

# INPLASY

## Echocardiographic assessment of cardiac structure and function of centenarians: a systematic review

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### ADMINISTRATIVE INFORMATION

**Support** - N/A.

**Review Stage at time of this submission** - Preliminary searches.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2024110010

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 November 2024 and was last updated on 3 November 2024.

### INTRODUCTION

**Review question / Objective** During the last two decades only a few echocardiographic studies have provided a detailed assessment of the cardiac structure and function in individuals aged  $\geq 100$  yrs. These studies analyzed limited sample sizes of centenarians, by using different methodologies. The present systematic review has been primarily designed to summarize the main findings of these studies and to examine the overall influence of extremely advanced age on cardiac mechanics. Pathophysiological mechanisms underpinning the cardiac remodeling occurring in centenarians will be discussed as well.

**Rationale** Cardiovascular disease is frequent in centenarians and represents the most common cause of mortality of this special population (PMID: 3827543, PMID: 11527481, PMID: 16079208). However, the exact mechanisms responsible for cardiac dysfunction and death in centenarians are still not fully understood. Transthoracic

echocardiography (TTE) is an essential tool for the evaluation of age-associated structural and functional changes. This noninvasive imaging modality allows to obtain useful information on cardiac chamber internal dimensions, left ventricular (LV) diastolic function, biventricular systolic function, morphology and function of the heart valves and pulmonary hemodynamics. To date, cardiac remodeling has poorly investigated in the “oldest-old” individuals (PMID: 21809160).

**Condition being studied** The aging of the world's population is rapidly increasing. According to the World Health Organization (WHO), the number of people aged 80 years and older is expected to triple between 2020 and 2050 and reach 426 million (World Health Organization Global Strategy and Action Plan on Ageing and Health. 2017. [(accessed on 17 April 2023)]. Available online: <https://www.who.int/publications/i/item/global-strategy-and-action-plan-on-ageing-and-health>). More remarkably, the number of centenarians has doubled every decade since the 1950s and is

estimated to increase five-fold by the year 2050 (Eurostat. Publication Office of the European Union: Ageing Europe - Statistics on Population Developments. 2019. 10.2785/811048). For this reasons, centenarians are more frequently encountered in the clinical practice (PMID: 12093397). Their longevity is favoured by the interaction of genetic and environmental factors (PMID: 27371745, PMID: 30024423).

## METHODS

**Search strategy** A comprehensive search of all echocardiographic studies evaluating the cardiac structure and function in individuals aged  $\geq 100$  yrs will be carried out by two independent reviewers (A.S. and M.L.) by using Medline and EMBASE databases. The search strategy will include the following terms: “centenarians” AND “transthoracic echocardiography” AND “cardiac function” OR “left ventricular ejection fraction” OR “left ventricular mechanics”. Search will be limited to full-text articles published in English, whereas non-English language studies will be excluded. There will be no time frame restriction for the inclusion of studies.

**Participant or population** Individuals aged  $< 100$  yrs: inpatients, outpatients or in-home patients.

**Intervention** The present systematic review has been primarily designed to examine the overall influence of extremely advanced age on cardiac structure and function. Pathophysiological mechanisms underpinning the cardiac remodeling occurring in centenarians will be discussed as well.

**Comparator** N/A.

**Study designs to be included** Observational Cohort and Cross-Sectional Studies.

**Eligibility criteria** All imaging studies evaluating the echocardiographic characteristics of centenarians, regardless of the time frame, will be included. Conversely, studies conducted on centenarians without echocardiographic data or with incomplete echocardiographic data, studies involving individuals aged  $< 100$  yrs, non-clinical articles, animal studies, duplicate articles, case reports, conference presentations, reviews, correspondences, editorials, letters without data, and abstracts, will be excluded.

**Information sources** A comprehensive search of all echocardiographic studies evaluating the cardiac structure and function in individuals aged  $\geq 100$  yrs, will be carried out by two independent

reviewers (A.S. and M.L.), by using PubMed, Scopus and EMBASE databases.

**Main outcome(s)** The present systematic review has been primarily designed to examine the overall influence of extremely advanced age on cardiac structure and function.

### Quality assessment / Risk of bias analysis

Articles included in this systematic review will be assessed for risk of bias (RoB) using the National Institutes of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (). All the studies will be assigned a “yes”, “no”, or “other” to each of the 14 criteria outlined in the appraisal tool. Notably, for each study included in the present systematic review, when the single criterion will be satisfied we will assign a “yes”, when it will not be satisfied we will assign a “no”, when it will not be evaluated we will assign a “not specified (NS)”. Then, by considering each criterion, the investigators will evaluate the overall quality of the study and assign an overall “good” (met 11–14 criteria), “fair” (met 6–10 criteria), “poor” (met 0–5 criteria) rating to each study. The quality rating will be independently estimated by two authors (A.S. and G.L.N.). Disagreement will be resolved by consensus.

**Strategy of data synthesis** Two reviewers (A.S. and M.L.) will screen the databases according to the inclusion criteria and perform data extraction independently. Following information concerning centenarians: 1) demographics (age and sex); 2) anthropometrics [body surface area (BSA) and body mass index (BMI)]; 3) prevalence of the most common cardiovascular risk factors (hypertension, smoking, type 2 diabetes and dyslipidemia); 4) previous history of coronary artery disease (CAD), heart failure and/or transient ischemic attack (TIA)/ stroke; 5) comorbidity burden and comorbidity indexes, such as the Charlson comorbidity index (CCI) (PMID: 3558716) and the Katz index (PMID: 14044222); 6) physical examination [systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate]; 7) electrocardiographic (ECG) data, such as the cardiac rhythm and the pattern of intraventricular conduction; 8) biochemical parameters, such as serum levels of hemoglobin, creatinine, cholesterol and brain natriuretic peptide (BNP); 9) 2D-TTE parameters, including cardiac chambers cavity size, LV diastolic function and LV filling pressures measured by E/A ratio and E/e' ratio respectively, biventricular systolic function assessed by LVEF and tricuspid annular plane systolic excursion (TAPSE) respectively, degree of concomitant valvular heart disease and pulmonary hemodynamics; 10) the current medical treatment;

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11) follow-up data (if any), will be independently collected by the two reviewers. Possible discrepancies between reviewers will be resolved through a consensus discussion with the involvement of a third author (G.L.N.), who will check the extracted data to ensure accuracy, completeness, and consistency.

**Subgroup analysis** N/A.

**Sensitivity analysis** N/A.

**Country(ies) involved** Italy.

**Keywords** Centenarians, cardiac structure, cardiac function, left ventricular ejection fraction, transthoracic echocardiography.

**Contributions of each author**

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