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ORIGINAL RESEARCH

Impact of Uncontrolled Hypertension at 3 Months After Intracerebral Hemorrhage

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BACKGROUND: Survivors of intracerebral hemorrhage (ICH) are at high risk for recurrent stroke, which is associated with blood pressure control. Because most recurrent stroke events occur within 12 to 18 months of the index ICH, rapid blood pressure control is likely to be crucial. We investigated the frequency and prognostic impact of uncontrolled short-term hypertension after ICH.

METHODS AND RESULTS: We analyzed data from Massachusetts General Hospital (n=1305) and the University of Hong Kong (n=523). We classified hypertension as controlled, undertreated, or treatment resistant at 3 months after ICH and determined the following: (1) the risk factors for uncontrolled hypertension and (2) whether hypertension control at 3 months is associated with stroke recurrence and mortality. We followed 1828 survivors of ICH for a median of 46.2 months. Only 9 of 234 (4%) recurrent strokes occurred before 3 months after ICH. At 3 months, 713 participants (39%) had controlled hypertension, 755 (41%) had undertreated hypertension, and 360 (20%) had treatment-resistant hypertension. Black, Hispanic, and Asian race/ethnicity and higher blood pressure at time of ICH increased the risk of uncontrolled hypertension at 3 months (all $P<0.05$). Uncontrolled hypertension at 3 months was associated with recurrent stroke and mortality during long-term follow-up (all $P<0.05$).

CONCLUSIONS: Among survivors of ICH, >60% had uncontrolled hypertension at 3 months, with undertreatment accounting for the majority of cases. The 3-month blood pressure measurements were associated with higher recurrent stroke risk and mortality. Black, Hispanic, and Asian survivors of ICH and those presenting with severe acute hypertensive response were at highest risk for uncontrolled hypertension.

Key Words: hypertension ■ intracerebral hemorrhage ■ stroke

Intracerebral hemorrhage (ICH) is the most severe form of stroke, accounting for almost half of all stroke-related morbidity and mortality.[1,2] Survivors of ICH are at high risk of recurrent ischemic and hemorrhagic strokes, which are generally more severe and lethal than the initial acute cerebrovascular event.[3–5] Control of elevated blood pressure (BP) represents the cornerstone of secondary stroke prevention after ICH.[3,6,7] Because the majority of recurrent strokes and mortality occurs within the first 12 to 18 months after primary ICH,[3,8–11] identification of survivors at risk for inadequate hypertension control early after hemorrhagic

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CLINICAL PERSPECTIVE

What Is New?

- The present study provides novel evidence that uncontrolled hypertension at 3 months after intracerebral hemorrhage predicts poor long-term blood pressure control as well as increased stroke recurrence and mortality risk.

What Are the Clinical Implications?

- Providers caring for survivors of intracerebral hemorrhage should focus on comprehensive evaluation and optimization of hypertension management at 3 months because it may represent a unique opportunity to improve quality of care and outcomes for survivors of hemorrhagic stroke.

Nonstandard Abbreviations and Acronyms

HK-ICH	Intracerebral Hemorrhage Study at University of Hong Kong
ICH	intracerebral hemorrhage
MGH-ICH	Intracerebral Hemorrhage Study at Massachusetts General Hospital

stroke would allow for corrective measures that are likely to improve long-term outcomes.

Despite the universal recommendation of hypertension control for secondary stroke prevention after ICH, <50% of survivors of ICH consistently achieve adequate BP control, as defined by international guidelines, in real-world data.[3,5,12–14] Unfortunately, existing evidence provides limited insight into risk factors and mechanisms accounting for poor BP control after ICH. Uncontrolled hypertension is most commonly attributed to underlying resistant hypertension (defined as BP that remains above the desired BP goal despite the use of ≥3 antihypertensive medication classes[15]) or inadequate prescription of antihypertensive medications. Although patients with ICH, when hospitalized, frequently have severe hypertension, studies of resistant hypertension beyond the acute setting are limited.[16] Furthermore, the extent of inadequate prescription of antihypertensive medications has yet to be assessed in survivors of ICH.[17] Therefore, we sought to investigate (1) the frequency and risk factors for undertreated and treatment-resistant hypertension at 3 months after ICH and (2) the impact of poorly controlled hypertension at 3 months after ICH on long-term risk of stroke and mortality.

METHODS

Participating Studies and Enrollment Eligibility Criteria

Participants were individuals aged 18 years or older presenting with an acute, primary ICH initially identified via daily manual review of medical records and confirmed by brain computed tomography (CT) scan obtained within 24 hours of symptom onset. Individuals with intracranial hemorrhage secondary to trauma, conversion of an ischemic infarct, rupture of a vascular malformation or aneurysm, and brain tumor were excluded. The MGH-ICH (Intracerebral Hemorrhage Study at Massachusetts General Hospital) is a single-center, longitudinal cohort study of ICH.[3,6] Participants were recruited among consecutive patients presenting to Massachusetts General Hospital between January 2006 and December 2017. The HK-ICH (Intracerebral Hemorrhage Study at University of Hong Kong) is a single-center stroke registry that enrolled consecutive patients with ICH from January 2011 to March 2019. The study protocols were approved by the institutional review boards at all participating institutions, and written informed consent was obtained from all participants.

Baseline Data Collection

Trained study staff collected demographic, social, and medical histories in both studies via in-person interviews of patients (and/or reliable informants) and a review of electronic medical records at the time of enrollment. Participants and/or informants provided self-identified race and ethnicity, choosing from categories recommended by the National Institutes of Health for use in research studies.[6] All available CT scans were deidentified, digitalized, and uploaded to the neuroimaging repository at both sites. Admission (ie, first available) CT scans were analyzed to determine ICH location, hematoma volume, and presence of intraventricular blood according to previously validated methodology.[3] All neuroimaging was analyzed blinded to clinical information.

Longitudinal Follow-Up

For the MGH-ICH, survivors of ICH and their caregivers were interviewed by dedicated study staff (blinded to baseline and neuroimaging information) at 3, 6, and 12 months after the index ICH and every 6 months thereafter based on established protocols.[3] Participants from the HK-ICH were followed up by clinicians every 3 to 6 months or more frequently if clinically indicated.[7] We supplemented patient-based collection of follow-up data with semiautomated review of longitudinal

electronic medical records to confirm and augment participant-reported information. We specifically collected information on antihypertensive medication use during follow-up. Patients with discrepancies between self-reported versus electronic medical record–derived data on medication use (medication name, route, dosing, or duration of use) were excluded from all analyses. If patients or caregivers reported new neurologic symptoms, recurrent stroke, hospital admission, or death, pertinent medical records and radiology reports were reviewed by study staff.[3] Adjudication of recurrent ischemic and hemorrhagic stroke events required direct review of neuroimaging scans.

Capture of BP and Antihypertensive Medication Data

MGH-ICH and HK-ICH research staff collected information on BP measurements obtained in a medical setting (outpatient clinic or inpatient ward) by medical personnel (self-reported or home measurements were not taken into consideration) according to previously published methods.[3,6,7] Of note, at-home BP measurements (whether from a visiting medical professional or self-monitoring) were not considered for the purpose of our analyses. We focused on BP measures 3 months after ICH on the assumption that (1) most recurrent stroke events occur after 3 months from the initial ICH[3,8] and (2) 3 months provides clinicians adequate time for titration of antihypertensive agents to a target BP goal. All patients with missing BP measurements or medication use data at any time point during follow-up were excluded.

Variable Definitions

Age at index ICH was analyzed as a continuous variable. Race/ethnicity was analyzed as a set of dichotomous variables. Measurements of systolic and diastolic BP were calibrated on 10 mm Hg increases. Outcomes of interest include controlled versus undertreated versus treatment-resistant hypertension as well as recurrent stroke (both ischemic and hemorrhagic) and mortality after ICH. Although the (currently in effect) 2015 American Heart Association/American Stroke Association ICH guideline recommends a follow-up BP target of <130/80 mm Hg, we defined our BP control goal at <140/90 mm Hg (the previously recommended guideline target) as most of the patients included in the present study received care before 2015.[5] Uncontrolled hypertension was therefore defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg. We defined resistant hypertension as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg despite use of ≥3 agents.[15] In contrast, undertreated hypertension was defined as systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg while on ≤2 agents. We also calculated average systolic and diastolic BP values during long-term follow-up using all available values except (1) from the index ICH hospitalization, (2) from the 3-month time point after ICH, or (3) from hospitalization for recurrent stroke. The number of antihypertensive agents prescribed was analyzed as an ordinal variable with levels corresponding to concomitant use of 0, 1, 2, or ≥ agents. Recurrent stroke was defined as the first episode of new-onset neurological symptoms representing recurrent ICH or incident ischemic stroke as confirmed by CT and/or magnetic resonance imaging.

Statistical Analysis

Overall Analysis Plan

We first sought to confirm whether the majority of recurrent stroke events after ICH occur in the first 12–18 months after ICH. We subsequently investigated the following: (1) the frequency of controlled and uncontrolled hypertension at 3 months after ICH; (2) the proportional representation of undertreated and treatment-resistant hypertension; (3) the association of BP measurements at 3 months with long-term hypertension control, recurrent stroke risk, and mortality; and (4) risk factors for uncontrolled (versus controlled) and treatment resistant (versus undertreated) hypertension at 3 months. Because of the limited availability of BP measurements before 3 months after index ICH, we initiated the follow-up for long-term outcomes (hypertension control, recurrent stroke, mortality) at 3 months after ICH.[3] All analyses were first conducted separately in the MGH-ICH and HK-ICH and then in a combined data set with adjustment for data source (see Univariable and Multivariable Analyses). We conducted tests of heterogeneity for all associations tested, but found no evidence of differential effects based on data source (all heterogeneity $P>0.20$).

Univariable and Multivariable Analyses

Continuous variables were expressed as either mean with standard deviation or median with interquartile range (IQR). Categorical data were expressed as number and percentage of subtotal. Categorical variables were compared using chi-square or the Fisher exact test (2-tailed) and continuous variables using the Mann–Whitney rank sum or Student *t* test, as appropriate. We used multivariable logistic regression models to identify risk factors for uncontrolled (versus controlled) and treatment-resistant (versus undertreated) hypertension at 3 months. We determined factors associated with stroke recurrence and mortality in univariable analyses using Kaplan–Meier plots, with significance testing via the log-rank test. All analyses of stroke recurrence and mortality

risk used 3 months after ICH as the initial time for statistical modeling purposes. Patient data were censored only in case of death or loss to follow-up. We performed multivariable analyses of survival outcomes using competing risk regression models via the Fine and Gray method to account for competing risks between stroke recurrence and death.[18] For all multivariable models, we initially included all factors associated with outcomes of interest in univariable analyses at a significance level of $P<0.20$. We subsequently used backward elimination procedures to arrive at a minimal model including only variables associated with ICH at $P<0.05$. We prespecified adjustment for study (dichotomous variable indicating MGH-ICH versus HK-ICH data source) and year of index ICH (in 2-year increments). The proportional hazard assumption was tested for all survival analyses using graphical checks and Schoenfeld residuals-based tests.

Multiple Testing Adjustments

We corrected for multiple testing using the Benjamini-Hochberg false discovery rate method for adjustment.[19] We report P values after false discovery rate adjustments applied to all predictors included in the univariable and multivariable models (because of multiple models being created as part of planned analyses). All significance tests were 2 tailed, and significance was set at $P<0.05$ (after adjustment). All analyses performed using R software version 3.6.2 (R Foundation for Statistical Computing).

Data Availability

The authors certify they have documented all data, methods, and materials used to conduct the research presented. Anonymized data pertaining to the research presented will be made available upon reasonable request from external investigators.

RESULTS

Study Participants

A total of 3254 consecutive patients with ICH were identified at initial screening (MGH-ICH, n=2354; HK-ICH, n=891). After application of inclusion and exclusion criteria (Figure 1), 1828 survivors of ICH (MGH-ICH, n=1305; HK-ICH, n=523) were included in all subsequent analyses. Racial and ethnic backgrounds differed substantially between the MGH-ICH and HK-ICH (Table 1). Survivors of ICH enrolled in the MGH-ICH were also more likely to be female and older and to have a prior medical history of hypertension, coronary artery disease, and atrial fibrillation and to use statins before index ICH (all $P<0.05$). Study participants enrolled in the HK-ICH presented with higher systolic and diastolic BP at time of hospital admission (both $P<0.05$). Antihypertensive agent prescription patterns also differed between studies (Table 1).

Recurrent Stroke Risk After ICH

We followed participants enrolled in the MGH-ICH for a total of 5973 person-years, with a median of 50.6 months (IQR, 41.6–62.3 months); the yearly loss to follow-up rate was 1.1%. During follow-up we identified 129 recurrent ICH events for an annual rate of 4.2% (95% CI, 3.4%–5.4%) and 43 ischemic stroke events for an annual rate of 1.4% (95% CI, 0.7%–2.1%). The HK-ICH participants were followed for a total of 1710 person-years, with a median of 34.6 months (IQR, 23.5–49.8 months); the yearly loss to follow-up rate was 1.4%. In the HK-ICH, we observed 37 recurrent ICH events during follow-up (annual rate, 2.9%; 95% CI, 2.0%–3.6%) and 25 ischemic strokes (annual rate, 1.6%; 95% CI, 1.1%–2.7%). The large majority of recurrent strokes (96%) occurred later than 3 months from index ICH in both studies (Figure 2).

Hypertension Control at 3 Months After ICH

A total of 1115 survivors of ICH (61%) did not achieve target BP control goal at 3 months. Undertreated hypertension accounted for 755 individuals (68% of uncontrolled hypertension), whereas 360 participants (32% of uncontrolled hypertension) received a diagnosis of treatment-resistant hypertension (Table 2 and Figure 3). We found strong correlations between BP measurements at 3 months and average values during the long-term follow-up (Figure 4). Systolic BP at 3 months after ICH (mean±SD, 141±8) did not significantly differ ($P=0.45$) from the average during long-term follow-up (mean±SD, 140±7). Diastolic BP at 3 months after ICH (mean±SD, 85±6) also did not significantly differ ($P=0.16$) from the average value during long-term follow-up (mean±SD, 84±6). Among 755 participants diagnosed with undertreated hypertension at 3 months, the majority (n=695, 92%) received the same diagnosis at least once more during follow-up. Among 360 participants with treatment-resistant hypertension at 3 months, the vast majority (n=339, 94%) qualified for the same diagnosis at least once more during follow-up. Overall, hypertension control status at 3 months (ie, uncontrolled versus undertreated versus treatment resistant) predicted the corresponding long-term control status with a sensitivity of 0.98 (95% CI, 0.97–0.99), specificity of 0.85 (95% CI, 0.82–0.87), positive predictive value of 0.89 (95% CI, 0.86–0.90), and negative predictive value of 0.98 (95% CI, 0.96–0.99). In univariable analyses, undertreated

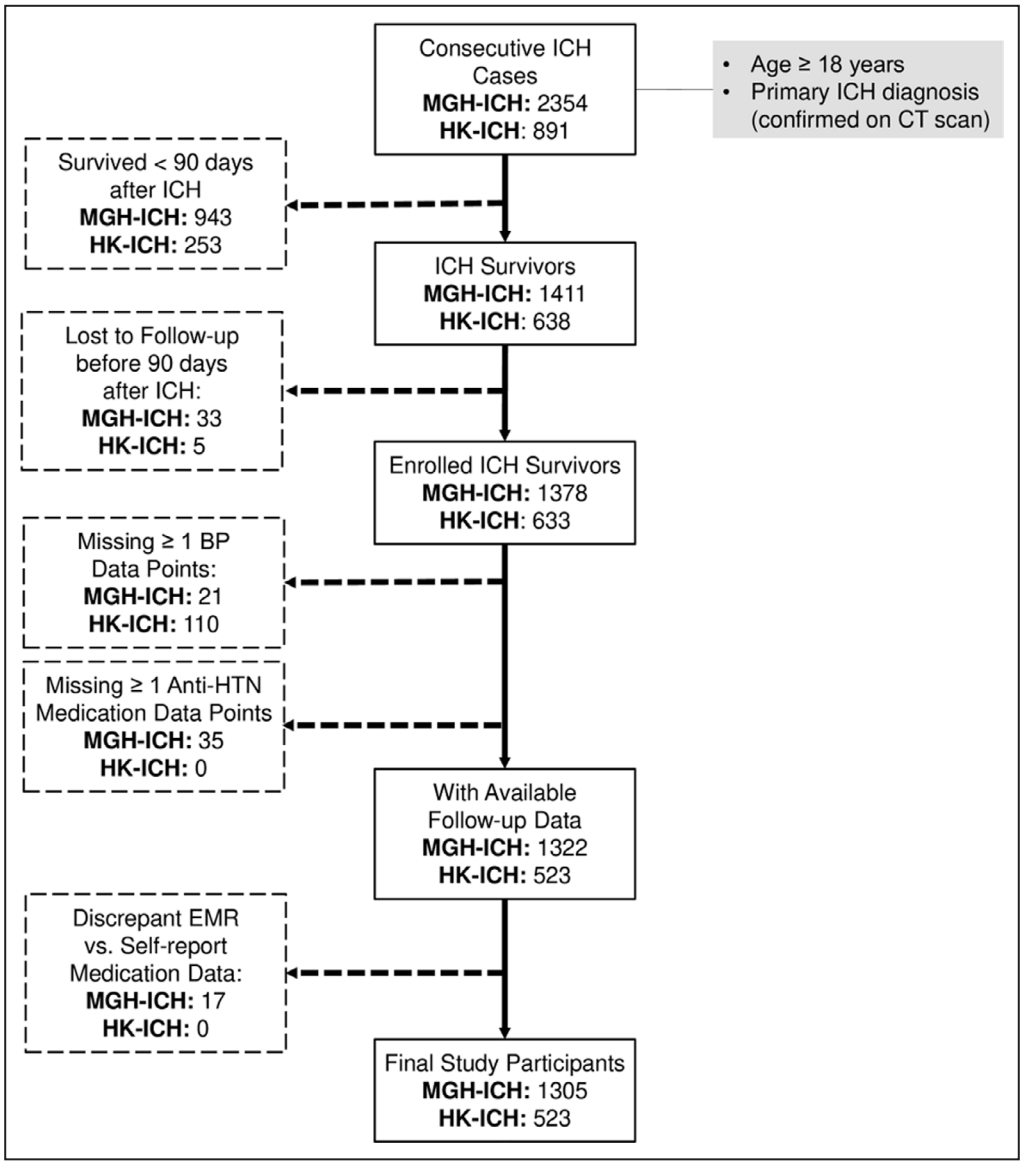

Figure 1. Flow diagram of study inclusion and exclusion criteria.
BP indicates blood pressure; CT, computed tomography; EMR, electronic medical record; HK-ICH, Intracerebral Hemorrhage Study at University of Hong Kong; HTN, hypertension; ICH, intracerebral hemorrhage; and MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital.

and treatment-resistant hypertension at 3 months after ICH were associated with recurrent stroke and mortality risk (all $P<0.05$; Figure 5 and Table S1). In multivariable analyses, both undertreated and treatment resistant hypertension at 3 months were consistently associated with recurrent ICH, ischemic stroke, and mortality (Table 3).

Risk Factors for Uncontrolled and Treatment-Resistant Hypertension

In univariable analyses, history of hypertension before ICH, BP measurements at time of admission for acute ICH, and number of antihypertensive agents prescribed at discharge were all associated with risk of uncontrolled hypertension 3 months after ICH (all $P<0.05$ in both studies). These associations proved independent in multivariable models (Table 4). In joint analyses of the MGH-ICH and HK-ICH data sets, we identified self-reported Black, Hispanic, or Asian race/ethnicity as associated with uncontrolled hypertension at 3 months after ICH (after adjustment for enrollment site). Associations with 3-month treatment-resistant hypertension in univariable analyses included younger age, history of hypertension before ICH, and BP measurements at time of admission for acute ICH (all $P<0.05$ in both studies), all of which were confirmed in multivariable models (Table 4). Self-reported Black and Asian

Table 1. Study Participant Characteristics

Variable	MGH-ICH	HK-ICH	*P* Value
Participants	1305 (100)	523 (100)	…
Demographics			
Age, y*	69.5±12.1	67.3±14.4	0.011
Sex, male*	696 (53)	326 (62)	<0.001
Race/ethnicity*			<0.001
White	1125 (86)	3 (1)	
Black	49 (4)	0 (0)	
Hispanic	59 (5)	0 (0)	
Asian	48 (4)	517 (99)	
More than one race	11 (1)	3 (1)	
Medical history			
Hypertension*	1021 (78)	305 (58)	<0.001
Diabetes mellitus	249 (19)	99 (19)	0.99
Coronary artery disease*	255 (20)	35 (7)	<0.001
Atrial fibrillation*	213 (16)	38 (7)	<0.001
Prior ICH	64 (5)	31 (6)	0.39
Prior ischemic stroke	121 (9)	66 (13)	0.054
Medication use			
Before index ICH			
Antiplatelet agents	250 (19)	107 (20)	0.54
Oral anticoagulation	123 (9)	42 (8)	0.36
Statins*	455 (35)	122 (23)	<0.001
After index ICH			
Antiplatelet agents	153 (12)	72 (14)	0.25
Oral anticoagulation	25 (1)	13 (3)	0.46
Statins	382 (29)	170 (33)	0.19
BP at time of index ICH			
Admission SBP, mmHg*	179±28	183±29	0.008
Admission DBP, mmHg*	95±21	99±19	0.034
Hypertension management			
No. of antihypertension agents			0.11
0	114 (9)	26 (5)	
1	296 (23)	157 (30)	
2	447 (34)	185 (35)	
≥3	448 (34)	155 (30)	
Antihypertension agent classes*			0.021
ACE inhibitor or ARB	811 (62)	265 (51)	
Calcium channel blockers	503 (39)	413 (79)	
Diuretics	295 (23)	31 (6)	
β-Blockers	756 (58)	188 (36)	
α-Blockers	124 (10)	86 (16)	

Data are presented as number (percentage) or mean±SD. *P* values represent the results of univariable comparisons between the MGH-ICH and HK-ICH studies. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; DBP, diastolic blood pressure; HK-ICH, Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; and SBP, systolic blood pressure.

*Statistically significant difference between the MGH-ICH and HK-ICH studies after multiple testing adjustments via the Benjamini-Hochberg method.

race/ethnicity were also independently associated with treatment-resistant hypertension in joint analyses of both studies (after adjustment for enrollment site).

DISCUSSION

In joint analyses of 2 single-center studies of ICH, we confirmed previous findings[3,8–11] that recurrent stroke rates substantially rise beyond 3 months after the initial hemorrhagic stroke event. Because BP control is a potent predictor of recurrent stroke after ICH, we examined rates of controlled hypertension at 3 months and observed that only a minority of patients (39%) were controlled. Furthermore, BP measurements at 3 months were highly correlated with subsequent BP measurements during long-term follow-up. Thus, uncontrolled hypertension at 3 months was associated with increased risk of recurrent stroke and mortality during long-term follow-up.

Our findings support the hypothesis that lowering BP and ensuring adequate hypertension control before this critical time point may result in a substantial decrease in recurrent stroke events. However, we found that most survivors of ICH fail to achieve adequate BP control in the short term. Participants of Black, Hispanic, and Asian self-reported race/ethnicity were at higher risk for uncontrolled hypertension at 3 months from ICH. In turn, short-term uncontrolled hypertension was associated with higher average BP during subsequent long-term follow-up and increased risk for death and recurrent stroke. Of note, nearly two thirds of individuals with inadequate early BP control were not prescribed adequate antihypertensive treatment and frequently remained undertreated for the remainder of follow-up. Overall, our results indicate that reevaluation of hypertension control shortly after ICH represents a clear opportunity to identify critical shortcomings in care, which could be leveraged to ensure appropriate hypertension treatment that might have an enduring impact on long-term outcomes for these patients.

Black, Hispanic, and Asian self-reported race/ethnicity conferred higher risk for both undertreated and

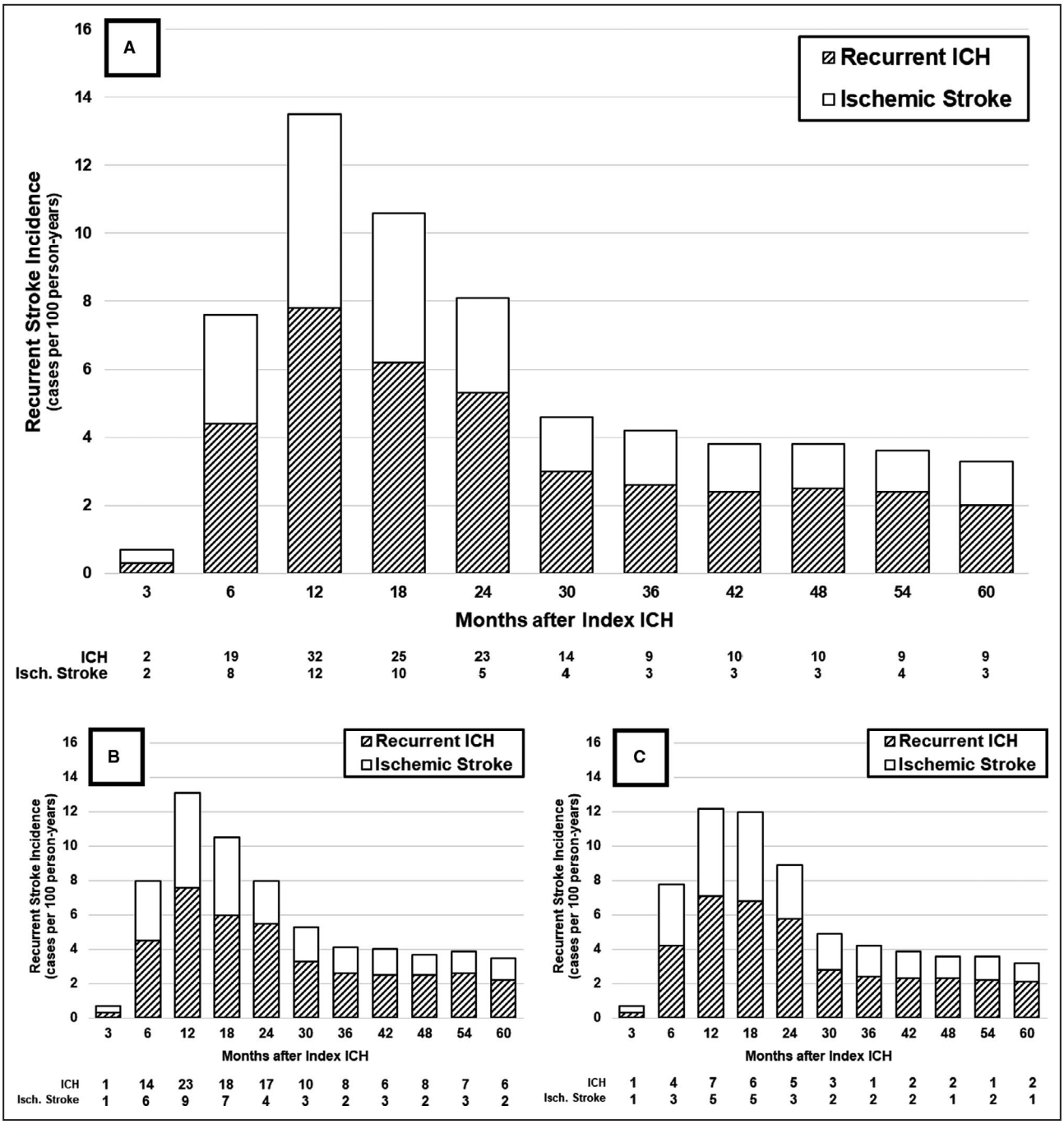

Figure 2. Recurrent stroke risk after ICH.
Incidence of recurrent ICH and ischemic stroke after index ICH in cases per 100-person years in both studies combined (**A**) and separately in the Intracerebral Hemorrhage Study at Massachusetts General Hospital (**B**) and the Intracerebral Hemorrhage Study at University of Hong Kong (**C**). Incidence rates were calculated as number of recurrent events (recurrent ICH or ischemic stroke) occurring between follow-up time points (ie, 6-month time periods, except 3 months between index ICH and first follow-up) over the sum of the follow-up period for all individuals remaining in the study during that time period, and finally normalized to 100 person-years. Number of ICH and ischemic stroke events are presented below each graph. ICH indicates intracerebral hemorrhage; and Isch., ischemic.

resistant hypertension. These findings expand on a previous joint analysis from the MGH-ICH and the ERICH (Ethnic/Racial Variations of Intracerebral Hemorrhage) study that found Black and Hispanic survivors of ICH have higher average BP after ICH.[6] The ERICH study investigators separately reported that untreated hypertension conferred greater risk for first-ever ICH among Black and Hispanic individuals.[20] Because we used

Table 2. Study Participants and Hypertension Treatment Status at 3 Months After ICH

Variable	Hypertension Treatment Status					
	MGH-ICH			HK-ICH		
	Controlled	Undertreated	Resistant	Controlled	Undertreated	Resistant
Participants	574	489	242	139	266	118
Demographics						
Age, y	68.8±12.7	71.0±12.3*	67.8±12.6	65.8±15.0	68.9±13.6*	61.5±14.2†
Sex, male	310 (54)	245 (50)	141 (58)	93 (67)	145 (55)	88 (75)
Race/ethnicity						
White	493 (86)	440 (90)*	192 (79)†	0 (0)	2 (1)	1 (1)
Black	25 (4)	9 (2)	15 (6)	0 (0)	0 (0)	0 (0)
Hispanic	31 (5)	10 (2)	18 (7)	0 (0)	0 (0)	0 (0)
Asian	20 (3)	13 (3)	15 (6)	138 (99)	263 (99)	116 (98)
More than one race	5 (1)	4 (1)	2 (1)	1 (1)	1 (1)	1 (1)
Medical history						
Hypertension	436 (76)	350 (72)*	235 (97)†	84 (60)	145 (55)*	76 (64)†
Diabetes mellitus	103 (18)	76 (16)	70 (29)	30 (22)	46 (17)	23 (20)
Coronary artery disease	109 (19)	83 (17)	63 (26)	11 (8)	8 (3)	16 (14)
Atrial fibrillation	103 (18)	51 (10)	59 (24)	14 (10)	26 (10)	8 (7)
Prior ICH	35 (6)	17 (3)	12 (5)	8 (6)	17 (6)	6 (5)
Prior ischemic stroke	63 (11)	29 (6)	29 (12)	23 (17)	35 (13)	8 (7)
Medication use						
Before index ICH						
Antiplatelet agents	98 (17)	104 (21)	48 (20)	21 (15)	62 (23)	24 (20)
Oral anticoagulation	63 (11)	39 (8)	21 (9)	13 (9)	21 (8)	8 (7)
Statins	183 (32)	187 (38)	85 (35)	27 (19)	69 (26)	26 (22)
After index ICH						
Antiplatelet agents	58 (10)	68 (14)	27 (11)	15 (11)	42 (16)	15 (13)
Oral anticoagulation	15 (3)	6 (1)	4 (2)	4 (3)	7 (3)	2 (2)
Statins	159 (28)	152 (31)	71 (29)	30 (22)	96 (36)	44 (37)
BP at time of index ICH						
Admission SBP, mmHg	174±33	181±22*	190±16†	175±29	189±32*	197±31†
Admission DBP, mmHg	93±23	95±22	98±19†	97±18	108±24*	110±26†
Hypertension management						
No. of antihypertension agents						
0	35 (6)	79 (16)*	0 (0.0)	5 (4)	21 (8)*	0 (0)
1	115 (20)	181 (37)*	0 (0.0)	42 (30)	115 (43)*	0 (0)
3	218 (38)	229 (47)*	0 (0.0)	55 (40)	130 (49)*	0 (0)
≥3	206 (36)	0 (0)*	242 (100)†	37 (27)	0 (0)*	118 (100)†
Antihypertension agent classes						
ACE inhibitor or ARB	373 (65)	249 (51)	189 (78)	72 (52)	98 (37)	95 (81)
Calcium channel blockers	218 (38)	92 (19)	193 (80)	108 (78)	192 (72)	113 (96)
Diuretics	126 (22)	46 (9)	123 (51)	9 (7)	7 (3)	15 (13)
β-Blockers	321 (56)	240 (49)	195 (81)	48 (35)	51 (19)	89 (75)
α-Blockers	53 (9)	29 (6)	42 (17)	21 (15)	21 (8)	44 (37)

Data are presented as number, number (percentage), or mean±SD. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; DBP, diastolic blood pressure; HK-ICH, Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; and SBP, systolic blood pressure.

*Statistically significant difference between controlled hypertension (reference) and undertreated hypertension after multiple testing adjustments via the Benjamini-Hochberg method.

†Statistically significant difference between controlled hypertension (reference) and resistant hypertension after multiple testing adjustments via the Benjamini-Hochberg method.

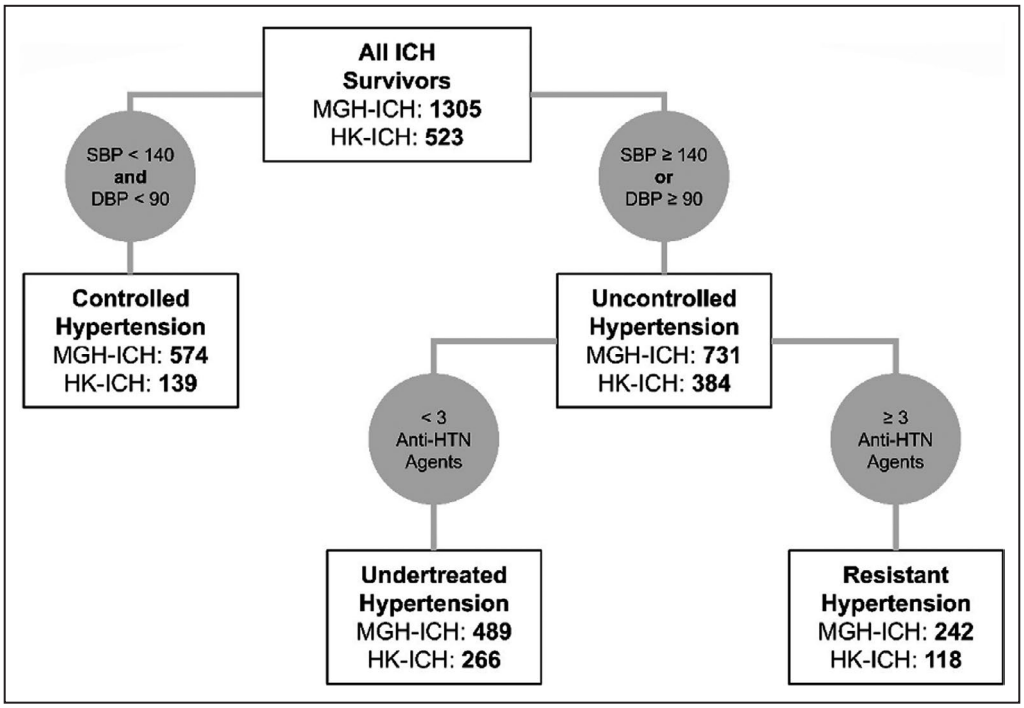

Figure 3. Hypertension control 3 months after ICH.
Anti-HTN indicates antihypertensive; DBP, diastolic blood pressure; HK-ICH, Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; and SBP, systolic blood pressure.

self-reported race/ethnicity, our findings likely reflect a complex combination of cultural and socioeconomic factors leading to disparities in post-ICH care. Taken in the context of existing evidence pointing to racial/ethnic disparities in ICH care,[6,21,22] our present results place control of hypertension among minority survivors of ICH as a priority for future public health policies and research efforts.

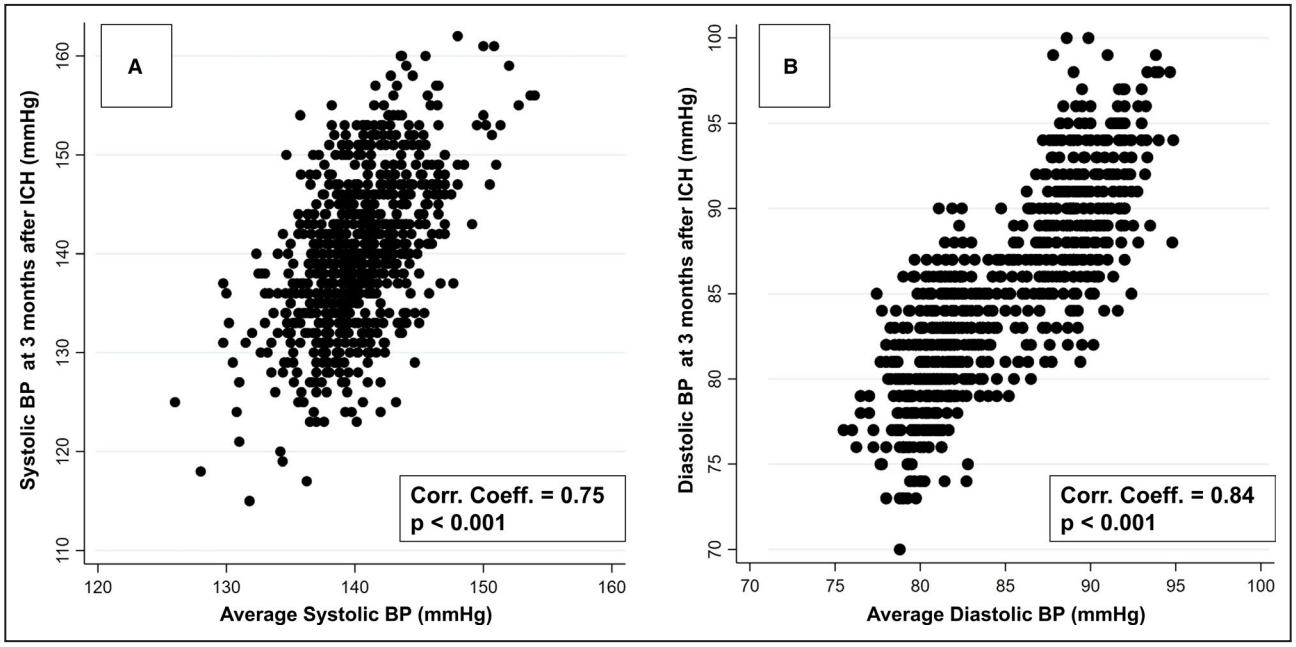

Figure 4. Correlation between BP measured 3 months after ICH and average BP during long-term follow-up.
Correlation scatter plots for systolic BP (**A**) and diastolic BP (**B**) at 3 months after ICH compared with the average values during overall study follow-up. BP indicates blood pressure; Corr. Coeff., correlation coefficient; and ICH, intracerebral hemorrhage.

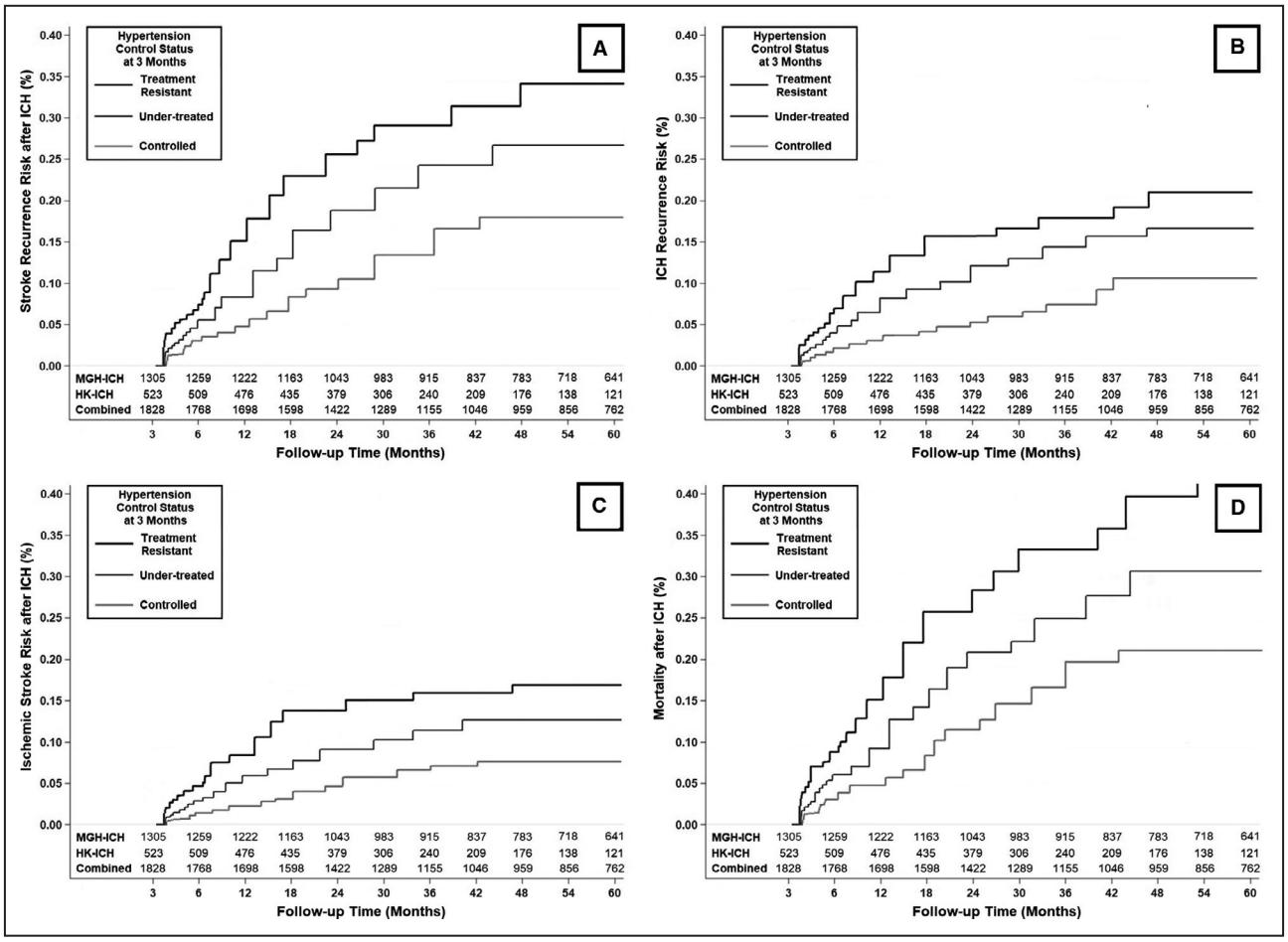

Figure 5. Hypertension control at 3 months and risk of recurrent stroke after ICH.
Cumulative incidence function curves for stroke recurrence risk (all cause; **A**), recurrent ICH (**B**), ischemic stroke (**C**), and mortality (**D**) based on hypertension control status (controlled, undertreated, or treatment resistant) at 3 months from index ICH. All survival analyses have 3 months after ICH as time zero. Sample size at each time point for the participating studies and the combined study sample during follow-up is listed above the horizontal axis. HK-ICH indicates Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; and n, sample size.

We also found that systolic and diastolic BP at time of acute ICH were associated with undertreated and treatment-resistant hypertension at 3 months. These findings suggest a link between severity of the acute, ICH-related hypertensive response and more chronic hypertension. In some patients, a more severe acute hypertensive response may reflect chronically untreated or undertreated hypertension[23] as well as a genetic predisposition to elevated BP.[24] Our findings suggest that patients with ICH initially presenting with severe BP elevation should be monitored closely for uncontrolled hypertension long term.

Our approach has several limitations. First and foremost, hypertension treatment in both studies was determined by treating providers in an unblinded fashion. Second, both enrollment sites are tertiary care centers with expertise in ICH care, both acute and long term. This is likely to have introduced severity bias in our analyses (severe ICH cases with harder-to-control BP may be more likely to receive care at expert centers). Third, we relied on office-based BP measurements as exposure of interest, potentially overestimating the prevalence of uncontrolled hypertension attributed to white coat hypertension.[25] However, the consistent associations between BP measurements at 3 months and recurrent stroke support the hypothesis that our methodology focused (at least partially) on a "true" biological link between short-term hypertension control and post-ICH outcomes.[26] Fourth, we use a currently outdated definition of hypertension[15]; however, said BP control goal (ie, systolic BP <140 mm Hg and diastolic BP <90 mm Hg) was recommended by guidelines for the majority of the studies' enrollment periods.[13,27] Fifth, most patients of Asian race/ethnicity were enrolled at 1 site (HK-ICH). However, Asian participants enrolled

Table 3. Hypertension Control at 3 Months After ICH and Risk of Recurrent Stroke and Death

Variable	MGH-ICH			HK-ICH			Combined		
	SHR	95% CI	*P* Value	SHR	95% CI	*P* Value	SHR	95% CI	*P* Value
Recurrent stroke (ICH or ischemic stroke)									
Controlled hypertension	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Undertreated hypertension	2.65	1.19–5.89	0.027*	2.41	1.15–5.05	0.027*	2.53	1.32–4.84	0.009*
Treatment-resistant hypertension	2.88	1.32–6.27	0.014*	2.59	1.12–5.99	0.034*	2.82	1.37–5.78	0.008*
Recurrent ICH									
Controlled hypertension	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Undertreated hypertension	2.94	1.27–6.79	0.018*	2.38	1.24–4.59	0.018*	2.74	1.62–4.63	0.002*
Treatment-resistant hypertension	3.48	1.46–8.32	0.009*	2.79	1.18–6.61	0.029*	3.04	1.97–4.70	<0.001*
Ischemic stroke									
Controlled hypertension	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Undertreated hypertension	2.38	1.07–5.28	0.044*	2.50	1.00–6.21	0.074	2.47	1.46–4.18	0.005*
Treatment-resistant hypertension	2.56	1.14–5.77	0.032*	2.63	0.95–7.31	0.088	2.58	1.23–5.42	0.023*
Mortality									
Controlled hypertension	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Undertreated hypertension	3.85	1.79–8.30	0.011*	3.39	1.56–7.39	0.008*	3.45	1.94–6.12	<0.001*
Treatment-resistant hypertension	4.41	2.00–9.75	<0.001*	3.78	1.70–8.39	0.004*	4.12	2.28–7.46	<0.001*

Multivariable analyses of the associations between hypertension control status at 3 months after ICH and outcomes of interest. All analyses were adjusted, for age, sex, race/ethnicity, enrollment site, enrollment year, and past medical history of hypertension. Death was considered a competing risk in all recurrent stroke models. HK-ICH indicates Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; and SHR, subhazard ratio.

* Statistically significant result after multiple testing adjustments via the Benjamini-Hochberg method.

Table 4. Risk Factors for Uncontrolled and Treatment-Resistant Hypertension at 3 Months After ICH

Variable	MGH-ICH			HK-ICH			Combined		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Uncontrolled vs. controlled hypertension									
History of pre-ICH hypertension	1.55	1.04–2.34	0.015*	1.46	1.06–2.01	0.031*	1.49	1.11–1.88	0.004*
Race/ethnicity†									
White	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Black	1.37	1.05–1.78	0.029*	…	…	…	1.37	1.05–1.78	0.029*
Hispanic	1.22	1.02–1.45	0.041*	…	…	…	1.22	1.02–1.45	0.041*
Asian	1.51	0.75–3.04	0.29	…	…	…	1.42	1.08–1.06	0.026*
Admission SBP (10 mm Hg increments)	1.19	1.02–1.39	0.039*	1.12	1.00–1.26	0.068	1.15	1.03–1.28	0.011*
Admission DBP (10 mm Hg increments)	1.14	0.98–1.32	0.097	1.21	1.01–1.45	0.059	1.17	1.03–1.30	0.009*
No. of antihypertension agents									
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1	0.64	0.34–1.21	0.22	0.80	0.52–1.22	0.36	0.74	0.46–1.00	0.085
2	0.46	0.25–0.84	0.022*	0.53	0.28–1.00	0.084	0.49	0.26–0.72	0.004*
≥3	0.52	0.28–0.95	0.043*	0.62	0.40–0.96	0.042*	0.58	0.36–0.79	0.003*
Treatment-resistant vs. nonresistant hypertension									
Age (per 10-y increase)	0.82	0.72–0.93	0.003*	0.73	0.63–0.85	<0.001*	0.78	0.70–0.87	<0.001*
History of pre-ICH hypertension	1.32	1.03–1.69	0.038*	1.39	0.91–2.13	0.16	1.34	1.06–1.69	0.023*
Race/ethnicity†									
White	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Black	1.75	1.18–2.63	0.009*	…	…	…	1.75	1.18–2.63	0.009*
Hispanic	1.28	0.96–1.70	0.11	…	…	…	1.29	0.96–1.70	0.11
Asian	1.37	0.83–2.27	0.26	…	…	…	1.62	1.13–2.32	0.017*
Admission SBP (10 mm Hg increments)	1.13	1.05–1.21	0.003*	1.15	1.01–1.31	0.041*	1.13	1.06–1.21	<0.001*
Admission DBP (10 mm Hg increments)	1.21	1.09–1.34	<0.001*	1.16	1.00–1.34	0.056	1.19	1.09–1.29	<0.001*

DBP indicates diastolic blood pressure; HK-ICH, Intracerebral Hemorrhage Study at University of Hong Kong; ICH, intracerebral hemorrhage; MGH-ICH, Intracerebral Hemorrhage Study at Massachusetts General Hospital; OR, odds ratio; and SBP, systolic blood pressure.

* Statistically significant result after multiple testing adjustments via the Benjamini-Hochberg method.

†Because of skewed distributions in race/ethnicity, associations with hypertension control were not tested in the HK-ICH. Multivariable analyses of the predictors of hypertension control status at 3 months after ICH. All analyses also included adjustment for sex, enrollment site, and enrollment year.

in the MGH-ICH showed nonsignificant associations with hypertension outcomes of highly similar magnitude to those enrolled in the HK-ICH. We also could not control for some competing covariates influencing risk of recurrent stroke (eg, social determinants of health, smoking, physical activity, diet) that were not part of the originally collected data. Finally, we did not have reliable measurements of treatment adherence, thus affecting our estimates of resistant hypertension.

Our study also displays several strengths. By joint analysis of data from 2 large longitudinal studies with highly compatible recruitment and follow-up methodologies, we managed to include a large number of survivors of primary ICH, a highly lethal cerebrovascular condition.[2] Both studies employed dedicated and consistent methodologies for BP capture during follow-up, which allowed for jointly planned analyses yielding highly concordant findings. Considering the disparity between participating studies in terms of geographical location, health care delivery system, racial and ethnic demographics, and sociocultural factors, the remarkable consistency of our primary findings suggest good generalizability to survivors of ICH at large. Finally, we were able to correlate BP measurements from participants to highly relevant clinical end points during follow-up, emphasizing the immediate, real-world relevance of our findings to ICH clinical care.

In summary, we demonstrated that most survivors of ICH have uncontrolled hypertension at 3 months, with undertreatment accounting for the majority of cases. Undertreated and treatment-resistant hypertension were more prevalent among non-White survivors of ICH and those with a more severe acute hypertensive response. Comprehensive evaluation and optimization of hypertension management at 3 months after ICH may represent a unique opportunity to improve quality of care for survivors of hemorrhagic stroke.

ARTICLE INFORMATION

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Supplementary Material

Table S1

REFERENCES

1. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation*. 2019;139:e56–e528. DOI: 10.1161/CIR.0000000000000659.
2. Poon MT, Fonville AF, Al-Shahi SR. Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2014;85:660–667. DOI: 10.1136/jnnp-2013-306476.
3. Biffi A, Anderson CD, Battey TW, Ayres AM, Greenberg SM, Viswanathan A, Rosand J. Association between blood pressure control and risk of recurrent intracerebral hemorrhage. *JAMA*. 2015;314:904–912. DOI: 10.1001/jama.2015.10082.
4. Huhtakangas J, Lopponen P, Tetri S, Juvela S, Saloheimo P, Bode MK, Hillbom M. Predictors for recurrent primary intracerebral hemorrhage: a retrospective population-based study. *Stroke*. 2013;44:585–590. DOI: 10.1161/STROKEAHA.112.671230.
5. Hemphill JC III, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, Fung GL, Goldstein JN, Macdonald RL, Mitchell PH, et al.; American Heart Association Stroke C, Council on C, Stroke N and Council on Clinical C. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:2032–2060. DOI: 10.1161/STR.0000000000000069.
6. Rodriguez-Torres A, Murphy M, Kourkoulis C, Schwab K, Ayres AM, Moomaw CJ, Young Kwon S, Berthaud JV, Gurol ME, Greenberg SM, et al. Hypertension and intracerebral hemorrhage recurrence among white, black, and Hispanic individuals. *Neurology*. 2018;91:e37–e44. DOI: 10.1212/WNL.0000000000005729.
7. Teo KC, Lau GKK, Mak RHY, Leung HY, Chang RSK, Tse MY, Lee R, Leung GKK, Ho SL, Cheung RTF, et al. Antiplatelet resumption after antiplatelet-related intracerebral hemorrhage: a retrospective hospital-based study. *World Neurosurg*. 2017;106:85–91. DOI: 10.1016/j.wneu.2017.06.015.
8. Bae H, Jeong D, Doh J, Lee K, Yun I, Byun B. Recurrence of bleeding in patients with hypertensive intracerebral hemorrhage. *Cerebrovasc Dis*. 1999;9:102–108. DOI: 10.1159/000015906.
9. Chen ST, Chiang CY, Hsu CY, Lee TH, Tang LM. Recurrent hypertensive intracerebral hemorrhage. *Acta Neurol Scand*. 1995;91:128–132. DOI: 10.1111/j.1600-0404.1995.tb00418.x.
10. Gonzalez-Duarte A, Cantu C, Ruiz-Sandoval JL, Barinagarrementeria F. Recurrent primary cerebral hemorrhage: frequency, mechanisms, and prognosis. *Stroke*. 1998;29:1802–1805. DOI: 10.1161/01.STR.29.9.1802.
11. Hill MD, Silver FL, Austin PC, Tu JV. Rate of stroke recurrence in patients with primary intracerebral hemorrhage. *Stroke*. 2000;31:123–127. DOI: 10.1161/01.STR.31.1.123.

12. Zahuranec DB, Wing JJ, Edwards DF, Menon RS, Fernandez SJ, Burgess RE, Sobotka IA, German L, Trouth AJ, Shara NM, et al. Poor long-term blood pressure control after intracerebral hemorrhage. *Stroke*. 2012;43:2580–2585. DOI: 10.1161/STROKEAHA.112.663047.
13. Steiner T, Salman R-S, Beer R, Christensen H, Cordonnier C, Csiba L, Forsting M, Harnof S, Klijn CJM, Krieger D, et al. European Stroke Organisation (ESO) guidelines for the management of spontaneous intracerebral hemorrhage. *Int J Stroke*. 2014;9:840–855. DOI: 10.1111/ijs.12309.
14. Lim MK, Ha SCN, Luk KH, Yip WK, Tsang CSH, Wong MCS. Update on the Hong Kong reference framework for hypertension care for adults in primary care settings-review of evidence on the definition of high blood pressure and goal of therapy. *Hong Kong Med J*. 2019;25:64–67. DOI: 10.12809/hkmj187701.
15. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *Hypertension*. 2018;71:e13–e115. DOI: 10.1161/HYP.0000000000000065.
16. Hong D, Stradling D, Dastur CK, Akbari Y, Groysman L, Al-Khoury L, Chen J, Small SL, Yu W. Resistant hypertension after hypertensive intracerebral hemorrhage is associated with more medical interventions and longer hospital stays without affecting outcome. *Front Neurol*. 2017;8:184. DOI: 10.3389/fneur.2017.00184.
17. Schelleman H, Klungel OH, Kromhout D, de Boer A, Stricker BH, Verschuren WM. Prevalence and determinants of undertreatment of hypertension in the Netherlands. *J Hum Hypertens*. 2004;18:317–324. DOI: 10.1038/sj.jhh.1001672.
18. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. *Circulation*. 2016;133:601–609. DOI: 10.1161/CIRCULATIONAHA.115.017719.
19. Keselman HJ, Cribbie R, Holland B. Controlling the rate of Type I error over a large set of statistical tests. *Br J Math Stat Psychol*. 2002;55:27–39. DOI: 10.1348/000711002159680.
20. Walsh KB, Woo D, Sekar P, Osborne J, Moomaw CJ, Langefeld CD, Adeoye O. Untreated hypertension: a powerful risk factor for lobar and nonlobar intracerebral hemorrhage in whites, blacks, and hispanics. *Circulation*. 2016;134:1444–1452. DOI: 10.1161/CIRCULATIONAHA.116.024073.
21. Leasure AC, King ZA, Torres-Lopez V, Murthy SB, Kamel H, Shoamanesh A, Al-Shahi Salman R, Rosand J, Ziai WC, Hanley DF, et al. Racial/ethnic disparities in the risk of intracerebral hemorrhage recurrence. *Neurology*. 2020;94:e314–e322. DOI: 10.1212/WNL.0000000000008737.
22. Cruz-Flores S, Rodriguez GJ, Chaudhry MRA, Qureshi IA, Qureshi MA, Piriyawat P, Vellipuram AR, Khatri R, Kassar D, Maud A. Racial/ethnic disparities in hospital utilization in intracerebral hemorrhage. *Int J Stroke*. 2019;14:686–695. DOI: 10.1177/1747493019835335.
23. Alqadri SL, Sreenivasan V, Qureshi AI. Acute hypertensive response management in patients with acute stroke. *Curr Cardiol Rep*. 2013;15:426. DOI: 10.1007/s11886-013-0426-7.
24. Falcone GJ, Biffi A, Devan WJ, Brouwers HB, Anderson CD, Valant V, Ayres AM, Schwab K, Rost NS, Goldstein JN, et al. Burden of blood pressure-related alleles is associated with larger hematoma volume and worse outcome in intracerebral hemorrhage. *Stroke*. 2013;44:321–326. DOI: 10.1161/STROKEAHA.112.675181.
25. Abolbashari M, White coat hypertension and cardiovascular diseases: innocent or guilty. *Curr Cardiol Rep*. 2018;20:25. DOI: 10.1007/s11886-018-0964-0.
26. Li W, Jin C, Vaidya A, Wu Y, Rexrode K, Zheng X, Gurol ME, Ma C, Wu S, Gao X. Blood pressure trajectories and the risk of intracerebral hemorrhage and cerebral infarction: a prospective study. *Hypertension*. 2017;70:508–514. DOI: 10.1161/HYPERTENSIONAHA.117.09479.
27. Morgenstern LB, Hemphill JC III, Anderson C, Becker K, Broderick JP, Connolly ES Jr, Greenberg SM, Huang JN, Macdonald RL, Messé SR, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2010;41:2108–2129. DOI: 10.1161/STR.0b013e3181ec611b.

SUPPLEMENTAL MATERIAL

Table S1. Univariable Analyses of Hypertension Control at 3 months after Intracerebral Hemorrhage and Risk of Recurrent Stroke and Death.

Outcome	Variable	MGH-ICH	HK-ICH	Combined
		p	p	p
Recurrent Stroke (ICH or Ischemic Stroke)	Controlled Hypertension	Ref.	Ref.	Ref.
	Undertreated Hypertension	**0.018**	**0.021**	**0.007**
	Treatment-Resistant Hypertension	**0.019**	**0.042**	**0.011**
Recurrent ICH	Controlled Hypertension	Ref.	Ref.	Ref.
	Undertreated Hypertension	**0.008**	**0.011**	**0.002**
	Treatment-Resistant Hypertension	**0.004**	**0.025**	**<0.001**
Ischemic Stroke	Controlled Hypertension	Ref.	Ref.	Ref.
	Undertreated Hypertension	**0.039**	**0.035**	**0.002**
	Treatment-Resistant Hypertension	**0.028**	0.065	**0.021**
Mortality	Controlled Hypertension	Ref.	Ref.	Ref.
	Undertreated Hypertension	**0.021**	**0.003**	**<0.001**
	Treatment-Resistant Hypertension	**<0.001**	**<0.001**	**<0.001**

Univariable (Log-rank test) analyses of the associations between hypertension control status at 3 months after ICH and outcomes of interest. HK-ICH = Intracerebral Hemorrhage Study conducted at University of Hong Kong, ICH = Intracerebral Hemorrhage, MGH-ICH= Intracerebral Hemorrhage Study conducted at Massachusetts General Hospital.