TIME TO RETIRE MICROALBUMIN
“the affirmative case”
AACB 53rd Annual Scientific Conference
September 2015

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TIME TO RETIRE MICROALBUMIN
“the affirmative case”
It is time for microalbuminuria to step down!

A paradigm of Diabetic Kidney Disease based solely on microalbuminuria needs to be questioned!

Microalbuminuria X
- Microalbuminuria = A2
- High Variability
- Low Specificity
- Spontaneous Regression
- $\Delta$ AER $\neq \Delta$ GFR

Microalbuminuria √
- Good prognostic marker
What is microalbuminuria?
Microalbuminuria refers to a range of urinary albumin excretion

<table>
<thead>
<tr>
<th>Classification</th>
<th>AER (μg/min)</th>
<th>ACR (mg/mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Females</td>
</tr>
<tr>
<td>Normoalbuminuria</td>
<td>&lt;20</td>
<td>&lt;3.5</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>20–200</td>
<td>3.5–35</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>&gt;200</td>
<td>&gt;35</td>
</tr>
</tbody>
</table>

ACR, albumin:creatinine ratio; AER, albumin excretion rate.
Microalbuminuria DOES NOT refer to fragments of urinary albumin

Microalbuminuria as a prognostic marker
Higher levels of urinary albumin excretion within the normal range predict faster decline in glomerular filtration rate in diabetic patients

Babazono T et al. Diabetes Care 2009;32:1518-1520
Measurable Urinary Albumin Predicts Cardiovascular Risk even among Normoalbuminuric Patients with Type 2 Diabetes

Why has microalbuminuria reigned so long as the preeminent marker of diabetic kidney disease?
An Immunoassay method for urinary albumin at low concentrations
H. Keen & C. Chlouverakis

THE LANCET
1963, 2(7314): 913-914
### Summary of early studies demonstrating that microalbuminuria predicts diabetic nephropathy* (DN) in type 1 diabetes

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>63</td>
<td>23</td>
<td>43</td>
<td>71</td>
</tr>
<tr>
<td>Age (years)</td>
<td>40</td>
<td>32</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Follow-up (years)</td>
<td>14</td>
<td>6</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Proposed discrimination rate (µg/min)</td>
<td>30</td>
<td>30</td>
<td>15</td>
<td>70</td>
</tr>
<tr>
<td>Development of DN below discrimination value</td>
<td>2/55</td>
<td>2/15</td>
<td>0/29</td>
<td>3/64</td>
</tr>
</tbody>
</table>

*Definition of DN included: protein excretion > 500 mg/24 h, AER > 150 µg/min, AER > 200 µg/min or albustix positive depending on the study

“According to evaluations and discussions among the present authors, the following criteria may be used for the classification and renal involvement in the insulin-dependent patient only, both in clinical work and in research projects. 

Microalbuminuria is present when urinary albumin excretion rate is greater than 20 µg/min less than or equal to 200 µg/min.”
Evolution of Diabetic CKD

- **Normoalbuminuria** (AER < 20 μg/min)
- **Microalbuminuria** (AER 20-200 μg/min)
- **Macroalbuminuria** (AER > 200 μg/min)

Incipient Nephropathy

Overt Nephropathy

**GFR**

100 (ml/min)

Log AER

Evolution over time:
- 10 years
- 15 years
- 20 years

**GFR**

Incipient Nephropathy

Overt Nephropathy
Microalbuminuria-variability
High intra-individual day-to-day variation (CV) of urinary albumin excretion (40-50%)
Seasonal variations of urinary albumin creatinine ratio in Japanese subjects with type 2 diabetes and early nephropathy?

Wada et al. Diabetic Medicine 2012,29:506-508
Microalbuminuria-specificity
The disease spectrum of microalbuminuria and its role as an indicator of inflammation

Microalbuminuria as a Risk Predictor in Diabetes: The Continuing Saga
Bakris GL & Molitch M Diabetes Care 2014,37:867-875
The disease spectrum of albuminuria and its associated CV risk and kidney disease presence

Microalbuminuria as a Risk Predictor in Diabetes: The Continuing Saga
Bakris GL & Molitch M Diabetes Care 2014,37:867-875
Does microalbuminuria represent an irreversible stage of Diabetic Kidney Disease?
## Microalbuminuria: Rates of remission/regression vs progression

<table>
<thead>
<tr>
<th>Type 1 diabetes</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>386 patients with micro</td>
<td>216 patients with micro</td>
</tr>
<tr>
<td>6 years</td>
<td>6 years</td>
</tr>
<tr>
<td>220 patients studied</td>
<td>113 patients studied</td>
</tr>
<tr>
<td>88/220 (40%)</td>
<td>23/113 (20%)</td>
</tr>
<tr>
<td>99/220 (45%)</td>
<td>66/113 (58%)</td>
</tr>
<tr>
<td>33/220 (15%)</td>
<td>21/113 (19%)</td>
</tr>
<tr>
<td><strong>Normo</strong></td>
<td><strong>Normo</strong></td>
</tr>
<tr>
<td><strong>Micro</strong></td>
<td><strong>Micro</strong></td>
</tr>
<tr>
<td><strong>Macro</strong></td>
<td><strong>Macro</strong></td>
</tr>
</tbody>
</table>

Factors associated with regression:
- Microalbuminuria of short duration, low A1c/SBP & lipid levels
- Microalbuminuria of short duration, RAS blockers, low A1c/SBP
Does kidney structure and function correlate with microalbuminuria?
Prevalence of low glomerular filtration rate (GFR < 60 ml/min/1.73m²) and normoalbuminuria

GFR < 60 ml/min/1.73m²)

'Progressive diabetic nephropathy. How useful is microalbuminuria?: contra’
MacIsaac et al RJ Kidney Int 2014, 86:50
Biopsy findings in microalbuminuric patients with type 2 diabetes and preserved renal function

Is microalbuminuria a valid surrogate end point in clinical trials?
‘Progressive diabetic nephropathy. How useful is microalbuminuria?: contra’
MacIsaac RJ et al Kidney Int 2014, 86:50
Summary
IS IT TIME TO RETIRE MICROALBUMINURIA?

Vote: YES

Problems with urinary albumin within the microalbuminuric range

- Microalbuminuria = A2
- High Variability
- Low Specificity
- Spontaneous Regression
- AER ≠ GFR
IS IT TIME TO RETIRE MICROALBUMINURIA?

Retire the name-  

Retire micro-albuminuria from its preeminent role in CKD in diabetes  

VOTE YES
IS IT TIME TO RETIRE MICROALBUMINURIA?
IS IT TIME TO RETIRE MICROALBUMINURIA?

YES
Progression versus remission/regression of microalbuminuria

‘Progressive diabetic nephropathy. How useful is microalbuminuria?: contra’
MacIsaac RJ et al. Kidney Int 2014, 86:50