ORIGINAL RESEARCH

Lower Blood Pressure Is Not Associated With Decreased Arterial Spin Labeling Estimates of Perfusion in Intracerebral Hemorrhage

Ana C. Klahr, PhD; Jayme C. Kosior, PhD; Dariush Dowlatshahi, MD, PhD; Brian H. Buck, MD, MSc; Christian Beaulieu, PhD; Laura C. Gioia, MD, MSc; Hayrapet Kalashyan, MD; Alan H. Wilman, PhD; Thomas Jeerakathil, MD, MSc; Derek J. Emery, MD, MSc; Ashfaq Shuaib, MD; Kenneth S. Butcher, MD, PhD

***Background*—**Subacute ischemic lesions in intracerebral hemorrhage (ICH) have been hypothesized to result from hypoperfusion. Although studies of cerebral blood flow (CBF) indicate modest hypoperfusion in ICH, these investigations have been limited to early time points. Arterial spin labeling (ASL), a magnetic resonance imaging technique, can be used to measure CBF without a contrast agent. We assessed CBF in patients with ICH using ASL and tested the hypothesis that CBF is related to systolic blood pressure (SBP).

***Methods and Results*—**In this cross-sectional study, patients with ICH were assessed with ASL at 48 hours, 7 days, and/or 30 days after onset. Relative CBF (rCBF; ratio of ipsilateral/contralateral perfusion) was measured in the perihematomal regions, hemispheres, border zones, and the perilesional area in patients with diffusion-weighted imaging hyperintensities. Twenty-patients (65% men; mean±SD age, 68.5±12.7 years) underwent imaging with ASL at 48 hours (N=12), day 7 (N=6), and day 30 (N=11). Median (interquartile range) hematoma volume was 13.1 (6.3–19.3) mL. Mean±SD baseline SBP was 185.4±25.5 mm Hg. Mean perihematomal rCBF was 0.9±0.2 at 48 hours at all time points. Baseline SBP and other SBP measurements were not associated with a decrease in rCBF in any of the regions of interest ($P \geq 0.111$). rCBF did not differ among time points in any of the regions of interest ($P \geq 0.097$). Mean perilesional rCBF was 1.04±0.65 and was unrelated to baseline SBP ($P=0.105$).

***Conclusions*—**ASL can be used to measure rCBF in patients with acute and subacute ICH. Perihematomal CBF was not associated with SBP changes at any time point.

***Clinical Trial Registration*—**URL: http://www.clinicaltrials.gov. Unique identifier: NCT00963976. **(*J Am Heart Assoc*. 2019;8: e010904. DOI: 10.1161/JAHA.118.010904.)**

Key Words: arterial spin labeling • blood pressure • intracerebral hemorrhage • magnetic resonance imaging

Management of acute hypertension in patients with an intracerebral hemorrhage (ICH) remains an area of clinical equipoise.[1] The most recent large randomized clinical trial demonstrated a trend to worse outcomes when systolic blood pressure (SBP) was aggressively lowered (<140 mm Hg).[1–3] Several magnetic resonance imaging (MRI) studies have demonstrated subacute ischemic lesions in patients with ICH. One of the hypothesized causes for both these ischemic lesions and worse outcomes after aggressive SBP lowering is impairment of cerebral perfusion.

Multiple studies of cerebral blood flow (CBF) in patients with ICH have demonstrated that there is a modest degree of regional hypoperfusion.[4–7] In addition, one randomized study demonstrated that the magnitude of hypoperfusion was unaffected by SBP reduction.[8,9] All of these studies of CBF have been limited to single assessments of perfusion at only one time point relatively early after symptom onset. Serial CBF measurements were not obtained because of the safety concerns associated with the contrast agents used to obtain perfusion measurements in these studies.

Arterial spin labeling (ASL) is an MRI technique that can be used to measure relative CBF (rCBF) without the need for a

From the Division of Neurology (A.C.K., J.C.K., B.H.B., L.C.G., H.K., T.J., A.S., K.S.B.), and Departments of Biomedical Engineering (C.B., A.H.W.) and Radiology and Diagnostic Imaging (D.J.E.), University of Alberta, Edmonton, Alberta, Canada; Division of Neurology, University of Ottawa, Ottawa, Ontario, Canada (D.D.); and Prince of Wales Clinical School, University of New South Wales, Sydney, New South Wales, Australia (K.S.B.)

Accompanying Tables S1 through S3 and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.010904

Correspondence to: Kenneth S. Butcher, MD, PhD, Prince of Wales Hospital, Edmund Blacket Bldg, First Floor South Wing, Randwick, New South Wales 2031, Australia. E-mail: ken.butcher@unsw.edu.au

Received January 7, 2019; accepted March 22, 2019.

Clinical Perspective

What Is New?

- Using arterial spin labeling (a magnetic resonance technique that does not require contrast) to measure cerebral blood flow in patients with acute and subacute intracerebral hemorrhage, perihematomal cerebral blood flow was not associated with systolic blood pressure changes at any time point.

What Are the Clinical Implications?

- Our results add to the body of literature showing that subacute ischemic lesions occurring in patients with an intracerebral hemorrhage are not related to blood pressure, which is relevant to antihypertensive therapy in this patient population.

gadolinium-based contrast agent.[10–12] We used ASL to measure CBF in patients with acute and subacute ICH. We tested the hypothesis that ASL measures of CBF are linearly related to SBP.

Materials and Methods

Patients

All patients were prospectively recruited into the study, as part of the ongoing ICH ADAPT II (Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial II; ***Clinical Trial Registration***—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00963976). The data will be added to The Virtual International Stroke Trials Archive (VISTA) ICH database once the ICH ADAPT II is completed. The data that support the findings of this study are available from the corresponding author on reasonable request. Patient inclusion/exclusion criteria for this trial have been previously published.[13] Briefly, this is a randomized evaluation of SBP reduction targets on the frequency of diffusion-weighted imaging (DWI) lesions in patients with ICH. Patients aged ≥18 years, presenting with computed tomography–confirmed acute primary ICH within 6 hours of symptom onset and baseline SBP >180 mm Hg, were eligible. Exclusion criteria included evidence of secondary ICH, planned surgical resection, and contraindications to antihypertensive therapy or MRI. Patients were randomly assigned to SBP <140 or <180 mm Hg. BP was monitored using labetalol, enalapril, and/or hydralazine. Informed consent was obtained in all cases. The trial was approved by the human research ethics board at the University of Alberta (Edmonton, Alberta, Canada). Analysis of the ASL data, obtained as part of this trial, was completed by investigators (A.K. and K.B.) who remain blinded to the randomized SBP treatment target.

Clinical Assessment

Baseline demographic information and medical history were collected as part of the trial case report form. The National Institutes of Health Stroke Scale score was obtained at time of admission. SBP was recorded during the first 24 hours.

Imaging Acquisition Protocol

Noncontrast computed tomographic scans (Siemens Somatom, Erlangen, Germany) were acquired within 6 and 24 hours after symptom onset. The computed tomography consisted of 5-mm slices, with no gap (120 peak kV, 300 mA per slice) through the entire brain (18–20 slices with a 512×512 matrix). MRI was performed on a 3.0-T instrument (Siemens Magnetom Prisma, Erlangen, Germany) with a 64-element phased array at 48 hours, day 7, and/or day 30 from symptom onset. The MRI protocol included pulsed ASL (voxel size, 2 mm, isotropic: repetition time, 4600 ms; echo time, 18.8 ms; voxel size, 3 mm: repetition time, 3500 ms; echo time, 16.2 ms), susceptibility-weighted

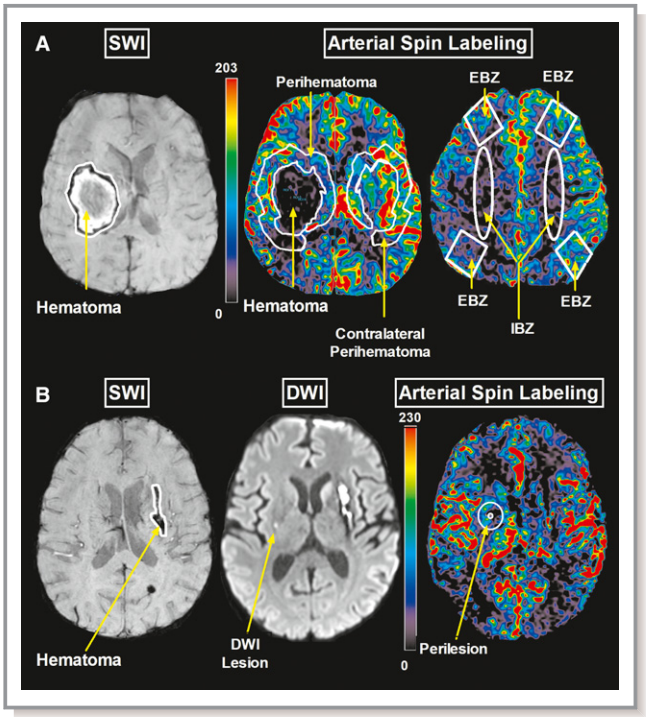

Figure 1. **A**, The hematoma was delineated using susceptibility-weighted images (SWIs; **left**), which were then coregistered with arterial spin labeling (ASL) scans (**right**). Regions of interest included perihematoma, hemisphere, internal and external border zones (IBZs and EBZs, respectively), and the contralateral homologous regions. **B**, Ischemic lesions were identified with diffusion-weighted imaging (DWI) and coregistered with ASL scans. The area surrounding the ischemic lesion was compared with a homologous contralesional area.

Table 1. Baseline Patient Characteristics

Characteristics	Values
Age, mean±SD, y	68.50±12.72
Sex, % men	65
NIHSS score, median (quartile 1–quartile 3)	12 (9–16)
Acute hematoma volume, median (quartile 1–quartile 3), mL	13.1 (6.3–19.3)
Hematoma volume at 24 h, median (quartile 1–quartile 3), mL	15.6 (7.3–35.5)
Edema at 24 h (5–23 HU), median (quartile 1–quartile 3), mL	2.5 (1.2–9.3)
SBP, mean±SD, mm Hg	185.4±25.5
Hematoma location	
Cortical	4
Subcortical	15
Cerebellum	1

HU indicates Hounsfield unit; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

imaging (voxel size, $0.7\times0.7\times2.0$ mm^3: repetition time, 28.0 ms; echo time, 20.00 ms), and DWI (voxel size, $0.7\times0.7\times1.5$ mm^3: repetition time, 4890 ms; echo time, 51.0 ms; b values of 1000 s/mm^2; 20 gradient directions). The acquisition used 3-dimensional Turbo gradient-spin-echo (TGSE) Flow-sensitive Alternating Inversion Recovery Quantitative Imaging of Perfusion Using a Single Subtraction II (FAIR QUIPSS) tagging with bolus duration of 700 ms and inversion time of 1990 ms.

Image Analysis

Planimetric assessment of acute and 24-hour computed tomographic hematoma volumes was performed using Quantomo software, a semiautomated, threshold-based, seed-growing algorithm.[14] Perihematomal edema and susceptibility-weighted imaging hematoma volumes were calculated with the Analyze 11.0 software package (Biomedical Imaging Resource, Mayo Clinic).

ASL data were used to generate maps of CBF with MIStar (Apollo Medical Imaging Technology, Melbourne, Victoria, Australia; Figure 1).[11,15] The maps of CBF were coregistered to susceptibility-weighted imaging and DWI images for region of interest (ROI) analysis. ROIs included the perihematomal region (1 cm surrounding the hematoma), ipsilateral and contralateral hemispheres, internal border zones, and external border zones. rCBF was calculated as the ratio of the mean values within each ROI/contralateral homologous regions at each time point.[8,9] Perilesional ROIs consisted of a 1-cm ring surrounding DWI hyperintensities (ischemic lesions).

Table 2. Absolute ASL Intensity Difference Values and rCBF Measurements

Region of Interest	Ipsilateral Absolute Value	Contralateral Absolute Value	rCBF
48-Hour perihematoma	76.2±34.4	88.9±41.6	0.9±0.2
48-Hour hemisphere	92.1±25.8	97.7±25.4	1.0±0.1
48-Hour internal border zone	37.1±23.4	42.2±29.7	1.0±0.2
48-Hour external border zone	54.9±27.3	62.0±29.4	0.9±0.2
Day 7 perihematoma	52.9±22.2	62.7±28.0	0.9±0.3
Day 7 hemisphere	65.9±31.1	71.4±32.0	0.9±0.1
Day 7 internal border zone	40.4±37.5	39.7±31.5	1.0±0.2
Day 7 external border zone	42.7±34.4	44.8±28.6	1.0±0.3
Day 30 perihematoma	65.1±29.7	73.5±30.9	0.9±0.2
Day 30 hemisphere	60.85±26.09	64.32±30.39	1.0±0.2
Day 30 internal border zone	32.8±26.8	34.9±25.2	0.9±0.2
Day 30 external border zone	40.3±21.4	45.2±26.4	1.0±0.4
DWI lesions (all time points; N=4)	70.0±49.2	77.3±86.8	1.0±0.7

Data are given as mean±SD. ASL indicates arterial spin labeling; DWI, diffusion-weighted imaging; rCBF, relative cerebral blood flow.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics 21.0 2008 (IBM, Armonk, NY). Weighted average SBPs were calculated as the area under the curve describing pressures >24 hours, as previously described.[8,16] Low SBP load was defined as the percentage of time spent at <140 mm Hg and high SBP load was defined as the percentage of time spent at >180 mm Hg within the first 24 hours from symptom onset.[8,17] There were insufficient SBP measurements available to calculate loads over time in one patient who had scans at the 48-hour, day 7, and day 30 time points. Absolute ASL signal intensity values at each time point were analyzed with a 1-way ANOVA to determine differences in perfusion between hemispheres. rCBF values at each time point were compared using the related-samples Friedman's ANOVA on ranks. Univariate linear regression was used to assess the relationships between SBP at the time of the scan, SBP change from baseline, SBP weighted average, percentage of time spent with SBP <140 and SBP >180 mm Hg within the first 24 hours, hematoma size, and rCBF at each time point. All nonnormally distributed variables were log transformed before regression.

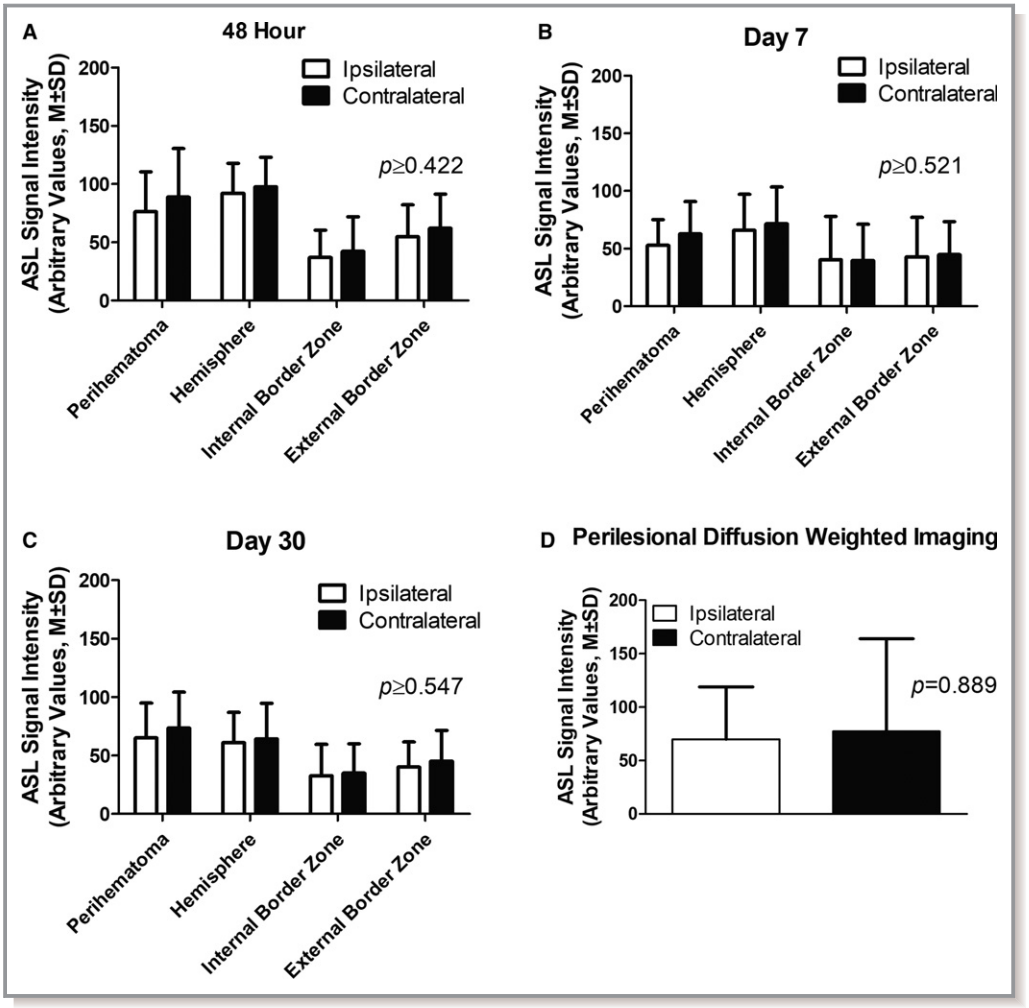

Figure 2. Absolute arterial spin labeling (ASL) signal intensity values in the perihematomal, hemispheric, and internal and external border zone areas in the ipsilateral and contralateral sides to the hematoma at 48 hours (**A**), on day 7 (**B**), and on day 30 (**C**) were not different. **D**, The ipsilateral and contralateral absolute ASL signal intensity values were combined for all the time points for the participants with diffusion-weighted imaging lesions, which did not differ either.

Results

Patient Characteristics

Twenty patients underwent imaging with ASL at 48 hours (N=12) and/or day 7 (N=6) and/or day 30 (N=11). Three patients had scans at all time points. Seven patients had scans at 48 hours only, 2 had scans at day 7 only, and 5 had scans at day 30 only. Two patients had a scan at 48 hours and day 30, and one patient had scans at day 7 and day 30. At 48 hours, 2 patients did not receive a scan, and 6 were scanned without the ASL protocol. At day 7, 2 patients died, 2 patients withdrew from the study, 9 patients did not receive a scan, and 1 patient was acquired without the ASL protocol. At day 30, 5 patients did not receive a scan. The ASL protocol was not used in every MRI scan as the acquisition requires patient cooperation for several minutes, which was not always possible in the patients with ICH. When ASL data were not obtained, SBP data and other parameters were excluded from summative data and regression analyses. Mean±SD times from symptom onset to scan at each of the 3 time points (48 hours, day 7, and day 30) were 57.1±24.1 hours, 9.2±2.3 days, and 39.3±12.5 days, respectively. Baseline patient characteristics are described in Table 1.

Measurements of CBF

Measurements of CBL are described in Table 2. There were no differences in ASL perfusion measurements at any time points in any of the ROIs ($P \geq 0.422$; Figure 2A through 2C). There were no differences in rCBF at any time points in any of

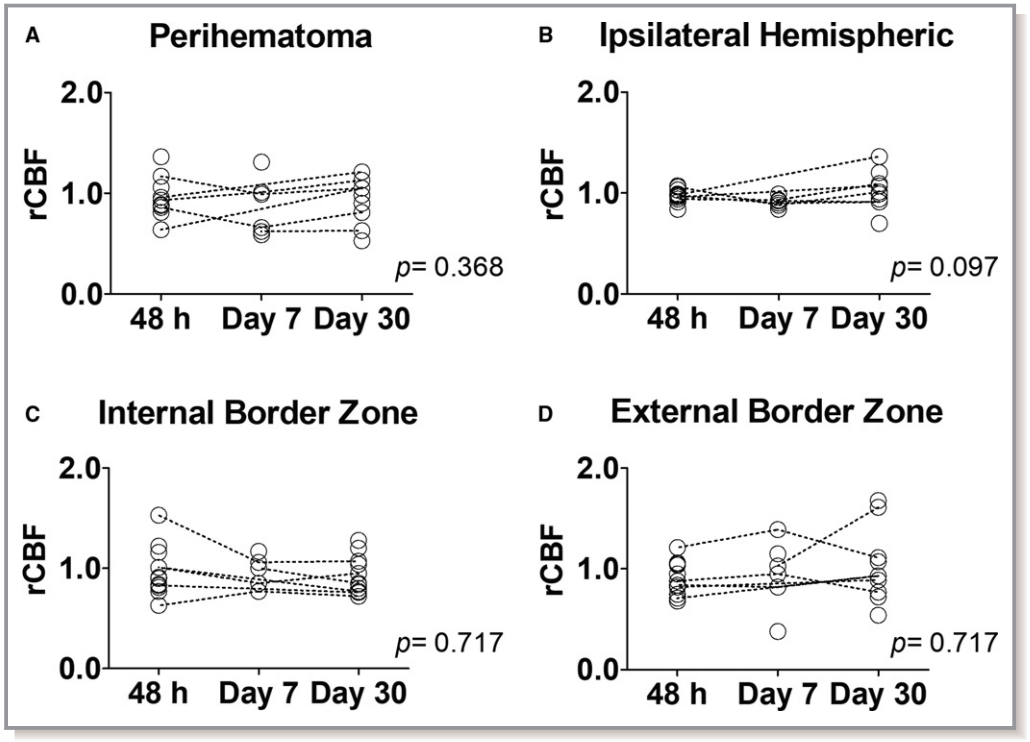

Figure 3. Perihematomal (**A**), ipsilateral hemispheric (**B**), and internal (**C**) and external (**D**) border zone relative cerebral blood flow (rCBF) values in individual patients. ANOVA results indicated no differences over time in any of the regions examined.

the other ROIs ($P \geq 0.097$; Figure 3). We also separately compared the rCBF of those patients who had ≥1 follow-up scans and did not find a difference between baseline and follow-up ($P \geq 0.198$; Table S1). Four patients developed DWI ischemic lesions at 27 hours, 6 days, 35 days, and 36 days (Table 2 and Figure S1). There were no differences in ASL perfusion measures within the areas of diffusion restriction (Figure 2D).

Temporal BP Profile

The mean±SD SBP was 145.0±19.5, 133.3±19.5, and 139.1±12.3 mm Hg at 48 hours, day 7, and day 30, respectively (Figure 4A). The SBP decreased by a mean±SD of 46.6±20.7, 57.6±32.4, and 53.0±30.1 mm Hg at 48 hours, day 7, and day 30, respectively. The mean±SD weighted average SBP was 146.2±17.3 mm Hg (N=17). The median (quartile 1–quartile 3) SBP load of <140 mm Hg at 48 hours was 18.7% (4.2%–35.4%; N=17). The median (quartile 1–quartile 3) SBP load of >180 mm Hg at 48 hours was 0% (0%–4.2%; N=17).

Relationship Between SBP and CBF

SBP was not associated with rCBF in any region at any time point ($P \geq 0.111$; Figure 4B through 4D; Table 3, Tables S2 and S3). SBP, including at the time of baseline, was also not associated with perilesional rCBF in those patients with DWI lesions ($P \geq 0.105$).

Hematoma volume was associated with decreased day 7 hemispheric rCBF ($\beta = -0.892$, $P = 0.042$), but no other regions of interest ($P \geq 0.074$), including perilesional rCBF in those patients with DWI lesions ($\beta = -0.689$, $P = 0.311$).

Discussion

We have shown that ASL measurements of rCBF up to 30 days after ICH are feasible. Consistent with other studies of perfusion in ICH, ASL measurements failed to demonstrate lower rCBF in patients with lower BP. In a limited number of patients with ischemic lesions, we found evidence of perilesional hypoperfusion in the patients with scans at 48 hours and on day 7 and slight hyperperfusion in the 2 remaining patients with day 30 scans, but CBF did not appear related to SBP.

Evidence from small and large clinical trials suggests that although aggressive antihypertensive therapy to 140 to 150 mm Hg has failed to improve patient outcome, it is relatively safe.[1–3] In a positron emission tomography study, reduction of mean arterial pressure in 14 patients with ICH by 15% between 6 and 22 hours from symptom onset

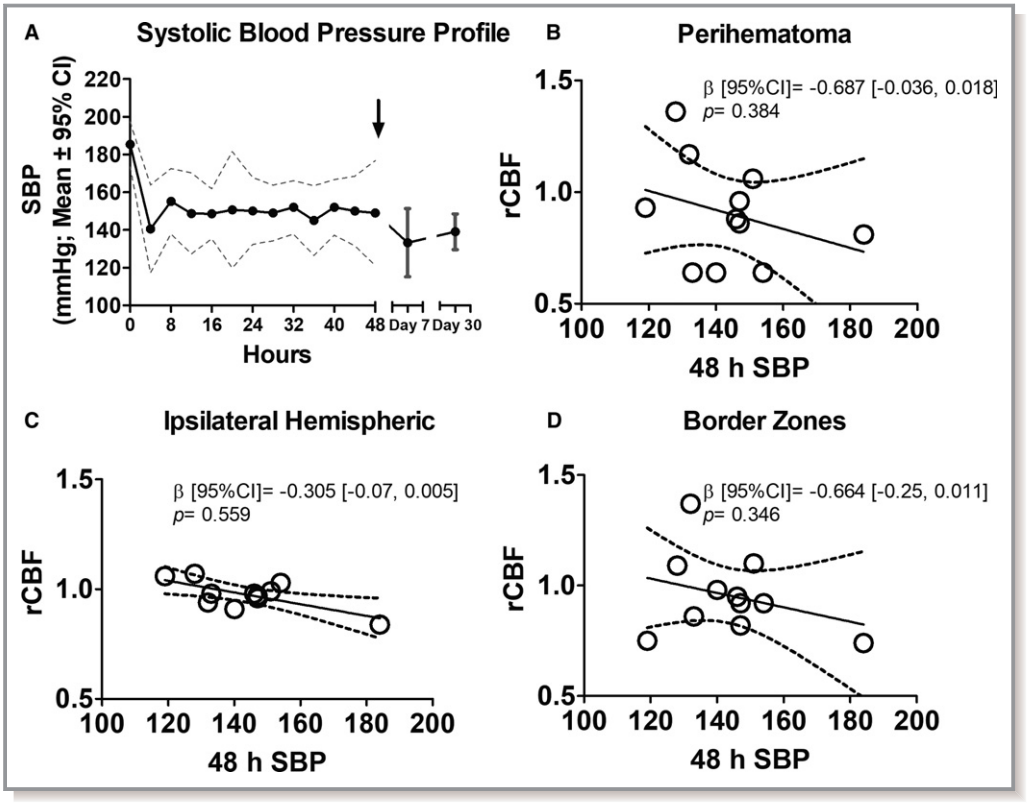

Figure 4. **A**, Temporal profile of mean (95% CI) of systolic blood pressure (SBP) profile up to 48 hours, as well as at day 7 and day 30. SBP at 48 hours was not associated with relative cerebral blood flow (rCBF) in the perihematoma (**B**), hemisphere (**C**), or border zones (**D**).

did not lead to decreased perihematomal or hemispheric CBF.[18] In the ICH ADAPT I, in which patients were randomized to a conservative (<180 mm Hg) or aggressive (150 mm Hg) SBP target, perfusion was not affected by decreased SBP.[9]

In this study, we also found that SBP changes were unrelated to rCBF in different regions of interest and across all time points, up to 30 days after ICH. Our results are consistent with previous research suggesting that there are no adverse effects on brain autoregulation caused by decreased SBP.

Remote ischemic lesions are found within a week of ICH onset in 14% to 41% of patients, and they have been associated with higher rates of morbidity and mortality.[19–25] Previously reported associations include hematoma volume, leukoaraiosis, amyloid angiopathy, microbleeds, and history of antihypertensive and antiplatelet therapy.[19–24] Retrospective studies are contradictory with respect to the association between SBP lowering and DWI lesions.[20,25,26] We found no consistent perilesional hypoperfusion in the 4 patients with ICH and remote DWI hyperintensities. Although larger hematoma volumes were associated with lower hemispheric perfusion at day 7, ischemic lesions were not. Most important, we did not find a relationship between perilesional rCBF and SBP. The ICH ADAPT II, which is currently ongoing, is a prospective randomized and blinded trial that will shed light on the impact of aggressive SBP lowering on DWI lesion frequency after ICH.[13]

Limitations of this study include the relatively small number of patients and loss to follow-up caused by morbidity and mortality, which may have led to selection bias. ASL sequences are several minutes long and require a cooperative and stable patient, which is often not the case shortly after ICH. The relative ASL measurements may have masked more global decreases in cerebral perfusion. Nonetheless, our findings are consistent with the bulk of evidence to date suggesting that lower SBP is not associated with hypoperfusion in patients with ICH.

Summary/Conclusions

This is the first study that measured CBF using ASL, a noninvasive MRI technique, to measure perfusion in patients with ICH. Although we found no evidence that lower pressures were associated with subacute or late changes in cerebral

Table 3. Univariate Relationships Between rCBF and BP Control at 48 Hours in the Perihematomal Region, Ipsilateral Hemisphere, and Internal and External Border Zones

rCBF at 48 h	No. of Patients*	β Value	Unstandardized B Value	95% CI	*P* Value
Perihematoma					
SBP change from baseline	11	−0.005	−0.00004	−0.013 to 0.013	0.993
Weighted average SBP	10	−0.621	−0.008	−0.092 to 0.076	0.783
SBP load <140 mm Hg	10	−1.450	−1.137	−5.719 to 3.445	0.487
SBP load >180 mm Hg	10	−0.354	−0.382	−3.186 to 2.422	0.694
Hemisphere					
SBP change from baseline	11	−0.193	0.000	−0.003 to 0.002	0.622
Weighted average SBP	10	2.114	0.009	−0.010 to 0.027	0.233
SBP load <140 mm Hg	10	2.076	0.511	−0.480 to 1.502	0.199
SBP load >180 mm Hg	10	−0.657	−0.222	−0.829 to 0.384	0.328
Internal border zone					
SBP change from baseline	11	−0.209	−0.002	−0.018 to 0.014	0.725
Weighted average SBP	10	0.882	0.013	−0.090 to 0.116	0.712
SBP load <140 mm Hg	10	−0.240	−0.218	−5.809 to 5.373	0.909
SBP load >180 mm Hg	10	−0.514	−0.643	−4.064 to 2.778	0.592
External border zone					
SBP change from baseline	11	−0.015	−0.00008	−0.008 to 0.008	0.978
Weighted average SBP	10	1.490	0.013	−0.042 to 0.067	0.515
SBP load <140 mm Hg	10	0.438	0.226	−2.739 to 3.192	0.824
SBP load >180 mm Hg	10	−0.817	−0.580	−2.394 to 1.234	0.384

BP indicates blood pressure; rCBF, relative cerebral blood flow; SBP, systolic BP.
*There were insufficient data points to calculate weighted average SBP in one patient.

perfusion, a randomized trial is required to definitively determine if aggressive BP targets affect CBF.

Sources of Funding

This study was supported by grant-in-aid funding from the Heart and Stroke Foundation of Canada (G-14-0006004). Klahr received Fellowship funding from the Quality Improvement and Clinical Research Alberta Stroke Program. Butcher holds a Canada Research Chair in Cerebrovascular Disease and a Professorship from the Heart and Stroke Foundation of Alberta, NWT, and Nunavut.

Disclosures

None.

References

1. Chu S, Sansing L. Evolution of blood pressure management in acute intracerebral hemorrhage. *F1000Res*. 2017;6:1–11.
2. Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, Lindley R, Robinson T, Lavados P, Neal B, Hata J, Arima H, Parsons M, Li Y, Wang J, Heritier S, Li Q, Woodward M, Simes RJ, Davis SM, Chalmers J. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med*. 2013;368:2355–2365.
3. Hanley DF, Hsu CY, Martin RL, Moy CS, Silbergleit R, Steiner T, Suarez JI, Toyoda K, Wang Y, Yamamoto H, Yoon B-WW, Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, Moy CS, Silbergleit R, Steiner T, Suarez JI, Toyoda K, Wang Y, Yamamoto H, Yoon B-WW; ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *N Engl J Med*. 2016;375:1033–1043.
4. Butcher KS, Baird T, MacGregor L, Desmond P, Tress B, Davis S. Perihematomal edema in primary intracerebral hemorrhage is plasma derived. *Stroke*. 2004;35:1879–1885.
5. Olivot J-M, Mlynash M, Kleinman JT, Straka M, Venkatasubramanian C, Bammer R, Moseley ME, Albers GW, Wijman CAC. MRI profile of the perihematomal region in acute intracerebral hemorrhage. *Stroke*. 2010;41:2681–2683.
6. Herweh C, Juttler E, Schellinger PD, Klotz E, Schramm P. Perfusion CT in hyperacute cerebral hemorrhage within 3 hours after symptom onset: is there an early perihemorrhagic penumbra? *J Neuroimaging*. 2010;20:350–353.
7. Rosand J, Eskey C, Chang Y, Gonzalez RG, Greenberg SM, Koroshetz WJ. Dynamic single-section CT demonstrates reduced cerebral blood flow in acute intracerebral hemorrhage. *Cerebrovasc Dis*. 2002;14:214–220.
8. Gould B, Mccourt R, Gioia LC, Kate M, Hill MD, Asdaghi N, Dowlatshahi D, Jeerakathil T, Coutts SB, Demchuk AM, Emery D, Shuaib A, Butcher K. Acute blood pressure reduction in patients with intracerebral hemorrhage does not result in borderzone region hypoperfusion. *Stroke*. 2014;45:2894–2900.
9. Butcher KS, Jeerakathil T, Hill M, Demchuk AM, Dowlatshahi D, Coutts SB, Gould B, Mccourt R, Asdaghi N, Findlay JM, Emery D, Shuaib A; ICH ADAPT Investigators. The intracerebral hemorrhage acutely decreasing arterial pressure trial. *Stroke*. 2013;44:620–626.

10. Bokkers RPH, Hernandez DA, Merino JG, Mirasol RV, van Osch MJ, Hendrikse J, Warach S, Latour LL; National Institutes of Health Stroke Natural History Investigators. Whole-brain arterial spin labeling perfusion MR imaging in patients with acute stroke. *Stroke*. 2012;43:1290–1294.
11. Bivard A, Krishnamurthy V, Stanwell P, Levi C, Spratt NJ, Davis S, Parsons M. Arterial spin labeling versus bolus-tracking perfusion in hyperacute stroke. *Stroke*. 2013;45:127–134.
12. Wang DJJ, Alger JR, Qiao JX, Hao Q, Hou S, Fiaz R, Gunther M, Pope WB, Saver JL, Salamon N, Liebeskind DS. The value of arterial spin-labeled perfusion imaging in acute ischemic stroke comparison with dynamic susceptibility contrast-enhanced MRI. *Stroke*. 2012;43:1018–1024.
13. Gioia L, Klahr A, Kate M, Buck B, Dowlatshahi D, Jeerakathil T, Emery D, Butcher K. The Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial II (ICH ADAPT II) protocol. *BMC Neurol*. 2017;17:100.
14. Kosior JC, Idris S, Dowlatshahi D, Alzawahmah M, Eesa M, Sharma P, Tymchuk S, Hill MD, Aviv RI, Frayne R, Demchuk AM. Quantomo: validation of a computer-assisted methodology for the volumetric analysis of intracerebral haemorrhage. *Int J Stoke*. 2011;6:302–305.
15. Alsop DC, Detre JA, Golay X, Matthias G, Hendrikse J, Hernandez-Garcia L, Lu H, Macintosh BJ, Parkes LM, Smits M, Van Osch MJP, Wang DJJ, Wong EC, Zaharchuk G. Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: a consensus of the ISMRM Perfusion Study Group and the European Consortium for ASL in Dementia. *Magn Reson Med*. 2015;116:102–116.
16. Aslanyan S, Fazekas F, Weir CJ, Horner S, Lees KR. Effect of blood pressure during the acute period of ischemic stroke on stroke outcome: a tertiary analysis of the GAIN International Trial. *Stroke*. 2003;34:2420–2425.
17. Zachariah PK, Sheps SG, Ilstrup DM, Long CR, Bailey KR, Wiltgen CM, Carlson CA. Blood pressure load—a better determinant of hypertension. *Mayo Clin Proc*. 1988;63:1085–1091.
18. Powers WJ, Zazulia AR, Videen TO, Adams RE, Yundt KD, Aiyagari V, Grubb RL, Diringer MN. Autoregulation of cerebral blood flow surrounding acute (6 to 22 hours) intracerebral hemorrhage. *Neurology*. 2001;57:18–24.
19. Gioia LC, Kate M, Choi V, Sivakumar L, Jeerakathil T, Kosior J, Emery D, Butcher K. Ischemia in intracerebral hemorrhage is associated with leukoaraiosis and hematoma volume, not blood pressure reduction. *Stroke*. 2015;46:1541–1547.
20. Menon RS, Burgess RE, Wing JJ, Gibbons MC, Shara NM, Fernandez S, Jayam-Trouth A, German L, Sobotka I, Edwards D, Kidwell CS. Predictors of highly prevalent brain ischemia in intracerebral hemorrhage. *Ann Neurol*. 2012;71:199–205.
21. Prabhakaran S, Gupta R, Ouyang B, John S, Temes RE, Mohammad Y, Lee VH, Bleck TP. Acute brain infarcts after spontaneous intracerebral hemorrhage: a diffusion-weighted imaging study. *Stroke*. 2010;41:89–94.
22. Garg RK, Liebling SM, Maas MB, Nemeth AJ, Russell EJ, Naidech AM. Blood pressure reduction, decreased diffusion on MRI, and outcomes after intracerebral hemorrhage. *Stroke*. 2012;43:67–71.
23. Kang DW, Han MK, Kim HJ, Yun SC, Jeon SB, Bae HJ, Kwon SU, Kim JS. New ischemic lesions coexisting with acute intracerebral hemorrhage. *Neurology*. 2012;79:848–855.
24. Murat Arsava E, Kayim-Yildiz O, Oguz KK, Akpinar E, Topcuoglu MA. Elevated admission blood pressure and acute ischemic lesions in spontaneous intracerebral hemorrhage. *J Stroke Cerebrovasc Dis*. 2013;22:250–254.
25. Singer OC, Kurre W, Humpich MC, Lorenz MW, Kastrup A, Liebeskind DS, Thomalla G, Fiehler J, Berkefeld J, Neumann-Haefelin T. Risk assessment of symptomatic intracerebral hemorrhage after thrombolysis using DWI-ASPECTS. *Stroke*. 2009;40:2743–2748.
26. Kimberly WT, Gilson A, Rost NS, Rosand J, Viswanathan A, Smith EE, Greenberg SM. Silent ischemic infarcts are associated with hemorrhage burden in cerebral amyloid angiopathy. *Neurology*. 2009;72:1230–1235.

Supplemental Material

Table S1. Relative cerebral blood flow (rCBF) of patients with a 48 hour and follow up scan.

48 Hour and Day 7 Follow Up	**Mean ± SD**	**Paired t-test *p* value**
48 hours Perihematoma rCBF (N=3)	0.99±0.16	0394
Day 7 Perihematoma rCBF (N=3)	0.89±0.20	
48 hours Hemisphere rCBF (N=3)	0.99±0.06	0.230
Day 7 Hemisphere rCBF (N=3)	0.90±0.02	
48 Hours Internal Borderzone rCBF (N=3)	1.05±0.45	0.463
Day 7 Internal Borderzone rCBF (N=3)	0.89±0.15	
48 Hours External Borderzone rCBF (N=3)	0.98±0.20	0.319
Day 7 External Borderzone rCBF (N=3)	1.05±0.30	
48 Hour and Day 30 Follow Up	**Mean ± SD**	**Paired t-test *p* value**
48 hours Perihematoma rCBF (N=5)	0.91±0.19	0.228
Day 30 Perihematoma rCBF (N=5)	1.05±0.15	
48 hours Hemisphere rCBF (N=5)	0.98±0.05	0.249
Day 30 Hemisphere rCBF (N=5)	1.08±0.17	
48 Hours Internal Borderzone rCBF (N=5)	1.00±0.33	0.198
Day 30 Internal Borderzone rCBF (N=5)	0.85±0.15	
48 Hours External Borderzone rCBF (N=5)	0.89±0.19	0.584
Day 30 External Borderzone rCBF (N=5)	0.92±0.12	

Table S2. **Linear regression between Day 7 rCBF and systolic blood pressure (SBP), SBP difference from baseline, weighted average SBP, and SBP loads.**

	N	β	Unstd B	95% CI	P value
Predictor of Day 7 perihematoma rCBF					
Day 7 SBP	5	-0.479	-0.006	-0.047, 0.035	0.602
SBP change from baseline	5	0.435	0.004	-0.025, 0.033	0.634
Weighted Average SBP	4	-1.146	-0.031	-0.371, 0.309	0.457
SBP load <140 mmHg	4	-0.521	-0.508	-11.71, 10.70	0.667
SBP load >180 mmHg	4	1.042	2.647	-29.11, 34.40	0.482
Predictor of Day 7 ipsilateral hemisphere rCBF					
Day 7 SBP	5	0.552	0.001	-0.004, 0.006	0.507
SBP change from baseline	5	0.084	0.000	-0.004, 0.006	0.914
Weighted Average SBP	4	-0.312	-0.001	-0.094, 0.091	0.893
SBP load <140 mmHg	4	-0.370	-0.067	-3.112, 2.979	0.827
SBP load >180 mmHg	4	0.331	0.155	-8.477, 8.787	0.857
Predictor of Day 7 internal borderzone rCBF					
Day 7 SBP	5	0.729	0.005	-0.014, 0.024	0.386
SBP change from baseline	5	-0.188	-0.001	-0.015, 0.013	0.803
Weighted Average SBP	4	0.504	0.005	-0.022, 0.032	0.496
SBP load <140 mmHg	4	-1.067	-0.545	-1.766, 0.676	0.111
SBP load >180 mmHg	4	-0.234	-0.295	-3.301, 2.712	0.431
Predictor of Day 7 external borderzone rCBF					
Day 7 SBP	5	0.356	0.003	-0.026, 0.033	0.675
SBP change from baseline	5	-0.642	-0.004	-0.025, 0.017	0.473
Weighted Average SBP	4	0.020	0.001	-0.505, 0.506	0.991
SBP load <140 mmHg	4	0.268	0.329	-16.35, 17.01	0.844
SBP load >180 mmHg	4	0.670	2.142	-45.13, 49.134	0.668

The weighted average SBP and the loads were missing for one patient in this study.

Table S3. **Linear regression between Day 30 rCBF and systolic blood pressure (SBP), weighted average SBP, SBP difference from baseline and SBP loads.**

	N	β	Unstd B	95% CI	P value
Predictor of Day 30 perihematoma rCBF					
Day 30 SBP	9	-0.111	-0.002	-0.015, 0.019	0.794
SBP change from baseline	9	-0.740	-0.008	-0.037, 0.022	0.188
Weighted Average SBP	8	-0.880	-0.016	-0.128, 0.096	0.321
SBP load <140 mmHg	8	-0.074	-0.072	-3.667, 3.523	0.842
SBP load >180 mmHg	8	0.234	0.480	-10.39, 11.35	0.675
Predictor of Day 30 ipsilateral hemisphere rCBF					
Day 30 SBP	9	0.048	0.001	-0.013, 0.015	0.902
SBP change from baseline	9	-0.584	-0.003	-0.053, 0.046	0.549
Weighted Average SBP	8	-0.139	-0.001	-0.191, 0.188	0.940
SBP load <140 mmHg	8	0.553	0.301	-5.800, 6.402	0.644
SBP load >180 mmHg	8	0.013	0.015	-18.43, 18.46	0.993
Predictor of Day 30 internal borderzone rCBF					
Day 30 SBP	9	-0.312	-0.005	-0.018, 0.008	0.413
SBP change from baseline	9	0.016	0.000	-0.102, 0.102	0.991
Weighted Average SBP	8	-1.038	-0.013	-0.402, 0.376	0.748
SBP load <140 mmHg	8	-1.029	-0.682	-13.20, 11.84	0.614
SBP load >180 mmHg	8	0.251	0.351	-37.50, 38.20	0.925
Predictor of Day 30 external borderzone rCBF					
Day 30 SBP	9	0.336	0.010	-0.016, 0.036	0.377
SBP change from baseline	9	-0.297	-0.004	-0.125, 0.116	0.721
Weighted Average SBP	8	2.238	0.059	-0.402, 0.521	0.925
SBP load <140 mmHg	8	1.461	2.084	-12.76, 16.930	0.707
SBP load >180 mmHg	8	-1.433	-4.314	-49.19, 40.56	0.662

The weighted average SBP and the loads were missing for one patient in this study.

Figure S1. Relative cerebral blood flow (rCBF) in the perilesional region of the four patients (one at 48 hours, one at Day 7, and two at Day 30) with DWI lesions remote to the hematoma.