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Diastolic left ventricular dysfunction in ankylosing spondylitis—A systematic review and meta-analysis

Sjoerd C. Heslinga, MD[a,b,c], Carlo J. Van Dongen, MD, PhD[a], Thelma C. Konings, MD[d], Mike J. Peters, MD, PhD[c], Irene E. Van der Horst-Bruinsma, MD, PhD[a,b], Prof. dr. Yvo M. Smulders[c], Michael T. Nurmohamed, MD, PhD[a,b,c,*]

[a] Department of Rheumatology, Reade, Amsterdam, the Netherlands
[b] Department of Rheumatology, VU University Medical Centre, Amsterdam, the Netherlands
[c] Department of Internal Medicine, VU University Medical Centre, Amsterdam, the Netherlands
[d] Department of Cardiology, VU University Medical Centre, Amsterdam, the Netherlands

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ABSTRACT

Objectives: Ankylosing spondylitis (AS) is associated with increased mortality largely due to cardiovascular disease. Diastolic left ventricular (LV) dysfunction serves as a precursor to chronic heart failure and may cause morbidity and mortality. A systematic literature search was conducted to determine the prevalence of diastolic LV dysfunction in patients with AS.
Methods: We identified all echocardiographic studies investigating diastolic LV function in patients with AS. The initial search yielded 166 studies of which 11 met the inclusion criteria.
Results: Compared to control subjects, AS patients had a worse E/A ratio [mean difference −0.13 m/s (95% CI: −0.19 to −0.07)], a prolonged deceleration time [mean difference 13.90 ms (95% CI: 6.03–21.78)], and a prolonged mean isovolumetric relaxation time [mean difference 8.06 ms (95% CI: 3.23–12.89)], all suggestive of diastolic LV dysfunction. The best way to establish diastolic LV dysfunction, however, is to combine E/A ratio, deceleration time, and isovolumetric relaxation time. The latter has been done in 3 studies, all reaffirming an increased prevalence rate of diastolic LV dysfunction in AS patients as compared with control subjects, i.e., 9% versus 0%, 30% versus 12%, and 45% versus 18%, respectively.
Conclusions: Our observations support the current evidence base for an increased risk of diastolic LV dysfunction in AS. However, larger studies are needed to investigate the exact magnitude of diastolic LV dysfunction and its clinical relevance in patients with AS.

Introduction

In ankylosing spondylitis (AS), cardiovascular disease increases mortality approximately 2-fold compared to the general population, and heart failure (HF) is an important contributor to the number of circulatory deaths [1–4]. HF develops when structural or functional cardiac disorders impair the ability of the left ventricle to fill with or eject blood. A disturbed filling pattern, termed as diastolic left ventricular (LV) dysfunction, is caused by impaired relaxation of the left ventricle and may eventually lead to HF with preserved ejection fraction (HFpEF) [5]. Failing pump function of the heart is termed systolic LV dysfunction and may lead to HF with reduced ejection fraction (HFrEF) [5].

In RA, multiple studies have shown an increased prevalence of diastolic LV dysfunction but not systolic LV dysfunction [6]. Systemic inflammation appears to be an important risk factor for diastolic LV dysfunction and HFpEF, as systemic inflammation gradually damages the cardiomyocytes and causes increased collagen deposition in the heart [7]. Against this background, we hypothesize that AS patients are at an increased risk for diastolic LV dysfunction and its sequelae HFpEF. To address this item, we conducted a systematic review and meta-analysis to summarize all available studies investigating diastolic LV functioning in AS.

Methods

Search

A systematic literature search was conducted to identify all articles published from January 1990 to April 2013 that assessed

* Corresponding author at: Department of Internal Medicine, VU University Medical Center, P.O. Box 7057, Amsterdam 1007 MB, the Netherlands.
E-mail address: mt.nurmohamed@vumc.nl (M.T. Nurmohamed).

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diastolic LV function with echocardiography in AS. As technological advances in echocardiographic techniques may lead to discrepancies in the results, we only included studies published from 1990 onwards. We performed the search in Medline, EMBASE, and Cochrane library. The search details are shown in Figure 1. The complete search, including search terms, is described in detail in Supplement 1. References of included articles were manually scanned for other relevant studies.

Study eligibility

Two reviewers (S.H. and C.V.D.) screened all titles and abstracts that were retrieved by the search. Studies that met the following inclusion criteria were included: cross-sectional studies with a control group, patients diagnosed with AS fulfilling the New York 1984 criteria, and use of echocardiography [8]. Studies were excluded if the language was not English or when data on echocardiographic measurements associated with diastolic LV function were lacking.

Definitions

The cardiac cycle encompasses 2 phases, namely systole (contraction and ejection) and diastole (relaxation and filling). Systolic LV function is described using ejection fraction (EF), which is defined as the stroke volume (the volume of the left ventricle that is ejected with each contraction) divided by this LV end-diastolic volume, multiplied by 100%. Normal systolic LV function usually ranges from an EF of 55% to 70% [9]. Systolic LV dysfunction is defined as an EF $< 50\%$.

The transthoracic echocardiographic parameters commonly used to assess diastolic LV function include peak early filling velocity (E-wave) divided by late diastolic filling velocity (A-wave) (E/A ratio), deceleration time (DT), early diastolic lateral annular velocity (Em), and isovolumetric relaxation time (IVRT) (Table 1). According to these parameters, diastolic LV dysfunction is graded into the following 3 categories: mild (grade I), moderate/pseudonormal (grade II), and restrictive (grade III) [10]. Since most studies did not use this combination of echocardiographic parameters for grading diastolic LV dysfunction, we included all studies with at least 1 reported parameter for diastolic LV dysfunction. Studies not specifically designed to assess diastolic LV function, but nonetheless reporting on single echocardiographic parameters were also included.

Data extraction

Two reviewers (S.H. and C.V.D.) individually extracted data from the included studies. In case of disagreement, the opinion of a third reviewer was sought (M.N.) to reach consensus. The following data were retrieved: title, authors, year of publication, study design, inclusion and exclusion criteria, number of patients and controls, mean age, percentage male, disease duration, echocardiographic methods, the definition of diastolic LV dysfunction used, and the prevalence of diastolic LV dysfunction.

Pooling of the data

If possible, outcomes of separate studies on diastolic LV dysfunction were pooled in order to calculate a point estimate for diastolic LV dysfunction. Meta-analysis was performed using Review Manager version 5.1 (Cochrane Collaboration). Heterogeneity was estimated using I^2 index. If $I^2 > 75\%$, we used a random-effects model to calculate overall effect sizes for all individual components, with mean differences and 95% confidence intervals. Publication bias was checked visually by creating a funnel plot with the precision plotted against the mean difference of single diastolic LV parameters.

Quality assessment

All studies were scored for quality using the Newcastle–Ottawa Scale for case–control studies. This score consists of 3 categories to evaluate quality, namely selection of cases and controls, comparability of cases and controls, and ascertainment of exposure. A maximum number of points are scored for each category (4, 2, and 3 points, correspondingly), with a higher score indicating higher methodological quality.

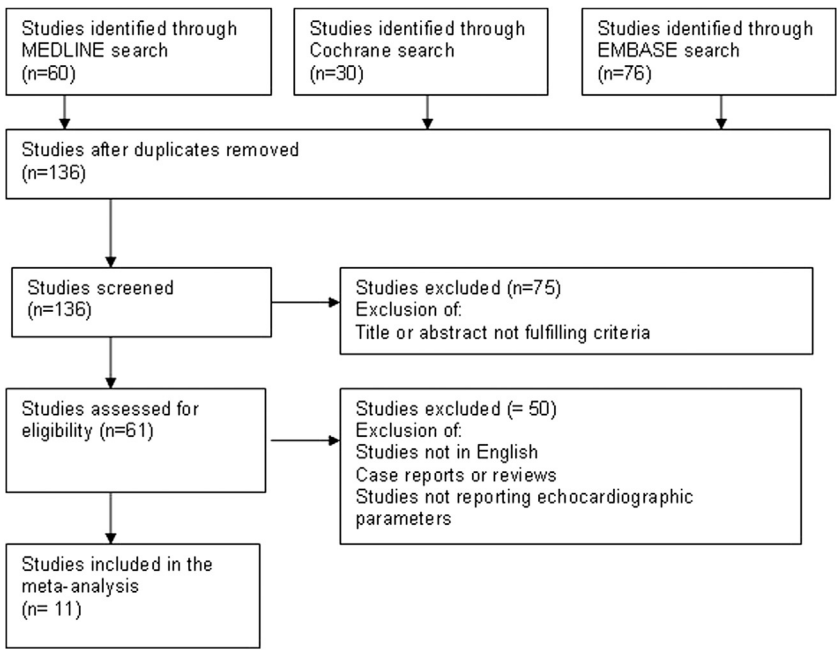

Fig. 1. Flowchart literature search.