

# Normoalbuminürik diyabetik nefropati

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# DIYABETİK NEFROPATİ

- Diyabetik nefropati, çoğunlukla intraglomerüler arteriollerin hasarına bağlı olarak progressif böbrek fonksiyonların bozulması ile ortaya çıkan tablodur

- Diyabetik Nefropati
  - Tip1DM %25-40
- •Tip2DM %5-40
  - Tanıda mikroalbuminuri  $\approx$ %20
- Standl E *Diabetologia* 1993; 36:1017
- –Hemodiyalizdeki diyabetlilerde Tip 2 DM oranı > %80

- spot idrar alb/kr oranı ( UDDK )
- Normal <30 mg/g kreatin
- Yüksek  $\geq 30$  mg/g kreatin

- 24 saatlik idrarda
- Normal 30 mg/24 s
- Mikroalbüminuri 30-300 mg/24 s
- Proteinuri >300 mg/24 s

# Diyabetik nefropati etiyopatogenez

- Kan şekeri kontrolü
- Genetik yatkınlık
- Hipertansiyon
- Sigara
- Obezite
- Yaş
- OKS kullanımı
- Riskli gruplar hispanikler, pima yerlileri

# DN patogenez-patoloji

## Patogenez



## Patoloji

- Glomerulopati
  - Mezengial proliferasyon
  - Bazal membran kalınlaşması
  - Glomeruloskleroz
    - Diffüz
    - Nodüler (Kimmelstiel-Wilson lezyonu)
- Tubulopati
- Vaskülopati

# DN SINIFLAMA TDDK KILAVUZ 2015

Tanım	GFR (ml/dak/1.73 m <sup>2</sup> vücut yüzeyi için)
Normal veya artmış GFR ile böbrek hasarı	≥ 90
Hafif azalmış GFR ile böbrek hasarı	60-89
Orta derecede azalmış GFR	30-59
Ciddi derecede azalmış GFR	15-29
Son dönem böbrek yetmezliği	< 15 veya diyaliz

# Normoalbuminürük diyabetik nefropati

- GFH`nın 60 ml/dk dan daha düşük olduđu buna karşılık idrarda albumin atılımının normal olduđu tabloya normoalbuminürük diyabetik nefropati (DN)



# Normoalbuminurik diyabetik nefropati sıklığı

- Tip 1 DM`lu olgularda DCCT-EDIC % 23.6
- Tip 2 DM`lu olgularda
  - DEMAND % 35.1
  - NEFRON % 56.5
  - RIACE %56.5
  - ADVANCE %61.6
  - JDDM %55.0

# DEMAND

- 24151 olgu
- 11.833 kreatin değeri mevcut 11573 olgu tamamlanmış
- Normoalbuminurik DN sıklığı % 35.1
  
- Normoalbuminurik 6072 olgudan 1044 KBH (%17)
- Mikroalbuminurik 4409 olgudan 1207 KBH (%27)
- Makroalbuminurik 1092 olgudan 335 KBH (%31)

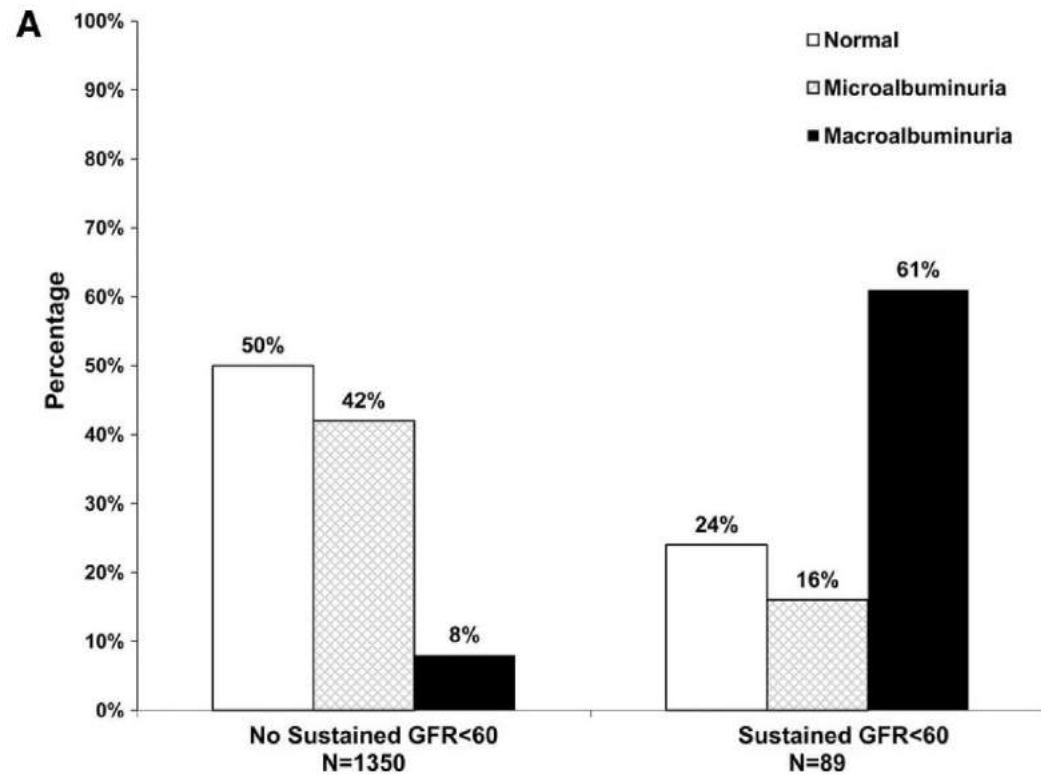
# NEPHRON(National evaluation of the Frequency of Renal Impairment Co-existing with NIDDM)

- 3893 Tip 2 DM li olgu
- %23 .1 GFH > 60 ml/dk
  - % 55 normoalbuminuri

# UKPDS 74

- % 38 olgu albuminuri
- % 29 olgu böbrek yetmezliđi
- % 51 olgu  $GFR < 60$  ml/ dk ve normoalbuminurik

# DCCT-EDIC



- Tip 1 DM % 24  
normoalbuminurik diyabetik  
nefropati

# ETİYOPATOGENEZ

- Renal iskemi
  - İskemik vasküler hastalık
  - Kolesterol mikroemboli
- İntertisyel fibrozis
- Genetik eğilim
- RAS blokajı

# Genetik eğilim

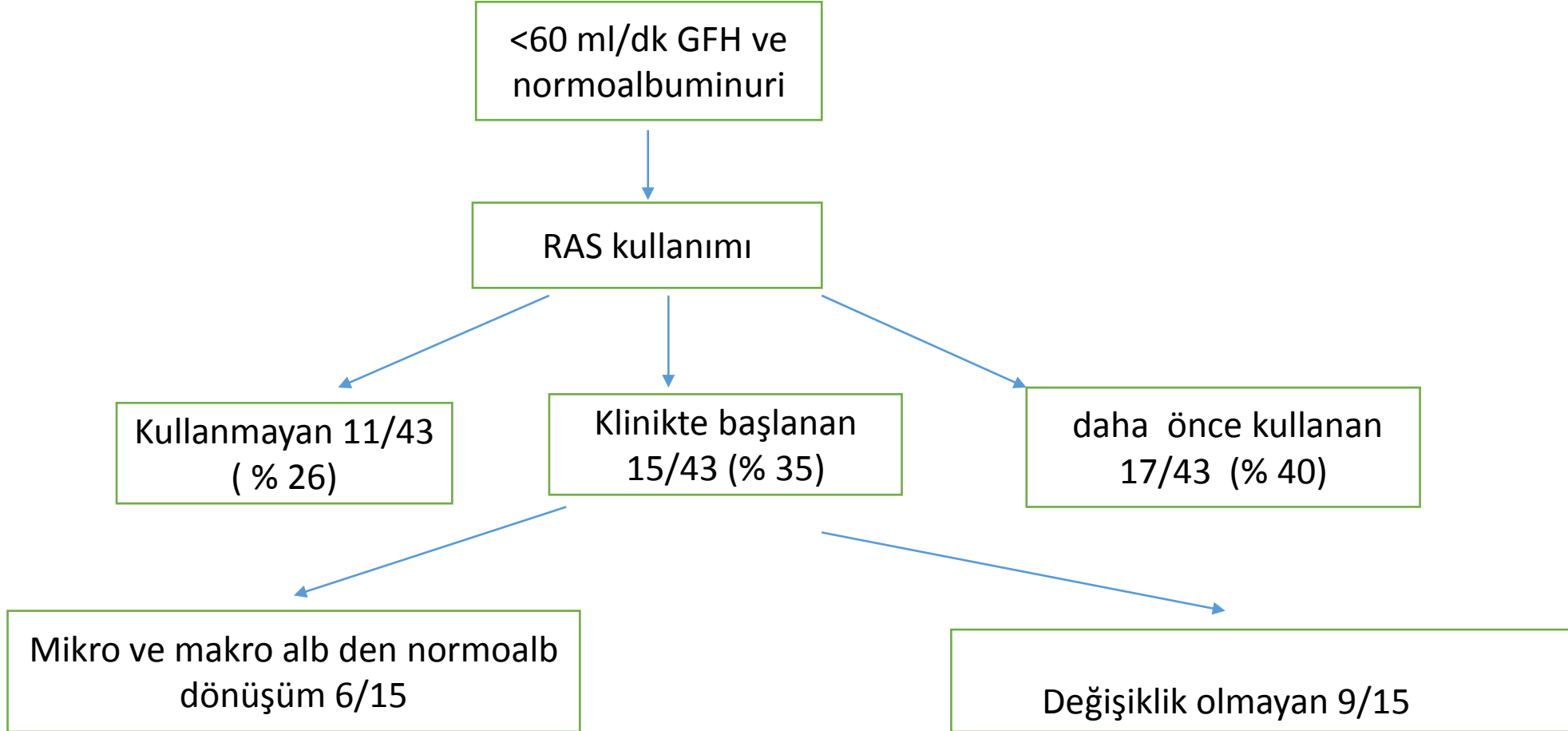
- PKC  $\beta$  gen polimorfizmi sıklığında artış

# RAS Blokajı

- RAS blokajının artmasıyla normoalbuminurik diyabetik nefropati sıklığı arasında ilişki
- RIACE çalışmasında albuminurik olgularda daha fazla RAS blokajı



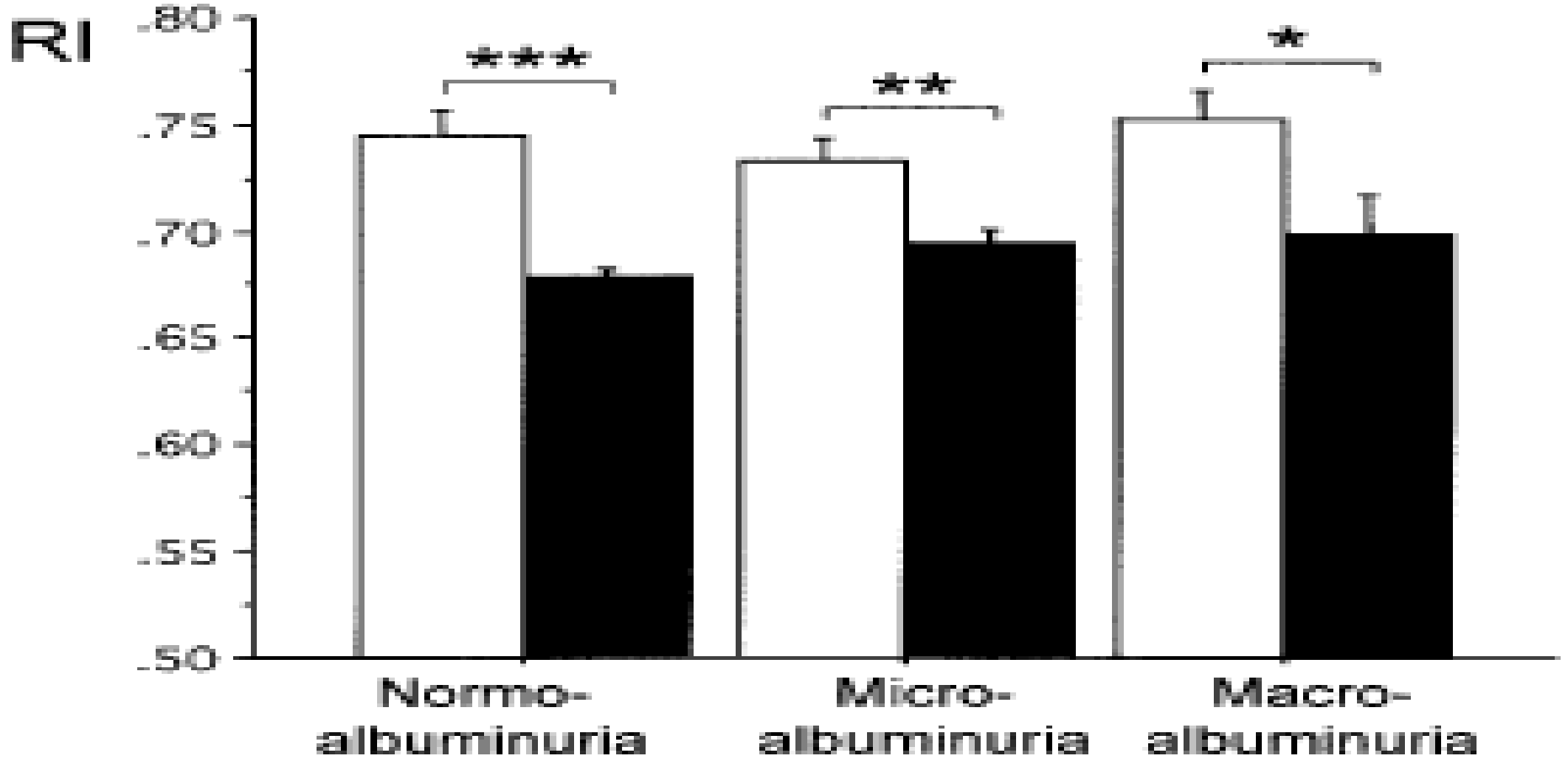
# RAS BLOKAJI



# RENAL İSKEMİ

- 325 Tip 2 DM`lu olgu
- Dopler USG ile rezistans indeksi ölçümü
- Tek nefron düzeyinden daha çok tüm böbrek düzeyinde arteryel direnci ölçüyor
- Renal arter stenozunu değerlendiremiyor
- İntrarenal arteryel rezistans indeksi ile GFR arasında ters ilişki

II

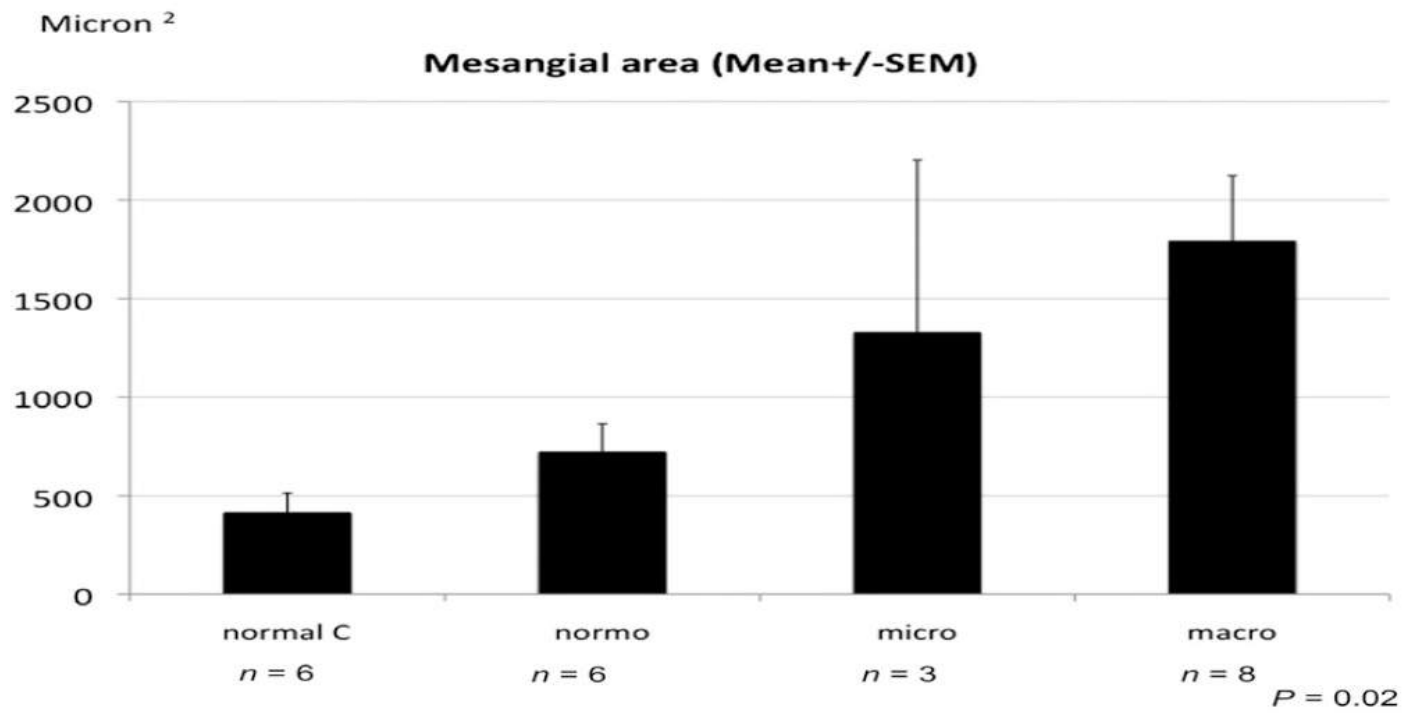


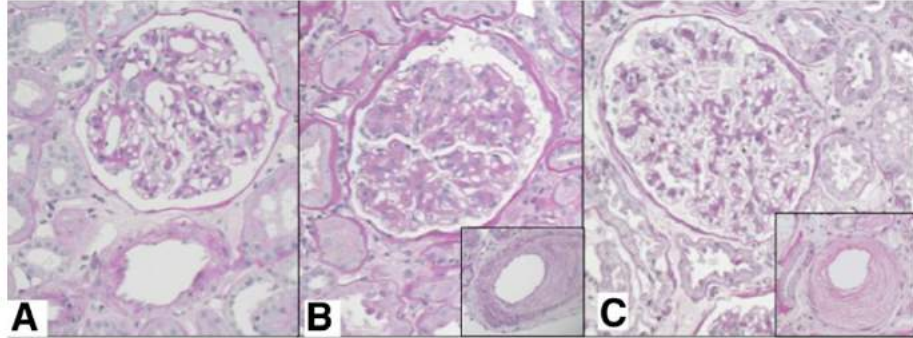
# Normoalbuminurik tip 2 DM`lu olgularda renal yapı

- 8 normoalbuminurik Tip 2 DM
- 6 mikroalbuminurik Tip 2 DM
- 17 makroalbuminurik Tip 2 DM

Patient study number	Fioretto category	ICC	GS score (0–3)	Mesangial expansion (0–3)	TA/IF (0–3)	Arteriolar hyalinosis (0–3)	Arteriosclerosis (0–3)	GBM thickness (on EM, nm)		Summary
								NR males 250–430 nm,	females 230–395 nm	
1	C1	U	1	0	0	0	0	244 WNR		Not DN, mild IgA nephropathy, no cause for renal impairment found
2	C1	U	2	0	1	1	1	#		Mild nonspecific changes, not DN
3	C2	III	1	3	2	3	2	#		Typical advanced DN
4	C2	IIa	1	1	1	1	1	276 WNR		Typical early DN
5	C2	IIa	1	1	0	1	2	321* ULN		Typical early DN
6	C3	U	1	0	1	2	1	260 WNR		Renovascular, not DN
7	C3	U	1	0	1	0	2	253 WNR		Renovascular, not DN
8	C3	I	3	1	3	1	3	395 >normal		Atypical DN, mild glomerular changes + severe vascular and tubulointerstitial disease

C1, defined by normal or near-normal histology; C2, defined by histology reflecting typical DN with predominantly glomerular changes; C3, defined by atypical histology, with disproportionately severe interstitial, tubular, or vascular damage and few or no glomerular changes; ICC, 2010 International Consensus Classification of DN; NR, normal range; U, unclassified; ULN, upper limit normal; WNR, within normal range. Normal range of GBM on EM reference (29). #EM not performed. \*On EM, GBM had abnormal homogenized quality highly suggestive of DN.





- Normoalbuminürük olgularda klasik DN aksine yaş, hipertansiyon ve intrarenal vasküler hastalığa ilişkin patolojik bulgular mevcut

- 105 normoalbuminurik Tip 1 DM
- 82 olgu Kr klirensi  $\geq 90$  ml/dk
- 23 olgu kr klirensi  $< 90$  ml/dk



	Normal GFR group	Low GFR group	<i>P</i>
<i>n</i>	82	23	
Sex (male/female)	36/46	4/19	0.021
Age (years)	35.2 ± 9.5	36.0 ± 8.0	NS
Age at diabetes onset (years)	12.9 ± 7.0	11.3 ± 7.9	NS
Diabetes duration (years)	22.2 ± 9.6	24.6 ± 8.0	NS
HbA <sub>1c</sub> (%)	8.5 ± 1.6	8.4 ± 1.1	NS
Serum creatinine (mg/dl)*	0.84 ± 0.17	0.96 ± 0.21	0.005
SBP (mmHg)	119.8 ± 10.9	116.8 ± 12.9	NS
DBP (mmHg)	71.2 ± 7.8	71.7 ± 7.3	NS
MBP (mmHg)	87.6 ± 8.2	86.5 ± 8.4	NS
Hypertension (yes/no)	27/55	11/12	NS
Antihypertensive treatment (yes/no)	13/69	9/14	0.022
ACEI or AARB (yes/no)	4/78	3/20	NS
GFR (ml · min <sup>-1</sup> · 1.73 m <sup>-2</sup> )†	121.2 ± 16.6	75.9 ± 11.7	ND
AER (μg/min)	7.7 (2.8-19.9)	7.7 (2.0-17.6)	NS
Retinopathy (none/background/proliferative)	33/31/15	2/11/10	0.006

	Control	Normal GFR	Low GFR	<i>P</i>
GBM width (nm)	331.5 ± 45.7	469.4 ± 84.2	544.5 ± 140.7	<0.001
V <sub>v</sub> (Mes/glom)	0.20 ± 0.03	0.28 ± 0.06	0.34 ± 0.08	<0.001
V <sub>v</sub> (MM/glom)	0.09 ± 0.02	0.15 ± 0.04	0.20 ± 0.06	<0.001
V <sub>v</sub> (MC/glom)	0.08 ± 0.02	0.08 ± 0.02	0.10 ± 0.02	<0.001
S <sub>v</sub> (PGBM/glom) (μm <sup>2</sup> /μm <sup>3</sup> )	0.126 ± 0.018	0.116 ± 0.019	0.094 ± 0.021	<0.001

**Klasik DN ye özgün ileri derecede glomeruloskrozun olduğu mikroskopik bulgular**

# Cohen diyabetik rat

- Tipik glomeruloskleroz
- Albuminüri saptanmıyor
- Nonproliferative diyabetik retinopati

- 8 GFR düşük normoproteinurili olgu
- 19 normal GFR ve normoproteinurili olgu
- 7 normal GFR mikroalbuminurili olgu
- 7 düşük GFR mikroalbuminurili olgu
- normoproteinurik düşük GFR ile mikroalbuminurik düşük GFR li olgular benzer glomeruler yapı gösteriyor ( klasik DN)

# NGAL( n6trotrofil gelatinaz iliřkili lipokalin)

- Klinik ve deneysel nefrolojide tubuler biyobelirteç
- Akut tubuler hasar g6stergesi
- Tehlikeli durumda b6brek tubuler h6crelerinde saatler iinde y6kselir
- Otozomal PKB ve glomerulonefrit etyopatogeneğinde rol oynuyor

- Diyabetik hastalarda daha yüksek
- S NGAL Hba1c düzeyiyle doğrusal orantılı
- Albüminüri ile doğru orantılı
- S NGAL 77.4 ng/ ml %88 özgüllük
- U NGAL 9.3 ng/ml % 100

- 260 Tip 2 DM lu olgu
- Böbrek biyopsisi ile kanıtlanmış diyabetik nefropati
- 8.1 yıl izlem
- 95 olgunun idrar albümin atılım kayıtları mevcut
- 10 ( %10.5 )normoalbuminuri
- 31 (% 32.6) mikroalbuminuri
- 54 (% 54.9) makroalbuminuri
- Dm süresi  $11.9 \pm 7.1$  yıl
- % 79.5 retinopati

- Tubulointertisyel deęişiklikler
- Arterioskleroz
- İntertisyel inflamasyon
- Arterioller hyalinozis

	Normoalbuminuria (normal proteinuria)		Micro-/macroalbuminuria (mild/severe proteinuria)		P for normo (normal) vs. micro (mild)/macro (severe)	
	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>
n	28	15	78	139		
<b>Clinical parameters</b>						
Age (years)	48.8 ± 13.8	62.5 ± 6.2**	53.8 ± 10.8	62.1 ± 9.6††	0.10	0.74
Male	53.6	46.7	65.4	65.5	0.27	0.15
Serum creatinine (mg/dL)	0.7 ± 0.1	1.2 ± 0.4**	0.7 ± 0.2	1.9 ± 1.5††	0.95	<0.01
eGFR (mL/min/1.73 m <sup>2</sup> )	86.0 ± 16.4	46.0 ± 10.6**	89.0 ± 26.4	36.4 ± 15.5††	0.81	<0.05
Hematuria	4.2	7.7	32.8	51.9†	<0.01	<0.01
Diabetes duration (years)	8.0 ± 7.4	7.4 ± 6.4	9.6 ± 6.6	13.1 ± 8.8††	0.21	<0.05
Diabetic retinopathy	41.7	50.0	81.7	87.9	<0.01	<0.01
HbA <sub>1c</sub> (%)	8.5 ± 2.4	8.3 ± 2.2	8.4 ± 2.5	7.4 ± 2.0††	0.53	0.35
HbA <sub>1c</sub> (mmol/mol)	65.0 ± 26.2	64.1 ± 25.1	68.8 ± 27.1	57.1 ± 22.3††	0.53	0.35
BMI (kg/m <sup>2</sup> )	23.5 ± 2.2	22.2 ± 2.2	22.9 ± 4.8	23.5 ± 3.4†	0.07	0.34
Systolic blood pressure (mmHg)	132.0 ± 17.1	129.3 ± 14.3	138.8 ± 22.1	146.9 ± 21.0††	0.31	<0.01
Diastolic blood pressure (mmHg)	75.0 ± 11.2	75.6 ± 10.0	77.6 ± 12.0	76.8 ± 12.4	0.26	0.91
Total cholesterol (mg/dL)	192.7 ± 37.4	196.6 ± 51.5	215.0 ± 54.4	227.6 ± 100.6	0.07	0.31
Hemoglobin (g/dL)	14.2 ± 1.6	13.0 ± 1.8	13.2 ± 2.1	11.1 ± 2.2††	<0.05	<0.01
<b>Pathological parameters</b>						
Diffuse lesion (0–4)	0.9 ± 0.6	1.5 ± 0.9*	2.0 ± 0.9	2.4 ± 0.8†	<0.01	<0.01
Nodular lesion	0.0	20.0*	44.7	65.1††	<0.01	<0.01
Exudative lesion	0.0	6.7	25.0	44.1††	<0.01	<0.01
Mesangiolytic	0.0	0.0	29.6	30.2	<0.01	<0.05
IFTA (0–3)	1.1 ± 1.0	2.3 ± 0.7**	1.6 ± 0.9	2.1 ± 0.9††	<0.05	0.41
Interstitial inflammation (0–2)	0.9 ± 0.8	1.5 ± 0.5**	0.9 ± 0.5	1.2 ± 0.5††	0.61	<0.05
Arteriolar hyalinosis (0–3)	1.4 ± 1.1	2.4 ± 0.8**	1.8 ± 1.0	2.2 ± 0.8††	0.07	0.33
Arteriosclerosis (0–2)	0.7 ± 0.6	1.9 ± 0.4**	1.2 ± 0.7	1.5 ± 0.5††	<0.01	<0.05

# Normoalbuminürik DN olgularının klinik özellikleri

- Kadınlarda
- Diyabet süresi kısa olanlarda
- Retinopati
- Nöropati
- Sigara içme
- HbA1C
- Trigliserid
- Hemogloblin
- HDL- K düzeyleri
- İleri yaş
- Metabolik sendrom



# GFR < 60 ml/dk albuminuri ( NEPHRON)

- Hipertansiyon
- Retinopati
- Makrovasküler hastalık
- Birinci derece akrabada KBH

# GFR < 60 ml/dk normoalbuminuri ( NEPHRON)

- Hipertansiyon
- Retinopati
- Makrovasküler hastalık
- Birinci derece akrabada KBH ile ilgi yok

# UKPDS 74 GFR azalması belirteçleri

- Kadın
- Düşük bel çevresi ölçümü
- İnsülin duyarlılığında artma
- Yaş

# UKPDS 74 albüminuri belirteçleri

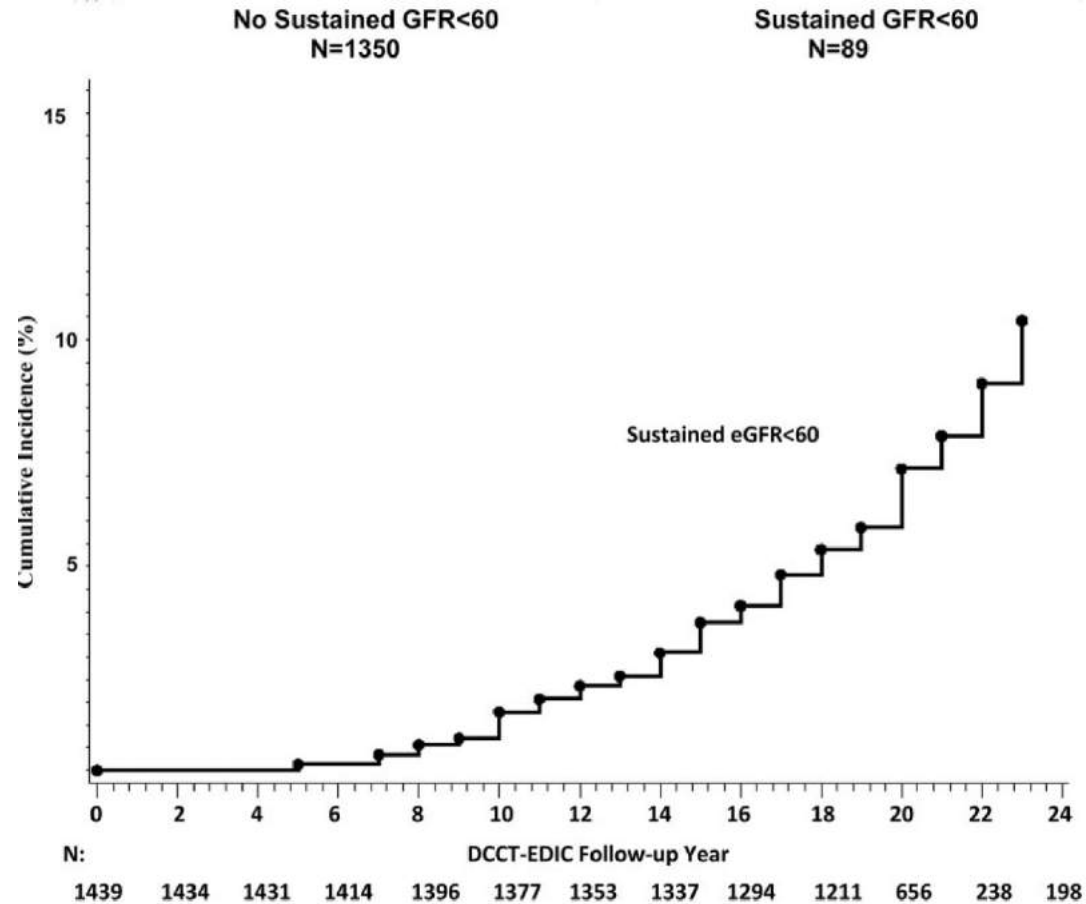
- Erkek
- Sigara
- Artmış bel çevresi
- TG, LDL-K yüksekliği
- Hba1C yüksekliği
- Retinopati öyküsü
- BK sayısında artma

# Tip 2DM lu olgularda normoalbuminürik böbrek hastalığı

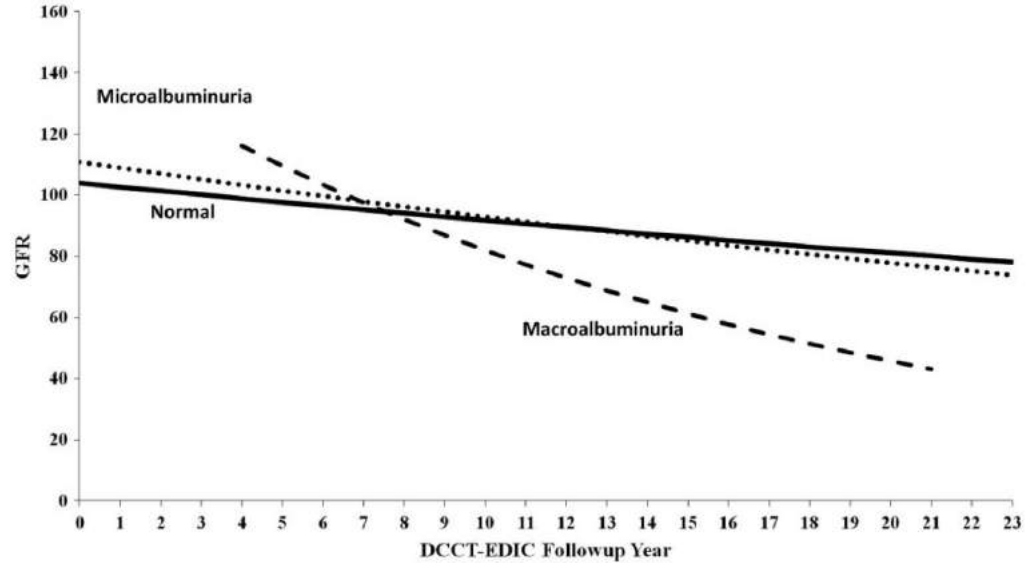
	eGFR		P
	>60 ml/min per 1.73 m <sup>2</sup>	15–60 ml/min per 1.73 m <sup>2</sup>	
n	576	84	—
Female subjects	444 (77.4)	51 (60.2)	0.002
Age (years)	56.8 ± 9.5	62.9 ± 10.3	<0.001
Diabetes duration (years)	9.3 ± 7.1	10.1 ± 7.0	0.318
BMI (kg/m <sup>2</sup> )	28.9 ± 5.2	29.0 ± 5.4	0.841
Male waist circumference (m)	0.98 ± 0.11	0.100 ± 0.65	0.449
Female waist circumference (m)	0.95 ± 0.12	0.98 ± 0.12	0.348
Obesity	18 (3.1)	75 (89.7)	0.375
Smoking	97 (16.4)	9 (11.4)	0.474
Systolic blood pressure (mmHg)	130.0 ± 22.2	146.0 ± 23.7	0.069
Diastolic blood pressure (mmHg)	86.0 ± 12.3	87.0 ± 16.9	1.000
Hypertension	334 (58.7)	56 (67.5)	0.140
HOMA-IR*	4.84 (0.3–45)	11.4 (1.6–44.7)	0.015
A1C (%)	7.07 ± 2.18	6.74 ± 2.35	0.259
Fasting plasma glucose (mg/dl)	175 ± 70.2	164 ± 76.7	0.521
Cholesterol (mg/dl)			
Total	205.3 ± 43.9	222.8 ± 52.0	0.014
HDL	46.4 ± 11.9	44.9 ± 10.6	0.288
LDL	122.1 ± 40.1	143.0 ± 46.0	0.028
Triglycerides (mg/dl)	158 (55–549)	176 (47–842)	0.006
UAE rate (mg/d)	4 (0.1–28.5)	2.35 (1–17)	0.181
Creatinine (mg/dl)	0.9 (0.5–1.2)	1.22 (0.98–2.6)	—
eGFR (ml/min per 1.73 m <sup>2</sup> )	88.0 (60.7–186.5)	34.2 (31.3–39.7)	—
Metabolic syndrome	403 (70.2)	68 (81.9)	0.027

- NHANES III % 13 erişkin tip 2 DM li olguda GFR < 60ml/dk
- KBH lı % 30 olguda
  - Diyabetik retinopati yok
  - İdrar albümin atılımı normal

# KLİNİK GİDİŞ DCCT EDIC



# DCCT EDIC GFR AZALMASI



mal:	1283	1285	1247	1241	1249	1144	1052	1056	1072	1095	987	1068	1062	1038	1035	1031	1018	1004	977	789	527	316	197	170
roalbumin:	156	140	168	163	156	153	147	161	156	201	163	182	180	181	187	166	170	168	159	136	92	51	31	32
roalbumin:	0	6	7	14	21	24	30	37	33	38	34	54	56	78	80	74	75	77	63	58	33	29	18	13

- Normolbuminurili % 1.2
- Mikroalbüminuri % 1.8
- Mikroalbuminuri öyküsü %1.4
- Makroalbuminuri %5.7

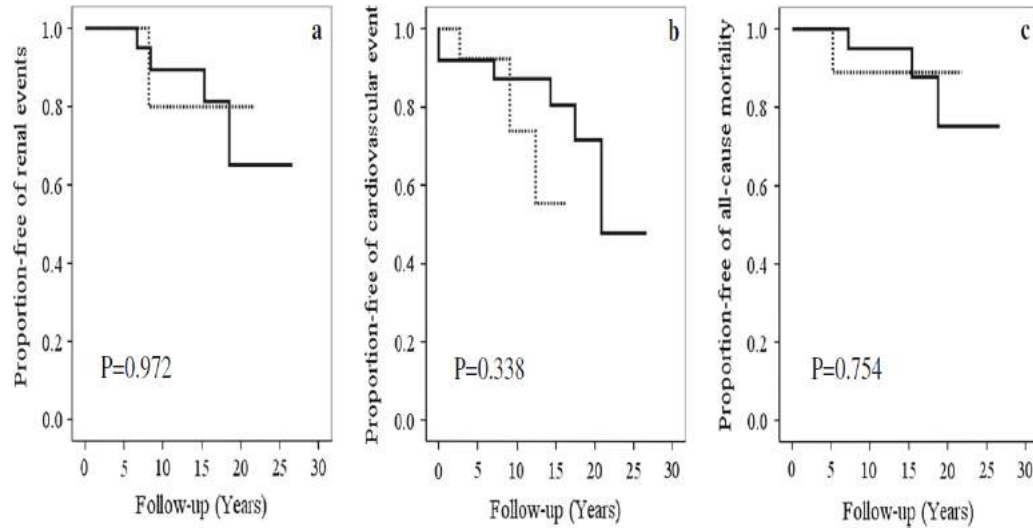


# DEMAND (Developing Education on Microalbuminuria for Awareness of Renal and Cardiovascular risk in Diabetes)

- 24151 olgu
- 11.833 kreatin değeri mevcut  
11573 olgu tamamlanmış
- Normoalbuminurik 6072  
olgudan 1044 KBH (%17)
- Mikroalbuminurik 4409  
olgudan 1207 KBH (%27)
- Makroalbuminurik 1092  
olgudan 335 KBH (%31)

CKD	n	Normoalbuminuria	Microalbuminuria	Macroalbuminuria
Total	24,151 (100%)	51%	39%	10%
Stage 1	3,132 (13%)	56%	36%	8.4%
Stage 2	5,855 (24%)	56%	36%	8.5%
Stage 3	2,428 (10%)	41%	47%	12%
Stage 4	141 (0.6%)	26%	48%	26%
Stage 5	17 (0.07%)	29%	47%	24%
Unknown	12,578 (58%)	51%	39%	10%

# KLİNİK SEYİR



- Renal olay
- KVH olay
- Toplam mortalite
- Normoalbuminurik olgularda daha düşük

# Klinik Gidiş

	Normoalbuminuria (normal proteinuria)		Micro-/macroalbuminuria (mild/severe proteinuria)		P for normo (normal) vs. micro (mild)/macro (severe)	
	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>	eGFR ≥60 mL/min/1.73 m <sup>2</sup>	eGFR <60 mL/min/1.73 m <sup>2</sup>
n	28	15	78	139		
<b>Clinical parameters</b>						
Age (years)	48.8 ± 13.8	62.5 ± 6.2**	53.8 ± 10.8	62.1 ± 9.6††	0.10	0.74
Male	53.6	46.7	65.4	65.5	0.27	0.15
Serum creatinine (mg/dL)	0.7 ± 0.1	1.2 ± 0.4**	0.7 ± 0.2	1.9 ± 1.5††	0.95	<0.01
eGFR (mL/min/1.73 m <sup>2</sup> )	86.0 ± 16.4	46.0 ± 10.6**	89.0 ± 26.4	36.4 ± 15.5††	0.81	<0.05
Hematuria	4.2	7.7	32.8	51.9†	<0.01	<0.01
Diabetes duration (years)	8.0 ± 7.4	7.4 ± 6.4	9.6 ± 6.6	13.1 ± 8.8††	0.21	<0.05
Diabetic retinopathy	41.7	50.0	81.7	87.9	<0.01	<0.01
HbA <sub>1c</sub> (%)	8.5 ± 2.4	8.3 ± 2.2	8.4 ± 2.5	7.4 ± 2.0††	0.53	0.35
HbA <sub>1c</sub> (mmol/mol)	65.0 ± 26.2	64.1 ± 25.1	68.8 ± 27.1	57.1 ± 22.3††	0.53	0.35
BMI (kg/m <sup>2</sup> )	23.5 ± 2.2	22.2 ± 2.2	22.9 ± 4.8	23.5 ± 3.4†	0.07	0.34
Systolic blood pressure (mmHg)	132.0 ± 17.1	129.3 ± 14.3	138.8 ± 22.1	146.9 ± 21.0††	0.31	<0.01
Diastolic blood pressure (mmHg)	75.0 ± 11.2	75.6 ± 10.0	77.6 ± 12.0	76.8 ± 12.4	0.26	0.91
Total cholesterol (mg/dL)	192.7 ± 37.4	196.6 ± 51.5	215.0 ± 54.4	227.6 ± 100.6	0.07	0.31
Hemoglobin (g/dL)	14.2 ± 1.6	13.0 ± 1.8	13.2 ± 2.1	11.1 ± 2.2††	<0.05	<0.01
<b>Pathological parameters</b>						
Diffuse lesion (0–4)	0.9 ± 0.6	1.5 ± 0.9*	2.0 ± 0.9	2.4 ± 0.8†	<0.01	<0.01
Nodular lesion	0.0	20.0*	44.7	65.1††	<0.01	<0.01
Exudative lesion	0.0	6.7	25.0	44.1††	<0.01	<0.01
Mesangiolytic	0.0	0.0	29.6	30.2	<0.01	<0.05
IFTA (0–3)	1.1 ± 1.0	2.3 ± 0.7**	1.6 ± 0.9	2.1 ± 0.9††	<0.05	0.41
Interstitial inflammation (0–2)	0.9 ± 0.8	1.5 ± 0.5**	0.9 ± 0.5	1.2 ± 0.5††	0.61	<0.05
Arteriolar hyalinosis (0–3)	1.4 ± 1.1	2.4 ± 0.8**	1.8 ± 1.0	2.2 ± 0.8††	0.07	0.33
Arteriosclerosis (0–2)	0.7 ± 0.6	1.9 ± 0.4**	1.2 ± 0.7	1.5 ± 0.5††	<0.01	<0.05

- Glomeruler lezyonlarda
- İntertisyel fibrozis ve tubuler atrofide mortalite ve SDBY daha yüksek

# KLİNİK SEYİR

	Normoalbuminuric	Albuminuric	P	Microalbuminuric	Macroalbuminuric
n	15	74		36	38
AER (mg/24 h)	20.7 ± 6.2	712 ± 876	0.003	123.7 ± 78.7	1,270 ± 922*†
Serum creatinine (μmol/l)	122 ± 27	160 ± 71	0.04	135 ± 44	183 ± 84*†
% Serum creatinine <120 μmol/l	71	33	0.006	35*	30*
Isotopic GFR (ml/min per 1.73 m <sup>2</sup> )	47.5 ± 19.9	45.2 ± 31.4	0.79	51.8 ± 27.4	39.0 ± 33.6
MDRD e-GFR (ml/min per 1.73 m <sup>2</sup> )	45.6 ± 8.9	40.4 ± 13.7	0.17	43.8 ± 12.2	37.2 ± 14.5
Correlation between MDRD e-GFR and isotopic GFR	r = 0.69, P < 0.005	r = 0.45, P < 0.001		r = 0.53, P < 0.001	r = 0.34, P < 0.05
% MDRD estimations within					
Isotopic GFR ± 10%	26	24	0.84	22	26
Isotopic GFR ± 30%	73	60	0.56	61	60
Isotopic GFR ± 50%	86	79	0.72	83	76
Sex (% female)	66	40	0.058	52	29*
Diabetes type (% type 2)	80	75	0.48	73	76
Age (years)	68 ± 9	64 ± 12	0.17	65 ± 11	62 ± 13
Diabetes duration (years)	14 ± 5	19 ± 11	0.06	19 ± 12	19 ± 10
BMI (kg/m <sup>2</sup> )	27.0 ± 4.5	26.9 ± 4.3	0.89	27.1 ± 4.4	26.7 ± 4.3
A1C (%)	9.0 ± 1.3	8.5 ± 1.6	0.31	8.6 ± 1.3	8.5 ± 2.0
Cholesterol (g/l)	2.37 ± 0.67	2.10 ± 0.48	0.07	2.03 ± 0.38	2.16 ± 0.56
LDL cholesterol (g/l)	1.26 ± 0.46	1.19 ± 0.40	0.54	1.14 ± 0.32	1.25 ± 0.47
HDL cholesterol (g/l)	0.64 ± 0.28	0.52 ± 0.17	0.04	0.56 ± 0.19	0.49 ± 0.15*
Triglycerides (g/l)	1.91 ± 1.86	1.76 ± 1.09	0.67	1.56 ± 0.09	1.96 ± 1.23
Systolic blood pressure (mmHg)	143 ± 16	147 ± 19	0.47	145 ± 19	149 ± 19
Diastolic blood pressure (mmHg)	79 ± 8	81 ± 10	0.56	79 ± 9	83 ± 10
Number of antihypertensive drugs	2.5 ± 1.8	2.4 ± 1.2	0.68	2.2 ± 1.0	2.5 ± 1.3
% on ACE inhibitors	40	59	0.25	69	50
% on angiotensin 2 receptor inhibitors	20	16	0.71	16	17
Hemoglobin level (g/dl)	13.3 ± 1.4	12.3 ± 1.4	0.01	12.6 ± 1.3	12.0 ± 1.4*
% With previous cardiac event	13	38	0.058	31	46
% With diabetic retinopathy	26	66	0.01	61*	71*
% Cigarette smoking	20	52	0.054	41	63*

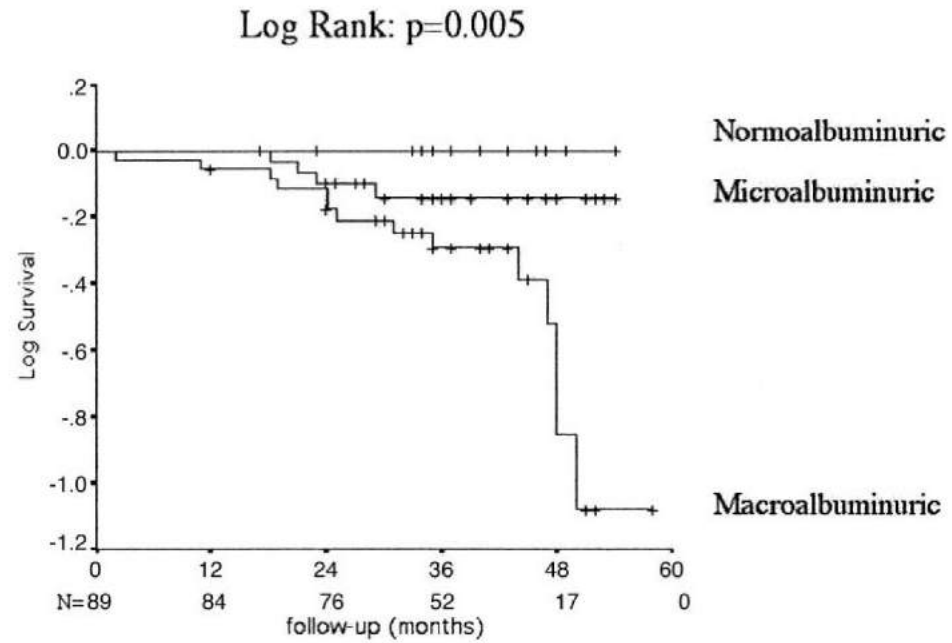
- 89 Tip 2 DM

- 15 normoalbuminurik

- ↓Diabetik retinopati sıklığı

- HDL ve Hb düzeyi yüksek ( Rigallau V, diabetes care 2034-9)

# KLİNİK SEYİR



# KLİNİK SEYİR

Rigalleau V Diabetes care 2007 2034-2039

	normoalbuminüri	mikroalbuminüri	makroalbuminüri
n	15	36	38
izlem (ay)	40 ±8	38 ±11	37 ±13
AER mg/24 s	18±9	271.1±342.2	1508.3±417.4
Kreatin µmol/l	123 ±25	142± 44	265 ±107
GFR MDRD mg/dk	45.8 ±8.5	43± 12.8	29.5 ±21.1
Dializ başlama	0	2	10
Ölüm	0	3	7

# KLİNİK SEYİR

- Normoalbuminurik ancak saptanabilir idrar albümin atılımı olanlarda Kardiyovasküler risk artıyor  
(BENEDICT) (Ruggenti P J Am soc nephrol 1717-1724)
- Normal ancak saptanabilir idrar albümin atılımı olanlarda GFR de hızlı düşme KVH riskinde artış ( Babazono T, 2009 1518-20)

# SONUÇ

- Normoalbuminurik diyabetik nefropati azımsanmayacak bir oranda
- Etiyopatogenezi tam olarak açık değil
- Retinopati saptanmayan KBH lı olgularda, kadınlarda dikkat edilmeli
- Klinik gidiş albuminurik olgulara göre daha selim olsa da saptanabilir albumin atılımının ve hızlı GFR azalmasının KVH risk etkeni olduğu unutulmamalıdır