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Real-world analysis of two ischaemic stroke and TIA systolic blood pressure goals on 12-month mortality and recurrent vascular events

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ABSTRACT

Introduction Whether obtaining the more intensive goal systolic blood pressure (SBP) of <130 mm Hg, rather than a less intensive SBP goal of <140 mm Hg poststroke/transient ischaemic attack (TIA) is associated with incremental mortality and recurrent vascular event benefit is largely unexplored using real-world data. Lowering SBP excessively may result in poorer outcomes.

Methods This is a retrospective cohort study of 26 368 Veterans presenting to a Veterans Administration Medical Center (VAMC) with a stroke/TIA between October 2015 and July 2018. Patients were excluded from the study if they had missing or extreme BP values, receiving dialysis or palliative care, left against medical advice had a cancer diagnosis, were cared for in a VAMC enrolled in a stroke/TIA quality improvement initiative, died or had a cerebrovascular or cardiovascular event within 90 days after their index stroke/TIA. The analytical sample included 12 337 patients. Average SBP during 90 days after discharge was assessed in categories (≤105 mm Hg, 106–115 mm Hg, 116–130 mm Hg, 131–140 mm Hg and >140 mm Hg). Separate multivariable Cox proportional hazard regressions were used to examine the relationship between average SBP groups and time to: (1) mortality and (2) any recurrent vascular event, from 90 days to up to 365 days after discharge from the index emergency department visit or inpatient admission.

Results Compared with those with SBP>140 mm Hg, patients with SBP between 116 and 130 mm Hg had a significantly lower risk of recurrent stroke/TIA (HR 0.77, 95% CI 0.60 to 0.99) but not cardiovascular events. Patients with SBP lower than 105 mm Hg, compared with those with >140 mm Hg demonstrated a statistically significant higher risk of death (HR 2.07, 95% CI 1.43 to 3.00), but no statistical differences were found in other SBP groups.

Discussion Data support a more intensive SBP goal to prevent recurrent cerebrovascular events among stroke/TIA patients by 90 days poststroke/TIA compared with less intensive goal. Very low SBPs were associated with increased mortality risk.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Hypertension control is exceedingly important within the ischaemic stroke and transient ischaemic attack (TIA) population in order to mitigate future vascular events. Given the paucity of data from completed randomised controlled trials examining relationships between different systolic blood pressure (SBP) targets and poststroke/TIA outcomes, such questions as 'what should the goal blood pressure be for my patient after a discharge for stroke/TIA?' and 'how low does one go?', remain open.

WHAT THIS STUDY ADDS

⇒ This observational study using real-world data from the Veterans Health Administration (VHA) reports on the value of obtaining a more intensive SBP goal (ie, <130 mm Hg), instead of a less intensive SBP goal of <140 mm Hg, by 90 days after discharge from an ischaemic stroke/TIA admission. Obtaining the more intensive goal is significantly associated with lower risk of recurrent cerebrovascular events but not cardiovascular events within 12 months after discharge, compared with obtaining a less intensive SBP goal. Furthermore, very low SBPs (ie, <105 mm Hg) are associated with increased mortality.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ When possible, clinicians caring for patients with an ischaemic stroke/TIA should consider an SBP<130 mm Hg and greater than 105 mm Hg to reduce recurrent cerebrovascular events and not to contribute to increased mortality.

INTRODUCTION

In recent years, a more intensive blood pressure (BP) target of <130/80 mm Hg over a less intensive goal of <140/90 mm Hg has been endorsed by multiple guidelines in order to improve postischaemic stroke and transient ischaemic attack (TIA) outcomes.[1–5] The Systolic Blood Pressure Intervention Trial noted that a target SBP of 120 mm Hg vs 140 mm Hg was associated with lower rates of cardiovascular events and all-cause mortality. However, patients with cerebrovascular events were excluded from this primary prevention study.[6] Randomised controlled trials (RCTs) focused on BP lowering among patients

with cerebrovascular events, including The European Society of Hypertension-Chinese Hypertension League-Stroke in Hypertension Optimal Treatment Trial (ESH-CHL-SHOT) and Recurrent Stroke Prevention Clinical Outcome (RESPECT), were stopped early.[7–9] A systematic review and meta-regression analysis of 14 secondary prevention RCTs noted benefits for reduction in recurrent stroke and all-cause mortality[10]; only 2 included trials randomising patients to more versus less intensive SBP goals.[10–12]

Given the paucity of data from completed RCTs examining the relationship between different BP goals and outcomes, clinicians should also recognise that overtreating BP can lead to adverse outcomes including falls and orthostasis.[13 14] Combining the uncertainty regarding issues of BP lowering among those with a cerebrovascular event, and recognising that real-world data can both complement RCT data and generate findings that may be more generalisable than more stringent study designs,[15] we conducted a post hoc analysis of administrative data from the (Protocol-guided Rapid Evaluation of Veterans Experiencing New Transient neurological symptoms (PREVENT), NCT02769338 to determine within a real-world healthcare setting, whether: (1) an SBP of <130/90 mm Hg 90 days postdischarge after an ischaemic stroke/TIA was associated with incremental risks of mortality and recurrent vascular event compared with an SBP of <140 mm Hg and (2) having an SBP substantially below these goals might increase the risk of mortality or recurrent cerebrovascular or cardiovascular events. We hypothesised that: (1) lower rates of mortality and recurrent vascular events would be observed among patients obtaining more intensive, rather than less intensive SBP and (2) a lower limit of SBP would be identified, below which, patients experienced increased mortality or recurrent vascular events.

METHODS

Study sample and data sources

This analysis relies on VHA data intended to examine care quality for a national cohort of Veterans admitted from a VA Emergency Department (ED) or Veterans Administration Medical Center (VAMC) with ischaemic stroke or TIA from October 2014 to September 2018.[1 16] Valid primary diagnosis codes (International Classification of Diseases, Ninth Revision, ICD-9) were used to identify patients with ischaemic stroke (433.X1, 434.00, 434.X1 and 436) and TIA (435.0, 435.1, 435.3, 435.8 and 435.9) during the index ED visit or inpatient admission (please see online supplemental file 1).[1 17 18] These codes were also used to define recurrent stroke and TIA. Mortality was obtained from the VHA Vital Status File.[19] Vascular events were identified using a combination of both VHA and fee-basis data (which describes healthcare services that were paid for by the VA but that were obtained by Veterans in non-VHA facilities).

Our study cohort began with 26 368 stroke or TIA patients who had an index ED visit or inpatient admission to any of 133 VAMCs from October 2015 to September 2018 (figure 1). From this cohort, we excluded 2553 patients who were receiving care at one of 7 VAMCs which had an ongoing quality improvement project directed at improving BP.[1 20] In addition, another 8236 patients were excluded who: had a cancer diagnosis (n=1435), received dialysis prior to, during or within 90 days of cerebrovascular event hospitalisation (n=383) or palliative care or hospice in the year prior to the index cerebrovascular event (n=1358), left against medical advice from a VAMC (n=751), had any combination of being transferred to another acute care facility, being prescribed ≥4 hypertension medications at discharge or were pregnant were also excluded (n=3640). Patients were excluded from the, for several reasons, including that these patients: (1) most likely had the most severe and treatment-resistant hypertension, and hence, would not be representative of patients more commonly encountered in routine practice; (2) may have had secondary causes of hypertension and/or different biological mechanisms linking BP to our outcomes of interest; (3) are oftentimes excluded when considering performance measurements for BP control and;[1 21] (4) were excluded from the ESH-CHL-SHOT and RESPECT trials.[8 9]

Our analysis focused on BP control within 90 days after discharge and outcomes experienced by ischaemic stroke and TIA patients beyond 90 days after discharge. Patients dying or having a recurrent vascular event within 90 days were excluded from the sample. We wanted to ensure that all patients in the sample had a full 90 days to achieve SBP control, and we wanted to avoid outcome occurring shortly after discharge that could be attributed to the quality of inpatient care or other causes unrelated to SBP control. In addition to excluding patients who died or had a recurrent vascular event (ie, cerebrovascular and cardiovascular) within 90 days after their index ED visit or inpatient admission (n=742), we excluded patients with missing BP values during the 90-day period after the index admission (n=2494), and extremely low BP values that may represent either implausible or very hypotensive outliers (ie, SBP<80 mm Hg or DBP<40 mm Hg; n=6).

Measures

Our primary predictor of interest was the average SBP within the first 90 days after discharge. SBP over this time period has been used in other research[13] to examine longer-term outcomes and was chosen because stroke/TIA patients would be beyond the acute cerebrovascular disease period, were considered by their treating providers to be neurological and haemodynamically stable for discharge, and would have allowed for adequate initial outpatient follow-up.[1 5 16] Additionally, patients who have been beyond the acute phase (ie, first 48 hours) of their acute cerebrovascular event.[22] SBP values were taken from outpatient clinic where hypertension could be actively managed, including those from primary care

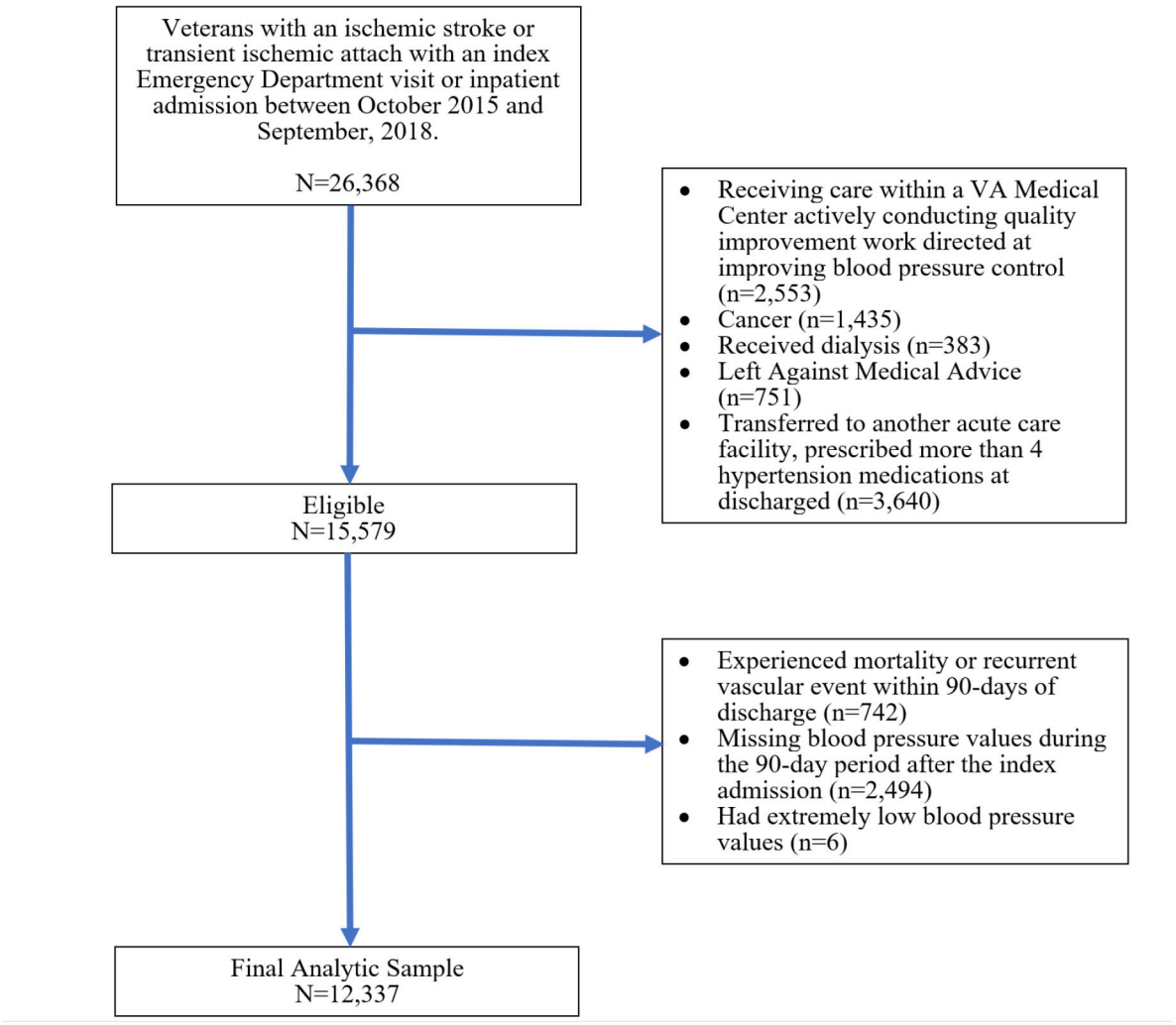

Figure 1 Flow chart of eligible veterans with ischaemic stroke and TIA to examine the relationship between systolic blood pressure control at 90 days and mortality and recurrent vascular events at 12 months. TIA, transient ischaemic attack.

clinic appointments (please see online supplemental file for clinic listing). As part of a previously developed and validated electronic quality measure algorithm related to poststroke/TIA BP control,[18] patients with BP values excluded from the construction of this variable are those who died during the hospitalisation or within 90 days of discharge, those discharged to hospice, or those transferred to another non-VHA acute care facility. These exclusion criteria reflect instances where BP values would be unavailable within VHA administrative data. Average SBP was chosen as the primary predictor of interest, rather than a single (including most recent) value, noting that an average value may more accurately reflect a persistent BP value,[23] and that clinicians may opt for more than a single data point before changing BP management. The average SBP was categorised into five groups: (1) ≤105 mm Hg, (2) 106–115 mm Hg, (3) 116–130 mm Hg, (4) 131–140 mm Hg and (5) >140 mm Hg. Categorisation incorporated recognised definitions for 'more intensive' (ie, <130/80 mm Hg) vs 'less intensive' (ie, <140/90 mm Hg).[3 24] The categories are also clinically meaningful categories which have been used previously to assess the J-curve pattern in the association between BP and outcomes.[2 13 25–30] Prior studies have suggested that overtreating BP may do more harm than good for some patients[13 14] and, more specifically, that stroke risk and mortality benefit decreases when values of SBP<115 mm Hg occur.[31] We considered average SBP groups with the 131–140 mm Hg group as meeting only the less intensive goal[3] and the SBP under 130 mm Hg as meeting the more intensive SBP goal.[24] SBP was chosen because of the importance placed in professional guidelines[5 24 32] J-curve association between SBP and outcomes,[25 33] and a stronger association that SBP has with vascular risk compared with diastolic BP.[30 34]

The primary outcomes were all-cause mortality, recurrent stroke/TIA, cardiovascular events (ie, myocardial infarction/acute coronary syndrome, ventricular arrhythmias)[35] and total vascular events (stroke/TIA and cardiovascular events) from 90 to 365 days postdischarge from the index ED visit or inpatient admission. We refer to these outcomes as '12-month' mortality, cerebrovascular or cardiovascular events. Follow-up ended prior to day 365, if a person died or experienced either any type of

Table 1 Baseline characteristics of ischaemic stroke/TIA patients cohort surviving 90 days postcerebrovascular event cohort (N=12 337)

Characteristic	Mean (SD) or %
Sociodemographic	
Age	69.05 (10.8)
Sex, male	95.3
Race	
White	70.2
Black	24.5
Asian	0.7
Other	0.6
Unknown	4.0
Hispanic	7.5
Systolic blood pressure groupings (mm Hg)	
≤105	3.6
106 to ≤115	10.3
116 to ≤130	34.9
131 to ≤140	27.4
> 140	23.7
Index Cerebrovascular Event-Final Diagnosis	
Ischaemic stroke	64.0
TIA	36.0
FY of presentation	
FY2016	37.3
FY2017	36.5
FY2018	26.2
Healthcare utilisation	
No of admissions in 1 year prior to presentation	0.31 (0.78)
No of ED presentations in 1 year prior to presentation	1.25 (2.12)
Length of hospitalisation stay (days)	3.90 (7.12)
ED presentation of index event	91.0
Hospital admission of index event	83.5
Medical history*	
Ischaemic stroke	56.7
TIA	26.0
Hemiplegia	34.3
Hypertension	79.0
Hyperlipidaemia	64.1
Diabetes	43.0
Atrial fibrillation	13.9
Other arrhythmia	11.0
CHF	11.9
MI	6.2
CEA/carotid stent	0.9
PAD	12.6
OSA	14.9
Chronic kidney disease	15.6
Current smoker	33.3
Alcohol dependence	9.7
Dementia	7.3
Depression	22.5
Additional clinical indicators	
CCI	2.20 (2.22)
Modified APACHE III score	9.73 (6.36)
Concomitant illness within 1 day of cerebrovascular event presentation	
MI	2.6
CHF	1.6

*Medical history variables identified by International Classification of Diseases, Ninth Edition Code.
APACHE, Acute Physiology and Chronic Health Evaluation; CCI, Charlson Comorbidity Index; CEA, carotid endarterectomy; CHF, congestive heart failure; ED, emergency department; FY, fiscal year; MI, myocardial infarction; OSA, obstructive sleep apnoea; PAD, peripheral arterial disease; SBP, systolic blood pressure; TIA, transient ischaemic attack; VA, Veterans Affairs.

recurrent vascular event or up to the end of follow-up period (ie, right-censored).

Patient demographics included age, sex and race/ethnicity. Medical history was based on the 5 years prior to the cerebrovascular event index date and included ischaemic stroke, TIA, hypertension, hyperlipidaemia, diabetes, atrial fibrillation, other arrhythmias, congestive heart failure (CHF), myocardial infarction, carotid endarterectomy, carotid stent, peripheral vascular disease, obstructive sleep apnoea, being a current smoker, alcohol dependence, dementia and depression. Additional clinical indicators were Charlson Comorbidity Index and modified Acute Physiology and Chronic Health Evaluation score, which were measured during the index ED visit or inpatient admission. Please see online supplemental file for comparisons of demographics and comorbidity profiles across SBP strata.

Statistical analysis

For descriptive analyses, we calculated mean and SD for continuous variables, and frequency and percentage for categorical variables. A χ^2 test or one-way analysis of variance was used to compare differences across SBP strata and outcomes. Multivariable Cox proportional hazard models were used to assess the association between 5 SBP groups and the survival from 90 days to up to 365 days after discharge with corrections for right-censoring. We employed backward selection to identify a subset of predictors at a significance level of 0.05, except age, sex

Table 2 Descriptive table of 12-month patient outcomes stratified by SBP levels (N=12 337)

	SBP≤105(1)	105<SBP≤115(2)	115<SBP≤130(3)	130<SBP≤140(4)	SBP>140(5)	Total	P value*
Total (%)	3.6	10.3	34.9	27.4	23.7	100	
SBP measurements							
Mean (SD)	2.39 (1.92)	2.90 (2.01)	3.19 (2.23)	3.22 (2.28)	3.15 (2.00)	3.14 (2.16)	<0.001†
Outcomes							
Recurrent ischaemic stroke/TIA	22 (7.7)	66 (6.3)	236 (5.6)	214 (6.2)	212 (6.4)	750 (6.1)	0.438
Cardiovascular events‡	5 (1.7)	15 (1.4)	83 (2.0)	72 (2.1)	58 (1.8)	233 (6.1)	0.671
Total vascular events§	24 (8.4)	80 (7.7)	304 (7.2)	275 (8.0)	260 (7.8)	943 (7.7)	0.732
All-cause mortality	28 (9.8)	38 (3.7)	143 (3.4)	98 (2.8)	123 (3.7)	430 (3.5)	<0.001

*P values from $\chi 2$ or one-way ANOVA.
†Significant contrasts from one-way ANOVA (Scheffe test, p<0.05): (1) less than (2–5); (2) greater than (1); (3) greater than (1, 2); (4) greater than (1, 2) and (5) greater than (1, 2).
‡Cardiovascular Events: myocardial infarction/acute coronary syndrome, ventricular arrhythmias.
§Total Vascular Events: recurrent stroke/TIA, myocardial infarction/acute coronary syndrome, ventricular arrhythmias.
ANOVA, analysis of variance; SBP, systolic blood pressure; TIA, transient ischaemic attack.

and race/ethnicity which were forced into all models regardless of significance level. For recurrent events, we modelled cerebrovascular recurrence, cardiovascular recurrence and all recurrent events separately using Cox proportional hazard regression, with death as a competing risk event.[36 37] Proportional hazard assumption test was performed, and p values were provided where applicable.

RESULTS

Baseline characteristics of ischaemic stroke and TIA patients surviving 90 days postcerebrovascular event

The 12 337 patients in the cohort had a mean age of 69 years (SD±10.8); 70% were white, 25% black and 7.5% Hispanic; and 95% were male (table 1). At their index ED visit or inpatient admission, 64% of patients had a stroke and 36% had a TIA diagnosis; 84% were admitted to the hospital and 16% were seen only in the ED. Most patients had a prior history of ischaemic stroke (57%) or TIA (26%). Unadjusted mortality was highest in the SBP≤105 mm Hg (9.8% vs 2.8%–3.7%), whereas SBP categories did not differ significant in the percentages with recurrent ischaemic stroke or TIA or recurrent cardiovascular events over the same period (table 2).

Distribution of postischaemic stroke and TIA SBP values

From the first day to 90 days postdischarge, 24 872 BP measurements were recorded in outpatient clinics. A majority either had 1 (40.75%), 2 (32.7%) or 3 (16.5%) SBP readings during this time (table 3). The highest percentage of SBP readings occurred on days 7 (2.77%) and 14 (2.78%) postdischarge. A gradual decline in postdischarge SBP readings occurred beyond 21 days postdischarge (figure 2). For the sample as a whole, the mean number of BP readings in the 90 days after discharge was 3.14 (SD=2.16) with a range of 2.39 for the SBP≤105 category to 3.19 for the 115<SBP≤130 group (table 2). Although the mean number of readings was significantly greater for top three categories (SBP>115) compared with the bottom 2, there were no significant differences among the top three categories.

Association between 12-month mortality and SBP goals

Compared with patients with an average SBP>140 mm Hg over the first 90 days after discharge for their index event,

Table 3 Distinct systolic blood pressure readings postdischarge per ischaemic stroke/TIA patient (N=12 337)

Distinct blood pressure measurements	n	(%)
1	5016	40.75
2	4020	32.66
3	2028	16.47
4	785	6.38
5	309	2.51
6	95	0.77
7	34	0.28
8	17	0.14
9	4	0.03
10	0	0.00
11	2	0.02

TIA, transient ischaemic attack.

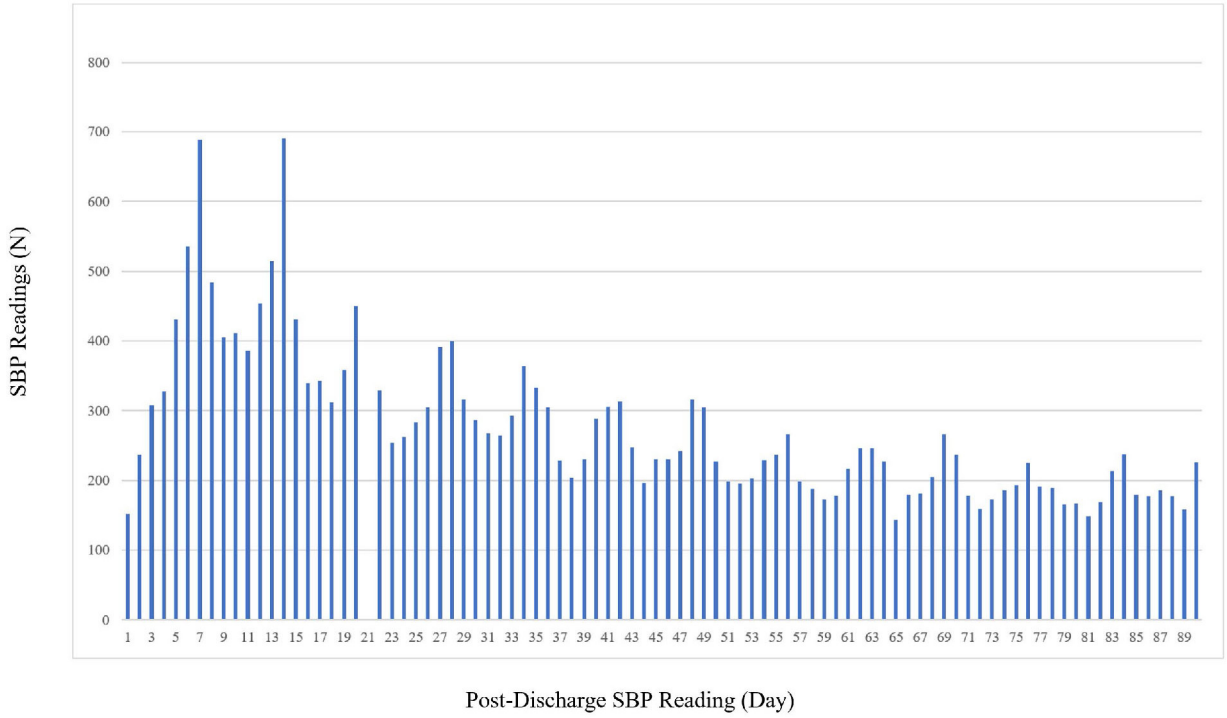

Figure 2 Number of systolic blood pressure readings by postischaemic stroke/TIA discharge day. SBP, systolic blood pressure; TIA, transient ischaemic attack.

patients in the lowest SBP group (≤105 mm Hg) had 2.07 times higher risk of death in the 12 months postdischarge (95% CI 1.43 to 3.00, p<0.001, satisfies PH assumption; table 2). The patients in the other SBP groups did not have a significant difference in survival (table 4, figure 3). Please see online supplemental file for additional information regarding point estimates for full models.

Association between 12-month vascular event recurrence and SBP goals

Cerebrovascular event recurrence

Compared with patients with >140 mm Hg, patients in the 116–130 mm Hg SBP group had significantly lower risk of cerebrovascular recurrence (HR 0.77, 95% CI 0.60 to 0.99; table 5). Other SBP groups, including patients in less intensive SB group, did not show a significant difference in cerebrovascular recurrence rates. Please see online supplemental file for additional information regarding point estimates for full models.

Cardiovascular and any vascular event recurrence

No significant differences between the SBP groups in the models for cardiovascular and combined cerebrovascular and cardiovascular event recurrence were found. Patients meeting either more intensive or less intensive SBP goals had no lower risk for cardiovascular or combined vascular event recurrence than patients above these goals (SBP>140 mm Hg).

DISCUSSION

In this large, real-world sample of Veterans with ischaemic stroke/TIA, we found no significant difference in 12-month all-cause mortality when patients obtained either more intensive or less intensive SBP goals by 90 days postcerebrovascular event. Patients with the lowest SBP experienced a twofold increase in 12-month all-cause mortality compared with patients with SBP>140 mm Hg. When considering recurrent vascular events, patients obtaining an SBP<130 mm Hg had a modestly lower risk of cerebrovascular event recurrence. In contrast, we did not detect a similar degree of protection in cardiovascular event recurrence nor in the combined vascular event recurrence.

Cerebrovascular disease-specific studies have yielded equivocal findings about the protective effect of various SBP ranges.[2 10 12 38] After 12 months, the SPS3 study reported a non-significant reduction in all stroke, disabling/fatal stroke and the composite of myocardial infarction/vascular death among those with a recent lacunar stroke between groups meeting more intensive compared with less intensive SBP goals.[12] In observational data from the National Health and Nutrition Examination Surveys (1998–2004) researchers examined the relationship between baseline SBP categories of <120 mm Hg, 120–140 mm Hg and ≥140 mm Hg and all-cause mortality among 455 participants with self-reported stroke over a 2-year assessment period. Compared with participants with SBP≥140 mm Hg, those with SBP<120 mm Hg had a higher all-cause mortality (HR 1.96: 95% CI 1.13 to 3.39).[38]

Table 4 Multivariable Cox proportional hazard regression for survival (N=12 337)*

Variable	Survival since 90 days after discharge up to 12 months	
	HR (95% CI)	PH assumption test
Systolic blood pressure groupings (mm Hg)		
≤105	2.07 (1.43 to 3.00)	0.58
106 to ≤115	1.14 (0.83 to 1.57)	0.11
116 to ≤130	0.91 (0.71 to 1.17)	<0.001
131 to ≤140	0.82 (0.63 to 1.07)	0.11
>140	Ref	
Age	1.06 (1.05 to 1.07)	0.16
Yes	0.77 (0.54 to 1.10)	<0.001
Healthcare utilisation		
No of admissions in 1 year prior to presentation	1.20 (1.07 to 1.35)	0.63
Length of stay		
No of ED presentations in 1 year prior to presentation	0.94 (0.89 to 1.00)	0.95
Medical history†		
Hyperlipidaemia		
No	Ref	
Yes	0.68 (0.56 to 0.83)	0.32
Atrial fibrillation		
No	Ref	
Yes	1.27 (1.02 to 1.59)	0.79
OSA		
No	Ref	
Yes	0.66 (0.48 to 0.91)	0.16
Dementia		
No	Ref	
Yes	1.80 (1.41 to 2.29)	0.21
CCI	1.11 (1.06 to 1.16)	0.74
APACHE	1.02 (1.00 to 1.03)	0.37

*PH assumption test=proportional hazard assumption test. A p≥0.05 indicates that the HR is constant over time. A p<0.05 indicates violation of the proportional hazard assumption for the model.
†Medical history variables identified by International Classification of Diseases, Ninth Edition Code.
APACHE, Acute Physiology and Chronic Health Evaluation; CCI, Charlson Comorbidity Index; ED, emergency department; OSA, obstructive sleep apnoea; PH, proportional hazard; TIA, transient ischaemic attack.

Across these studies and our current work, the lowest tiers of SBP are associated with increased postcerebrovascular event mortality. While some of the observed relationship may be attributable to reverse causality (ie, the sickest patients have the lowest BP), we excluded patients with cancer, end-stage renal disease, and palliative care and adjusted for degree of acute illness encountered during the hospitalisation, burden of medical comorbidities and conditions associated with lower BP (eg, CHF). When treating BP, clinicians also do so with the intention of reducing the likelihood of future vascular events. Here, we report that the relationship between SBP and vascular event recurrence varies on the type of postevent vascular event (ie, cerebrovascular vs cardiovascular vs composite vascular). This is not altogether unexpected when considering that hypertension is more strongly associated with cerebrovascular than cardiovascular events.[30 39] In considering recurrent ischaemic strokes, a post hoc analysis performed with PRoFESS data noted that those who maintained SBP values other than 120–129 mm Hg had a lower hazard of stroke compared with patients with an SBP 130–139 mm Hg, after adjusting for sociodemographic characteristics, prior cerebrovascular event type, vascular risk factors and National Institutes of Health Stroke Scale (NIHSS) score.[2] We similarly report that patients with an SBP<130 mm Hg but greater than 105 mm Hg experience less cerebrovascular recurrence than patients with higher SBP. The Blood Pressure and Clinical Outcome in TIA or Stroke observational trial examined the relationship between mean self-measured

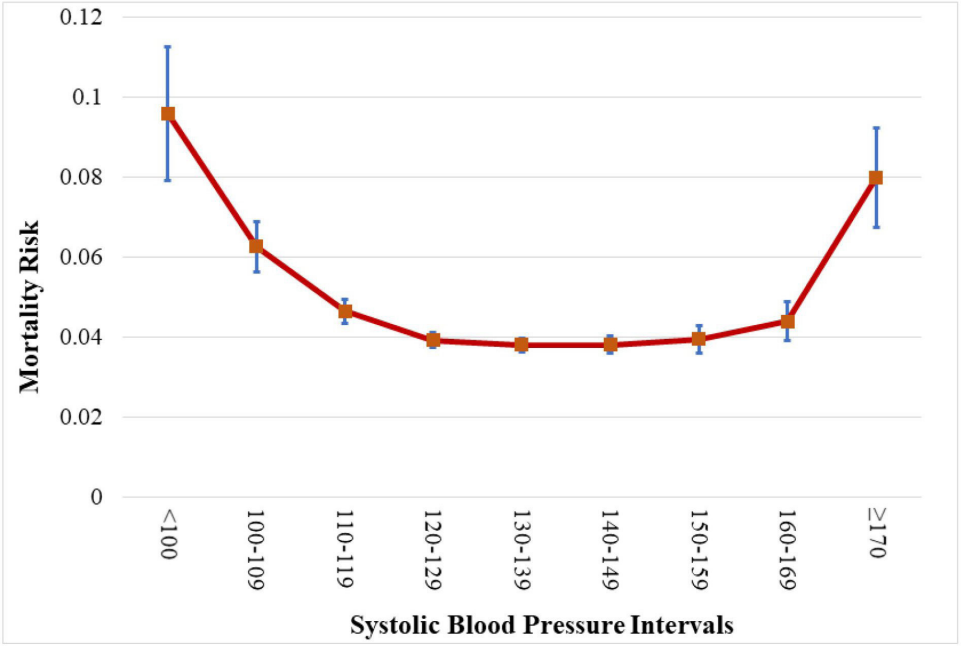

Figure 3 Predicted probability (with CIs) for mortality within 12 months by systolic blood pressure intervals (N=9065). Predicted probability of all-cause mortality within 12 months by systolic blood pressure obtained at 90 days postischaemic stroke/transient ischaemic attack.

SBP at 90 days postcerebrovascular event and both stroke recurrence and combined vascular events. At 1-year post-cerebrovascular event, the lowest rates of both outcomes occurred among patients with SBP 115–124 mm Hg, suggesting that this may be an optimal SBP target for 90 days postcerebrovascular event to lower stroke recurrence.[13] A systematic review and meta-regression analysis of 14 randomised controlled secondary cerebrovascular prevention trials reported that a mean SBP target of <130 mm Hg effectively reduced recurrent cerebrovascular events (p=0.048), compared with those who with SBP between 130 and 140 mm Hg and greater than 140 mm Hg. Data from the RESPECT trial were combined with three other RCTs examining BP control post cerebrovascular event, the risk ratio favoured (RR) a goal BP of <130/80 mm Hg (RR 0.78; 95% CI 0.64 to 0.96; p=0.02).[9] A similar association between cardiovascular events and reaching SBP of <130 mm Hg compared with the two aforementioned SBP categories was not observed (p=0.291).[10]

The strengths of our study include the large sample size, use of competing risk models to understand the relationship between fine gradations of SBP seen at 90 days postcerebrovascular event and several important clinical outcomes, inclusion of both ischaemic stroke and TIA patients and patient comorbidities that were routinely excluded from secondary cerebrovascular prevention trials though routinely managed in real-world healthcare settings, and multivariable analysis with statistical controls for many potential confounders.

Limitations of the study should also be noted. As our observational study consisting of largely older, white Veteran men, both our ability to infer causality and study generalisability are limited. While we cannot control for the effects of unmeasured variables, we report on SBP values obtained during routine care of hypertension among patients with ischaemic stroke and TIA. Furthermore, while providers are encouraged to incorporate recommendations regarding 'goal' BP, our current study cannot comment on whether BP was actively managed by providers to reach specific BP thresholds. Next, we focused on SBP obtained over the 90 days postdischarge and subsequent mortality and vascular outcomes, we cannot generalise to other time points (eg, at time of discharge). Also, we used all available SBP readings; however, most stroke/TIA patients had 1–3 readings within the 90 days postdischarge. While the number of BP readings were not as standardised as would be seen in an RCT, we would not expect the same degree of rigour in a real-world analysis of hypertensive stroke/TIA patients who were diagnosed and care for by various types of clinicians. Additionally, we cannot control for bias that providers may have when determining who should return for more frequent BP measurements.

Our study included a wide range of ischaemic stroke and TIA patients; however, unlike other studies,[2 12] we did not have information on stroke subtypes. We did not include measures of antihypertensive medication or other treatments to control SBP. A systematic review and meta-analysis of BP reduction in stroke prevention trials did not demonstrate a relationship between class of antihypertensive medication and recurrent stroke, suggesting that the BP is more important than the pharmacotherapy used to obtain that BP.[10] Stroke/TIA patients were excluded from this current analysis if they were receiving four or more antihypertensive medications, as these patients likely

Table 5 Multivariable Cox proportional hazard regression for cerebrovascular recurrence, cardiovascular recurrence and both combined, with death as a competing risk (N=12 337)

	Model 1—recurrent cardiovascular event*	Model 2—recurrent cerebrovascular event†	Model 3—recurrence of either vascular event‡
Characteristic	HR (95% CI)		
Systolic blood pressure groupings (mm Hg)			
≤105	0.90 (0.63 to 1.30)	0.87 (0.51 to 1.47)	0.92 (0.55 to 1.53)
106 to ≤115	0.95 (0.74 to 1.21)	0.99 (0.71 to 1.38)	0.89 (0.62 to 1.28)
116 to ≤130	0.92 (0.77 to 1.10)	0.77 (0.60 to 0.99)	1.09 (0.84 to 1.41)
131 to ≤140	1.02 (0.84 to 1.23)	1.10 (0.86 to 1.40)	0.89 (0.66 to 1.19)
>140	Ref	Ref	Ref
Age	1.01 (1.00 to 1.02)	1.01 (1.00 to 1.02)	1.01 (1.00 to 1.02)
No of ED presentations in 1 year prior to presentation	1.09 (1.07 to 1.11)	1.07 (1.05 to 1.10)	1.11 (1.08 to 1.13)
ED presentation of index event			
No	Ref		
Yes	1.33 (1.02 to 1.73)	—	—
Medical history§			
Ischaemic stroke			
No	—	Ref	—
Yes	—	1.26 (1.04 to 1.52)	
Hemiplegia			
No	—	—	Ref
Yes	—	—	0.72 (0.58 to 0.90)
Diabetes			
No	Ref	Ref	—
Yes	1.28 (1.10 to 1.50)	1.47 (1.23 to 1.77)	—
Atrial fibrillation			
No	Ref		Ref
Yes	1.34 (1.12 to 1.59)	—	1.65 (1.29 to 2.12)
CHF			
No	Ref		Ref
Yes	1.76 (1.46 to 2.12)		2.77 (2.13 to 3.61)
MI			
No	Ref	—	Ref
Yes	1.45 (1.17 to 1.80)	—	1.65 (1.23 to 2.21)
Current smoker			
No	—	Ref	—
Yes	—	1.32 (1.09 to 1.61)	—
CCI	1.05 (1.02 to 1.09)	—	1.10 (1.05 to 1.14)
APACHE	1.01 (1.00 to 1.02)	—	1.02 (1.01 to 1.04)

*Model 1—Recurrent cerebrovascular events only with death as a competing risk.
†Model 2—Recurrent cardiovascular events only with death as a competing risk.
‡Model 3—Combined recurrent cerebrovascular events and recurrent cardiovascular events with death as a competing risk.
§Medical history variables identified by International Classification of Diseases to Ninth Edition Code.
APACHE, Acute Physiology and Chronic Health Evaluation; CCI, Charlson Comorbidity Index; CHF, congestive heart failure; ED, Emergency Department; MI, myocardial infarction.

represent those with the most severe hypertension and treatment-resistant group of patients.[21]

We were unable to adjust for variables which are not routinely available within administrative data, including measures of functional disability (eg, modified Rankin scale) and neurological status (eg, NIHSS) at discharge, severity of conditions (eg, dementia) which may have led to reverse causality between SBP and mortality, the provider type (eg, vascular neurologist) who coded a stroke/TIA diagnosis and reasons why patients may have received more or less SBP measurements. In our modelling, we did include neurological deficits for which ICD-9 codes were available and have been used to identify stroke patients using electronic health record data[40]; of these, hemiplegia was found both to be common and an important predictor of vascular event recurrence. While hemiplegia is not specific to stroke, given the composition of our cohort, it is likely that hemiplegia is attributable to a cerebrovascular event. Also, we adjusted for the presence of conditions, which may have led to reverse causality; however, given the larger associated noted between SBP and mortality compared with SBP and vascular outcomes, reverse causality likely contributed to some of our current findings. Of note, many studies included in the aforementioned systematic review and meta-regression analysis[10] excluded patients from clinical trial participation (eg, prior ipsilateral carotid endarterectomy)[5 10 12] were included in our real-world data analysis.

CONCLUSIONS

Healthcare providers managing postischaemic stroke and TIA BP should recognise the benefit for patients in obtaining more intensive SBP lowering for preventing cerebrovascular event recurrence. Using real-world data, poststroke/TIA SBP<130 mm Hg and greater than 105 mm Hg appears reasonable to reduce recurrent cerebrovascular events and not to contribute to increased mortality. Future work is needed to thoroughly understand the roles that the interrelated concepts of reverse causality, BP trajectories, medication adherence and intensification, and healthcare utilisation have on post-cerebrovascular event outcomes.

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