Does baseline hypotension predict incident depression in a cohort of community-dwelling older people? Data from The Irish Longitudinal Study on Ageing (TILDA)

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Abstract

Background: hypotension is now recognised as a risk factor for syncope, cardiovascular events and mortality, but it may also represent a risk factor for late life depression (LLD). The aim of this study was to clarify the longitudinal relationship between hypotension and incident LLD.

Methods: this is a longitudinal study involving community-dwelling participants aged ≥50 years, using data from The Irish Longitudinal Study on Ageing. The Centre for Epidemiological Studies Depression Scale (CES-D) was administered at baseline and at follow-up 2 years later. Blood pressure (BP) was measured at baseline. Participants with a CES-D score ≥16 at baseline and those taking antidepressants were excluded and considered to have a current diagnosis of depression. A score of ≥16 at follow-up was used to define incident depression.

Results: about 4,525 participants were included and 200 participants had diagnosis of incident LLD. The incident depression group had lower systolic BP at baseline than the non-depressed group (132.8 ± 1.43 mm Hg vs. 136.0 ± 0.30 mm HG, P = 0.025). Logistic regression showed those with systolic BP <130 mm HG had an unadjusted odds ratio of 1.31 (1.01–1.68) for incident depression. This persisted after adjustment for confounding factors.

Conclusion: systolic BP <130 mm Hg increased the likelihood of incident depression in a cohort of community-dwelling older adults. These findings are important because systolic hypertension may represent a potentially modifiable risk factor for LLD. They are also relevant in the context of BP treatment targets for older people.

Keywords: depression, hypotension, blood pressure, older people

Introduction

Late life depression (LLD), defined as depression presenting in later life or persisting into later life, is common, affecting 8% of a population-representative sample of older participants in The Irish Longitudinal Study on Ageing (TILDA) [1]. LLD also represents a distinct clinical entity to depression at an earlier age, with different...
clinical features and presentations [2], on a background of significant underlying medical complexity such as heart disease and frailty [3, 4]. As well as these intrinsic factors, extrinsic influences including social isolation and bereavement also contribute to this high prevalence of depressive illness in later life.

Depression in later life is, therefore, underpinned by different underlying aetiological mechanisms. One such factor is the strong influence of cardiovascular disease, including stroke and heart disease [3]. The vascular basis of LLD is now well recognised [5], and initially emerged when it was noted that patients with LLD had higher rates of cerebrovascular disease, reflected by cerebral white matter hyperintensities (WMHs) on magnetic resonance imaging studies compared to those with earlier onset depression [6]. Given this relationship, one would expect to find a close association with blood pressure (BP) control and there is an increasing body of evidence to suggest that hypotension, rather than hypertension in later life, may be an important factor in development of LLD [7].

Hypotension in later life is now recognised as a risk factor for falls and syncope [8], cardiovascular events [9] and all-cause mortality [10]. While the potentially detrimental effects of hypotension in later life are reflected by current Joint National Committee guidelines for BP targets in older adults [11], the recent Systolic Blood Pressure Intervention Trial (SPRINT) trial demonstrated the possible benefits of aggressive BP lowering in a subgroup of older patients and this may have important implications for more aggressive BP target recommendations in future guidelines [12].

The aim of this study is to clarify the longitudinal relationship between hypotension and LLD. Our hypothesis is that hypotension at baseline increases the risk of incident depression. A specific challenge in studies of this type is that hypotension can represent an end-point for several diverse disease processes in the older person, including heart failure and lung disease [13]. Rates of depression are also significantly higher in older persons with more profound chronic medical illness [14] and while both depression and hypotension are markers of poor physical health, this could mediate the relationship between the two [15]. Therefore, controlling for the myriad of confounding factors, including physical dependency, frailty and accumulating medical illness, can be complex. The comprehensive TILDA data set allows us to control for these potentially confounding factors however.

Methods

This is a longitudinal study in a cohort of community-dwelling participants aged 50 years and over, examining the relationship between baseline BP and incident depression at 2-year follow-up.

Study design

Data were analysed from the 1st and 2nd wave of TILDA, a nationally representative study of community-dwelling older people, collected between 2009 and 2012. The TILDA study design has been outlined in previous studies [16]. Each participant undertakes a computer assisted personal interview, involving specific questions with a focus on health, social and economic factors. This takes place in their own home. Participants are also invited to a health centre for a comprehensive health assessment, involving measures such as gait and orthostatic BP analysis. All assessments are completed by trained nursing staff.

Participants with a history of dementia, based on a prior physician diagnosis, were excluded.

The TILDA study received ethical approval from the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin and informed consent was obtained from all participants.

Depression

The Centre for Epidemiological Studies Depression Scale (CES-D) was used to measure depressive symptoms. The CES-D is a 20-item scale examining four key factors: depressed affect, absence of positive affect or anhedonia, somatic activity or inactivity and interpersonal challenges [17]. The response values are 4-point Likert scales, with range 0–3, yielding a total possible score of 60, with higher scores indicating greater depressive symptoms.

The CES-D has been validated in an older population, and a value of 16 or more has been shown to have a sensitivity of 92% and a specificity of 87% for diagnosis of LLD [18]. The CES-D was administered at baseline and at Wave 2 follow-up 2 years later. Participants with a score of 16 or more on the CES-D at baseline were excluded from the study. Participants were also excluded if they were taking antidepressants. A score of 16 or more at follow-up was used to define incident depression.

Blood pressure

BP was measured twice by a trained research nurse in the seated position using the OMRON™ digital automatic BP monitor and the mean value of the 2 BP readings was used for analysis.

Other measures

The CAGE questionnaire was administered to screen for alcohol dependency with a score of two or more indicative of same. Functional impairment was defined as having one or more impairment in activities of daily living (ADL), including dressing, washing, bathing, eating, getting in and out of bed and using the toilet. The Mini Mental State Examination (MMSE) was used as a marker of cognitive performance. Chronic illness burden was assessed by recording the absolute number of chronic illnesses self-reported from the following list: lung disease, arthritis, cancer, liver disease, Parkinson’s disease, previous hip or wrist fracture, peptic ulcer disease and cataracts. Frailty status was defined using the fried frailty criteria [19], defining participants as either frail, pre-frail or non-frail. Loneliness was measured using...
the University of California, Los Angeles (UCLA) Loneliness Scale [20]. Cardiovascular disease burden was assessed by self-report of a history of diabetes, stroke, myocardial infarction (MI) or angina. Chronic pain was based on the self-report of moderate to severe pain. Additionally, medication lists were examined for antihypertensive medication use, specifically calcium channel blockers, Angiotensin converting enzyme inhibitors and Angiotensin receptor blocking agents, alpha-blockers, beta-blockers, hydralazine or diuretics.

Results
Baseline characteristics
In total 5,857 participants were aged 50 years and above and completed both a home interview and health assessment, including BP measurement. Of these, 872 participants were excluded because they were prescribed antidepressants or their baseline CES-D score was 16 or more. Four hundred sixty participants did not complete 2-year follow-up, resulting in a study population of 4,525 participants. See Figure 1.

Table 1 shows baseline characteristics of both the incident depression group and the non-depressed group.

BP and depression
Table 2A shows the mean baseline BP values of the incident depression group compared to the non-depressed group. The incident depression group had lower systolic BP at baseline compared to the non-depressed group. There was no statistically significant difference in diastolic BP between the two groups.

Discussion
This study demonstrates that in a cohort of older people with no depression at baseline, lower values for systolic BP...
increased the likelihood of incident depression at 2-year follow-up. The group with incident depression was more likely to be female and smokers, and had higher rates of alcohol dependence, chronic disease, functional impairment and frailty. However, the association with lower systolic BP persisted after controlling for these potentially confounding factors.

Cross-sectional studies, while limited in their ability to attribute causality, have demonstrated a consistent relationship between hypotension and depression in later life [7]. Longitudinal studies up to now have demonstrated conflicting results however. Paterniti et al. [21] demonstrated that low diastolic BP at enrolment predicts future depression, but that depression at baseline did not predict subsequent low BP. Tikhonoff et al. [22] found that the burden of depressive illness in early and middle age contributes to lower BP in later life, while Gao et al. [23] showed that the systolic BP of a group of participants aged over 60 years with incident depression increased significantly more prior to this diagnosis than in those without depression.

There are marked methodological differences between these studies, which may explain these discordant findings, including age at enrolment, as well as the methods used to assess depressive symptoms and measure BP. No studies to date have controlled for frailty, in addition to functional status. These findings are important because, despite its prevalence, the aetiological basis of LLD is not yet fully understood and hypotension may represent a potentially modifiable risk factor for LLD. They are also relevant in the context of setting BP treatment targets and guidelines for older people.

There are several potential mechanisms that may underlie this association. Hypotensive episodes lead to a reduction in cerebral blood flow, causing cerebral hypoperfusion and the development of WMH [24]. These WMHs can disrupt the frontal-subcortical circuitry resulting in psychomotor retardation, loss of interest and executive dysfunction; hallmarks of LLD [5] and have been shown to be a predictor for severity of depression in older subjects after adjusting for quality of life [25]. Other mechanisms that may mediate this observed association include hypocortisolemia occurring in the setting of LLD [26], monoaminergic dysfunction [24] and immune dysregulation [27].

Previous work in the TILDA population has demonstrated a cross-sectional association between symptomatic orthostatic hypotension (OH) and depression [28]. OH and baseline hypertension represent two distinct clinical entities; however, and patients with OH are frequently hypertensive at baseline [29]. Both associations may be mediated by WMHs due to cerebral hypoperfusion; however, and a significant association was only found in subjects who developed symptoms of orthostatic intolerance in the setting of OH, which may correlate with lower nadir orthostatic BP.

These findings also parallel the association between low BP and dementia, where late life hypotension have been identified as a risk factor [30]. This is against the backdrop of overlapping clinical features between LLD and dementia, including the presence of executive dysfunction, and may demonstrate a common aetiological pathway shared between the two when we consider the impact of white matter disease and loss of frontal lobe integrity on neurophysiological status in older people.

The strengths of this study include the fact that data were collected prospectively. The breadth of data collected as part of the TILDA study also allows us to control for factors, such as frailty, which has not previously been possible in longitudinal studies examining this relationship.

There are some weaknesses of this study which must also be considered. A CES-D score of 16 or more was used to define depression, rather than the gold standard structured psychiatric interview. The CES-D was developed in order to identify populations at risk of developing depression and was not intended to be used as diagnostic tool; however, in the setting of large population-based studies, performance of a structured psychiatric interview is
often impractical or impossible, and the high sensitivity and specificity of the CES-D means it is a reliable alternative to a structured interview in this setting. Additionally, BP values were based on automated oscillometric readings. While this represents the most commonly used method in clinical practice, it provides only a static measurement of BP, a highly dynamic variable, and, therefore, may not be reflective of true 24 h BP average. Additionally, while our study demonstrates a significant association between hypotension and LLD, this should not be assumed to indicate a causal relationship and further studies are required to clarify this.

LLD currently affects 1 in 10 older adults. In this study, systolic BP less than 130 mm Hg increased the likelihood of incident depression in a cohort of community-dwelling older adults, suggesting that systolic hypotension may represent a potentially modifiable risk factor for LLD. Given projected future demographic changes, in conjunction with the detrimental effect depression can have on the independence of older people, the burden of depression in this cohort is likely to increase significantly in the near future and studies directly testing this hypothesis are warranted. Furthermore, given recent findings directing more aggressive BP treatment in older people, there is also a need for specific studies examining beneficial and adverse effects of BP lowering specifically in an older population.

Key points

- Hypotension in later life can increase the risk of falls, syncpe, cardiovascular events and all-cause mortality.
- However, the SPRINT trial demonstrated the possible benefits of aggressive BP lowering in a subgroup of older patients.
- We found that systolic BP <130 mm Hg increased the likelihood of incident depression in older adults at 2-year follow-up.
- Systolic hypotension may represent a potentially modifiable risk factor for late life depression.
- These findings are also important in the context of BP treatment targets for older people.

Conflicts of interest

None declared.

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References

Interaction of obstructive sleep apnoea and cognitive impairment with slow gait speed in middle-aged and older adults

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Abstract

Objective: to investigate whether slow gait speed is associated with cognitive impairment and further whether the association is modified by obstructive sleep apnoea (OSA).

Methods: in total, 2,222 adults aged 49–80 years, free from dementia, stroke and head injury were asked to walk a 4-m course at fast and usual gait speeds. The time taken to walk was measured. All participants completed the Korean Mini-Mental State Examination, which was validated in the Korean language, to assess cognitive function. Additionally, the participants completed a polysomnography test to ascertain OSA (defined as an apnoea–hypopnoea index ≥15). Multivariable linear regression models were utilised to test the associations.

Results: time taken to walk 4 m showed significant inverse associations with cognitive scores (P value = 0.001 at fast gait speed and P = 0.002 at usual gait speed). Furthermore, a significant interaction according to OSA on the association between time to walk and cognitive impairment was found (P value for interaction = 0.003 at fast gait speed and P value for interaction = 0.007 at usual gait speed).

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