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The 453rd International Symposium on Therapy

The 453rd International Symposium on Therapy was held by the Zoom Webinar on March 17, 2022. Dr. Tsutomu Yamazaki, Director of the International Medical Society of Japan (IMSJ), presided over the meeting.

New catheter treatment in the cardiovascular field

Introductory Message from the Chair

Tsutomu Yamazaki, MD, PhD
Director, IMSJ

The program was structured with the following theme: New catheter treatment in the cardiovascular field.

Lectures were given by the following professors on the following topics: Koichiro Sugimura, MD, PhD, Professor, Department of Cardiology, International University of Health and Welfare, Narita Hospital, on Novel Therapeutic Approaches for Chronic Thromboembolic Pulmonary Hypertension and Akio Kawamura, Chairman and Professor, Department of Cardiology, International University of Health and Welfare, School of Medicine, on Percutaneous Closure of Patent Foramen Ovale.

Designated as an intractable disease, pulmonary hypertension is common in young women. Among the various types of pulmonary hypertension, chronic thromboembolic pulmonary hypertension, commonly referred to as CTEPH, is thought to have a relatively good prognosis. Professor Sugimura demonstrated that balloon pulmonary angioplasty, which has been further developed in Japan following its initial development, has largely contributed to the relatively good prognosis of CTEPH. Professor Kawamura explained that

while paradoxical embolism caused by patent foramen ovale is well known as a textbook topic, it is also a significant clinical challenge as it is considered to be one of the causes of cerebral infarction of undetermined cause in young adults. He demonstrated that percutaneous closure can be safely performed in a relatively short time for treating patent foramen ovale. The lectures enabled us to gain knowledge about the latest advances in the rapidly advancing catheter treatments.

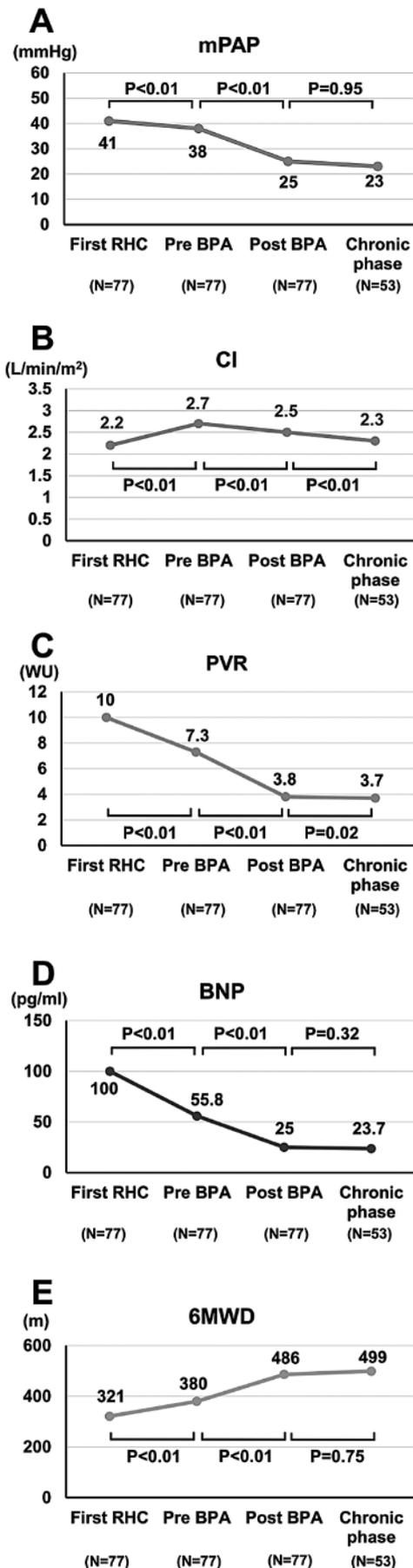
Lecture I

Novel Therapeutic Approaches for Chronic Thromboembolic Pulmonary Hypertension

Koichiro Sugimura, MD, PhD
Professor
Department of Cardiology
International University of Health and Welfare
Narita Hospital

Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by persistent pulmonary arterial obstruction due to organized thrombus and fibrous tissue. Although balloon pulmonary angioplasty (BPA) improves hemodynamics and short-term prognosis in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), the long-term effects of BPA and procedure-related complications remain to be fully elucidated. From July 2009 to October 2016, we performed a total of 424 BPA sessions in 84 consecutive patients with inoperable CTEPH. We used 3D reconstructed computed tomography

to determine target lesions of pulmonary arteries and optical computed tomography to select balloon size, if needed. Before we started BPA treatment, all patients had been treated with appropriate combination therapy with vasodilators and warfarin. In 77 patients (92%) who completed the BPA treatment (65 ± 14 [SD] y.o., male/female 14/63), we examined hemodynamics parameters, exercise capacity and serum levels of brain natriuretic peptide (BNP) and compared the data before first BPA session and those at 6 months after last BPA session. Moreover, in 53 patients (63%), we examined the same parameters in the chronic phase (at the time of >12 months after last BPA sessions. Although medical treatment improved hemodynamics and exercise capacity, the BPA treatment significantly and additionally improved mean pulmonary arterial pressure (38 ± 10 to 25 ± 6 mmHg), pulmonary vascular resistance (7.3 ± 3.2 to 3.8 ± 1.0 Wood units) and 6-min walk distance (380 ± 138 to 486 ± 112 meters) (all $P < 0.01$), and the improvements persisted throughout the follow-up period (43 ± 27 months) ($N = 53$). To examine the BPA procedure-related complications, all 424 sessions in 84 patients were reviewed. Pulmonary arterial dissection and hemoptysis were noted in 30 (7%) and 60 sessions (14%), respectively. Hemoptysis was noted in 45 sessions during BPA procedures and in 15 sessions after the procedure. None of the patients with PA dissection needed any additional trans-catheter or surgical procedures or NPPV. NPPV was used in 33 sessions (8%); 29 for hemoptysis, and 4 for segmental pulmonary edema. NPPV was used for hemostasis except for 4 cases with segmental pulmonary edema. Only one patient with hemoptysis subsequently required oral intubation and mechanical ventilation due to aspiration pneumonia. In all the remaining patients, NPPV effectively controlled hemoptysis and improved pulmonary edema. Furthermore, 5-year survival was 98.4% without peri-procedural death (only one patient died of colon cancer). These results indicate that BPA improves hemodynamics and exercise capacity in inoperable CTEPH patients with acceptable complication rate and that the beneficial hemodynamic effects of BPA persist for years with resultant good long-term prognosis.



Lecture II

Percutaneous closure of patent foramen ovale

Akio Kawamura
Chairman and Professor
Department of Cardiology, School of Medicine
International University of Health and Welfare

Paradoxical embolism is a condition where blood clot formed in the venous circulation is embolized to the arterial circulation through right-to-left shunt. Without right-to-left shunt,

blood clot migrating into the heart is captured at the pulmonary vasculature, the condition called pulmonary embolism. If the clot is small in size, that does not cause big clinical problem. However, even tiny thrombus migrating into the arterial circulation can cause grave organ damage (stroke, myocardial infarction, renal infarction, etc.) Patent foramen ovale has been on the spotlight as one of the causes of paradoxical embolism. This anatomical anomaly is also associated with platypnea-orthodeoxia syndrome (hypoxia worsened in the upright position), migraine headache, or diver's disease.

As a baby grows in the womb, the foramen ovale is present in between the right and left top chambers of the heart (atria). It is a vital anatomy for a baby to deliver oxygen rich blood from mother to the brain. It normally closes during infancy. When the foramen ovale doesn't close, it's called a patent foramen ovale. It is estimated that 10-25% of adults have patent foramen ovale. Interestingly, patent foramen ovale has been found in about 50% of patients suffering from stroke without clear cause (atherosclerosis, atrial fibrillation, etc.). In Japan, paradoxical embolism was found in 5% of acute stroke patients. Every year, more than 200,000 patients develop stroke in Japan, and 5% of them (10,000 patients) seem to be caused by paradoxical embolism.

The diagnosis of paradoxical embolism is made when there is a right-to-left shunt, deep venous thrombosis or pulmonary embolism, imaging study suggesting arterial embolism without clear cause of stroke such as atrial fibrillation, infective endocarditis, cardiac tumor, and atherosclerosis of aorta or carotid arteries. To detect right-to-left shunt, cardiac ultrasound with contrast bubble study is useful. When right-to-left shunt is found, patent foramen ovale, congenital heart disease, or pulmonary arteriovenous fistula are potential differential diagnosis.

The mainstay of treatment of paradoxical embolism is the secondary prevention. For this purpose, anticoagulants (warfarin and direct thrombin inhibitors) are the first-line options. Catheter-based closure of patent foramen ovale has been on the scene for decades, but it has not been approved in the US or Japan until recently because of lack of strong evidence. In 2017, 3 randomized clinical studies were published in the New England Journal of Medicine, and this treatment were given green light by FDA. A couple years later, it has become available in Japan as well. When this new option is considered for patients, however, we need to give some considerations. First, in the 3 randomized studies, this treatment was shown to be superior to antiplatelets therapy mostly with aspirin, but it was not clear whether it is superior to anticoagulation therapy with warfarin or direct thrombin inhibitors. Second, the patients included in those studies were under 60 years old. Elderly are more likely to have other risk factors of stroke such as atrial fibrillation, diabetes, and hypertension. For these patients, patent foramen ovale can be rather a by-stander than a real culprit. Therefore, at present, it would be prudent to select this new treatment for young patients without clear causes of stroke.

For primary prevention of stroke, catheter closure of patent foramen ovale is not recommended. Indeed, it can play a role in the prevention of stroke in long airplane travel and divers' sickness in individual with patent foramen ovale. These are interesting topics but awaits future researches.

Discourse

Introduction of the speaker of discourse

Tsutomu Yamazaki, MD, PhD
Director, IMSJ

Ken Matsui, CEO of ugo, Inc., spoke on The Future Work Style Opened Up by the Avatar Robot "ugo". Mr. Matsui is one of the key businesspeople representing the millennials. He introduced one area of applied robot science, which has been dramatically changing amidst the third robot boom that began in mid-2010s. Avatar robots are expected to further evolve through collaboration with various sensors, AI, facial recognition systems, etc. (open innovation).

Discourse: The future work style opened up by the avatar robot "ugo"

Ken Matsui
CEO
ugo, Inc.

A wide range of services for supporting everyday life are provided in the cities and towns we live in. The people who have jobs essential for maintaining everyday life and activities are called essential workers.

Meanwhile, when we look at Japan's labor force projections, it has been estimated that Japan's labor force will drop by 14 million people in the next 20 years. Furthermore, needs for manpower reduction and remote work/operation have been rising in almost all sectors in the past few years as businesses have been forced to continue providing remote and non-contact services due to the spread of COVID-19.

In response to those needs, we have developed the next generation avatar robot "ugo" to serve as people's avatar. We provide systems for digitally transforming tasks by utilizing this robot.

Our problem-solving approach is a robotics service that enables workers to remotely perform tasks from a distant location by placing network-connected robots at the worksites in facilities. This enables businesses to assign workers regardless of their location. Furthermore, tasks can be gradually automated based on the data accumulated by the remote operation of robots.

At present, our systems are utilized mainly in office buildings as well as a wide range of facilities including factories, commercial facilities, condominiums, storage buildings, and nursing facilities.

We also provide a methodical system called UEOSU that features robots capable of moving to other floors on their own by using elevators. The robots can either physically manipulate buttons with their arm to use elevators or use elevators through communication by linking with the building's system. UEOSU expands the range of robot motion, enhancing the benefits of adopting robots.

◆ Formula for integrating people, robots, and AI: Worksite tasks DX framework

Instead of handling robots as fixed equipment, we have been developing systems for engineering work styles that use robots as tools for expanding human capabilities. Starting from using systems for remote operation, businesses can optimize or expand their scale by outsourcing business processes once the tasks have been gradually automated and the accuracy has been established to a certain degree.

When the automation rate rises gradually, the know-how of tasks is turned into explicit knowledge and profitability increases as this knowledge is shared by the entire organization. To this end, it must be possible at the worksites to flexibly shift from remote operation to automation of all basic elements of tasks.

We have developed a system for making this shift called ugo Platform, a web app for easily setting remote operation and automation of robots on a browser. Providing the basic functions commonly required by various solutions, ugo Platform serves as a framework for building solutions for a wide range of sectors.

◆ Security DX solution utilizing avatar robots

The biggest challenge of the security industry these days is the severe shortage of workers. At 6.2, the industry's jobs-to-applicants ratio is exceptionally high in comparison to that of other industries. In response to this situation, we began to provide a security digital transformation (DX) solution utilizing ugo robots together with Taisei Co., Ltd., a comprehensive building maintenance service provider. The security DX solution materializes a structure for guards at a building's disaster management center to remotely guard the building through ugo robots 24 hours a day, 365 days a year; stand guard duties are remotely performed during the day and multiple ugo robots patrol each floor during late-night hours.

◆ The world brought about by ugo tasks DX

Performing all sorts of tasks, a wide range of robots already exist in the spaces we live in.

In a world where humans and robots work together cooperatively, there is a need for a setting of common recognition that seamlessly links the physical world and the digital world to optimize each other's activities by mutually recognizing the environment where each other's activities take place.

Our avatar robot ugo is optimal for serving the role of periodically moving and collecting data in the physical world to build and update the setting of common recognition. Once the wide range of data obtained from the physical world can be built and updated in the digital world, the world where human and robot activities take place can be visualized, making it easy to obtain new insights by analyzing the visualized world and conducting simulations. Tasks and plans to be carried out by humans and robots can be optimized by feeding back those results to the physical world. The ugo tasks DX framework realizes the worksite tasks optimization cycle by implementing this feedback loop that links the physical world and the digital world.

As these systems expand human capabilities by seamlessly integrating people, robots, and AI, businesses utilizing them will be able to realize new work styles in which workers can perform their tasks at any time in the day at any location.