Editorial

Pulmonary arterial hypertension in systemic lupus erythematosus: should we bother?

Pulmonary arterial hypertension (PAH) in SLE: should we bother? Yes, but, as we shall discuss, only in patients with increased chance to develop this complication.

PAH is thought to be a life-threatening complication of CTDs, which is mainly based on reports of patients with SSc. Before advanced therapies became available, the prevalence of PAH in SSc was estimated to be between 7.5 and 12% with a 1-year survival rate of only 45% [1]. Despite the lack of data on survival and efficacy of therapeutic intervention in SSc–PAH, early diagnosis was advocated, which made sense. With the introduction of advanced therapies such as prostanooids, endothelin-receptor antagonists (ERAs) and phosphodiesterase (PDE) V inhibitors [2, 3] for PAH, clinicians now have the tools to improve pulmonary haemodynamics, functional status and probably even survival of patients with SSc–PAH. In this era of modern treatment, 1-year survival of SSc–PAH has increased from 45 to 78% [4].

Data on prevalence and survival of PAH in other forms of CTDs, such as SLE, are rare and merely based on figures obtained from tertiary referral centres. Therefore, should screening for PAH in SLE be recommended? We are uncertain. Ideally, screening is performed in patients at risk who are selected on the basis of identified risk factors. Cost effectiveness of the screening depends on its true prevalence; i.e. its occurrence in an unselected SLE cohort, the availability of a reliable and sensitive screening method and the identification of risk factors involved.

Screening should lead to early diagnosis, but clinical diagnosis of PAH is difficult. Symptoms of PAH, such as exertional dyspnoea, fatigue, weakness, angina, exertional syncope and abdominal distension, as well as its signs such as distended jugular veins, peripheral oedema, a loud pulmonary second heart sound, hepatomegaly and ascites, are unspecific, thereby making it difficult to suspect the presence of PAH on clinical grounds [5]. Early diagnosis, therefore, depends on additional methods of screening.

In this issue of the journal, Prabu et al. [6] provides important data on the prevalence of PAH in a large cohort of SLE patients. None of the patients evaluated were given sildenafil or bosentan. In contrast to what might have been expected from earlier studies, the prevalence of PAH was found to be 4.2%, which was based on echocardiographic screening. Moreover, only 3 of the 12 patients had severe disease [systolic pulmonary arterial pressure (ERVSP) > 40 mmHg]. These results are of particular interest, because the cohort, in contrast to other reports, has a community, non-tertiary background and seems not biased by the patient selection, and therefore might very well be considered as representative of the general SLE population.

The major issue that remains is the method of screening. Although widely accepted as the screening method of choice, echocardiography has its drawbacks. Estimated right ventricular systolic pressure (ERVSP) on echocardiography, which is equivalent to the pulmonary artery systolic pressure (PASP) in the absence of pulmonary outflow obstruction, showed a moderate correlation with right catheterization values of PASP [7]. ERVSP (or PASP) increases with age and BMI and, therefore, can give false positive results in elderly or obese patients [8]. In this study, in only one of the five patients, previously thought to have PAH by echocardiography, this diagnosis could be confirmed.

Additional (combinations of) screening tests for PAH may prevent under- and over-diagnosis of PAH. These tests might include biomarkers such as N-terminal pro-brain-natriuretic peptide (N-TproBNP) [9]. N-TproBNP levels in patients with scleroderma-associated PAH were significantly higher than those found in SSc patients without PAH [1474 pg/ml (s.d. 2642) vs 139 pg/ml (s.d. 151)] and correlated positively with mean PAP (r = 0.62; P < 0.0001) [9]. Although N-TproBNP levels were also of prognostic value in this group of SSc–PAH patients, their precise role, and the role of other potentially interesting biomarkers, in screening for PAH–CTD needs to be determined.

In another small study comprising 20 patients with SSc–PAH and 20 sex-matched healthy controls, levels of endoglin, endothelin-1, PDGF, TNF-α, TGF-β2 and IL-8 were assessed. Of these, endoglin, endothelin-1, TNF-α and IL-8 levels were all significantly elevated in SSc–PAH patients [10].

Unfortunately, in the study by Prabu et al. [6], levels of N-TproBNP or other biomarkers were not measured and, apart from the presence of LAC, no other risk factor was found to identify patients at risk. Questionnaires for respiratory symptoms and 6-min walk test did not differentiate between patients with or without PAH. Although in SSc patients a decrease in the diffusion capacity for carbon monoxide without concomitant changes of restrictive lung function was found as a risk factor for the development of PAH [11], such relation was not found within SLE patients.

Therefore, besides confirmation of the current data in other cohorts, efforts should be made to develop an optimal screening strategy based on reliable tools and risk factors that have been proven to be of prognostic value. Furthermore, data on survival of SLE patients with PAH and intervention with modern drugs like ERAs and PDE V inhibitors are eagerly awaited. Preliminary data suggest that SLE patients have a significantly better prognosis than SSc patients (3-year survival rate of 74 vs 47%) [4]. Altogether, when additional data become available, the data will offer the possibility to develop guidelines for screening and management of PAH in patients with SLE. Until then, on the basis of data in this issue, it seems appropriate to screen for the presence of PAH in those SLE patients at risk, i.e. those with LAC and those planning a pregnancy [6].

Disclosure statement: The authors have declared no conflicts of interest.

Marc Bijl, Hendrika Bootsma, Cees G. M. Kalenberg

1Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Accepted 21 July 2009

Correspondence to: Marc Bijl, Department of Rheumatology and Clinical Immunology, University Medical Center Groningen,
References