REVIEW ARTICLE—EDUCATIONAL TRACK

The Cooperative Relationship Between ASNC and JSNC: Joint Symposium in JSNC 2021 and More!

Takashi Kudo, MD, PhD

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Abstract

The Japanese Society of Nuclear Cardiology (JSNC) and the American Society of Nuclear Cardiology (ASNC) has a cooperative relationship through a memorandum of understanding (MOU), based on which we hold a joint symposium in the JSNC annual meeting in early summer. In addition to the joint symposium this year, a joint webinar was held in early June. The theme of the joint symposium and webinar was cardiac amyloidosis. We consider the success of this collaborative work to be the fruit of the close friendship between JSNC and ASNC. The cooperative relationship between JSNC and ASNC will continue to grow.
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The Japanese Society of Nuclear Cardiology (JSNC) holds an annual scientific meeting in the early summer. It is a two-day meeting that consists of lectures and symposiums with fruitful discussions. Due to the COVID-19 pandemic, the JSNC annual meeting this year was held virtually from the city of Fukushima.

JSNC and the American Society of Nuclear Cardiology (ASNC) have a cooperative relationship through a memorandum of understanding (MOU). We regularly hold a joint symposium in the annual meeting of JSNC and invite speakers from ASNC. The theme for the joint symposium this year was cardiac amyloidosis, which is one of the most recent and important topics in nuclear cardiology. Due to the COVID-19 pandemic, the joint symposium was held virtually in JSNC 2020 and JSNC 2021. The joint symposium this year was chaired by Prof. Taishiro Chikamori (Tokyo Medical University) and me and consisted of two parts: video lectures in English by invited speakers from the United States and lectures in Japanese by three Japanese speakers. It was web-based and transmitted from the conference headquarters in Fukushima. Discussions between presenters and the audience were possible using the textbase Q and A system on a web conference system.

JSNC invited Dr. Sharmila Dorbala as a speaker from ASNC for this year's symposium. Dr. Dorbala is the immediate past president of ASNC and one of the leading researchers in nuclear cardiology, including cardiac amyloidosis. She gave a pre-recorded video presentation of approximately 40 min.

To my surprise and gratitude, Dr. Dorbala began by dedicating her lecture to Dr. Keiichiro Yoshinaga, who passed away last October (1). I would like to express my deep appreciation to her for her kind words and actions, both as the President of JSNC and as a friend of Dr. Yoshinaga. She then presented an excellent review of cardiac amyloidosis through its initial diagnosis and therapy (2, 3). Dr. Dorbala emphasized the timeliness of discussions on cardiac amyloidosis by demonstrating that this once untreatable and fatal disease is now treatable (4, 5). However, according to Dr. Dorbala, Transthyretin (ATTR) cardiac amyloidosis remains a prevalent, but underdiagnosed disease entity. The first important note in her presentation was the prominent regional differences in the prevalence and death rate of cardiac amyloidosis in the US (6,7). Since the US has a highly skewed ethnic distribution and ethnic differences have been reported in the incidence of cardiac amyloidosis, this skewed distribution may be affected by the ethnic composition. However, another possibility suggested by Dr. Dorbala is that differences in the awareness of cardiac amyloidosis by physicians may contribute to this biased distribution of this

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Department of Radioisotope Medicine, Atomic Bomb Disease Institute, Nagasaki University, Nagasaki, Japan

disease, which was previously considered to be rare. Since cardiac amyloidosis is still an underdiagnosed disease, as well as in Japan, future research is needed to investigate whether regional differences in disease awareness exist in Japan, similar to the US. After presenting a large amount of evidence and describing her vast experience diagnosing cardiac amyloidosis, Dr. Dorbala summarized some of the following pitfalls associated with bone tracer scintigraphy. She stressed that delayed images need to be taken in order to reduce blood pool activity. She also cautioned about the low sensitivity of bone tracers for hereditary ATTR cardiac amyloidosis. Furthermore, she discussed the exclusion of light chain (AL) amyloidosis, even in cases that test positive for bone tracers. Dr. Dorbala also demonstrated that not all bone tracers are equally helpful for reaching a diagnosis in some cases. She continued her presentation by describing three steps that need to be taken in cardiac nuclear medicine in order to diagnose cardiac amyloidosis. SPECT needs to be performed because its metrics are superior to planar images. However, SPECT/CT is the optimal imaging modality because it is superior to SPECT. Dr. Dorbala used case images to demonstrate the superiority of SPECT/CT to SPECT alone and how it may prevent misdiagnoses. Furthermore, absolute quantitative measurements need to be obtained and analyzed. Dr. Dorbala introduced a number of studies that examined the relationship between bone tracer accumulation in the myocardium and the prognosis of patients, suggesting that mild amyloid deposition in the myocardium is associated with a better prognosis than its severe deposition (8–10). These findings indicated that quantitative imaging will become more important in the future. Dr. Dorbala summarized these studies as "Quantitation of cardiac ^{99m}Tc-pyrophosphate (PYP) using SPECT/CT: The next frontier in ATTR cardiac amyloidosis". She indicated that many recent studies have performed quantitative measurements of bone tracers (^{99m}Tc-PYP/DPD (Diphosphono-1, 2-propanodicarboxylic acid)/HMDP (Hydroxymethylene diphosphonate) using SPECT technology, such as cadmium zinc telluride detector scanners. She then moved onto the diagnosis of AL amyloidosis and the importance of PET imaging for this disease entity. As many will know, PET tracers for amyloid deposition in Alzheimer's disease are widely used, such as ^{11}C PiB (Pittsburgh Compound B), ^{18}F-Florbetapir, ^{18}F-Florbetaben, and ^{18}F-Fultemetamor. Dr. Dorbala proposed that these amyloid PET tracers, which were developed for the imaging of brain amyloid deposition, are also highly useful for cardiac amyloidosis, particularly AL amyloidosis, citing her own research and findings from other researchers. Moreover, she introduced a study showing that PET tracer kinetics differed between ATTR amyloidosis and AL amyloidosis, (11) indicating that a proper image acquisition time after the injection of PET tracers is crucial for the imaging of cardiac amyloidosis. At the end of her talk, she expressed her opinion that the diagnosis of cardiac amyloidosis by biopsy will be replaced by nuclear imaging combined with the exclusion of AL amyloidosis using a serum assay. Dr. Dorbala summarized her presentation by stating that cardiac amyloidosis is a very challenging target for nuclear cardiology, and also that further research on quantitative imaging is warranted to assess responses to therapy. We, the members of JSNC, would like to express our deep gratitude to Dr. Dorbala for her excellent and detailed lecture at this joint symposium.

After Dr. Dorbala's video presentation, we moved onto the second part of the symposium, a session in Japanese. The second part of the symposium invited three speakers, Dr. Hiroaki Kitaoka from Kochi University, Dr. Seitaro Oda from Kumamoto University, and Dr. Kenji Fukushima from Saitama Medical University.

Dr. Kitaoka presented his experience of diagnosing and treating cardiac amyloidosis from the viewpoint of a cardiologist. He suggested that cardiac amyloidosis is actually a relatively common disease, particularly in patients with heart failure with a preserved ejection fraction (HFpEF). In the case of HFpEF with left ventricular hypertrophy, the prevalence of cardiac amyloidosis is approximately 14% (12). He noted that many societies are committing their efforts to the establishment of common diagnostic criteria, with statements being published in multiple journals (13-15). Dr. Kitaoka himself is the team leader for the establishment of guidelines by the Japanese Circulation Society for cardiac amyloidosis. He emphasized that although various therapies and drugs have been developed for cardiac amyloidosis and may improve the prognosis of patients, cardiac amyloidosis is still a progressive and fatal disease. Therefore, it is very important to have a palliative care perspective in addition to aggressive treatment. This is one of the crucial messages from this joint symposium.

Dr. Oda presented his experience and opinions of imaging cardiac amyloidosis using echo, CT, and MRI. He described echo as an essential and convenient method for diagnosing cardiac amyloidosis; however, its sensitivity and specificity for classical findings, such as "granular sparkling", are not high (16). Dr. Oda showed the very high utility of MRI for the diagnosis of cardiac amyloidosis. Although delayed contrast enhancement is a very well-known MRI finding in cardiac amyloidosis, he emphasized that T1 mapping and its use to image the extracellular volume is highly specific for diagnosing cardiac amyloidosis. On the other hand, Dr. Oda stressed that since the majority of patients with cardiac amyloidosis already have a pacemaker, the use of MRI is limited. In light of this, Dr. Oda stated that it is important to make measurements of the extracellular volume, which is performed in MRI, also possible in CT. He considers this to be the direction to aim for in the future.

Dr. Fukushima presented his experience in nuclear medicine for the diagnosis of cardiac amyloidosis. He noted that the use of bone tracers for cardiac amyloidosis is not a novel finding; it was already known by experienced nuclear cardiology physicians. He also referred to a large body of evidence showing that bone tracers are very useful for diagnosing cardiac amyloidosis, particularly with high specificity (17). Dr. Fukushima also expressed his agreement with Dr. Dorbala's opinion that the future direction of nuclear cardiology in cardiac amyloidosis will be quantitative measurements and introduced the preliminary data of his ongoing study on quantitative measurements of bone tracers using SPECT/CT.

Unfortunately, due to the COVID-19 pandemic, we were unable to hold face-to-face discussions between the Japanese presenters and Dr. Dorbala at this meeting. Nevertheless, through this ASNC-JSNC joint symposium, we shared international knowledge and efforts to diagnose cardiac amyloidosis from different viewpoints, namely, those from the US and Japan, as well as perspectives for cardiology, radiology, and nuclear medicine.

The joint activities of JSNC and ASNC this year were not limited to this joint symposium. On June 4th, we also held a joint webinar on cardiac amyloidosis entitled "Cardiac Amyloidosis; Read with Experts in Japan". This webinar is part of the ASNC education program on cardiac amyloidosis. This year, ASNC is holding multiple international webinars in local languages in many countries, including Latin America and Europe. The webinar conducted in June was the first international webinar held by ASNC in Asia, and was planned and organized in collaboration with JSNC. We, JSNC, consider this webinar to be the result of a long and fruitful cooperation between JSNC and ASNC. Dr. Toru Kubo (Kochi University) and Dr. Kenichi Tsujita (Kumamoto University) were invited as speakers for this webinar. I, Takashi Kudo, also made a presentation and held the role of chairperson. This webinar accepted audience comments through a Q and A system, similar to the joint seminar held in JSNC 2021. In this webinar, Dr. Kubo initially reviewed basic knowledge and essential findings on cardiac amyloidosis, such as Echo, electrocardiogram (ECG), nuclear medicine, and clinical findings. He also emphasized the importance of considering cardiac amyloidosis when clinicians encounter patients with heart failure and arrhythmia. Dr. Tsujita presented a diagnostic algorithm for cardiac amyloidosis and also introduced criteria that he developed to screen highly probable cases of amyloidosis. These criteria involve a high troponin level, thickened left ventricular posterior wall, and wide QRS on ECG as the three red flags for cardiac amyloidosis. These criteria are well known as the "Kumamoto Criteria". He also discussed several imaging methods for cardiac amyloidosis and emphasized the advantages of using ^{99m}Tc-PYP imaging to track the natural history of this disease. I also demonstrated how to image patients with ^{99m}Tc-PYP and described some of the pitfalls associated with this technique. Nearly 200 audience members joined this webinar. The materials presented are now available on the ASNC home page.

We, the Japanese Society of Cardiology and Nuclear Medicine, would like to express our deep gratitude to the executives and all other members and staff of ASNC for their cooperation in this joint symposium. We hope that we will be able to invite speakers from ASNC directly to the next venue in JSNC 2022 in Tokyo next year and hold face-to-face discussions. The cooperative relationship between JSNC and ASNC will continue to grow.

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Conflicts of interest

None.

Reprint requsts and correspondence:
Takashi Kudo, MD, PhD
Department of Radioisotope Medicine, Atomic Bomb Disease Institute, Nagasaki University, 1-12-4 Sakamoto, Nagasaki, 852-8523 Japan
E-mail: tkudo123@nagasaki-u.ac.jp

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