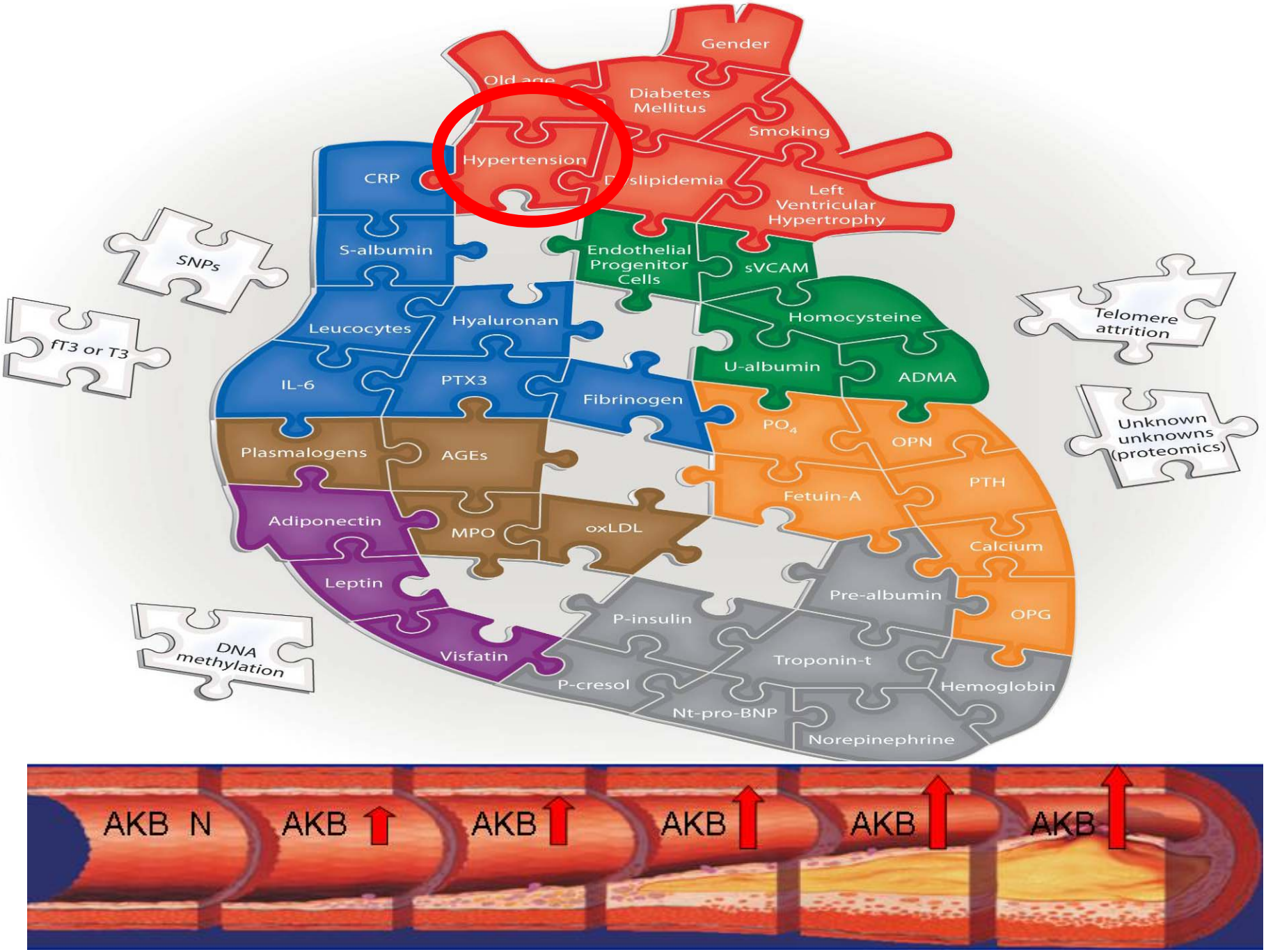
Konstrüksiyon
Büyümenin artışı
Protrombotik
Proinflamatuar
Pro-oksidan

ENDOTEL



Endotel disfonksiyonu




Gender
Old age
Diabetes Mellitus
Smoking
Hypertension
Dyslipidemia
Left Ventricular Hypertrophy
CRP
S-albumin
SNPs
fT3 or T3
Endothelial Progenitor Cells
sVCAM
Homocysteine
Telomere attrition
Leucocytes
Hyaluronan
U-albumin
ADMA
IL-6
PTX3
Fibrinogen
Unknown unknowns (proteomics)
PO4
OPN
Plasmalogens
AGEs
PTH
Fetuin-A
Adiponectin
MPO
oxLDL
Calcium
Leptin
Pre-albumin
OPG
P-insulin
DNA methylation
Visfatin
Troponin-t
P-cresol
Hemoglobin
Nt-pro-BNP
Norepinephrine
AKB N
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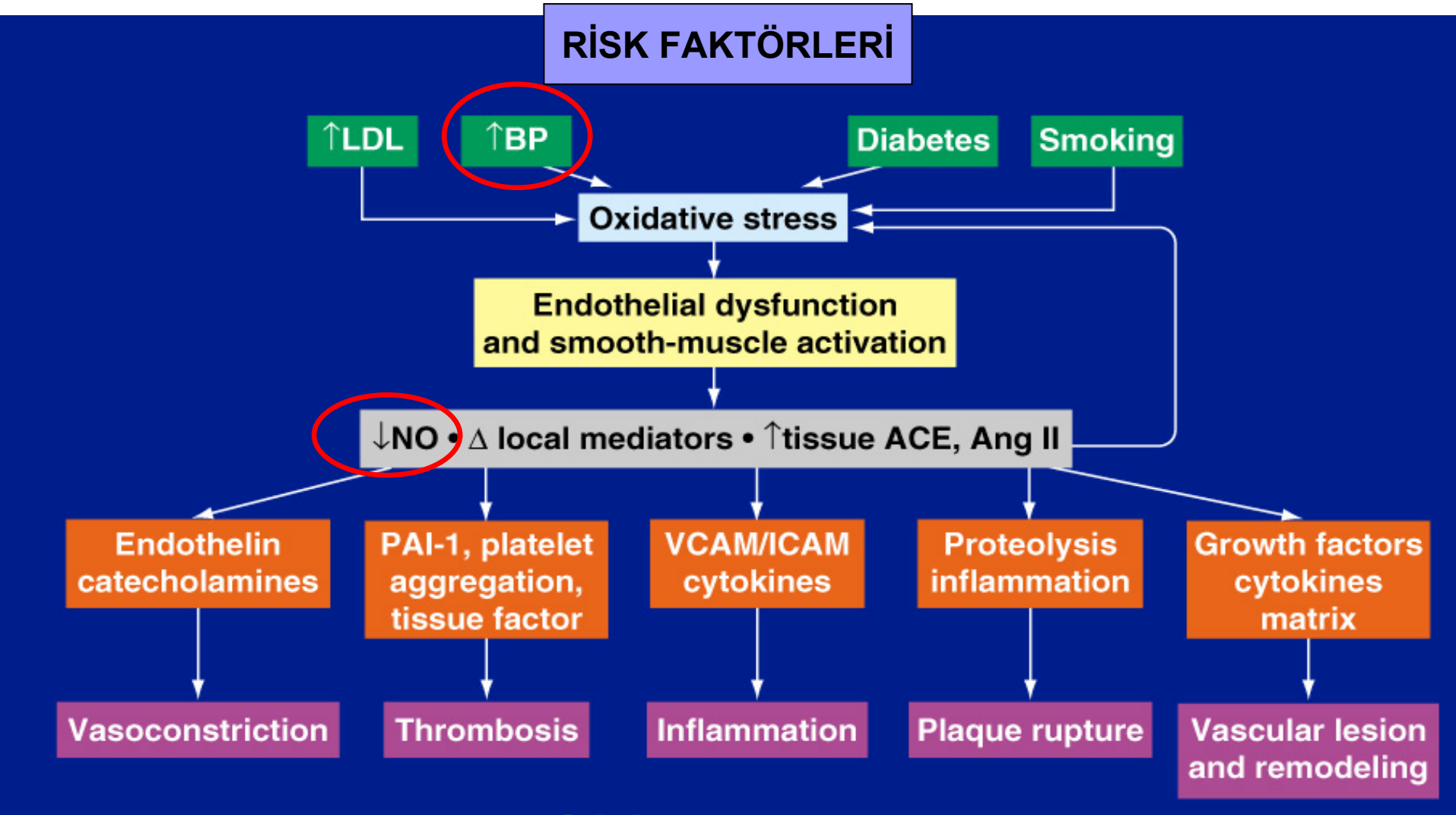

RİSK FAKTÖRLERİ
↑LDL
↑BP
Diabetes
Smoking
Oxidative stress
Endothelial dysfunction and smooth-muscle activation
↓NO • Δ local mediators • ↑tissue ACE, Ang II
Endothelin catecholamines
PAI-1, platelet aggregation, tissue factor
VCAM/ICAM cytokines
Proteolysis inflammation
Growth factors cytokines matrix
Vasoconstriction
Thrombosis
Inflammation
Plaque rupture
Vascular lesion and remodeling

KBH VE KV HASTALIK

- Klasik risk faktörleri
- KBH a özgü risk faktörleri
  - Vasküler kalsifikasyon
  - Hiperhomosisteinemi
  - Anemi (LVH)
  - **Oksidatif stres**
  - Dislipidemi
  - **Asimetrik dimetilarginin ↑**
  - Advanced glycation end products
  - İnflamasyon (CRP ↑)
  - **Endotel disfonksiyonu**
- **Hipertansiyon**
  - %50-%75
  - Kronik volüm yüklenmesi
  - KronikRAAS aktivasyonu
  - Kronik SSS aktivasyonu
  - Oksidatif stres ve inflamasyon> **endotel disfonksiyonu**
  - Vasküler kalsifikasyon

Hipertansiyon

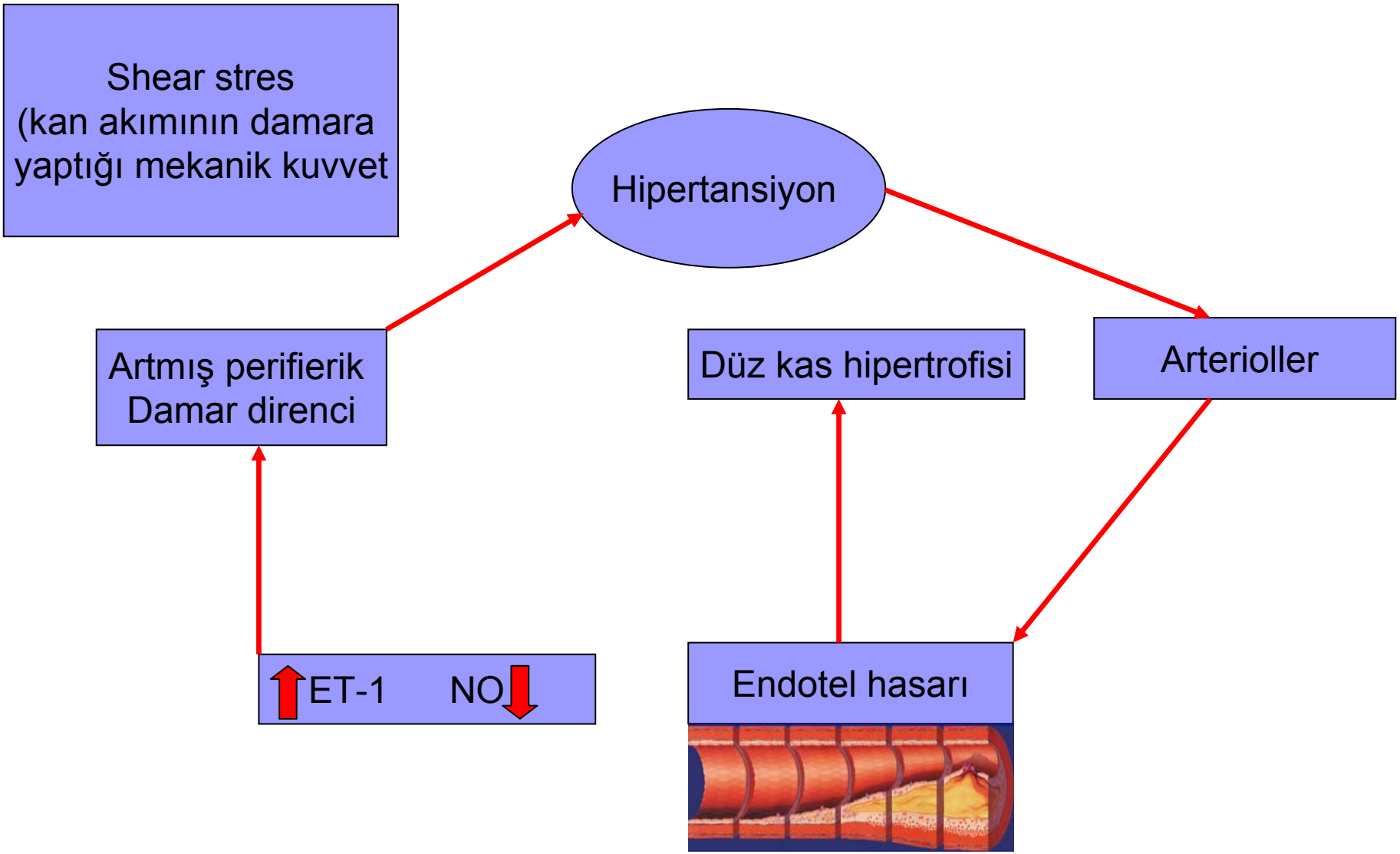
- Endotel
- Damar düz kas fonksiyonu
- Damar düz kas kitlesinde artış

ET-1

- Plazma ET-1 düzeyi HT'li hastalarda daha yüksek
- Böbrek yetmezlikli ve HT'li hastalarda normal sağlıklılara göre plazma endotelin düzeyi daha yüksek saptanmıştır.

Scichiri M, et al. JAMA, 1990

Hipertansif kısır döngü



KBH' NIN PROGRESYONUNU ARTIRAN FAKTÖRLER

- Artmış RAAS aktivitesi
  - Glomerüler hipertansiyon
  - Fibrotik süreç aktivasyonu
- Hipoksi
  - Serbest radikal artışı
  - Tubuler epitel apoptosisi
- Vasküler kalsifikasyon
- Artmış oksidatif stres
- Advanced glycation end products
- NO eksikliği
- Sistemik hipertansiyon
- İnflamasyon (hipoksi, fibrogenez, oksidatif stres)

RENAL

SİSTEMİK

ARTMIŞ KARDİYOVASKÜLER RİSK

Kardiyo Vasküler Olaylar

Renal endotelial disfonksiyon

Sistemik endotelial disfonksiyon

Genetics NO?

Genetics NO?

ROS Hcys

↓NO

ADMA ROS Hcys

↓NO ↓EDHF

Traditional risk factors

Susceptibility to renal injury

Microalbuminuria

Renoprotective therapeutic response

Renal insufficiency incl. ESRD

ENDOTEL FONKSİYONUNU ARAŞTIRMADA …….

- Klinik çalışmaları
- Hayvan çalışmaları

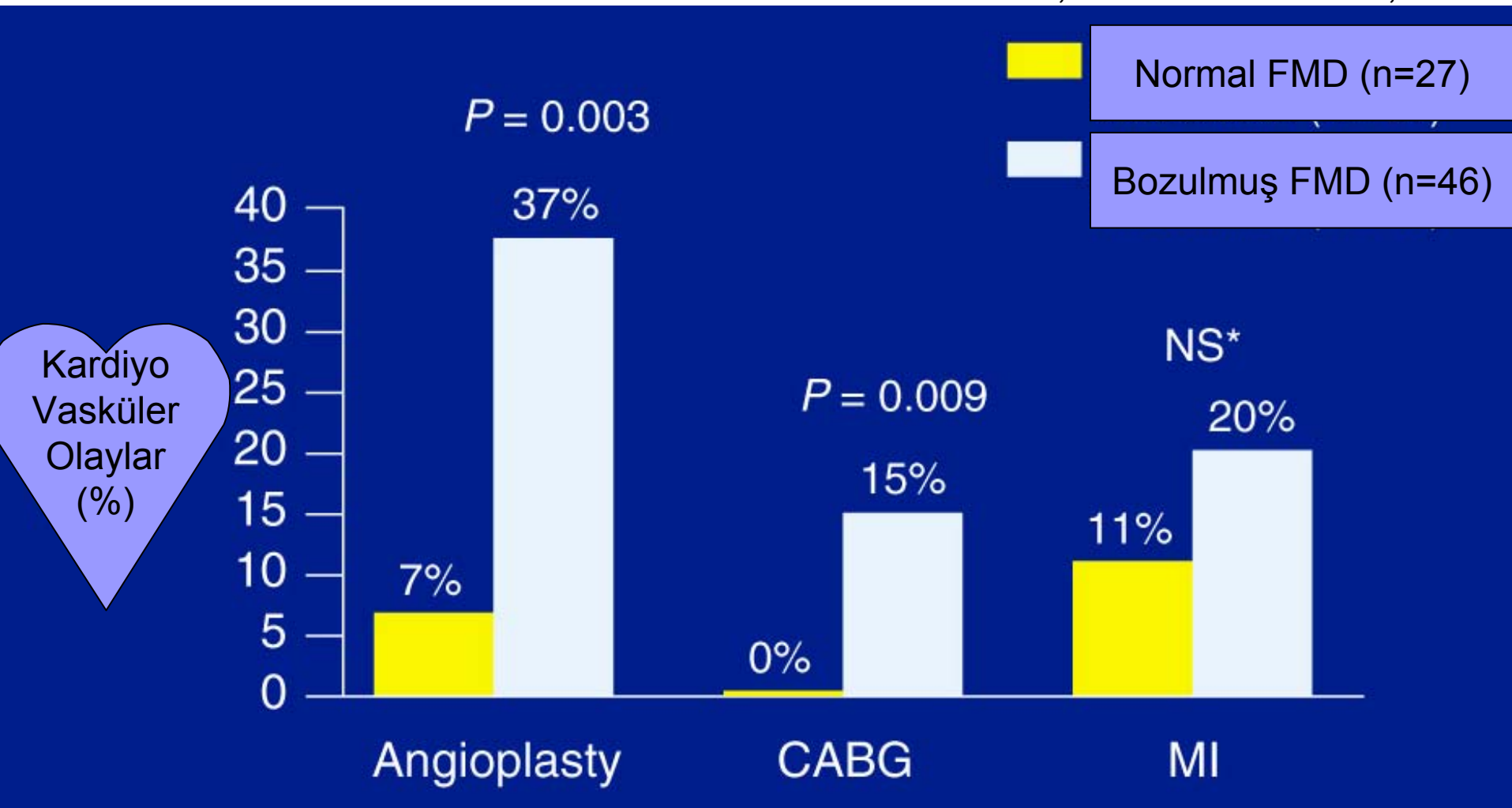
Endotel fonksiyon göstergeleri

- Dolaşımdaki belirteçleri
1. ADMA
2. vWF
3. t-PA
4. PAI-1
5. ICAM-1
6. VCAM-1

- NO'e bağlı vazomotor aktivitenin bazı fonksiyonel testler ile ölçümü
1. İnvaziv koroner testi
2. İnvaziv ön kol testi: Pletismografi metodu
3. Non-invaziv koroner testi: PET
4. Non-invaziv ultrason metodu (akıma aracılı vazodilatasyon): FMD

Endotel disfonksiyonu kardiyovasküler olayları öngörebilir

Neunteufl T, et al. Am J Cardiol, 2000



Endotel bağımlı vazodilatasyon
FMD (Akım aracılı vazodilatasyon)

- 1992'de Celermajer ve arkadaşları
- Brakiyal arter çapı bazal olarak ölçülür ve daha sonra manşon sistolik değerin üstünde bir basınçta şişirilir
- 3-5 dakika boyunca kol iskemik kalacak şekilde arteriyel akım engellenmiş ve oluşan İskemi sonucunda damarda vazodilatasyon gelişmektedir.
- Takiben vazodilatasyona uyum için kısa süreli bir yüksek akım dönemi (reaktif hiperemi) oluşur.
- Manşet basıncı indirildikten 60 saniye sonra brakiyal arter çapı tekrar ölçülerek reaktif hiperemiye yanıt olarak oluşan FMD yüzde olarak değerlendirilir:
- FMD = % hiperemik akım sonrası ortalama çap - bazal çap/ Bazal çap

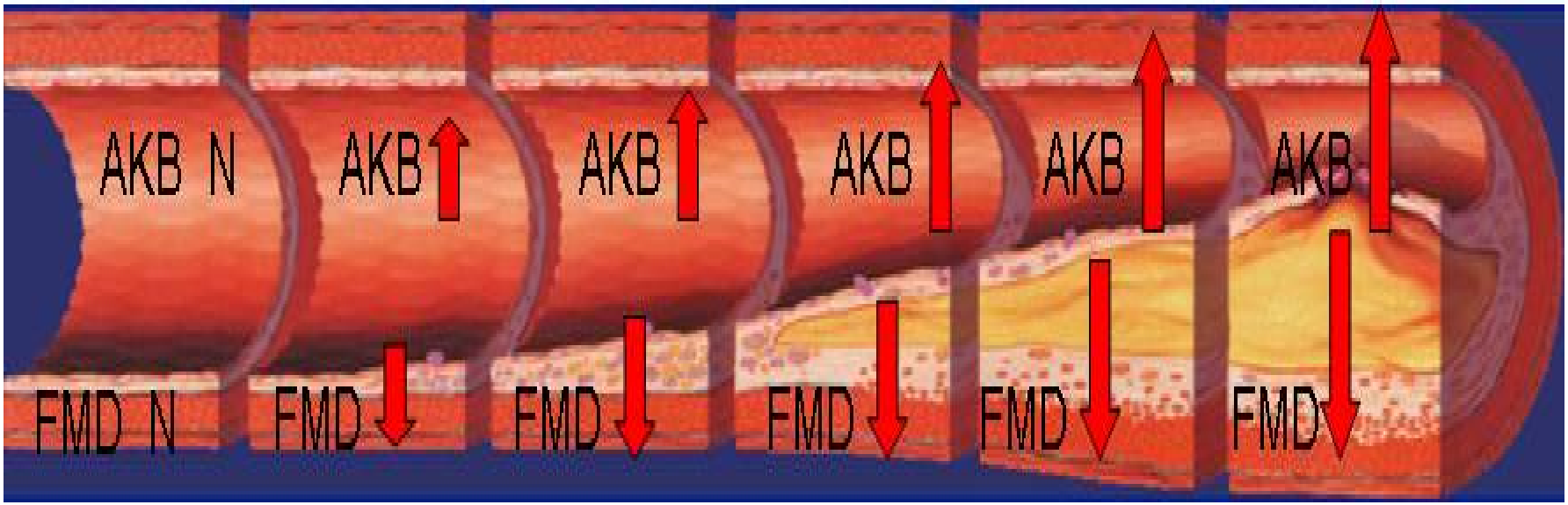
Endotelden bağımsız dilatasyon
NMD (Nitrogliserin aracılı vazodilatasyon)

- Endotelden bağımsız dilatasyon (NMD) ölçümü içinse, bazal bir ölçüm yapılmasının ardından 15 dakika sonra sublingual 400 µg glyceryl trinitrate uygulanır ve 3 dakika sonra ikinci bir ölçüm yapılır.
- NAD değeri ise ilaç uygulanması sonrası bulunan ortalama çaptan bazal çapın çıkarılması ve bunun bazal çapa bölünmesiyle % olarak ifade edilmiştir.

Nelere dikkat edelim?

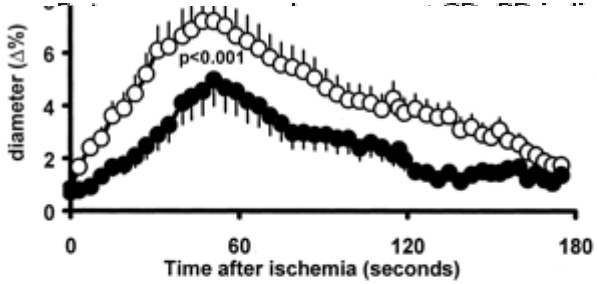
- Damarda akım etkisiyle oluşan yanıtları ortam sıcaklığı, beslenme, ilaçlar ve sempatik uyaranlar gibi pek çok faktörden etkilendiğinden çalışma, sessiz ve sıcaklığı kontrol altında olan bir ortamda yapılır.
- Hastaların egzersizden kaçınmış olmasına, son 4-6 saatte kafein, fazla yağlı gıdalar, C vitamini gibi antioksidanlar almamasına dikkat edilmelidir.

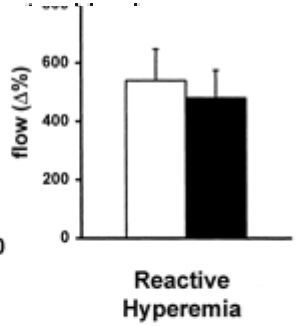
Hipertansiyon-FMD

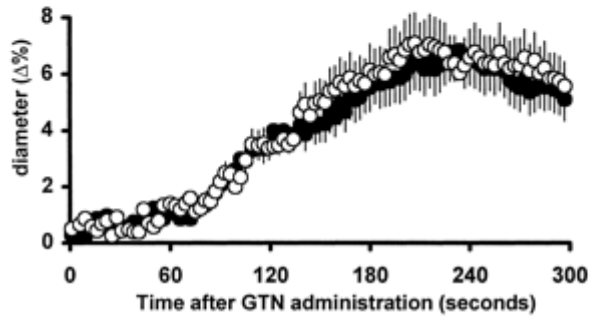


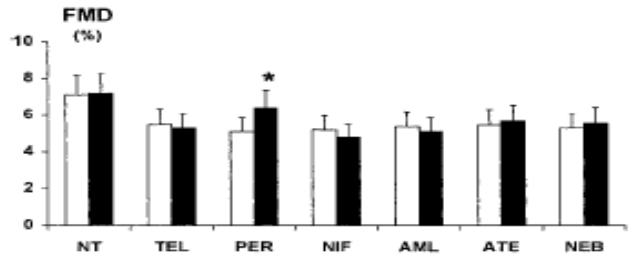
Hipertansiyon-FMD

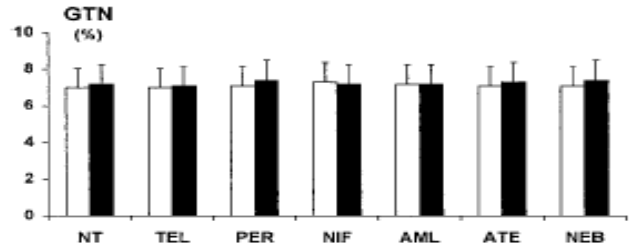
Parameter	Perindopril Group (n=28)	Telmisartan Group (n=29)	Nifedipine Group (n=28)	Amlodipine Group (n=28)	Atenolol Group (n=29)	Nebivolol Group (n=28)
Gender, M/F	18/10	18/11	17/11	17/11	18/11	17/11
Age, y	51±11	50±9	52±11	53±8	53±9	53±8
Higher drug dose (%)	28 (100)	28 (100)	18 (64)	19 (68)	22 (76)	22 (79)
Diuretic added (%)	7 (25)	6 (21)	2 (7)	3 (11)	10 (34)	7 (25)
Patients with BP <140/90 mm Hg (%)	22 (79)	22 (76)	22 (79)	23 (82)	24 (83)	21 (75)







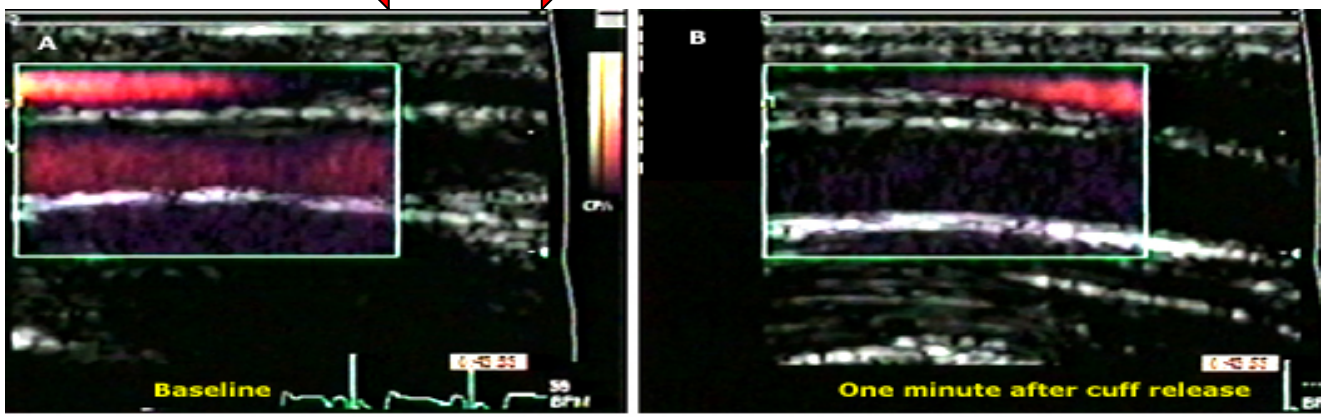




Ghiadoni L, et al. Hypertension, 2003

FMD- SKB/DKB

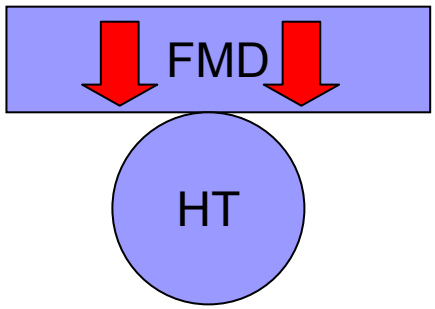
- 155 HT'lu hasta
- 40 normotansif kontrol
- HT'lu hastalarda FMD ve NMD bozulmuş
- FMD ⟷ SKB
- FMD ⟷ DKB

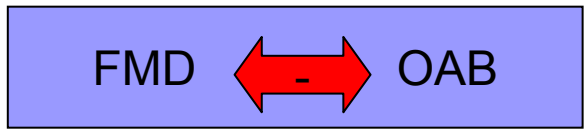


Ward NC, et al. J Hypertension, 2004

FMD-OAB

- 70 yaşındaki hipertansif hastalar
- 72 yaşındaki sağlıklı kontrollerle karşılaştırılmış





Kimura Y, et al, Can J Cardiol, 1999

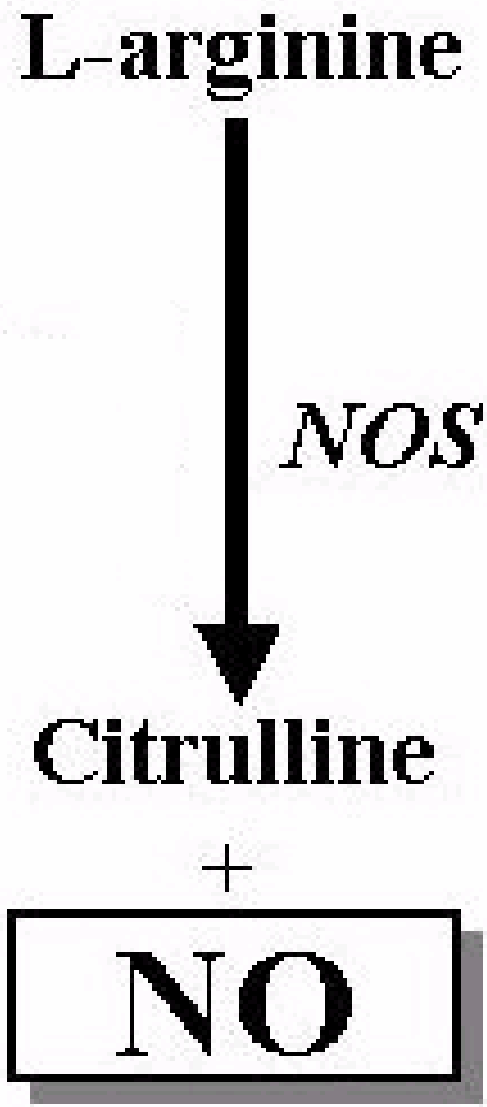
NO, bir endojen antiaterosklerotik molekül

- NO'in kardiyovasküler sistem için koruyucu bir rolü vardır

1. Vasküler kas hücresi proliferasyonunu
2. Platelet agregasyonunu
3. Monositlerin endotele adezyonunu inhibe eder

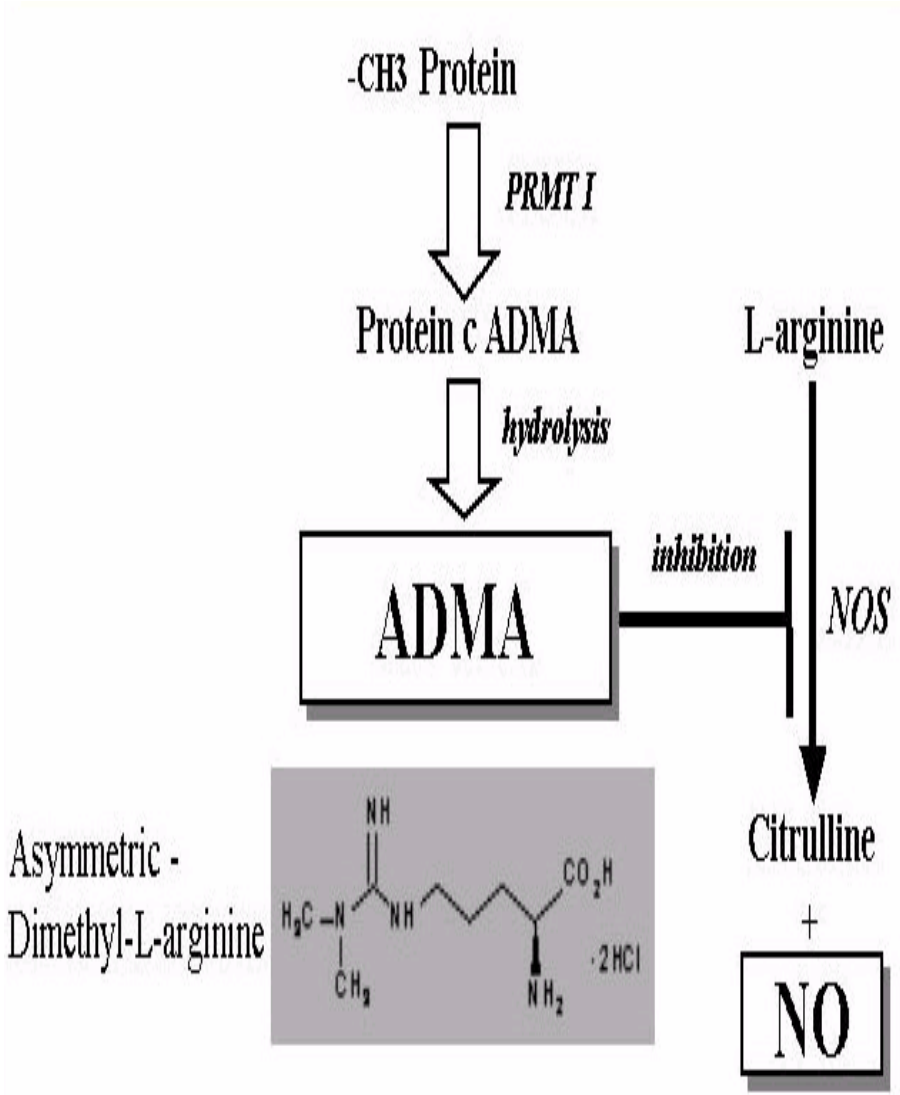
NO

- Normal şartlar altında, NO endotelde, L-arjinini NO ve sitrline çeviren NO sentaz (NOS) enzimi tarafından devamlı bir şekilde üretilir.



ADMA ve NO

- NOS, endojen metilarjininler tarafından inhibe edilebilir ve asimetrik dimetilarjinin (ADMA), bu endojen NOS inhibitörlerinin en önemlisi gibi görünmektedir.
- ADMA, doğal olarak ortaya çıkan, plazmada dolaşan, idrar ile atılan ve doku ve hücrelerde bulunan bir amino asittir



ADMA ve kardiyovasküler risk faktörleri

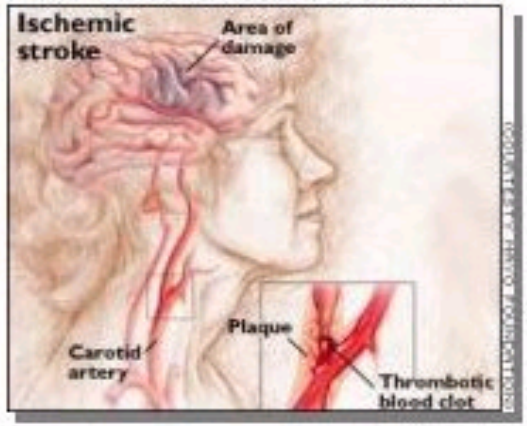
Miyazaki *Circulation* 1999
Kielstein *Circulation* 2003

Lin *Circulation* 2002
Yasuda *Eur Heart J* 2006

Miyazaki *Circulation* 1999
Zoccali *J Am Soc Nephrol* 2002
Furuki *Atherosclerosis* 2006

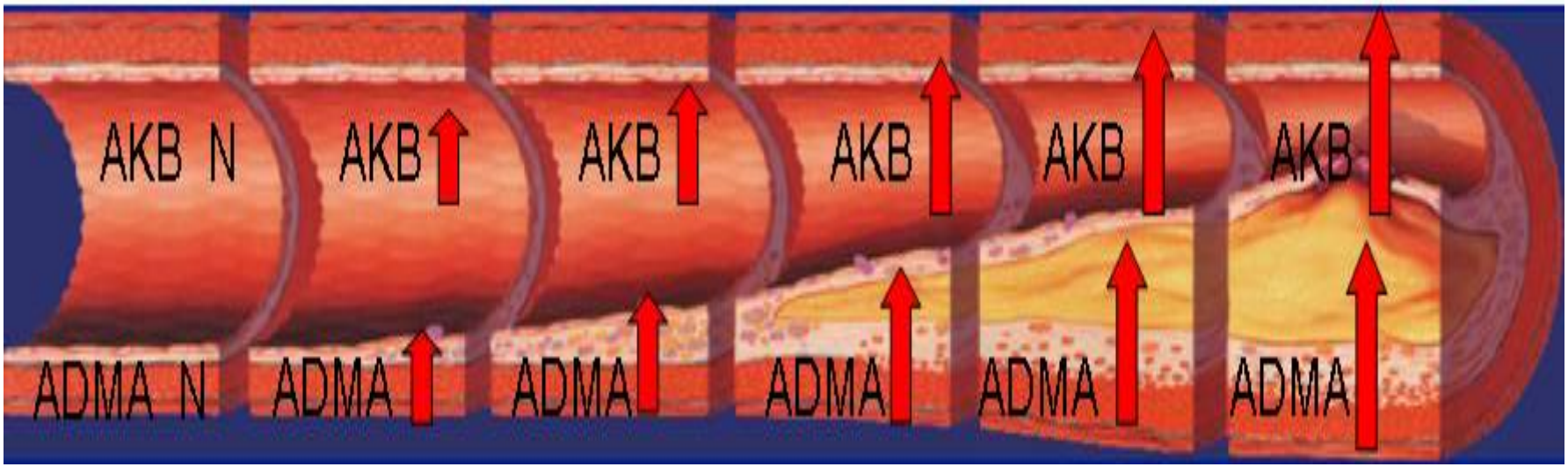
Boeger *Circulation* 1998
Paiva *Metabolism* 2004

Boeger *Circulation* 1997
Kielstein *J Am Soc Nephrol* 1999



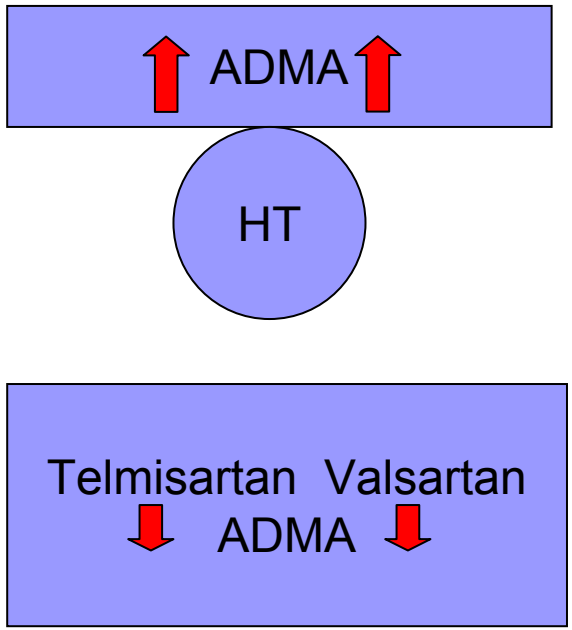
Yoo *Atherosclerosis* 2001

HT-ADMA



HT-ADMA

- 40 hipertansif hasta



Tomiyama H, et al., 2007, Am J Hypertens

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Asymmetric Dimethylarginine, L-Arginine, and Endothelial Dysfunction in Essential Hypertension

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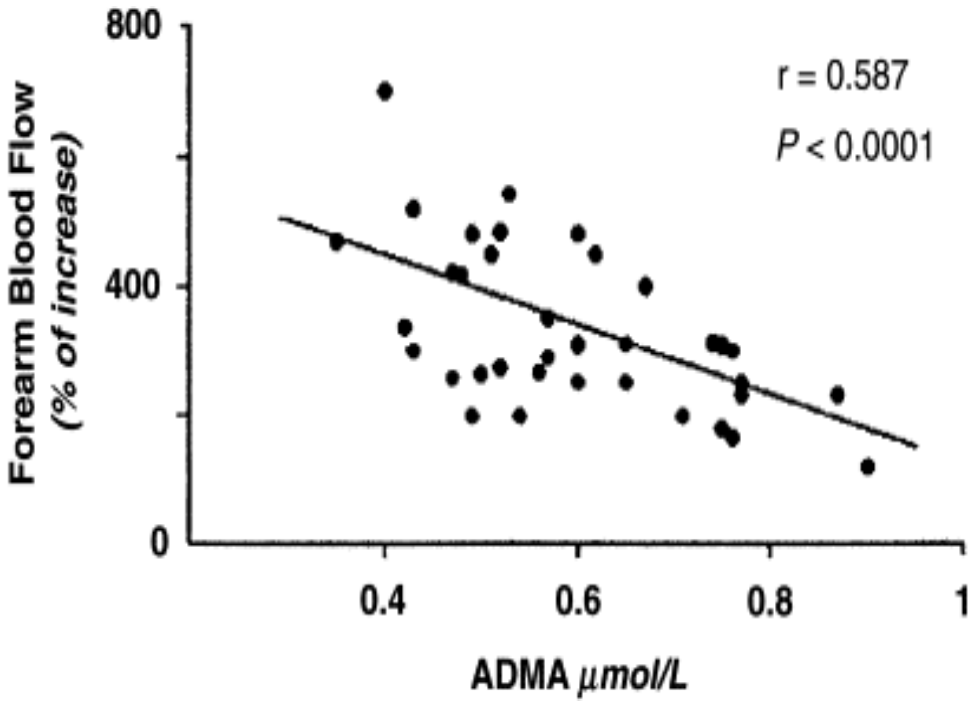

	Hypertensives (n = 36)	Normotensives (n = 8)	p Value
Gender (males/females)	28/8	4/4	0.247
Age (yrs)	44.2 ± 8.8	44.5 ± 5.8	0.927
Body mass index (kg/m^2)	27.2 ± 2.8	26.2 ± 4.0	0.404
Heart rate (beats/min)	74.5 ± 8.5	75.8 ± 11.2	0.714
Systolic BP (mm Hg)	155.9 ± 8.3	124.4 ± 4.1	0.000
Diastolic BP (mm Hg)	93.1 ± 7.3	69.1 ± 4.8	0.000
Pulse pressure (mm Hg)	62.8 ± 7.8	55.4 ± 6.0	0.016
Fasting glucose (mg/dl)	92.4 ± 8.4	90.4 ± 12.5	0.581
Total cholesterol (mg/dl)	194.6 ± 25.3	186.7 ± 29.0	0.444
LDL cholesterol (mg/dl)	126.4 ± 27.4	121.1 ± 31.4	0.632
HDL cholesterol (mg/dl)	48.0 ± 10.4	46.0 ± 8.3	0.614
Triglycerides (mg/dl)	100.6 ± 21.9	98.1 ± 35.4	0.797
Creatinine (mg/dl)	0.87 ± 0.10	0.83 ± 0.11	0.312
FBF (m · 100 ml^{-1} of tissue · min^{-1})	3.36 ± 0.28	3.49 ± 0.23	0.229
Vascular resistance (U)	33.2 ± 4.3	26.3 ± 2.5	0.000

Role of Asymmetrical Dimethylarginine in Renal Microvascular Endothelial Dysfunction in Chronic Renal Failure with Hypertension

Ken OKUBO, Koichi HAYASHI, Shu WAKINO, Hiroto MATSUDA, Eiji KUBOTA, Masanori HONDA, Hirobumi TOKUYAMA, Tokunori YAMAMOTO*, Fumihiko KAJIYA**, and Takao SARUTA

Hypertens Res 2005; 28: 181–189

	Control	CRF
n	7	7
Body weight (kg)	12.2±1.1	10.4±1.0*
MAP (mmHg) (conscious)	96±3	119±2**
HR (beats/min) (conscious)	114±4	95±8*
Hematocrit (%)	49±2	39±2**
Serum creatinine (μmol/l)	64.6±2.7	188.5±26.5**
Total cholesterol (mmol/l)	3.25±0.05	3.35±0.25
HDL-cholesterol (mmol/l)	2.69±0.11	2.77±0.12
Triglyceride (mmol/l)	0.21±0.03	0.38±0.05*
Creatinine clearance (ml/min)	31.3±1.5	13.2±0.8**

	Control	CRF
N	7	7
von Willebrand factor (%)	11.3±0.8	31.0±8.0*
PAI-1 (nmol/l)	352±127	848±190#
Homocysteine (μmol/l)	6.8±0.4	12.2±0.7**
ADMA (μmol/l)	1.50±0.08	2.60±0.13**

CRF, chronic renal failure; PAI-1, plasminogen activator inhibitor-1; ADMA, asymmetrical dimethylarginine. Data are expressed as the mean±SEM. *$p<0.05$ *vs.* controls. **$p<0.01$ *vs.* controls. #$p=0.05$ *vs.* controls.

Improving Proteinuria, Endothelial Functions and Asymmetric Dimethylarginine Levels in Chronic Kidney Disease: Ramipril versus Valsartan

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Erdinc Cakir[d] Yasemin Kurt[d] Tayfun Eyileten[a] Mustafa Tasar[b]
Cengizhan Acikel[e] Yusuf Oguz[a] Abdulgaffar Vural[a] Mujdat Yenicesu[a]

Blood Purification; 2007; 25(4):327-335

	Patients (n = 66)	Controls (n = 36)	p*
Age, years	47.1 ± 6.2	46.9 ± 5.4	0.846
BMI	26.66 ± 2.33	26.62 ± 2.31	0.935
eGFR, ml/min/1.73 m²	42.73 ± 11.52	111.83 ± 8.18	<0.001
Triglyceride, mg/dl	116.26 ± 25.38	134.86 ± 16.00	0.084
Total cholesterol, mg/dl	177.34 ± 24.04	170.05 ± 36.69	0.498
LDL cholesterol, mg/dl	108.36 ± 22.49	104.41 ± 21.27	0.114
HDL cholesterol, mg/dl	44.92 ± 6.04	47.72 ± 4.71	0.227
ADMA, μmol/l	1.55 ± 0.28	0.88 ± 0.13	<0.001
SDMA, μmol/l	1.64 ± 0.28	0.82 ± 0.17	<0.001
L-Arginine, μmol/l	81.5 ± 8.8	94.1 ± 7.9	<0.001†
L-Arginine/ADMA ratio	55.6 ± 13.7	105.8 ± 16.7	<0.001†
hsCRP, mg/l	12.63 ± 3.49	2.38 ± 0.72	<0.001
Systolic BP, mm Hg	153.15 ± 7.55	117.13 ± 13.77	<0.001
Diastolic BP, mm Hg	92.95 ± 3.18	81.36 ± 2.22	<0.001
FPG, mg/dl	87.69 ± 5.89	87.97 ± 4.55	0.794
Insulin, μU/ml	5.10 ± 1.05	4.55 ± 0.93	0.007
HOMA	1.10 ± 0.23	0.98 ± 0.21	0.013
Proteinuria, mg/day	1,483.33 ± 382.89	122.34 ± 18.35	<0.001
NMD, %	12.92 ± 0.53	13.10 ± 0.59	0.012
FMD, %	6.74 ± 0.59	8.86 ± 1.31	<0.001

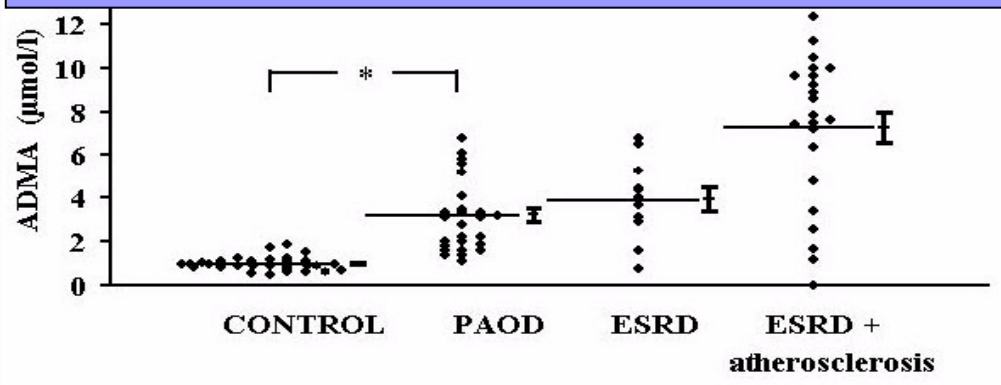
Improving Proteinuria, Endothelial Functions and Asymmetric Dimethylarginine Levels in Chronic Kidney Disease: Ramipril versus Valsartan

Mahmut Ilker Yilmaz[a, f] Mutlu Saglam[b] Alper Sonmez[c] Kayser Caglar[a]
Erdinc Cakir[d] Yasemin Kurt[d] Tayfun Eyileten[a] Mustafa Tasar[b]
Cengizhan Acikel[e] Yusuf Oguz[a] Abdulgaffar Vural[a] Mujdat Yenicesu[a]

Blood Purification; 2007; 25(4):327-335

	Group I ACE inhibitor (ramipril) n = 32 (16 M, 16 F), 5 mg/day		Group II AT II blocker (valsartan) n = 34 (17 M, 17 F), 160 mg/day	
	baseline	3 months	baseline	3 months
eGFR, ml/min/1.73 m²	44.00 ± 11.79	41.87 ± 11.67	39.79 ± 11.51	38.47 ± 11.54
ADMA, μmol/l	1.52 ± 0.24	1.13 ± 0.18*	1.57 ± 0.31	1.17 ± 0.25*
SDMA, μmol/l	1.63 ± 0.22	1.52 ± 0.24*	1.66 ± 0.28	1.56 ± 0.27*
L-Arginine, μmol/l	81.1 ± 10.2	91.5 ± 8.9*	82.0 ± 7.5	85.3 ± 10.6
L-Arginine/ADMA ratio	57.1 ± 13.7	83.8 ± 22.7*	54.3 ± 13.9	77.9 ± 28.1*
hsCRP, mg/l	12.34 ± 1.99	7.81 ± 2.24*	12.90 ± 4.49	7.17 ± 3.58*
SBP, mm Hg	154.84 ± 7.84	131.87 ± 7.85*	151.55 ± 7.02	135.94 ± 9.17*
DBP, mm Hg	94.59 ± 2.90	86.56 ± 4.33*	91.41 ± 2.65	88.47 ± 3.13*
FPG, mg/dl	84.75 ± 5.80	69.43 ± 6.49*	90.47 ± 4.46	70.38 ± 5.64*
Insulin, μU/ml	5.20 ± 1.11	4.13 ± 0.97*	5.01 ± 1.00	4.55 ± 1.49*
HOMA	1.08 ± 0.24	0.71 ± 0.19*	1.12 ± 0.22	0.79 ± 0.26*
Proteinuria, mg/day	1,485.31 ± 286.66	697.34 ± 221.31*	1,481.47 ± 409.98	957.64 ± 361.56*
NMD, %	12.86 ± 0.42	12.93 ± 0.52*	12.80 ± 0.52	13.00 ± 0.59*
FMD, %	7.07 ± 0.44	8.25 ± 0.74*	6.43 ± 0.55	7.67 ± 0.79*

Kielstein JT, et al. JASN 1999



Miyazaki H, et al. Circulation 1999

116 sağlıklı insan

ADMA ↑ ADMA-CIMT ↑ CIMT

Zoccali C, et al. Kidney Int 2002

SDBY olan 225 hastada artmış plazma ADMA
Ortalama 33.4 aylık takip
120 major kardiyovasküler olay ve toplam 83 ölüm
ADMA ve yaş

Zoccali C, et al. JASN 2002

90 SDBY

ADMA ↑ ADMA-CIMT ↑ CIMT

Nijveldt RJ , et al. Clin Nutr 2003

Yoğun bakım ünitesindeki hastalarda

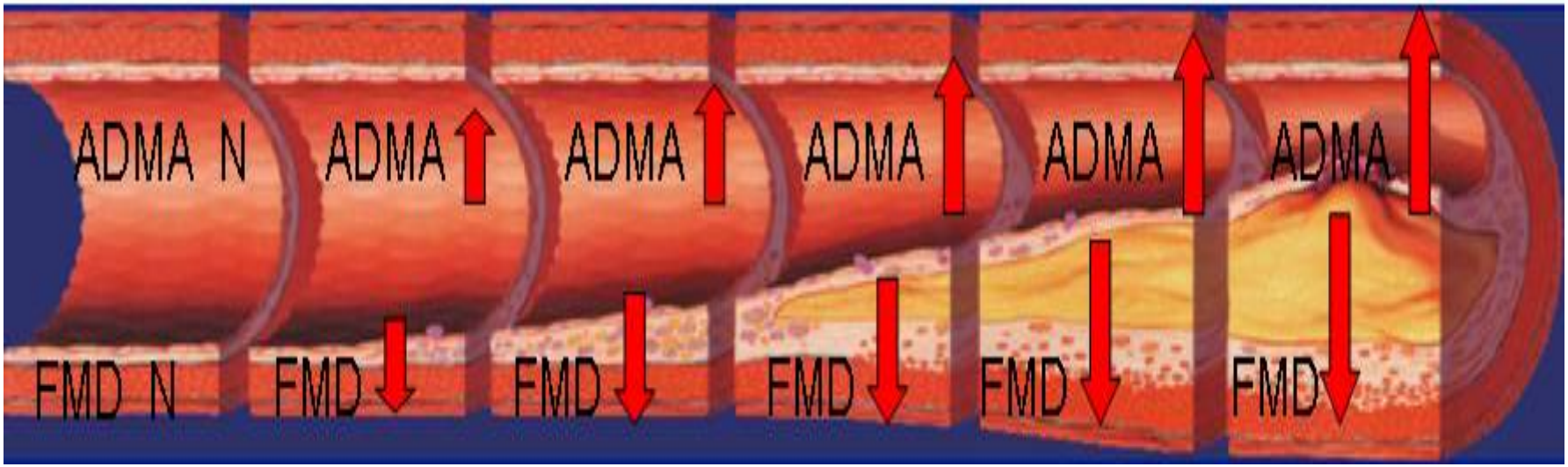
ADMA → Mortalite 17 kat

Volkanen, et al. Lancet 2001

150 orta yas sigara icen

ADMA 3.9 → Akut koroner olay

FMD-ADMA ilişkisi



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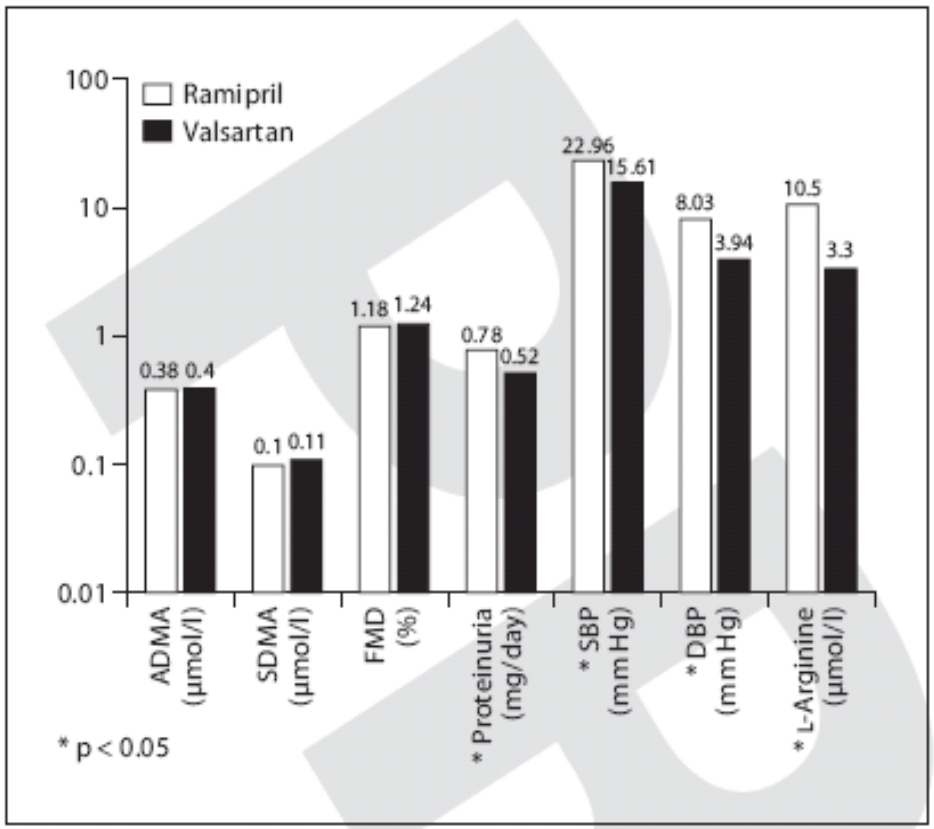

	ADMA µmol/l	SDMA µmol/l
Age, years	NS	NS
GFR, ml/min/1.73 m^2	–0.379*	–0.361*
Serum albumin, g/dl	NS	NS
BMI	NS	NS
hsCRP, mg/l	0.532**	0.270*
HOMA	NS	NS
L-Arginine, µmol/l	–0.369*	–0.305*
L-Arginine/ADMA ratio	–0.884**	–0.541**
Proteinuria, mg/day	0.823**	0.553**
FMD, %	–0.409**	–0.370*
NMD, %	NS	NS

ADMA Levels Correlate with Proteinuria, Secondary Amyloidosis, and Endothelial Dysfunction

Mahmut Ilker Yilmaz,*† Alper Sonmez,‡ Mutlu Saglam,§ Abdul R. Qureshi,† Juan Jesus Carrero,† Kayser Caglar,* Tayfun Eyileten,* Erdinc Cakir,‖ Yusuf Oguz,* Abdulgaffar Vural,* Mujdat Yenicesu,* Bengt Lindholm,† Peter Stenvinkel,† and Jonas Axelsson†

J Am Soc Nephrol, 19:388, 2008

	Healthy, age and sex-matched controls (n=50)	Non-nephrotic proteinuria (<3.5 g/day) (n=43)	Nephrotic-range proteinuria without amyloidosis (>3.5 g/day) (n=39)	Nephrotic-range proteinuria with amyloidosis (>3.5 g/day) (n=39)	Differences between the two nephrotic groups[1] (p)	ANOVA (p)
Clinical parameters						
eGFR (ml/min/ 1.73 m^2)	103±4	102±9	90±6	93±7	NS	NS
Proteinuria (g/day)	0.1±0.03	2.5±0.8	4.9±1.3	5.3±1.2	NS	<0.001
Metabolic markers						
Total Cholesterol (mg/dl)	189±18	203±27	283±33	281±55	NS	<0.001
Triglycerides (mg/dl)	122 (84-155)	134 (78-58)	214 (151-243)	215 (128-265)	NS	<0.001
LDL Cholesterol (mg/dl)	112±14	112±15	158±27	158±20	NS	<0.001
Serum albumin (g/dl)	4.1±0.3	4.1±0.4	3.1±0.6	3.0±0.4	NS	<0.001
Inflammation and glucose homeostasis						
hsCRP (mg/l)	2.3±0.9	11.5±2.8	14.5±2.8	14.6±3.4	NS	<0.001
HOMA	1.2 (0.8-2.1)	2.1 (1.1-4.3)	2.2 (1.1-5.3)	3.0 (1.0-7.4)	<0.001	<0.001
Endothelial function and methylarginines						
FMD (%)	8.8±1.2	7.1±0.6	6.6±0.6	5.8±0.7	<0.001	<0.001
L-Arginine (μmol/l)	96.5±9.1	96.2±7.9	93.1±5.7	92.1±7.9	NS	0.02
L-Arginine/ADMA	108 (70-232)	61 (46-98)	32 (19-56)	22 (15-31)	0.027	<0.001
ADMA/SDMA ratio	1.2±0.3	0.75±0.11	0.89±0.13	0.93±0.07	<0.001	<0.001
SDMA (μmol/l)	0.8 (0.5-1.3)	2.2 (1.2-2.4)	3.2 (1.8-4.8)	4.6 (3.2-5.5)	<0.001	<0.001
ADMA (μmol/l)	0.9 (0.5-1.2)	1.6 (1.1-1.8)	3.0 (1.9-4.4)	4.2 (3.1-5.0)	<0.001	<0.001

CLINICAL RESEARCH www.jasn.org

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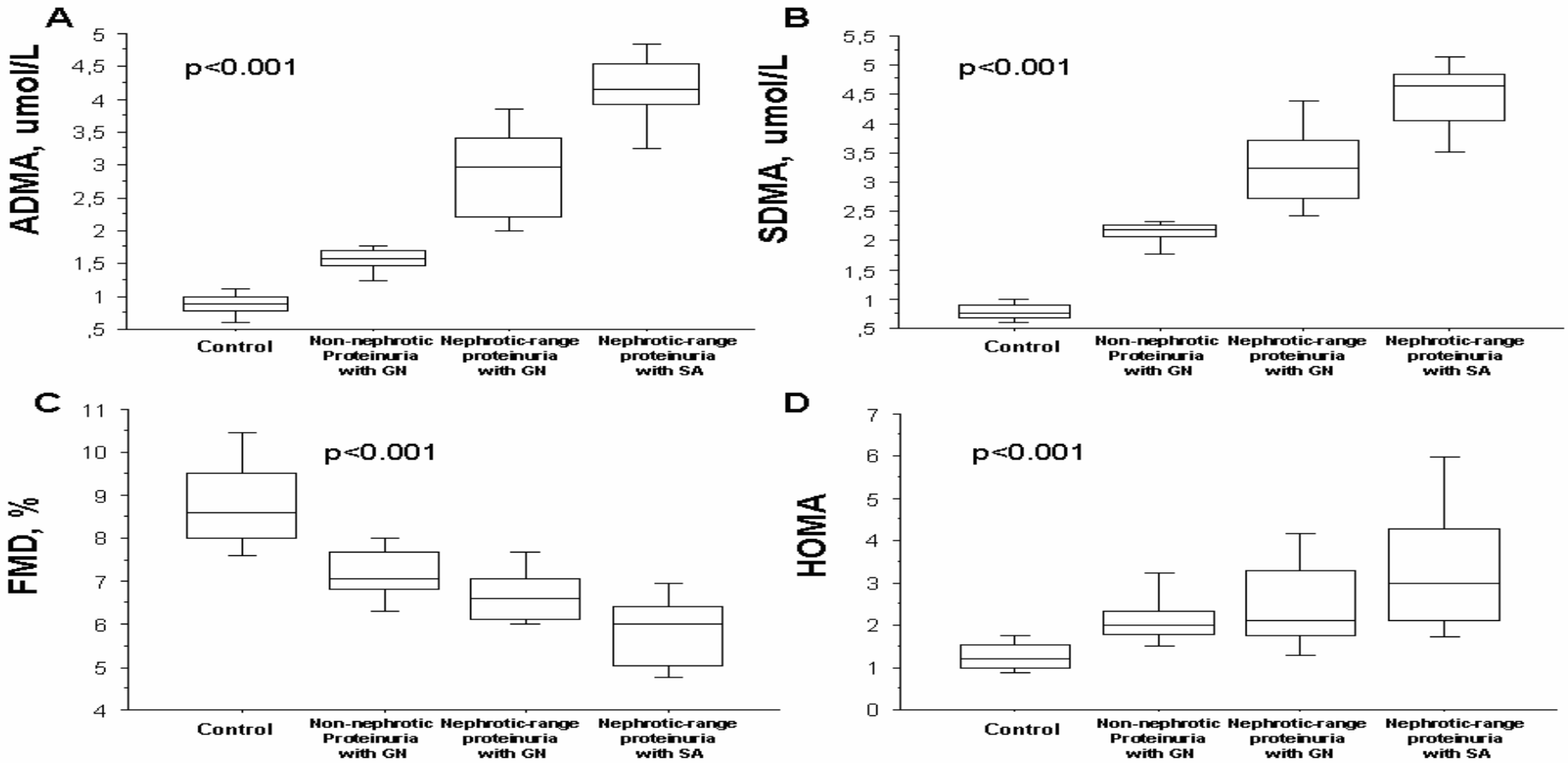

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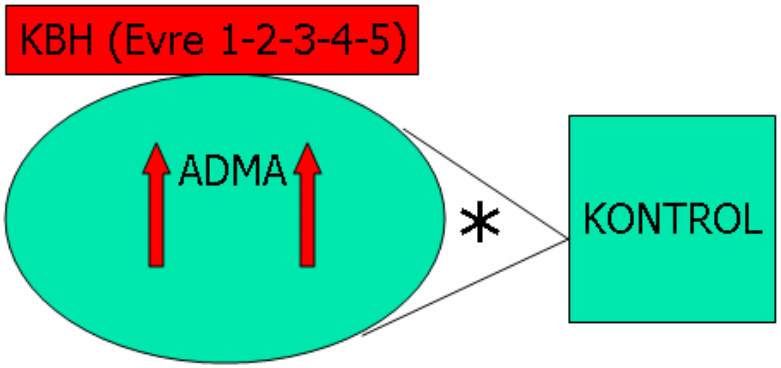
A) FMD%. *The initial model included sex (male vs female), high age (>33 years), high proteinuria (>2.5 g/day, yes/no), high serum albumin (>3.5 g/dl), high hs CRP (>10 mg/l), high HOMA (> 2.1), high total cholesterol (>200 mg/dl), high triglycerides (>150 mg/dl), high SDMA (>3.16 µmol/l) and high ADMA (>2.76 µmol/l).*

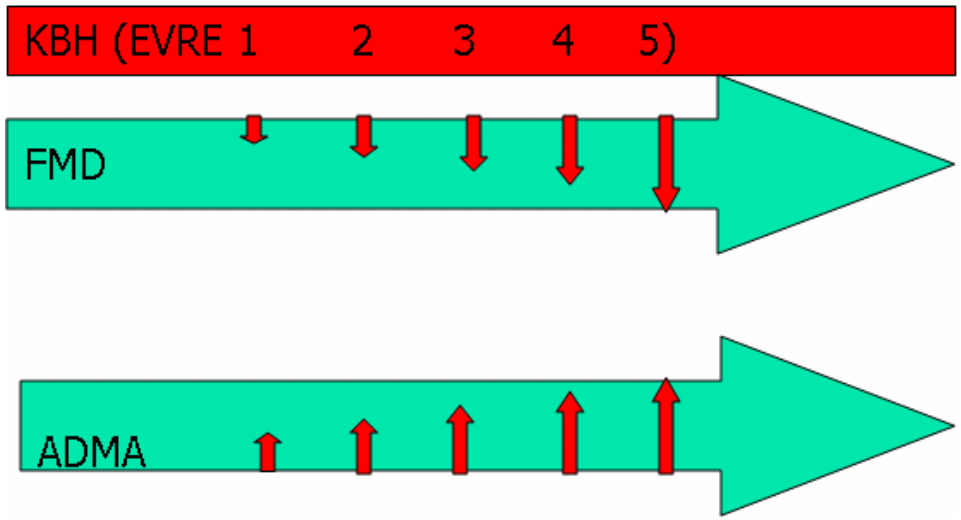
	Estimate	Standard error	Partial r^2	p value
Intercept	7.3	0.12		<0.0001
ADMA (µmol/l) (>2.76 µmol/l)	-0.60	0.16	0.27	0.0002
Serum albumin, >3.5 g/dl	-0.44	0.15	0.21	0.004
HOMA (>2.1)	-0.35	0.13	0.10	0.01

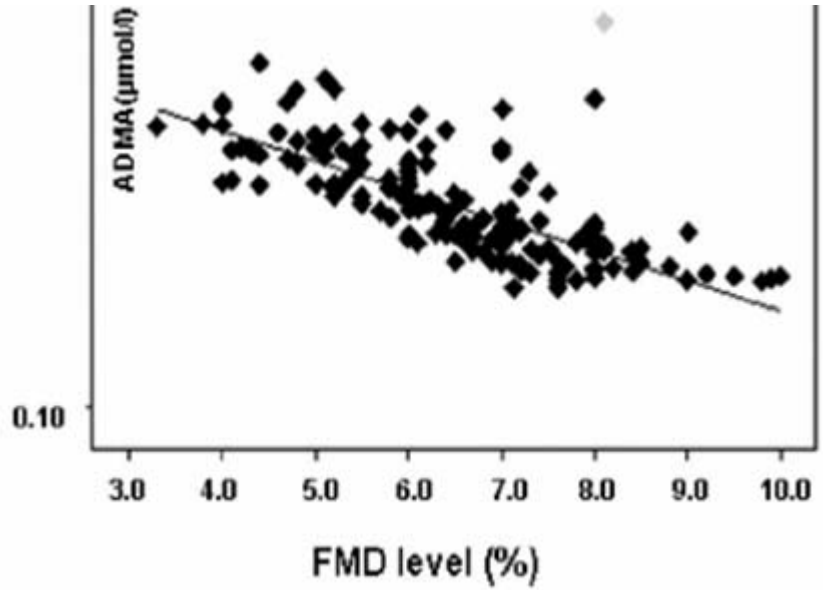
The Determinants of Endothelial Dysfunction in CKD: Oxidative Stress and Asymmetric Dimethylarginine

Mahmut Ilker Yilmaz, MD, Mutlu Saglam, MD, Kayser Caglar, MD, Erdinc Cakir, MD, Alper Sonmez, MD, Taner Ozgurtas, MD, Ahmet Aydin, MD, Tayfun Eyileten, MD, Omer Ozcan, MD, Cengizhan Acikel, MD, Mustafa Tasar, MD, Gultekin Genctoy, MD, Kemal Erbil, MD, Abdulgaffar Vural, MD, and Carmine Zoccali, MD

Am J Kidney Dis. 2006 Jan;47(1):42-50.







Neler söyledim?

- Endotel disfonksiyonu hipertansiyon ve kronik böbrek hastalığı gibi kronik hastalıklarda ki mortalite ve morbidite ile yakından ilişkilidir.
- Endotel fonksiyonunu ölçmede bir çok metod vardır.
- Bu metodlardan serumda ADMA ölçümü ile fonksiyonel testlerden biri olan FMD uygun ölçümler olarak kullanılabilir.