A.S.O. "S.Croce e Carle"
Cuneo

S.C. Endocrinologia, Diabetologia e Metabolismo
S.S. Malattie Metaboliche e Diabetologia
S.C. Nefrologia

con richiesta di Patrocinio a:
- Associazione Medici Endocrinologi (AME) Piemonte e Valle d'Aosta
- Associazione Medici Diabetologi (AMD) Piemonte e Valle d'Aosta
- Ordine dei Medici Chirurghi e Odontoiatri della Provincia di Cuneo
- Società Italiana di Nefrologia (SIN)

DIABETE IN OSPEDALE:
il paziente
con insufficienza renale

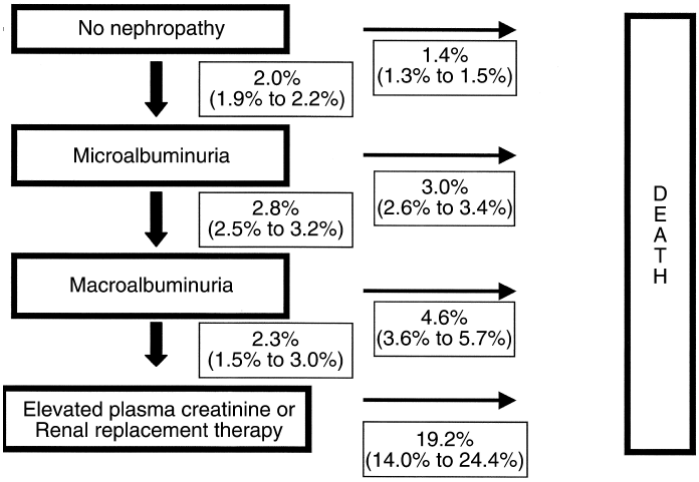
Sabato, 25 Gennaio 2014

Le nefropatie diabetiche

Andrea Guarnieri

SC Nefrologia e Dialisi
ASO S Croce e Carle Cuneo

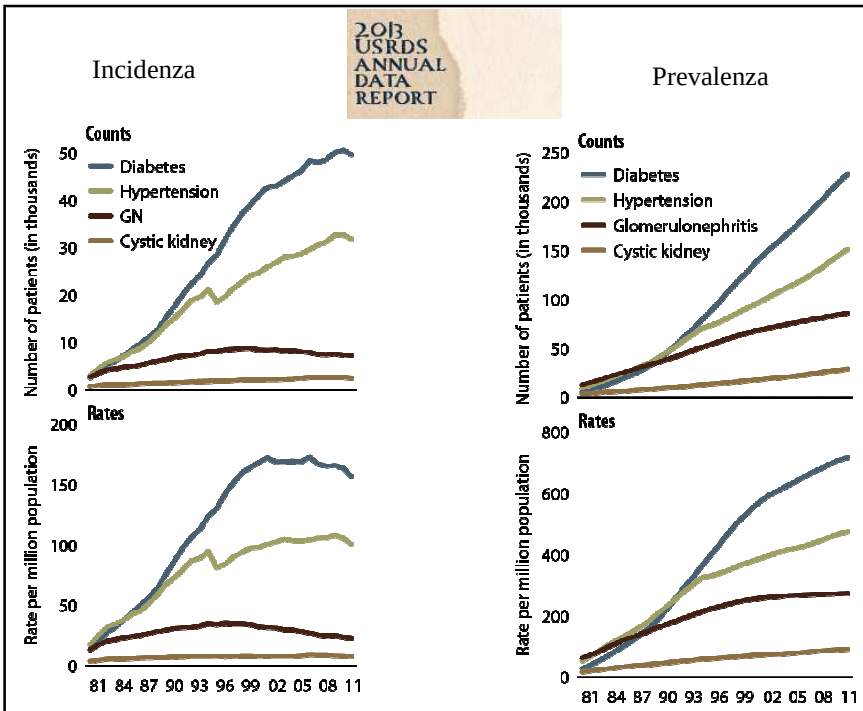
Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64)



Kidney International, Vol. 63 (2003), pp. 225–232

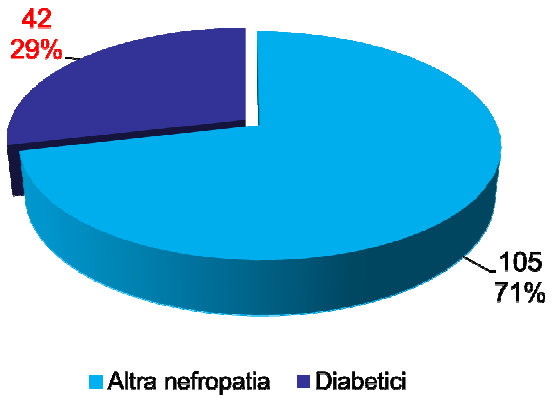
Incidenza

Prevalenza

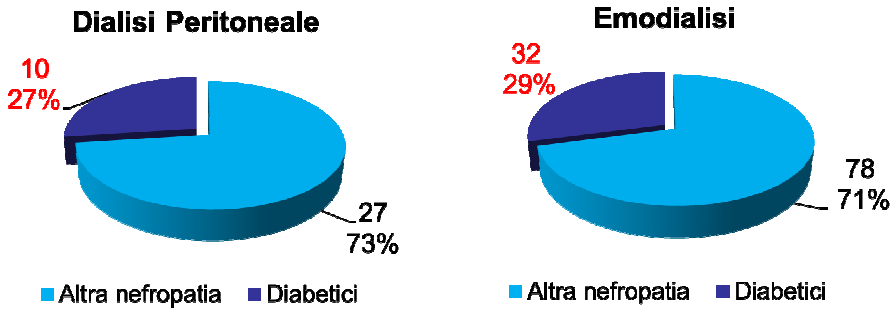


SC Nefrologia e Dialisi – Cuneo

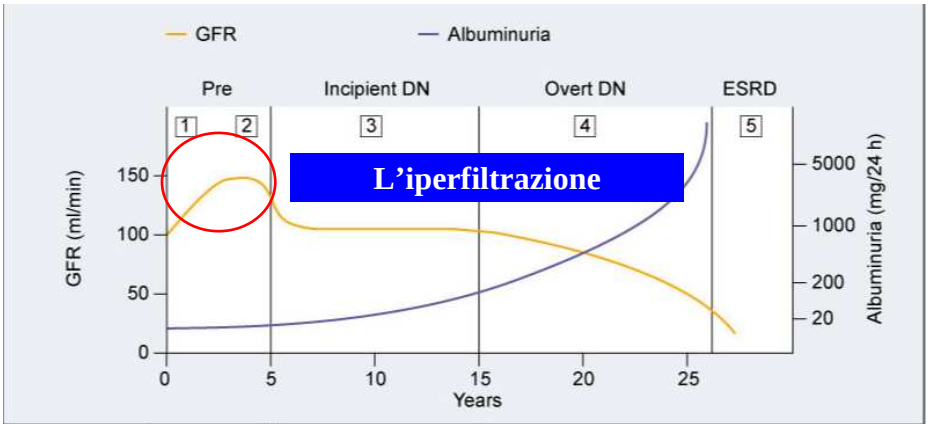
Pazienti in trattamento sostitutivo (HD + PD)



SC Nefrologia e Dialisi - Cuneo

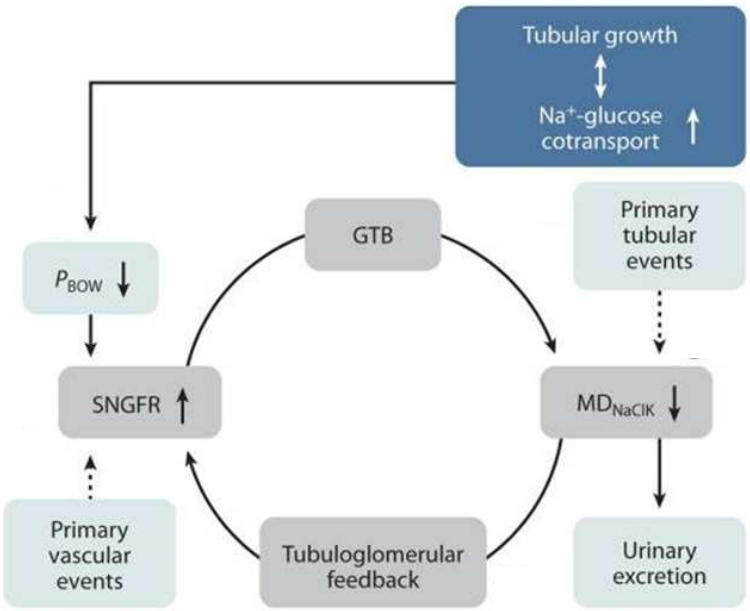


Nefropatia diabetica: storia naturale

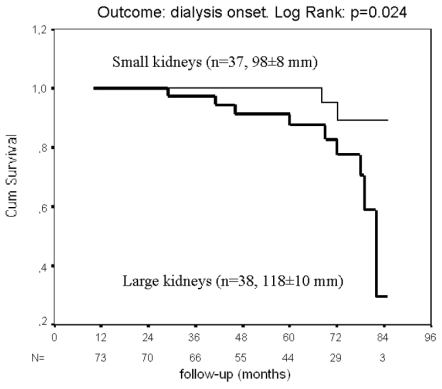


Stage	Pre	Incipient	Overt
Functional	GFR ↑ (25%–50%)	Microalbuminuria, hypertension	Proteinuria, nephrotic syndrome, GFR ↓

Iperfiltrazione: l'ipotesi «tubulare»

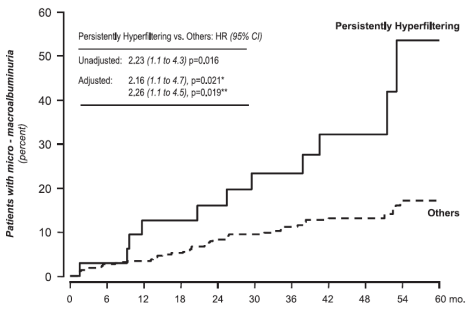


Large kidneys predict poor renal outcome in subjects with diabetes and chronic kidney disease



Rigalleau *et al. BMC Nephrology* 2010, **11**:3

Glomerular Hyperfiltration and Renal Disease Progression in Type 2 Diabetes



Diabetes Care 35:2061–2068, 2012

Iperglicemia: possibili meccanismi patogenetici

- Può indurre direttamente l'espansione mesangiale determinando l'aumento della produzione di matrice o attraverso la glicazione delle proteine della matrice mesangiale con la formazione di prodotti avanzati della glicosilazione (AGE).

Harris RD KI 1991, Singh AK JASN 1998

- Aumenta l'apoptosi delle cellule mesangiali.

Mishra R KI 2005

- Determina l'attivazione della protein kinasi C (iperfiltrazione glomerulare, albuminuria, sintesi di TGF-β).

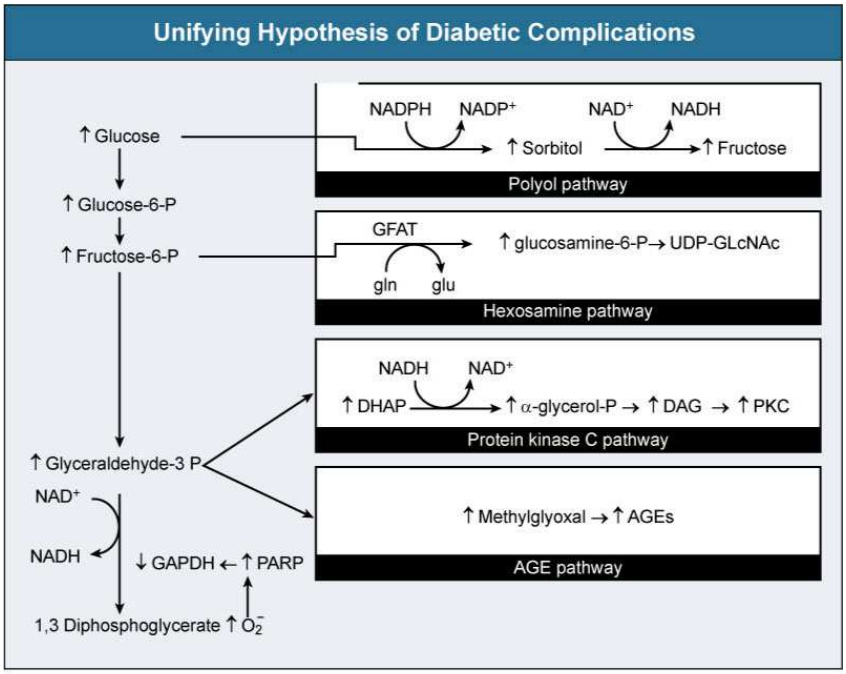
Coopr Me Lancet 1998

- Aumenta l'espressione dell'eparanasi e la riduzione dell'eparan solfato della membrana cellulare che ne consegue può contribuire all'aumentata permeabilità all'albumina.

Van den Hoven MJ KI 2006

- Stimola l'espressione di citochine pro-fibrotiche e pro-infiammatorie, fattori di crescita vascolare (VEGF, TGF-β).

Wolf G KI 1999



Nature 2001; 414:813-820

Role of Intensive Glucose Control in Development of Renal End Points in Type 2 Diabetes Mellitus

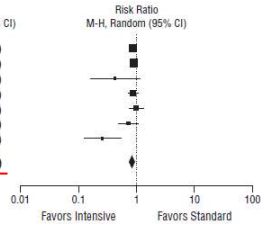
Systematic Review and Meta-analysis

Steven G. Coca, DO, MS; Faramarz Ismail-Beigi, MD, PhD; Nowreen Haq, MD, MPH; Harlan M. Krumholz, MD, SM; Chirag R. Parikh, MD, PhD

A Microalbuminuria

Study or Subgroup	Intensive Therapy Events	Intensive Therapy Total	Standard Therapy Events	Standard Therapy Total	Weight, %	Risk Ratio M-H, Random (95% CI)
ACCORD[8,14]	720	3250	828	3273	27.3	0.88 (0.80-0.96)
ADVANCE[12]	1318	5571	1434	5569	29.3	0.92 (0.86-0.98)
Kumamoto[4,15]	5	52	11	50	1.3	0.44 (0.16-1.17)
UKPDS 33[16]	368	2277	172	938	19.6	0.88 (0.75-1.04)
UKPDS 34[17]	79	342	95	411	12.2	1.00 (0.77-1.30)
VADT[11]	43	442	61	463	7.6	0.74 (0.51-1.07)
VA Feasibility Trial[5]	7	42	30	46	2.5	0.26 (0.13-0.52)
Total (95% CI)		**11 976**		**10 750**	**100.0**	**0.86 (0.76-0.96)**
Total events	**2540**		**2631**			

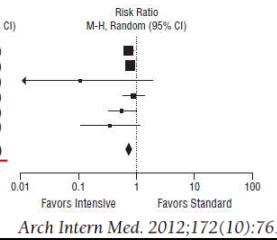
Heterogeneity: $\tau^2 = 0.01$; $\chi^2_6 = 16.71$; $P = .01$; $I^2 = 64\%$
Test for overall effect: $z = 2.60$; $P = .009$



B Macroalbuminuria

Study or Subgroup	Intensive Therapy Events	Intensive Therapy Total	Standard Therapy Events	Standard Therapy Total	Weight, %	Risk Ratio M-H, Random (95% CI)
ACCORD[8,14]	195	4397	272	4424	39.3	0.72 (0.60-0.86)
ADVANCE[12]	230	5571	292	5569	42.5	0.79 (0.67-0.93)
Kumamoto[4,15]	0	52	4	50	0.2	0.11 (0.01-1.94)
UKPDS 33[16]	72	2277	33	938	10.4	0.90 (0.60-1.35)
VADT[11]	20	693	36	703	6.2	0.56 (0.33-0.96)
VA Feasibility Trial[5]	3	24	10	28	1.4	0.35 (0.11-1.13)
Total (95% CI)		**13 014**		**11 712**	**100.0**	**0.74 (0.65-0.85)**
Total events	**520**		**647**			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_5 = 5.73$; $P = .33$; $I^2 = 13\%$
Test for overall effect: $z = 4.24$; $P = .001$

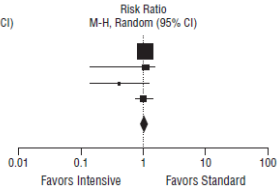


Arch Intern Med. 2012;172(10):761-769

A Doubling of the Serum Creatinine Level

Study or Subgroup	Intensive Therapy Events	Intensive Therapy Total	Standard Therapy Events	Standard Therapy Total	Weight, %	Risk Ratio M-H, Random (95% CI)
ACCORD[8,14]	392	5041	357	5035	62.5	1.10 (0.96-1.26)
ADVANCE[12]	67	5571	61	5569	15.6	1.10 (0.78-1.55)
UKPDS 33[16]	7	2150	7	895	1.9	0.42 (0.15-1.18)
VADT[11]	78	882	78	884	20.0	1.00 (0.74-1.35)
Total (95% CI)		**13 644**		**12 383**	**100.0**	**1.06 (0.92-1.22)**
Total events	**544**		**503**			

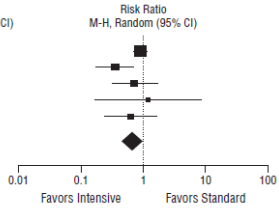
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_3 = 3.46$; $P = .33$; $I^2 = 13\%$
Test for overall effect: $z = 0.76$; $P = .44$



B ESRD

Study or Subgroup	Intensive Therapy Events	Intensive Therapy Total	Standard Therapy Events	Standard Therapy Total	Weight, %	Risk Ratio M-H, Random (95% CI)
ACCORD[8,14]	138	5119	151	5115	43.2	0.91 (0.73-1.15)
ADVANCE[12]	11	5571	31	5569	21.2	0.35 (0.18-0.70)
UKPDS 33[16]	16	2729	9	1138	17.3	0.74 (0.33-1.67)
UKPDS 34[17]	2	342	2	411	4.2	1.20 (0.17-8.49)
VADT[11]	7	882	11	884	14.1	0.64 (0.25-1.64)
Total (95% CI)		**14 643**		**13 117**	**100.0**	**0.69 (0.46-1.05)**
Total events	**174**		**204**			

Heterogeneity: $\tau^2 = 0.09$; $\chi^2_4 = 7.08$; $P = .13$; $I^2 = 43\%$
Test for overall effect: $z = 1.72$; $P = .09$

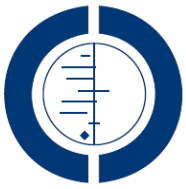


Arch Intern Med. 2012;172(10):761-769

Targeting intensive glycaemic control versus targeting conventional glycaemic control for type 2 diabetes mellitus

Hemmingsen B, Lund SS, Gluud C, Vaag A, Almdal TP, Hemmingsen C, Wetterslev J

End-stage renal disease Follow-up: median 63.6 years	**16 per 1000**	**14 per 1000** (11 to 17)	**RR 0.87** (0.71 to 1.06)



Ethnicity and long-term vascular outcomes in Type 2 diabetes: a prospective observational study (UKPDS 83)

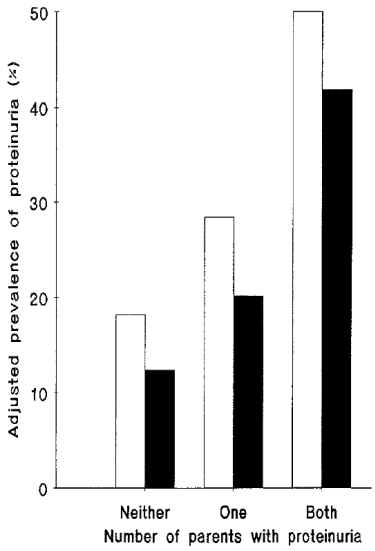
T. M. E. Davis[1], R. L. Coleman[2] and R. R. Holman[2] for the UKPDS Group

End point and ethnic group	Number of events	Person years	Absolute risk/1000 person-years	Age and sex-adjusted relative risk (95% CI)*	Adjusted relative risk (95% CI)†
Any diabetes-related end point					
White Caucasian	2066	45 681	45.2	1.00	1.00
Afro-Caribbean	172	4142	41.5	0.98 (0.97–0.99)	1.01 (0.91–1.12)
Asian Indian	230	5320	43.2	1.12 (1.02–1.22)	1.18 (1.07–1.29)
Diabetes-related death					
White Caucasian	869	58 560	14.8	1.00	1.00
Afro-Caribbean	36	5460	6.7	0.71 (0.61–0.83)	0.75 (0.64–0.88)
Asian Indian	52	7188	7.2	0.82 (0.72–0.94)	0.90 (0.79–1.03)
All-cause mortality					
White Caucasian	1606	59 349	27.1	1.00	1.00
Afro-Caribbean	86	5512	15.6	0.82 (0.74–0.90)	0.84 (0.76–0.93)
Asian Indian	90	7231	12.4	0.82 (0.74–0.90)	0.89 (0.80–0.97)
Myocardial infarction					
White Caucasian	922	55 397	16.6	1.00	1.00
Afro-Caribbean	26	5339	4.9	0.48 (0.37–0.61)	0.55 (0.43–0.71)
Asian Indian	89	6726	13.2	1.00 (0.86–1.15)	1.11 (0.96–1.28)
Stroke					
White Caucasian	343	56 734	6.0	1.00	1.00
Afro-Caribbean	35	5319	6.6	1.13 (0.93–1.36)	1.18 (0.97–1.43)
Asian Indian	23	7012	3.3	0.89 (0.70–1.11)	0.98 (0.78–1.23)
Peripheral vascular disease					
White Caucasian	132	57 421	2.3	1.00	1.00
Afro-Caribbean	3	5389	0.6	0.50 (0.28–0.86)	0.55 (0.33–0.93)
Asian Indian	2	7135	0.3	0.37 (0.19–0.73)	0.43 (0.23–0.82)
Microvascular disease					
White Caucasian	623	53 512	11.6	1.00	1.00
Afro-Caribbean	76	4756	16.5	1.21 (1.03–1.42)	1.06 (0.90–1.24)
Asian Indian	73	6542	10.9	0.92 (0.78–1.08)	0.89 (0.75–1.05)

Accepted 26 October 2013

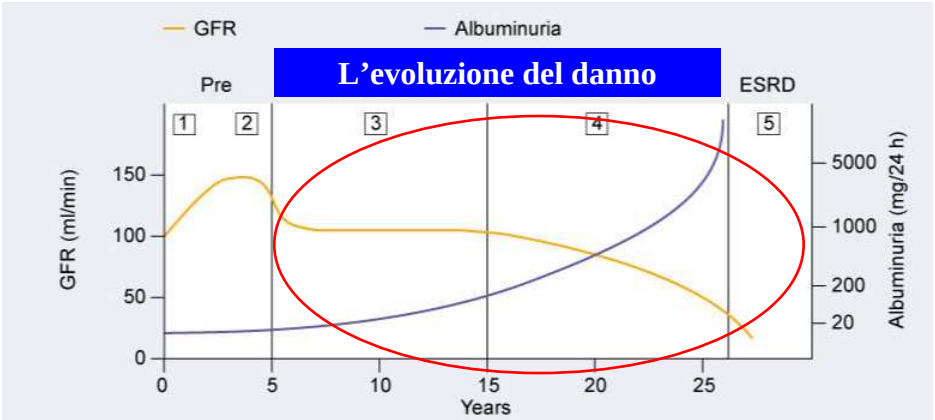
Familial predisposition to renal disease in two generations of Pima Indians with Type 2 (non-insulin-dependent) diabetes mellitus

D. J. Pettitt[1], M. F. Saad[1], P. H. Bennett[1], R. G. Nelson[2] and W. C. Knowler[1]

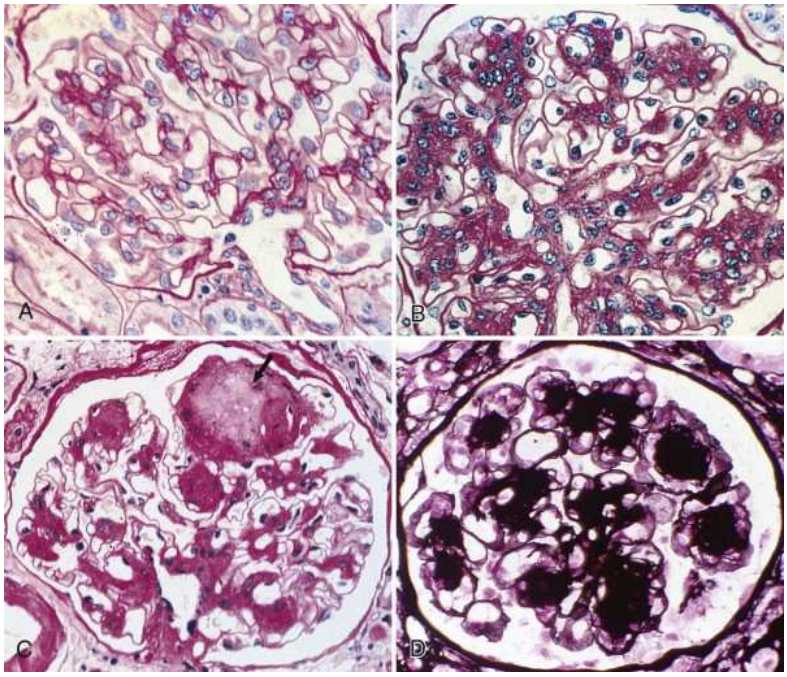


Diabetologia (1990) 33: 438–443

Nefropatia diabetica: storia naturale



Structural	Renal hypertrophy	Mesangial expansion, GBM thickening, arteriolar hyalinosis	Mesangial nodules (Kimmelstiel-Wilson lesions) Tubulointerstitial fibrosis



Pathologic Classification of Diabetic Nephropathy

Class	Description	Inclusion Criteria
I	Mild or nonspecific LM changes and EM-proven GBM thickening	Biopsy does not meet any of the criteria mentioned below for class II, III, or IV GBM > 395 nm in female and >430 nm in male individuals 9 years of age and older[a]
IIa	Mild mesangial expansion	Biopsy does not meet criteria for class III or IV Mild mesangial expansion in >25% of the observed mesangium
IIb	Severe mesangial expansion	Biopsy does not meet criteria for class III or IV Severe mesangial expansion in >25% of the observed mesangium
III	Nodular sclerosis (Kimmelstiel–Wilson lesion)	Biopsy does not meet criteria for class IV At least one convincing Kimmelstiel–Wilson lesion
IV	Advanced diabetic glomerulosclerosis	Global glomerular sclerosis in >50% of glomeruli Lesions from classes I through III

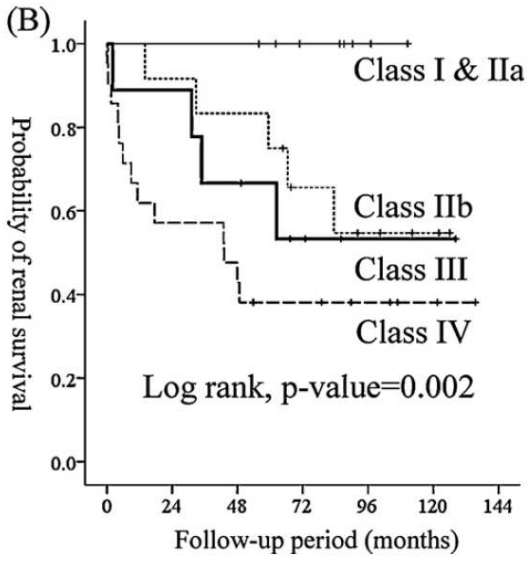
J Am Soc Nephrol **21:** 556–563, 2010

Table 2. Interstitial and vascular lesions of DN

Lesion	Criteria	Score
Interstitial lesions		
IFTA	No IFTA	0
	<25%	1
	25% to 50%	2
	>50%	3
interstitial inflammation	Absent	0
	Infiltration only in relation to IFTA	1
	Infiltration in areas without IFTA	2
Vascular lesions		
arteriolar hyalinosis	Absent	0
	At least one area of arteriolar hyalinosis	1
	More than one area of arteriolar hyalinosis	2
presence of large vessels	–	Yes/no
arteriosclerosis (score worst artery)	No intimal thickening	0
	Intimal thickening less than thickness of media	1
	Intimal thickening greater than thickness of media	2

J Am Soc Nephrol **21:** 556–563, 2010

Clinical implications of pathologic diagnosis and classification for diabetic nephropathy



Fattori di rischio

- **Età di insorgenza**

1. Avanzata

Tapp RJ Am J Kidney Dis 2004

2. Precoce

Pavkov ME JAMA 2006

- **Pressione arteriosa**

Earle K KI 1994

- **Obesità**

de Boer IH JASN 2007

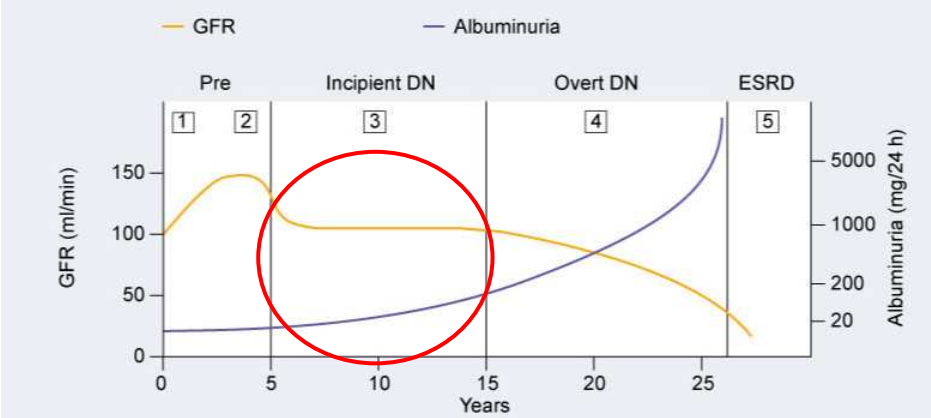
- **Fumo**

Nilsson PM Diabetes Metab 2004

- **Contraccettivi orali (?)**

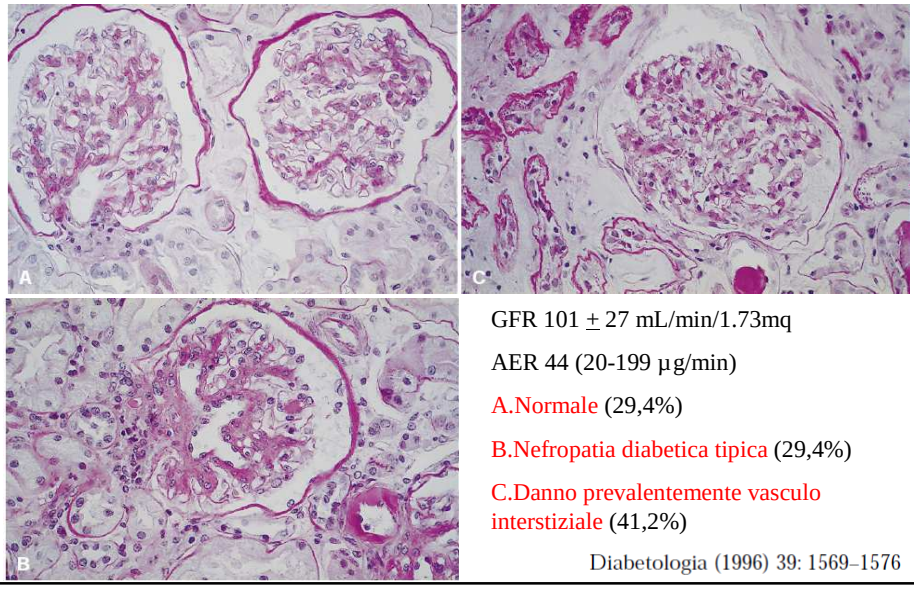
Ahmed SB Diabetes Care 2005

Nefropatia incipiente



Patterns of renal injury in NIDDM patients with microalbuminuria

P. Fioretto[1], M. Mauer[2], E. Brocco[1], M. Velussi[3], F. Frigato[3], B. Muollo[3], M. Sambataro[3], C. Abaterusso[1], B. Baggio[1], G. Crepaldi[1], R. Nosadini[1, 4]



GFR 101 ± 27 mL/min/1.73mq

AER 44 (20-199 µg/min)

A.Normale (29,4%)

B.Nefropatia diabetica tipica (29,4%)

C.Danno prevalentemente vasculo interstiziale (41,2%)

Diabetologia (1996) 39: 1569–1576

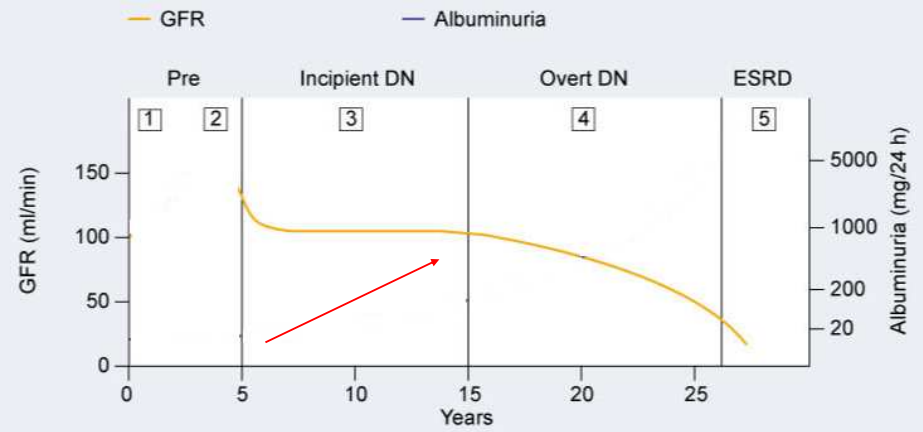
Table 1. Clinical features of patients divided into three renal structural categories

Category	male/female	%	Age (years)	Known NIDDM duration (years)	BMI (kg/m²)	HbA_{1c} (%)
C I	5/5	23.4	54 ± 9	8 ± 3	31 ± 4[b]	7.5 ± 0.8
C II	9/1	29.4	60 ± 6	14 ± 6[a]	26 ± 4	9.6 ± 1.8[d]
C III	12/2	41.2	61 ± 6	10 ± 8	30 ± 3[b]	8.5 ± 1.3[c]
p values						

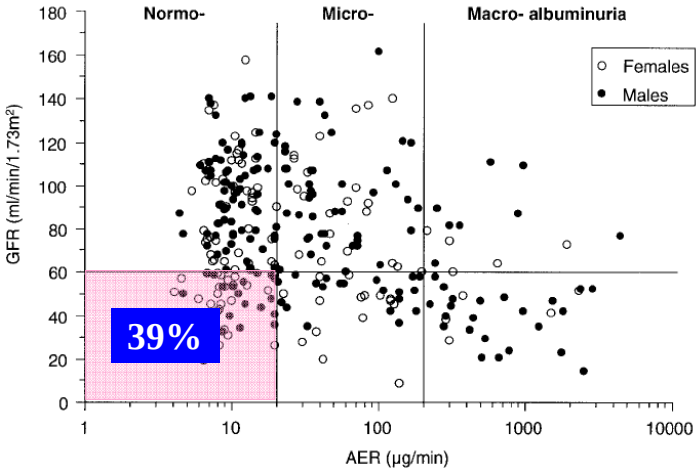
Table 3. Diabetic retinopathy in relation to patterns of renal injury

Category	Diabetic retinopathy		
	Absent	Background	Proliferative
C I	5	5	0
C II	0	5	5
C III	6	8	0

Nefropatia diabetica: storia naturale ?



Nonalbuminuric Renal Insufficiency in Type 2 Diabetes



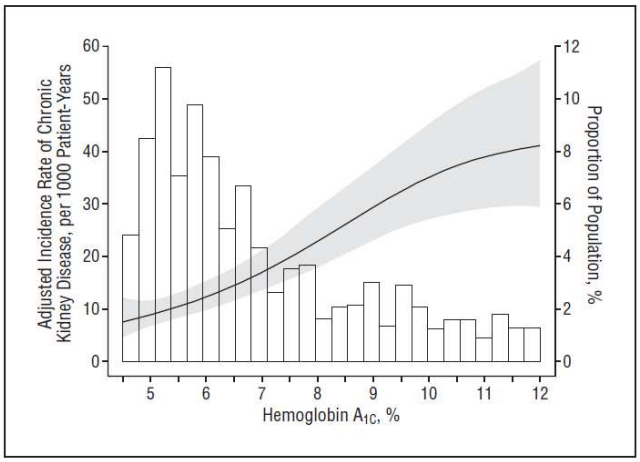
Diabetes Care 27:195–200, 2004

IRC normoalbuminurica: caratteristiche cliniche

- Sesso femminile ↑
- Durata del diabete ↓
- Ipertensione arteriosa ↓
- Retinopatia ↓
- Neuropatia ↓
- Precedenti CV ↓
- Fumo ↓
- HbA1C ↓
- Trigliceridi ↓
- HDL ↑
- Hb ↑

Yokoyama H NDT 2009; Penno G J Hypert 2011; Rigalleau V Diabetes Care 2007

Poor Glycemic Control in Diabetes and the Risk of Incident Chronic Kidney Disease Even in the Absence of Albuminuria and Retinopathy

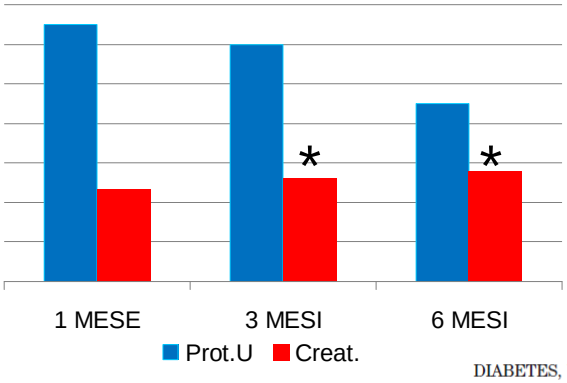


Neither albuminuria nor retinopathy (66 of 675[b])						
No. of events	73 of 707	31 of 393	22 of 173	6 of 58	14 of 83	
Incidence per 1000 person-years	8.05	6.10	9.95	8.17	13.42	<.001
Adjusted HR[c] (95% CI)	1.27 (1.08-1.51)[d]	1 [Reference]	1.46 (0.80-2.65)	1.17 (0.43-3.19)	3.51 (1.67-7.39)	.004

Arch Intern Med. 2008;168(22):2440-2447

Nonproteinuric Diabetes-Associated Nephropathy in the Cohen Rat Model of Type 2 Diabetes

Chana Yagil,[1] Adiel Barak,[2] David Ben-Dor,[3] Eliezer Rosenmann,[1] Joel Bernheim,[4] Mordechai Rosner,[5] Yael Segev,[6] Sarah Weksler-Zangen,[7] Itamar Raz,[8] and Yoram Yagil[1]



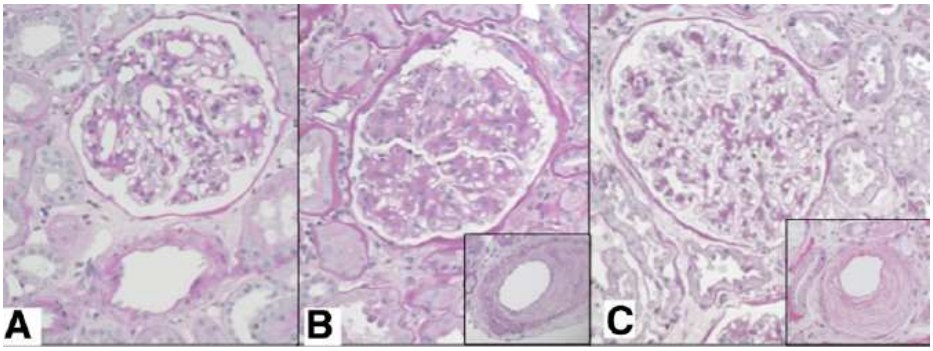
DIABETES, VOL. 54, MAY 2005

Renal Structure in Normoalbuminuric and Albuminuric Patients With Type 2 Diabetes and Impaired Renal Function

Group	Normoalbuminuria (n = 8)
Sex	3 M, 5 F
Age (years)	67 ± 2.0
Duration (years)	12 ± 2.4
BMI (kg/m^2)	34 ± 1.6
Smoking	0/8
Retinopathy (proliferative or nonproliferative diabetic retinopathy)	4/8
AER (μg/min)	7.9 ± 1.2
eGFR (mL/min/1.73 m^2)	41 ± 3.0
Brochner-Mortensen corrected DTPA GFR (mL/min/1.73 m^2)	47 ± 7 (performed in 5 of 8 patients)
HbA_{1c} (%) (mmol/mol)	6.8 ± 0.2 51 ± 2.2
Triglycerides (mmol/L)	2.6 ± 0.4
Cholesterol (mmol/L)	4.4 ± 0.2

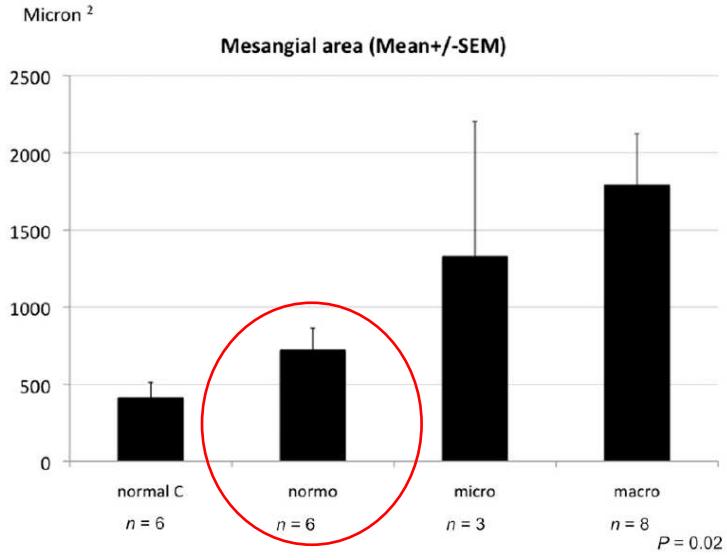
Diabetes Care 36:3620–3626, 2013

Ridotto GFR e normoalbuminuria



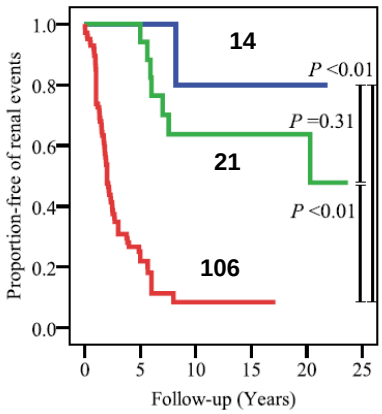
Reperto normale: **2 paz.** Nefropatia diabetica: **3 paz.** Danni vascolari: **3 paz.**

Diabetes Care 36:3620–3626, 2013



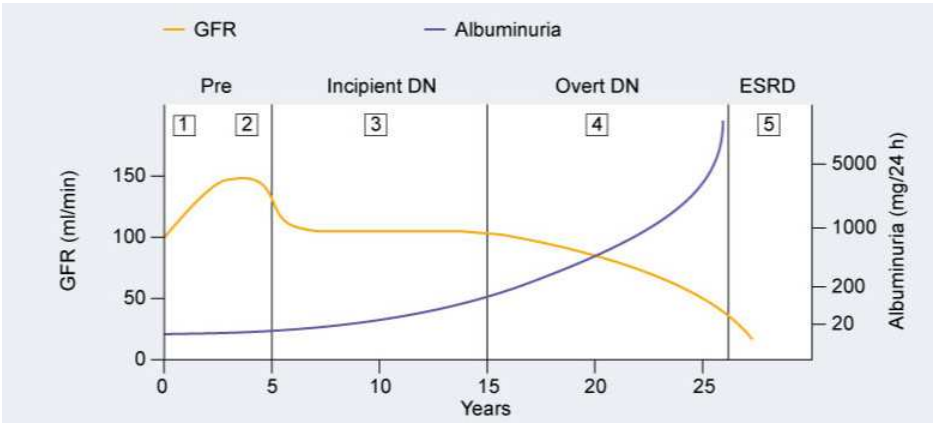
Diabetes Care 36:3620–3626, 2013

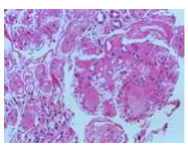
Long-Term Outcomes of Japanese Type 2 Diabetic Patients With Biopsy-Proven Diabetic Nephropathy

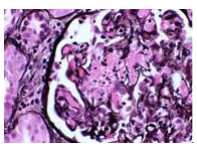


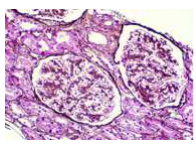
Diabetes Care 36:3655–3662, 2013

Altre nefropatie



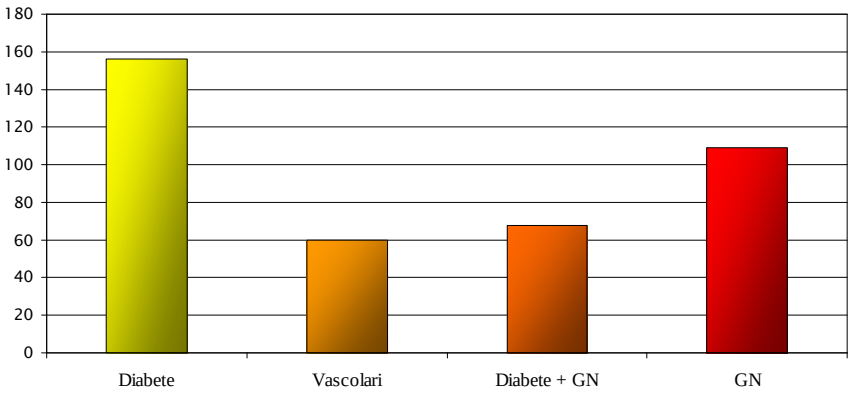






Different Patterns of Renal Damage in Type 2 Diabetes Mellitus: A Multicentric Study on 393 Biopsies

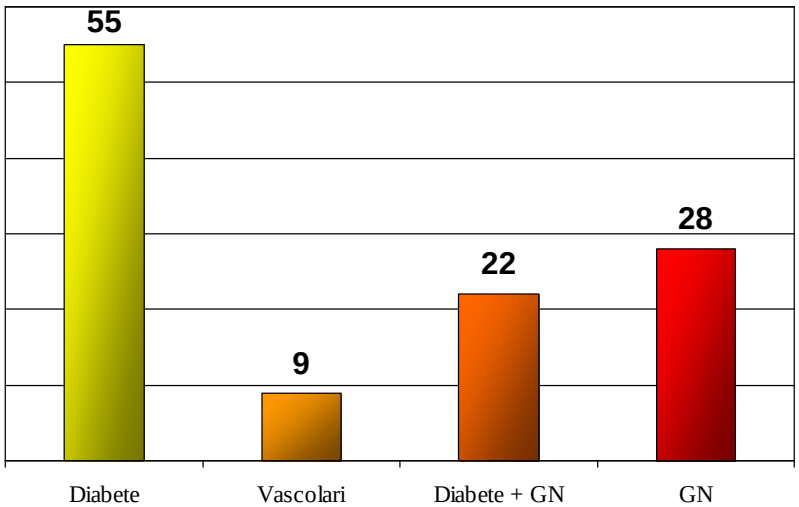
Gianna Mazzucco, MD, Tullio Bertani, MD, Mirella Fortunato, MD, Monica Bernardi, MD, Monica Leutner, MD, Renzo Boldorini, MD, and Guido Monga, MD



American Journal of Kidney Diseases, Vol 39, No 4 (April), 2002: pp 713-720

SC Nefrologia e Dialisi – Cuneo

Biopsie renali su diabetici 1993 - 2013



The Modern Spectrum of Renal Biopsy Findings in Patients with Diabetes

Shree G. Sharma, Andrew S. Bomback,† Jai Radhakrishnan,† Leal C. Herlitz,‡ Michael B. Stokes,‡ Glen S. Markowitz,‡ and Vivette D. D'Agati‡*

Table 1. Key demographic and clinical data at time of kidney biopsy

Characteristics	DN Alone	DN Plus NDRD	NDRD Alone
Participants (*n*)	227	164	220
Age (yr)	59 (49–65)	63 (55–72)[a]	63 (54–70)[b]
Male sex	129 (56.8)	100 (61.0)	142 (64.6)
Race			
Unknown	108 (47.6)	57 (34.8)[a]	104 (47.3)[c]
White	62 (27.3)	63 (38.4)[a]	70 (31.8)
African American	39 (17.2)	33 (20.1)	29 (13.2)
Hispanic	12 (5.3)	7 (4.3)	8 (3.6)
Asian	4 (1.8)	4 (2.4)	7 (3.2)
Other	2 (0.9)	0 (0.0)	2 (0.9)
DM type 1	9 (4.0)	5 (3.1)	2 (0.9)[b]
Duration of DM (yr)	13 (8–17)	10 (7–18)	5 (3–10)[b,c]
Serum creatinine (mg/dl)	2.3 (1.6–3.8)	3.1 (1.7–5.2)[a]	2.3 (1.5–4.4)[c]
eGFR (ml/min per 1.73 m^2)	31.3 (17.5–55.2)	21.4 (12.5–46.6)[a]	32.5 (14.3–60.0)[c]
Proteinuria (g/d)	5.0 (2.8–8.8)	5.0 (2.0–8.0)	2.9 (1.4–7.1)[b,c]

Types of NDRD (n)
Acute tubular necrosis (109)
FSGS (69)
Primary FSGS (6)
Secondary FSGS (63)[b]
HTN related
HTN plus obesity related
Obesity related
Other[c]
Hypertensive nephrosclerosis (70)[b]
IgA nephropathy (35)
Membranous GN (23)
Pauci-immune crescentic GN (19)
Acute interstitial nephritis (18)
Amyloidosis (10)
Myeloma cast nephropathy (10)
Acute postinfectious GN (6)
Atheroembolic disease (5)
Others (10)

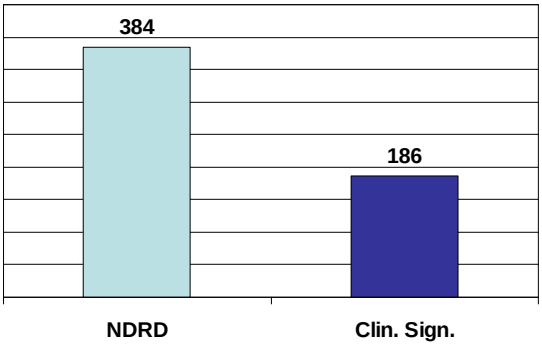


Table 4. Association of key clinical predictors and biopsy findings of nondiabetic renal disease

Variables	OR (95% CI)	*P* Value
Proteinuria (mg/d)		
<500	1.00 (reference)	
500–3500	1.28 (0.39 to 4.20)	0.68
>3500	0.55 (0.19 to 1.66)	0.29
eGFR (ml/min per 1.73 m^2)		
>60	1.00 (reference)	
30–60	0.89 (0.35 to 2.25)	0.81
15–30	1.42 (0.53 to 3.82)	0.49
≤15	1.54 (0.48 to 4.96)	0.47
Age	1.03 (1.00 to 1.06)	0.06
Male sex	1.05 (0.54 to 2.02)	0.89
Race		
Unknown	1.00 (reference)	
White	0.93 (0.46 to 1.91)	0.85
Black	1.38 (0.49 to 3.84)	0.54
Hispanic	1.07 (0.27 to 4.23)	0.93
Asian	1.66 (0.26 to 10.67)	0.59
Duration of diabetes	0.95 (0.91 to 0.98)	0.004
AKI	1.44 (0.67 to 3.07)	0.35
Low complements	4.70 (0.49 to 45.42)	0.18
M-spike (serum or urine)	1.50 (0.51 to 4.37)	0.46

Clin J Am Soc Nephrol 8: 1718–1724, October, 2013

Identifying Parameters to Distinguish Non-Diabetic Renal Diseases from Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis

- Assenza di retinopatia
- Minor durata di malattia
- Valori inferiori di HbA1c
- Valori inferiori di PAS e PAD

Non Significativo

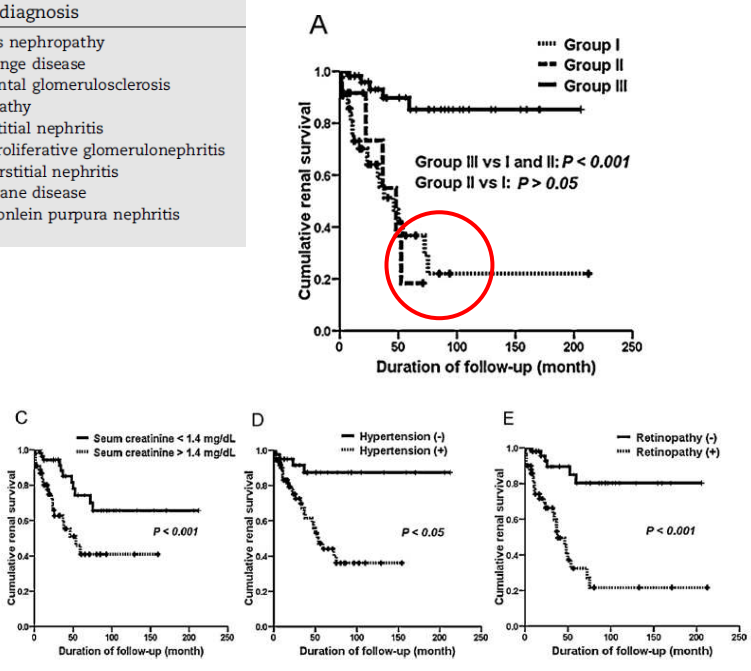
- Età
- Proteinuria
- Creatininemia, GFR, Clearance della creatinina

PLOS ONE | www.plosone.org May 2013 | Volume 8 | Issue 5 | e64184

Renal outcomes in patients with type 2 diabetes with or without coexisting non-diabetic renal disease

	Group I ($n = 43$)	Group II ($n = 12$)	Group III ($n = 64$)	P-value
Age (years)	50.6 ± 10.9	51.8 ± 10.3	54.9 ± 10.5	<0.05
Gender (male)	21 (48.8)	6 (50)	37 (57.8)	NS
Duration of diabetes (years)	10.6 ± 6.5*	9.7 ± 4.8	5.9 ± 5.9	<0.001
Presence of retinopathy	34 (79.1)*	8 (66.7)	9 (14.1)	<0.001
Presence of proteinuria	41 (95.3)	12 (100)	60 (93.8)	NS
Presence of hematuria	24 (55.8)	10 (83.3)	31 (48.4)	NS
Presence of hypertension	35 (81.4)*	8 (66.7)	34 (53.1)	<0.05
Systolic blood pressure (mmHg)	145 ± 18*	140 ± 19	132 ± 17	<0.01
Diastolic blood pressure (mmHg)	87 ± 11	87 ± 6	83 ± 10	NS
Kidney size (cm)	11.6 ± 1.1*	11.1 ± 1.2	10.8 ± 0.8	<0.05
Laboratory findings				
Hemoglobin (g/dl)	10.2 ± 1.7*	10.5 ± 2.3**	12.7 ± 2.3	<0.001
Serum creatinine (mg/dl)	2.2 ± 1.3*	2.0 ± 1.7	1.4 ± 0.8	<0.01
Serum albumin (g/dl)	2.9 ± 0.7	3.0 ± 0.7	2.9 ± 1.0	NS
Total cholesterol (mg/dl)	233.3 ± 94.7	243.4 ± 90.9	276.9 ± 128.2	NS
Fasting glucose (mg/dl)	178.9 ± 68.8	186.6 ± 99.7	155.9 ± 51.2	NS
Hemoglobin A1c (%)	8.4 ± 2.2	8.3 ± 2.1	7.8 ± 2.2	NS
Proteinuria (g/24 h)	6.4 ± 4.9	7.1 ± 3.9	8.1 ± 6.4	NS
Albuminuria (g/24 h)	4.3 ± 3.1	4.5 ± 2.4	5.8 ± 4.5	NS
Creatinine clearance (ml/min)	42.5 ± 24.2*	40.5 ± 25.7	59.7 ± 28.7	<0.05

Pathologic diagnosis
Membranous nephropathy
Minimal change disease
Focal segmental glomerulosclerosis
IgA nephropathy
Acute interstitial nephritis
Membranoproliferative glomerulonephritis
Chronic interstitial nephritis
Thin membrane disease
Henoch-Schonlein purpura nephritis
Others



Conclusioni

- Il coinvolgimento renale nel DMT2 ha importanti implicazioni in termini di morbilità (ESRD) e mortalità.
- La diagnosi di certezza di nefropatia diabetica è solo bioptica anche se alcune caratteristiche clinico anamnestiche (durata della malattia, controllo glicometablico e pressorio, ecc.) possono aiutare a formulare una diagnosi presuntiva.
- Non c'è una costante correlazione tra quadro clinico e anatomo-patologico.
- La frequenza di nefropatie non diabetiche, associate o meno alla diabetica, è rilevante e la loro individuazione può avere importanti ripercussioni terapeutiche e prognostiche.

Resveratrol Attenuates Diabetic Nephropathy via Modulating Angiogenesis

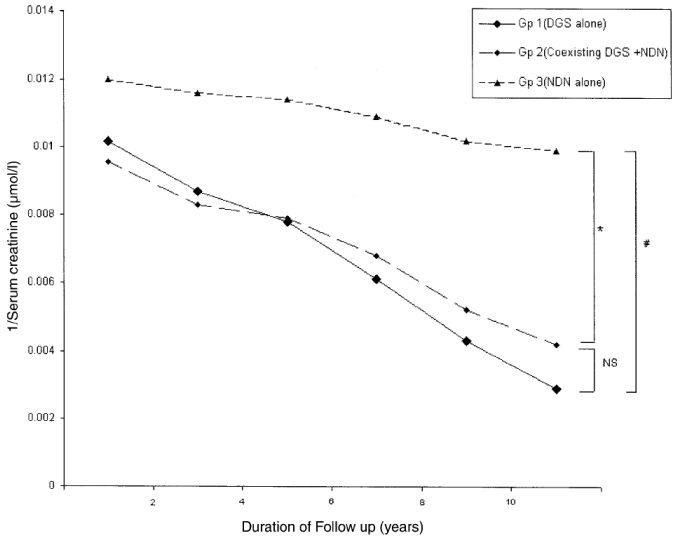
Variable	Macroalbuminuria (*N* events = 420) HR (95% CI)	*P*	Creatinine clearance ≤60 ml/min per 1.73 m^2 (*N* events = 1,428) HR (95% CI)	*P*
Age at diagnosis (per 5 years)	1.06 (0.97–1.16)	0.18	2.07 (1.98–2.17)	<0.0001
Sex (male)	1.42 (1.05–1.93)	0.023	0.53 (0.48–0.59)	<0.0001
Ethnicity				
White Caucasian	1		1	
Afro-Caribbean	0.94 (0.52–1.70)	0.84	1.17 (0.98–1.41)	0.085
Indian Asian	1.72 (1.13–2.62)	0.011	0.76 (0.62–0.93)	0.0065
Smoking status				
Never	1		1	
Ever	1.31 (0.96–1.79)	0.088	0.93 (0.83–1.04)	0.19
Urinary albumin (per 20 mg/l)	1.010 (1.007–1.013)	<0.0001	1.003 (0.999–1.008)	0.14
Plasma creatinine (per 10 μmol/l)	1.010 (1.038–1.157)	0.00093	1.18 (1.14–1.21)	<0.0001
Weight (per 5 kg)	1.05 (1.01–1.10)	0.014	0.762 (0.745–0.779)	<0.0001
Waist (cm)	1.021 (1.014–1.029)	<0.0001	0.960 (0.955–0.965)	<0.0001
Height (cm)	1.00 (0.99–1.01)	0.75	1.07 (1.05–1.08)	<0.0001
Systolic blood pressure (per 10 mmHg)	1.18 (1.10–1.26)	<0.0001	1.20 (1.17–1.23)	<0.0001
Diastolic blood pressure (per 10 mmHg)	1.16 (1.00–1.34)	0.047	1.07 (1.02–1.13)	0.0062
Hypertensive	1.74 (1.31–2.33)	0.00016	1.90 (1.71–2.11)	<0.0001
On antihypertensive therapy	1.52 (1.10–2.10)	0.012	1.74 (1.55–1.97)	<0.0001
FPG (mmol/l)	1.08 (1.03–1.13)	0.00081	1.021 (1.007–1.035)	0.0036
A1C (%)	1.10 (1.02–1.18)	0.015	1.05 (1.02–1.08)	0.0016
HOMA %B (per 10%)	0.97 (0.94–1.01)	0.18	0.97 (0.95–0.98)	0.000034
HOMA %S (per 10%)	0.95 (0.91–0.99)	0.019	1.02 (1.01–1.03)	0.000012
Total cholesterol (mmol/l)	1.20 (1.06–1.36)	0.0037	1.20 (1.15–1.26)	<0.0001
LDL cholesterol (mmol/l)	1.17 (1.02–1.34)	0.026	1.22 (1.15–1.28)	<0.0001
HDL cholesterol (mmol/l)	0.53 (0.28–0.99)	0.048	1.85 (1.50–2.28)	<0.0001
Plasma triglycerides mmol/l)*	1.19 (1.11–1.27)	<0.0001	0.96 (0.86–1.07)	0.44
White cell count (10^9/l)	1.07 (1.00–1.14)	0.056	0.98 (0.95–1.00)	0.093
Previous retinopathy	1.46 (1.05–2.05)	0.027	1.38 (1.18–1.61)	0.000043
Previous sensory neuropathy	1.40 (1.01–1.96)	0.045	1.36 (1.21–1.54)	<0.0001
Previous CVD	1.64 (1.18–2.28)	0.003	1.71 (1.51–1.93)	<0.0001

DIABETES, VOL. 55, JUNE 2006

	Normo-albuminuria	Micro-albuminuria	Macro-albuminuria	*P*
n	43	38	28	
AER (μg/min)	9.3 ×/÷ 1.1	61 ×/÷ 1.2	671 ×/÷ 1.2	<0.0001
Age (years)	73 ± 1	72 ± 2	67 ± 2	<0.01
Females (%)	56	45	18	<0.01
Duration of diabetes (years)	14 ± 1	16 ± 1	15 ± 2	0.64
BMI (kg/m^2)	30.8 ± 1.0	29.3 ± 0.7	31.6 ± 1.4	0.26
Retinopathy (%)	26	50	41	0.11
CHD (%)	49	51	64	0.42
CVD (%)	21	27	18	0.67
PVD (%)	23	35	46	0.12
Smoking (%)	38	53	62	0.19
HbA_{1c} (%)	7.3 ± 0.3	7.9 ± 0.2	7.9 ± 0.3	0.23
SBP (mmHg)	138 ± 3	147 ± 3	147 ± 3	0.02*
DBP (mmHg)	75 ± 2	78 ± 1	77 ± 1	0.37
TC (mmol/l)	4.4 ± 0.2	4.5 ± 0.2	4.3 ± 0.2	0.91
LDL-C (mmol/l)	2.6 ± 0.1	2.8 ± 0.1	2.5 ± 0.2	0.43
HDL-C (mmol/l)	1.15 ± 0.05	1.19 ± 0.06	0.97 ± 0.05	0.02*
TG (mmol/l)	1.9 ×/÷ 1.1	1.8 ×/÷ 1.1	2.0 ×/÷ 1.1	0.86
GFR (ml · min^{-1} · 1.73 m^{-2})	47 ± 2	47 ± 2	39 ± 2	0.01
Creatinine (μmol/l)	110 (87–146)	112 (101–136)	150 (123–200)	0.001
RAS inhibitor (%)	74	74	81	0.76
Anti-HT (%)	95	95	96	0.95

Diabetes Care 27:195–200, 2004

Renal Outcome in Type 2 Diabetic Patients With or Without Coexisting Nondiabetic Nephropathies



Diabetes Care 25:900–905, 2002

FRONTIERS IN NEPHROLOGY

J Am Soc Nephrol 14: 1396–1405, 2003

Diabetic Nephropathy in Type 2 Diabetes Prevention and Patient Management

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Table 2. Indications for renal biopsy in albuminuric patients with type 2 diabetes

- Nephritic sediment (dysmorphic erythrocytes, acanthocytes, numerous casts, particularly composed of red cells)
- History of nondiabetic renal disease
- Fast increase in proteinuria (over weeks)
- Proteinuria > 5 g/24 h
- Albuminuria in the absence of retinopathy
- Decrease in renal function in the absence of proteinuria
- Fast decline of renal function without obvious explanation