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Chest 2007;132;373-379; Prepublished online March 30, 2007;
DOI 10.1378/chest.06-2913

ISSN:0012-3692

CHEST

Original Research

PULMONARY HYPERTENSION

Registry and Survival Study in Chinese Patients With Idiopathic and Familial Pulmonary Arterial Hypertension*

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Background: **To evaluate the clinical features and survival data of patients with idiopathic pulmonary arterial hypertension (PAH) and familial PAH in Chinese patients.**
Methods: **Seventy-two patients with idiopathic PAH and familial PAH were enrolled in the study from 1999 to 2004 and were classified into two groups according to World Health Organization (WHO) functional class (I/II and III/IV). Clinical and hemodynamic data were recorded.**
Results: **The mean age of the 72 patients was 35.9 years with female patient/male patient ratio of 2.4:1. A significant difference was identified in the clinical presentation between two WHO functional class groups at baseline. Echocardiography showed a mean pulmonary systolic pressure of 98 mm Hg. Left ventricular end-diastolic diameter was significantly smaller in the group of patients in WHO functional class III/IV than in those in class I/II group. After follow-up for a mean (± SD) duration of 40.1 ± 20.0 months, the survival rates at 1, 2, 3, and 5 years were 68.0%, 56.9%, 38.9%, and 20.8%, respectively. A significant difference was identified in survival rate between the class I/II and class III/IV groups (p = 0.02 [log rank test]).**
Conclusions: **The baseline characteristics and survival rates of our cohort study are close to those of the National Institutes of Health Registry in the 1980s, and the 1-year survival rate is obviously lower for patients in this registry than for those in the French registry between 2002 to 2003. Lack of effective treatment was the main cause of poor survival in this study. Our results support the need of an appropriate treatment strategy for this devastating disease in China.**
(CHEST 2007; 132:373–379)

Key words: pulmonary arterial hypertension; registry; survival rate

Abbreviation: LVEDD = left ventricular end-diastolic diameter; NIH = National Institutes of Health; PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure; PPH = primary pulmonary hypertension; RHC = right heart catheterization; WHO = World Health Organization

Idiopathic pulmonary arterial hypertension (PAH) and familial PAH were described as primary pulmonary hypertension (PPH) before 2003; PAH is a devastating disease that is associated with increased pulmonary vascular resistance and the development of right heart failure or even death.[1,2] In 1951, Dresdale and colleagues[2] first defined PPH as a rare disease that is characterized by elevated pulmonary artery pressure (PAP) with no apparent cause. The diagnosis is usually made by excluding other known causes of pulmonary hypertension.[3] From 1981 to 1987, National Institute of Health (NIH) performed a multicenter PPH registry study in United States to get more information on this disease. In that study, 187 PPH patients were enrolled, and clinical data and outcomes were followed and summarized.[4] These results became the most important basic data for learning about the epidemiology, clinical characteristics, and prognosis of PPH in the long term. From 2002 to 2003, another national PAH registry study in France[5] provided us with greater insight into this disease. But it is not yet known whether the results of these studies can be extended to other populations. So, it was extremely important to initi-

ate a PAH registry study in another population, like China, because these international data can enrich our knowledge of this disease.

China is a multinational country, not only in terms of its large population, but also by remarkable differences in race, lifestyle, customs, and environment relative to Western countries.

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The most effective treatments (*eg*, epoprostenol and bosentan) are not affordable for Chinese patients, and this has led to difficulty in preventing and treating pulmonary hypertension in China. Therefore, it was necessary to initiate PAH registry study in China to explore the clinical characteristics and survival data in Chinese patients with PAH.

Materials and Methods

Patients

This registry study was conducted at Fu Wai Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College from January 1999 to October 2004. A total of 72 consecutive patients in whom idiopathic and familial PAH had been diagnosed were enrolled into this study. Patients with suspected pulmonary hypertension were admitted to a hospital ward for further evaluation. PAH was defined as a mean PAP of > 25 mm Hg at rest by right heart catheterization (RHC)[6] or systolic PAP exceeding 40 mm Hg by echocardiography in patients without RHC.[7] These patients were followed up to 2006, and a 6-min walk test and RHC were conducted in 12 of them who did not have hemodynamic data at the time of the first evaluation. The complementary RHC confirmed the diagnosis of idiopathic and familial PAH.

Before the patient was discharged from the hospital, individual information and patient demographics were collected and recorded on the standard registry form, including the following: (1) name, gender, nationality, and date of birth; (2) the onset of symptoms and time; (3) medical history; (4) personal history and family history; (5) physical examination findings; (6) laboratory test results; (7) ECG; (8) chest radiograph; (9) echocardiograph; (10) RHC; and (11) clinical diagnosis.

According to the World Health Organization (WHO) functional classification at baseline, all patients were divided into either a class I/II group or a class III/IV group. Echocardiographic variables, hemodynamic parameters, and survival rate were compared between the two groups.

According to the time of enrollment, the patients were divided into the following three groups: the 1999-to-2000 group; the 2001-to-2002 group; and the 2002-to-2004 group. The duration from the onset of symptoms to diagnosis was also compared among the three groups.

All the patients were followed up by three experienced PAH specialists and completed standard follow-up forms before June 2005. The primary end points were death and WHO functional class, which were evaluated either over the telephone or by mail. The death date and causes were recorded. Clinical outcomes were compared between WHO functional class I/II group and class III/IV group. A survival analysis was performed, and the results were compared with those of the NIH registry and French registry.[4,5] The treatment of these patients was recorded and summarized in the period of follow-up.

The study was approved by the Institutional Review Boards of Fu Wai Hospital, the Chinese Academy of Medical Sciences, and the National Ministry of Science and Technology of China. Informed consent was obtained from each participant.

Statistical Analysis

All the of the registry forms were coded. The data were separately input by two doctors using appropriate software (Epidata, version 3.1 [free software]). A statistical software package (SPSS, version 13.0; SPSS; Chicago, IL) was applied to data management. Baseline and follow-up data were expressed as the mean ± SD or as the frequency and proportions. Differences between proportions were compared with a χ^2 test, differences between two groups were assessed by independent sample *t* test, and differences between multiple groups were performed by analysis of variance. Survival comparison was tested by Kaplan-Meier estimate. p Values of < 0.05 were considered to be significant.

Results

Demographic Characteristics and Comparison With NIH Registry and French Registry

Of the 72 patients enrolled in this study, 21 were men and 51 were women (Table 1). The female patient/male patient ratio was 2.4:1. The mean age was 35.9 ± 12.2 years (range, 9.7 to 73.8 years). According to different genders, there was no difference in patients' age when they received the first medical examination ($p = 0.36$). Of these 72 patients, 11.1% (8 patients) were < 20 years old, 56.9% (41 patients) were 20 to 39 years old, 27.8% (20 patients) were 40 to 59 years old, and 4.2% (3 patients) were > 60 years old. The patients between 20 and 59 years of age accounted for 84.7% of all

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This study was supported by research grant No. 2002BA711A08 ("National Key Technologies R&D Program") from the National Ministry of Science and Technology, People's Republic of China.
The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Manuscript received December 7, 2006; revision accepted February 26, 2007.

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DOI: 10.1378/chest.06-2913

Table 1—*Baseline Characteristics of Chinese Registry, NIH Registry, and French Registry

Characteristics	Chinese Registry (IPAH/FPAH)	NIH Registry (PPH)	French Registry (PAH)
Cases, No.	72	187	674
Age, yr	35.9 ± 12.2	36 ± 15	50 ± 15
Gender, No.			
Male	21	69	234
Female	51	118	440
Ethnicity, No.			
Han nationality	67		
Others	5		
Family history	4 (5.6)	12 (6)	26 (3.9)
Initial symptoms			
Breathless on exertion, fatigue	71 (98.6)	60%	
Chest pain	21 (29.2)	7%	
Syncope	19 (26.4)	13%	
Hemoptysis	15 (20.8)		
Palpitation	7 (9.7)	5%	
Edema of lower limb	3 (4.2)	3%	
Chest distress	2 (2.8)		
Time to diagnosis from onset of symptoms, mo	26.4 ± 27.6	24.4 ± 58.8	27
Physical examination, %			
Accentuated P2	88.9	93	
WHO functional class			
I/II	2/37	0/29	1/24
III/IV	44/17	71	63/12
Cyanosis	21 (29.2)	20%	
Jugular venous distention	10 (13.9)		
Edema of lower limb	8 (11.1)		
ECG			
Right-axis deviation	52 (72.2)	79%	
Right ventricular hypertrophy	55 (76.4)	87%	

*Values are given as the mean ± SD or No. (%), unless otherwise indicated. IPAH = idiopathic PAH; FPAH = familial PAH.

patients (61 patients). A total of 93.1% of patients were reported as being of Han nationality.

Medical and Family History

Familial PAH was diagnosed in four patients (5.6%). A gene mutation test was completed in one family, and a bone morphogenetic protein receptor-II mutation was found in this family.[8]

Symptoms

The mean duration from the onset of symptoms to diagnosis was 26.4 ± 27.6 months. The most common symptom was breathlessness on exertion (98.6% of patients). Other common symptoms were chest pain (29.2% of patients), syncope (26.4% of patients), hemoptysis (20.8% of patients), palpitation (9.7% of patients), and edema of the lower limbs (4.2% of patients).

Physical Examination

Physical examination showed an accentuated pulmonic second sound (P_2) in 88.9% of patients, cyanosis in 29.2% of patients, as well as jugular venous distention in 13.9% of patients.

Chest Radiograph Examination and ECG

The main finding on the chest radiograph was a heart/chest ratio of > 0.44, which was found in all patients. The incidence of right ventricular hypertrophy seen on the ECG was 76.4%; right-axis deviation was 72.2%. A regression analysis showed that the heart/chest ratio was not related to PAP as detected by either echocardiography or RHC, and nor was right ventricular hypertrophy as detected by ECG.

Echocardiography and RHC

The results of echocardiography were listed in Table 2. The mean systolic PAP was 97.8 ± 28.9 mm Hg, and the mean left ventricular end-diastolic diameter (LVEDD) was 35.7 ± 9.7 mm, which was lower than the normal range (male patients, < 55 mm; female patients, < 50 mm) in 97.2% of patients; the mean left ventricular ejection fraction was 66.4 ± 9.0%.

Table 2—*Echocardiographic Variables in Different WHO Functional Classes

Variables	WHO Class I/II	WHO Class III/IV	Total
Cases, No.	28	44	72
Aortic diameter, mm	30.0 ± 7.3	31.4 ± 4.6	30.8 ± 5.8
Right ventricular diameter, mm	32.5 ± 6.9	35.0 ± 9.2	34.0 ± 8.4
TV regurgitant velocity, m/s	4.2 ± 1.0	4.7 ± 0.6	4.7 ± 0.8
Pulmonary artery systolic pressure, mm Hg	91.1 ± 35.8	101.6 ± 23.8	97.8 ± 28.9
LVEDD, mm	41.2 ± 11.7	32.3 ± 6.3†	35.7 ± 9.7
EF, %	67.4 ± 9.3	65.8 ± 8.9	66.4 ± 9.0

*Values are given as the mean ± SD, unless otherwise indicated. TV = tricuspid valve; EF = ejection fraction.
†$p < 0.001$ (class I/II vs class III/IV).

The variables of echocardiography in patients with different WHO functional classes were analyzed as well, and it was found that LVEDD was much smaller in the group of patients in functional class III/IV than in group in functional class I/II (32.3 vs 41.2 mm, respectively; $p < 0.001$), but systolic PAH and tricuspid regurgitant velocity were similar in the two groups.

RHC was performed in 20 patients at the initial examination and was repeated in 12 patients during the follow-up period. The baseline data show that the mean right atrial pressure was 12.8 ± 5.6 mm Hg, mean systolic right ventricular pressure was 84.0 ± 32.2 mm Hg, systolic PAP was 89.7 ± 24.5 mm Hg, diastolic PAP was 44.7 ± 15.1 mm Hg, and mean PAP was 64.1 ± 17.2 mm Hg; pulmonary vascular resistance was 1634.8 ± 642.0 dyne · s · cm^{-5}. According the NIH registry study, female patients did not differ significantly from male patients in hemodynamic findings, so we only selected data from female patients to compare with those from our study; we also compared the data with those from the French registry which was published in 2006 (Table 3). Similar to the NIH and French registries, a significant difference was found in right atrial pressure in patients from different WHO functional classes. The mean right atrial pressure was significantly lower in the class I/II group (7.8 ± 2.6 mm Hg) than in the class III/IV group (14.4 ± 6.2 mm Hg; $p = 0.01$); the mean PAP, systolic PAP, diastolic PAP, and pulmonary vascular resistance were higher in class III/IV group than in the class I/II group but did not reach statistical significance. During the follow-up period, the pulmonary hemodynamic data showed that the pulmonary capillary wedge pressure was < 15 mm Hg (Table 4), which supported that the diagnosis of idiopathic and familial PAH was correct.

Duration From Onset of Symptoms to Diagnosis

The mean duration from the onset of symptoms to diagnosis was 26.4 ± 27.6 months (Table 1); the longest duration was in 1999 to 2000 (32.06 ± 31.18 months). From 2001 to 2002, this duration was shortened to 29.34 ± 30.85 months. After 2003, the mean time required for diagnosing idiopathic and familial PAH was shortened to 18.79 ± 18.84 months, which was significantly less than the time of diagnosis in 1999 to 2000 ($p = 0.028$) [Table 5].

Therapy

During the period of this study, only conventional therapy was available in China; all treatment was recorded and is summarized in Table 6. The results

Table 3—*Variables of RHC in Different WHO Functional Classes

Variables	Class I/II	Class III/IV	Total	NIH Registry (Female)	French Registry (IPAH)
Cases, No.	11	9	20	118	259
RAP, mm Hg	7.8 ± 2.6	14.4 ± 6.2†	12.8 ± 5.6	9 ± 6	9 ± 5
RVP, mm Hg	82.5 ± 29.8	85.6 ± 37.0	84.0 ± 32.2		
Systolic PAP, mm Hg	83.6 ± 20.6	92.8 ± 29.1	89.7 ± 24.5	91.7 ± 23.0	
Diastolic PAP, mm Hg	41.7 ± 15.5	47.7 ± 15.0	44.7 ± 15.1	43.3 ± 14.1	
Mean PAP, mm Hg	59.1 ± 14.7	69.1 ± 18.8	64.1 ± 17.2	60 ± 18	56 ± 14
PVR, dyne · s · cm^{-5}	1,600.8 ± 722.2	1,681.5 ± 557.3	1,634.8 ± 642.0		1,824 ± 800

*Values are given as the mean ± SD, unless otherwise indicated. RAP = right atrial pressure; RVP = right ventricular pressure; PVR = pulmonary vascular resistance.
†$p = 0.01$ (class I/II vs class III/IV).

Table 4—*Data From Clinical and Hemodynamic Follow-up for 12 IPAH Patients

Variables	IPAH (n = 12)
Age, yr	32.42 ± 13.05
Sex	
Male	2
Female	10
BSA, m^2	1.55 ± 0.19
WHO functional class	
I/II	9
III/IV	3
Mean PAP, mm Hg	57.33 ± 24.97
PCWP, mm Hg	6.27 ± 2.53
CI, L/min/m^2	2.97 ± 1.49
PVR, Wood units	15.02 ± 8.63
Svo_2, %	64.07 ± 12.44
Acute vasodilator responders	3 (25)
6MWD (m)	399.55 ± 125.77

*Values are given as the mean ± SD or No. (%). BSA = body surface area; PCWP = pulmonary capillary wedge pressure; CI = cardiac index; Svo_2 = mixed venous saturation; 6MWD = 6-min walk distance. See Table 3 for abbreviation not used in the text.

showed that calcium channel blockers was the most popular form of therapy in China before 2006.

Survival Analysis

All patients were followed up by three experienced specialists in PAH according to the standard follow-up forms from March to June 2005. The mean duration of follow-up was 40.1 ± 20.0 months. Of the 72 patients, 52 were followed up successfully (72.7%). Twenty-two patients were still alive at the cutoff day, and the survival rate was 42.3% (22 of 52 patients); 30 patients had died, and the mortality rate was 57.7% (30 of 52 patients). The mean survival time was 29.2 ± 21.3 months.

In this study, the survival rates at 1, 2, 3, and 5 years were 68.0%, 56.9%, 38.9%, and 20.8%, respectively, with conventional therapy (Table 7). Table 7 also shows no statistical difference in survival rate compared with those of the NIH registry ($p > 0.05$), but were obviously poorer compared with those of the French Registry. There was a significant difference in survival rate between the class I/II group and the class III/IV group by log-rank test ($p = 0.02$) [Fig 1]. A paired *t* test showed no improvement in WHO functional class status in 22 patients who survived ($p = 0.13$), indicating that current therapies have no effect on the functional class of patients with idiopathic and familial PAH in China.

Table 5—*Comparison of the Duration From Symptom Onset to Diagnosis in the Three Groups

Periods of Diagnosis	Patients, No.	Time From Symptom Onset to Diagnosis, mo
1999–2000	26	32.06 ± 31.18
2001–2002	20	29.34 ± 30.85
2003–2004	26	18.79 ± 18.84†

*Values are given as mean ± SD, unless otherwise indicated.
†$p = 0.028$ (2003–2004 vs 1999–2000).

Table 6—*Conventional Therapy During Period From 1999–2004

Therapy	Patients
Calcium channel blockers	65 (90.3)
Oral anticoagulation	36 (50.0)
Diuretics	58 (80.6)
Digoxin	41 (56.9)

*Values are given as No. (%).

Discussion

The present study is the first report from China on data concerning idiopathic and familial PAH. Dyspnea on exertion is the most common symptom of disease onset, occurring in 98.6% of Chinese patients with idiopathic and familial PAH, predominantly in women (women/men ratio, 2.4:1); idiopathic and familial PAH can occur at any age but most often occurred between the ages of 20 and 59 years. The survival rate decreased dramatically after 5 years. These results were similar to those in the report of the NIH registry,[4] but the 1-year survival rate was poorer in this group of patients than in the group of patients in the French registry.[5]

The diagnosis of idiopathic and familial PAH, however, is often delayed; the mean duration from the onset of symptoms to diagnosis was 26.4 ± 27.6 months in this study, which is similar to that from NIH registry (24.4 ± 58.8 months) reported by Rich et al[4] in 1987 and from the French registry (27 months) reported by Humbert et al[5] in 2006. This indicated that the early diagnosis of pulmonary hypertension is still a challenge. According to different enrollment times, we divided the patients into the 1999-to-2000 group, the 2001-to-2002 group, and the 2002-to-2004 group, showing that the duration from the onset of symptoms to diagnosis was shortened gradually after some years. We found that the acknowledgment of the diagnosis and the awareness of the disease have been improving gradually in the last 5 years.

No special finding was identified in the results of the physical examination and chest radiograph in this study compared with other studies. The ECG showed right ventricular hypertrophy in 76.4% of patients that was not correlated to the hemodynamic

Table 7—*Comparison of Survival Rates Among China Registry, NIH Registry, and French Registry

Registry	1 Year	2 Years	3 Years	5 Years
Chinese	68.0	56.9	38.9	20.8
NIH	77	52	41	27
French†	89.3			

*Values are given as %.

†Including idiopathic pulmonary arterial hypertension, familial pulmonary arterial hypertension, and anorexigen-associated pulmonary arterial hypertension.

variable ($p > 0.05$), suggesting that right ventricular hypertrophy is common in PAH patients; however, the absence of right ventricular hypertrophy does not rule out the diagnosis of PAH. The ECG had limited value in evaluating and diagnosing PAH.

Two-dimensional transthoracic echocardiography with Doppler flow is the most commonly used tool to screen PAH. Murata et al[7] reported that systolic PAP estimated by echocardiography is often higher than that estimated by RHC. We also found a variation in results with the use of these two methods (97.8 ± 28.9 vs 89.7 ± 24.5 mm Hg, respectively; $p = 0.03$). Furthermore, LVEDD was decreased while left ventricular ejection fraction had no change in 97.7% of patients; this observation was consistent with the literature.[9]

RHC is the "gold standard" for documenting the presence of PAH, and many international trials[6,10,11] have used RHC parameters as the main indicators. But the RHC test is not generally used in China; only a few patients with severe PAH have accepted the use of the RHC test. The major reason for this is that RHC is invasive and relatively expensive in China. Regarding the RHC analysis of 20 idiopathic and familial PAH in the study, we found that systolic PAP, diastolic PAP, and mean PAP were increased to a similar extent as that of Rich et al[4]; moreover, 95% of patients had elevated right atrial pressures, suggesting that right heart failure is more likely to develop in Chinese patients, who are more likely to have a poorer condition at the first evaluation. Much effort should be made to shorten the time from the onset of symptoms to diagnosis. The earlier the treatment, the better the clinical outcome.

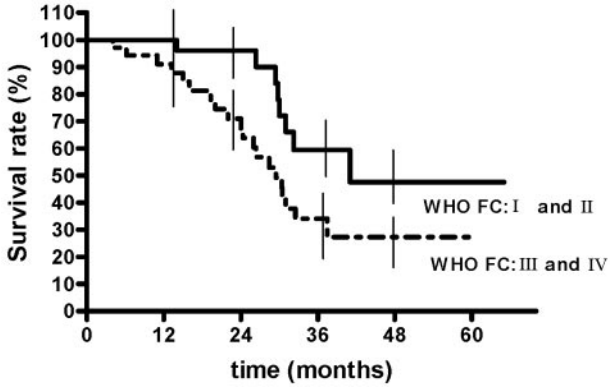

FIGURE 1. Survival rate comparison of patients in WHO functional class I/II vs those in class III/IV ($p = 0.02$ [log rank test]). FC = functional class.

Based on WHO functional class, 72 patients were divided into two groups (WHO functional class I/II and WHO functional class III/IV) to evaluate the impact of different functional class on prognosis. The results showed that the survival of patients in WHO functional class I/II was much better than those in class III/IV ($p = 0.02$). This phenomenon was consistent with the report by Kawut et al.[12] WHO functional class at diagnosis can predict the prognosis.

In China, the conventional therapy for idiopathic and familial PAH includes diuretics and anticoagulation (Table 6). The survival rates at 1, 2, 3, and 5 years for patients with idiopathic and familial PAH in this study were 68.0%, 56.9%, 38.9%, and 20.8%, respectively, which are close to the survival rates reported in the 1991 study by D'Alonzo et al[13] (77%, 52%, 41%, and 27% respectively). Obviously, the prognosis of these patients with conventional therapy is much poorer than that of the patients in the French registry[5] in which epoprostenol or bosentan were used.

In 2002, Sitbon and colleagues[14] reported that the survival rates at 1, 2, and 5 years for patients receiving continuous infusion of prostacyclin were 85%, 70%, and 55%, respectively. In 2005, McLaughlin et al[15] reported that the survival rate of in PPH patients after receiving monotherapy with bosentan can be improved to 85% and 70%, respectively, at the end of 12 and 24 months. By the end of 2004, no specific treatment was available for PAH in China. Though therapy with sildenafil and beroprost has been launched, these drugs have no indication for the treatment of PAH. Currently, the available treatment for PAH in China is still the same as that in the era before 1992 in Western countries. The main reasons for this are as follows: (1) the price of effective and specific drugs is too high for most Chinese patients; (2) many drugs, like sildenafil, are still in the process of further investigation; (3) beroprost can only be prescribed to PAH patients in Japan, which means that the clinical value of this product is limited; and (4) calcium channel blockers are widely used without an acute vasoreactivity test.

These problems should prompt us to develop some cheap but effective medicines for developing countries; it is not only an economic problem but also a key strategy to save the poor patients who

cannot afford these expensive but advanced therapies. Furthermore, it is necessary to perform epidemiology studies in these regions and to explore suitable treatment strategies.

As a result of significant advances in the immense research on PAH, we now have a better understanding of this disease. Along with the progress in therapeutics, the clinical outcomes of patients with PAH have improved remarkably, as was shown in the French registry, although we are still faced with many challenges. For example, the known BMPR-II gene mutation is the pathogenic factor in patients with familial PAH, but this mutation is not found in all patients with familial PAH while other patients with idiopathic PAH are carriers.[16,17] Another study[12] has shown that race is an important prognostic factor for idiopathic PAH, indicating that the outcomes for patients with idiopathic PAH in the Asian population may be poorer. The correlation and roles of environmental factors and genetic predisposition need to be explored further. Most of the current data come from Western countries. Very few reports could be found from developing countries such as China, Brazil, or Africa. More studies and screening programs should be carried out in these target populations.

References

1 Galie N, Torbicki A, Barst R, et al. Guidelines on diagnosis and treatment of pulmonary arterial hypertension: the Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. Eur Heart J 2004; 25:2243–2278

2 Dresdale DT, Schultz M, Michtom RJ. Primary pulmonary hypertension: I. Clinical and hemodynamic study. Am J Med 1951; 11:686–705

3 Wood P. Pulmonary hypertension with special reference to the vasoconstrictive factor. Br Heart J 1958; 21:557–570

4 Rich S, Dantzker DR, Ayres SM, et al. Primary pulmonary hypertension: a national prospective study. Ann Intern Med 1987; 107:216–223

5 Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France results from a national registry. Am J Respir Crit Care Med 2006; 173:1023–1030

6 McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004; 126(suppl):14s–34s

7 Murata I, Takenaka K, Yoshinoya S, et al. Clinical evaluation of pulmonary hypertension in systemic sclerosis and related disorders: a Doppler echocardiographic study of 135 Japanese patients. Chest 1997; 111:36–43

8 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; 315:1033–1038

9 Bossone E, Chessa M, Butera G, et al. Echocardiographic assessment of overt or latent unexplained pulmonary hypertension. Can J Cardiol 2003; 19:544–548

10 McLaughlin VV, Shillington A, Rich S. Survival in primary pulmonary hypertension: the impact of epoprostenol therapy. Circulation 2002; 106:1477–1482

11 Hoeper MM, Oudiz RJ, Peacock A, et al. End points and clinical trial designs in pulmonary arterial hypertension. J Am Coll Cardiol 2004; 43:48s–55s

12 Kawut SM, Horn EM, Berekashvili KK, et al. New predictors of outcome in idiopathic pulmonary arterial hypertension. Am J Cardiol 2005; 95:199–203

13 D'Alonzo GE, Barst RJ, Ayres SM, et al. Survival in patients with primary pulmonary hypertension: results from a national prospective registry. Ann Intern Med 1991; 115:343–349

14 Sitbon O, Humbert M, Nunes H, et al. Long-term intravenous epoprostenol infusion in primary pulmonary hypertension: prognostic factors and survival. Am Coll Cardiol 2002; 40:780–788

15 McLaughlin VV, Sitbon O, Badesch DB, et al. Survival with first-line bosentan in patients with primary pulmonary hypertension. Eur Respir J 2005; 25:244–249

16 Carcamo J, Zentella A, Massague J. Disruption of transforming growth factor β signaling by a mutation that prevents transphosphorylation within the receptor complex. Mol Cell Biol 1995; 15:1573–1581

17 Elliott CG. Genetics of pulmonary arterial hypertension: current and future implications. Semin Respir Crit Care Med 2005; 26:365–371

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