



## In memoriam: a tribute to Masao Ishii, MD PhD

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**Dr Masao Ishii**

Dr Masao Ishii passed away in December of 2022. He had a central role in the activity of the Japanese Society of Hypertension (JSH) and was the president of the 15th JSH scientific meeting in Yokohama held in 1992. “A great star has fallen” with the death of the person driving basic, translational and clinical research on hypertension in our

country. He was born in 1932 in Mito, Ibaraki, Japan, and graduated from the Faculty of Medicine, The University of Tokyo in 1958. Dr Ishii worked in the nephrology–hypertension group led by Professor Tsuneaki Sugimoto in the Department of Internal Medicine II, Tokyo University, and start his research to examine contributing factors of regulation of circulatory system including blood pressure (BP). He then went to the Hypertension, Kidney, and Electrolyte Division, Department of Internal medicine, University of Minnesota Hospital and School of Medicine, Minneapolis, Minnesota, USA, from 1967 through 1970 and studied the pathogenesis of hypertension with focus on the derangement of kidney papillary function as evidenced by low interstitial cell granules, sodium and urea in the “hypertensive” papilla of chronic Goldblatt hypertension model under the mentorship of Dr Louis Tobian [1].

After returning to Japan, Dr Ishii was appointed as a Professor in the Department of Internal Medicine II, Yokohama City University in 1987. Even after being seriously injured in a traffic accident while on a business trip to attend 10th Scientific Meeting of The Inter-American Society of Hypertension (La Jolla, CA, USA) in April 1993, Dr Ishii made a remarkable recovery. He continued to energetically direct a lot of research in the field of hypertension including basic, translational and clinical research for identification of regulators of circulatory and kidney function including BP with focus on pathological role of the prostaglandin and intracellular calcium handling, ATP-adenosine axis, and natriuretic peptide system in hypertension and its related disease [2–4]. In addition, in the field of hypertension-related basic research, Dr Ishii and Dr Satoshi Umemura showed possible contributions of several genetic mutations of alpha-adrenergic receptors and renin-angiotensin system components including angiotensinogen and angiotensin I converting enzyme in human hypertension and cardiovascular disease, by employing analysis of

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restriction fragment length polymorphisms [5, 6]. Dr Ishii had a collaboration with Dr Kazuo Murakami, Institute of Applied Biochemistry, University of Tsukuba to examine transcriptional mechanism of renin and angiotensinogen genes in pathogenesis of hypertension [7], and he showed important anatomical and physiological consequences by angiotensinogen gene-knockout in mice [8].

The enormous fluctuations occurring in BP over a 24-h period can involve as many as 100,000 directly measured intra-arterial BP values and  $\approx$ 100 measurements made indirectly by ambulatory BP monitoring (ABPM). In clinical research, Dr Ishii and Dr Eiji Miyajima showed an important pathophysiological role of the muscle sympathetic nerve activity (MSNA) of the tibial nerve in essential hypertension [9]. In addition, Dr. Ishii and Dr. Osamu Tochikubo examined physiological and pathological importance of long-term and short-term BP variation, and showed that statistical base BP obtained by ABPM was closely related to the severity of hypertensive organ damage and was highly reproducible, suggesting the statistical base BP as a representative BP value in an individual subject [10].

In 1998, Dr Ishii moved to the Yokohama Seamen's Insurance Hospital, (currently JCHO Yokohama Hodogaya Central Hospital) in Yokohama, Japan, as a director. Then, Dr Ishii, Dr Takao Saruta, Dr. Toshio Ogihara and other principal members of JSH played a central role in the successful accomplishment of the Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS), which was nation-wide randomized controlled trial by JSH in collaboration with Japan Physicians Association [11]. This study was performed to examine the benefits of lowering a systolic BP below 140 mmHg in elderly hypertension and patients with essential hypertension (65–85 years old, with a pretreatment systolic BP > 160 mmHg) were randomly assigned to receive strict treatment ( $n = 2212$ ) or mild treatment ( $n = 2206$ ). The results of JATOS gave us important insights in the management of elderly hypertensive patients, and significantly contributed to the JSH Guidelines for the Management of Hypertension as an important evidence from Japan [12].

We believe that Dr Ishii have been one of great mentors of JSH and Department of Internal Medicine II, Yokohama City University (currently Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine). Please accept our deepest

sympathy for his death, we pray that his soul may rest in peace.

## Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

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