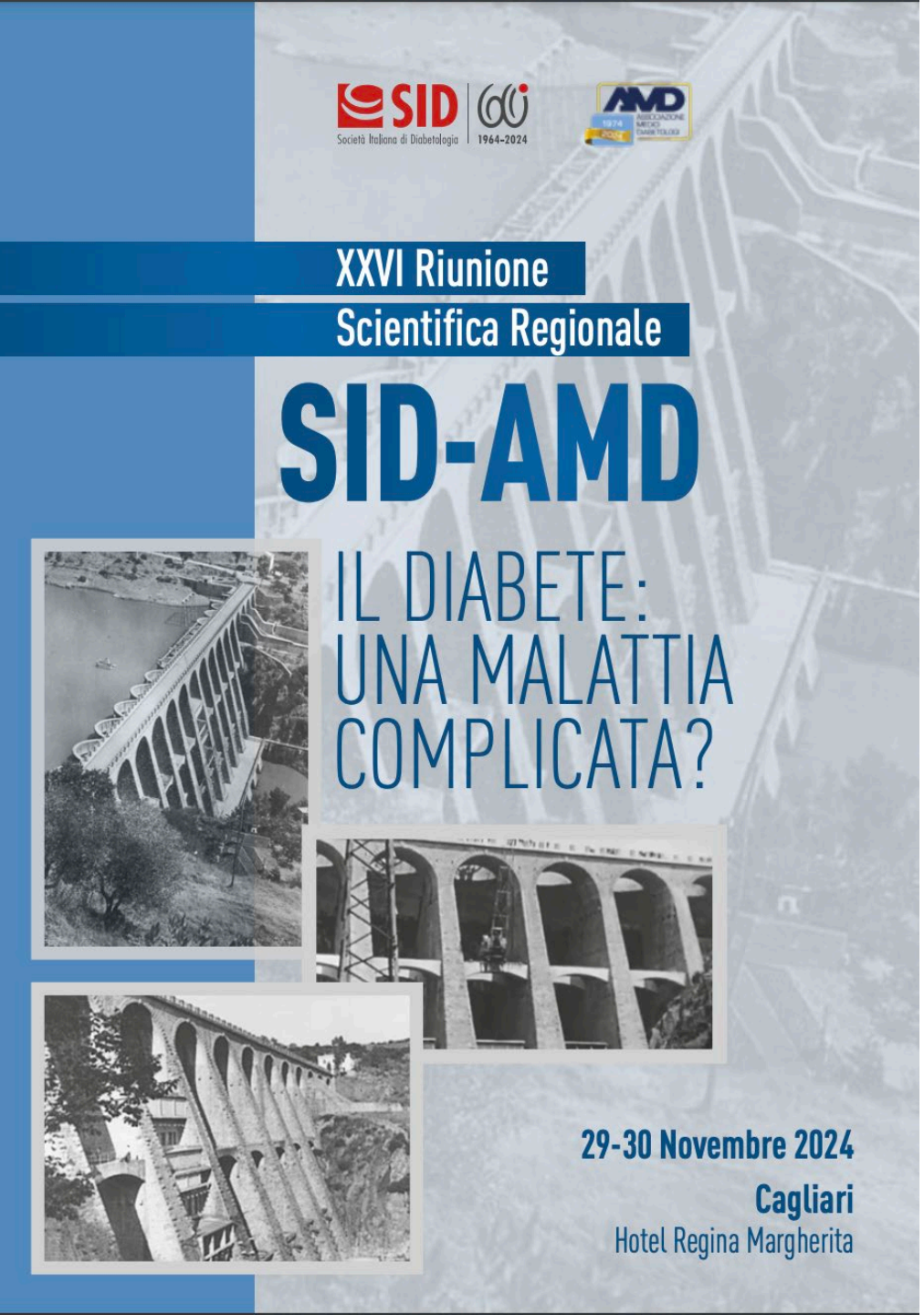

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Il paziente diabetico nefropatico: necessità di un corretto approccio diagnostico

Matteo Floris

ARNAS G. Brotzu

SCDU Nefrologia, Dialisi e Trapianto Renale

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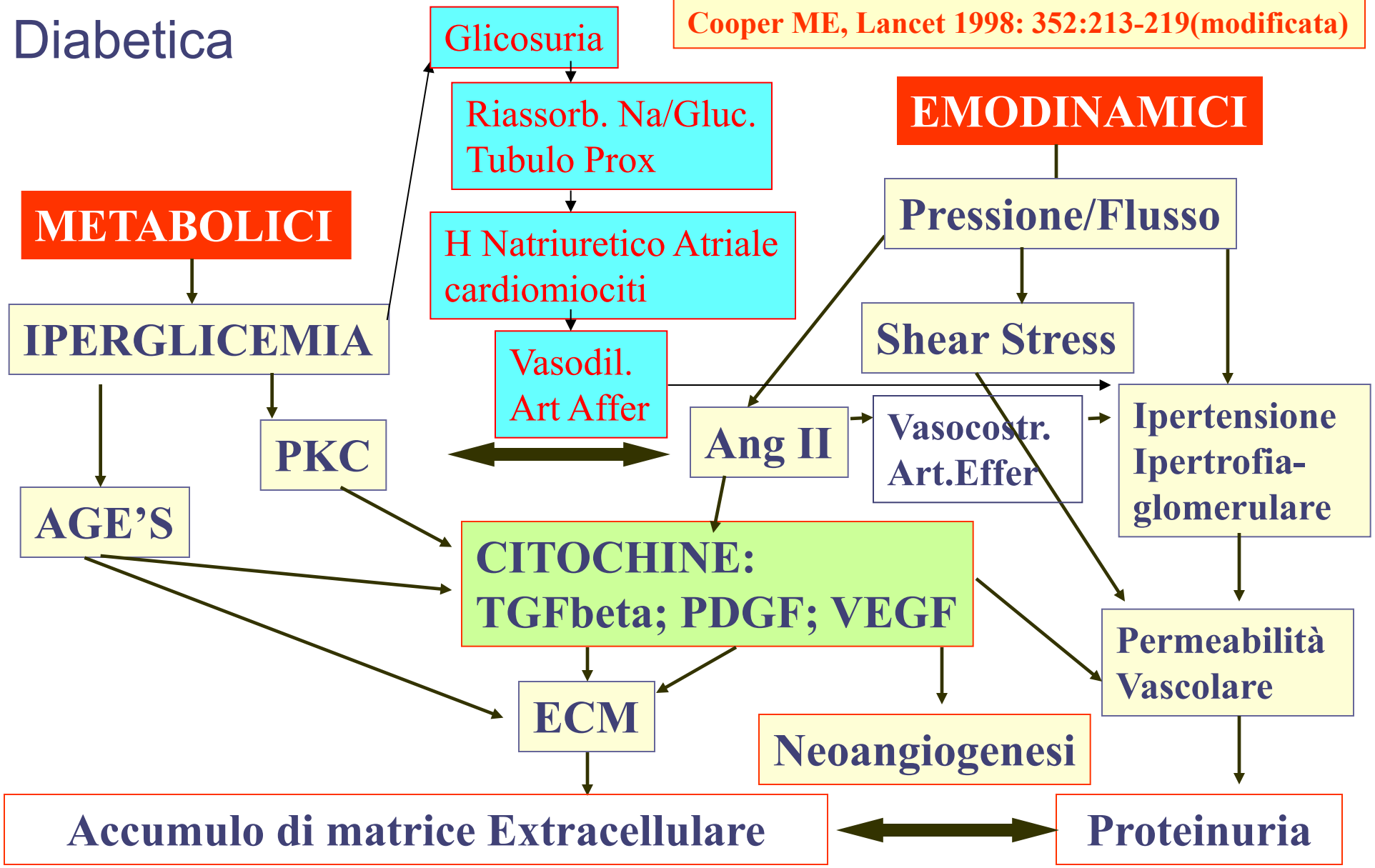
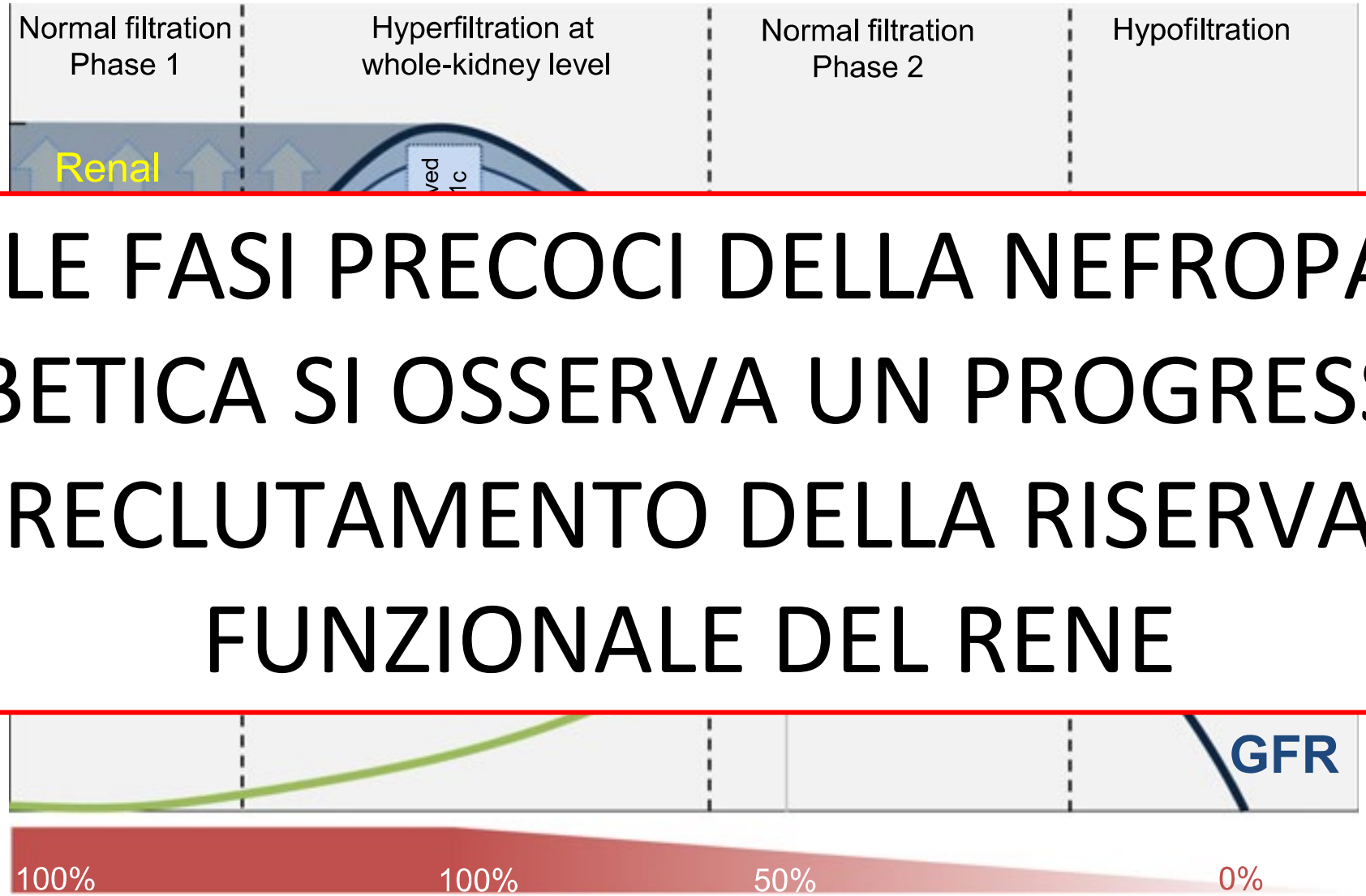
Agenda

1. Definizione e Storia Naturale della **«Diabetic Kidney Disease»(DKD)**
2. Recenti «Concetti» Patogenetici della DKD
3. Diabetic kidney disease vs Non Diabetic kidney disease
4. Attuali Indicazioni alla Biopsia Renale e quali dati di letteratura ci hanno portato a tali indicazioni
5. Eterogeneità delle Lesioni Renali della DKD e Diversi Fenotipi
6. Indicazioni per la Pratica Clinica e Indicazioni per la Ricerca e i RCT
7. Conclusioni

Schema sui Meccanismi Patogenetici della Nefropatia Diabetica

Cooper ME, Lancet 1998: 352:213-219(modificata)



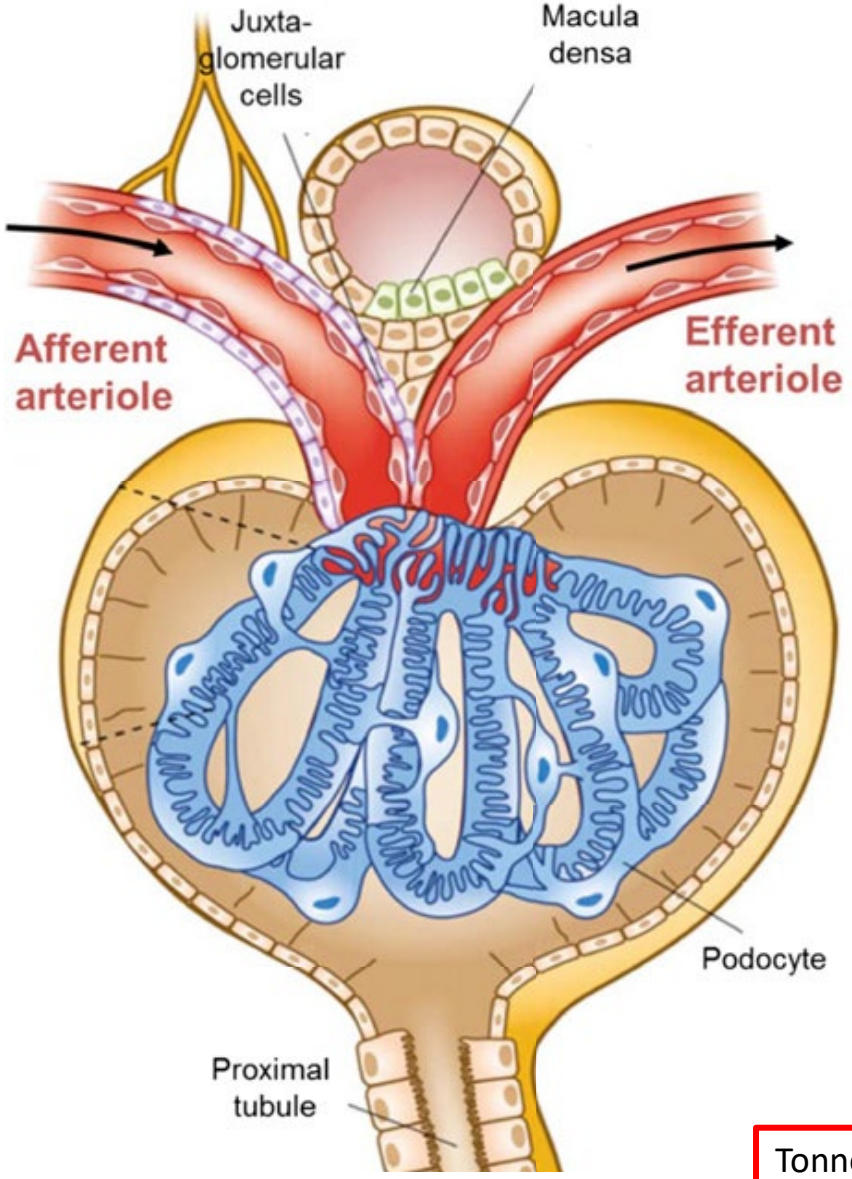


NELLE FASI PRECOCI DELLA NEFROPATIA DIABETICA SI OSSERVA UN PROGRESSIVO RECLUTAMENTO DELLA RISERVA FUNZIONALE DEL RENE

Tonneijck L. et Al. J Am Soc Nephrol 28: 1023–1039, 2017

Schematic (net) effect of factors implicated in the pathogenesis of glomerular hyperfiltration in diabetes.

Factors causing a net reduction of <u>afferent</u> arteriolar resistance
Vascular factors
Nitric oxide bioavailability
COX-2 prostanoids
Kalikrein-kinins
Atrial natiuretic peptide
Angiotensin(1-7)
Hyperinsulinemia *per se*
Tubular signals
Inhibition of tubuloglomerular feedback (macula densa signals)



Factors causing a net increase of <u>efferent</u> arteriolar resistance
Vascular factors
Angiotensin-II
Thromboxane A2
Endothelin-1 (ETA receptor)
Reactive oxygen species

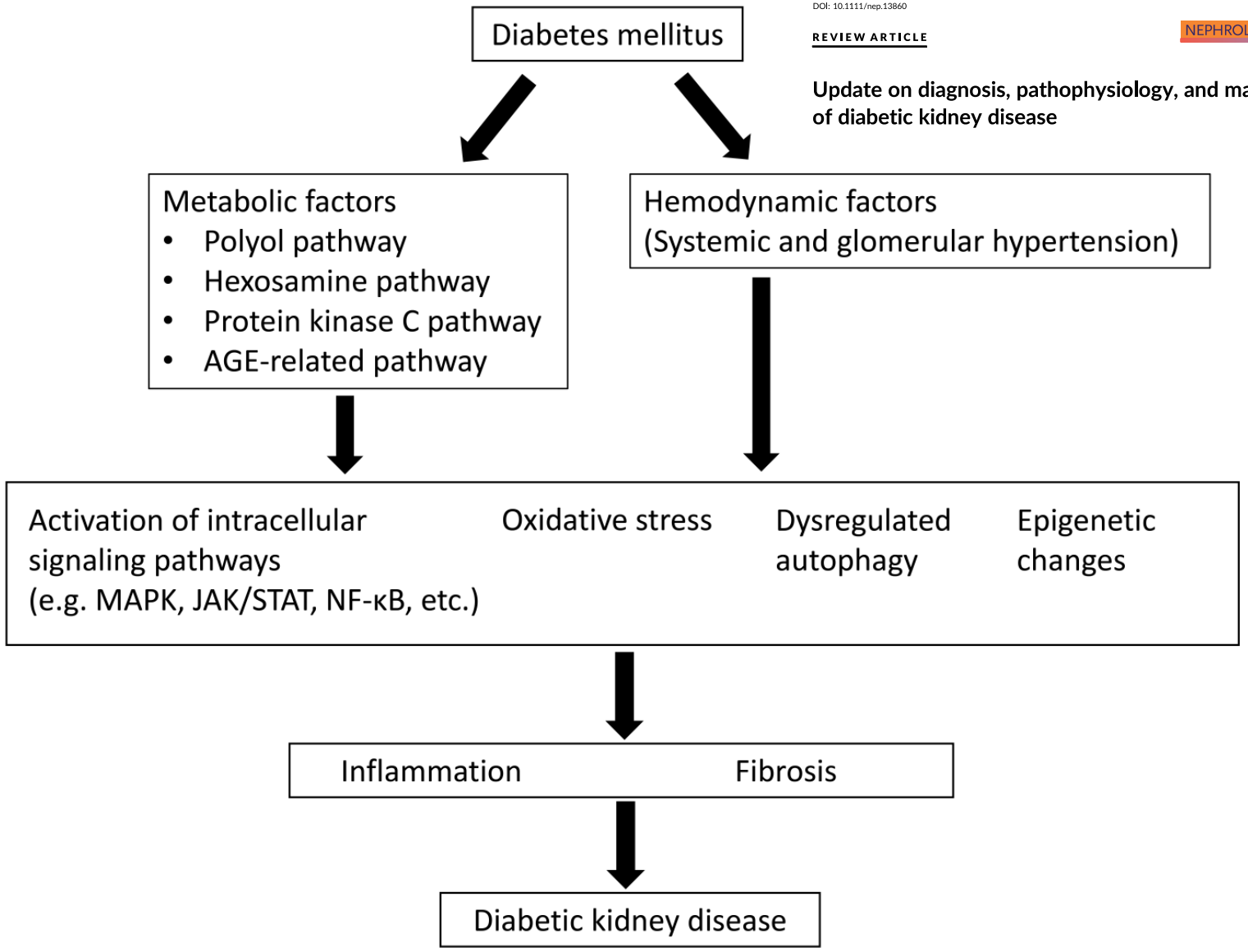
Tonneijck L. et Al. J Am Soc Nephrol 28: 1023–1039, 2017

The pathogenesis of DKD

Received: 4 January 2021 | Accepted: 2 February 2021
DOI: 10.1111/nep.13860
REVIEW ARTICLE
NEPHROLOGY WILEY

Update on diagnosis, pathophysiology, and management of diabetic kidney disease

2021



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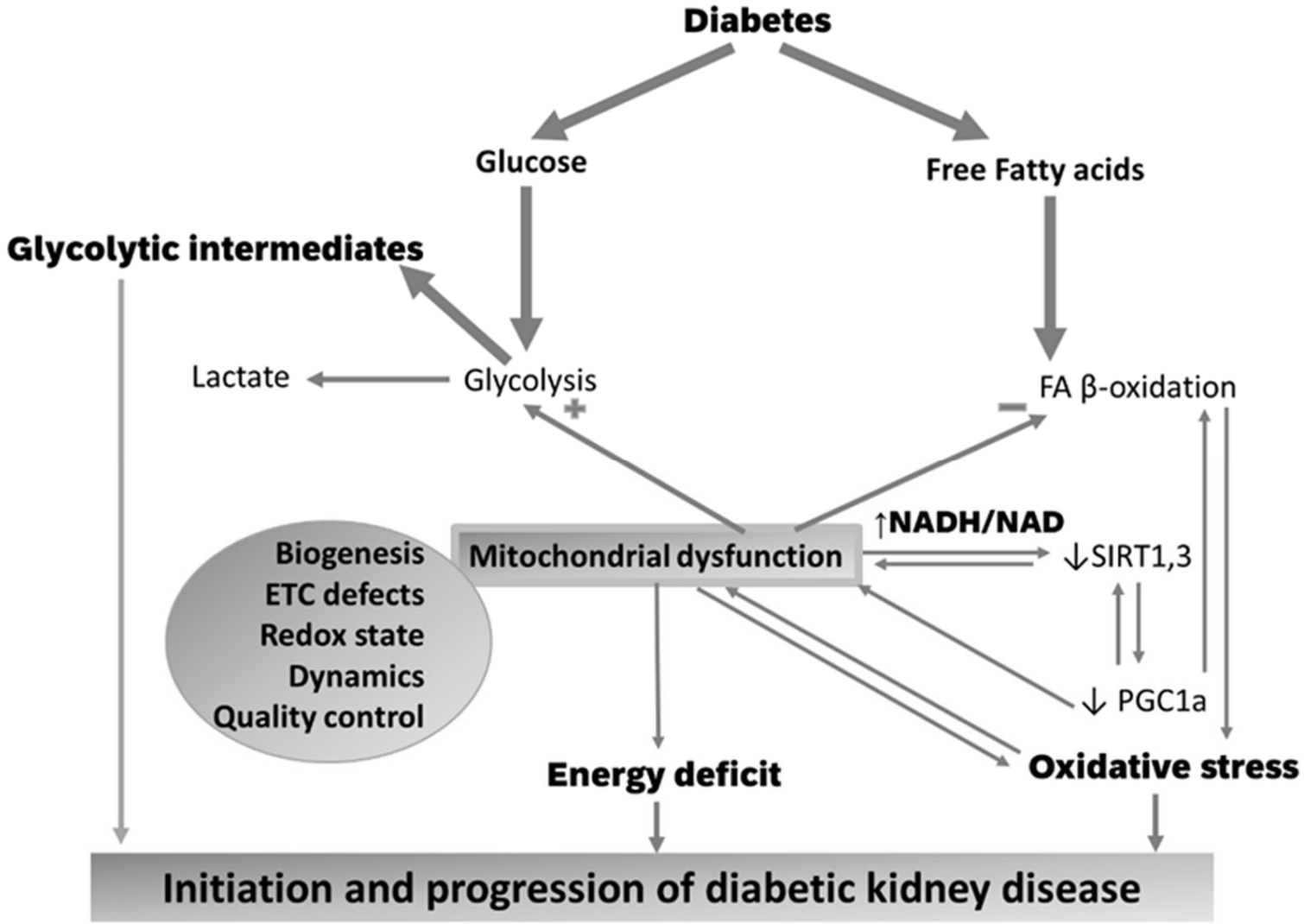
Excessive energetic substrates in diabetes leads to mitochondrial defects that cause reductive stress, oxidative stress, and energy deficit.



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REVIEWS

Innate immunity in diabetic kidney disease

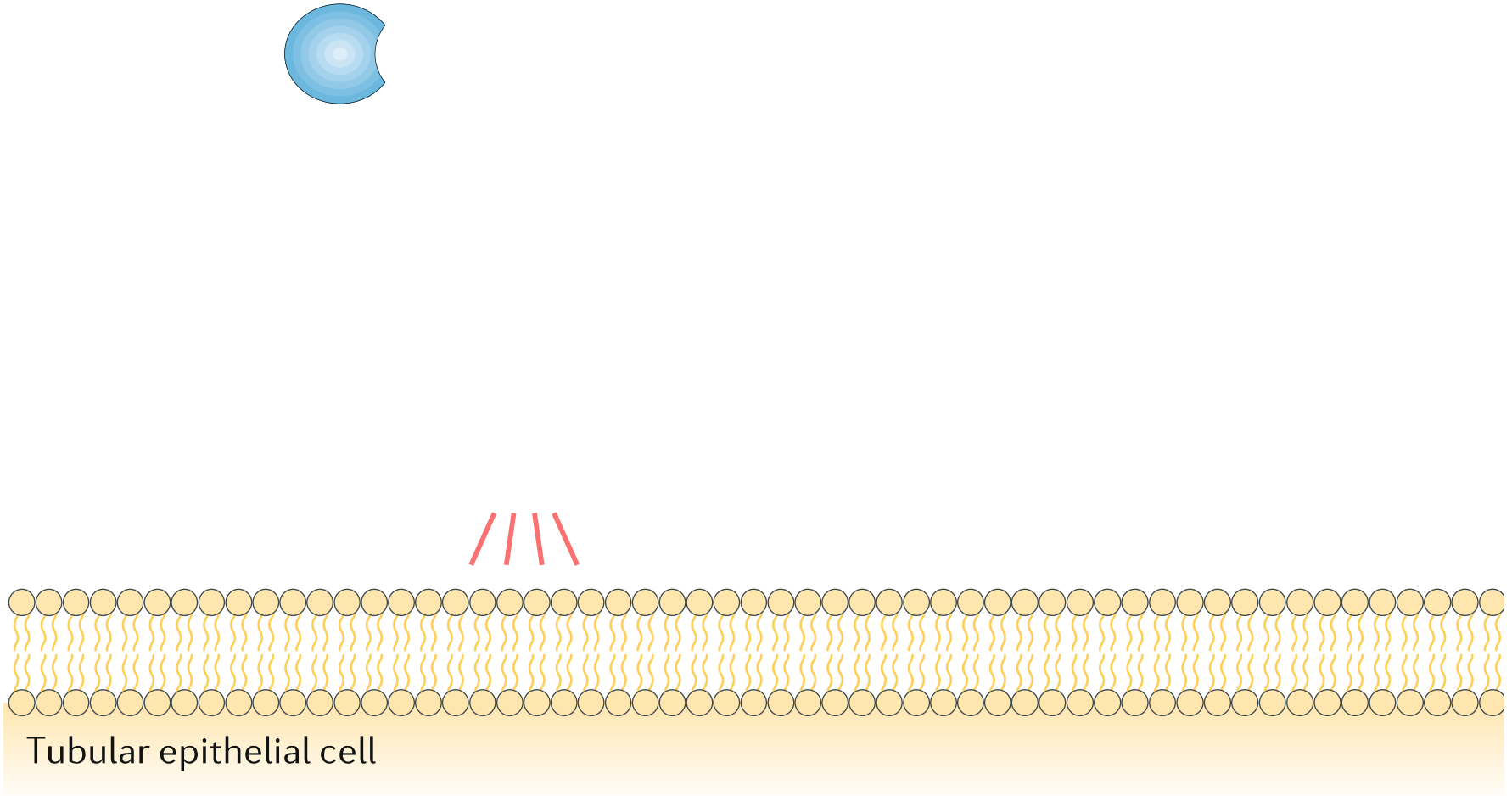
Sydney C. W. Tang * and Wai Han Yiu*

The role of inflammation in the pathogenesis of diabetic kidney disease

intracellular damage-associated molecular patterns

From Gilbert RE, Marsden PA. Activated protein C and diabetic nephropathy. N Engl J Med. 2008;358:1628–1630.

Potential mechanisms of complement activation in diabetic kidney disease.



LE PIU' RECENTI EVIDENZE ARRICCHISCONO LE CONOSCENZE CIRCA LA PATOGENESI DELLA NEFROPATIA DIABETICA SOTTOLINEANDO IL RUOLO DELL'INFIAMMAZIONE, DELLA DISFUNZIONE MITOCONDRIALE, DEL SISTEMA DEL COMPLEMENTO E LA CENTRALITA' DEL DANNO TUBULARE

Clinical diagnosis of DKD

Normoalbuminuria
Normal GFR

↓

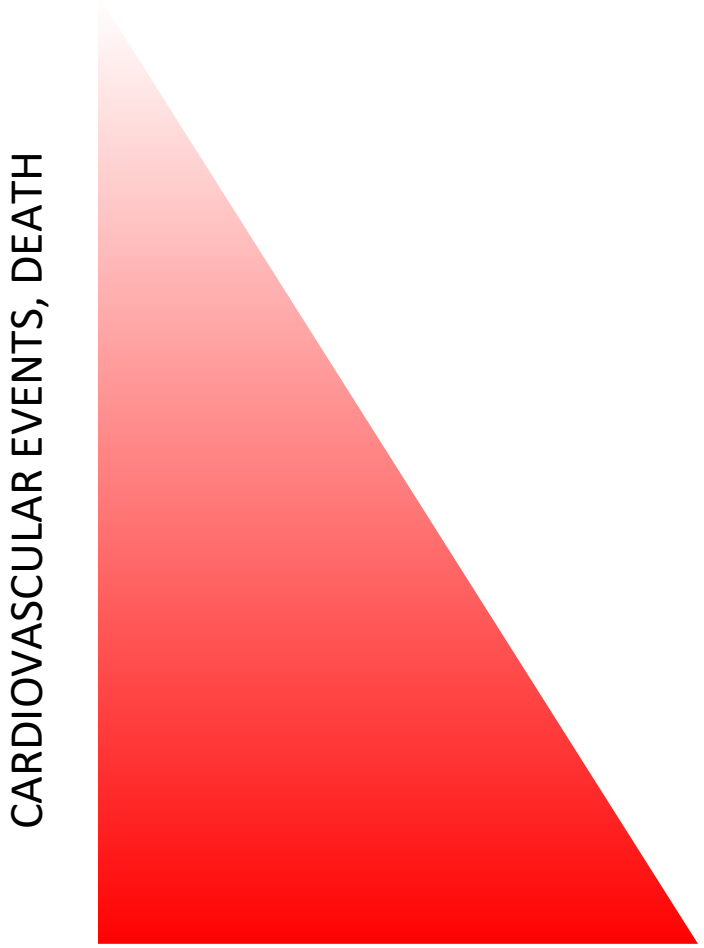
Microalbuminuria

↓

Macroalbuminuria

↓

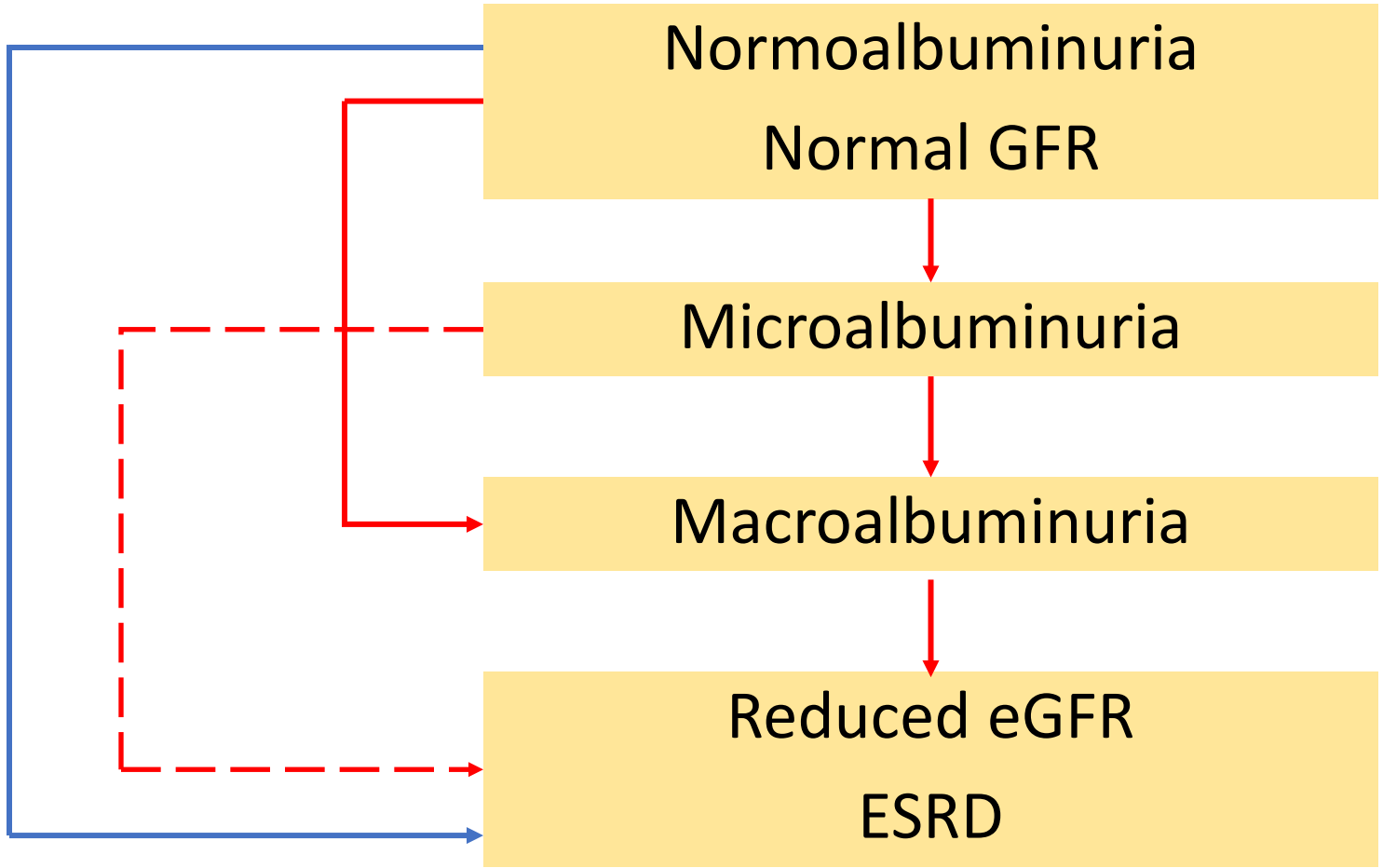
Reduced eGFR
ESRD

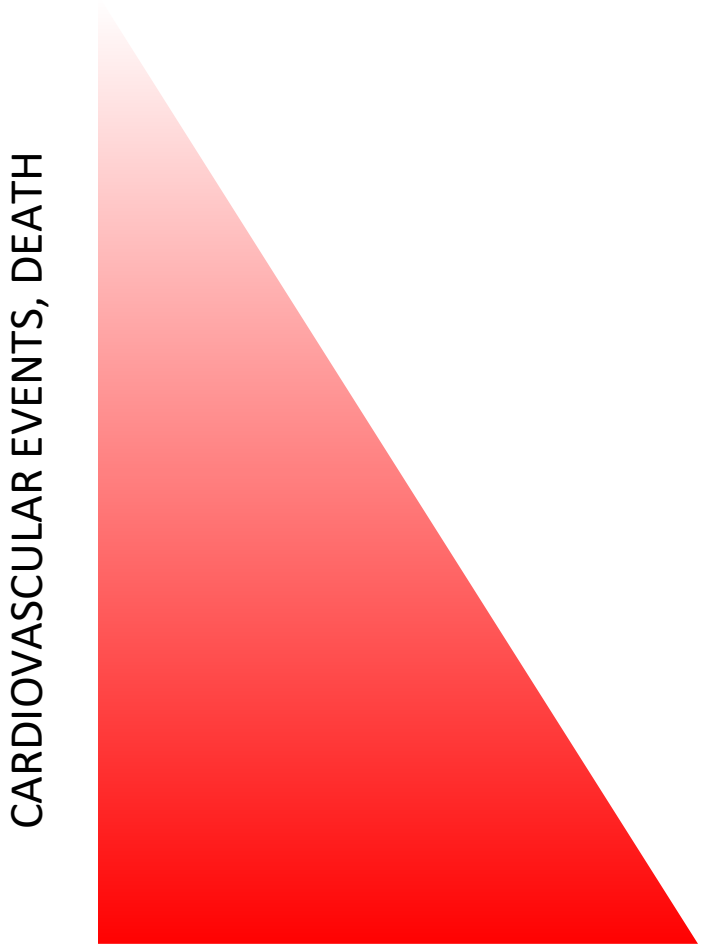


Natural history of DKD «non albuminuric» pattern

Natural history of DKD «albuminuric» pattern

Clinical diagnosis of DKD





Natural history of DKD «non albuminuric» pattern

Natural history of DKD «albuminuric» pattern

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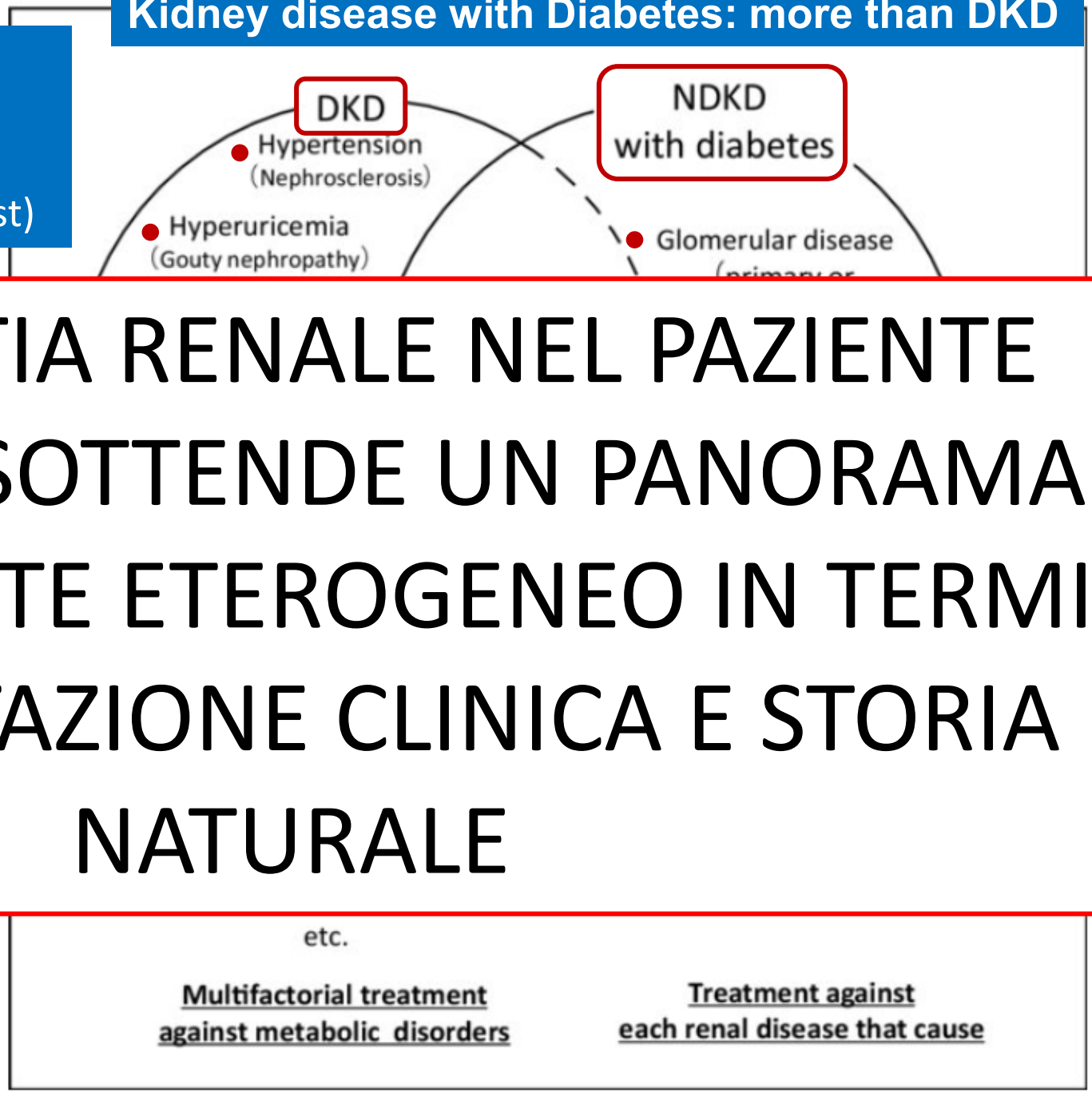
DMT2

~4 million (Italy)

CKD ≈ 30% (at least)

Kidney disease with Diabetes: more than DKD



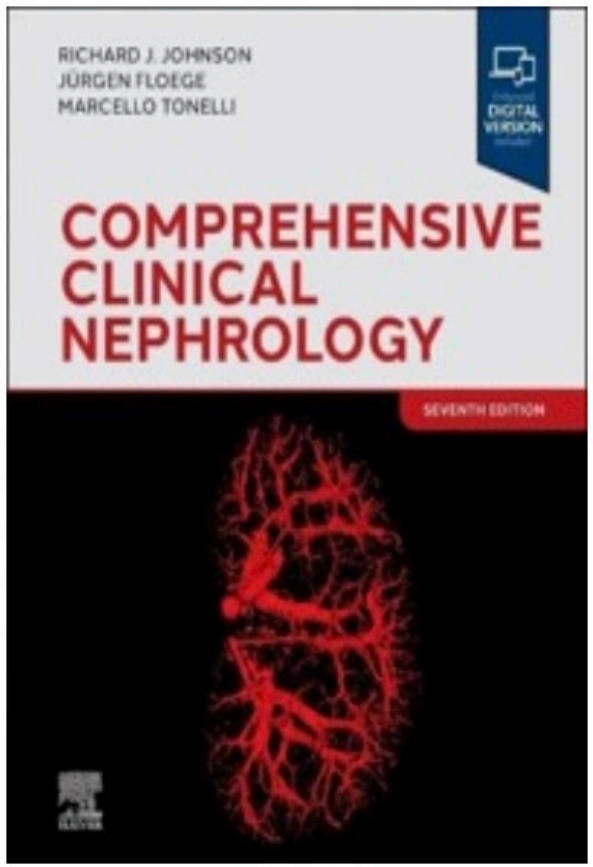
LA MALATTIA RENALE NEL PAZIENTE DIABETICO SOTTENDE UN PANORAMA ESTREMAMENTE ETEROGENEO IN TERMINI DI PRESENTAZIONE CLINICA E STORIA NATURALE

Clinical Evaluation of Diabetic Nephropathy

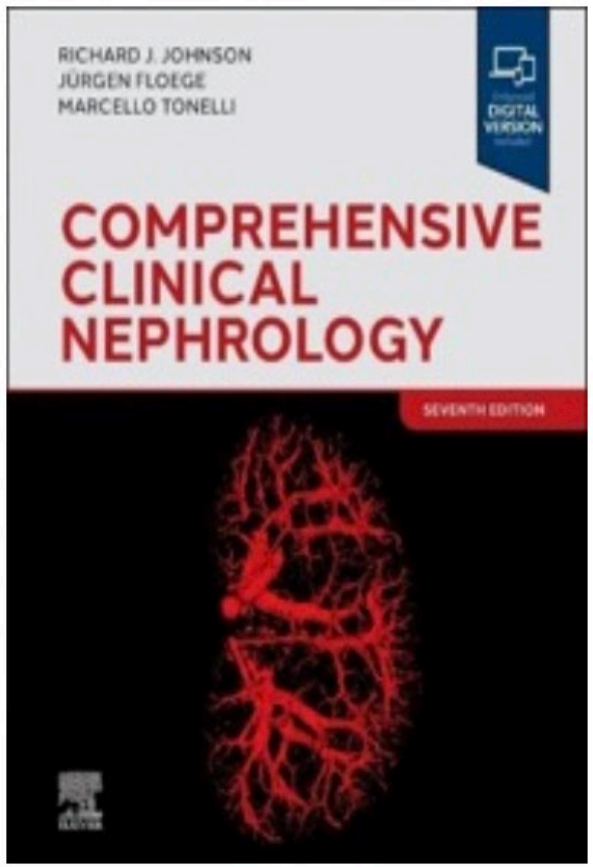
Diabetes proteinuria

↓

Exclude urinary tract infection
Urine microscopy: red cells, white cell casts?
Quantitate proteinuria
Renal ultrasonography
Serology if glomerulonephritis suspected
ANCA, DNA antibodies, C3, C4



Clinical Evaluation of Diabetic Nephropathy



Diabetes proteinuria

Exclude urinary tract infection
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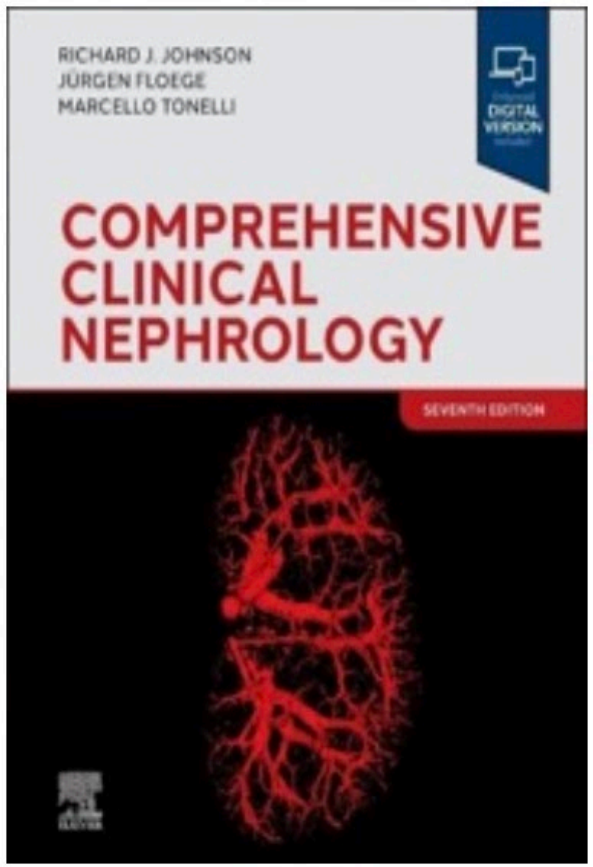
Typical diabetic nephropathy
Type 1 diabetes for >10 years
Retinopathy
Previous microalbuminuria
No macroscopic hematuria
No red cell casts
Enlarged kidneys on ultrasound

No renal biopsy

Clinical Evaluation of Diabetic Nephropathy



Diabetes proteinuria

- Exclude urinary tract infection
- Urine microscopy: red cells, white cell casts?
- Quantitate proteinuria
- Renal ultrasonography
- Serology if glomerulonephritis suspected ANCA, DNA antibodies, C3, C4

Typical diabetic nephropathy

- Type 1 diabetes for >10 years
- Retinopathy
- Previous microalbuminuria
- No macroscopic hematuria
- No red cell casts
- Enlarged kidneys on ultrasound

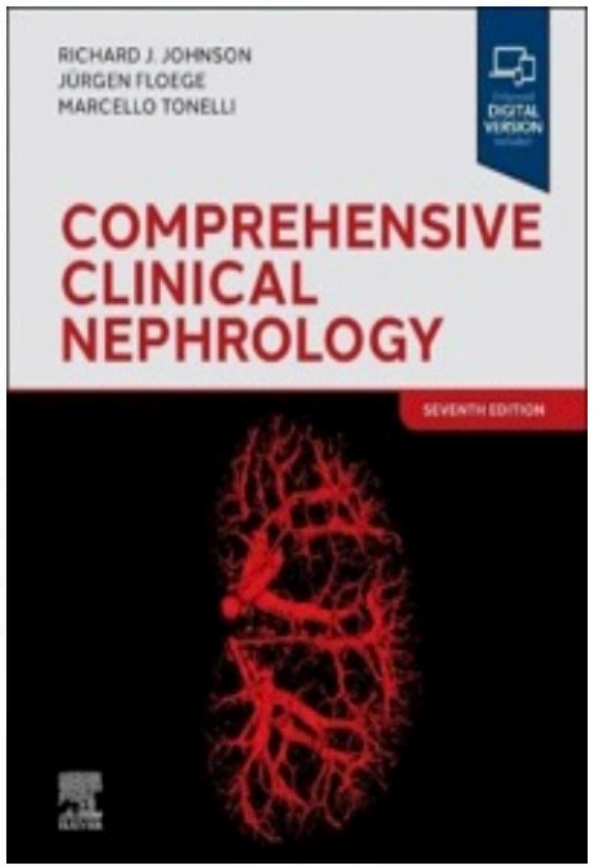
→ No renal biopsy

Atypical proteinuria

- Type 1 diabetes for <10 years
- No retinopathy
- Nephrotic-range proteinuria without progression through microalbuminuria
- Macroscopic hematuria
- Red cell casts

→ Renal biopsy

Clinical Evaluation of Diabetic Nephropathy



Diabetes proteinuria

Exclude urinary tract infection
Urine microscopy: red cells, white cell casts?
Quantitate proteinuria
Renal ultrasonography
Serology if glomerulonephritis suspected
ANCA, DNA antibodies, C3, C4

Typical diabetic nephropathy
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No macroscopic hematuria
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Enlarged kidneys on ultrasound

→ No renal biopsy

Atypical proteinuria
Type 1 diabetes for <10 years
No retinopathy
Nephrotic-range proteinuria without progression through microalbuminuria
Macroscopic hematuria
Red cell casts

→ Renal biopsy

Atypical
Azotemia with proteinuria <1 g/day
Papillary necrosis (pyuria, hematuria, scarring)
Tuberculosis (pyuria, hematuria)
Renovascular disease (other occlusive vascular disease)

→ No renal biopsy

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Classical indications for renal biopsy in patients with diabetes

Biopsy not indicated when

- Typical evolution of renal disease
- Concomitant retinopathy

Biopsy should be considered when

- Renal manifestations are seen atypically (<10 years) early in type 1 diabetes
- Dysmorphic erythrocytes/casts are found (nephritic sediment)
- Rapid deterioration of renal function of unknown cause is noted
- Elevated serum creatinine without urine abnormalities
- Heavy proteinuria (>5–8 g/day) persists despite lowering of blood pressure

UpToDate

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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

1997-2000 -> Biopsia renale in 393 pazienti affetti da diabete mellito tipo 2 in 3 Centri Italiani: Torino, Novara (restricted policy, CRPs) e Bergamo (unrestricted policy, CUP)

Restricted policy (CRPs)

- Ematuria
- Sindrome nefrosica
- Proteinuria > 2 g/d senza retinopatia diabetica
- Insufficienza renale rapidamente evolutiva
- Insufficienza renale di ndd

Unrestricted policy (CUP)

- Proteinuria > 0.5 g/d
- Ematuria
- Riduzione della funzione renale

Pazienti con lunga storia di DM e segni di severo danno d'organo microangiopatico non venivano sottopostia a biopsa renale (diagnosi clinica di ND)

Mazzucco et al AJKD 2002

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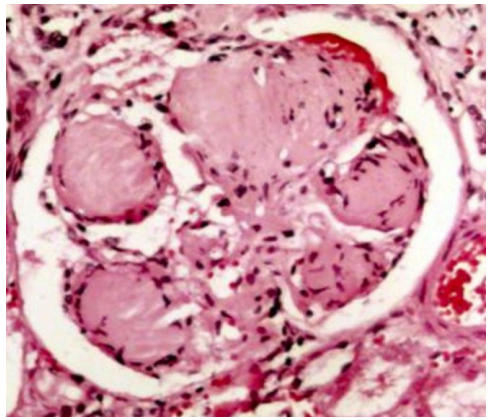
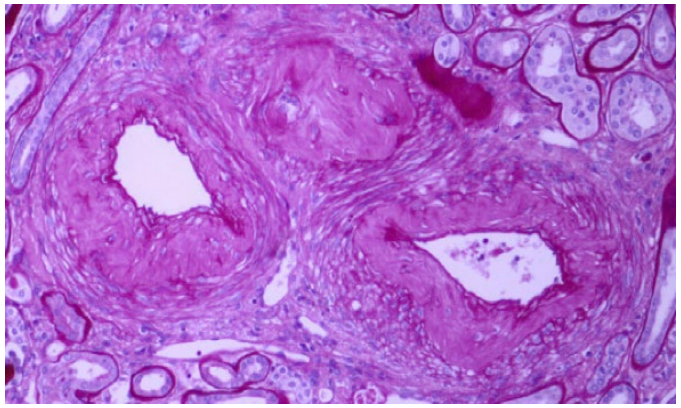
3 CLASSI SULLA BASE DEL DATO ISTOLOGICO

Classe 1



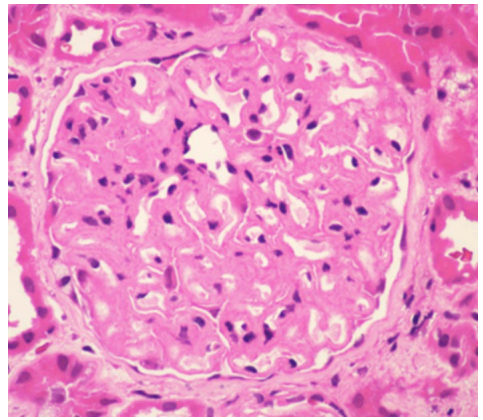
Glomerulosclerosi diabetica

Classe 2



Lesioni vascolari

Classe 3



Nefropatia non-diabetica associata a nefropatia diabetica (3a) o non associata (3b)

Mazzucco et al AJKD 2002

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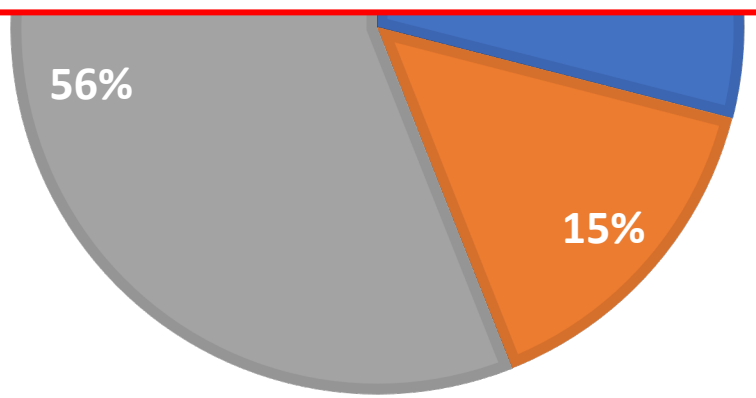
Different Patterns of Renal Damage in Type 2 Diabetes Mellitus: A Multicentric Study on 393 Biopsies

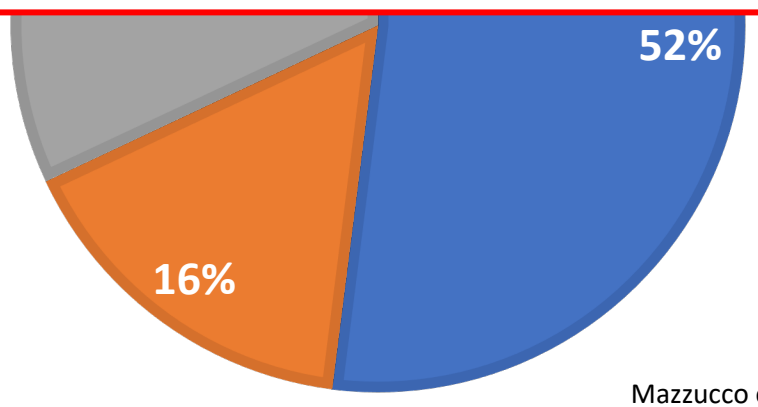
Gianna Mazzucco, MD, Tullio Bertani, MD, Mirella Fortunato, MD, Monica Bernardi, MD, Monica Leutner, MD, Renzo Boldorini, MD, and Guido Monga, MD

DIFFERENTI INDICAZIONI ALLA BIOPSIA RENALE DETERMINANO UNA SIGNIFICATIVA DIFFERENZA IN TERMINI DI LESIONI RENALI OSSERVATE ALL'ESAME ISTOLOGICO



Classe 2: N.S.

Classe 3: P< 0.0001



Mazzucco et al AJKD 2002

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Perché effettuare una biopsia renale in un paziente diabetico?

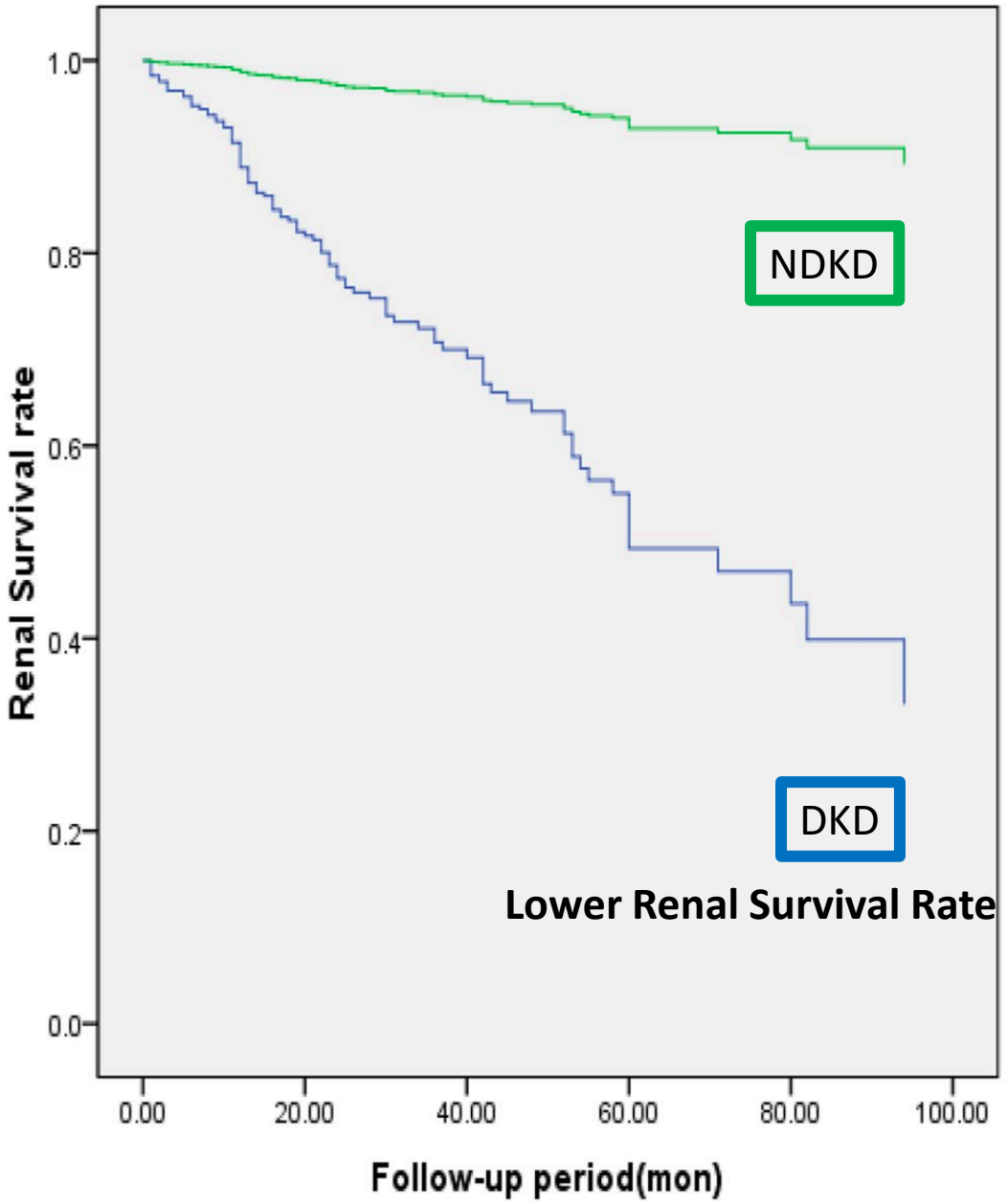
1) Identificare pazienti affetti da diabete mellito con lesioni renali NON secondarie alla patologia di base (non-diabetic kidney disease:**NDKD**)

ORIGINAL ARTICLE

Identification of clinical predictors of diabetic nephropathy and non-diabetic renal disease in Chinese patients with type 2 diabetes, with reference to disease course and outcome

Jiali Wang[1,2] · Qianqian Han[1] · Lijun Zhao[1] · Junlin Zhang[1] · Yiting Wang[1] · Yucheng Wu[1] · Tingli Wang[1] · Rui Zhang[1] · Premesh Grung[1] · Huan Xu[3] · Fang Liu[1]

A total of 505 T2DM patients with renal disease were eligible and enrolled in the present study. Renal biopsy revealed that 302 patients **(59.8%) had DN**, 174 **(34.5%) had NDRD**, and **29 (5.7%) had NDRD superimposed on DN**.



Wang et al Acta Diabetologica 2019

Renal biopsy in patients with diabetes: a pooled meta-analysis of 48 studies

Marco Fiorentino[1], Davide Bolignano[2,3], Vladimir Tesar[4], Anna Pisano[2], Wim Van Biesen[3], Giovanni Tripepi[2], Graziella D'Arrigo[2] and Loreto Gesualdo[1] on behalf of the ERA-EDTA Immunonephrology Working Group

The prevalence of DN, NDRD and mixed forms ranged from 6.5 to 94% (mean 50.1), 3 to 82.9% (mean 36.9) and 4 to 45.5% (mean 19.7) of the overall diagnoses, respectively. IgA nephropathy was the most common NDRD

Conclusions. NDRD are highly prevalent in patients with diabetes. Clinical judgment alone can lead to wrong diagnoses and delay the establishment of adequate therapies.

Fiorentino et al NDT 2016

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Renal biopsy in patients with diabetes: a pooled meta-analysis of 48 studies

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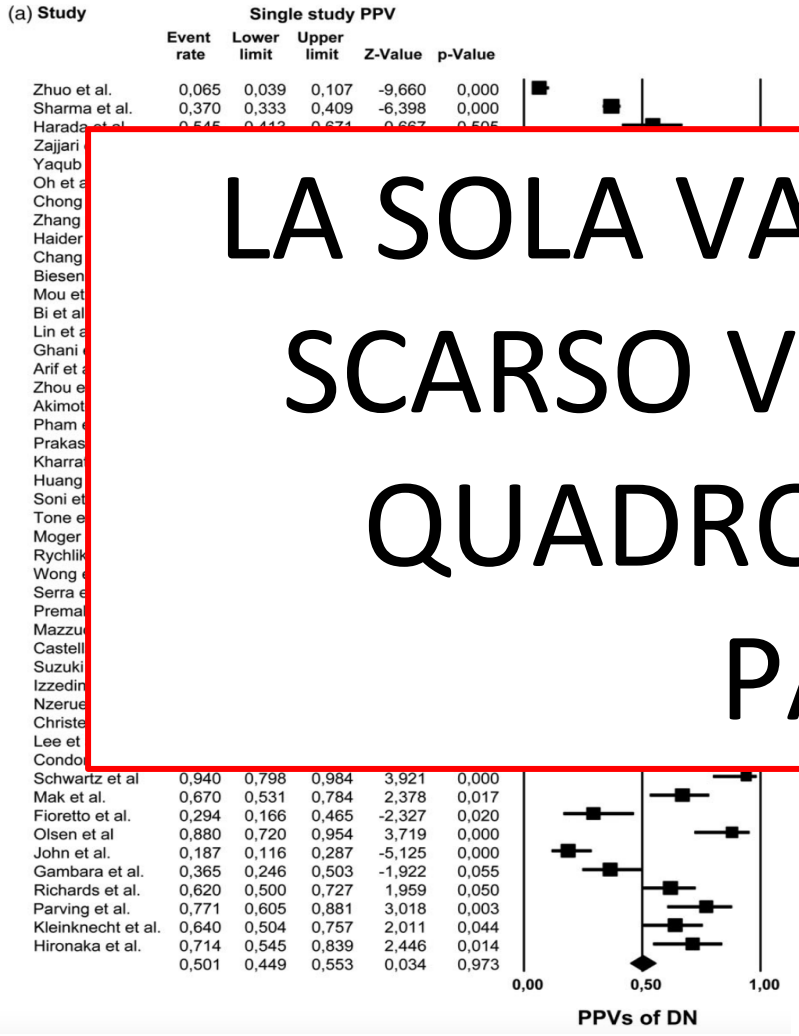

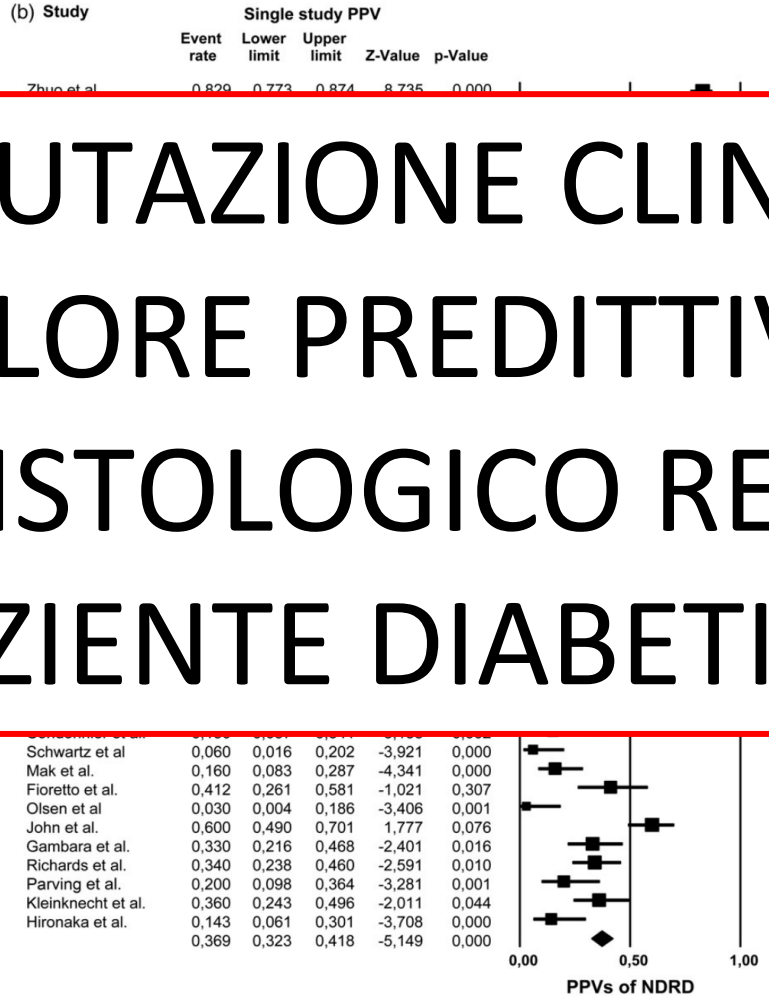

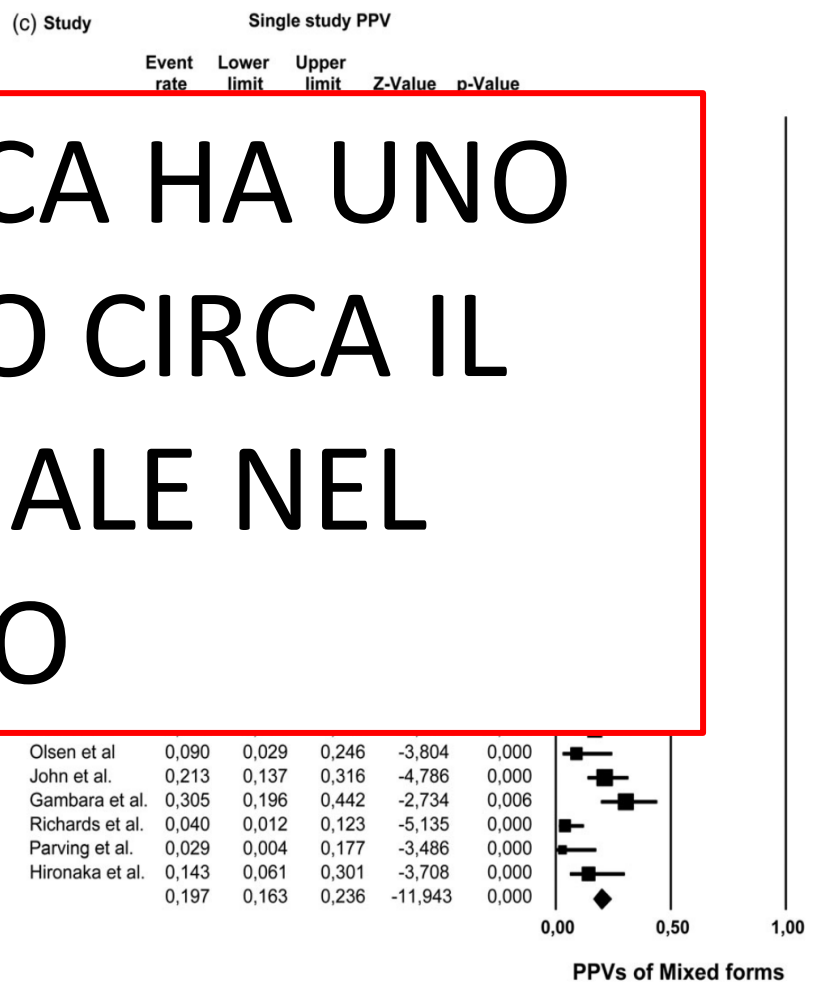

LA SOLA VALUTAZIONE CLINICA HA UNO SCARSO VALORE PREDITTIVO CIRCA IL QUADRO ISTOLOGICO RENALE NEL PAZIENTE DIABETICO

Fiorentino et al NDT 2016

Nefropatia Diabetica, Non Diabetica, forme miste

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‡*

CJASN 2013

Analisi di 2642 biopsie: 620 erano pazienti diabetici

LA DIAGNOSI ISTOLOGICA HA PERMESSO DI MODIFICARE L'APPROCCIO TERAPEUTICO IN CIRCA UN PAZIENTE DIABETICO SU TRE

186 (30%) pz avevano lesioni che hanno richiesto terapie particolari

Sharma SG, CJASN 2013

Nefropatia Diabetica, Non Diabetica, forme miste

36,6%

26,4%

35,4

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]

Of 620 patients with diabetes who underwent biopsy, 611 had adequate tissue for diagnosis. Categorical variables are expressed as *n* (%); continuous variables are expressed as median (interquartile range). DN, diabetic nephropathy; NDRD, nondiabetic renal disease; DM, diabetes mellitus; eGFR, estimated GFR.

[a]$P<0.05$ for comparison of DN plus NDRD versus DN alone subgroups.

[b]$P<0.05$ for comparison of NDRD alone versus DN alone subgroups.

[c]$P<0.05$ for comparison of NDRD alone versus DN plus NDRD subgroups.

Sharma SG, CJASN 2013

Tipo di Nefropatia Non Diabetica

Table 2. Summary of NDRD, with and without DN, found on biopsies of patients with diabetes

Types of NDRD (n)	NDRD Alone (*n*=220)	DN Plus NDRD (*n*=164)	*P* Value[a]
Acute tubular necrosis (109)	38 (17.3)	71 (43.3)	<0.001
FSGS (69)	48 (21.8)	21 (12.8)	0.02
Primary FSGS (6)	6 (2.7)	0 (0.0)	0.03
Secondary FSGS (63)[b]			
HTN related	19 (8.6)	10 (6.1)	0.35
HTN plus obesity related	16 (7.3)	10 (6.1)	0.65
Obesity related	4 (1.8)	1 (0.6)	0.30
Other[c]	3 (1.4)	0 (0.0)	0.13
Hypertensive nephrosclerosis (70)[b]	39 (17.7)	31 (18.9)	0.77
IgA nephropathy (35)	23 (10.5)	12 (7.3)	0.29
Membranous GN (23)	18 (8.2)	5 (3.0)	0.04
Pauci-immune crescentic GN (19)	15 (6.8)	4 (2.4)	0.05
Acute interstitial nephritis (18)	11 (5.0)	7 (4.3)	0.73
Amyloidosis (10)	10 (4.5)	0 (0)	0.01
Myeloma cast nephropathy (10)	8 (3.6)	2 (1.2)	0.14
Acute postinfectious GN (6)	3 (1.4)	3 (1.8)	0.72
Atheroembolic disease (5)	2 (0.9)	3 (1.8)	0.43
Others (10)	5 (2.3)	5 (3.0)	0.64

Values are expressed as *n* (%). NDRD, nondiabetic renal disease; DN, diabetic nephropathy; HTN, hypertension.
[a]*P* value is from a two-sample test of proportions
[b]Thirteen cases of secondary FSGS in the NDRD alone subgroup and 16 cases of secondary FSGS in the DN plus NDRD subgroup also showed features of hypertensive nephrosclerosis.
[c]Includes increased muscle mass (*n*=1), solitary kidney (*n*=1), and familial FSGS (*n*=1)

Sharma SG, CJASN 2013

Durata del diabete e altro……..

- **5.9 anni nefropatia non diabetica vs 10.6 anni nefropatia diabetica (p <0.001 - Chang, 2011)**

"Whereas AKI, low complements, and positive M-spike suggest an increased likelihood of finding NDRD on biopsy, long duration of DM emerged as the strongest predictor of finding DN alone".

Approximately one-quarter of all renal biopsies are performed in patients with DM. Judicious use of renal biopsy has uncovered NDRD alone or superimposed on DN in the majority of such biopsies. ATN is emerging as an important category of NDRD, which has not been reported previously.

Sharma SG, CJASN 2013

Our experience (1994-2012)

From 1374 renal biopsies performed in our division (S.C.D.U. Nefrologia, Dialisi e Trapianto, ARNAS Brotzu) from January 1994 to February 2012

Patient profile: mean age (yrs): 61.7±13.9; M/F: 1.59; Type I Diabetes (%): 8; onset of diabetes (yrs): 11.9±9.5; onset of microalbuminuria (yrs): 5.3±5.4.

Renal Biopsy Clinical Criteria:
1.Rapid onset of: nephrotic syndrome, hematuria, proteinuria ≥0.5 to 1 g/24h, proteinuria ≥1 to <3 g/24h; proteinuria >3 g,
2.Nephritic Syndrome;
3.Acute Kidney Injury;
4.RPGN

Histological diagnosis	n	%	%ap
ACUTE TUBULAR NECROSIS	4	7.0	4.5
AMYLOIDOSIS	1	2.0	1.1
CAST NEPHROPATHY	2	3.9	2.3
PAUCIIMMUNE G.N.	4	7.0	4.5
CRYOGLOBULINEMIA	3	5.9	3.4
FSGS, SECONDARY	3	5.9	3.4
IgAN	5	9.8	5.7
INTERSTITIAL NEPHRITIS	6	11.8	6.8
MEMBRANOUS G.N.	8	16	9.1
MESANGIOPROLIFERATIVE G.N.	1	2.0	1.1
MINIMAL CHANGE DISEASE	3	5.9	3.4
MPGN TYPE 1	1	2.0	1.1
NEPHROANGIOSCLEROSIS	6	12	6.8
NON HODGKIN LYMPHOMA	1	2.0	1.1
NORMAL KIDNEY	1	2.0	1.1
POSTINFECTIOUS G.N.	1	2.0	1.1
THROMBOTIC MICROANGIOPATHY	1	2.0	1.1
TOTAL (EXCLUDED DGS)	51	100	58
NDRD	39		44.3
NDRD + DGS	12		13.7
DIABETIC GLOMERULOSCLEROSIS	37		42.0
TOTAL BIOPSIES	88		100

Figure 1: Histological diagnosis in selected patients and prevalence of NDRD, NDRD & DGS, AND DGS alone. Number of cases (n); relative percentages in patients affected with NDRD (%); percentages obtained considering DGS patients

Unpublished data

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Criteria of Kidney biopsy in Diabetes, suspecting a NDKD

LA PRESENZA DI UNA DI QUESTE CONDIZIONI RAPPRESENTA UN'INDICAZIONE ASSOLUTA ALL'ESECUZIONE DI BIOPSIA RENALE NEL PAZIENTE DIABETICO

(personal opinion condivisa nel nostro centro)

Di Paolo S. et al Nutr Metabol Cardiovasc Diseases 2020

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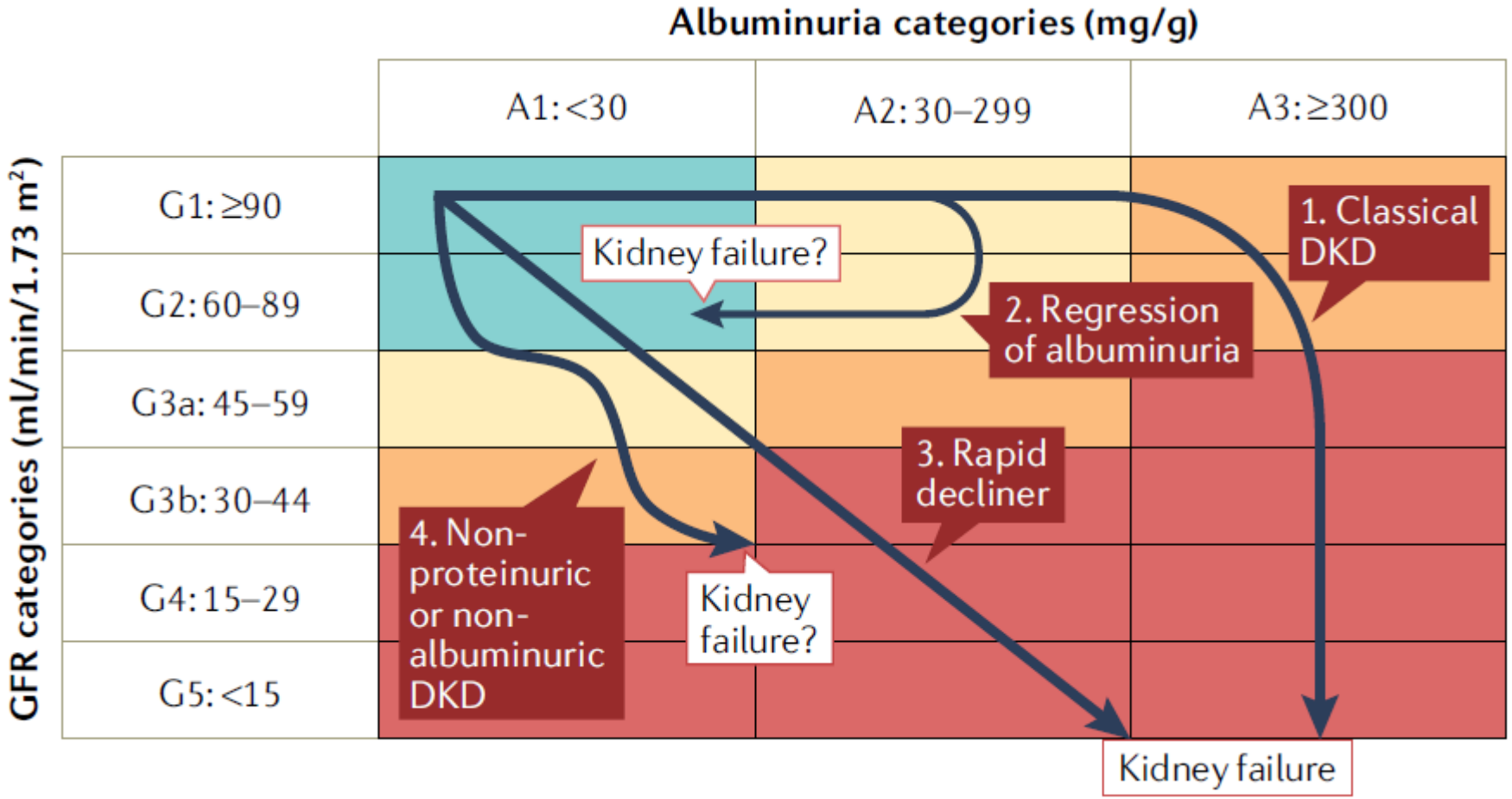
Perché effettuare una biopsia renale in un paziente diabetico? (2)

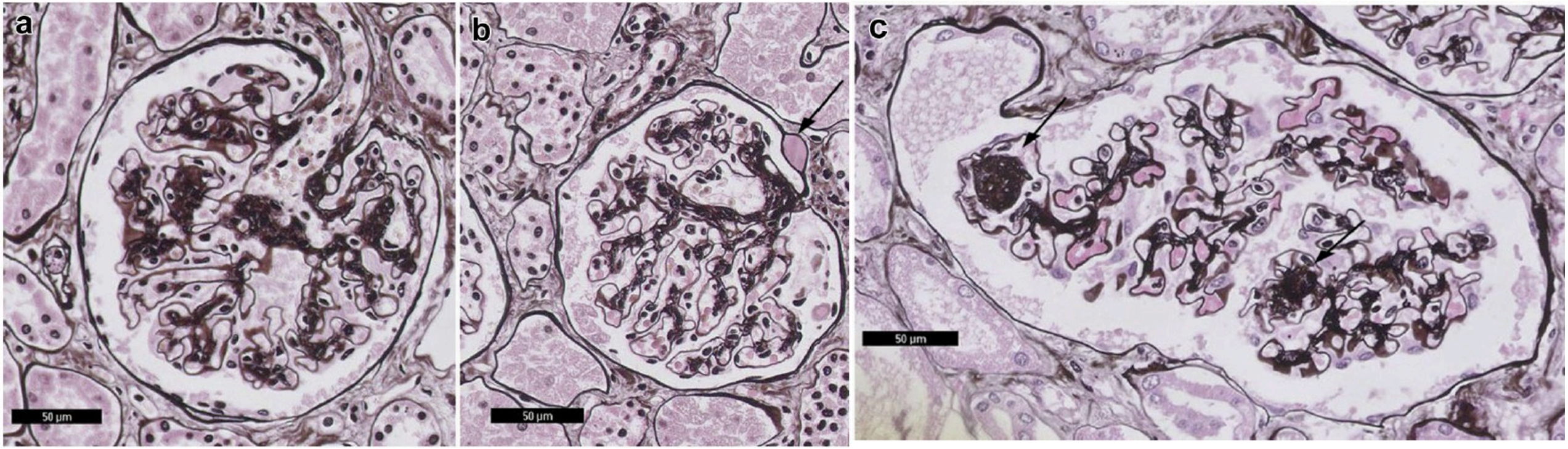
2) Identificare il fenotipo del paziente con DKD (diabetic kidney disease) e personalizzare l'approccio terapeutico

Can the progression to ESKD be prevented before it is too late?



Oshima M et al Nat Rev Nephrol 2021

Are clinical patterns in DKD sufficiently sensible and specific? Based on autopsy studies, when clinical manifestations appear DKD is too “late”



Mesangial expansion (stage II)

Capsular drops

KW nodules (stage III)

Klessens CQF et al KI 2015

Is the progression to ESKD due to multiple factors? The rise of clinical and histological patterns

KDIGO: Prognosis of CKD by GFR and albuminuria categories

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk. GFR, glomerular filtration rate.

Furuiki K. et al NDT 2016

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Is the progression to ESKD due to multiple factors?
The rise of clinical and histological patterns

LA PRESENZA DI LESIONI GLOMERULARI IDENTIFICA UN GRUPPO DI PAZIENTI CON ELEVATO RISCHIO DI ESRD ANCHE IN ASSENZA DI ALBUMINURIA E CON FUNZIONE RENALE NORMALE O MINIMAMENTE RIDOTTA

Furuiki K. et al NDT 2016

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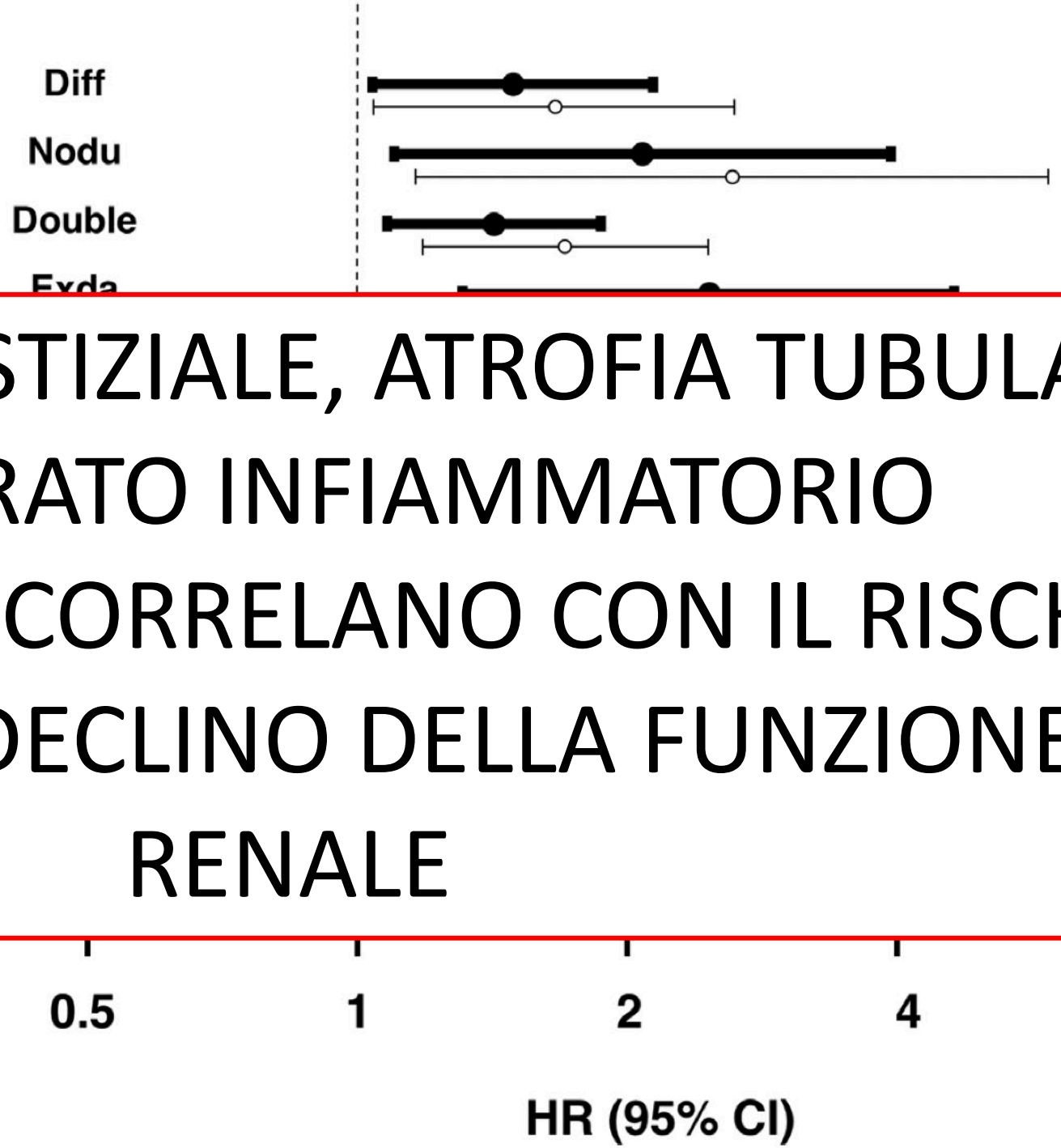
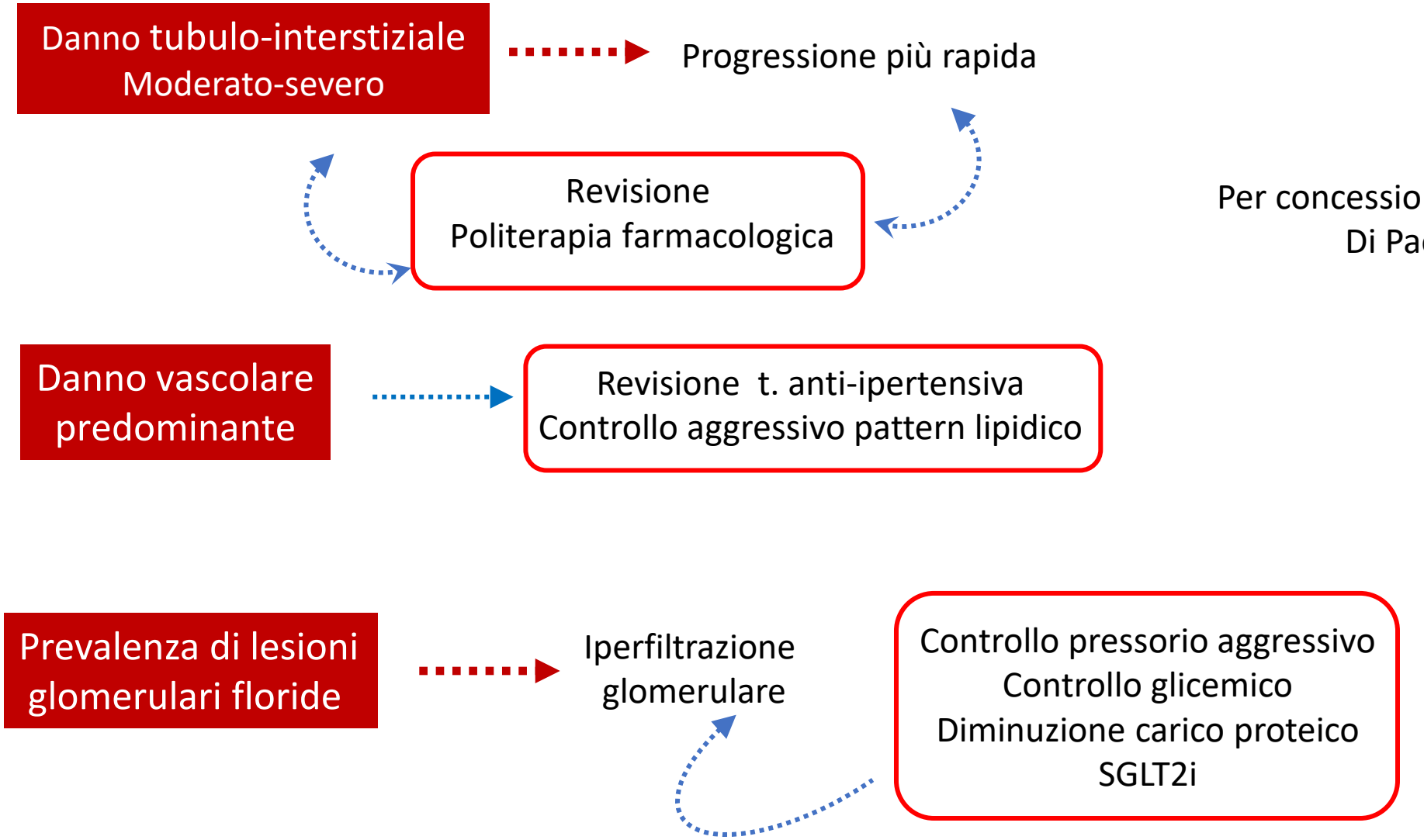
BMJ Open Diabetes Research & Care



FIBROSI INTERSTIZIALE, ATROFIA TUBULARE E INFILTRATO INFIAMMATORIO INTERSTIZIALE CORRELANO CON IL RISCHIO DI RAPIDO DECLINO DELLA FUNZIONE RENALE

Quale potenziale valore prognostico-terapeutico dei riscontri bioptici?



Per concessione del dott.
Di Paolo

Razionale per biopsia renale in paziente con sospetta DKD

PRO

- Le lesioni istologiche della DKD sono eterogenee e presentano un impatto prognostico significativo circa la progressione verso ESRD e il rischio CV
- La diagnosi clinica di DKD è talora fallace e spesso può giungere in maniera tardiva nella storia naturale della malattia
- Il profilo di DKD ”non albuminurico” assume un peso crescente nell’ambito dei pazienti diabetici
- Il profilo fenotipico evidenziato dall’istologia renale potrebbe permettere un approccio personalizzato alla terapia

CON

- Difficoltà nella pratica clinica ad estendere l’indicazione bioptica a pazienti non albuminurici con funzione renale normale o lievemente ridotta (fasi precoci della DKD “non albuminurica”)
- Perplessità circa l’impatto reale sulla modifica dell’approccio terapeutico (in considerazione dell’attuale standard of care)

STUDY PROTOCOL Open Access

Prognostic imaging biomarkers for diabetic kidney disease (iBEAt): study protocol

Kim M. Gooding[1,2*], Chrysta Lienczewski[3], Massimo Papale[4], Niina Koivuviita[5,6], Marlena Maziarz[7], Anna-Maria Dutius Andersson[7], Kanishka Sharma[8], Paola Pontrelli[4], Alberto Garcia Hernandez[9], Julie Bailey[10], Kay Tobin[11], Virva Saunavaara[12], Anna Zetterqvist[7], David Shelley[10,13], Irvin Teh[14], Claire Ball[2], Sapna Puppala[10], Mark Ibberson[15], Anil Karihaloo[16], Kaj Metsärinne[5], Rosamonde E. Banks[17], Peter S. Gilmour[18], Michael Mansfield[10], Mark Gilchrist[1], Dick de Zeeuw[19,20], Hiddo J. L. Heerspink[19,20], Pirjo Nuutila[5,6], Matthias Kretzler[3,21], Matthew Welberry Smith[11], Loreto Gesualdo[4], Dennis Andress[22], Nicolas Grenier[23], Angela C. Shore[1,2], Maria F. Gomez[7†], Steven Sourbron[8†] and for the BEAt-DKD consortium

Biopsy in DKD: research

Patient's Phenotyping

Histopathological
Clinical
Imaging
Omics

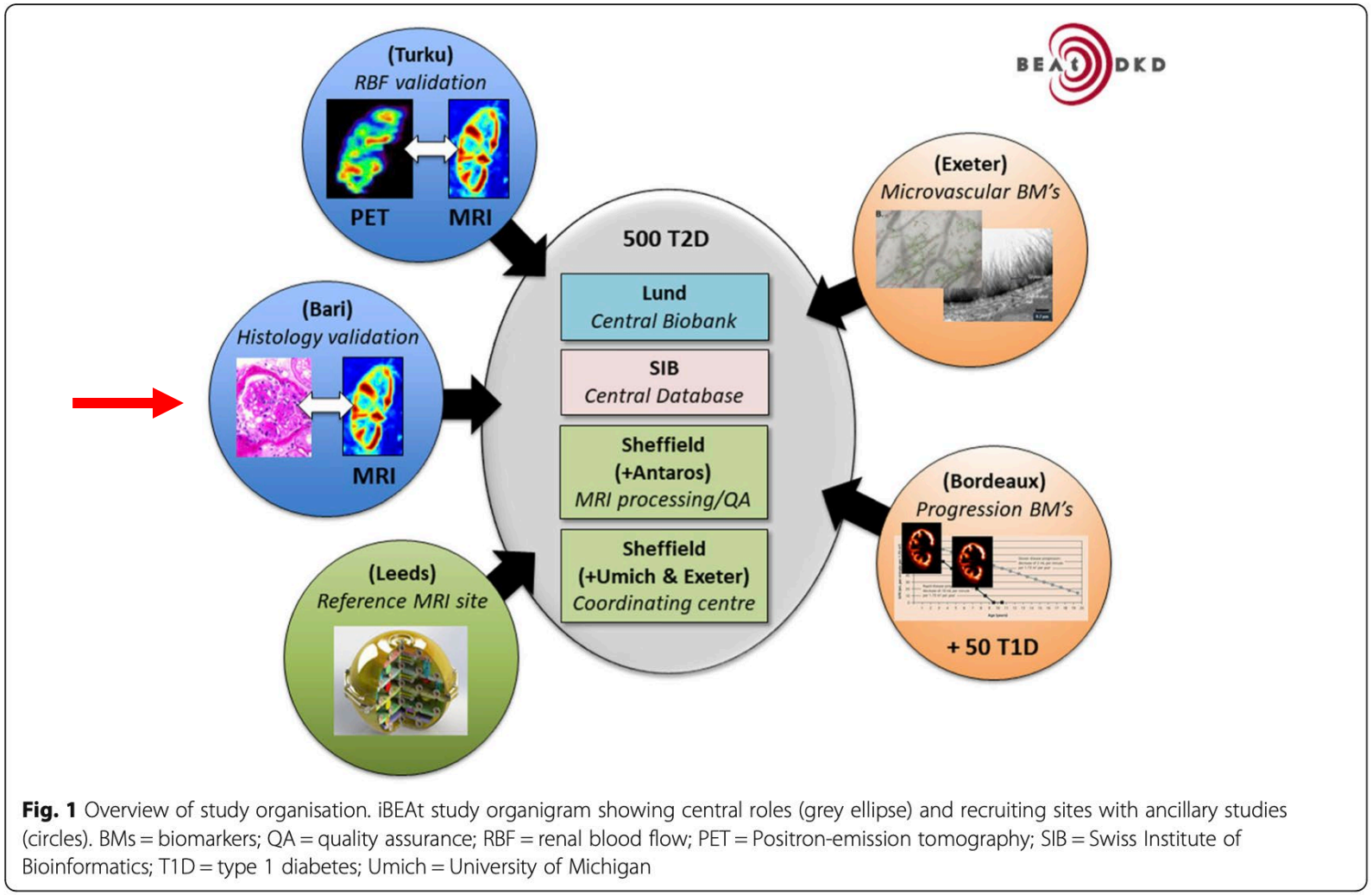


Fig. 1 Overview of study organisation. iBEAt study organigram showing central roles (grey ellipse) and recruiting sites with ancillary studies (circles). BMs = biomarkers; QA = quality assurance; RBF = renal blood flow; PET = Positron-emission tomography; SIB = Swiss Institute of Bioinformatics; T1D = type 1 diabetes; Umich = University of Michigan

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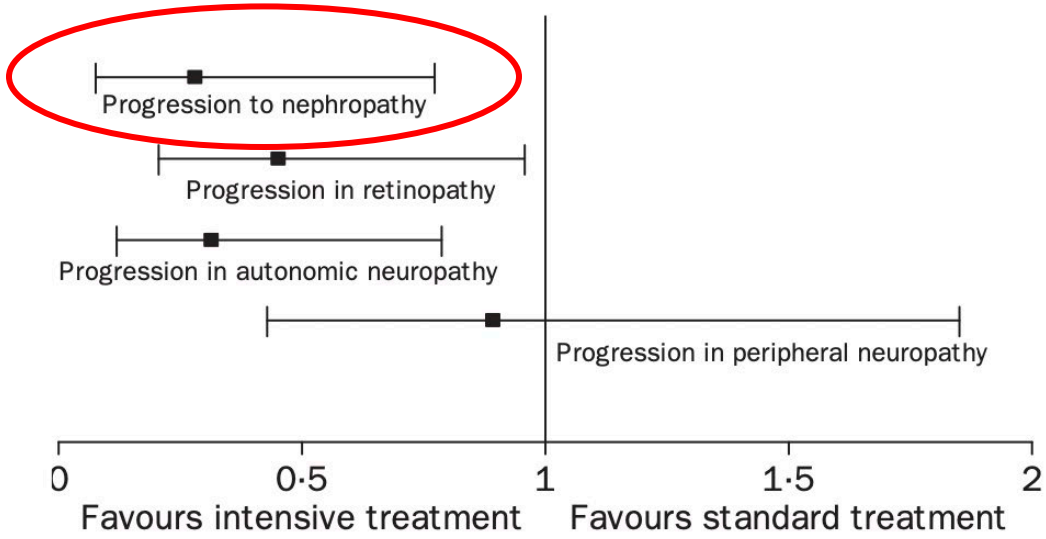
TAKE HOME MESSAGES

- La malattia renale nel paziente diabetico comprende un ampio spettro di condizioni sia conseguenti alla patologia diabetica (DKD) sia indipendenti da essa (NDKD)
- I pazienti con NDKD presentano una prognosi renale migliore rispetto ai pazienti con DKD
- La probabilità clinica di una condizione di NDKD aumenta in assenza di retinopatia diabetica e con storia di diabete mellito < 5 anni
- La diagnosi della NDKD è una diagnosi istologica
- Il fenotipo della DKD è eterogeneo sia clinicamente sia istologicamente
- Le lesioni vascolari sono un elemento precoce nella storia naturale della DKD non albuminurica
- L'estensione delle indicazioni bioptiche nei pazienti con verosimile DKD in ambito di ricerca rappresenta un passaggio necessario per una miglior comprensione dei fenotipi di DKD e per la validazione di nuovi biomarkers

TAKE HOME MESSAGES: NO DKD WITHOUT DIABETES!

Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study

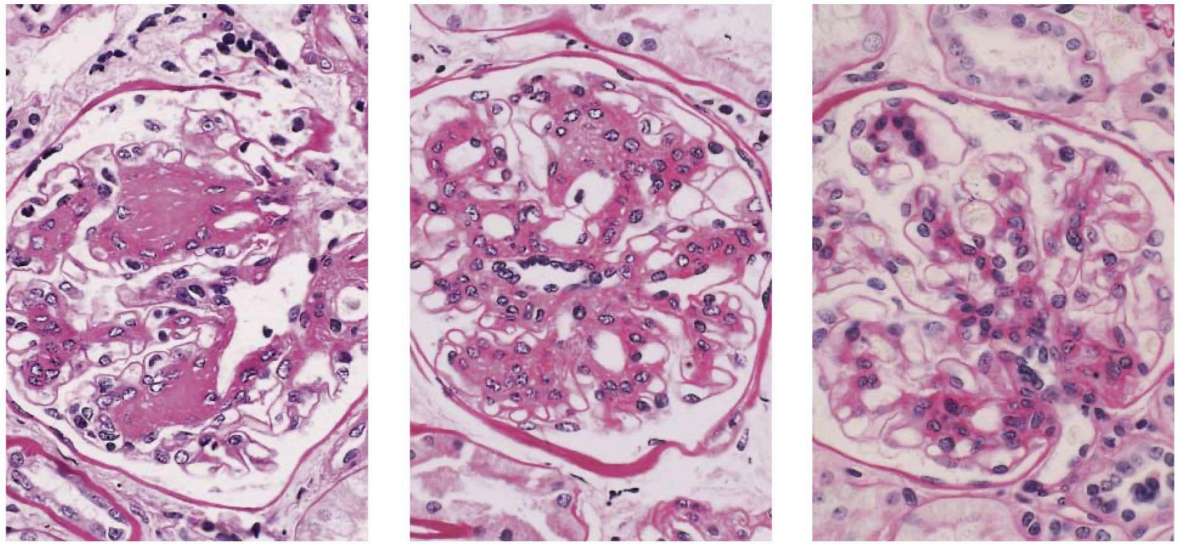
Peter Gæde, Pernille Vedel, Hans-Henrik Parving, Oluf Pedersen



REVERSAL OF LESIONS OF DIABETIC NEPHROPATHY AFTER PANCREAS TRANSPLANTATION

REVERSAL OF LESIONS OF DIABETIC NEPHROPATHY AFTER PANCREAS TRANSPLANTATION

PAOLA FIORETTO, M.D., PH.D., MICHAEL W. STEFFES, M.D., PH.D., DAVID E.R. SUTHERLAND, M.D., PH.D., FREDERICK C. GOETZ, M.D., AND MICHAEL MAUER, M.D.




Dr. Nicola Lepori
Prof. Antonello Pani


nal recovery
No
Yes
censored
censored
A. ANGIOI
Dr. Andrea Angioi


Grazie
感谢您的时间
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