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# Asymptomatic systolic and diastolic dysfunction in patients with risk factors referred for echocardiography. The DAVES study by the Italian Society of Cardiovascular Echography

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### Abstract

*Objectives:* This study aims to determine the prevalence of left ventricular dysfunction in subjects without signs and symptoms of heart failure referred for echocardiography essentially for the presence of one or more cardiovascular risk factors.

*Materials and methods:* The DAVES study (Disfunzione Asintomatica del Ventricolo Sinistro, left ventricular asymptomatic dysfunction) is a multicenter cross-sectional observational study based on echocardiography. Among 16,099 screened subjects from 75 Centers, we enrolled 3,537 subjects without signs or symptoms of heart failure. The prevalence of depressed left ventricular systolic (left ventricular ejection fraction  $\leq$  50%) and diastolic function was analyzed.

*Results:* The overall prevalence of asymptomatic left ventricular systolic dysfunction was 9.4%, while diastolic dysfunction was detected in 39.1% of subjects. The rate of systolic and diastolic dysfunction increased proportionally to the number of cardiovascular risk factors (1 or  $\geq$  5 risk factors), ranging from 8.1% to 27.1% and from 37.5% to 45.0%, respectively. At multivariate analysis, independent variables predictive for systolic dysfunction were male gender (p < 0.001), family history of cardiovascular disease (p = 0.002) and diabetes (p = 0.027); while for diastolic dysfunction they were age (p < 0.001), hypertension (p < 0.001) and diabetes (p < 0.05).

*Conclusions:* In a large sample of subjects without symptoms of heart failure referred to echocardiography, we found a significant prevalence of left ventricular systolic and diastolic dysfunction, both related to the number of cardiovascular risk factors.

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Key words: Left ventricular dysfunction; Echocardiography; Diastole; Systole; Heart failure.

# Riassunto: Disfunzione asintomatica sistolica e diastolica del ventricolo sinistro in pazienti con fattori di rischio cardiovascolare sottoposti ad ecocardiografia. Lo studio DAVES della Società Italiana di Ecografia cardiovascolare

*Obiettivi:* Valutare la prevalenza della disfunzione del ventricolo sinistro in soggetti senza segni o sintomi di scompenso cardiaco sottoposti a ecocardiografia in relazione alla presenza di uno o più fattori di rischio cardiovascolare.

*Materiali e metodi:* Lo studio DAVES (Disfunzione Asintomatica del Ventricolo Sinistro) è uno studio osservazionale multicentrico. Sono stati valutati 16.099 pazienti provenienti da 75 Centri e arruolati 3.537 soggetti senza segni o sintomi di scompenso cardiaco. È stata valutata la funzione sistolica e diastolica del ventricolo sinistro, osservando una prevalenza di disfunzione sistolica (frazione di eiezione  $\geq$  50%) del 9,4% e diastolica del 39,1%.

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*Risultati:* La presenza di disfunzione sistolica e diastolica aumentava proporzionalmente al numero dei fattori di rischio cardiovascolare, rispettivamente, dall'8,1% al 27,1% e dal 37,5% al 45,0%. All'analisi multivariata, variabili predittive indipendenti per la disfunzione sistolica erano il sesso maschile (p < 0,001), una familiarità nota per malattie cardiovascolari (p = 0,002) e il diabete mellito (p = 0,027), mentre per la disfunzione diastolica erano l'età (p < 0,001), l'ipertensione arteriosa (p < 0,001) e il diabete mellito (p < 0,05).

*Conclusioni:* In un ampio campione di soggetti asintomatici per scompenso cardiaco sottoposti a ecocardiogramma abbiamo riscontrato una significativa prevalenza di disfunzione sistolica e diastolica, correlata al numero di fattori cardiovascolari.

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Parole chiave: Disfunzione del ventricolo sinistro; Ecocardiografia; Diastole; Sistole; Scompenso cardiaco.

### 1. Introduction

The prevalence of heart failure (HF) in general population ranges between 0.4% and 2% and increases with age<sup>1,2</sup>. In Italy, every year about 190,000 subjects with HF seek hospital care and about 65,000 of them are admitted<sup>3</sup>. Symptomatic HF is usually determined by systolic left ventricular dysfunction (LVD); however a significant proportion of subjects with HF has a normal left ventricular systolic function which translates into the clinical condition of "heart failure with preserved ejection fraction"<sup>4,5</sup>. Thus, cardiac ultrasound has a pivotal role in the quantification of left ventricular ejection fraction (LVEF) and classification of diastolic pattern, both identifying LVD type and severity.

Recent 2008-focused updated American College of Cardiology/American Heart Association (ACC/AHA) guidelines for HF have confirmed four stages in the development of HF, with stages A and B characterized respectively by the presence of clinical cardiovascular risk factors and structural abnormalities without symptoms<sup>6</sup>. These silent abnormalities may lead over time to symptomatic LVD, and the progression of the disease can be positively affected by early treatment  $^{7-9}$ . Thus, the early detection of subclinical forms of LVD is of paramount importance to delay HF evolution. However, most of the published studies on the epidemiology of HF include only symptomatic subjects and data on the prevalence of asymptomatic LVD in the general population are still lacking<sup>10,11</sup>. The identification of individuals who are at risk for HF is useful for the implementation of HF prevention strategies. Furthermore, it is not yet clear whether all subjects in stage A or only those at high risk for developing HF should be submitted to serial non invasive assessment for LV ventricular function.

Based on these concepts, the *Italian Society of Cardiovascular Echography* (SIEC) has planned a national multicenter observational study, with the aim of establishing the prevalence of asymptomatic LVD in subjects with cardiovascular risk factors referred for conventional echocardiography.

#### 2. Materials and methods

#### 2.1. Study Population

The DAVES study (Disfunzione Asintomatica del Ventricolo Sinistro, left ventricular asymptomatic dysfunction) is a multicenter cross-sectional survey designed by the *Italian Society of Cardiovascular Echography* (SIEC) which enrolled 3,537 subjects admitted to 75 echolabs for conventional echocardiography. All laboratories were selected according to the competence of the operators, level 3 in agreement with the *American Society of Echocardiography* (ASE) requirements<sup>12</sup>. The study was approved by the local research ethic committees.

Subjects older than 20 years referred for a transthoracic echocardiogram were enrolled in the study. All subjects had normal electrocardiogram (ECG) tracings with a normal clinical examination, in presence of one or more cardiovascular risk factors (stage A of HF). All these selected subjects performed 2D echocardiography for the evaluation of LV functional and structural findings. Exclusion criteria were: patients with clear symptoms or clinical signs of HF; ischemic heart disease; valvular heart disease more than mild; cardiomyopathies; atrial fibrillation; previous stroke; previous cardiac surgery intervention; bad acoustic window. All subjects gave written informed consent and provided detailed medical history, and gave consent to the eventual assumption of drug therapies.

For study purposes six cardiovascular risk factors were considered as follows: hypertension (systolic blood pressure  $\geq 140$  mmHg, or diastolic blood pressure  $\geq 90$  mmHg, or in drug treatment), diabetes mellitus (fasting glycaemia  $\geq 7.0$  mmol  $L^{-1}$ , or in drug treatment), hypercholesterolemia (> 200 mg/dL, or in drug treatment), family history of cardiovascular disease, smoking ( $\geq 1$  cigarette/day, cessation of smoking < 10 years was still considered as smoking), obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) (Table 1).

Table 1

Characteristics of the 3,537 subjects enrolled in the study.

|  | No (%)       |
|--|--------------|
| Men                                      | 1,795 (50.7) |
| Women                                    | 1,742 (49.3) |
| Hypertension                             | 1,872 (52.9) |
| Family history of cardiovascular disease | 1,168 (33.0) |
| Dyslipidemia                             | 985 (27.8)   |
| Smoking                                  | 721 (20.04)  |
| Obesity                                  | 496 (14.6)   |
| Diabetes mellitus                        | 291 (8.2)    |
| Angiotensin converting enzyme inhibitors | 921 (26.03)  |
| Diuretics                                | 395 (11.1)   |
| Angiotensin II receptor blockers         | 355 (10.03)  |
| Calcium channel blockers                 | 255 (7.2)    |
| Beta-blockers                            | 575 (16.2)   |
| Alfa-blockers                            | 152 (4.29)   |
| Aspirin                                  | 393(11.1)    |
| Statins                                  | 652 (18.4)   |

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