Evaluating proteinuria in patients with diabetes and chronic kidney disease

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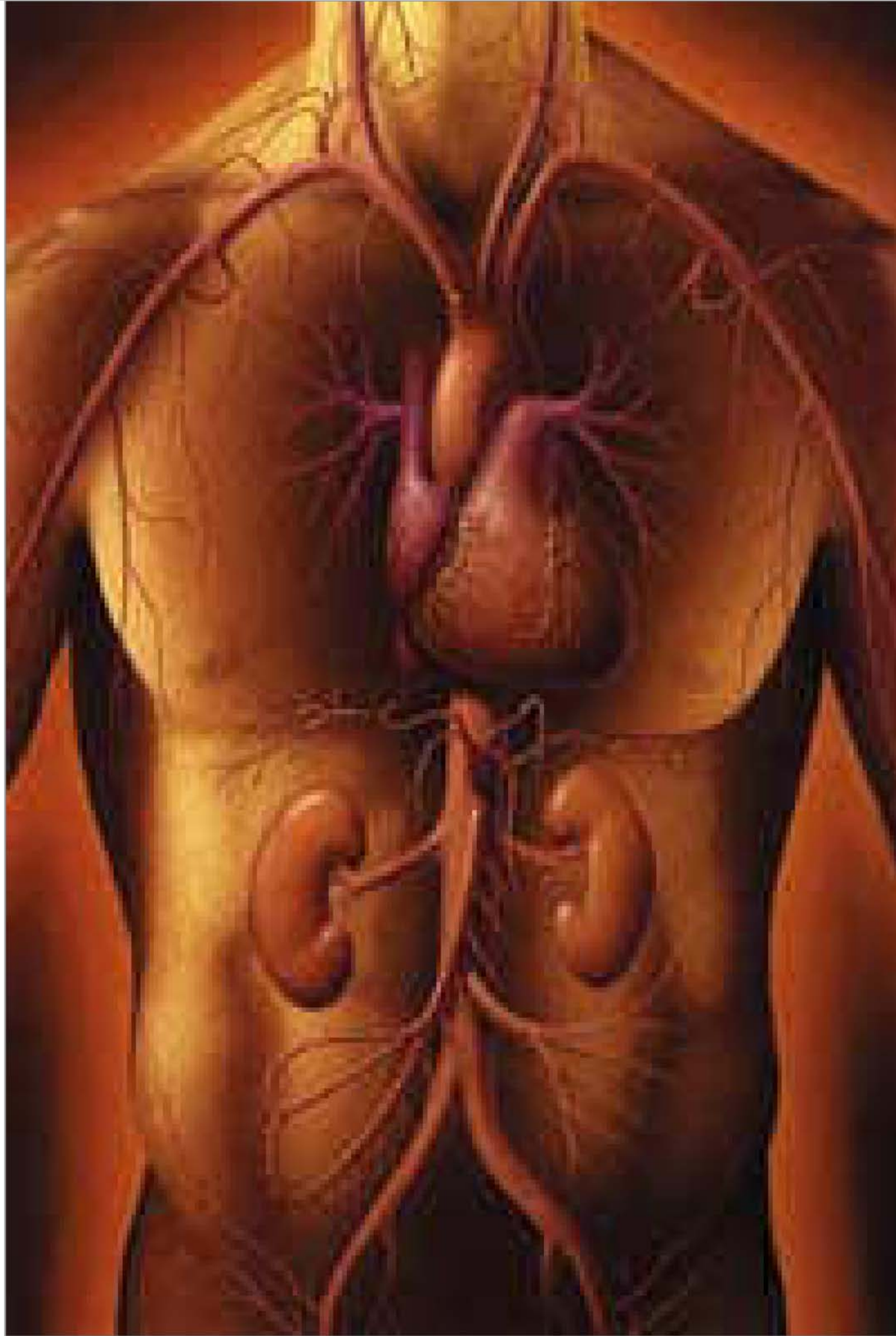


Objectives

- Review how to measure proteinuria in clinical practice including caveats for measurement
- Understand the prognostic significance of proteinuria
- How and when to treat proteinuria and targets for treatment
- Who should I refer?

Common clinical scenario, what would you advise?

62 year old woman, non-diabetic, BP 130/80 with an ACR of 7.8 – 15 mg/mmol, Cr 85, GFR 70, Urinalysis normal

- Does she have CKD?
- What would you tell her re significance?
- Would you prescribe any therapy?
- Would you refer her? To whom?

Chronic Kidney Disease is a growing problem

Stage	Description	GFR (ml/min/1.73 m²)	Prevalence 1 Extrapolated directly from US	Prevalence 2 Extrapolated US data, adjusted Cdn dialysis prevalence
1	Kidney Damage with Normal or ↑ GFR	>90	792,000	478,500
2	Kidney Damage with Mild ↓ GFR	60-89	720,000	435,000
3	Moderate ↓ GFR	30-59	1,032,000	***623,500***
4	Severe ↓ GFR	15-29	48,000	***29,000***
5	Kidney Failure	<15 or (or dialysis)	(24,000)	14,500

Over 50% of what is considered CKD is patients with normal GFR and microalbuminuria

Adapted from Am J Kidney Dis 2002; 39 (2, Suppl. 1): S17-S31 ; Stigant CMAJ 2003

Estimated % of patients with microalbuminuria (ACR 3-30mg/mmol)

- General population
  - Caucasian 5-10%
  - Other 15% +
- Hypertension 10-20%
- Diabetes 15-50%
- Acute MI 34%

Up to 40% of people over 70 have CKD using this definition

True or False?

There is virtually no role for 24-hour urine collections for the evaluation of proteinuria in primary care

True

How to measure proteinuria

- Dipstick tests – pick up 300mg albumin or an ACR of 30 or higher
- Urine ACR – test of choice
  - **Confirm ACR >3 with at least 2 more samples (need 2 of 3 positive)**
    - Remember, albuminuria has large day to day variation and is affected by BP control, glucose control, CHF, exercise, UTI
- 24 hr urine - UNNECESSARY in primary care

Urine ACR is the test of choice for measuring urine protein

	ACR (mg/mmol)	Dipstick	mg/day
Normal	<3	Negative	<30mg/d
Microalbuminuria	3-30	Negative, +1	30-300mg/d
Overt nephropathy	30-300	+2, +3	300-3000mg/d
Nephrotic range	>300	+4	>3000mg/d

Urine testing — don’t forget the urine microscopy!

- Urine microscopy
  - persistent WBC in absence of infection
  - persistent RBC
  - cellular casts (not hyaline)
  - protein (over 300mg/day)

Urine test abnormalities, even with normal eGFR values indicate abnormal kidney function and usually require referral

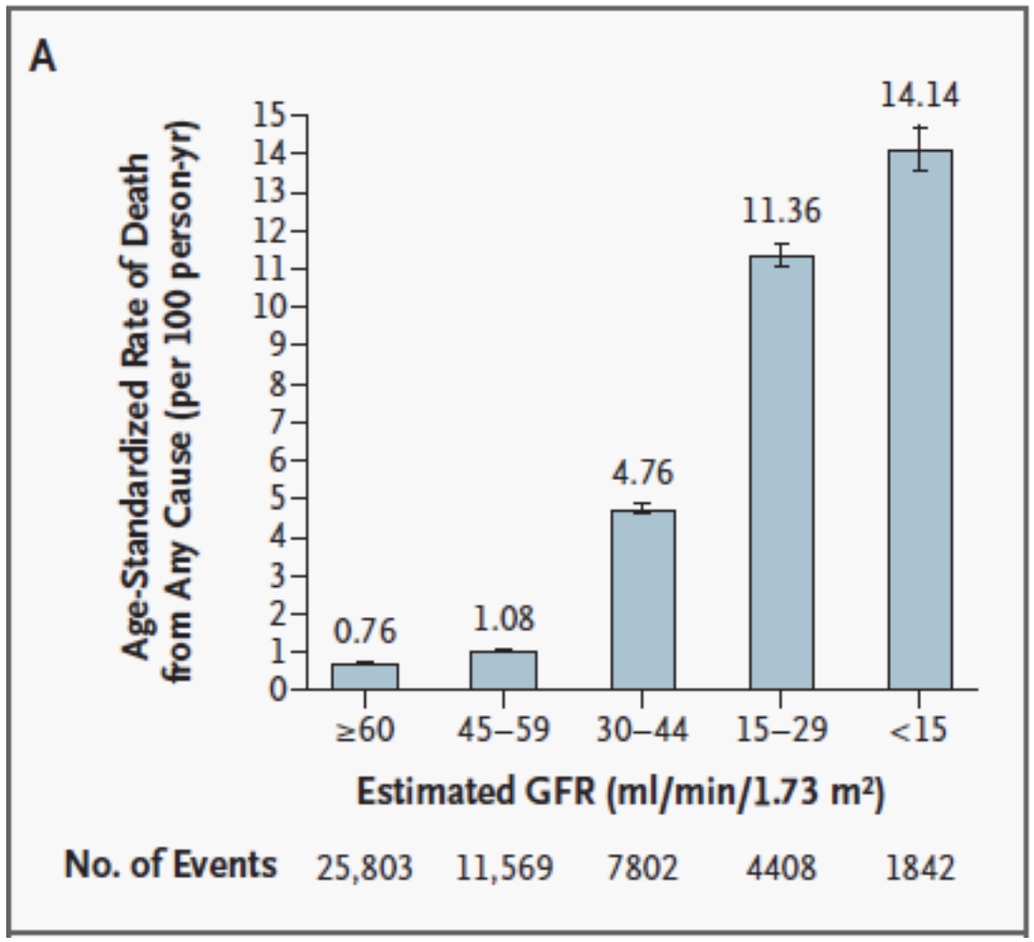
True or False?

A patient with a GFR of 45 mL/min and an ACR of 1.0 mg/mmol (normal) has a similar risk of adverse events (cardiovascular and renal) as a patient with a GFR of 70 mL/min and an ACR of 15 mg/mmol

True

What are the outcomes/implications of CKD diagnosis?

- associated with increased age standardized risk of
  - mortality
    - cardiovascular disease
- risk of Acute Kidney Injury (transient or sustained)
- in minority — risk of progressive CKD, associated complications, and need for RRT



Go AS et al. N Engl J Med 351:1296-1305(2004)

The Patient with early stage CKD is 5 to 10 times more likely to die from a cardiovascular event than progress to ESRD

Foley RN et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. J Am Soc Nephrol 2005; 16:489-95

What are the outcomes/implications of having proteinuria?

Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis

*Chronic Kidney Disease Prognosis Consortium**

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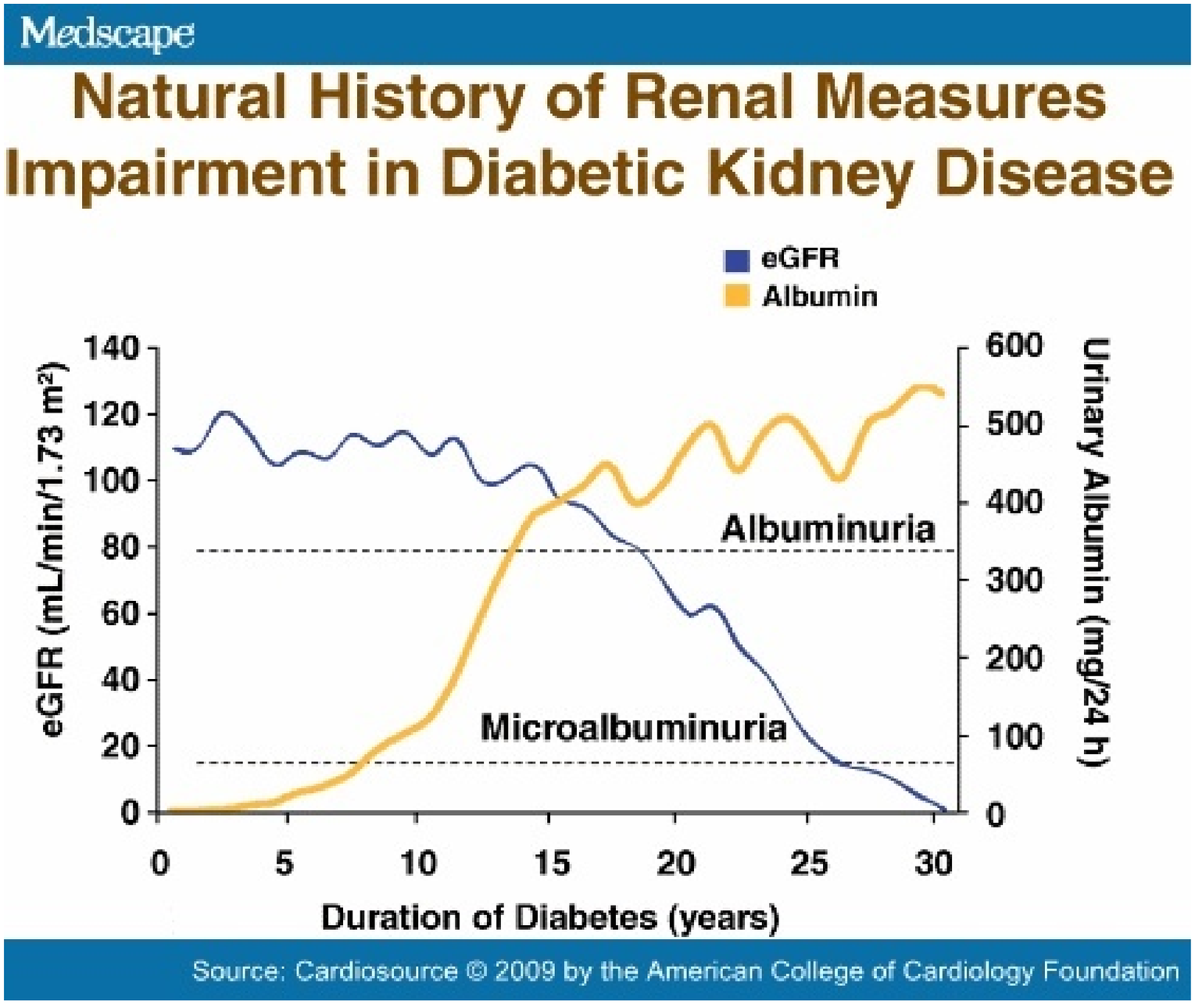
Prognostic significance of abnormal ACR

- Albuminuria was linearly related to events along its entire distribution indicating it may be even more informative than eGFR

- An ACR >3 is not normal and is associated with complications including higher risk of CKD, AKI, cardiovascular mortality, all cause mortality, even if GFR normal

- These effects are independent of GFR and independent of traditional cardiac risk factors

Albuminuria predates GFR decline in diabetic nephropathy by 10-20 years



How should you treat this patient?

Mr. Smith is a 70 yr old man with dyslipidemia and PVD. His BP is 130/80, eGFR 70mL/min. He is on ASA and statin therapy. An ACR is done and is 21 - 25 mg/mmol (normal <3) on 3 occasions. His U/A is normal.

You should:

(a)Continue to optimize his other CV risk factors, counsel to avoid precipitants of AKI (no NSAIDS) and follow ACR and renal function q 6-12mo

(b)Do the above plus start ACE-I or ARB as his ACR is significantly elevated

(c)Do (a) and (b) and refer to nephrology as ACR is significantly elevated

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When to treat with an ACE or ARB?

	ACR <3	ACR 3-30	ACR >30
DM, no HTN	No	Yes	Yes
DM, HTN	Yes	Yes	Yes
No DM, No HTN	No	**No**	Yes
No DM and HTN	No	Yes	Yes

Pharmacologic choices to treat proteinuria

- ACE-I or ARB – yes
- Combination of ACE or ARB - no
- Combination ACE or ARB and DRI – no

Antiproteinuric effect is enhanced by a low Na diet or a diuretic

Targets of therapy

- Reduce urine ACR to < 40 mg/mmol or as low as possible
- Blood pressure <130/80
- Stabilize creatinine/eGFR — < 1-2 mL/min loss per year
- Educate patients to
  - avoid nephrotoxins (dye, NSAIDS)
  - **if acute illness/ECFV contraction, etc... ⟶ hold ACEi, ARB, diuretic, metformin**
- Regular follow-up/monitoring

What to do with the ACR result? - Referral Decision Making by GFR and Albuminuria

	ACR < 3	**ACR 3.1 - 29**	**ACR >30**
GFR >60	Monitor	Monitor	Refer
GFR 45-59	Monitor	Monitor	Refer
GFR 30-44	Monitor	Refer	Refer
GFR <30	Refer	Refer	Refer

And in all patients with albuminuria – CV risk reduction, BP control, DM control, avoid precipitants of AKI

Common clinical scenario, what would you advise?

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Summary

- Proteinuria is common and associated with worse cardiovascular and renal outcomes
    - You hope your ACR is normal!
- Treat elevated ACR in patients with DM or HTN with ACE or ARB
    - The specific treatment of ACR 3-30 in patients without HTN or DM is less clear
    - But always treat CV risk factors
- Refer to nephrology if ACR is consistently above 30 mg/mmol

Questions?


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