PH Registry: China's Experience

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Our research is a Chinese state-backed project, and is the largest and the most authoritative pulmonary hypertension registry study in China. It is led by Prof. Jian-Guo He from Fuwai Hospital and has 60 participating centers distributing across China (which can ensure the representativeness of enrolled patients). Our project was initiated in Aug. 2009 and has been conducting smoothly for 5 years.

Our project consists of four parts, including a national, prospective, multi-center pulmonary arterial hypertension (PAH) registry, a registry for chronic thromboembolic pulmonary hypertension (CTEPH), a registry for pulmonary hypertension due to left heart disease and a heart function study of pulmonary hypertension. The objectives of our study are to establish a national-wide information platform for Chinese PH patients (WHO Group 1, 2 and 4), to study the epidemiology, to illustrate the actual clinical characteristics, diagnosis and treatment strategies of Chinese PH patients, and to explore the changes of prognosis, analyze prognostic factors, and establish a survival prognostic model of Chinese PH patients (WHO Group 1, 2 and 4). Our registry studies have been recorded on the ClinicalTrials.gov website.

We have made detailed protocols for our studies, and they all have strict inclusion and exclusion criteria for patient enrollment.

For heart function study, eligible patients still need to receive echocardiogram examination, PET and cardiac magnetic resonance (CMR) within one week. And their blood samples will be collected and stored for further study. All patients will be followed-up every 6 months (±2 weeks) by telephone, letter, e-mail, outpatient or hospitalization. Main outcomes including death, receiving atrial septostomy, receiving Lung/Heart-lung transplantation, re-hospitalization due to PH aggravation and lost followup, will be re-corded. Research data will be recorded on electronic case report (eCRF) forms by trained researchers immediately after patient`s enrollment to avoid data missing and memory bias.

Each center has its unique user name and password to keep the confidentiality of data. Data from each local center will be reviewed by a General Center, and mistakes and suggestions will be fed back by e-mail. Inspectors, from General Center, will also be sending to local centers to guide their work regularly. We have also made some standards for the conducting of protocols, for examples, we applied modified NYHA/WHO Functional Class to assess patient`s heart function, we performed 6MWT and Borg score according to ATS statement, we even made standard procedures for echocardiogram examination and RHC. In the end, every study has its own patient informed consent.

Jian-Guo He

In the PAH registry study, we have enrolled 1562 patients, and our preliminary research results show that, Chinese PAH patients have some different features comparing with US REVEALstudy and French registry study. Our patients are much younger with better WHO-FC. They have longer 6MWD and better cardiac index even with higher mPAP and worse PVR. For CTEPH registry, 195 patients have been enrolled, and our patients are also much younger with worse PVR comparing with a UK study. For PH due to left heart disease, we want to illustrate how PH will affect the prognosis of patients with left heart diseases, we only enroll patients who have received RHC a month prior to registry and about 261 patients have been enrolled. But in other Group 2 registrystudies, patients only received echocardiogram examination to measure pressure of pulmonary artery, which is inaccurate. So our research is very important and meaningful.

In the heart function study, we found some echocardiographic parameters like TAPSE, S` correlated well with hemodynamics measured by RHC or CMR, which can reflect right ventricular function, and the ratio of transverse diameter of RV to LV can predict mortality of IPAH patient. In the PET study, we found some parameters like RV SUV and RV/LV SUV in both fasting and glucose loading conditions can reflect RV function, and RV/LV SUV in fasting condition can even predict survival in patients with IPAH and HPAH. The CMR study showed that some parameters can assess RV function noninvasively. We also found biomarkers like red blood cell distribution width (RDW), CXCL10, 12, 16 and YKL-40 can not only reflect RV function, but also predict prognosis.

In summary, our researchis supported by Chinese government, and is the largest and the most authoritative pul-monary hypertension registry study in China, covering PH WHO group 1, 2 and 4. All the enrolled patients are confirmed PH cases by RHC. We also involved a PH heart function study. Imaging methods (PET, CMR and Echocardiogram) and biomarkers are applied to help evaluated heart function and predict prognosis. Our preliminary results of this project have been published on international journals, and have received wide attentions.

Therapeutic Strategies of Intermediate Risk Pulmonary Embolism: Present and Future

Prof. Chen WANG will give us a speech on the therapeutic strategies of intermediate risk pulmonary embolism (PE). He will introduce the brief history, definition and diagnostic criteria of PE risk stratification. The prognosis and outcome of PE are affected by risk stratification. There are controversies and uncertainties in the field of intermediate risk PE. Randomized clinical trials that test fibrinolytic agents versus heparin alone in patients with acute pulmonary embolism have enrolled, in total, fewer than 1000 patients over the past 40 years. Although these drugs have been shown to rapidly improve hemodynamic variables, their effects on the clinical outcome, particularly in patients without hemodynamic instability at presentation, have not been determined. The Pulmonary Embolism Thrombolysis (PEITHO) trial was designed to investigate the clinical efficacy and safety of fibrinolytic therapy with a single–bolus injection of tenecteplase, in addition to standard anticoagulation therapy with heparin, in normotensive patients with acute pulmonary embolism and an intermediate risk of an adverse outcome. Thrombolysis reduces the primary end point of death or hemodynamic collapse within 7 days of randomization. However, thrombolytic therapy significantly increased risk of major bleeding. In the subgroup analysis, agingincreases bleedings. A recent meta–analysis which enrolls 5 clinical trials finds that low–dose rt–PA does not increase the major bleeding but remain similar efficacy.A Multi–Center RCT is performed by the CHINA VTE Investigating Group, to investigate the efficacy and safety of thrombolysis with low dose rt–PA in normotensive patients with acute intermediate–risk PE (both treatment arms receive LMWH anticoagulation). The preliminary data will be presented in this speech. In this field, further study and analysis remain to be done. Alternative endpoints including clot burden, RV dysfunction, pulmonary hypertension and life quality need to be reconsidered. The indications and contraindicationsof thrombolysis also need to be revaluated.Further stratification of intermediate risk PE is an important problem to be solvedin the future.