

Managing vascular risk in hypertension with a focus on microalbuminuria: attitude and practices

Wu A Y T, Low L P

ABSTRACT

Introduction: Elevated blood pressure is a principal risk factor for cardiovascular and renal diseases. Early detection and adequate treatment of hypertension are essential components in the primary prevention of these end-stage events. Microalbuminuria is recognised as an early marker of renal disease and increased cardiovascular risk. Screening alerts physicians to implement timely intervention strategies to delay disease progression and minimise consequent complications. Although the value and significance of microalbuminuria screening has been widely documented, its use is still suboptimal.

Methods: Survey forms were sent to randomly-selected general practitioners in Singapore to capture their self-reported attitudes and practices regarding microalbuminuria screening in the management of hypertension.

Results: Results from this survey revealed that microalbuminuria screening was practised by 88 percent of the physicians surveyed; however, only 56 percent of hypertensive patients without risk factors were screened. Quantitative analysis of urine samples was the preferred screening method of 90 percent of the physicians surveyed.

Conclusion: A concerted effort should be made to address the lack of public awareness on the importance of screening for microalbuminuria. Continuing medical education should also emphasise the usefulness of surrogate markers in the therapeutic prevention of end-organ damage in hypertensive patients. There is also a need to form a consensus guideline on microalbuminuria screening, to aid in the standardisation of practice.

Keywords: cardiovascular risk factor, health screening, hypertension, microalbuminuria, renal disease

Singapore Med J 2009;50(10):976-981

INTRODUCTION

Worldwide, hypertension is estimated to cause 7.1 million premature deaths.⁽¹⁾ Treatment of hypertension has been associated with a 40% reduction in the risk of stroke and 15% reduction in the risk of myocardial infarction.⁽²⁾ Early detection and adequate treatment of hypertension are thus essential components in the primary prevention of these end-stage events.

There has recently been a plethora of information on microalbuminuria.⁽³⁾ Microalbuminuria provides a more sensitive marker of early nephropathy development and acts as an indicator of increased cardiovascular risk.⁽⁴⁾ Furthermore, the association between elevated blood pressure and diabetic complication is well established,⁽⁵⁾ and microalbuminuria has also been identified as a marker for the development of hypertension.⁽⁶⁾ Therefore, early screening for microalbuminuria allows risk reduction measures to be implemented earlier, for possibly more effective prevention of progressive organ damage. The clinical value of screening for microalbuminuria has been acknowledged in the 2007 Guidelines for the Management of Arterial Hypertension by the European Society of Hypertension (ESH) and European Society of Cardiology (ESC). Both societies recommended microalbuminuria screening as an essential component in the assessment of organ damage because of its easy detection and low cost.⁽⁷⁾ It was also advised that screening for microalbuminuria be considered as a routine procedure for all hypertensive patients, including subjects with metabolic syndrome, even in the presence of only high-normal blood pressure.⁽⁷⁾

The paucity of information on the incidence of microalbuminuria in hypertensive patients with type 2 diabetes mellitus in Singapore prompted a local prevalence study. Albuminuria was detected in 72% of hypertensive patients with type 2 diabetes mellitus in Singapore (48.5% with microalbuminuria and 23.5%

Wu Nephrology and Medical Clinic, Mount Elizabeth Medical Centre, 3 Mount Elizabeth, #16-12, Singapore 228510

Wu AYT, MBBS, FRACP, FAMS Consultant

Low Cardiology Clinic, Mount Elizabeth Medical Centre, 3 Mount Elizabeth, #11-05/06, Singapore 228510

Low LP, MBBS, FRACP, FACC Consultant

Correspondence to: Dr Akira Y T Wu
Tel: (65) 6732 1819
Fax: (65) 6734 8266
Email: akirawu@pacific.net.sg

Table I. Average number of patients seen each week with hypertension, diabetes mellitus or both.

Base	No. (%) of patients seen by general practitioners in:			
	Total (n = 735)	Private sector (n = 639)	Public sector (n = 17)	Medical groups (n = 79)
Average no. of patients	189	190	173	184
Hypertension	28 (14.8)	28 (14.7)	22 (12.7)	25 (13.6)
Diabetes mellitus	22 (11.6)	22 (11.6)	22 (12.7)	22 (12.0)
Both conditions	19 (10.1)	18 (9.5)	20 (11.6)	20 (10.9)

with macroalbuminuria).⁽⁸⁾ Such a high prevalence indicates a need for a more aggressive management of glycaemia and blood pressure in hypertensive patients with diabetes mellitus. It also suggests that screening for microalbuminuria has not been undertaken as frequently as would be desired. The objective of this present study was to understand the attitude and the practices of physicians in Singapore regarding the management of vascular risk in hypertension with special emphasis on microalbuminuria.

METHODS

This paper reports the results of a survey on the management of hypertension among general practitioners in Singapore. Survey respondents were randomly selected from various areas across Singapore. Screening questions were administered prior to recruitment, to ensure that respondents met the inclusion criteria (i.e. physicians in local practice with a minimum of three years' practice experience to date and a minimum of 20 hypertension patients attended to per month). Locums were excluded from this survey, which was conducted from October 2006 to February 2007.

The semi-structured questionnaire was provided by GFK Healthcare Asia (Singapore) and approved by an expert committee which included nephrologists, cardiologists, endocrinologists and general practitioners. The duration of the main interview was between 15 and 20 minutes, and a token was provided to the respondent after the completion of the interview. A combination of face-to-face interviews, telephone interviews and faxes was used as suited to the respondents' convenience. Specifically, to determine the screening methods of microalbuminuria, the doctors were asked to choose from the following answer options: (1) Use urine dip-sticks in my clinic; (2) Perform a quantitative test in my clinic; (3) Send urine samples for laboratory analysis; and (4) Others.

RESULTS

1,000 general practitioners were selected, and the screening questions were administered. All 735 doctors who met the inclusion criteria, returned the completed questionnaire

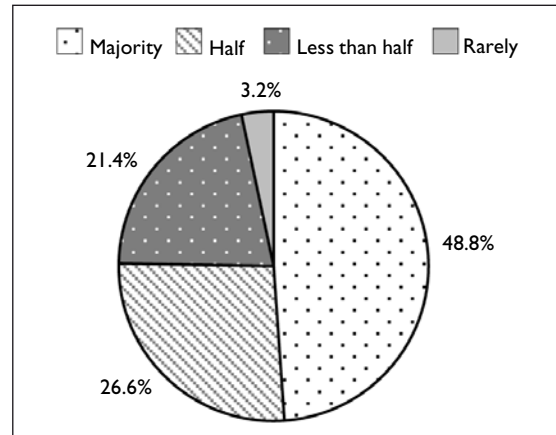


Fig. 1 Pie chart shows the proportion of doctors who screen for microalbuminuria in their hypertensive patient population.

(100% response rate). Out of the 735 doctors polled in this survey, 639 (86.9%) were from the private sector, 17 (2.3%) were from the public sector and 79 (10.8%) were from private medical groups. The questionnaire sought to profile the demographics of patients who were treated for hypertension and the frequency of testing for microalbuminuria in Singapore. An average of 189 patients was seen weekly by the participating physicians. The mean proportion of patients who were hypertensive, diabetic or suffering from both disease conditions were 14.8% (n = 28), 11.6% (n = 22) and 10.1% (n = 19), respectively (Table I).

Identification of high-risk hypertensive patients was through abnormal ankle-brachial index measurement (21.5%; n = 158), fundoscopy (32.8%; n = 241), electrocardiography (47.9%; n = 352) or a history of concomitant disease (82.6%; n = 607). Fundoscopy was performed more frequently by general practitioners in the public sector (82.4%; n = 14) than those in the private sector (32.1%; n = 205) or the medical groups (27.8%; n = 22). In identifying high-risk hypertensive patients, public sector general practitioners used electrocardiography more frequently (64.7%; n = 11) than those in the private sector or medical groups (58.2%; n = 46). This may be attributed to the availability of such screening facilities in the public healthcare institutions compared to the private sector and medical groups.

Table II. Profile of patients screened for microalbuminuria.

Patient profile	No. (%) of patients seen by general practitioners in:			
	Total (n = 735)	Private sector (n = 639)	Public sector (n = 17)	Medical groups (n = 79)
Hypertension without risk factors*	366 (49.8)	323 (50.5)	9 (52.9)	34 (43.0)
Hypertension with diabetes mellitus	505 (68.7)	443 (69.3)	11 (64.7)	51 (64.6)
Hypertension with other risk factors	461 (62.7)	400 (62.6)	11 (64.7)	50 (63.3)
Diabetes mellitus	542 (73.7)	477 (74.6)	11 (64.7)	54 (68.4)
Combination of one of the above conditions	62 (8.4)	55 (8.6)	0	7 (8.9)
Combination of two of the above conditions	117 (15.9)	106 (16.6)	0	11 (13.9)
Combination of three of the above conditions	28 (3.8)	2 (0.3)	2 (11.8)	24 (30.4)
Combination of four of the above conditions	273 (37.1)	242 (37.9)	9 (52.9)	22 (27.8)

* non-diabetic cardiovascular risk factors include hypertension, high low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol, tobacco use, physical inactivity, menopause, psychological stress and family history of cardiovascular disease.

Table III. Recommended first-line therapies for management of microalbuminuria among general practitioners.

Recommended first-line therapy	No. (%) of patients seen by general practitioners in:			
	Total (n = 735)	Private sector (n = 639)	Public sector (n = 17)	Medical groups (n = 79)
No advice	197 (26.8)	174 (27.2)	6 (35.3)	17 (21.5)
Lifestyle modifications	359 (48.8)	314 (49.1)	7 (41.2)	38 (48.1)
Aggressive global cardiovascular risk reduction	205 (27.9)	173 (27.1)	8 (47.1)	24 (30.4)
Pharmacological intervention with ACEI or ARB	332 (45.1)	293 (45.9)	6 (35.3)	33 (41.8)
Others	11 (1.5)	9 (1.4)	1 (5.9)	1 (1.3)

ACEI: angiotensin converting enzyme inhibitors; ARB: angiotensin II receptor blockers.

A large proportion of the general practitioners (88.8%; n = 653) screened their hypertensive patients for microalbuminuria, while 48.7% of the doctors implemented screening in the majority (> 50%) of their patients (Fig. 1). The main reason cited for not screening for microalbuminuria in hypertensive patients was the lack of conviction about the value of screening for this abnormality. Other reasons cited included the patient's unwillingness to be screened, the cost of screening and the lack of resources.

General practitioners usually selected patients for microalbuminuria screening if they were diabetic, hypertensive without risk factors, hypertensive with diabetes mellitus, hypertensive with other high risk factors or a combination of the listed factors (Table II). Only 56.0% of hypertensives without risk factors were screened. To ascertain their motivation behind a change towards inclusion of microalbuminuria screening, the participating physicians were requested to list the factors that influenced their decisions. Among the responses noted were: (1) cost-effectiveness of including microalbuminuria screening; (2) awareness of the emerging clinical evidence pertaining to the value of such screening; (3) patient's compliance with such screening; (4) automatic inclusion of microalbuminuria

screening in the general check-up package; (5) provision of a government subsidy; (6) availability of resources; and (7) recommendations of local guidelines.

Two methods were adopted to screen for microalbuminuria: the use of urine dip-sticks (semi-quantitative) and quantitative analysis of urine samples, either available in their own practice or sent to an external vendor. Quantitative analysis of urine samples was the preferred screening method among participating physicians (90.8%; n = 593). Doctors also expressed satisfaction with the current microalbuminuria screening methodologies employed. A small proportion indicated that the current microalbuminuria screening was a significant additional cost deterrent factor to patients.

Lifestyle modifications were the most frequently recommended type of first-line therapy for patients with increased microalbuminuria. This was closely followed by pharmacological interventions, specifically angiotensin II receptor blockers (ARBs) or angiotensin converting enzyme inhibitors (ACEIs). A smaller proportion (31.4% of all participants) advised aggressive global cardiovascular risk reduction by targeting all identifiable risk factors, but this approach was most frequently adopted by public sector practitioners (57.1%) (Table III).

DISCUSSION

An assessment of cardiovascular risk is recommended in individuals with elevated blood pressure.⁽⁹⁾ The Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure⁽¹⁰⁾ recommends fulfilling three objectives when evaluating patients with documented hypertension: (1) lifestyle assessment for identification of other cardiovascular risk factors or concomitant disorders that may affect prognosis and guide treatment; (2) identification of the causes of high blood pressure; and (3) an audit of the presence or absence of target organ damage and cardiovascular disease. Much of this information can be acquired via a thorough review of the patient's medical history and a physical examination. Routine laboratory tests and other diagnostic procedures are recommended before the initiation of therapy to ascertain the secondary causes of hypertension or to obtain results that may significantly influence the management of the patient.⁽¹¹⁾ One such examination is microalbuminuria screening.

Patients with diabetes mellitus often have elevated blood pressure which increases their risk of cardiovascular complications,⁽¹²⁾ and contributes to a 20%–40% lifetime risk for development of nephropathy.⁽¹²⁾ Microalbuminuria is the earliest easily-detectable marker of renal damage. Although more than 80% of general practitioners screen for microalbuminuria in their hypertensive patients, this survey also revealed that only half of the hypertensive patients without risk factors were screened. The ESH-ESC 2007 guidelines for the management of arterial hypertension recommend screening for microalbuminuria in all hypertensive patients as an important indicator of the presence of organ damage.^(7,13,14) There is therefore a need for improvement in screening for microalbuminuria in the assessment of all hypertensive patients.

Microalbuminuria screening is a simple, inexpensive and relatively efficient technique. Presently, three methods are commonly employed for microalbuminuria screening: (1) measurement of the albumin-to-creatinine ratio in a random spot collection; (2) 24-hour collection with creatinine, allowing the simultaneous measurement of creatinine clearance; and (3) timed collection.⁽¹⁵⁾ Although the measurement of albumin excretion rate in a timed urine sample is the gold standard for the definition of microalbuminuria, it is not a practical procedure.⁽¹⁶⁾ The measurement of albumin-to-creatinine ratio in a random spot collection is generally preferred because of its simplicity and accuracy.⁽¹⁵⁾ Screening with sensitive semi-quantitative urine dip-sticks, specifically designed with detection limits for identification of microalbuminuria, affords an alternative.⁽¹⁵⁾ In North America, more than

nine in ten doctors employ this screening technique. Quantitative assay is another viable option which has been used widely,⁽¹⁷⁾ although they have been utilised less frequently by general practitioners. This is different from the findings of this study, where most local doctors (90.8%) preferred the use of quantitative assays.

Upon diagnosis of hypertension with microalbuminuria, the most popular responses were to advise the patient on lifestyle modifications and to recommend pharmacological interventions. This conforms to the American Diabetes Association guidelines on the advantages of treatment with ARBs or ACEIs, to delay the development of diabetic nephropathy and for the reduction of albuminuria.⁽¹⁸⁾ The 2007 ESH-ESC guidelines reinforce the advisability of early pharmacotherapy intervention⁽⁷⁾ by recommending that the presence of microalbuminuria should prompt the use of antihypertensive drug treatment even when the initial blood pressure is within the high-normal range, as well as the preferred use of renin-angiotensin system blockers which have a pronounced antiproteinuric effect.

Overall, the survey revealed that doctors in the public sector were more active in screening high-risk, hypertensive patients for increased cardiovascular and renal risks, and in adopting a global cardiovascular risk reduction strategy. However, in terms of implementing therapy, doctors in the private sector were more likely to initiate pharmacotherapy. The reasons for these differences in practice trends are unclear and require further clarification. A comparison with the prescription habits from a microalbuminuria prevalence study conducted in 2006⁽⁸⁾ suggests that there has only been a slight improvement in the prescribing habits for antihypertensive drug therapy in patients with microalbuminuria (ACEIs and ARBs were prescribed in 34% and 23% of patients, respectively, compared to 50.8% prescription of ARBs or ACEIs, observed in the present study). One limitation of this survey was the small sample size of participating doctors from the public sector ($n = 17$), resulting in a sample bias towards doctors from the private sector ($n = 639$), which comprised 86.9% of the total sample. Hence, the results of the survey may not accurately reflect the clinical and drug prescription practices of the general practitioner community as a whole.

In essence, despite the desirable characteristics of the available screening tests and the existence of authoritative clinical recommendations, there remains a significant gap in screening for microalbuminuria in patients with diabetes mellitus. According to the Singapore National Health Survey 1998,⁽¹⁹⁾ a significant increase in the prevalence rates of hypertension among Singaporeans

aged 30–69 years was observed (i.e. from 22.5% in 1992 to 26.6% in 1998).^(19,20) This suggests the need for earlier intervention strategies to combat the rise in prevalence. Published reports evaluating microalbuminuria and macroalbuminuria screening have generally reported suboptimal rates.^(21,22) This is probably attributed mainly to patients being unaware of the need for microalbuminuria screening and physicians not uniformly well-informed about the value of screening and the available techniques.⁽²³⁾ This warrants a call for action to address these inadequacies in physician and patient education. At present, there are also no existing standardised testing methods. This may be an additional barrier to implementing the recommendations for microalbuminuria screening.

To achieve the goal of optimal antihypertensive therapy, evidence from studies on the value of such screening will be essential. A concerted effort should also be made to address the gap in public awareness. Formulation of consensus guidelines for microalbuminuria screening to aid in the standardisation of practice, will significantly promote the use of this effective and simple screening test. Recommendation should be made to include routine screening of microalbuminuria in all hypertensive patients, including primary hypertension. The detection of microalbuminuria should alert a doctor to optimise control of all cardiovascular risk factors in a patient. Microalbuminuria may also direct the doctor to exclude an underlying renal disease. Doctors' awareness of the clinical importance of microalbuminuria in hypertensive patients may be enhanced by incorporating the test in routine general health screening, by lowering the cost of the test and by continuous education to emphasise the usefulness of surrogate markers in the therapeutic prevention of end-organ damage.

ACKNOWLEDGEMENTS

This work was made possible through the research support and editorial assistance provided by Sanofi-aventis. We would like to take this opportunity to thank the following for their contributions: Titus Lau WL (Department of Medicine, National University Hospital, Singapore); Lee CH (Lee Chung Horn Diabetes and Endocrinology, Gleneagles Medical Centre, Singapore); Lim SC (Diabetes Centre, Alexandra Hospital, Singapore); Kevin Tan EK (Kevin Tan Clinic for Diabetes, Thyroid and Hormones Pte Ltd, Mount Elizabeth Medical Centre, Singapore); Tan HH (Singapore Polyclinics [HQ], Health Promotion Board Building, Singapore); Chee TS (Chee Heart Specialists Clinic Pte Ltd, East Shore Medical Centre, Singapore); Ang PK (P K Ang Family Clinic &

Surgery, Singapore); and Tan YT (Tan Medical Clinic Pte Ltd, Singapore).

REFERENCES

1. World Health Organization. The World Health Report 2002: Reducing risks, promoting healthy life. Geneva: World Health Organization, 2002. Available at: www.who.int/whr/2002/Overview_E.pdf. Accessed August 2007.
2. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease. Part 2. Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990; 335:827-38.
3. Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. *Am J Hypertens* 2004; 17:986-93.
4. Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kidney Dis* 1999; 33:1004-10.
5. Mogensen CE. Microalbuminuria and hypertension with focus on type 1 and type 2 diabetes. *J Intern Med* 2003; 254:45-66.
6. Knudsen ST, Andersen NH & Mogensen CE. Ambulatory pulse pressure and progression of albuminuria in type 2 diabetes: evidence provided, new questions emerge. *Hypertension* 2006; 48:207-8.
7. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2007; 25:1105-87.
8. Wu AY, Tan CB, Eng PH, et al. Microalbuminuria prevalence study in hypertensive patients with type 2 diabetes mellitus in Singapore. *Singapore Med J* 2006; 47:315-20.
9. National Institute for Health and Clinical Excellence. Hypertension: management of hypertension in adults in primary care. 2006. NICE clinical guidelines CG34. Available at: www.nice.org.uk/CG034. Accessed August 2007.
10. National Institutes of Health & National Heart Lung and Blood Institute. The Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. 2004. Available at: www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf. Accessed August 2007.
11. Ministry of Health Singapore. MOH Clinical Practice Guidelines 2/2005. Hypertension. 2005. Available at www.moh.gov.sg/mohcorp/uploadedFiles/Publications/Guidelines/Clinical_Practice_Guidelines/HPT-Booklet.pdf. Accessed August 2007.
12. American Diabetes Association. Standards of medical care in diabetes--2007. *Diabetes Care* 2007; 30 Suppl 1:S4-41.
13. Madison JR, Spies C, Schatz IJ, et al. Proteinuria and risk for stroke and coronary heart disease during 27 years of follow-up: the Honolulu Heart Program. *Arch Intern Med* 2006; 166:884-9.
14. Borch-Johnsen K, Feldt-Rasmussen B, Strandgaard S, Schroll M, Jansen JS. Urinary albumin excretion. An independent predictor of ischemic heart disease. *Arterioscler Thromb Vasc Biol* 1999; 19:1992-7.
15. Molitch ME, DeFronzo RA, Franz MJ, et al. Nephropathy in diabetes. *Diabetes Care* 2004; 27:S79-83.
16. Marshall SM. Screening for microalbuminuria: which measurement? *Diabet Med* 1991; 8:706-11.
17. Reinauer H, Home PD, Kanagasabapathy AS, Heuck CC. Laboratory diagnosis and monitoring of diabetes mellitus 2002. Available at: whqlibdoc.who.int/hq/2002/9241590483.pdf. Accessed August 2007.
18. Molitch ME, DeFronzo RA, Franz MJ, et al. Diabetic nephropathy. *Diabetes Care* 2003; 26 Suppl 1:S94-8.
19. Singapore National Health Survey 1998. Epidemiology and

- Disease Control Department, Ministry of Health Singapore, 1999.
20. Tan CE, Emmanuel SC, Tan BY, Jacob E. Prevalence of diabetes and ethnic differences in cardiovascular risk factors. The 1992 Singapore National Health Survey. *Diabetes Care* 1999; 22:241-7.
21. Kraft SK, Lazaridis EN, Qiu C, Clark CM Jr, Marrero DG. Screening and treatment of diabetic nephropathy by primary care physicians. *J Gen Intern Med* 1999; 14:88-97.
22. Mainous AG 3rd, Gill JM. The lack of screening for diabetic nephropathy: evidence from a privately insured population. *Fam Med* 2001; 33:115-9.
23. Iltz JL, Setter SM, Campbell RK. Microalbuminuria screening for patients with diabetes 2005. Available at: www.uspharmacist.com/index.asp?show=article&page=8_1490.htm. Accessed August 2007.

Singapore Medical Journal Honour Roll of Editors

<i>Honorary Editor</i>	<i>Term of Service</i>
<i>Dr Gwee Ah Leng</i>	<i>1960 - 1971</i>
<i>Dr Tan Kheng Khoo</i>	<i>1971 - 1975</i>
<i>Prof Lim Pin</i>	<i>1975 - 1978</i>
<i>Prof Feng Pao Hsüi</i>	<i>1978 - 1987</i>
<i>Prof Chee Yam Cheng</i>	<i>1988 - 1995</i>
<i>Prof Tan Choon Kim</i>	<i>1995 - 1996</i>
<i>Prof Kua Ee Heok</i>	<i>1996 - 1999</i>
<i>A/Prof C Rajasoorya</i>	<i>2000 - 2003</i>
<i>Prof Wilfred CG Peh</i>	<i>2004 - 2009</i>