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Older people remain on blood pressure agents despite being hypotensive resulting in increased mortality and hospital admission

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Abstract

Background: the use of antihypertensive medication in older people in order to prevent cardiovascular events is well established. The use of such agents has been encouraged by incentive schemes in the United Kingdom including the Quality and Outcomes Framework. In addition, many guidelines recommend good blood pressure (BP) control in the elderly. However, in older people antihypertensives can cause adverse effects related to hypotension.

Aim: the aim of this study was to assess the prevalence of low BP and impact on outcomes, particularly in the presence of antihypertensive treatment, in a primary care population of older people.

Design: a retrospective observational cohort study in people over the age of 70 years registered with primary care providers in Kent.

Results: a total of 11,167 patients over 70 years old were analysed, 6,373 female (57%). Systolic blood pressure (SBP) was below 120 mmHg in 1,297 people (844 on antihypertensives), below 110 mmHg in 474 (313 on antihypertensives) and below 100 mmHg in 128 (89 on antihypertensives). Hypotension was independently associated with mortality, acute kidney injury and hospital admission.

Conclusions: the results demonstrate that low SBP is associated with adverse events, it is possible that the pursuit of BP control at a population level may lead to over-treatment in certain groups of patients. This may result in an increased incidence of adverse events particularly in older people.

Keywords: *older people, hypotension, hospital admission, acute kidney injury, mortality*

Introduction

Randomised controlled trials show that treating hypertension in old age reduces strokes and other cardiovascular events [1, 2]. However in elderly patients with multiple co-morbidities there is a trade-off between using antihypertensives to reduce the risk of future disease and increased risk due to adverse effects of medication [3–5].

Most older people have hypertension and many older patients also have other co-morbidities therefore they are at risk of adverse effects of drugs used to treat each condition [3, 5–9]. Drug treatments for symptomatic relief of other conditions common in old age such as prostatism, Parkinson's disease and depression have hypotensive effects [7–9]. Preventative treatments used in accordance with national guidelines for heart failure (HF) and chronic kidney

disease (CKD) may also cause hypotension [10, 11]. Adverse effects due to hypotension include syncope and falls, which can cause serious injury such as hip fracture, and head injury as well as a number of symptoms, which impair daily quality of life for the older population [3, 5], including dizziness, unsteadiness and fear of falling [12]. Atypical presentations common in older people such as weakness, lethargy, 'off legs', confusion and visual impairment may also be due to drug side effects [5, 6]. Physiological changes of ageing affect drug metabolism and increase the propensity to side effects of medication [6]. The risks of hypotension in older people are compounded by other age-related changes including postural instability increasing the risk of falls [13]. Once medication is initiated, it is not always regularly reviewed and titrated to adjust for physiological changes associated with ageing and the effects of additional drugs [5, 6].

Adverse reactions to medications are implicated in a significant number of hospital admissions [14, 15]. Rising acute admissions especially of older patients with multiple co-morbidities are contributing to ever-increasing NHS costs, once admitted older people with multiple co-morbidities have longer lengths of stay [16, 17]. An emergency admission to hospital is a disruptive and unsettling experience for the older person exposing them to new clinical and psychological risks and increasing their dependency [18]. Admissions of frail elderly people to care homes are frequently precipitated by a hospital admission [19]. Acute kidney injury (AKI) is a common occurrence in hospital and is associated with increased short- and long-term mortalities.

There is no clear guidance or drug trial evidence to inform how far to lower blood pressure (BP) with antihypertensives in the older old [1, 4, 20, 21]. A review of hypertension trials data indicated that for octogenarians Systolic blood pressure (SBP) <130 mmHg and diastolic BP <65 mmHg should be avoided [4]. The need for randomised controlled trial evidence on a representative sample of older people with multiple co-morbidities has been highlighted [3]. NICE Hypertension Guidance advises that for the oldest old (80 and over) the target BP is higher than in younger people [20]. Some guidance extends the 150/90 target to patients over 65s [21]. Accompanying guidance included yearly face-to-face medication review to look for side effects and titrate dosage according to symptoms and BP in older patients on antihypertensives [20].

Aims

The aim of this study was to assess the prevalence of low BP in the presence of antihypertensive treatment, and its impact on outcomes particularly in a primary care population. In this study, outcomes of patients on antihypertensives with SBP <120 mmHg were analysed. These were stratified into three groups those with SBP <120 and ≥ 110 mmHg, <110 and ≥ 100 mmHg and those with SBP <100 mmHg.

Methods

This study used a prospectively collected database developed from an unrelated study investigating automated intervention in CKD. Data collection commenced in 2005 by extracting data from primary care databases using MIQUEST [22]. All patients who had serum creatinine checked in primary care had a data set extracted usually at around monthly intervals between 2005 and 2015, the application is known as System for Early intervention in Kidney Disease (SEIK) [23]. This study used a retrospective analysis of data obtained from this database. Data on the medication, BP, blood results and co-morbidity of patients aged 70 was obtained. Co-morbidity data were obtained directly from the primary care record, these were coded by primary care doctors caring for the patients.

Medication record was extracted directly from electronic prescription data used in primary care systems. The primary aim was to estimate the prevalence of hypotension of older people in primary care, associated medication prescribed and co-morbidity. Data were obtained from the 13 practices actively participating in SEIK.

Inclusion criteria:

- Patients with a serum creatinine estimation.
- Patients with a BP measurement between 30 June 2011 and 01 January 2012.
- Patients registered in participating practices.

Exclusion criteria:

- Patients not screened after 01 June 2013.
- Patients under 70 years of age.
- Request to be withdrawn from the study/database.

The BP and medication data were collected according to the schedule in Figure 1. Definition of index BP was the first one after 30 June 2011. Definition of ‘previous blood pressures’ was all systolic and diastolic BPs 12 months prior to and including the index BP. Follow-up BPs were all the systolic and diastolic BPs in the 12 months following the index BP. Current medication was defined as medication prescribed between the index BP and in the 4 months previous. Follow-up medications were all medications prescribed between 8 and 12 months after the index BP date. Current co-morbidity included all those extracted and reported prior to the index BP date. Follow-up co-morbidity included any reported up to 12 months after the index date. Changes in numbers of antihypertensives were assessed by BP strata.

The data were stratified into four groups according to index SBP:

- SBP ≥ 120 mmHg.
- SBP <120 mmHg but ≥ 110 mmHg.
- SBP <110 mmHg but ≥ 100 mmHg.
- SBP <100 mmHg

Data on admissions, episodes of AKI and mortality were obtained from hospital records.

The association between SBP strata and survival was examined. The primary outcome assessed was all cause mortality. The results were expressed as unadjusted Kaplan–Meier survival curves.

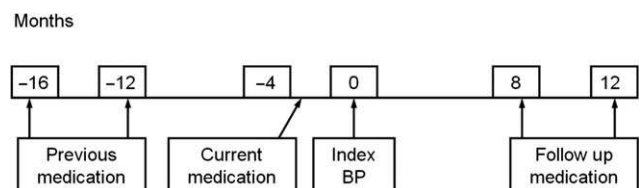


Figure 1. Schedule of data collection. Index BP was defined as the first BP reading after 30 June 2011. Follow-up and data collection period displayed in months.

Binary logistic regression analysis was used to assess factors associated with death and AKI in follow-up.

Finally, the probability of dying at 1 year was estimated using logistic regression analysis. To allow for possible confounding variables, a series of three models were fitted with varying adjustments for other variables to allow comparison between the categories

The models fitted were as follows:

- Unadjusted relationship between strata of SBP and death.
- The relationship between strata of SBP and death, adjusted for age and gender only.
- The relationship between strata of SBP and death, adjusted for age, gender, antihypertensive use and comorbidities.

Results

Data were included from a total of 11,167 patients aged 70 and over, 6,373 female (57.1%). The mean index SBP was 138 mmHg (SD 19, range 90–220). The mean index diastolic BP was 75 mmHg (SD 11, range 40–120).

The mean SBP prior to the index BP ($n = 8,758$) was 140 mmHg, SD 16 (range 82–193 mmHg). The mean diastolic BP before index ($n = 8,771$) was 76 mmHg, SD 9 (range 35–117 mmHg).

Baseline characteristics of patients included in the study are described in Table 1. Coded co-morbidities at index were as follows (see Table 1): 12.4% had a diagnosis of hypertension, 7.0% diabetes, 4.2% coronary artery disease (CAD), 8.6% CKD and 1.3% HF. The patients were taking between 0 and 5 antihypertensives at index: 34.1% were taking an angiotensin converting enzyme inhibitor (ACEI),

17.6% were taking a diuretic, 16.4% an angiotensin receptor blocker (ARB), 13.2% a calcium channel blocker, 13.0% a beta-blocker, 3.9% an alpha-blocker and 0.4% a centrally acting antihypertensive.

Of patients over 70 years old, 128 (1.2%) patients had a SBP <100 mmHg at index. Of these, 39 (30.5%) were not taking antihypertensives, 40 (31.3%) were taking one antihypertensive, 22 (17.2%) were taking two, 22 (17.2%) were taking three, 4 (3.1%) were taking four and 1 (0.8%) was taking five antihypertensives. Patients in the strata with lower BP were on more antihypertensive medication ($P < 0.001$). The majority of patients either had their antihypertensives increased or unchanged over the study period. Patients with an index SBP of <100 mmHg 41% had no change in medication, 34% had their medication reduced. In contrast those with an index SBP of ≥ 120 mmHg, 36% had no change in medication and 43% had their medication increased.

Unadjusted analysis of survival by index SBP strata demonstrated that 1 year survival was poorer in those with lower BP (97.1% BP >120 mmHg vs. 83.6% BP <100 mmHg), this result is displayed graphically using survival curves in Supplementary Figure 2 (see Supplementary data are available in *Age and Ageing* online).

Using binary logistic regression analysis factors significantly associated with mortality included age, gender, index diagnoses of stroke and HF, index BP <100 mmHg, average SBP <100 mmHg in 1 year pre-index. The number of antihypertensives used was not significantly associated with mortality (data not shown). Multiple logistic regression analysis showed that age, gender, index BP <100 mmHg and index diagnoses of stroke and HF were significant variables associated with mortality (Table 2).

Table 1. Baseline characteristics of study patients

	All patients	Index SBP (mmHg)			
		<100	100–109	110–119	≥ 120
<i>n</i>	11,167	128	346	823	9,870
Age, mean (SD)	79 (6)	81 (7)	80 (7)	80 (7)	79 (6)
Gender (% male)	42.9	57.8*	52.3*	49.8*	41.8*
<i>Proportion of patients taking antihypertensives (%)</i>					
No antihypertensives	38.1	30.5	35.5	35.4	38.6
One antihypertensive	37.8	31.3	35.3	36.9	38.0
Two antihypertensives	14.4	17.2	16.5	16.2	14.1
Three antihypertensives	7.2	17.2	10.4	8.4	6.9
Four antihypertensives	2.1	3.1	2.0	2.8	2.1
Five antihypertensives	0.3	0.8	0.3	0.2	0.4
Six antihypertensives	0.0	0.0	0.0	0.1	0.0
<i>Coded diagnosis</i>					
Diabetes mellitus, <i>n</i> (%)	786 (7.0)	8 (6.5)	21 (6.1)	77 (9.4)	680 (6.9)
CAD, <i>n</i> (%)	466 (4.2)	11 (8.6)*	23 (6.6)*	59 (7.2)*	373 (3.8)*
Hypertension, <i>n</i> (%)	1,387 (12.4)	6 (4.7)*	16 (4.6)*	52 (6.3)*	1,313 (13.3)*
Stroke, <i>n</i> (%)	249 (2.2)	2 (1.6)	15 (4.3)	18 (2.2)	214 (2.2)
CKD, <i>n</i> (%)	961 (8.6)	12 (9.4)	37 (10.7)	83 (10.1)	829 (8.4)
HF (%)	148 (1.3)	10 (7.8)*	17 (4.9)*	23 (2.8)*	98 (1.0)*

SBP strata were based on index SBPs, number of antihypertensive medications were based on prescription data at the time of index SBP. Coded diagnoses figures were calculated from the proportion of patients with read codes relating to the particular diagnosis.

* $P < 0.0001$ ANOVA, between groups.

Of the total 11,167 patients, 1,637 were admitted to hospital once over the 1-year follow-up, 755 twice, 1,438 three or more times. Variables were significantly associated with age (1.03, 1.02–10.4), male gender (0.89, 0.82–0.97) and average SBP <100 mmHg (1.68, 1.18–2.41) and index diagnoses of coronary heart disease (1.51, 1.25–1.83), stroke (1.54, 1.19–1.99) and HF (1.90, 1.35–2.66).

Over 1-year follow-up, 10.6% of patients had an episode of AKI, 0.8% had two episodes and 0.3% had three episodes. Of the 128 patients with index SBP <100 mmHg, 30 patients (23%) had an episode of AKI in follow-up compared to 11% in those with SBP \geq 100 mmHg (χ^2 20.9, P < 0.05). Variables significantly associated with AKI included age, gender, index SBP <100 mmHg, current number of antihypertensive groups and index diagnoses of diabetes, HT, stroke, CKD and HF. Of the 44 patients with average BP <100 mmHg, 7 (16%) had AKI in follow-up.

Table 2. Multilevel logistic regression examining the association between index SBP other variables with death in follow-up

Variable	Category/term	Odds ratio (95% CI)	P-value
Model 1			
SBP	>120	1	<0.001
	<100	6.51 (4.02–10.55)	
	100–109	2.70 (1.78–4.09)	
	110–120	2.3 (1.73–3.15)	
Model 2			
SBP	>120	1	<0.001
	<100	5.14 (3.07–8.60)	
	100–109	2.27 (1.47–3.48)	
	110–120	2.01 (1.54–2.86)	
Age	Linear term	1.14 (1.12–1.16)	<0.001
Gender	Male	1	0.01
	Female	0.76 (0.62–0.95)	
Model 3			
SBP	>120	1	<0.001
	<100	4.51 (2.65–7.69)	
	100–109	2.09 (1.35–3.24)	
	110–120	2.00 (1.46–2.73)	
Age	Linear term	1.14 (1.12–1.15)	<0.001
Gender	Male	1	0.08
	Female	0.75 (0.60–0.93)	
Diuretic		3.86 (0.50–30.28)	NS
Beta-blocker		2.32 (0.297–18.19)	NS
Alpha-blocker		2.85 (0.34–24.00)	NS
ACEI		1.67 (0.22–12.95)	NS
ARB		2.30 (0.29–18.04)	NS
Calcium-blocker		2.26 (0.29–17.93)	NS
Renin antagonist		2.01 (0.26–15.57)	NS
CHD		1.33 (0.87–2.04)	NS
Hypertension		1.06 (0.76–1.48)	NS
Stroke		1.87 (1.15–3.06)	0.01
CKD		1.30 (0.95–1.78)	NS
HF		2.32 (1.35–3.97)	0.02

Odds ratios describe the effect of all variables on outcome. For variable measured on a categorical scale, the odds ratios represent the odds of death in each category relative to baseline category. For the continuous variables, the odds represent the change in odds for one-unit increase in that variable. Three models were examined, each considering the effect of BP on outcome.

Discussion

This study has demonstrated that a small but clinically significant proportion of primary care population of patients remains on antihypertensive drugs despite being hypotensive (SBP <100 mmHg, <110 mmHg and <120 mmHg). It was not within the scope of the study to ascertain the clinical correlates of the low BP recordings of individual patients. Binary logistic regression analysis indicated that hypotension was independently associated with acute admission, AKI and mortality. However, it is not possible to say whether the hypotension was the result of a severe illness, which was the primary cause of the admission, or whether it was the hypotension itself, which caused the admission. Some of the hypotensive patients also had a diagnosis of HF and it is possible that hypotension in these cases was as a direct result of this and antihypertensives were continued in order to manage their underlying condition (e.g. ACEI/ARB, beta-blockers and diuretics).

The low BP in HF patients can be as a consequence of appropriate treatment [12]. However, the results of the multivariate analysis demonstrated that BP was an independent predictor of poor outcome (mortality, AKI and hospital admission). A further limitation of this study is that it uses coded data for co-morbidities and these are likely to underestimate the prevalence of co-morbidities, in addition not all co-morbidity data were available (for example disability and dementia), which may have had an influence on the result. This is demonstrated by the fact that only 12% of the total population are coded as hypertensive, despite considerably more being on antihypertensive medication. It is therefore possible that excess mortality in the hypotensive patient may be attributed to an un-coded (or under coded) co-morbidity such as HF. One of the groups of antihypertensives included in the study was diuretics, which may be used for the treatment of HF rather than hypertension. This group of agents included thiazide diuretics, loop diuretics and aldosterone antagonists, the latter two agents may be indicated for the treatment of hypertension particularly in the context of CKD but are more commonly used in the treatment of oedema. Finally, the data set did not include the entire prescription information, some medications known to lower BP have not been included in the analysis (e.g. drugs to treat prostatic hypertrophy and Parkinson's disease).

However despite these limitations the finding that a clinically significant proportion of elderly people on antihypertensive drugs is hypotensive is of importance. Clinical trials have demonstrated that antihypertensive treatment prevents cardiovascular disease in older people but recent research has underscored the importance of assessing the risk benefit ratio in individual patients especially those with co-morbidities [1–3]. Common clinical sequelae of hypotension in older people include falls, syncope and fear of falling [3, 5, 7–9, 12]. The consequences of hypotension due to drugs are potentially costly to the NHS and have a negative effect on the quality of life of older patients [14–19].

When medication is used primarily for the prevention of future disease (for example in the case of antihypertensives to prevent cardiac and cerebrovascular events) in frail elderly patients, it is important to regularly review treatment in order to balance the risk and benefits [3, 5]. A target clinic BP <150/90 mmHg for treated hypertension in older people aged 80 and over and 140/90 for younger patients is specified in NICE guidance [20]. These targets are also Quality and Outcomes Framework (pay for performance) indicators. However consideration of how far BP is reduced below the target in frail older people is also important. A SBP of 110 mmHg or below in older people is associated with an increased risk of falls, which potentially can be associated with serious clinical consequences [3, 8]. Regular face-to-face medication review to monitor the effects of antihypertensive treatment in older patients was also advised in the NICE Hypertension guideline. In this regard checking for postural hypotension and using ambulatory BP monitoring can be useful to detect the potential for hypotensive side effects in older people.

The participants in the randomised clinical trials upon which clinical guidelines are based (which demonstrated the benefit of antihypertensives in reducing cardiovascular events) suffered from fewer co-morbid conditions than an age-matched clinical population [3]. Randomised controlled trials involving a representative sample of older people are needed to best distinguish, which older people are most likely to derive more benefit than harm from treatment including effects on function and mortality [3]. Moreover, it has been suggested that in future clinical trials of long-term preventative treatments it would be useful to consider patient centred-outcomes such quality of life along with hard outcomes such as mortality and cardiovascular events [24].

However factors other than chronological age are important when assessing the risks and benefits of antihypertensive treatment in older people. There is recent evidence that patients with cognitive impairment, frailty and those in care homes require special consideration regarding antihypertensive prescribing [25–27]. For example in older patients with frailty (as indicated by slower walking speed) higher BP was not associated with higher mortality, whereas in patients with higher walking speeds high BP was associated with increased mortality [24]. These are important areas for further research.

The important role of the generalist physician to take a holistic overview of patients on multiple medications has been acknowledged [5, 6, 28]. Patients with co-morbidities may be prescribed BP lowering medication to treat other conditions, e.g. prostatism, Parkinson's, depression or cardiac conditions, and a regular holistic medication review is advised. In the face of a multiplicity of single disease guidelines, an evolving evidence-based clinical decision-making requires judgement and treatment has to consider patient circumstances and preferences [5, 6, 28]. Additionally, there is further scope for the development of clinical systems to aid decision-making in the care of elderly patients with multiple medications and co-morbidities [5, 6, 29]. Validated

assessment tools have been shown to aid detection and prevention of adverse drug events and iatrogenic illness in primary and secondary care [29]. The development of integrated IT systems, which enable closer integration between primary and secondary care, could help guide the management of patients with co-morbidities [6].

In conclusion, this study suggests that some older patients in primary care on antihypertensive drugs are hypotensive. This could be of clinical importance in some older patients particularly if they have co-morbidities.

Key points

- A significant proportion of the over 70s remain on antihypertensives despite hypotension.
 - Hypotension in older people is associated with an increased mortality.
 - Hypotension in older people is associated with hospital admission and acute kidney injury.
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Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

Authors' contribution

Study design, data analyses and interpretation, manuscript draft: Y.M., M.B., C.K.T.F. Data acquisition: J.I. and M.B. Results interpretation and manuscript revision: all authors.

Conflicts of interest

None declared.

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Ethical approval

Ethical approval had previously been sought to extract anonymised patient data from primary care practices in Kent. Approval was subsequently sought to reanalyse the data set for the purposes of this study. The Trust Research and Development Department gave approval for the study.

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