Circ J 2017; **81:** 1261–1267
doi:10.1253/circj.CJ-17-0706

Overview of the 81st Annual Scientific Meeting of the Japanese Circulation Society

— Cardiovascular Medicine for the Next Generation —

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The 81st Annual Scientific Meeting of the Japanese Circulation Society was held in Kanazawa, Japan, on March 17–19, 2017 under a miraculously clear sky. The frontlines of healthcare and medicine are dramatically changing. Thus, "Cardiovascular Medicine for Next Generation" was chosen as the main theme of this meeting. The program was constructed around major identified issues, including renewal of our understanding of basic cardiovascular medicine, translational research, and preventive molecular medicine, all of which are anticipated to transcend the medical field over the next generation. Despite the provincial location, 15,672 participants, including more than 400 from overseas countries, attended the 3-day meeting, and there were in-depth discussions in the various sessions. In particular, to our great pleasure, Her Imperial Highness Princess Takamado kindly attended the opening ceremony and extended congratulations to us. The meeting successfully completed and we sincerely appreciate the great cooperation and support from all affiliates.

Key Words: Cardiovascular medicine; Japanese Circulation Society; Next generation

Overview and Meeting Theme

The 81st Annual Scientific Meeting of the JCS was held in Kanazawa, Japan, on March 17–19 (http://www2.convention.co.jp/jcs2017/) with "Cardiovascular Medicine for Next Generation" as the main theme. We were blessed with miraculous good weather for early spring in Hokuriku region. This was the 15th Anniversary of the International Joint Sessions. Historically, the 36th JCS Scientific Meeting was held 45 years ago in Kanazawa in 1972, when Dr. Mototaka Murakami, an honorary Professor of Medicine, Kanazawa University, served as the Congress Chairperson.

Ishikawa Ongakudo was the main venue (**Figure 1A**), while Hotel Nikko Kanazawa, etc. were also used concurrently. We were able to concentrate the venues in the JR Kanazawa Station area (10-min walk from the station) for attendees' convenience (**Figure 1B**). Moreover, the recent extension of the Hokuriku Shinkansen, a bullet train from Kanazawa to Tokyo, which opened on March 14, 2015, enabled participants to more easily access Kanazawa. Despite the provincial location, 15,672 people, including medical doctors, healthcare professionals, and management staff, attended the meeting during the 3 sessional days, and there were in-depth discussions in the various sessions (**Figure 2**). Importantly, the number of attendees from abroad was recorded to be 424 at this meeting. Of 3,758 entries received for regular abstracts, 2,479 were accepted (acceptance rate, 66.0%). For the late-breaking sessions, of 95 entries received 66 were finally selected (69.5%). All told, 501 members accepted the session Chair role, of which 63 were female members (12.5%).

During the Congress Chairperson's lecture entitled "Perspectives in Cardiovascular Medicine for the Next Generation", Dr. Masakazu Yamagishi (**Figure 3A**,**B**) stated

Received June 30, 2017; accepted July 6, 2017; released online August 8, 2017
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ISSN-1346-9843

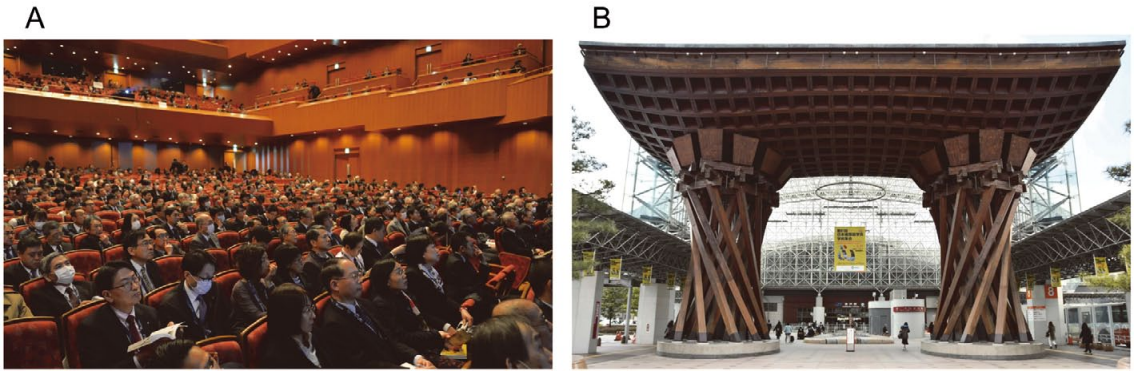

Figure 1. (**A**) Main hall of Ishikawa Ongakudo. (**B**) Tsudumi-mon at Kanazawa Station.

Figure 2. (**A**) Oral presentations. (**B**) Poster presentations. (**C**) Exhibition hall.

that the most important Japanese national health issue through the 1960s had been infectious diseases such as tuberculosis, which his father researched. He showed the data for the transition of national disease in Japan resulting from the change in life style of Japanese and talked about present issues and findings in cardiology with his own department's research.[1,2] Finally he concluded with his perspectives on cardiovascular medicine for the next generation.

Dr. Masabumi Shibuya (**Figure 3C**), honorary professor of The University of Tokyo and President of Jobu University, conducted the Mashimo Memorial Lecture, entitled "Vascular Endothelial Growth Factor and Its Receptor System: A Critical Regulator for Physiological and Pathological Angiogenesis". He talked about the discovery of a new receptor-type tyrosine kinase carrying 7 Ig-domains, named Fms-like tyrosine kinase-1 (Flt-1), and related distinguished work as a pioneer in the field of vascular endothelial research. Dr. Christine E. Seidman (**Figure 3D**), world-renowned professor at Harvard Medical School in

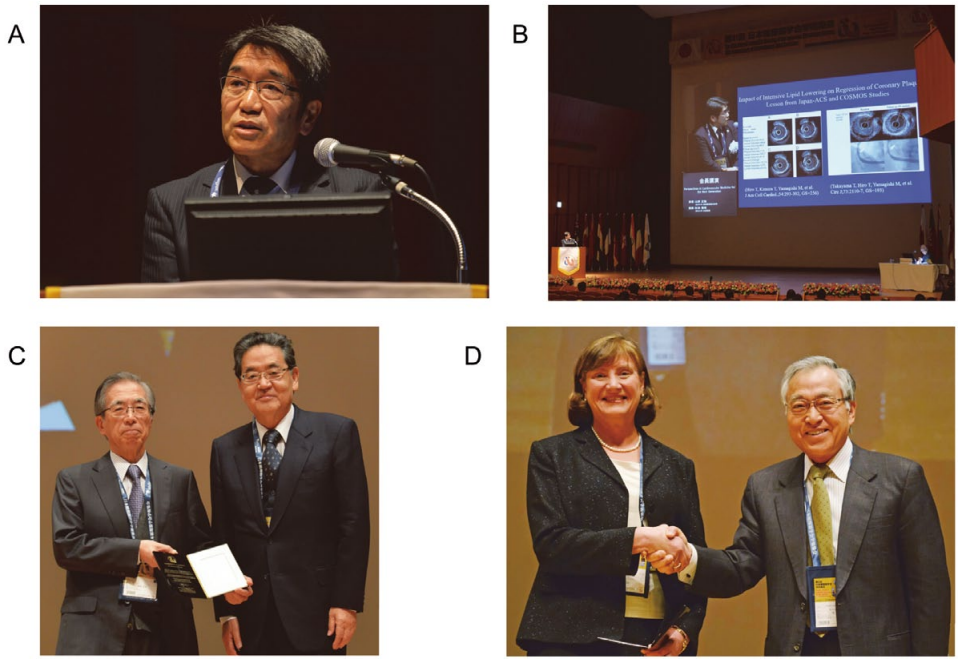

Figure 3. (**A**,**B**) Masakazu Yamagishi, MD, PhD, Professor of Kanazawa University Graduate School of Medicine, presenting the Congress Chairperson's Lecture. (**C**) Masabumi Shibuya with the session's chairperson, Yoshio Yazaki, at the Mashimo Memorial Lecture. (**D**) Christine E Seidman with the session's chairperson, Masatsugu Hori, at the Mikamo Lecture.

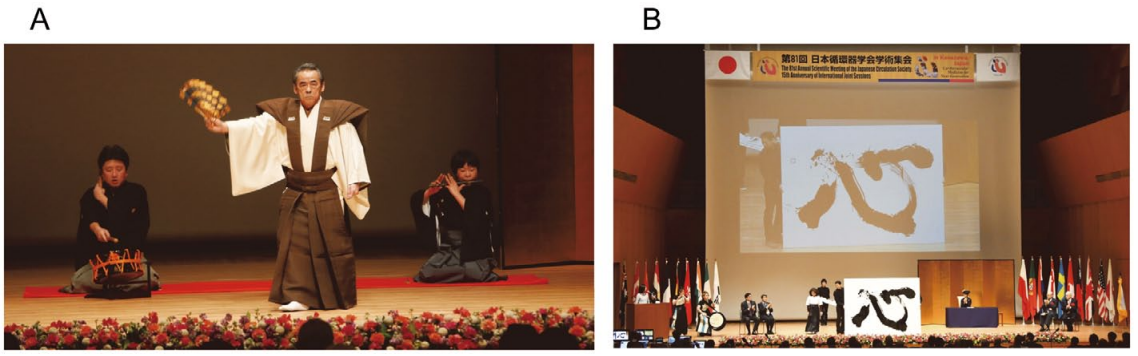

Figure 4. (**A**) Kaga-Hosho-Noh. (**B**) Calligraphy of the "Heart".

the USA, presented the Mikamo Lecture on Genetics of Heart Disease. She was the first female researcher to speak in the Lecture. She reviewed recent insights into the molecular basis of congenital heart defects, the hypertrophic and dilated (DCM) cardiomyopathies,[3] which have had strong impact on further development of basic clinical research.

In this scientific meeting, there were 15 special lectures, 10 plenary sessions, and 20 symposia, 6 joint symposia with foreign academic societies, including the AHA, ESC, ACC, and those of Asian nations, 2 Meet the ESC in Japan sessions, 7 roundtable discussions, 8 topic sessions, 8 controversy sessions, 11 meet-the-expert sessions, 29 morning lectures, and more. In the special lectures, Dr. Anthony N. DeMaria, University of California, USA, gave a lecture entitled "Emerging Advances in Cardiac Ultrasound". He showed the importance of echocardiography, especially intracavitary (intraventricular) flow in pathologic conditions, in the management of cardiac disease.

Opening Ceremony and Kanazawa Declaration

The opening ceremony began with a song "With your eyes", about the spread of AEDs. We welcomed members with a show of Kaga-Hosho-Noh (**Figure 4A**). After greetings from the Congress Chairperson and President of the JCS, it was our great honor to have a message from Her Imperial

Highness Princess Takamado who strongly inspired us in terms of further development of the JCS. There was calligraphy of the "Heart" at the end of the ceremony (**Figure 4B**).

Special Sessions

Kanazawa Declaration: Stop CVD

In Special Session 4, Protection of Youngsters from Cardiovascular Disease: A Recommendation for the Kanazawa Declaration, "Stop CVD" was adopted. The Declaration says in summary that the JCS again realizes the importance of prevention in cardiovascular disease (CVD). The JCS declares that we promote activity to prevent the CVD throughout life and to increase healthy life expectancy through educational activity of CVD prevention for society as a whole, including children and youngsters.

Current and Future Perspectives of Cardiovascular Genetics

One of the major themes of this meeting was the great advancement of the cardiovascular genetics and its clinical perspectives. Dr. Seidman (Harvard Medical School, USA) presented the Mikamo Lecture on the genetics of heart disease, especially cardiomyopathy. Dr. Kathiresan (Massachusetts General Hospital, USA) provided an idea of cardiovascular genetics as discovery, biology, and clinical translation.[4] Dr. Fatkin (Victor Chang Cardiac Research Institute, Australia) reported genetic data for DCM. In addition to lecturers from abroad, 5 Japanese speakers presented original data in Symposium 14 entitled "Precision Medicine Based on Genetic Information". Dr. Tada (Kanazawa University) presented the power of common SNPs predicting coronary heart disease, comparing those of family history, and metabolic risk factors.[5] Dr. Tanaka (Tokyo Medical and Dental University) presented the historical development of GWAS for coronary artery disease (CAD). Dr. Ebana (Tokyo Medical and Dental University) presented a combined analysis using GWAS and array data for detecting associated pathways and shared genomic structure. Dr. Shimizu (Nippon Medical School) showed data regarding the genetics of inherited arrhythmia syndrome. Dr. Nomura (The University of Tokyo) presented data on the genetics of cardiomyopathy. It was emphasized throughout this annual meeting that rare as well as common genetic variations could be useful for the discovery of drug targets, precision medicine, and understanding the biology of human diseases.[6,7]

Current and Future Perspectives on Diagnoses and Therapies for Dyslipidemia

Although lipid-lowering therapies such as statins are effective in lowering low-density lipoprotein cholesterol (LDL-C), a proportion of patients do not achieve target LDL-C goals with statins or are intolerant to statins necessitating other treatment options. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are a new class of agents that reduce LDL-C beyond the maximum achievable LDL-C reductions with statins. Against this background, Plenary Session 1 entitled "Future Perspective on Diagnoses and Therapies for Dyslipidemia" was held with Professor Stein (Metabolic & Atherosclerosis Research Center) and Professor Hirata (Kobe University). Dr. Stein nicely summarized the current understanding of PCSK9 inhibitors. Dr. Kataoka (National Cerebral and Cardiovascular Center) presented data regarding PCSK9 concentration as a marker for familial hypercholesterolemia (FH). Dr. Kawashiri (Kanazawa University) highlighted the efficacy of PCSK9 inhibitors in withdrawing regular LDL apheresis. Dr. Koba (Showa University) reported the importance of small dense LDL particles as a strong residual risk factor. Dr. Toh (Kobe University) presented a novel approach to assessing dysfunctional high-density lipoprotein for cardiovascular risk stratification. The efficacy of PCSK9 inhibitors has been shown in a large RCT, supporting the "the lower, the better" concept in CAD. It was quite interesting that controversy regarding the role of CETP seemed to be concluded in this scientific session.[8]

Current Outstanding Issues in CAD

One of the current topics in the field of CAD is the optimal duration of dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation. In Controversy 5, Professor Lüscher (University Hospital Zurich, Switzerland) gave the keynote lecture entitled "Dual-antiplatelet Therapy after Percutaneous Coronary Intervention: How to Get the Correct Answer". Professor Nakamura (Toho University) summarized the evidence in terms of optimal DAPT duration after DES deployment. Dr. Sakata (Kanazawa University) reported the optimal extended DAPT duration, particularly for patients with acute coronary syndrome (ACS). Dr. Natsuaki (Saiseikai Fukuoka General Hospital) reported short DAPT duration after everolimus-eluting stent implantation. Professor Ako (Kitasato University) presented DAPT and concomitant anticoagulant therapy. Dr. Abe (Dokkyo Medical University) considered the duration of DAPT after zotalimus-eluting stent implantation.

In Symposium 16, Dr. Ueda (Ryukyu University) introduced residual risk in coronary heart disease. Dr. Nakahashi (Kanazawa University) reported decreased LDL-C level on admission as a residual risk in patients with ACS. Dr. Yagi (Tokushima University) suggested the n-3 polyunsaturated fatty acids are a promising target for the prevention of cardiovascular events. Dr. Yamashita showed gut microbiota was both a residual risk and a novel therapeutic target in CAD. Dr. Masuda focused on the accumulation of chylomicron remnants as a residual risk. Dr. Sawano showed the residual risk among Japanese PCI patients and its prognostic implication.

Recent Advances in Heart Failure (HF) Research

The Plenary Session 2 entitled "Challenges for Elucidating the Pathogenesis of Heart Failure: From Genome to Organs" focused on the recent understanding regarding the pathogenesis of HF and future perspectives for novel therapeutic targets. Dr. Otsu (King's College London, UK) lectured on the role of autophagy in the pathogenesis of HF.[9,10] Autophagy is a protein degradation system that plays an important role in cardiac remodeling in response to pressure overload-induced HF. Regulation of the degradation system might be a novel therapeutic target. Dr. Waagstein (Sahlgrenska University, Sweden) spoke on the progression of HF treatment with neurohumoral antagonists such as β-blockers and RAAS antagonists.

Dr. Yamaguchi (Osaka University) reported the function of Bcl-2-like protein 13 (BCL2L13), inducing mitochondrial fission and mitophagy. The mitochondrial quality control regulated by BCL2L13 might be a novel mechanism of HF. Dr. Nagata (Kanazawa University) reported that 'upregulated during skeletal muscle growth 5' (USMG5)

as a component of ATP synthase might regulate ATP production in the myocardium and could be a novel therapeutic target for HF. Dr. Saito (Nippon Medical School) reported that the absence of autophagic vacuoles in the myocardium evaluated with electron microscopy might relate to LV dysfunction and the poor prognosis of HF patients. Dr. Matsushima (Kyushu University) reported that Fyn, a Src family tyrosine kinase, negatively regulated cell death in the failing heart as a sensor and regulator of NOX4-derived reactive oxygen species in mitochondria.

Recent Advances in Cardiovascular Imaging

The sessions on imaging were "Recent Advances in Coronary Imaging and Intervention" (ESC-JCS Joint Symposium), "Imaging guided PCI vs FFR guided PCI" (Controversy 7), "What is the Best Imaging modality for Less Invasive Treatment of Structural Heart Diseases" (Plenary Session 7), "Cardiovascular Molecular Imaging in Future" (Topic 5), and "How to Enhance the Intravascular Ultrasound in Future" (Special Session 13). Special Session 13 focused on the future potential of coronary plaque imaging. Dr. Matsuo (Gifu Heart Center) presented the usefulness of fraction flow reserve CT angiography and Dr. Noguchi (National Cerebral and Cardiovascular Center) showed the utility of coronary magnetic resonance angiography to noninvasively assess the characteristics of coronary plaque.

Management of Arrhythmia: Basic and Clinical Point of Views

Many significant papers were also reported in the field of arrhythmia. In the Late Breaking Cohort Studies 2, biomarkers and genetic markers for cardiovascular events were discussed. Dr. Yamagata (National Cerebral and Cardiovascular Center) reported that probands with Brugada syndrome (BrS) and SCN5A mutations had more conduction abnormalities on ECG, and exhibited a higher risk for cardiac events.[11] In the Late Breaking Cohort Studies 4, environmental factors of atrial fibrillation (AF) and treatment were discussed. Dr. Okumura (Hirosaki University) et al combined the data of 5 major AF registries in Japan and estimated significant risk factors for ischemic stroke in non-valvular AF patients. Prior stroke, low body weight (<50 kg), age (>75 years), AF type (permanent/persistent), and hypertension (HT) were significant risk factors for ischemic stroke. C-statistics for ischemic stroke using the novel scoring system, which consists of these factors, was higher than that using the CHADS2 score.

In symposium 15, both the utility and limitation of new approaches for cardiac arrhythmia were discussed. Dr. Tsuchiya (EP Expert Doctors-Team Tsuchiya) reported on rotor mapping-guided voltage-based ablation for persistent AF. They showed that this ablation technique revealed the arrhythmogenic low-voltage zone with regionally meandering rotors and was effective for the treatment of persistent AF.

Cardiovascular Basic Sciences

In addition to developments in clinical cardiology, basic research is still important in terms of seeking the basic mechanism of cardiovascular diseases. For this purpose, a lot of programs were incorporated during the scientific meeting. The topics regarded the role of vessel endothelium, with a couple of sessions including the Mashimo Memorial Lecture providing strong messages about the role of endothelial cells and the related tissues.[12]

Diagnosis and Treatment of Cardiomyopathy

Emerging technologies in genome sequencing enabled us to understand the underlying pathogenesis of inheritable cardiomyopathy. In the Mikamo Lecture, Dr. Seidman (Harvard Medical School, USA) reviewed recent insights into the molecular basis of cardiomyopathies. The limitations of gene testing for DCM are being overcome by next-generation sequencing techniques, which have revealed that titin mutations increase the risk for clinically significant arrhythmias in DCM patients. Gene mutations also cause hypertrophic cardiomyopathy (HCM).[13] Rare sarcomere gene variants, which were found in 0.6% in the general population, were associated with increased risk for adverse cardiovascular events even before formation of hypertrophy, suggesting that screening of these variants may improve risk stratification in the general population from the viewpoint of preemptive medicine. Dr. Teramoto (Kanazawa University) presented supportive data for detecting mutation-positive HCM patients using cardiac magnetic resonance in Symposium 14 entitled "Cardiomyopathies: A Diagnostic and Therapeutic Update".

Regeneration Medicine in Cardiology: Induced Pluripotent Stem Cells (iPSCs)

Human iPSCs are generated from patients with various kinds of genetic diseases and can be used as disease models in vitro. In Special Session 6 entitled "Present Situation and Prospect in Clinical Application of Disease-specific Human iPSCs", some researchers presented the molecular mechanism of cardiac arrhythmia. Dr. Yuasa (Keio University) and Dr. Hisadome (Tottori University) reported the characteristics of mutated ion channels using human iPSCs derived from patients with long QT syndrome and BrS. Dr. Yamashita (Kyoto University) showed a 3D heart tissue model of drug-induced torsades de pointes using human iPSCs-derived cardiac tissue sheets. Human iPSCs are a useful model for understanding human arrhythmic diseases.

Role of Cardiologists in Emergency Medicine

In Controversy 1 entitled "Cardiopulmonary Resuscitation for the Elderly in Super-aging Society", the next steps to reduce undesired cardiopulmonary resuscitation for elderly out-of-hospital cardiac arrest (OHCA) patients were discussed. Dr. Funada (Kanazawa University) reported that the annual OHCA events increased each year, especially, in patients aged ≥75 years using Japanese OHCA registry from 2005 to 2014.[14] Dr. Hamanabe (Tokyo Metropolitan Bokutoh Hospital) suggested that, given limited medical resources, the emergency medical service system in Japan might eventually collapse. Dr. Minooka (Minooka Clinic and Tokyo University) introduced a Japanese version of 'physician orders for life sustaining treatment (POLST)' that is advocated as being of paramount importance to alleviate and resolve ethical dilemmas relating to end-of-life care. Dr. Ozawa (Megumi Zaitaku Clinic) as a home care physician proposed that medical staff should learn how to support elderly patients not only regarding life extension but also end-of-life care as a whole. Dr. Inaba (The University of Tokyo) demonstrated the Japanese view of life and death and a history of medical treatment in Japan. Dr. Nonogi (Shizuoka General Hospital) and Dr. Yahagi (The University of Tokyo), as the Chair, summarized that if we did not reach a conclusion within the session, medical staff from each field would need to

Figure 5. Commemorative photograph of the doctors and staff of the Department of Cardiovascular and Internal Medicine, Kanazawa University.

cooperate and continue discussion about this issue.

Metabolic Medicine in Cardiology: Diabetes Mellitus and HT

Cardiovascular disease is the major cause of death and complications in patients with type 2 diabetes mellitus (DM). Recent trials evaluating a sodium-glucose cotransporter 2 inhibitor (SGLT2i), a new oral hypoglycemic agent, have shown reduced death from cardiovascular causes.[15] In Symposium 17, entitled "Heart Failure and Diabetes Mellitus", Dr. Laufs (Universitatsklinikum des Saalandes, Germany), an invited lecturer, presented novel data on the interaction of DM and HF events. New insights on the mechanism of HF induced by DM were also discussed in the Symposium. Team Medical Care Session Symposium 2 was provided jointly with the Japan Diabetes Society. For prevention of the onset of DM and cardiovascular complication, it is necessary for medical staff to cooperate and provide guidance about diet and lifestyle to patients. The members, including diabetes nurse educators and registered dietitians, discussed the importance of a team approach for diabetes management.

As for HT, Symposium 8, entitled "New Devices and methods for Treating Resistant Hypertension", was held in accordance with the theme of the meeting "Cardiovascular Medicine for the Next Generation". Professor Esler (Baker IDI Heart and Diabetes Institute, Australia) gave the keynote lecture on device revolution in severe and resistant HT therapy. Dr. Murai (Kanazawa University) reported how to assess renal sympathetic nerve activity to improve conventional renal denervation. Professor Ogita (Shiga University of Medical Science) showed the significance of dipeptidyl peptidase III. Dr. Koriyama (Osaka University) introduced a DNA vaccine for HT. Dr. Shiina (Tokyo Medical University) presented a renal sodium handling abnormality in obstructive sleep apnea-related HT.

In Featured Research Session 4 (HT), Dr. Harada (Nagoya University) reported that low skeletal muscle mass was an independent predictor of major adverse cardiovascular events in chronic kidney disease patients without hemodialysis. Dr. Gong (Zhongshan Hospital, China) showed cardiomyocyte secretory β-2 microglobulin contributes to myocardial fibrosis during pressure overload. Dr. Lim (Korea National Institute of Health, Korea) presented cardiovascular events and achieved pressure levels in hypertensive patients with and without type 2 DM in Korea. Professor Chinushi (Niigata University) revealed arrhythmogenesis in enhanced renal sympathetic activity and the therapeutic option of the proximal renal artery ablation for ventricular arrhythmia treatment. Dr. Takeda (Kanazawa University) presented the effect of a high-salt diet on angiotensinogen gene epigenesis in salt-sensitive hypertensive rats.

Current Perspectives in Cardiovascular Surgery

There were several sessions discussing the recent developments in cardiovascular surgery, for which is also important to consider the collaboration of physicians and surgeons. Minimally invasive cardiovascular surgery has become a common procedure in every field of cardiovascular surgery. Under these conditions, imaging during surgery can provide quite important information regarding the result and complications after surgery.[16] There was also discussion about the results of the Japan Cardiovascular Surgery Database.[17]

Pediatric Cardiology

As for pediatric cardiology, there were several programs, including the management of adult congenital diseases, Kawasaki disease and perinatal cardiac diseases. Particularly, there was quite interesting discussion regarding the cardiovascular involvement of rare diseases such as Danon disease.[18]

Closing Remarks

The 81st Annual Scientific Meeting of the JCS successfully offered future perspectives in cardiovascular medicine for the next generation. We believe that all participants were deeply satisfied with this meeting as well as the ambience of Kanazawa. We believe we completed our mission for this scientific meeting when every place was fully occupied with participants having robust discussion. This report is based on the viewpoints of both the authors and contributors. **Figure 5** is a commemorative photograph of the doctors and staff of the Department of Cardiovascular and Internal Medicine, Kanazawa University.

Acknowledgments

We thank Masayuki Takamura, MD, Kunio Ohta MD, Yoshifumi Sai, PhD, Masahiko Zuka, MD, Takumi Taniguchi, MD, Masahito Yamada, MD, and Yoh Takuwa, MD at Kanazawa University; Toshiaki Akita, MD, Kouji Kajinami, MD at Kanazawa Medical University; Naoki Yoshimura, MD at University of Toyama; and Takaaki Koshiji, MD at University of Fukui for their scientific advices. We also thank contributors listed below for their excellent reports regarding the scientific meeting, Kenji Sakata, MD, Tetsuo Konno, MD, Akira Funada, MD, Hayato Tada, MD, Chiaki Nakanishi, MD, Yoji Nagata, MD, Ryota Teramoto, MD, Ayako Wakayama, MD, Mitsuhiro Kometani, MD, Daisuke Aono, MD at Kanazawa University. We also thank all the staff and executive board members of the JCS and the staff of the Japan Convention Service Corporation and Ms. Yumiko Takase at Kanazawa University for their enthusiastic contributions to this scientific meeting.

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