

The specialty of pulmonary vascular medicine in China: historical development and future directions

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Abstract: Over the past 40 years, Chinese experts have made great progress on research, diagnosis, and therapy of pulmonary vascular disease, including pulmonary embolism and pulmonary hypertension. These theoretical and clinical advances have increased public awareness about this group of conditions, which are associated with significant morbidity and mortality in China and worldwide. With its theoretical basis combining knowledge from cardiovascular and pulmonary medicine, pulmonary vascular disease has developed into a separate, unique specialty in hospitals across China and worldwide. This article will provide a short historical perspective but also an outlook into the future of this exciting novel discipline. We provide a Chinese perspective, based on our research and clinic experience over the past decades.

Key Words: Specialty development; pulmonary vascular disease; pulmonary embolism; pulmonary hypertension



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In recent years, the discipline of pulmonary vascular disease, which combines knowledge from cardiovascular and respiratory medicine, has emerged as a separate medical specialty in China. With an improved understanding of the morbidity, mortality, and social burden associated with pulmonary embolism and pulmonary hypertension, public awareness and interest in pulmonary vascular disease has gradually increased. The theoretical basis of pulmonary vascular disease overlaps multiple specialties, including cardiology, pulmonology, hematology, immunology, etc. It is also essential for pulmonary vascular specialists to be proficient in a number of clinical skills and techniques, including ventilator management, vascular endoscopy, pulmonary angiography, right heart catheterization, bronchoscopy, and ultrasound technology.

The first pulmonary vascular department in China evolved from the National Research Center of Pulmonary Circulation at the Fuwai Hospital [<http://www.fuwaihospital.org/News/Main?siteId=527>] (Beijing, Xi Cheng District), which has contributed significantly to the diagnosis and treatment of pulmonary vascular disease. The department

was established in the 1970s by Professor Xiansheng Cheng, who is known as the pioneer of pulmonary vascular disease research in China (1-8). A focus of his early work was the dissemination of smoking cessation programs. At that time, and in particular in the poor countryside, smoking was highly prevalent and hardly anyone realized its relationship and significance with pulmonary vascular disease. Professor Xiansheng Cheng subsequently developed the first domestic guideline of diagnosing and treating pulmonary vascular disease based on its pathologic basis, autopsy findings, and his valuable clinical experiences (8).

In the 1980s, Professor Xinzhi Weng from Chaoyang Hospital [<http://www.bjcyh.com.cn/english/intro.shtml>] (Beijing, Chao Yang District) highlighted the importance of anticoagulation as supplementary therapy in pulmonary heart disease (9-14). In the mid-1990s, Professor Xiansheng Cheng (Fuwai Hospital, Beijing) standardized the thrombolytic therapy of pulmonary embolism and drafted the first Chinese guideline for its diagnosis and therapy based on a multi-center trial of pulmonary embolism diagnosis and thrombolytic therapy (7). That trial was part

of the National Medical Science and Technique Foundation during the 9th Five-Year Plan.

In response to the increasing incidence of pulmonary embolism, Professor Dayi Hu from Peking University Health Science Center (PKU-HSC) [<http://www.bjmu.edu.cn/>] (Beijing, Hai Dian District) set up a novel tract for pulmonary vascular disease at the 2001 Great Wall International Cardiovascular Conference (GWIC) (15-19). The GWIC is the most comprehensive cardiovascular conference in mainland China with participation of scientists from countries around the world [<http://en.gw-icc.org/>]. The pulmonary vascular science tract provides a platform for Chinese physicians and scientists to share their experience on treatment and research of pulmonary vascular disease with international experts in a bi-lingual environment. Its establishment at the GWIC marked a turning point and the knowledge of pulmonary vascular disease enjoyed growing popularity thereafter.

In 2003, in the aftermath of the SARS pandemic, Professor Ying Liang and Doctor Hua Luo from Anzhen Hospital (Beijing, Chao Yang District) [http://english.bjhb.gov.cn/AsktheDoctor/OlympicappointedHospitals/200708/t20070813_30848.htm] broke with international traditions of the heparin dosing nomogram and simplified the standard of anticoagulation on the basis of international RASCHE nomogram (20,21). Their efforts have allowed widespread standardized anticoagulation therapy and the authors were invited to present to an international forum at the American College of Chest Physicians (22,23). In the very same year, they defined unique national heparin dosage guidelines for anticoagulation (22,23), which were presented at the Asia Pacific Congress on Diseases of the Chest (APCDC) in 2003. Importantly, while based on international standards, these dosages for Chinese patient are different than those for other countries, likely reflecting differences in genetic traits. Their work contributed invaluable to standardized anticoagulant therapy of pulmonary embolism in China. However, on a global stage, it also demonstrated the need for individualization when applying international treatment and dosing guidelines to specific, national patient populations. As such, their work is an example of Chinese experts coming to the forefront of their field on an international level.

In 2005, Doctor Zhicheng Jing (24) (Shanghai Pulmonary Hospital, Shanghai, Yang Pu District) [<http://med.tongji.edu.cn/oldtj/english/P15.htm>], who at that time was studying at one of the most famous of pulmonary hypertension center in Europe (Center for Pulmonary Vascular Disease, Paris-Sud

University, Antoine Bécélère Hospital, Clamart, France), established the first official Chinese website of pulmonary hypertension (www.phachina.com), aiming to disseminate the growing knowledge about PHA in Chinese language. In 2006, as the youngest pulmonary vascular specialist at that time, he chaired the meeting of the National Census Registration Collaborative Group for Pulmonary Hypertension (Guilin, Guangxi province), [<http://www.phassociation.org/page.aspx?pid=1035>], which aroused great public awareness inside and outside the country and marked the opening of a new era of multi-disciplinary cooperation in China.

With the rapid sub-specialization of modern medicine, it became obvious that the discipline of pulmonary vascular disease would sooner or later separate from the cardiovascular and respiratory specialties. In 2008, after moving to Tongji University (Shanghai, Yang Pu District) [<http://www.tongji.edu.cn/english/>], Professor Zhicheng Jing established the Diagnosis and Treatment Center for Pulmonary Vascular Diseases at Tongji University (25-33). The center has been the first comprehensive modern research and treatment center for pulmonary hypertension in China, and is one of the leading centers in the world [<http://www.phassociation.org/page.aspx?pid=1035>]. It is also the training center for specialists from the Cardiology Branch of Chinese Medical Association and the National Base of Continuing Medical Education. The center is actively involved with international initiatives and contributes nationally and internationally to the accumulation of valuable epidemiological data on pulmonary hypertension. Another focus is clinical research of novel pharmaceutical and interventional treatment approaches for pulmonary hypertension.

Being the intellectual heir of Professor Xinzhi Weng, Professor Chen Wang, a nationally well-known respiratory expert from Chaoyang Hospital [<http://www.bjcyh.com.cn/english/intro.shtml>] (Beijing, Chao Yang District) has carried forward the standardized diagnosis and treatment for PTE on a national scale (34,35). In 2009, he affirmed 50 mg of r-tPA, half of the standard international dose, as the individual thrombolytic dosage for Chinese patients by performing one of the largest PTE RCT in the world (36), and has become an important author of Chinese PVD guidelines.

Mentored by Professor Dayi Hu, Doctor Hua Luo (Peking University Shenzhen Hospital, Shenzhen, Guangdong Province) [<http://www.pkusz.com/navigate.jsp?selectedCat=000>] has since 2007 devoting himself to turning pulmonary vascular medicine into an independent discipline at Peking University (PKU). He had founded



Figure 1 Shenzhen Hospital of Peking University

the first PVD Pioneer Tribune at PKU (www.pkupv.lingd.net) without any sponsor or reward. This website has become a bridge between PKU and the overseas, reporting international developments of PVD and original scientific research at PKU. Doctor Hua Luo has established the Anticoagulation Online Clinic and offered outpatients nationwide free consultation and follow-up. He has set up an innovative theoretical framework of PVD prevention and emphasized the importance of basic education. He wrote the first PVD proposal at PKU for its discipline development and has advocated education reform for training younger colleagues on the subject, which led to the first Chinese Student Association on PVD Prevention. With his help, a 21-year-old assistant Peng Yu (PKU-HSC, Beijing, Hai Dian District), performed the first domestic evaluation of college students' needs on PVD education. From 2003 to 2009, Luo had designed a series of trials to explore the individual treatment of PTE anticoagulation in China (37-43) and gained the recognition from the Great Wall International Cardiovascular Conference (October 14-17, 2010, the 21th Great Wall International Cardiovascular Conference, Beijing, China) [<http://www.gw-icc.org/2010/newslist.asp>; <http://www.365heart.com/show/43023.shtml>]. Based on his prospective trial in 2004, he verified 13 U/(kg·h) as the unique national heparin dosage, which was initially proposed in the retrospective study at 2003 APCDC by Professor Ying Liang. Furthermore, Luo has paid tremendous attention to PVD specialty development. In the May of 2012, he organized the first PKU working group with multi-disciplinary cooperation & the Patients Club for PVD at Shenzhen Hospital (*Figure 1*). Experts

in the working group are responsible for different fields of PVD, such as diagnosis and treatment, basic research and nursing care, prevention and follow-up, international communication and cooperation, etc. The specialists are expected develop the Patients Club into a communication platform between doctors and patients. A lifelong follow-up for PVD patients should be established in order to improve their life quality. His contributions to PVD in the PKU system will facilitate more standardized clinical pathways for building outpatient service aiming for chest pain, anticoagulation and pulmonary hypertension in Shenzhen Hospital (*Figures 2,3,4*). With no doubt, his attempt will provide precious experience for Peking University Health Science Center on developing this new specialty of pulmonary vascular medicine.

As described above, much interest has been focused on pulmonary vascular disease. However, apart from pulmonary hypertension and pulmonary thromboembolism, Chinese pulmonary vascular specialists have also directed their attention to right heart diseases, congenital heart disease, atrial fibrillation originated from the pulmonary veins, diagnosis and treatment of pulmonary vein stenosis (post radio frequency), arrhythmia originated from the right heart, pulmonary vasculitis, sleep apnea syndrome, research of bronchial circulation, diagnosis and interventional therapy of pulmonary vascular disease (right heart floating catheter, intravascular ultrasound, percutaneous pulmonic valve replacement) and many other conditions.

Contrary to traditional specialties, the novel discipline of pulmonary vascular disease does not adhere to an established, rigid theoretical and clinical framework. This



Figure 2 Spiral CT



Figure 3 ECT



Figure 4 DSA

is challenging in the context of treatment standardization. However, emerging conditions, including pulmonary hypertension crisis, pulmonary vascular remodeling, and pulmonary hypertension also provide opportunities for innovation.

As described above the goal is to perform cutting edge research and develop consensus treatment guidelines for domestic specialists based on accumulating global data. This will foster the role of Chinese scientists and clinicians as equal partners and leaders in the international scientific community. This approach, exemplified for pulmonary vascular disease, marks a new era of modernization and internationalization in the Chinese medical community,

with the ultimate goal to improved care for our patients in all parts of China.

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References

1. Cheng X, Zhang Z, Li J. Evaluating the national ECG diagnostic criteria of pulmonary heart disease from epidemiology. *J Electrocardiol* 1996;15:66-8.
2. Cheng X. Accurate diagnosis of lung infarction. *Zhonghua Nei Ke Za Zhi* 1996;35:512.
3. Cheng X. Chronic cor pulmonale: progress in the prevention, treatment and research. *Zhonghua Nei Ke Za Zhi* 1996;35:723-4.
4. Cheng X, Li J, Zhang Z. Analysis of basic data of the study on prevention and treatment of COPD and chronic cor pulmonale. *Zhonghua Jie He He Hu Xi Za Zhi* 1998;21:749-52.
5. Cheng X, Wu Y, Li J. Study on susceptible risk factors for COPD in smokers. *Zhonghua Jie He He Hu Xi Za Zhi* 1999;22:602-4.

6. Cheng X, Xiong C. To promote Chinese standardization of thrombolytic therapy for acute pulmonary thromboembolism. *Zhonghua Nei Ke Za Zhi* 2002;41:2-3.
7. Cheng X, He J, Gao M, et al. Multicenter clinical trial on the efficacy of thrombolytic therapy with urokinase and/or anticoagulant with low molecular weight heparin in acute pulmonary embolism. *Zhonghua Nei Ke Za Zhi* 2002;41:6-10.
8. Cheng X. eds. *Right Ventricular Diseases - Basis and Clinic*. Beijing: People's Medical Publishing House, 2008:110-1.
9. Weng XZ. Progress in the prevention and treatment of chronic pulmonary heart disease in Beijing region. *Journal of Capital Medical University* 1980;1:320-6.
10. Zhou YC, Weng XZ, Qiu HG. The therapeutic effect of defibrase on patients with an acute stage of chronic cor pulmonale. *Zhonghua Nei Ke Za Zhi* 1986;25:404-6, 444.
11. Zhou YC, Weng XZ, Qiu HG. Assessment of platelet aggregation and malondialdehyde production in patients with chronic cor pulmonale. *Zhonghua Nei Ke Za Zhi* 1987;26:638-40, 677.
12. Gao Y, Weng X, Chen S. The study of platelet function in patients with chronic pulmonary heart disease. *Zhonghua Jie He He Hu Xi Za Zhi* 1998;21:404-6.
13. Weng XZ. Anti-smoking campaign in China. *Chin Med J (Engl)* 1990;103:875-8.
14. Weng X. Physicians of the respiratory tract disease specialty should take the lead and be the example in the control of smoking. *Zhonghua Jie He He Hu Xi Za Zhi* 1998;21:579-80.
15. Weng X, Zhang H. Smoking and chronic obstructive pulmonary disease. *Zhonghua Nei Ke Za Zhi* 1999;38:797-8.
16. Hu D, Feng X. Improving recognition and diagnosis level of pulmonary embolism. *Zhonghua Yi Xue Za Zhi* 2001;81:1479-80.
17. Hu DY, Pan CY, Yu JM, et al. The relationship between coronary artery disease and abnormal glucose regulation in China: the China Heart Survey. *Eur Heart J* 2006;27:2573-9.
18. Hu DY, Jing ZC. To standardize the screening, diagnosis and treatment of pulmonary arterial hypertension. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007;35:977-8.
19. Hu D, Li J, Li X, et al. Investigation of blood lipid levels and statin interventions in outpatients with coronary heart disease in China: the China Cholesterol Education Program (CCEP). *Circ J* 2008;72:2040-5.
20. Hu DY, Sun YH. Anticoagulation as adjunctive therapy to thrombolysis for pulmonary embolism: when to start? *Zhonghua Nei Ke Za Zhi* 2008;47:623-4.
21. Raschke RA, Reilly BM, Guidry JR, et al. The weight-based heparin dosing nomogram compared with a "standard care" nomogram. A randomized controlled trial. *Ann Intern Med* 1993;119:874-81.
22. Liang Y, Luo H. Clinical design and application of body weight-based heparin dosing nomogram. *Chin J Tuberc Respir Dis* 2003;26:114-5.
23. Y. Liang, H. Luo, W. Zhang. The study of heparin anticoagulation dosage and its influencing factors in pulmonary thromboembolism. *Chest* 2003;supplement:109.
24. Y. Liang, H. Luo. Clinical design and application of body weight-based heparin dosing nomogram. *Chest* 2003; supplement:109.
25. Zhicheng J, Lihe L, Zhiyan H, et al. Bone morphogenetic protein receptor-II mutation Arg491Trp causes malignant phenotype of familial primary pulmonary hypertension. *Biochem Biophys Res Commun* 2004;315:1033-8.
26. Jing ZC, Xu XQ, Badesch DB, et al. Pulmonary function testing in patients with pulmonary arterial hypertension. *Respir Med* 2009;103:1136-42.
27. Jing ZC, Jiang X, Han ZY, et al. Iloprost for pulmonary vasodilator testing in idiopathic pulmonary arterial hypertension. *Eur Respir J* 2009;33:1354-60.
28. Jing ZC, Xu XQ, Ma CR, et al. Effects of bosentan in treatment of pulmonary arterial hypertension: a pilot study of 21 patients. *Zhonghua Yi Xue Za Zhi* 2008;88:2136-9.
29. Jing ZC. The current situation and strategies in management of pulmonary arterial hypertension in China. *Zhonghua Jie He He Hu Xi Za Zhi* 2007;30:643-4.
30. Jing ZC, Xu XQ, Han ZY, et al. Registry and survival study in Chinese patients with idiopathic and familial pulmonary arterial hypertension. *Chest* 2007;132:373-9.
31. Jing ZC, Jiang X, Wu BX, et al. Vardenafil treatment for patients with pulmonary arterial hypertension: a multicentre, open-label study. *Heart* 2009;95:1531-6.
32. Jing ZC, Xu XQ, Jiang X, et al. Feasibility and safety of right heart catheterization and pulmonary angiography through the antebraichium veins. *Zhonghua Xin Xue Guan Bing Za Zhi* 2009;37:142-4.
33. Jing ZC, Strange G, Zhu XY, et al. Efficacy, safety and tolerability of bosentan in Chinese patients with pulmonary arterial hypertension. *J Heart Lung Transplant* 2010;29:150-6.
34. Jing ZC, Yu ZX, Shen JY, et al. Vardenafil in pulmonary arterial hypertension: a randomized, double-blind,

- placebo-controlled study. *Am J Respir Crit Care Med* 2011;183:1723-9.
35. Wang C, Zhai Z, Yang Y, et al. Efficacy and safety of low dose recombinant tissue-type plasminogen activator for the treatment of acute pulmonary thromboembolism: a randomized, multicenter, controlled trial. *Chest* 2010;137:254-62.
 36. Wu Y, Wang C, Pang B, et al. The pathology of and the cardio-pulmonary functional changes in acute multiple pulmonary microthromboembolism in a canine model. *Zhonghua Jie He He Hu Xi Za Zhi* 2002;25:217-20.
 37. Wang C, Zhai Z, Yang Y, et al. Efficacy and safety of 2-hour urokinase regime in acute pulmonary embolism: a randomized controlled trial. *Respir Res* 2009;10:128.
 38. Luo H, Liang Y. Thrombin-activatable fibrinolysis inhibitor: a new modulator linking coagulation and fibrinolysis. *Basic Medical Sciences and Clinics* 2003;23:484-9.
 39. Luo H, Liang Y. The influencing factors of heparin anticoagulation guided by APTT. *Journal of Cardiovascular and Pulmonary Diseases* 2003;22:245-7.
 40. Luo H, Liang Y. Clinical assessment of diagnostic technology for pulmonary embolism. *Chinese Journal of Medicine* 2005; 40:15-7.
 41. Luo H, Liang Y, Yang JH, et al. The study of individual dosage of warfarin and its application in pulmonary thromboembolism. *Journal of Chinese Modern Medicine* 2006;3:491-4.
 42. Luo H, Liang Y. Initial study of heparin dosage and the time to achieve APTT target in pulmonary thromboembolism. *Journal of Cardiovascular and Pulmonary Diseases* 2009;3:178-82.
 43. Luo H, Liang Y. Initial Evaluation of Raschke Nomogram as Heparin Anticoagulation Guidance in Chinese Patients with Pulmonary Thromboembolism. *Contemporary Medicine* 2009;15:11-3.
 44. Luo H, Liang Y. Study of relationship among heparin dosage, concentration and APTT in pulmonary thromboembolism. *Journal of Cardiovascular and Pulmonary Diseases* 2009;4:269-72.

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