EPIDEMIOLOGY OF DKD

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Outline of the presentation

• The diabetes epidemic
• Consequences of DKD
• Screening tools (albuminuria)
• Tools to screen for renal function (eGFR)
• Prevalence of DKD
• Take home messages
The diabetes epidemic
The diabetes epidemic

Diabetes is a global epidemic

Whole world
2003 = 194 M
2025 = 333 M
↑ 72%

AFR
19.2 M
39.4 M
↑ 105%

EMME
19.2 M
39.4 M
↑ 105%

SEA
39.3 M
81.6 M
↑ 79%

WP
43.0 M
75.8 M
↑ 79%

NA
23.0 M
36.2 M
↑ 57.0%

EUR
48.4 M
58.6 M
↑ 21%

SACA
14.2 M
26.2 M
↑ 85%

Type 1 diabetes incidence continues to increase, faster than ever before.
Diabetic complications

- MI, Cardiac failure
- Nephropathy
- Neuropathy
- Retinopathy
- Stroke, PVD
Consequences of diabetic nephropathy and/or DKD
Mortality excess is confined to those with renal complications. Most patients do very well.


ESRD = end-stage renal disease
DKD is the major predictor of mortality in type 2 diabetes

Population-based study of 1,565 individuals with known type 2 diabetes who were resident in the town of Casale Monferrato in north-west Italy in 1988. There were 670 deaths during 10,780 person years of follow-up.

All-cause mortality in patients with type 2 diabetes stratified by baseline eGFR

10-year follow-up of 3288 patients in the South Tees Diabetes Mortality Study

Log rank P<0.0001

eGFR ≤29

eGFR 30-59

eGFR 60-89

eGFR >90

eGFR = estimated glomerular filtration rate

ADVANCE: Cardiovascular events

Cardiovascular risk is greatest when both diabetes and CKD are present

Among patients with diabetes and CKD, the rate of cardiovascular events is more than twice that among patients with diabetes only.

Changes in the numbers of ESRD cases due to diabetes in the US over 25 years

Number of people initiating treatment for ESRD 1980-2006

U.S. Renal Data System, USRDS 2008 Annual Data Report
Declining renal function also increases risk of severe hypoglycaemia

Increased risk most dramatic in patients with renal dysfunction and type 2 diabetes

Around 74% of sulphonylurea-induced severe hypoglycaemic events (loss of consciousness) occurs in patients with reduced renal function

Screening tools (albuminuria)
Screening for microalbuminuria

Courtesy of Hans-Henrik Parving
Definitions of albuminuria

**Normoalbuminuria:** a timed overnight urinary albumin excretion rate (AER) <20 µg/min or <30 mg/24 h or an albumin-creatinine ratio (ACR) of <2.5 mg/mmol for men and <3.5 for women in a first morning urine sample.

**Microalbuminuria:** AER 20-200 µg/min or 30-300 mg/24 h or an ACR of 2.5-25 mg/mmol for men and 3.5-35 for women in a first morning urine sample.

**Macroalbuminuria:** AER >200 µg/min or >300 mg/24 h or an ACR of >25 mg/mmol for men and >35 for women in a first morning urine sample.
Type 1 diabetes
Microalbuminuria in type 2 diabetes

**NEAR NORMAL HISTOLOGY (C1) - 30 %**

- (a) Both normal and totally destroyed glomeruli

**TYPICAL DIABETIC NEPHROPATHY (C2) - 30 %**

- (b) Severe arteriollohylalinosis

- (c) Tubulointerstitial fibrosis

**NON-SPECIFIC FINDINGS (C3) - 40 %**

Fioretto et al. Diabetologia 1998;41:233-236
Change in GFR (%) in patients with type 2 diabetes and microalbuminuria

(n=33, 4 year follow-up)

* p<0.05, C2 vs C1 ja C3

Progression of diabetic nephropathy

Proteinuria $\geq 500$ mg/24 h and average S-Crea 88 $\mu$mol/l at baseline

Graph showing the progression of GFR (ml/min) over years for Type 1 (n=16) and Type 2 (n=16) diabetic patients.

**Albuminuria: a risk factor for DKD**

Risk of developing sustained eGFR < 60 mL/min/1.73 m²

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Microalbuminuria</th>
<th>Macroalbuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hazard ratio</td>
<td>1.2</td>
<td>1.8*</td>
<td>5.7*</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(1.2–1.3)</td>
<td>(1.6–1.9)</td>
<td>(4.5–6.8)</td>
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* p < 0.001 versus normal.

Albuminuria: a risk factor for CVD

The risk of CV outcomes according to degree of albuminuria in patients with T2DM: The Renal Insufficiency and Cardiovascular Events Study, N = 15,773

Odds ratio (95% CI) for major acute CVD events

*Coronary events (including myocardial infarction and/or coronary revascularization); cerebrovascular events (including stroke and/or carotid revascularization; and peripheral events including ulcer/gangrene/amputation and/or lower limb revascularization). Solini et al. Diabetes Care. 2012:35:143–149.
Tools to estimate renal function (eGFR)
Estimation of renal function

The *Cockroft-Gault formula* provides an estimate of the creatinine clearance (eCCr)

*Cockcroft DW, Gault MH. Nephron 1976;16(1):31-41.*

The *MDRD-4 formula* provides an estimate of the glomerular filtration rate (eGFR)


The *CKD-EPI equation* provides an estimate of the glomerular filtration rate (eGFR)

Stages of renal function

Stage 1 - eGFR >90 ml/min + persistent albuminuria

Stage 2 - eGFR 60-89 ml/min + persistent albuminuria

Stage 3a - eGFR 45-59 ml/min

Stage 3b - eGFR 30-44

Stage IV - eGFR 15-29 ml/min

Stage V - eGFR <15 ml/min

KDOQI
Prevalence of DKD
Prevalence depends on the definition?

Impossible to make causal inference

"so it is clinically defined in patients with diabetes and an eGFR < 60 ml/min/1.73 m² and/or an elevated urinary ACR (≥30 mg/g)

= essentially CKD in diabetes or DKD
Scatter plots for eGFR against ACR in type 1 and type 2 diabetes

Type 1 diabetes

Type 2 diabetes

Shaded area denotes CKD defined as ACR ≥30 mg/g and/or eGFR < 60 ml/min/1.73 m²

The distribution of albuminuria and an eGFR <60 ml/min/1.73 m\(^2\) in patients with T2D in Australia

Nefron Study
N=3.893 patients with Type 2 diabetes
52% males

Thomas et al. MJA 2006, 185, 140-144

*The unshaded area denotes patients without chronic kidney disease (52.9%).
Global perspective

Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)

Epidemiology of CKD in diabetes

Varies considerably across countries and settings

- African Americans
- Middle Eastern
- Hispanic
- Asian
- Polynesian
- Indigenous peoples

Increased risk due to economic, social or educational disadvantage, access to and uptake of care, lower achievement of treatment goals, lower screening rates, suboptimal early treatment of complications, diet and lifestyle factors, smoking, obesity, genetic factors and probably also developmental programming.
Latin American perspective

N=22,000

Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)

Asian perspective

Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND)


N=9,111
Epidemiology of CKD in the UKPDS

After 15 years of follow-up

52% ALB

28% eGFR < 60

Only 14% developed both

UKPDS 74
Epidemiology of CKD in diabetes

HOW MANY OF THESE ACTUALLY HAVE DIABETIC KIDNEY DISEASE?

How many have age-related decline, hypertensive or dyslipidemic nephropathy, obesity-related, glomerular atherosclerosis?

DOES IT MATTER?
Epidemiology of CKD in diabetes

Do you need retinopathy to have DKD?

Do you need albuminuria to have DKD?

Do you need histology to have DKD?
Take home messages

- Diabetes is increasing with epidemic proportions all over the world
- DKD is a common complication
- The consequences of DKD are grim
- We have to take action which is the scope of this controversy meeting
Thank you for your attention

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