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Editorial Comment
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From Real-World Evidence to Consensus of Renal Denervation in Taiwan: A Call for the Incorporation of Ambulatory Blood Pressure Monitoring after Witnessed Intake of Medications

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Hypertension is the number one killer around the world.[1,2] Approximately one in four adults got hypertension globally. The burden of hypertension and its related comorbidities is rampant given the rapidly increasing aging people due to the improvement of healthcare in recent decades. To effectively reduce the burden, better and long-term control of hypertension is vital, particularly in the national perspective. Increasing the awareness of hypertension by promoting self-measurement of blood pressures,[3] reducing salt intake in hypertensive individuals,[4] and improving long-term adherence of blood pressure-lowering therapy are three major approaches to achieve this goal.[1,5]

Renal sympathetic denervation, as a one-time procedure to permanently block the sympathetic nerves surrounding the renal arteries and modulating the blood pressures, has been carefully studied worldwide to assess whether it could effectively reduce the burden of hypertension by achieving sustained and clinically meaningful reductions of blood pressures, without causing harms.[6] The clinical unmet need is huge, so are the challenges confronted. Through the ups and downs of initial clinical trials of renal denervation, the techniques and trial designs of renal denervation have progressed dramatically. The progresses are mainly driven by the better understanding of the spatial distribution of renal sympathetic nerves along the renal arteries and branches, the tissue penetration depth of energy applied to achieve nerve ablation, the human behavior of drug intakes, and the vulnerability of short-term blood pressure variations in the office setting.[7] To cope with all these factors, comprehensive ablation of renal artery branches, different energy modalities to achieve adequate tissue penetration depth, urine/plasma screening for drug adherence, the inclusion of sham group, and adoption of ambulatory blood pressure monitoring as the outcome measure have been implemented in most recent clinical trials of renal denervation. All these so-called second-generation renal denervation trials, including more than 400 patients in total, have demonstrated consistent and clinically meaningful ambulatory systolic blood pressure reductions (6-10 mmHg), further substantiating the role of renal sympathetic nerves in the pathogenesis of hypertension.[6] We are now waiting for the results of the ongoing SPYRAL PIVOTAL study, which was planned to include 433 drug-naïve, uncontrolled hypertensive participants and will decisively determine the fate of this radiofrequency technology.

Hypertension plays a more important role in causing morbidity and mortality in East Asian countries because a steeper blood pressure-vascular event relation has been consistently demonstrated in East Asian populations compared to that in Western populations.[1,2] With regard to the blood pressure-lowering effects of renal denervation, real-world data from Korea[8] and Taiwan,[9] which is published in this issue of the *Journal*, showed that the magnitudes of office blood pressure reductions were similar (25-35 mmHg) among patients from Korea, Taiwan, and Western countries in the first 12 months. However, after 12 months, systolic blood pressure reductions remained the same as the first 12 months in patients from Western countries, whereas for patients

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from Korea and Taiwan, systolic blood pressure continued declining following 1 year. The same phenomenon regarding the systolic blood pressure reductions following renal denervation became even more pronounced after 12 months was also observed in Japanese patients in Symplicity HTN-Japan study.[10] The uniqueness of the GSR-Taiwan registry 3-year follow-up results, reported by Lee CK et al., is that it provides the only long-term follow-up results of both branch and main renal artery ablation, the refined renal denervation strategy, in Asian patients with uncontrolled hypertension. Compared with the main renal artery ablations by using the single-electrode catheter, branch and main renal artery ablations resulted in a significantly greater number of ablations (median, 40.5 versus 19.5) within a significantly shorter procedural time (107.5 versus 144.5 minutes). The office systolic blood pressure reductions achieved by branch and main renal artery ablations were numerically greater throughout the follow-up period. The comprehensive branch and main renal artery ablations did not result in any acute or long-term renal events. Limitations of this real-world observational data from GSR-Taiwan include small number of patients (only 26) and lack of ambulatory blood pressures data. In other words, these results need further verification by either larger-sized studies or more reliable blood pressure measurements, i.e. ambulatory blood pressure monitoring.

In addition to the first Asian real-world data of branch and main renal artery ablation published in this *Journal*, we also published the first Consensus paper regarding renal denervation, following the publications of a series of second-generation renal denervation trials, issued by the Taiwan Hypertension Society and Taiwan Society of Cardiology in the May issue.[6] In that Consensus, 2 acronyms addressing the key issues of renal denervation, patient selection for renal denervation and pre/post renal denervation evaluations, were created to facilitate implementation. The first acronym is "RDNi2" to describe the five key features of indicated patients for renal denervation: R for resistant hypertension; D for diseased organ or vessels mediated by hypertension; N for non-adherent; i for intolerant; and 2 for treatment-resistant secondary hypertension. The other acronym is "RAS" for pre-renal denervation assessments: R for renal artery assessment by computed tomographic angiography or magnetic resonance angiography; A for ambulatory blood pressure monitoring; and S for secondary hypertension evaluation and treatment. Ambulatory blood pressure monitoring is regarded as a routine examination before renal denervation since it provides 24-hour blood pressure profile and is more reliable as stated before. An additional requirement for ambulatory blood pressure measurement, which was not mentioned in the Consensus, is that it should be done after witnessed taking of prescribed antihypertensive drugs.[11] This could be described as either "witnessed ambulatory blood pressure monitoring" or "directly observed therapy ambulatory blood pressure monitoring", and should be widely adopted in not only pre-renal denervation assessment, but also daily clinical practice. The main reason for incorporation of this witnessed ambulatory blood pressure monitoring in pre-renal denervation assessment is that poor adherence is an extremely common phenomenon and could only be detected by either urine/plasma drug screening or this very approach.[11] Because of limited clinical evidence of second-generation renal denervation, albeit good efficacy and safety being consistently demonstrated, the Taiwan renal denervation Consensus recommended renal denervation should be done in the context of either clinical studies or registries.

In the recent 2 years, our *Journal* published several pharmacological or instrumental interventional studies which did contribute to the progress of medical management.[12-19] We highly welcome the submission of clinical trials, particularly randomized clinical trials, into our Journal since the level of evidence is the greatest because of exclusion of various biases. However, the majority of articles submitted and published were correlation and observational studies, which should be of novel pathophysiologic significance or of important clinical implications. We particularly selected several articles as cited here for the readers' interest.[20-32] The science is continuously progressing through scientific publications. We will do our best to make our *Journal* contribute more in the global scientific society. We hope you enjoy the *Acta Cardiologica Sinica*, and any comment or suggestion is wholeheartedly welcomed by our editorial team.

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