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INTERNATIONAL PERSPECTIVES

Cardio-Oncology in China

We Are on the Go!

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As the most populous country in the world, in the year 2020, there will be approximately 4.5 million new cases of cancer in China (1). Cancer and cardiovascular disease are the 2 most common causes of mortality in China. However, because of the development of newer therapies, cancer patients are living longer, and as a consequence, also suffering from an increased risk of cardiovascular disease. This Perspective aims to present the recent development of cardio-oncology in China.

THE DEVELOPMENT AND GROWTH OF CARDIO-ONCOLOGY IN CHINA

In 2011, Dr. Bonnie Ky delivered a keynote lecture at the China Heart Congress, and first introduced the concept of cardio-oncology to medical specialists in China. At that time, most Chinese cardiovascular and oncology physicians never heard of cardio-oncology and lacked awareness of the treatment and prevention of cardiotoxicity in cancer patients. The first cardio-oncology-specific forum was then held at the China International Heart Failure Congress in March 2016, followed by the first cardio-oncology workshop in June 2016 in Dalian, China. This meeting was attended by 17 experts from different provinces and cities, and brought together experts from cardiology, oncology, hematology, and radiation oncology. During that conference, we collectively agreed to develop a formalized cardio-oncology program in China.

Since then, cardio-oncology clinics and multidisciplinary teams have been established across the entire country, including: 1) cardio-oncology clinics and multidisciplinary teams in general hospitals, such as The First Affiliated Hospital of Dalian Medical University and Zhongshan Hospital of Fudan University; 2) cardio-oncology clinics in cancer-specific hospitals, such as the Harbin Medical University Cancer Hospital; Chongqing Cancer Hospital; Cancer Hospital, Chinese Academy of Medical Science (CAMS); and the Peking Union Medical College (PUMC); 3) cardio-oncology clinics in cardiac-specific hospitals, such as the Fuwai Hospital, CAMS, and PUMC; and 4) multidisciplinary teams across cardiovascular and oncology hospitals, including collaborations between the cardiac-specific centers Fuwai Hospital, CAMS, and PUMC with cancer-specific centers in CAMS, PUMC, and the Beijing Cancer Hospital.

To date, there are more than 10 large cardio-oncology clinics or multidisciplinary groups in China (**Figure 1**). We anticipate these numbers will continue to grow to meet the demands of an increasing number of cancer patients. Alongside this, many professional cardio-oncology societies have also been established in China (**Figure 2**), providing professional and organizational platforms to promote the development of cardio-oncology programs across China.

CARDIO-ONCOLOGY EDUCATION AND TRAINING IN CHINA

With the leading efforts by major professional societies, many cardio-oncology congresses and specific forums have been held over the past 4 years. Cardio-oncology congresses include meetings such as the China CardioOncology Conference, China Cancer Management Symposium, and the International

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: CardioOncology* author instructions page.

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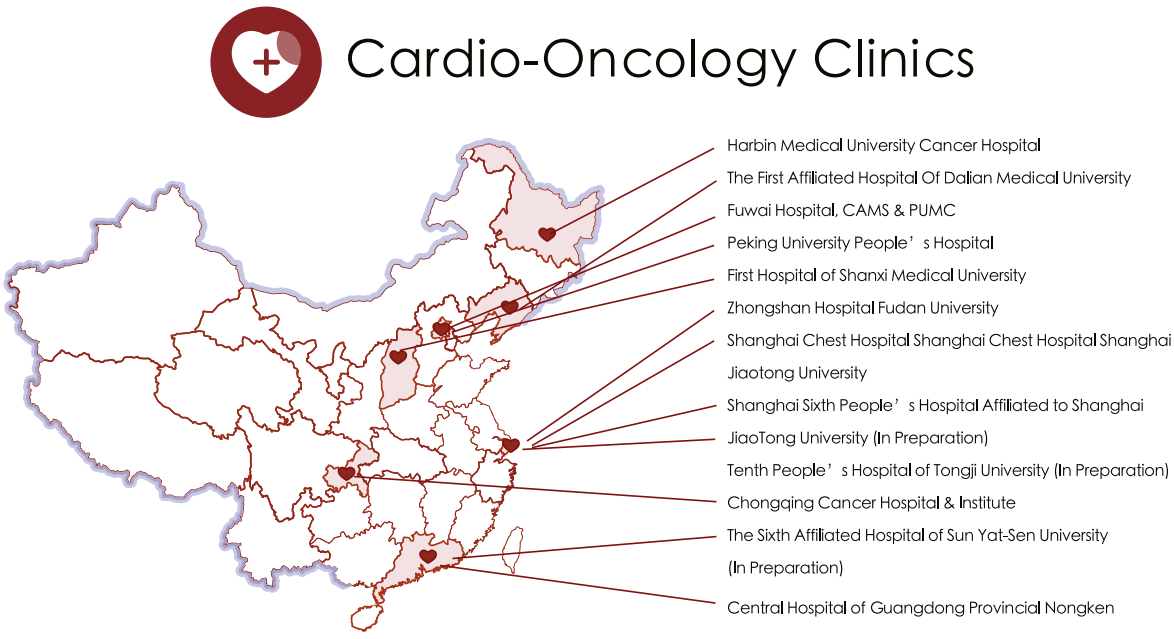
FIGURE 1 **Distribution of Major Cardio-Oncology Clinics in China**



Conference for Metabolic Disorders and Cancer Related Cardiovascular Diseases.

Cardio-oncology specific sessions have been held during the scientific meetings of cardiovascular and oncology societies, including the Integrated Cardio-Oncology Society of China Anti-Cancer Association, Chinese Society of Clinical Oncology, Great Wall International Congress of Cardiology, China Heart Congress, China International Heart Failure Congress, Chinese Society of Cardiology, Oriental Congress of Cardiology, and South China International Congress of Cardiology.

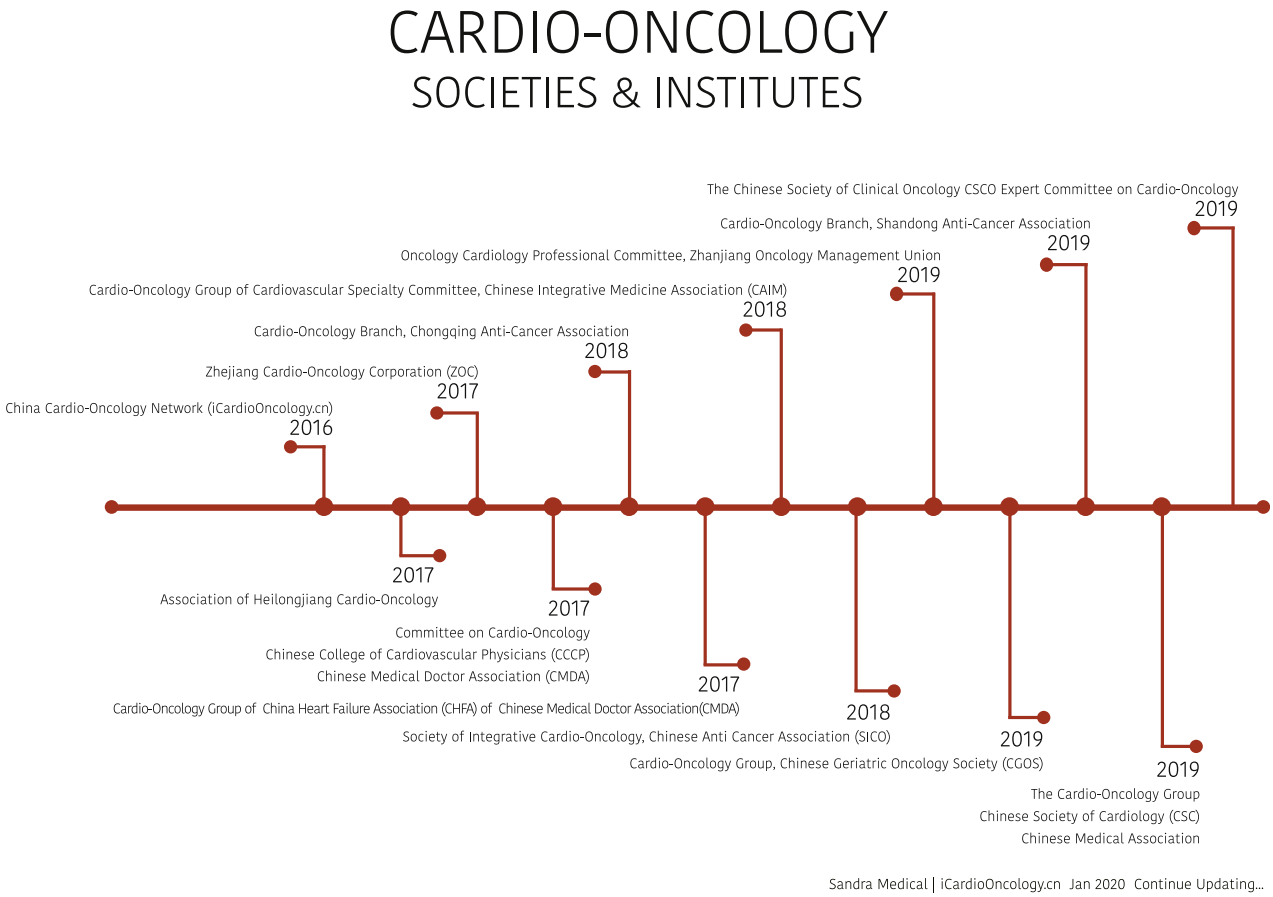
In 2018, the Integrated Cardio-Oncology Society launched the "CardioOncology Academy" and "Speaking Tour" program in several provinces. A total of 58 specific conferences on cardio-oncology have been held, and more than 10,000 physicians have attended these activities to help them exchange ideas and promote collaborations.

Academic websites, journals, and WeChat official accounts on nationwide social media platforms have been established to foster communications and dissemination of cardio-oncology clinical and research findings to clinicians and researchers. The iCardio-oncology account is one example of a specific WeChat network. The *Journal of Heart Failure and Cardiomyopathy* has also published a special column on *JACC: CardioOncology* highlighting each issue with translated synopses. Efforts are ongoing to also provide translated summaries of cardio-oncology papers published internationally as we believe this will enable physicians in China to access the leading papers and facilitate the practice of cardio-oncology according to the latest guidelines, recommendations, and research. Several textbooks have been translated, written, and published in China. Popular texts have also been written specifically for patients to empower them and increase awareness. Together, all of these efforts have produced great impact on the education and training of cardio-oncologists in China.

CARDIO-ONCOLOGY RESEARCH IN CHINA

There are many ongoing basic, clinical, and translational research programs in cardio-oncology, investigating the mechanisms, pathophysiology,

FIGURE 2 **Timeline Depicting the Development of Cardio-Oncology Societies in China**



epidemiology, evaluation, prevention, and management of cardio-oncology. For example, over the past 2 years in China, approximately 100 peer-reviewed publications have been published in Chinese and English journals.

In the clinical research field, Liu et al. (2) found that hypertension was the most prevalent cardiovascular risk factor (26.0%) among 22,500 newly diagnosed cancer patients; Liu et al. (3) reported a study which included 710,170 cancer patients, and showed that the presence of hypertension was associated with a higher all-cause mortality in patients with heart failure, myocardial infarction, atrial fibrillation, stroke, and diabetes. Cao et al. (4) found that increased radiation dose was associated with a higher risk of heart failure in breast cancer patients; Hu et al. (5) showed that thoracic cancer survivors who underwent radiotherapy have higher SYNTAX scores and were at a higher risk of developing anatomically severe coronary artery disease, independent of chemotherapy exposure. Meta-analyses conducted by Yuan et al. (6,7) showed the incidence of atrial fibrillation in breast cancer patients treated with trastuzumab was approximately 1.2%, with the highest incidence of atrial fibrillation occurring within 90 days after cancer diagnosis. In the Kailuan study, which included 68,759 Chinese male adults with approximately 8 years of follow-up, total cholesterol, low-density lipoprotein (LDL)-cholesterol, and non-LDL-cholesterol not only increased the risk of cardiovascular disease, but also negatively impacted cancer risk. Lipophilic statins have been shown to improve the prognosis of breast cancer patients (8). Xu et al. (9) found that echocardiographic 3-dimensional speckle tracking imaging with strain was useful in the early detection of myocardial injury caused by chemotherapeutic drugs. Anqi et al. (10) showed that segmental left ventricular strain, indicative of regions supplied by the left anterior descending coronary artery, was a more sensitive indicator of the cardiotoxicity of anthracyclines.

In basic research, An et al. (11) found that neuregulin-1 could attenuate doxorubicin-induced autophagy and apoptosis in cardiomyocytes. Xie

et al. (12) showed mitochondrial $ONOO^-$ represents an early biomarker to predict subclinical anthracycline cardiotoxicity. Li et al. (13) reported that L-arginine was effective in suppressing doxorubicin-induced vascular dysfunction by attenuating vascular NO release and apoptosis. Huang et al. (14) found that NH_4CL significantly improved doxorubicin-induced contractile dysfunction, inflammation, apoptosis, and autophagy in mice. Ma et al. (15) found that rituximab can prevent or reverse ventricular remodeling by interfering with B cells. Liu et al. (16) showed that autophagy-related single nucleotide polymorphisms were associated with chemotherapy-induced cardiotoxicity.

Some original studies and clinical trials are ongoing: Dr. Zhiren Zhang received funding from the National Natural Science Foundation of China to study the mechanisms of cardiotoxicity caused by anti-cancer medications; Dr. Yuhui Zhang launched a randomized clinical study on the prevention of cardiovascular toxicity with a traditional Chinese medicine; Dr. Yun Zhang is leading a multicenter study on the use of echocardiography to evaluate cardiotoxicity with chemotherapy and the role of targeted cardioprotective therapy in patients with breast cancer; Dr. Yunlong Xia initiated a multicenter clinical registry study on the preventive treatment of bevacizumab-related hypertension with olmesartan.

THE FUTURE OF CARDIO-ONCOLOGY IN CHINA

Over the next few years, we hope to focus on accomplishing the following goals: 1) Improving the awareness of cardio-oncology amongst both cardiovascular and oncology physicians; 2) Growing our cardio-oncology clinics and multidisciplinary teams to serve more cancer patients; 3) Establishing the standards for the diagnosis, evaluation, monitoring, and risk stratification for Chinese cardio-oncology patients; 4) Initiating multicenter registries to study cardiotoxicity in Chinese cancer patients; 5) Planning multicenter randomized clinical trials for cardioprotection prophylaxis in Chinese cancer patients, using not only Western but also traditional Chinese medicines; 6) Issuing guidelines and consensus statements on the diagnosis, prevention and treatment of the cardiotoxicity of cancer therapies tailored to Chinese cancer patients; 7) Developing educational platforms aimed to improve the quality of education for cardio-oncologists and physicians at all levels; and 8) Promoting international exchange and collaboration in cardio-oncology globally.

In the future, cardio-oncology will continue to rapidly evolve in China, and together we will face the challenges to maintain and develop the standards to best serve our patients. We are on the go!

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