



Guidelines for the appropriate use of renal denervation systems in Japan: endorsed by the Japanese Society of Hypertension (JSH), the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT), and the Japanese Circulation Society (JCS), and their positioning in the JSH 2025 guidelines

Kazuomi Kario¹ · Hisashi Kai² · Hiromi Rakugi^{3,4} · Satoshi Hoshide¹ · Koichi Node⁵ · Kenichi Katsurada¹ · Keisuke Shinohara⁶ · Yuichiro Maekawa⁷ · Yasushi Sakata⁸ · Yuya Matsue⁹ · Masaru Yamaki¹⁰ · Masahiko Fujihara¹¹ · Yoshio Kobayashi¹² · Ken Kozuma¹³ · Jiro Aoki¹⁴

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Abstract

This document presents the Guidelines for the Appropriate Use of Renal Denervation (RDN) Systems in Japan, jointly endorsed by the Japanese Society of Hypertension (JSH), the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT), and the Japanese Circulation Society (JCS). Based on the final consensus statement of the Joint Committee on RDN, these guidelines identify resistant hypertension as the principal indication for RDN treatment in Japan. Indicated resistant hypertension is strictly defined as uncontrolled blood pressure, confirmed by both office and out-of-office measurements (ambulatory blood pressure monitoring or home blood pressure monitoring), despite lifestyle modification and appropriate antihypertensive therapy with three or more drug classes, including a diuretic. RDN procedures should be performed by a multidisciplinary Hypertension Renal Denervation Treatment (HRT) team, composed of JSH-, CVIT-, and JCS-certified specialists, nurses, pharmacists, and registered dietitians, within accredited centers providing accessible outpatient care. Using standardized checklists and procedural manuals, the HRT team thoroughly evaluates lifestyle factors, pharmacological therapy, and patient background, and determines the indication for RDN based on a shared decision-making process with each patient. The Japanese Society of Hypertension Guidelines for the Management of Elevated Blood Pressure and Hypertension 2025 (JSH2025) explicitly state that RDN may serve as a novel adjunctive treatment option for resistant hypertension (recommendation strength: 2, evidence strength: B, consensus rate: 100%). This recognition represents a pivotal step toward integrating RDN into clinical practice in Japan. Moving forward, the Joint RDN Committee will revise and update indications and implementation guidance as appropriate, informed by real-world clinical evidence.

Keywords guidelines, renal denervation · hypertension · resistant hypertension · Japan, Hypertension Renal Denervation Treatment (HRT) team

Indication (approved indication)

RDN systems approved in Japan, is indicated as an adjunctive treatment to lower blood pressure (BP), for patients with resistant hypertension* whose BP cannot be adequately controlled by treatment in accordance with the Japanese Society of Hypertension Guidelines for the Management of Elevated Blood Pressure and Hypertension 2025 (JSH2025) including lifestyle modification, non-pharmacological therapy, and pharmacological therapy.

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✉ Kazuomi Kario
kkario@jichi.ac.jp

Extended author information available on the last page of the article

Graphical Opinion

Indication of Guidelines for the Proper Use of Renal Denervation Systems in Japan (2026)



**“True”
Resistant hypertension**

The renal denervation system is used to lower blood pressure (BP) as an additional treatment for patients with **resistant hypertension*** whose BP cannot be adequately controlled with treatment in accordance with Japanese Society of Hypertension JSH2025 guidelines for the management of hypertension (lifestyle modifications/non-pharmacological therapy and pharmacological therapy using 3 or more classes including diuretics) after evaluation of **Hypertension Renal Denervation Treatment (HRT)** team composed of specialists in hypertension (JSH), cardiovascular intervention (CVIT), cardiology (JCS), nurses, pharmacists, and registered dietitians in the JSH, CVIT, and JCS-certified special centers.

***Items to confirm before diagnosing resistant hypertension:**

- 1) Status of lifestyle modifications
- 2) Adherence to medication
- 3) Types and dosages of antihypertensive drugs
- 4) Correct blood pressure measurement and confirmation of target BP levels
- 5) Exclusion of secondary hypertension

Inclusion criteria

- 1) Office BP $\geq$ 140/90 mmHg AND ABPM: 24-hour BP $\geq$ 130/80 mmHg, daytime BP $\geq$ 135/85 mmHg, or nighttime BP $\geq$ 120/70 mmHg
- OR
- 2) Office BP $\geq$ 140/90 mmHg AND Morning or evening home BP $\geq$ 135/85 mmHg, or nighttime home BP $\geq$ 120/70 mmHg

Exclusion Criteria

- 3) Patients with renal artery aneurysms, stenosis, or anatomical structures of renal arteries unsuitable for treatment (primarily assessed via contrast-enhanced CT)
- 4) eGFR $<$ 40 ml/min/1.73 m²
- 5) Patients falling under contraindications or prohibited conditions listed in the product's package insert

Japanese Society of Hypertension (JSH); Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT); Japanese Circulation Society (JCS); Ambulatory blood pressure monitoring (ABPM)

*According to the JSH 2025, resistant hypertension is defined as BP that fails to reach the target level despite the use of three antihypertensive agents of different classes, including a diuretic.

Conditions of approval

- (1) Physicians and medical teams with sufficient knowledge and experience related to hypertension treatment shall appropriately select patients, and after fully acquiring skills in handling this product as well as knowledge of complications associated with the procedure, use this product at medical institutions where treatment systems are in place. Necessary measures shall be taken such as dissemination of Guidelines for the Appropriate Use of RDN Systems in Japan, training sessions, etc., in cooperation with the relevant academic societies, such as JSH, CVIT, and JCS.
- (2) Until data on a certain number of cases are accumulated, post-marketing surveillance (PMS) shall be conducted on all cases in which this product is used, and results of longitudinal analyses concerning long-term outcomes shall be reported to the Pharmaceuticals and Medical Devices Agency (PMDA) with appropriate measures as necessary.

Patient requirements (patients must satisfy all of the following conditions)

RDN treatment is intended, in accordance with the latest guidelines for the management of elevated BP and hypertension, for BP management of hypertensive patients whose BP control remains inadequate despite having received appropriate treatment such as lifestyle modification and antihypertensive medication guidance. The indication shall be determined by the Hypertension Renal Denervation Treatment (HRT) team, through multidisciplinary collaboration, after reviewing the patient's condition.

For appropriate patient selection in this treatment, screening shall be conducted using the Renal Denervation Appropriate Use Checklist shown in Appendix 1.

- (1) Items to be confirmed before judging poor BP control
 - Status of lifestyle modification.
 - Status of medication adherence.
 - Types and dosage of antihypertensive drugs.
 - Confirmation of proper BP measurement and target BP level.
 - Exclusion of secondary hypertension.

(2) Criteria for uncontrolled BP (Selection criteria)

- Office BP $\geq$ 140/90 mmHg and 24-hr BP $\geq$ 130/80 mmHg, or daytime BP $\geq$ 135/85 mmHg, or nighttime BP $\geq$ 120/70 mmHg by ambulatory BP monitoring (ABPM).
- OR
- Office BP $\geq$ 140/90 mmHg and morning home BP or evening home BP $\geq$ 135/85 mmHg, or nighttime home BP $\geq$ 120/70 mmHg by home BP monitoring (HBPM).

(3) Resistant hypertension (Selection criteria).

Resistant hypertension is defined as uncontrolled BP despite treatment with three or more classes of antihypertensive drugs including diuretics. However, antihypertensive drugs other than diuretics shall, in principle, be used at the maximum tolerated dose.

(4) Patients unsuitable for RDN (Exclusion criteria).

- Patients with renal artery aneurysm, renal artery stenosis, or anatomical structures of the renal artery unsuitable for the procedure evaluated, in principle, by contrast-enhanced CT.
- eGFR $<$ 40 ml/min/1.73 m².
- Patients who fall under the contraindications or prohibited matters described in the package insert.

Facility conditions (facilities must satisfy all of the following conditions)

- (1) The facility shall be a JSH RDN-related facility, a CVIT training or affiliated training facility, and a JCS cardiovascular training or affiliated training facility.
- (2) The following criteria must all be satisfied, and the facility must possess a certificate of accreditation issued by the Japan Renal Denervation Council organized by the JSH, CVIT and JCS:
 - 1) At least one JSH-certified hypertension specialist must reside, and a specialized outpatient department must be established and publicly displayed.
 - 2) At least one CVIT-certified physician or specialist or honorary specialist must reside.
 - 3) At least one JCS-certified cardiology specialist must reside.
- (3) The HRT team must function cooperatively through patient selection, lifestyle modification, medication

guidance, procedure, perioperative management, and post-operative follow-up.

- 1) The HRT team must be composed of at least a JSH-certified hypertension specialist, a CVIT-certified physician or specialist or honorary specialist, a JCS-certified cardiology specialist, nurse, pharmacist, a registered dietitian.
- 2) The participation of certified cardiovascular disease prevention educator is desirable.
- 3) If there is any change in HRT team members due to transfer or reassignment, it must be reported immediately to the Japan Renal Denervation Council, and the new members must be applied for. If the report and application cannot be confirmed, the facility accreditation may be revoked.
- (4) All cases must be registered in the PMS and in the registry designated by the Japan Renal Denervation Council. The PMS items are shown in Appendix 3.
 - 1) The data at the time of application for confirmation of RDN indication must be submitted to the Japan Renal Denervation Council.
 - 2) The Renal Denervation Appropriate Use Checklist (Appendix 1) and the Renal Denervation Follow-up Checklist (Appendix 2) must each be submitted to the Japan Renal Denervation Council at the time of indication determination and at follow-up visits, respectively.
 - 3) If registration cannot be confirmed, the facility accreditation will be revoked.

Operator physician requirements (physicians must meet all three requirements: (1) or (2), and (3) and (4))

- (1) CVIT-certified physician or specialist or honorary specialist.
- (2) The Japanese Society of Interventional Radiology-certified specialist (must collaborate with 4(1) during the procedure).
- (3) Must have completed the designated training course regarding the device and the relevant pathology
- (4) Must be proficient in measures for managing complications.

Others

Based on the accumulation of future evidence and the results of PMS of this product conducted in Japan, the content of Guidelines for the Appropriate Use of RDN Systems in Japan shall be reviewed periodically (at least once every three years).

Part 2. Evidence, guidelines, and regulatory science to implementation in Japan

Regulatory approval and JSH 2025 guidelines

In a historic regulatory milestone, 2025 marked the approval in Japan of two RDN systems—Otsuka Medical Devices' Paradise™ System and Medtronic's Symplicity Spyral™—as adjunctive therapies for resistant hypertension [1, 2]. It has been 10 years since SYMPPLICITY HTN-Japan—the first randomized controlled trial of catheter-based RDN in Asian patients—was initiated [3]. This dual approval was granted under a unified framework led by the JSH, the CVIT, and the JCS. This collaborative approach underscores the need for specialized clinical expertise and strict application of HRT team-based usage criteria, reflecting Japan's rigorous integration of device-based therapies into hypertension care [4]. The significance of this advancement cannot be overstated. It represents a paradigm shift in Japan's therapeutic arsenal against hypertension, particularly for patients whose BP remain uncontrolled despite optimized pharmacologic therapy and lifestyle management [1, 2]. The JSH has conducted a comprehensive systematic review of 12 randomized sham-controlled trials on RDN [5]. In addition, *Hypertension Research*, the official journal of JSH, has compiled and updated evidence from multiple perspectives, publishing review and position papers on RDN [6–26]. Based on the current body of evidence, the newly released *JSH2025* formally recommend RDN for patients with resistant hypertension as a Class II recommendation, Level of Evidence B, with 100% agreement [27]. This recommendation signals cautious optimism—acknowledging both the clinical potential of RDN and the need for careful patient selection by the HRT team and long-term outcome monitoring as specified in these Guidelines. This regulatory and academic endorsement marks a new chapter in hypertension management in Japan and may serve as a model for global integration of device-based therapies into evidence-based clinical practice.

International clinical data and regulatory status

The two approved systems have received CE marking in Europe. In 2023, the U.S. FDA approved both systems as adjunctive therapies for patients with uncontrolled hypertension. The Paradise system demonstrated consistent

efficacy and safety in trials such as RADIANCE-HTN SOLO, RADIANCE-HTN TRIO, and RADIANCE II, all of which proved significant BP-lowering effects compared to sham procedure in double-blinded manners under off-medication in patients with uncontrolled hypertension or treatment on-medication with a triple antihypertensive combination drug including a diuretic in patients with resistant hypertension [28–31]. Similarly, the Symplicity Spyral system has shown BP-lowering effects in global RCTs such as SPYRAL HTN-ON MED and SPYRAL HTN-OFF MED, with and without concurrent medication [32–36]. Across these programs, RDN reduces 24-hr BP, including nighttime and morning BP, in patients with resistant hypertension [28, 29, 36]. In addition, RDN has been associated with durable BP control and is expected to contribute to long-term hypertension management [37–40].

Resistant hypertension: indications in Japan

In Japan, the two approved RDN systems are indicated for patients with resistant hypertension who fail to achieve adequate BP control despite standard therapies including lifestyle modifications and medication, with indication determined by the multidisciplinary HRT team (hypertension and cardiovascular specialists including JSH-, CVIT-, and JCS-certified physicians), together with nurses, pharmacists, and registered dietitians.

Resistant hypertension is strictly defined as uncontrolled blood pressure, confirmed by both office and out-of-office measurements (ambulatory blood pressure monitoring or home blood pressure monitoring), despite lifestyle modification and appropriate antihypertensive therapy with three or more drug classes, including a diuretic [27]. RDN is a non-pharmacologic device therapy that reduces sympathetic nervous system activity by ablating renal sympathetic efferent and sensory afferent nerves via catheterization, resulting in sustained BP reduction [1, 2]. Its distinct mechanism of action differentiates it from pharmacologic therapies.

Candidates for RDN must meet all of the following (Fig. 1):

- Office BP $\geq 140/90$ mmHg and uncontrolled BP as defined by 24-hr BP $\geq 130/80$ mmHg, or daytime BP $\geq 135/85$ mmHg, or nighttime BP $\geq 120/70$ mmHg by ambulatory BP monitoring on ABPM or defined by morning home BP or evening home BP $\geq 135/85$ mmHg, or nighttime home BP $\geq 120/70$ mmHg on home BP monitoring (HBPM).
- Verified medication adherence, lifestyle assessment, accurate BP measurement, and exclusion of secondary hypertension.

Indication of Guidelines for the Proper Use of Renal Denervation Systems in Japan (2026)



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- 2) Office BP $\geq 140/90$ mmHg AND Morning or evening home BP $\geq 135/85$ mmHg, or nighttime home BP $\geq 120/70$ mmHg

Exclusion Criteria

- 3) Patients with renal artery aneurysms, stenosis, or anatomical structures of renal arteries unsuitable for treatment (primarily assessed via contrast-enhanced CT)
- 4) eGFR < 40 mL/min/1.73 m²
- 5) Patients falling under contraindications or prohibited conditions listed in the product's package insert

Japanese Society of Hypertension (JSH); Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT); Japanese Circulation Society (JCS); Ambulatory blood pressure monitoring (ABPM)

Fig. 1 Indication of Guidelines for the Appropriate Use of Renal Denervation Systems in Japan (2026) (Graphic abstract)

- Anatomical suitability of the renal arteries (contrast-enhanced CT-based evaluation) and eGFR ≥ 40 mL/min/1.73 m².

Implementation of the RDN procedure is limited to institutions with certified hypertension outpatient clinics recognized by JSH/CVIT/JCS, and all cases must be registered and performance monitored per the PMS and registry processes designated by the Japan Renal Denervation Council.

Advantage of RDN on 24-hr BP control in “true resistant hypertension”

In Japan, RDN is implemented for “true resistant hypertension,” referring to resistant hypertension that remains uncontrolled not only in the office but also on HBPM or ABPM—specifically elevated morning, evening (at bedtime), or nighttime home BPs, or daytime, nighttime, or 24-hr ambulatory BPs—despite treatment with 3 or more antihypertensive drug classes including a diuretic, after therapeutic inertia, non-adherence, poor adherence to lifestyle interventions, use of drugs causing hypertension, other causes of secondary hypertension, and poorly measured BPs have been excluded. The out-of-office BPs, such as ambulatory BP and self-measured home BP, are more closely associated with poor cardiovascular outcomes than

office BP [41–45]. The cardiovascular prognosis of such true resistant hypertension is extremely poor [46, 47]. Resistant hypertension defined by office and home blood pressure is an ultra-high-risk condition, with cardiovascular events occurring in as many as 35% of patients over 10 years [47].

As the number of antihypertensive medications increases, control of office BP and daytime BP improves; however, improvement is limited for nighttime and morning BPs [48–51]. Even among hypertensive patients receiving 3 or more classes of antihypertensive drugs, nighttime BP remains uncontrolled in 45%, and morning BP remains uncontrolled in 55% [48]. The cardiovascular risk associated with uncontrolled nighttime and morning hypertension is higher than that associated with uncontrolled office BP or uncontrolled daytime BP [50–58]. Disrupted circadian rhythms—such as a riser pattern of nighttime BP, an exaggerated morning BP surge, and sleep BP surges associated with sleep apneas—are associated with cardiovascular event risk [59–64]. These abnormal 24-hr BP profiles remain major challenges to suppress organ damage and subsequent cardiovascular events in hypertension management.

RDN provides 24-hr BP-lowering effects, and its greatest advantage is the suppression of nighttime and morning hypertension with improved 24-hr BP variability, resulting in the potential reduction of cardiovascular events in high-risk hypertensive patients [1, 33, 65–72].

Hypertension Renal Denervation Treatment (HRT) team for RDN implementation

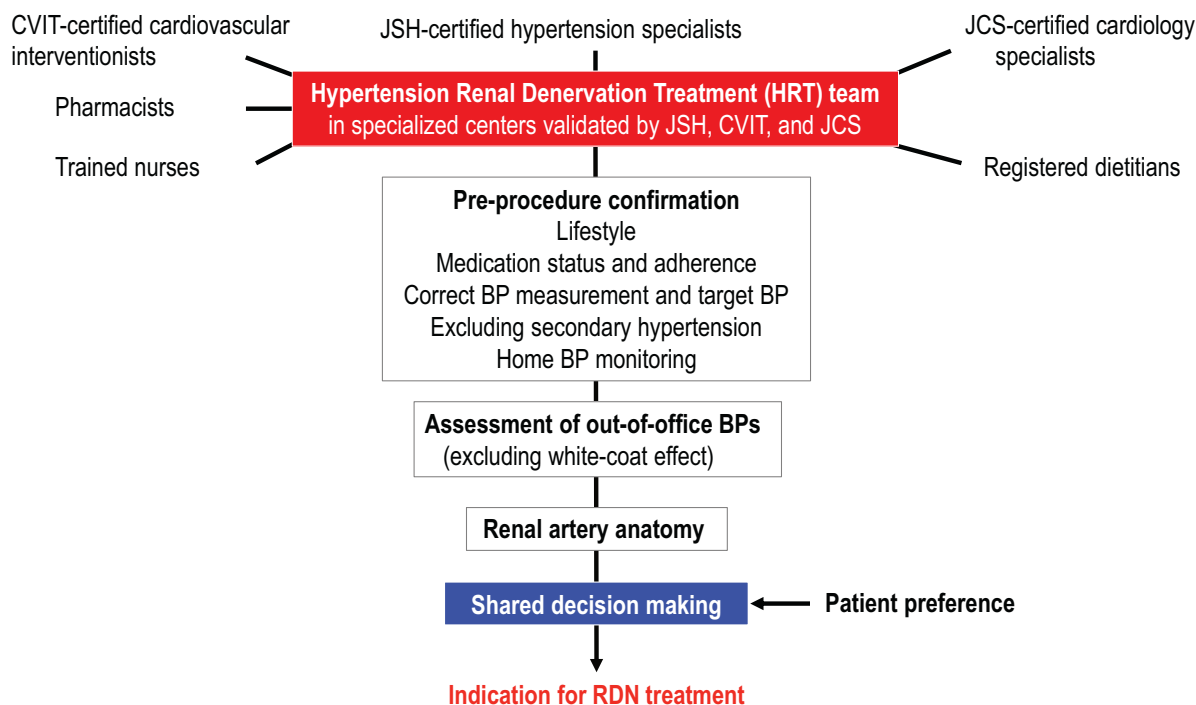


Fig. 2 Process to determine the presence of an indication for renal denervation. BP blood pressure CVIT, Japanese Association of Cardiovascular Intervention and Therapeutics, JCS Japanese Circulation Society, JSH Japanese Society of Hypertension, RDN renal denervation

Role of hypertension specialty centers

Successful implementation of RDN in Japan relies on precise patient screening and comprehensive perioperative management, centered around specialized hypertension centers and multidisciplinary HRT teams that can network with surrounding clinics (Fig. 2). Because RDN is a preference-sensitive intervention, patient selection and timing should be guided not only by clinical criteria but also by shared decision-making (SDM) that elicits the patient's goals, values, and preferences (e.g., willingness to continue medications, tolerance of side effects, expectations for BP reduction, and priorities regarding morning/nocturnal BP control). In this context, patient preference data from Japan are reassuring and broadly comparable with other countries: in a nationwide Japanese survey, 31.6% of treated patients expressed a preference for RDN, while a German survey reported that 28.2% of patients already on antihypertensive therapy (and 38.2% of those not yet on medication) would opt for RDN—supporting the need for structured counseling and, when available, decision aids to align care with informed patient preference [73, 74].

Led by JSH-certified hypertension specialists and supported by CVIT- and JCS-certified cardiologists, nurses, pharmacists, and dietitians, the HRT team should establish long-term

care systems. The RDN procedure is available only in JSH/CVIT/JCS-certified hypertension centers, as stipulated in these Guidelines. Specialist knowledge and coordinated care are essential for post-RDN follow-up, assessment of appropriate use, and long-term outcomes; importantly, follow-up should also revisit SDM over time, incorporating patient-reported outcomes, medication adjustment, and satisfaction with the chosen strategy. Expansion of hypertension centers and enhancement of specialist training are critical challenges. As case numbers grow and data accumulate, the optimal use and long-term outcomes of RDN are expected to become clearer, broadening treatment options.

Cost-effectiveness

From a health-system perspective, economic data are also encouraging: a Japan-specific model-based analysis estimated an incremental cost-effectiveness ratio (ICER) of ¥2,565,236 per quality-adjusted life year (QALY) gained versus a ¥5,000,000/QALY threshold (and became more favorable under scenarios incorporating added nighttime BP benefit), while a UK analysis co-authored by Schmieder reported an ICER of £13,482 per QALY—well below the NICE threshold of £20,000–30,000/QALY [75, 76].

Conclusion and perspectives

The regulatory approval of RDN represents a breakthrough in the treatment of resistant hypertension and has the potential to transform hypertension care in Japan. Introduction of RDN as a novel non-pharmacologic, device-based option is highly anticipated for this difficult-to-manage condition with the expectation that improved 24-hr BP control may contribute to suppression of organ damage and subsequent cardiovascular events. In addition, by providing a durable, adherence-independent BP-lowering effect, RDN may help overcome “implementation hypertension,” in which suboptimal real-world BP control persists because effective therapies are not fully implemented or sustained due to medication intolerance, poor adherence, or therapeutic inertia [77–79]. Evidence-based, cautious implementation in alignment with these Appropriate Use Guidelines, together with patient-centered multidisciplinary collaboration by the HRT team, will be key to its future success.

Compliance with ethical standards

Conflict of interest Kario K received grants from A&D, Omron Healthcare, Fukuda Denshi, CureApp; Honoraria from Daiichi Sankyo, Viartis, Novartis, Otsuka Pharmaceuticals, Medtronic, Otsuka Medical device, Omron Healthcare. Kai H received honoraria from Daiichi Sankyo, Novartis and Otsuka Medical Device. Rakugi H received honoraria from Daiichi Sankyo Co., Ltd., Novartis Pharma K.K., and Otsuka Pharmaceutical Co., Ltd.; research funding from Novartis Pharma K.K.; scholarship from Daiichi Sankyo Co., Ltd., Nippon Boehringer Ingelheim Co., Ltd., Takeda Pharmaceutical Company Ltd., and Sumitomo Pharma, Co., Ltd. Hoshide S received honoraria from Novartis. Node K received research grants from Otsuka Medical Devices, Medtronic, Astellas, Bayer Yakuhin, Boehringer Ingelheim Japan, Fujiyaku, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Novartis Pharma; Scholarship from Abbott, Boehringer Ingelheim Japan, Daiichi Sankyo, Mitsubishi Tanabe Pharma, Teijin Pharma; Honoraria from AstraZeneca, Bayer Yakuhin, Boehringer Ingelheim Japan, Daiichi Sankyo, Eli Lilly Japan, Kowa, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, MSD, Novartis Pharma, Novo Nordisk Pharma, Ono Pharmaceutical, Otsuka, Tsumura & Co. Katsurada K received honoraria from Otsuka Medical Device and Medtronic. Shinohara K received grants from Otsuka Medical Devices. Maekawa Y received scholarship funds from Abbott Medical Japan LLC, Medtronic Japan Co., Ltd., and BIOTRONIK JAPAN; and honoraria from Bristol-Myers Squibb Co., Ltd. Sakata Y received grants from Abbott Medical Japan, Otsuka Pharmaceutical, Nippon Boehringer Ingelheim, Boston Scientific Japan, BIOTRONIK JAPAN; Honoraria from AstraZeneca, Otsuka Pharmaceutical, Nippon Boehringer Ingelheim, Novartis Pharma and Bayer Yakuhin. Matsue Y received honoraria from Otsuka Pharmaceutical Co., Ltd., EN Otsuka Pharmaceutical Co., Ltd., Novartis Pharma K.K., Ono Pharmaceutical Co., Ltd., AstraZeneca K.K., Nippon Boehringer Ingelheim Co., Ltd., Bayer Yakuhin, Ltd., Kyowa Kirin Co., Ltd., Pfizer Japan Inc., and Alnylam Japan K.K. He also received collaborative research funding from Otsuka Pharmaceutical Co., Ltd., EN Otsuka Pharmaceutical Co., Ltd., Bayer Yakuhin, Ltd., Pfizer Japan Inc., Nippon Boehringer Ingelheim Co., Ltd., AstraZeneca K.K., Roche Diagnostics K.K., Grace Imaging Inc., and Omron Healthcare Co., Ltd. Yamaki M declares no conflict of interest. Fujihara M received consultation fees

from Abbott, Philips, Cordis, Kaneka, and BD, as well as honoraria from Boston Scientific, Medtronic, Gore, and Terumo. Kobayashi Y received lecture fees from Amgen, Novartis Japan, Medtronic, and Daiichi-Sankyo and research grants from Nipro, Kaneka Medical Products, OrbusNeich Medical, Win International, and Abbott Medical Japan. Kozuma K received remuneration for lecture from Boston Scientific, Abbott Medical, Medtronic, Otsuka Pharmaceutical and Medical Devices, Daiichi-Sankyo, Amgen, Novartis, Novo Nordisk, Shockwave medical, Research fund from Abbott Medical. Aoki J received Honoraria from Medtronic, Otsuka Medical Device, Otsuka Pharmaceutical, Daiichi Sankyo, Nippon Boehringer Ingelheim, and Novartis Pharma. **Role of Clinical Trials:** Kario K is an Executive Committee Principal Investigator for the Spyral OFF MED, the Spyral ON MED, the DUO and the REQUIRE; a Coordinating investigator for the TCD-16164 study; a Site Principal Investigator for the HTN-J, the Spyral OFF MED, the Spyral ON MED, the DUO, the REQUIRE and the TCD-16164 study. Kai H is a Site Sub-Investigator for the HTN-J; a medical expert for the DUO and the REQUIRE. Rakugi H is a Site Sub-Investigator for the HTN-J, the DUO and the REQUIRE. Hoshide S is a Site Sub-Investigator for the HTN-J, the Spyral OFF MED, the Spyral ON MED, the DUO, the REQUIRE and the TCD-16164 study; a medical expert for the REQUIRE. Node K is a Site Sub-Investigator for the REQUIRE. Katsurada K is a Site-sub-Investigator for the DUO. Shinohara K is a Site Principal Investigator for the DUO and the REQUIRE. Maekawa Y is a Site Principal Investigator for the DUO. Sakata Y is a Principal Investigator for the DUO and the REQUIRE; a Site Sub-Investigator for the HTN-J. Matsue Y has no role. Yamaki M is a Site Principal Investigator for the DUO and the REQUIRE. Fujihara M is a Site Principal Investigator for the REQUIRE. Kobayashi Y has no role. Aoki J is a Site Sub-Investigator for the HTN-J; a Site Principal Investigator for the Spyral OFF MED, the Spyral ON MED studies, the DUO and the REQUIRE.

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Affiliations

Kazuomi Kario¹ · Hisashi Kai² · Hiromi Rakugi^{3,4} · Satoshi Hoshide¹ · Koichi Node⁵ · Kenichi Katsurada¹ · Keisuke Shinohara⁶ · Yuichiro Maekawa⁷ · Yasushi Sakata⁸ · Yuya Matsue⁹ · Masaru Yamaki¹⁰ · Masahiko Fujihara¹¹ · Yoshio Kobayashi¹² · Ken Kozuma¹³ · Jiro Aoki¹⁴

¹ Division of Cardiovascular Medicine, Jichi Medical University School of Medicine, Tochigi, Japan

² Department of General Medicine and Community Healthcare Promotion, Yokokura Hospital, Fukuoka, Japan

³ Osaka Rosai Hospital, Sakai, Japan

⁴ Osaka University, Suita, Japan

⁵ Department of Cardiovascular Medicine, Saga University, Saga, Japan

⁶ Department of Cardiovascular Medicine, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan

⁷ Division of Cardiology, Internal Medicine III, Hamamatsu University School of Medicine, Hamamatsu, Japan

⁸ Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Osaka, Japan

⁹ Department of Cardiovascular Biology and Medicine Juntendo University Graduate School of Medicine, Tokyo, Japan

¹⁰ Department of Cardiology, Sapporo-Kosei General Hospital, Sapporo, Japan

¹¹ Department of Cardiology, Osaka Keisatsu Hospital, Osaka, Japan

¹² Department of Cardiovascular Medicine, Chiba University Graduate School of Medicine, Chiba, Japan

¹³ Department of Cardiology, Teikyo University Hospital, Tokyo, Japan

¹⁴ Department of Cardiovascular Medicine, St. Luke's International Hospital, Tokyo, Japan