From August 27th to 31st, the 2016 Annual Congress of the European Society of Cardiology (ESC 2016) was held in Fiera di Roma, Italy. Despite the socially unstable situation, more than 32,000 attendees, including clinical physicians, basic researchers, medical students, and paramedical personnel, as well as 5,000 exhibitors from 106 countries gathered in this historical city to share the latest findings and to discuss the present issues in cardiovascular medicine. There were scientific sessions, including 28 Hot Lines, 26 clinical trial updates, 24 registry studies, and 5 clinical practice guideline sessions. Japan had 1,170 attendees, with 1,743 submitted and 670 accepted abstracts, including the NIPPON trial presented in the hotline session. From 2011 to 2016, Japan has been the first abstract submitter and has had the most abstracts accepted, which indicates the great contribution of Japanese cardiologists and the Japanese Circulation Society. This report briefly introduces the key presentations and highlights from the ESC 2016 Scientific Sessions.

Key Words: Cardiology; Congress report; European Society of Cardiology

The Annual Congress of the European Society of Cardiology 2016 (ESC 2016) was held in Fiera di Rome from August 27th to 31st, 2016 (Figure 1). Surprisingly, it was the first time the world’s largest and leading cardiovascular society meeting had been held in this historical city.

Despite some unstable social conditions such as Brexit, terrorist activities, and the huge earthquake that struck Amatrice, a remote village 100 kilometers north-east of Rome just 2 days prior, the Congress attracted more than 32,000 medical professionals from 106 countries. During the 5 days, over 150 topics were discussed in 500 sessions, including 28 clinical Hot Line studies, 26 clinical trial updates, 24 registry studies, and 12 basic and translational science Hot Lines. In all 4,594 abstracts were selected from more than 11,000 submissions. This report presents some key abstracts and the highlights from the ESC 2016 Congress.

Opening Showcase

“There is no end. There is no beginning. There is only the infinite passion of life.” In the welcome address, Genevieve Derumeaux, Chair of the Congress Program Committee cited that famous phrase by the Italian film director, Federico Fellini, and emphasized all the advances in cardiovascular medicine there have ever been and should be achieved with the continuous work of medical professionals.

As new endeavors, the ESC Congress 2016 offered a new type of session called the Gladiator’s Arena in tribute to ancient Rome. In that session, there were heated, interactive debates between opinion leaders followed by voting by the audience.

The Spotlight of the ESC Congress 2016 was “The Heart Team”, which stressed the importance of teamwork and interaction among all professionals in treating cardiovascular disease (CVD) patients. In some Heart Team sessions, specific clinical cases such as aortic disease, athletic evaluations, metabolic disorders, and strokes were presented with films recorded in advance and the audience saw how the team worked well via cross-talk among all those involved.

Andreas Gruntzig’s Lecture

One of the greatest achievements in the care of CVD is the progress in catheter interventions in patients with coronary artery disease (CAD). Jean Fajadet (Toulouse, France) reviewed the history of the coronary interventions and ongoing challenges in Andreas Gruntzig’s Lecture entitled “From balloon to bio-resorbable scaffold: a 40-year journey in coronary intervention”, held on August 28th.

Fajadet engaged in the early BENESTENT, which was the first trial to show a lower rate of restenosis after coronary stenting compared with balloon angioplasty. Since then, he has played a significant role in over 40 clinical trials such as RAVEL, ENDEAVOR II, E-SIRIUS, and COMPARE ABSORB. He has also dedicated himself to education. He co-established the Euro-PCR for discussion, training, and sharing of experiences, which is now one of the largest coronary intervention groups with more than 12,000 attendees at the annual meeting. Nowadays, the remaining challenge is the metallic cages left in the
coronary arteries after releasing all the drugs. The latest development has been bioresorbable scaffolds, which release the drugs when restenosis prevention is required, then disappear to offer a more natural coronary environment. Although it is sometimes difficult to demonstrate any further significant advantage after the great advances in coronary intervention, efficacy and safety would be of great interest.

**Hot Line Sessions**

**DANISH**

To assess the effect of prophylactic implantable cardioverter defibrillator (ICD) implantation on clinical outcome, 1,116 patients with symptomatic systolic heart failure (HF) affected by a non-ischemic etiology were randomized into 2 groups: usual care (n=560) and an additional ICD (n=556). In both groups, 90% of the patients were taking angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-receptor blockers (ARBs), 90% had β-blockers, and 58% underwent cardiac resynchronization therapy (CRT). During the follow-up period of 5.6 years, all-cause death, defined as the primary endpoint, occurred in 131 patients in the usual care group and in 120 patients in the ICD group, which revealed no statistically significant difference (hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.68–1.12, P=0.28). The incidence of the secondary endpoint of sudden cardiac death was significantly lower in the ICD group, compared with the usual care group (HR 0.50, 95% CI 0.31–0.82, P=0.005).

The presenter, Lars Køber (Copenhagen, Denmark) showed the results of an additional analysis that suggested relatively younger patients may have the benefit of a prophylactic ICD implantation, and there was no difference in the ICD effect between patients with and without CRT.

**REM-HF & MORE-CARE**

Despite the advances in therapy, HF remains associated with a high risk of mortality and morbidity. The clinical question of whether the remote transmission of data obtained by cardiac implantable electronic devices (CIEDs) provides a beneficial outcome in HF patients has been of interest. The results of 2 clinical trials aiming to elucidate that question were presented.

In the REM-HF trial, in 9 English hospitals, 1,650 HF patients (70 years old, 86% male, NYHA class II–III, ejection fraction [EF] 30%) were recruited and randomized to usual care alone or usual care with weekly remote monitoring. The study was well controlled, completed with a more than 99% follow-up rate. ACEIs or ARBs, β-blockers, and CRT were given in 91%, 90%, and 53% of the patients, respectively. In the total of 3,574 remote monitoring incidences, 599 responses were performed. During a median follow-up period of 2.8 years, all-cause death and cardiovascular hospitalization as primary endpoints were neutral. The HR of the remote monitoring group was 1.01 (95% CI 0.87–1.18, P=0.87). Furthermore, there was no significant difference between the 2 groups for any of the secondary endpoints, and none of the baseline characteristics identified a group in which remote monitoring was more efficient than usual care. The presenting investigator, Martin Cowie (London, UK), concluded that the addition of weekly remote monitoring of CIEDs to usual care did not reduce the risk of death or unplanned hospitalizations and he commented that with high-quality HF services, CIEDs no longer provide additional benefit.

The next presenter, Giuseppe Boriani (Modena, Italy), presented the results of the MORE-CARE study. In all, 917 HF patients with CRT-D devices were randomized to remote and in-office device checks or the standard arm with all checks performed in the office. At a median follow-up period of 2.8 years, no difference between the study arms was found for the primary endpoint including all-cause death. CVD or device-related hospitalizations (29.7% vs. 28.7% HR 1.02, 95% CI 0.80–1.30, P=0.889) or its components. However, remote monitoring was related to healthcare and travel cost savings (2,899 euros per 100 patients and 145 euros per patient over 2 years).
ANTARCTIC
Platelet function testing is currently recommended in many countries to optimize the choice and dose of the antiplatelet drugs, especially in high-risk patients. The previous GRAVITY and ARCTIC studies both failed to show a significant advantage of platelet monitoring: low risk and elective stent-PCI patients were assigned to 2 groups (standard and increased doses of clopidogrel) based on platelet reactivity and there was no difference between them. To validate these results with a different medication and a more unstable patient population, ANTARCTIC enrolled 877 patients aged ≥75 years with coronary stents against ACS. All were started on a fixed dose of prasugrel (5 mg/day). In all, 442 patients were randomized to the conventional fixed dose therapy arm and 435 to the monitoring arm. Patients in the monitoring arm received 5 mg of prasugrel for 14 days, then the dose of prasugrel was adjusted according to platelet reactivity. In the monitoring arm 44.8% of the patients required a dose adjustment and were considered as over- or undertreated. However, there was no significant difference in the primary endpoint (bleeding, SV death, MI, urgent revascularization, stent thrombosis, and stroke) between the 2 groups (27.8% in the conventional group and 27.6% in the monitoring group). “The ANTARCTIC and ARCTIC studies confirmed that platelet reactivity monitoring failed to improve ischemic and safety outcomes,” concluded Senior Investigator Giles Montalescot (Paris, France), and he expected the guidelines and practice to change as a result.

CE-MARC 2
The results of the CE-MARC2 trial showed that cardiovascular magnetic resonance (CMR) and myocardial perfusion scintigraphy (MPS) could reduce unnecessary angiography without any penalty. The Principal Investigator, John Greenwood (Leeds, UK), said “Despite recommendations for non-invasive imaging in international guidelines, invasive angiography is too widely used,” in order to explain the background of the CE-MARC2 study. “Most of the populations with chest pain will have no significant obstructive CHD.” To compare CMR, MPS, and the National Institute for Health and Care Excellence (NICE) guidelines for reducing any unnecessary angiography, 1,202 symptomatic patients with suspected CHD were randomized into 3 groups (481 patients in the CMR, 481 patients in the MPS, and 240 patients in the NICE guideline group). The patients in the NICE guideline group were allocated to coronary CT, MPS, and direct coronary angiography according to their likelihood of CHD: low, intermediate, and high. The primary endpoint was unnecessary angiography defined by the absence of any significant stenosis measured by FFR and quantitative coronary angiography. In the NICE guideline group, 43% had direct angiography, 18% CMR, and 16% MPS. As a result, within 12 months 22% of the study subjects underwent coronary angiography. The CMR strategy group had fewer primary endpoints of an unnecessary angiogram, compared with the NICE guideline group, while there was no significant difference between the CMR and MPS groups. There was no significant difference in the secondary endpoint of MACE and positive angiography among the 3 groups (9.8% in the CMR, 8.7% in the MPS and 12.1% in the NICE group). This study also considered whether the CMR strategy had any financial benefit, and the results were expected.

ODYSSSEE ESCAPE
Currently, inhibition of the PCSK9-mediated hepatic catabolism of low-density lipoprotein (LDL) is attracting significant interest. Just after the presentation of Lpa apheresis for refractory angina, another apheresis study was presented by Patrick Moriarty (KS, USA). ODYSSEY ESCAPE investigated whether alirocumab, a fully human monoclonal antibody to inhibit PCSK9, can reduce the need for apheresis. In all, 62 patients with heterozygous familial hypercholesterolemia (HeFH) started with apheresis, and then randomized into the alirocumab (n=41) and placebo (n=21) groups. The apheresis rate was fixed until week 6 then adjusted from weeks 7–18, according to the individual LDL response. The change in the apheresis rate between weeks 1–6 and weeks 7–18 was -53.7% in the alirocumab group and +1.6% in the placebo group (P<0.0001). Furthermore, LDL decreased by 50% from baseline in the aliroximab group while it increased by 2% in the placebo group. Last of all, in his conclusion, Moriarty said he expected that “Alirocumab may provide patients with HeFH a chance to terminate or reduce the frequency of apheresis.”

NORSTENT
Current ESC guidelines recommend new drug-eluting stents (DES) over bare metal stents (BMS) as the default for coronary revascularization. Besides the idea of releasing anti-restenosis drugs continuously, the stent itself has been improved with new designs, materials, and thinner struts. Thus, based on the need for re-evaluation of modern BMS and DES, NORSTENT, the largest stent study, was conducted. In a total of 9,013 patients with stable or unstable CAD indicated for PCI were randomized into the DES (n=4,504) and BMS (n=4,509) arms, respectively. The vast majority (96%) of the DES used in the study were everolimus- or zotarolimus-eluting stents. The primary outcome was a composite of death from any cause and non-fatal spontaneous MI. The results at 6 years showed there was no significant difference in the primary outcome (16.6% in the DES and 17.1% in the BMS group) or all-cause death between DES and BMS. Also, there was no difference in the frequency and magnitude of angina-related symptoms such as physical limitation and quality of life. The 6-year rate of any repeat revascularization was higher in the DES group than in the BMS group. However, the difference was smaller than previously expected (16.5% vs. 19.8%, P=0.001). In conclusion, Kaare Bonaa (Tromso, Norway) said “Patients treated with DES do not live longer and do not live better than patients treated with BMS.”

ENSURE-AF
Current guidelines recommend 3 weeks of therapeutic anticoagulation for patients with atrial fibrillation (AF) undergoing cardioversion. Vitamin K antagonists (VKAs) such as warfarin have been standard anticoagulation drugs; however, they need titration with regular monitoring, and it takes time to reach the PT-INR within the therapeutic range of 2.0–3.0. Thus, anticoagulation with VKAs often delays cardioversion for at least several weeks. Currently available non-vitamin K-dependent oral anticoagulants (NOACs) are considered as a safe and effective alternative to VKAs, and there has been limited data on cardioversion. ENSURE-AF was the largest prospective randomized trial to compare the efficacy and safety of the NOAC, edoxaban, with conventional therapy (warfarin/enoxaparin) in patients with non-valvular AF (NVAF) undergoing cardioversion, and the results were presented by Andreas Goette (Paderborn, Denmark). In total, 2,199 NVAF patients were recruited from Europe and the USA and randomized into edoxaban (n=1,095) and warfarin/enoxaparin (n=1,104) groups. Notably, patients in the edoxaban group could start edoxaban as early as 2h prior to the cardioversion if they had access to transesophageal echocardiography (otherwise 3 weeks prior to
the cardioversion). A total of 988 and 966 patients had electrical and spontaneous cardioversions, respectively. The primary efficacy evaluation item was the incidence of the composite endpoints of stroke, MI, and CV death at day 28, which occurred in 0.5% in the edoxaban group and 1.0% in the conventional therapy group without any significant difference. There was also no difference in the primary safety evaluation items (composite of major and clinically relevant non-major bleeding at 30 days).

New Practice Guidelines

In 2016, the ESC presented 4 new ESC Clinical Practice Guidelines on HF, AF, CVD prevention, and dyslipidemia. Moreover, the ESC released 1 position paper on cardio-oncology, which should be a great issue in cardiovascular disease in the near future.

Heart Failure

New guidelines stress the potential of ACEIs, β-blockers, and statins in patients with arterial hypertension and CAD. HF with a mid-range EF (HFmrEF) is added as a new category to the existing categories of HFrEF and HFrEF (reduced and preserved EF, respectively). At present, therapeutic strategies to improve prognosis are established only in HFrEF. ACEIs, β-blockers, and mineralocorticoid receptor antagonists are the mainstay of therapy. If patients on optimal therapy are still symptomatic and have an EF <35% even after 3 months, presently 3 options can be considered. The first is using a combination of an angiotensin-receptor neprilysin inhibitor and an ARB (based on the PARADIGM-HF trial). CRT is also an option suitable for patients in sinus rhythm, and with a left bundle branch block QRS morphology and duration of >130 ms. The last option is using ivabradine for patients in sinus rhythm and with an elevated heart rate of >70 beats/min. Unfortunately, HF remains an unmet medical challenge and despite increasing insights, there are no major advances from the 2012 version for patients with HFrEF. In acute HF, time is an important factor. Prompt evaluation of perfusion and congestion will guide the initial therapy, and the acronym CHAMP (coronary, hypertensive crisis, arrhythmia, mechanical cause, and pulmonary embolism) will help clinicians take immediate action.

Atrial Fibrillation

The 2016 guidelines emphasize the importance of the early detection of asymptomatic AF. The diagnosis of AF requires a documented ECG (IB). In all patients older than 65 years, intensive ECG screening for AF is recommended (IB). Except for patients with the lowest risk of a stroke, almost all patients will benefit from anticoagulation (IA). NOACs are the frontline anticoagulation therapy (IA). Avoiding and minimizing modifiable bleeding risks is important; however, considering the overlap of stroke and bleeding risk, this guideline does not recommend any specific bleeding score. Catheter ablation is an option for rhythm control therapy in anticoagulated patients with a symptomatic recurrence of AF (IA for paroxysmal, IIaC in persistent), and is becoming a frontline alternative in selected patients.

Cardiovascular Disease Prevention

These guidelines were released in May this year, as a result of close communication among 10 societies. One of the new aspects added is a population-based approach to CVD prevention. In this chapter, the importance and measures aiming at the promotion of a healthy lifestyle are presented. The recommendations include a healthy diet, sufficient physical activity, and avoiding smoking through regulations, economic incentives, health education, and so on. The new guidelines focus on the total CV risk factors in specific groups of individuals such as

Figure 2. Contribution of Japanese Circulation Society (JCS). (A) Professor Nakamura presents the results of the NIPPON study in the Hot Line session. (B) The ESC-JCS Leadership Meeting was held on August 28, 2016. (C) Many cardiovascular professionals stopped at the exhibition booth to see our training stimulator. (D) The JCS secretaries convinced many foreign professionals to attend the upcoming JCS 2016 meeting to be held in Kanazawa.
women, younger and elderly persons, ethnic minorities, and patients treated for cancer.

Dyslipidemia
In the 2016 ESC/EAS (European Atherosclerosis Society) guidelines, the importance of assessing the total CV risk was discussed. Four categories (low, intermediate, high, and very high) were determined, and the guidelines also provided a table in which an intervention strategy for each category was described. Screening for dyslipidemia is recommended in all men >40 years and in women >50 or postmenopausal. Apolipoprotein B is proposed as an alternative risk marker in subjects with high triglyceride levels. Although the AHA/ACC guidelines 2014 have abandoned treatment targets, the ESC guidelines took a distinct approach to retain them. In patients with a very high CV risk, the recommended LDL-C goal is <70 mg/dl or a >50% reduction if the baseline LDL-C level is between 70 and 135 mg/dl. The benefit and potential side effects of statins are also argued. In the 2016 version, ezetimide and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are introduced for the first time. The effect of ezetimide is small but significant. PCSK9 inhibitors are introduced as very powerful LDL-C lowering drugs.

Contribution of the JCS to ESC 2016
The contribution of the Japanese Circulation Society (JCS) to the ESC is becoming greater year by year (Figure 2). The number of attendees at the ESC Congress was 605 in 2010 and has doubled in 2016. The JCS is also the first abstract submitter and has had the most accepted abstracts from 2011 to 2016. This year 670 abstracts were accepted and 1,170 Japanese medical professionals attended the ESC meeting in Rome. In the Hot Line session, Masato Nakamura (Tokyo, Japan) presented the results of the NIPPON trial, which showed the non-inferiority of 6 months of dual antiplatelet therapy (DAPT) compared with 18 months of DAPT. Osaka University also attended as an exhibitor to demonstrate a unique training simulator. Some centers are already participating in the EuroObservational Research Programme and the number should increase in the near future. During the Congress, the ESC-JCS Leadership Meeting was held at the ESC headquarters on August 28, 2016. Professor Issie Komuro (Tokyo, Japan), Professor Takashi Akasaka (Osaka, Japan), and Professor Yasushi Sakata (Osaka, Japan), and the next president, Professor Jeroen Bax (Leiden, the Netherlands) about the importance of a closer relationship between both leading cardiovascular societies.

Closing Remarks
The ESC 2016 Congress closed on August 31st with a historical event. His Holiness Pope Francis visited to address attendees at the meeting. He came in the popemobile and received a stethoscope as a gift from the cardiologists. Pope Francis told the cardiologists that he was thankful for their work, as “I’ve been in the hands of some of you”, and added, “You look after the heart. How much symbolism is enshrined in this word! How many hopes are contained in this human organ! In your hands you hold the beating core of the human body, and as such your responsibility is very great!”. His entire address is available at http://popevisit.escardio.org/, and is an encouraging message to all cardiologists.

Now, undoubtedly, the ESC presents the world’s leading congress, which provides the newest findings, relevant information, and updated guidelines. We hope this brief report stimulates young doctors in some way and drives them to submit >2,000 abstracts to the upcoming ESC 2017 Congress in Barcelona. It would be a great pleasure to discuss many issues there.

Acknowledgments
The authors thank all the members of the Osaka Cardiovascular Club (OCVC) who attended the ESC 2016 Congress for their suggestions and comments. We also thank Dr Patrick T. Siegrist and Mr John Martin for editing this manuscript.

Disclosures
Y.S. is a Fellow of the ESC (FESC). The authors have no conflicts of interest to disclose.

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