Microalbuminuria: monitoring and management

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This series is aimed at helping the busy GP diagnose and manage patients with diabetes and its complications. How would you confirm that this patient has microalbuminuria, and what are the implications of this finding?

Figure 1. Diabetic nephropathy. Microalbuminuria is the earliest sign of diabetic nephropathy.

Case history

As part of the monitoring of diabetes, you check your patient, Lisa, for microalbuminuria. Her spot urine albumin level is 70 mg/L.

Lisa is 63 years old and has had moderately controlled type 2 diabetes for 12 years (HbA_{1c} 7 to 9%). She has hypertension that is being treated (current blood pressure is 130–145/80–90 mmHg), and her recently measured lipid profile is: total cholesterol 5.7 mmol/L, LDL cholesterol 4.0 mmol/L, triglyceride 1.8 mmol/L, HDL cholesterol 0.8 mmol/L. She is slightly overweight (height 154 cm, weight 61 kg) but walks briskly for 30 to 40 minutes every day. She has never smoked and has one to two drinks per week.

Lisa sees the ophthalmologist every six months and finished her second course of laser therapy for retinopathy a month ago. She is up to date with her immunisation schedule (yearly influenza vaccination and pneumococcal vaccination two years ago) and with her other health monitoring (Pap smears and mammograms).

Her medications include metformin (850 mg twice daily), gliclazide (80 mg twice daily) and felodipine (10 mg daily).

What should you consider?

Given Lisa's urine albumin result, consider the following:

- What further investigations are indicated?
- Assuming the abnormal value is confirmed, how should you interpret the results?
- If Lisa does have microalbuminuria, what are the implications?
- What interventions should you recommend?

Further investigations

Lisa's urine albumin result suggests that she has microalbuminuria (defined as an excretion of 20 to 200 mg/L of albumin in the urine); however, the spot sample can produce false-positive results. The major reason for a false-positive test is use of an inappropriate specimen. Urinary albumin excretion is affected by exercise, posture and food intake. The recommended specimen is of urine that has been formed overnight. Thus the simplest specimen to test is the first voided morning urine since the collection process is easy to explain and for patients to do. When clinical proteinuria has developed, a 24-hour urine specimen for proteinuria is recommended.

The albumin to creatinine ratio (ACR) should be requested since the inclusion of creatinine as the denominator allows for any concentration or dilution of the urine (since creatinine excretion is assumed to be constant and determined by muscle mass). Since generally women have a lower proportion of muscle than men, their total creatinine excretion is less and a different normal range for ACR applies, as follows:

- men <2.5 mg/mmol
- women <3.5 mg/mmol.

Some specialists recommend timed overnight urine collection with patients collecting the urine formed overnight. Patients record the time they void into the toilet at bedtime and the time they awake in the morning, and collect any urine

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passed through the night and the first voided morning specimen. In this case, the albumin excretion rate should be requested, which is independent of urine concentration. No adjustment is needed for females; the normal range for all adults is <20 μg/minute.

Other causes of false-positive results include the patient having a fever, transient hyperglycaemia, urinary tract infection or urinary obstruction, all of which should be excluded.

If microalbuminuria is found, the abnormality should be confirmed on a second specimen since there is considerable intra-individual variability. If the second specimen is negative, a third specimen will confirm whether the overall test is positive or negative.

Generally, microalbuminuria should be investigated at least as often as retinopathy – i.e. at least two yearly. The Service Incentive for Payment schedule requires checking for microalbuminuria at least annually.

Interpreting the results

Microalbuminuria indicates renal damage and the likelihood of progression to macroalbuminuria and renal failure.

Microalbuminuria is likely to be diabetes-related if Lisa's retinopathy has been of the proliferative variety (which is probably the case since her retinopathy has been severe enough to need laser therapy). However, there are other causes of microalbuminuria that may need to be considered (e.g. IgA nephropathy), and consultation with a renal physician or endocrinologist might be useful.

Implications of having microalbuminuria

The implications of having microalbuminuria fall into several categories.

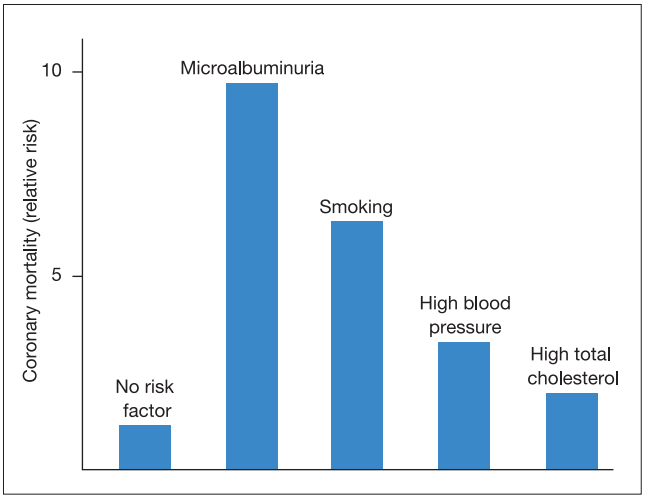

Figure 2. Cardiovascular risk factors.

Renal damage

As noted above, microalbuminuria indicates significant renal damage despite being the earliest clinically detectable abnormality. A renal biopsy in a patient with microalbuminuria will indicate considerable glomerular damage.

The development of microalbuminuria is less common than the development of detectable diabetic nephropathy (Figure 1), but when microalbuminuria occurs, this indicates that the patient is at risk of progressive renal damage and eventual renal failure. Intervention (see below) and close monitoring are indicated.

Cardiovascular events

Microalbuminuria is an indicator of a high risk of cardiovascular events. Indeed, microalbuminuria is a better predictor of future cardiovascular events than many of the other, better recognised, risk factors (Figure 2).

Other microvascular damage

Lisa has significant retinal and renal microvascular damage and other organs are likely to be similarly damaged. She is very likely to have the other characteristic microvascular complication, neuropathy, which may include autonomic neuropathy. It will be worthwhile checking Lisa for symptoms and signs of neuropathy (tingling, numbness, burning, loss of sensation, reflexes and muscle bulk and postural changes in blood pressure).

Recommended interventions

Renal interventions

Meticulous control of blood pressure (keeping it at least <130/85 mmHg) and glycaemia (HbA_{1c} <7%) will slow the progression of renal damage. An angiotensin receptor antagonist (ARA) or ACE inhibitor would be a better hypotensive agent than a calcium channel blocker. Calcium channel blockers dilate both the afferent and efferent arterioles in the glomeruli, whereas ARAs and ACE inhibitors preferentially dilate the efferent arterioles. Thus, ACE inhibitors and ARAs reduce glomerular pressure, glomerular filtration and albumin leakage to a greater extent than do calcium antagonists.

Cardiovascular interventions

Given Lisa's high risk of future cardiovascular events, it would be worth checking that she is on target controlling the other cardiovascular risk factors.

- **Lipids.** The targets are: total cholesterol <4 mmol/L, LDL-cholesterol <2.5 mmol/L, triglyceride <2 mmol/L, HDL-cholesterol >1 mmol/L. Lisa is eligible for a PBS subsidy for statin therapy given her low HDL-cholesterol (<1.0 mmol/L) and high total cholesterol (>5.5 mmol/L). The dose of statin could be adjusted to achieve the desired

level of control. An electrocardiogram would provide a baseline to help interpret any future ECGs that might be obtained because of an atypical presentation of myocardial infarction.

- **Blood pressure.** The target is: <125/75 mmHg (which is lower than the usual target of <130/85 mmHg because of Lisa's microalbuminuria). Blood pressure control will not only reduce the progression of renal damage, but will also reduce the risk of cardiovascular events. If Lisa needed an additional hypotensive agent the next step would be to consider a low dose thiazide diuretic or a beta blocker. Her high cardiovascular risk might prompt the use of a beta blocker.
- **Other cardiovascular interventions.** The use of prophylactic aspirin at a dosage of 75 to 150 mg/day will reduce Lisa's risk of a future cardiovascular event by approximately 25%.
- **Effectiveness of interventions.** The STENO 2 Study showed that active pursuit of targets for diabetes care in patients with microalbuminuria halved the risk of progression to diabetic nephropathy and of cardiovascular events.

Other interventions

If Lisa does have significant peripheral and/or autonomic neuropathy, specific measures could be considered. For example, a foot care education program might be indicated if she had significant peripheral neuropathy (especially if she had one of the other major risk factors: vascular disease, abnormal foot structure, or poor foot care or footwear). If she had autonomic neuropathy this might complicate management of her hypertension and/or make it more likely that she had gastroparesis slowing delivery of mealtime carbohydrate and putting her at greater risks of blood glucose swings. If either of these were a problem an endocrinologist might provide you with some advice.

Some doctors would check Lisa's *Helicobacter* antibody titres and consider eradication therapy if positive to reduce the future risk of gastrointestinal haemorrhage.

Summary

Microalbuminuria indicates a significant change in the risk of renal damage and cardiovascular events. Checking for microalbuminuria is an important part of the cycle of diabetes care. Microalbuminuria should be confirmed on a second appropriate sample (e.g. first voided urine albumin to creatinine ratio). It should trigger review and active management of glycaemia, blood pressure and cardiovascular risk. MT

Further reading

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