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ORIGINAL ARTICLE

Searching for the least invasive parameters used as predictors of survival in idiopathic pulmonary arterial hypertension

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KEYWORDS

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Abstract IPAH is a debilitating disease that is not curable and needs regular long term monitoring, where the gold standard for diagnosing and monitoring patients, is right heart catheter.

Aim: Searching for the least invasive parameters possible to use as predictors of survival in IPAH patients

Methodology: The study included 14 IPAH patients, for all PASP, SpO2, 6MWD, FC, PHQ9 depression score and targeted treatment pattern were assessed and the overall survival in 12, 24, 36, and 48 months in relation to the mentioned parameters was calculated.

Results: The overall survival was 64.29% in 12 months following diagnosis, 56.25% in 24 months, 46.88% in 36 months and 35.16% in 48 months. The overall survival was only statistically significant in the groups of depression measured by PHQ-9. Most patients presented in functional class II and III. Though SpO2, 6MWD and mono Versus combined therapy did not show statistical significance in the overall survival, yet there was obvious higher overall survival in patients with SpO2 $\geqslant$ 90%, 6MWD $>$ 300 m and in first year of treatment with combined therapy.

Conclusion: The most significant parameter affecting survival was depression score using PHQ-9. It was also observed that the highest mortality was in the first year of diagnosis although it was not statistically significant. Thus, a wider scale study is needed for the idiopathic pulmonary hypertension patients to better assess their survival pattern.

Introduction

Pulmonary arterial hypertension is a rare debilitating disease characterized by progressive increase in pulmonary arterial pressure and pulmonary vascular resistance leading to right ventricular failure and death [1]. The most commonly reported symptoms on presentation in individuals with PAH are dyspnea and fatigue. These symptoms limit physical function, and, by the time of diagnosis, most individuals have a marked functional limitation [2]. The symptoms of dyspnea and fatigue associated with PAH reflect both acute and chronic RV

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dysfunction, influence functional class and indirectly, predict survival [3].

Although PAH cannot be cured, medical therapy often allows the afflicted patient to live with the chronic illness, albeit with varying degrees of impairment which is usually physical [4].

By time, patient reaches a stage of disability, including physical and cognitive impairment as well as impaired quality of life, which is related to several factors underlying their disease process [6]. This frequently accumulates a number of life stressors that have been associated with development of depression [5].

The level of symptoms on exertion is used by clinicians to grade disease severity and prognosis in individuals with PAH [3], aiming for practical management and predicting outcome [7]. However many studies tackled this entity depending on the patients' hemodynamics based on performing right heart catheterization [8–11], there were many patients who refused performing invasive maneuvers [12].

Aim of work

Searching for the least invasive parameters possible that can be used as predictors of survival in patients with idiopathic pulmonary arterial hypertension.

Methodology

The study was held in the Chest department, Kasr Al-Aini hospital, Faculty of Medicine, Cairo University, during the year 2011.

Fourteen patients diagnosed as Idiopathic pulmonary arterial hypertension, were included in the study.

For all patients, certain parameters were used:

- PASP was used instead of m PAP as 6 patients out of the 14 patients refused performing the right heart catheter and pulmonary artery pressure was calculated only by echocardiography.
- Functional classification of pulmonary hypertension modified after New York Heart Association functional classification according to WHO 1998 [13].
- 6 minute walk distance was measured according to the standards of the ATS guidelines [14] and was classified into two groups either < 300 m or $\geqslant 300$ m.
- Oxygen saturation was measured by pulse oximetry at time of presentation and was classified into two groups $< 90\%$ or $\geqslant 90\%$.
- Patient Health Questionnaire-9 (PHQ9) for assessment of depression [15]. The results were sub classified into none and mild versus moderate and moderately severe.
- Treatment pattern was followed whether being on monotherapy or combined therapy.
- Calculating the survival time from time of diagnosis till the first of April 2015, in months or mentioning death event.
- Descriptive data were tabulated. Mean, median, standard deviations, maximum and minimum were calculated.
- Subcategories were presented in the form of absolute numbers and percentage of the total study population.
- Survival analyses were statistically analyzed and depicted as graphs.

Results

Along 42 months, 75% survival in the group $\geqslant 300$ m (no median was reached) while 30% in group < 300 m (median survival 15.3 months) (no statistical significance as p value was 0.2383).

In the group with none/mild depression, survival was 62.5% (median survival 42.63 months).

And in the group with moderate/moderately severe depression survival was 16.67% (median survival 8.13 months).

(Statistically significant with p value 0.048).

Along 4 years the group with SpO2 < 90 showed median survival 15.31 with 16.67% survival while for SpO2 $\geqslant 90$ the median was not reached with 62.5% survival (No statistical significance).

Knowing that number of patients receiving monotherapy were 10 (71.42%) in the form of sildenafil, 4 patients received combined therapy (28.58%) in the form of sildenafil and bosentan in 3 patients and sildenafil and treprostinil in 1 patient.

The group of monotherapy showed median of 10.17 months with 40% survival along 4 years while the group of combined therapy showed median of 32.53 months with 50% survival (No statistical significance).

After 1 year 90% survival was found in combined therapy and only 50% in the monotherapy group.

Discussion

The current study included 14 patients diagnosed as idiopathic pulmonary arterial hypertension. The study population was considered small which was attributed to the low incidence of the disease all over the world, where the incidence rate was stated, approximately 2–6 cases/million populations/year in the United States [16]. Recently the Registry to Evaluate Early and Long-Term PAH Disease Management "REVEAL" registry stated an annual incidence of 1–2 cases per million people in the US and Europe [17]. A prevalence of IPAH in France was found to be about 6 cases/million populations [16]. The estimated prevalence of PAH was found 15–50 cases/million [18], where IPAH accounts for at least 40% of its cases [19].

Table 1 shows that the mean age was 29 ± 8.8 years, which is consistent with the findings of Ni et al. (2009) who found the mean age of the 108 IPAH patients was 32.5 ± 12.6 years [20]. Also Pugh & Hemnes (2010), stated mean age of 34.9 ± 36.3 months [21], and National Institutes of Health (NIH) registry reported a mean ± SD age at diagnosis of 36 ± 15 years [22] while it was found in another age group 56 ± 16.4 years in other study [23]. Contemporary registry data indicate that the average age of patients diagnosed with PAH has increased, at least in the Western world [24].

Recent data from various PAH registries indicate that the demographics of IPAH patients have changed. In the US NIH registry in the 1980s PAH was typically diagnosed in young adults [22] but more recent registry data depict a shift toward diagnosing PAH in older patients [25–28].

There was evident female sex predilection as shown in Table 2, where the female: male ratio was 6:1, (no: ♀ = 12, ♂ = 2). It was found that, in the United States, the average female-to-male ratio reported in clinical trials and registries is close to 4:1 [17,21].