Ageing Research Reviews 18 (2014) 41–52

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

# Cognitive impairment and cardiovascular diseases in the elderly. A heart–brain continuum hypothesis

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ARTICLE INFO

*Article history:*
Received 19 March 2014
Received in revised form 9 July 2014
Accepted 17 July 2014
Available online 11 August 2014

*Keywords:*
Cardiovascular disease
Cognitive impairment
Dementia

ABSTRACT

The aging population is increasing and, therefore, a higher prevalence of cardiac disease is emerging; including hypertension, coronary artery disease, atrial fibrillation and chronic heart failure. Large cohort studies have revealed a relationship among increased risk for cognitive impairment and dementia in cardiovascular diseases probably due to embolic stroke or chronic cerebral hypoperfusion. Thus, the aim of the present review is to overview the studies that investigate the presence and/or the development of cognitive impairments and dementia in patients with varied types of cardiovascular disease. Finally, a continuum among hypertension, coronary artery disease, atrial fibrillation and chronic heart failure with to the development of cognitive impairment and progression to dementia has been hypothesized.


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http://dx.doi.org/10.1016/j.arr.2014.07.003
1568-1637/

## 1. Introduction

Cardiovascular diseases (CVD) including hypertension, coronary artery disease (CAD), atrial fibrillation and chronic heart failure (CHF) are highly prevalent in the elderly (Aronow, 2002). Moreover, CVDs are strongly related to cognitive impairment and dementia (Kerola et al., 2011; Eggermont et al., 2012). Although the etiology of cognitive changes in CVD disease remains unknown, the main mechanism of this relationship seems to involve embolic stroke or chronic cerebral hypoperfusion (Kalaria, 2012). Of course, cognitive impairment and dementia reduce the ability to manage the care of a complex chronic illness and reduced medication adherence (Insel et al., 2006). Interestingly, CVDs are capable of producing both Alzheimer's disease (AD) (de la Torre, 2002) and vascular dementia (VaD) (Román, 2002), the most common forms of dementia in the elderly.

We used MEDLINE, the National Research Register, Embase (1980–2006, OVID online) to search for studies that investigated the relationship between CVD and cognition, and which were published until May 2013. The search included the following key words: cardiovascular diseases; hypertension; heart failure; coronary artery disease; atrial fibrillation; cognitive impairment, dysfunction, deficit; neuropsychological functions; dementia, Alzheimer's disease, vascular dementia.

## 2. Cognitive function and cognitive impairment

Cognitive function involves various specific aspects referring to memory, attention, executive functioning, psychomotor speed, language, and visuo-spatial ability and it is a critical function for the consciousness of situation, needs, and goals (Borson, 2010). The Mini-Mental State Examination (MMSE) has been used as a screening measure for global cognitive performance in several studies studying the relationship between CVD and cognitive impairment (Vogels et al., 2007a,b). However, because of the lack of sensitivity of MMESE in the CVD population, other instruments with adequate test performance to detect cognitive impairment are used including the Clock Drawing Test, Mini-Cog, Memory Impairment Screen, Abbreviated Mental Test, Short Portable Mental Status Questionnaire, Free and Cued Selective Reminding Test, 7-Minute Screen, and Informant Questionnaire on Cognitive Decline in the Elderly. Medications approved (Lin et al., 2013).

Cognitive impairment is a broad term that generally describes a decline in cognitive functions. The severity of this impairment may range from mild symptoms to severe cognitive deficits that may justify the diagnosis of dementia. Mild cognitive impairment can be described as a transition phase between normal aging and dementia. This syndrome reflects the clinical situation in which a person has a reduction of objective measurements of cognitive impairment (around 1.5 standard deviations below normative data) along with intact daily functioning with or without memory impairment (Burns and Zaudig, 2002). Individuals with mild cognitive impairment are in increased risk of progression to dementia (Fleisher et al., 2007).

Dementia is defined by a decline in cognitive function from a prior baseline and a deficit in performance in $\geq$2 cognitive domains that are of sufficient severity to affect the subject's activities of daily living (Gorelick et al., 2011). After excluding reversible causes, four common dementia syndromes, namely, Alzheimer's disease, vascular dementia, dementia with Lewy body, and fronto-temporal dementia, account for 90% of all cases. These dementias have distinct clinical features, cognitive profiles, and imaging abnormalities (Fratiglioni et al., 2000; Ritchie and Lovestone, 2002). In particular, vascular dementia is probable when (1) there is cognitive impairment and imaging evidence of cerebrovascular disease and there is a clear temporal relationship between a vascular event (i.e., clinical stroke) and onset of cognitive deficits, or there is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology; (2) there is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder (Gorelick et al., 2011).

The association between cardiovascular diseases and cognitive impairment in older people is multifactorial and involves common risk factors such as atherosclerosis, hypertension, and diabetes mellitus (Román, 2004; Whitmer et al., 2005; Cukierman et al., 2005; Pullicino et al., 2008). Cognitive impairment may be also the result of strokes affecting cerebral structures (strategic strokes), multiple strokes and/or periventricular ischemic leukoencephalopathy (Román, 2003), and silent strokes (Vermeer et al., 2007) and may develop both Alzheimer and vascular disease (Hofman et al., 1997; Skoog et al., 1998; Ott et al., 1999). The huge limitation of the present review is the quality of psychometric data in CVD patients. This limitation depends both on the instrument used (i.e., MMSE is able to identify only global cognitive impairment and not specific domains) and on the time necessary for comprehensive neuropsychological batteries (i.e., fatigue is a common complaint in patients with CVD and may influence neuropsychological test scores) (Bauer et al., 2012).

## 3. Hypertension and cognitive impairment

Among people aged 65 years and over, the prevalence is estimated to be around 8% for dementia and 65% for hypertension (Qiu et al., 2005; Kearney et al., 2005). Moreover, hypertension represents the major risk factor for vascular dementia although vascular factors may be also involved in Alzheimer dementia (Launer, 2002; de la Torre, 2002). Thus, mixed vascular and neurodegenerative dementia has emerged as the leading cause of age-related cognitive impairment (Iadecola, 2013).

### 3.1. Hypertension and cognitive impairment: clinical evidences

When hypertension was defined as systolic blood pressure (BP) values equal or higher than 160 mmHg or clinically diagnosed (medical history and/or use of antihypertensive drugs) an association between hypertension and cognitive impairment in cross-sectional studies was found (Scherr et al., 1991; van Boxtel et al., 1997; Harrington et al., 2000; André-Petersson et al., 2001; Stewart et al., 2001; Kuo et al., 2004). Interestingly, it has been reported that diastolic, but not systolic BP, is predictive of cognitive impairment (Cacciatore et al., 1997). Moreover, the association between blood pressure and poor cognitive performance was also characterized by U-shaped curves (Morris et al., 2002; Waldstein et al., 2005). In fact, a link between low blood pressure and