Our Stance towards the 2017 ACC/AHA High Blood Pressure Clinical Practice Guideline: Has the Pendulum Swung Too Far?

Tzung-Dau Wang

High blood pressure remains the number one attributable cause of death worldwide.¹ In large-scale observational studies, the graded relations between both systolic and diastolic blood pressures and cardiovascular events become obvious and are in a log-linear manner since 115 mmHg and 75 mmHg, respectively.^{2,3} However, before release of results of the Systolic Blood Pressure Intervention Trial (SPRINT),⁴ there had been no studies demonstrating that lowering systolic blood pressures to < 130 mmHg, compared to \geq 130 mmHg, could achieve better clinical outcomes in patients with baseline systolic blood pressures of \geq 140 mmHg, either treated or untreated. In fact, there are several studies suggesting a potential harm with lowering systolic blood pressures to < 140 mmHg, compared to \geq 140 mmHg, in either elderly patients with baseline systolic blood pressures of \geq 160 mmHg or patients with low inherent cardiovascular risk (annual cardiovascular risk < 1%).⁵⁻⁷ This is the background why most international and national hypertension guidelines adopted a more conservative approach, setting systolic blood pressure target of < 140 mmHg in general and < 150 mmHg for vulnerable patients, mainly elderly, in the "pre-SPRINT" era.^{8,9}

On November 13, 2017, the American College of Cardiology/American Heart Association (ACC/AHA), together with other professional societies, issued the 2017 High Blood Pressure Clinical Practice Guideline in the annual meeting of AHA.¹⁰ In contrast to the 2014 Ameri-

Received: December 1, 2017 Accepted: December 18, 2017 Cardiovascular Center and Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei City, Taiwan.

Corresponding author: Dr. Tzung-Dau Wang, Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Zhong-Shan South Road, Taipei City 10002, Taiwan. Tel: 886-2-2312-3456 ext. 65632; Fax: 886-2-2391-3682; E-mail: tdwang@ntu. edu.tw

can hypertension guidelines,⁸ the current ACC/AHA guideline recommends a far more aggressive approach, which could be summarized in the following 3 aspects: 1) lowering the blood pressure definition of hypertension from \geq 140/90 mmHg to \geq 130/80 mmHg; 2) setting a unanimous target of blood pressure management of < 130/80 mmHg, irrespective of baseline cardiovascular risks and blood pressure levels; and 3) initiation of two first-line antihypertensive agents in patients with baseline blood pressures of \geq 140/90 mmHg (stage 2 by 2017 ACC/AHA guideline and stage 1 by all other guidelines). All these blood pressure targets are based on an average of ≥ 2 careful readings obtained from ≥ 2 occasions at clinic. The main evidence supporting the 2017 ACC/AHA guideline comes from the SPRINT trial, which includes 9,361 non-diabetic American patients with average blood pressures of 140/78 mmHg at baseline and showed statistically significant reductions in total mortality and fatal and non-fatal cardiovascular events of 27% and 25%, respectively, by targeting a systolic blood pressure of < 120 mmHg compared to < 140 mmHg.¹⁰

The drastic change in the approaches of hypertension management by 2017 ACC/AHA hypertension guideline evokes extensive discussions in numerous medical societies. According to the definition set by the 2017 ACC/AHA guideline, the number of people diagnosed as hypertensive will increase by approximately 40%, mostly in adults aged from 20 to 55.¹⁰ The tolerability in vulnerable patients managed by such an aggressive blood pressure-lowering approach is of serious concern, given that only 5% of participants in SPRINT had baseline systolic blood pressures of \geq 160 mmHg.

The Taiwan Society of Cardiology/Taiwan Hypertension Society released updated Taiwan Hypertension Guidelines in the May 2017 issue of *Acta Cardiologica Sinica*.¹ In the updated Taiwan Hypertension Guidelines, the main changes include: 1) the blood pressure targets for elderly (\geq 75 years) hypertensive patients are lowered from < 150/90 mmHg to < 140/90 mmHg at clinic; and 2) we recommend another set of unattended automated office systolic blood pressure target of < 120 mmHg for hypertensive patients with either coronary heart disease, chronic kidney disease, or age \geq 75 years, based on the SPRINT findings. It is obvious that these recommendations are more aggressive than most of the other hypertension guidelines. The underlying reasons for the aggressive approach are that East Asian populations, including Taiwan, are prone to develop hypertension, compared to Caucasians or South Asians with similar body habitus,¹¹ and susceptible to hypertension-related vascular events.¹

Given the aggressive manner of Taiwan Hypertension Guidelines, what should be our stance towards the even more aggressive 2017 ACC/AHA guideline? Should we follow the recommendations of 2017 ACC/AHA guideline? The simple answer is "No". Regarding the definition of hypertension, we will not change our definition of hypertension to \geq 130/80 mmHg because the treatment targets are not unanimous and include systolic blood pressures of < 120, < 130, and < 140 mmHg according to different risk profiles in Taiwan Hypertension Guidelines. We recognized that patients with East Asian ethnicity in the SPRINT trial are very few (< 2%). Hence, the generalizability of SPRINT findings are not certain in Taiwan. The Heart Outcome Prevention Evalutaion-3 (HOPE-3) trial included 3,691 Chinese patients out of 12,705 participants with a mean baseline blood pressure of 138/82 mmHg and showed patients with baseline systolic blood pressures of \leq 131.5 mmHg were associated with numerically higher major cardiovascular events.⁷ In the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS) trial, effects of lowering systolic blood pressure to < 140 mmHg were significantly smaller in patients \geq 75 years with regard to cerebrovascular events. We therefore refrain from recommending systolic blood pressure target of < 130 mmHg at clinic for elderly hypertensive patients in Taiwan. Likewise, we do not recommend to initiate two antihypertensive agents for all patients with baseline blood pressures of \geq 140/90 mmHg.

There are many other issues worthy to be clarified in the field of hypertension. In this issue of the *Journal*, Attar et al. explored whether spironolactone 25 mg daily was effective in lowering blood pressures in drug-naïve stage 1 hypertensive patients.¹² The authors found that spironolactone treatment for 4 weeks significantly reduced systolic blood pressure of 4.5 mmHg (placebocorrected), irrespective of baseline potassium levels. They did not examine plasma aldosterone: renin activity ratio, thus not knowing whether there is any differential effect relevant to this ratio. Although spironolactone has not been recommended as the first-line antihypertensive agent in all hypertension guidelines, it is associated with some cardiovascular beneficial effects beyond blood pressure-lowering.¹³ Its status in hypertension management deserves further evaluation. Another important issue is how to improve the cost effectiveness of hypertension management. Accurate risk stratification is essential in this regard. In the previous issues of our Journal, we published articles revealing increased epicardial adipose tissue,¹⁴ obstructive sleep apnea,¹⁵ nocturnal non-dipping,¹⁶ and subclinical hypothyroidism¹⁷ all had clinical adverse impacts in hypertensive patients. Despite whether incorporation of these "novel" risk factors may refine our risk-stratification tool merits further evaluation, it seems valid that assessment of these comorbidities and sharing results to the patients may enhance their adherence to antihypertensive treatments, which is essential for chronic disease management.¹⁸

REFERENCES

- 1. Chiang CE, Wang TD, Lin TH, et al. The 2017 Focused Update of the Guidelines of the Taiwan Society of Cardiology (TSOC) and the Taiwan Hypertension Society (THS) for the management of hypertension. *Acta Cardiol Sin* 2017;33:213-25.
- Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903-13.
- Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet* 2014;383:1899-911.
- Wright JT Jr, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103-16.
- 5. Goto Y, Ishii M, Saruta T, et al. Principal results of the Japanese trial to assess optimal systolic blood pressure in elderly hypertensive patients (JATOS). *Hypertens Res* 2008;31:2115-27.

- 6. Ogihara T, Saruta T, Rakugi H, et al. Target blood pressure for treatment of isolated systolic hypertension in the elderly: valsartan in elderly isolated systolic hypertension study. *Hypertension* 2010;56:196-202.
- Lonn EM, Bosch J, Lopez-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med* 2016;374:2009-20.
- James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014;311:507-20.
- 9. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC 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). *Eur Heart J* 2013;34:2159-219.
- Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Hypertension* 2017;Nov 13. doi: 10.1161/HYP. 000000000000065. [Epub ahead of print]
- 11. Wang TD, Goto S, Bhatt DL, et al. Ethnic differences in the relationships of anthropometric measures to metabolic risk factors in Asian patients at risk of atherothrombosis: results from the

WAN SO

REduction of Atherothrombosis for Continued Health (REACH) Registry. *Metabolism* 2010;59:400-8.

- Attar A, Sadeghi AA, Amirmoezi F, et al. Low dose spironolactone monotherapy in the management of stage I essential hypertension: a pilot randomized, double-blind, placebo-controlled trial. *Acta Cardiol Sin* 2018;34:59-65.
- 13. Topuz M, Cosgun M, Akkus O, et al. Effect of spironolactone on plasma apelin-12 levels in patients with chronic systolic heart failure. *Acta Cardiol Sin* 2016;32:690-7.
- 14. Ozturk MT, Ebinc FA, Okyay GU, et al. Epicardial adiposity is associated with microalbuminuria in patients with essential hypertension. *Acta Cardiol Sin* 2017;33:74-80.
- 15. Lin YS, Liu PH, Chu PH. Obstructive sleep apnea independently increases the incidence of heart failure and major adverse cardiac events: a retrospective population-based follow-up study. *Acta Cardiol Sin* 2017;33:656-63.
- Lin HJ, Wang TD. Nocturnal non-dipping: an overlooked clinical manifestation of subclinical hypothyroidism linking to increased cardiovascular risk. *Acta Cardiol Sin* 2017;33:495-7.
- 17. Polat Canbolat I, Belen E, Bayyigit A, et al. Evaluation of daily
- blood pressure alteration in subclinical hypothyroidism. *Acta Cardiol Sin* 2017;33:489-94.
- Wang TD, Chen YH, Huang CH, et al. Bidirectional adherence changes and associated factors in patients switched from free combinations to equivalent single-pill combinations of antihypertensive drugs. *Hypertension* 2014;63:958-67.