Should guidance for the use of antihypertensive medication in older people with frailty be different?

The benefits of antihypertensive treatments have been established in numerous large clinical trials. Although the Hypertension in the Very Elderly Trial (HYVET) confirmed the protective effect of blood pressure medication for healthy, older individuals without dementia over 80 years of age who do not live in a care home [1], the evidence for people who are also frail and/or have comorbidities remains unclear [2]. This is reflected in hypertension guidelines. For example, the guidelines of the European Society of Hypertension and European Society of Cardiology [3] recommend reducing the systolic blood pressure in older people who have a blood pressure of 160 mmHg or above, to between 140 and 150 mmHg with the caveat of those over 80 years of age should be in good physical and mental conditions to do so. The guidelines of the National Institute of Health and Care Excellence (NICE) for Hypertension [4] advise for people under 80 years of age a target blood pressure of 140/90 mmHg and for people over 80 years of age a target blood pressure of 150/90 mmHg. Furthermore, for people over 80 years of age, co-morbidities should be taken into account when deciding on antihypertensive treatment.

While this accepts that age and comorbidities should be considered when prescribing antihypertensive medication, several questions remain: is age only relevant if someone is younger or older than 80 years? Or, does the relationship between antihypertensive treatment, age and benefits continue to change? For example, a recent cross-sectional study including Polish centenarians suggested that higher blood pressure levels might be related to better health status and higher short-term survival [5]. Which co-morbidities should influence prescription decisions, and how should they be taken into account? Frailty, a condition in which the person is at increased risk of adverse health outcomes and/or dying after a destabilising event [6], might be particularly important in this context. In their recent review, Benetos et al. [2] suggested using the comprehensive geriatric assessment to evaluate the patient’s clinical and functional parameters before deciding on treatment.

While this highlights the importance of tailoring treatment, the Milan Geriatrics 75+ Cohort study (Ogliari et al.), which is included in this issue, is already one step further. Their study indicated that for people who are 75 years or older and have impaired functional and cognitive statuses, the relationship between blood pressure and 10-year mortality might be U shaped with a blood pressure of 165/85 mmHg being associated with the lowest mortality risk. This suggests that the relationship between blood pressure levels and mortality depends on functional and cognitive statuses, which should be taken into account when considering target blood pressure levels. This large cohort study (n = 1587) achieved what would currently be very difficult to do using a randomised controlled study design: without exposing participants to an unknown risk of cerebro- and cardiovascular events, the study investigated the relationship between blood pressure levels and mortality in a vulnerable older population over a 10-year period. Ethical motivation to not expose participants to an increased risk of cerebro- and cardiovascular events was among the reasons for the short follow-up period in the randomised controlled DANTE trial, which looked at the effects of withdrawing antihypertensive treatment on cognition in people with mild cognitive impairment [7].

The results of the Milan Geriatrics 75+ Cohort study reflect the findings of the National Health and Nutrition Examination Survey [8], which indicated that walking speed might affect the association between blood pressure and mortality. Fast walkers with blood pressure levels of 140 mmHg or higher had a higher mortality risk compared with those with lower blood pressure levels; in slow walkers, no relationship was observed; and in participants who did not complete the walk test, higher blood pressure levels (≥140 mmHg) were associated with lower mortality (diastolic: HR 0.38; CI 0.23–0.62; systolic: HR 0.10; CI 0.01–0.81). Although not completing the walking test in this study had different reasons, physical limitations were the most reported one. This suggests that frailty might be another factor that should influence prescribing decisions. However, it is important to note that the results of a sub-analysis of the HYVET study using a Frailty Index based on 60 different deficits did not show a significant effect of frailty on the impact of antihypertensive medication in terms of cardiovascular events, stroke or total mortality, although the P-values for the interaction between treatment and frailty were close to the significance levels for each of the three endpoints (P = 0.73 for cardiovascular events, P = 0.52 for stroke and P = 0.61 for total mortality) [9] and the generalisability of the results is still limited due to the characteristics of their participants.

Given these findings, hypertension guidelines should advise to take frailty into consideration when making treatment decisions. In addition, frequent monitoring is required for this population as the optimal blood pressure range is limited in a U-shaped relationship especially as blood pressure levels may decrease in women after the age of 70 [10]. Furthermore, considering the limited effect preventative medication might have for a person with a shorter life...
expectancy [11], it is important to acknowledge all benefits and harms of the treatment, not only mortality. When treating hypertension in people with dementia, for example, our review showed that in addition to cerebro- and cardiovascular events and mortality, a range of potential outcomes should be taken into account such as progression of the disease, falls, depression, hypotension, polypharmacy and interaction with cholinesterase inhibitors [12]. A similar range of outcomes might be relevant for older people with frailty. To provide evidence-based, individually tailored healthcare, large studies are needed to look at multiple outcomes simultaneously with enough statistical power to investigate these and their interactions, instead of focusing on one primary outcome.

Key points

• When making decisions regarding antihypertensive treatment, the functional and cognitive statuses of the patient should be taken into account.
• Frequent blood pressure monitoring is required for people with frailty.

References

5. Szewieczek J, Dulawa J, Francuz T et al. Mildly elevated blood pressure is a marker for better health status in Polish centenarians. Age (Dordrecht, the Netherlands) 2015; 37: 9738.

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Is frailty in the elderly linked to inflammation?

With an increase in life expectancy around the world, the period of life spent in dependency towards the later part of life has increased and is now a subject of great importance. This has a significant effect on quality of life in the later years. There have been a number of studies to investigate the causes of frailty in later years. A number of these have linked quality of life in later years to genetic factors. For example, a study of 349 elderly women found that there was a strong association with several single-nucleotide polymorphisms (SNPs) in genes encoding apoptotic and transcription regulation factors [1]. The role of inflammation in the pathogenesis of frailty in particular has also long been hypothesised [2].

The study by Mekli et al. shows a significant association between frailty and a SNP in the first intron of the interleukin (IL)-18 gene and a less significant one with that for the IL-12 gene. IL-18 is an inflammatory cytokine of the IL-1