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Quantification of pial collateral pressure in acute large vessel occlusion stroke: basic concept with patient outcomes

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Abstract

Purpose Pial collateral perfusion to the ischemic penumbra plays a critical role in determining patient outcomes in acute stroke. We aimed to assess the validity and reliability of an intra-procedural technique for measuring and quantifying the pial collateral pressure (QPCP) to ischemic brain tissue during acute stroke secondary to LVO. QPCP measurements were correlated with standard computed tomography angiography (CTA) and digital subtraction angiography imaging assessments of pial collateral perfusion and outcomes after mechanical endovascular revascularization (MER).

Methods This prospective cohort study included 60 consecutive patients with middle cerebral artery (MCA)–M1 and proximal M2 occlusions. QPCP measurements were obtained during MER. The validity of QPCP measurements was evaluated using four widely accepted collateral grading scales. QPCP measurements were also analyzed as a predictor of patient outcomes utilizing National Institute of Health Stroke Scale reduction at 24 h and modified Rankin Scale (mRS) scores at 30 days.

Results QPCP measurements and QPCP ratio (QPCP/systemic mean arterial blood pressure) showed a statistically significant association with single-phase pretreatment CTA Maas and American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology binary grading scales. Patient outcomes demonstrated for every 10-unit increase in QPCP, the odds of mRS 0-2 at 30 days increased by 76% ($p = 0.019$).

Conclusion QPCP measurements related best with the pretreatment CTA Maas collateral grading scale but were more strongly associated with patient outcomes than any of the four widely accepted collateral grading scales. Greater QPCP was significantly associated with better overall patient outcomes as defined by mRS at 30 days.

Keywords Large vessel occlusion · Patient outcomes · Pial collateral flow · Stroke · Thrombectomy

Introduction

Pial collateral perfusion to the ischemic penumbra plays a critical role in determining patient outcomes in acute stroke. Pial collaterals serve a vital function in providing blood flow to the ischemic penumbra and may influence total infarct volume and overall outcome [1–6]. Numerous studies utilizing various imaging modalities and grading systems have attempted to evaluate the role of collaterals in stroke outcomes. Few of these methods have been physiologically validated.

We attempted to quantify pial collateral pressure (QPCP) by directly measuring pressures during mechanical endovascular revascularization (MER) with a microcatheter downstream to the occlusion. In addition, we assessed the validity of our method by comparing these measurements with four widely accepted and validated collateral pretreatment computed tomography angiography (CTA) and digital subtraction angiography (DSA) grading scales. Patient outcomes were assessed for association with the intraprocedural QPCP measurements.

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Materials and methods

Technique

This prospective cohort study was conducted at our institution from June 2017 to September 2018. It was approved by our institutional review board (IRB# 11925), and signed consent was obtained from all patients. Sixty consecutive patients with acute middle cerebral artery (MCA)–M1 or proximal M2 occlusions were recruited. The patients underwent MER with microcatheter pressure measurements [7]. Common femoral arterial access was obtained and continuous arterial pressures were transduced from the 8-French sheath (Fig. 1). A Flow Gate™ (Stryker, Fremont, CA) balloon guide catheter was then used to catheterize the internal carotid artery (ICA) on the side of the occlusion. DSA images were obtained with the injection of Isovue-250 contrast. Using a coaxial technique with a 0.021″ microcatheter and 0.014″ microwire, the M2 inferior or superior division was catheterized distal to the M1 MCA occlusion. A super-selective angiographic run through the microcatheter was performed to visually confirm placement of the microcatheter distal to the occlusive lesion. The MAP distal to the MCA occlusion (QPCP) was then transduced from the microcatheter requiring only an additional 3 min (Fig. 2). Mechanical revascularization using a stent retriever was then performed in standard fashion.

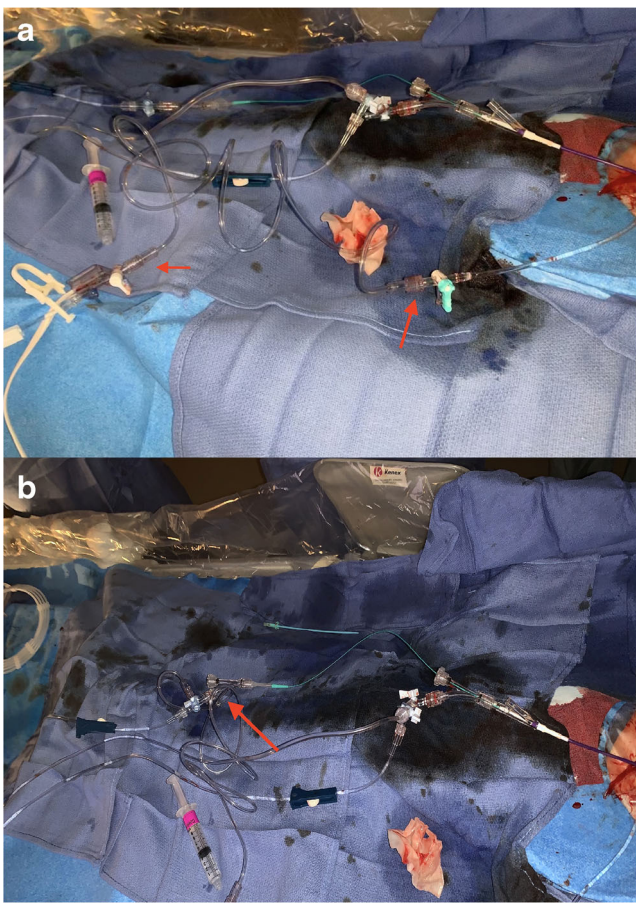

Fig. 1 Intra-procedural image showing arterial line transducer (small arrow) connected to the femoral sheath (large arrow) (top picture). Intra-procedural image showing arterial line transducer (small arrow) connected to the microcatheter (large arrow) (bottom picture)

Case illustration

A 27-year-old woman with diabetes mellitus type I and patent foramen ovale presented with a left MCA large vessel occlusion (LVO). She exhibited symptoms of aphasia and right hemiplegia with National Institute of Health Stroke Scale (NIHSS) 18. Her last known well was 102 min prior to admission. A head computed tomography (CT) scan showed no early signs of stroke with Alberta Stroke Program Early CT Score (ASPECTs) 10. Her CTA demonstrated a left M1 MCA occlusion with good pial collateralization (Fig. 3a arrow, b–e). She was assigned Miteff grade 3 (the vessels are reconstituted distal to the occlusion); Mass grade 3, equal to contralateral unaffected side; and Tan grade 3, for collateral supply filling entire territory (Fig. 3a–e). She was taken emergently for cerebral angiography and MER. Cerebral angiography showed a left M1 occlusion with good pial collateral from the anterior cerebral artery over the convexity retrograde filling the MCA

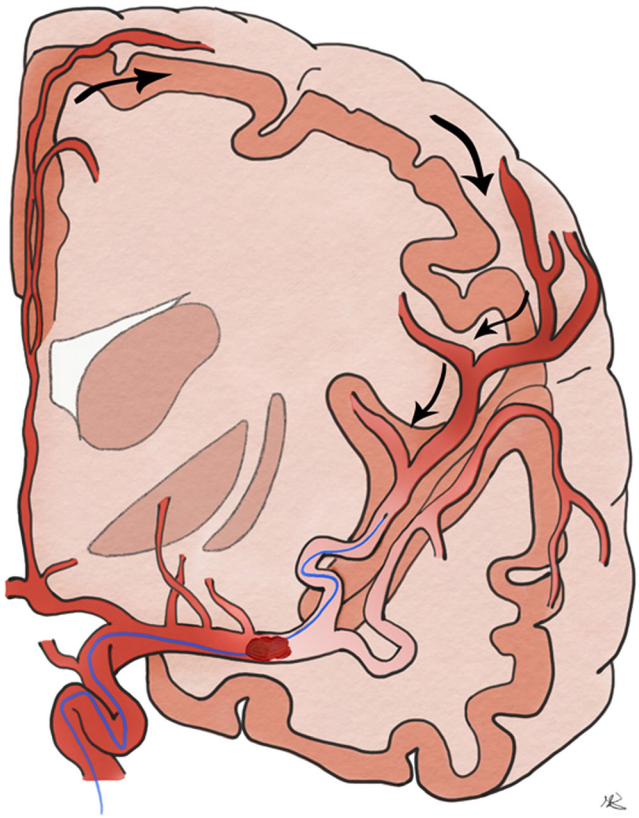

Fig. 2 Artist's depiction of microcatheter distal to left M1 large vessel occlusion in superior division with pial collateral flow generating back flow/pressure that can be recorded by the microcatheter. Arrows indicate pial collateral flow towards the microcatheter

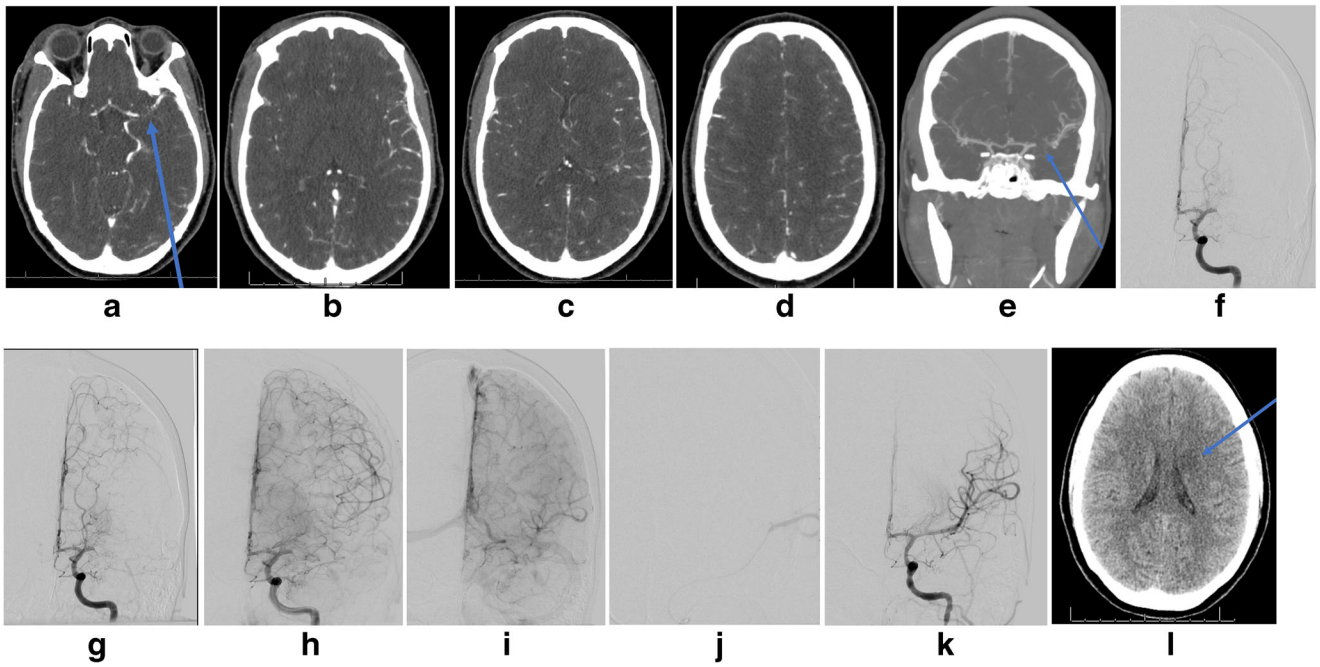

Fig. 3 Case illustration—axial computed tomography angiography (CTA) (**a**–**d**), and coronal CTA (e) showing left M1 MCA occlusion with good pial collateral. Left internal carotid injection in AP projections in early arterial to venous phase showing retrograde reconstitution of the middle cerebral artery territory (**f**–**i**). **j** demonstrates microcatheter injection in the inferior division M2 branch. **k** shows TICI 3 reperfusion after mechanical endovascular revascularization. **l** depicts 24-h head computed tomography with only small left frontal stroke

back to the bifurcation, American Society of Interventional and Therapeutic Neuroradiology (ASITN) grade 3, collaterals with slow but complete angiographic blood flow of the ischemic bed by late venous phase (Fig. 3f–i). The microcatheter pressure measurement in the proximal inferior division M2 distal to the M1 occlusion was 48 mmHg (Fig. 3j). The systemic MAP at the time of stent thrombectomy was 109 mmHg. TICI 3 reperfusion was achieved with one pass of the stentriever (Fig. 3k). The total procedure time from groin puncture to closure was 25 min. Her 24-h post head CT scan demonstrated a small 7-ml infarct (Fig. 3l). She recovered with minimal deficits, with a modified Rankin score of 1 at both 30 days and 3 months.

Collateral grading scale

All the collateral grade assignments were adjudicated together by a senior staff neuroradiologist (HM) and a vascular neurology fellow, blinded to the QPCP measurements and outcomes (Fig. 3). High-resolution CTA was performed on a 64-section multidetector helical scanner (Brilliance; Philips Healthcare, Best, the Netherlands), and the source images were reformatted into 3-mm-thick axial, coronal, and sagittal projections. MIPs were routinely provided as part of CTA; no 3D reconstructions were performed. Independent assessment of the pre-treatment single-phase CTA scan and DSA of each patient was performed according to the following four predefined scales:

A modified Maas et al. [8] grading system was used to assess pial collaterals on CTA. Pial collaterals were compared between affected and unaffected sides and graded as follows: absent collateral compared to contralateral unaffected side ("absent" score 1), less than compared to contralateral unaffected side ("partial" = score 2), and equal to contralateral unaffected side ("adequate" score = 3). The scores were further dichotomized into good (grade 2 and 3) or poor (grade 1).

The Miteff et al. system [9] is a 3-point grading system based on reconstitution of MCA by retrograde filling via collateral with respect to the Sylvian fissure. The grades are as follows: 3 = good (if the vessels are reconstituted distal to the occlusion), 2 = moderate (vessels seen in Svlvian fissure), or 1 = poor (when the contrast opacifies distal superficial branches) [9]. We dichotomized it further to good (grade 3) or poor (grade 1 and 2).

The Tan et al. system [10] is a four-point grading system ranging from 0 to 3. A score of zero indicates absent collateral supply to MCA territory. A score of 1 indicates collateral supply filling $\leq 50\%$ but $> 0\%$ of the occluded MCA territory. A score of 2 is given for collateral supply filling $> 50\%$ but $< 100\%$. A score of 3 is given for 100% collateral supply of the occluded MCA territory. Scores were dichotomized to good (grades 2 and 3) or poor (grades 0 and 1).

The American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading system [11] is a 5-point scale ranging from 0 (no visible collaterals) to 4 (complete and rapid

collateral by retrograde perfusion). As there were no patients with collateral grade 0, we dichotomized this grade into good (grades 2, 3, and 4) and poor (grade 1).

Data collection

Demographic, past medical history, preprocedural, procedural, and postprocedural data were collected including postprocedural thrombolysis in cerebral infarction (TICI) score as assessed and assigned by treating interventionalist (Table 1). Postprocedural analysis assessed for modified first pass effect (FPE) TICI≥2b [12]. The final infarct volume on postprocedural MRI prior to discharge was measured using a 1.5 Tesla MRI scanner by a senior staff neuroradiologist tracing the infarct area on diffusion-weighted imaging using Vitrea MRI Basic Stroke Software with semiautomatic post processing (https://www.vitalimages.com/product-information/mr-basic-stroke/). Symptomatic intracerebral hemorrhage (SICH) was defined as change in NIHSS > 4 and any ICH at 24 h. Early response was defined as > 10 improvement in NIHSS score on post-procedural day 1. Good clinical outcome was defined as mRS ≤ 2 at 30 days.

Statistical analysis

The distribution of all variables was examined using descriptive statistics, Shapiro-Wilk tests, histograms, and QQ plots. Univariate associations with QPCP were carried out using Kruskal-Wallis tests or Wilcoxon rank sum tests for categorical variables and using Spearman's rank correlation coefficients for continuous variables. Univariate associations between binary groups were carried out using chi-square or Fisher's exact tests for categorical variables. Linear regression models were used to examine the effect of QPCP on mRS at 30 days and at 3 months while controlling for premorbid mRS, with results presented as beta estimates with 95% confidence intervals. Logistic regression modeling was also used to examine these same effects when mRS at 30 days is dichotomized with results presented as adjusted odds ratios with 95% confidence intervals. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 60 patients were included in the study. The mean patient age was 67.4; SD ± 17.3 years; 55% female. The median presenting NIHSS scores and premorbid mRS were 18 (IQR 6.7) and 1 (IQR 2), respectively. Other relevant clinical and demographic variables are included in Table 1. Good collateral grades were noted in 50% (Maas), 80% (Tan), 50% (Miteff), and 60% (ASITN/SIR). Intra-procedural statistics revealed a mean time from groin puncture to recanalization 48 ± 35 min (Table 1). Fifty-three (88%) patients treated achieved (TICI 2b or greater) recanalization scores. The mean QPCP recorded was 40.5 ± 15.3 mmHg with a median value of 41.5 (IQR 18). The mean QPCP/Systemic MAP ratio was 0.43 ± 0.14 with a median of 0.42 (IQR 0.18). The mean of the Systemic MAP-QPCP was 54.6 ± 17.6 with a median value of 55.0 (IQR 24.5).

Follow-up MRI showed a final infarct volume at discharge as77.6 cc ± 97.3 cc with a median of 34 (IQR 106). The average NIHSS score difference/improvement postprocedure was 9 ± 8 with a median of 8 (IQR 14). Twenty-five (42%) patients were categorized as having an early response defined as greater than 10-point NIHSS score improvement on post-procedural day 1. No patient experienced a SICH, but 13 (22%) patients demonstrated radiographic evidence of hemorrhage on post-procedural CT scan. The mean mRS score at 30 days was 3.3 ± 1.9, median 3 (IQR 3) and 3 ± 2, and median 3 (IQR 4) at 3 months. Seventeen (30%) patients included in the study were deceased at 3 months.

Collateral grading scales

QPCP/systemic MAP ratio demonstrated a statistically significant association with Maas et al. grading scheme ($p = 0.021$) and ASITN/SIR binary 1,2 versus 3,4 grading ($p = 0.038$) [8, 11] (Table 2). When the Maas et al. scale was simplified to a binary grading scheme with poor vs. good collateral status, both QPCP and QPCP ratio maintained statistical significance ($p = 0.038$ and $p = 0.008$, respectively). None of the other collateral grading scales was associated with the QPCP measurements with statistical significance (Table 2). There was no relationship with admission systemic MAP and the collateral grading schemes except for ASITN/SIR with poor collateral grade having statistically significant higher admission MAP ($p = 0.013$). None of the collateral grading scales including Maas were independent predictors of clinical outcome (Table 3).

Patient variables and outcomes

We observed higher values of absolute QPCP and QPCP ratio associated with higher ASPECTS, lower presenting NIHSS score, and lower stroke volumes, but these did not reach statistical significance (Table 2). In addition, no significant relationship between last known well to reperfusion time and QPCP was found. There was a statistically significant correlation with systemic MAP and QPCP ($r = 0.441$, $p < 0.001$). There was a statistically significant ($r = -0.294$, $p = 0.033$) correlation between absolute QPCP and favorable functional outcome at 30 days (Table 2).

Table 1 Clinical and demographic information, intraprocedural variables, collateral grading scale and outcomes for patients undergoing mechanical endovascular revascularization (MER) for M1 occlusions

Variable	*N*	Mean (SD) Median (IQR) or *N* (%)
Age	60	67.4 (17.3) 67 (25)
BMI	60	27.6 (6.8) 27.2 (9.0)
Sex		
Male		27 (45.0%)
Female		33 (55.0%)
Race		
Black		23 (39.7%)
White		34 (58.6%)
Other		1 (1.7%)
Previous stroke		19 (31.7%)
Hypertension		44 (73.3%)
Diabetes mellitus		20 (33.3%)
Use of antiplatelet		32 (53.3%)
Use of anticoagulation		11 (18.3%)
Glasgow Coma Scale	60	11.5 (2.3) 11 (4.5)
Presenting NIHSS	60	17.9 (6.7) 18 (10)
Premorbid mRS	53	1.2 (1.4) 1 (2)
CT ASPECTS	60	8.9 (1.0) 9 (2)
CTA ASPECTS	60	8.3 (1.4) 8 (1)
Procedure time (min)	59	48 (35) 50 (61)
Side of occlusion		
Left		35 (58.3%)
Right		25 (41.7%)
MCA site of occlusion		
Proximal M1		19 (32%)
Distal M1		23 (38%)
Proximal M2		18 (30%)
Recording taken from		
Superior division		34 (57%)
Inferior division		26 (43%)
Systemic mean arterial pressure (mmHg)	60	95.1 (18.6) 93 (29)
QPCP (mmHg)	60	40.5 (15.3) 41.5 (18)
QPCP ratio	60	0.43 (0.14) 0.42 (0.18)
Systemic MAP-QPCP (mmHg)	60	54.6 (17.6) 55 (24.5)
Number of attempts at thrombectomy	60	2 (1.2) 1.5 (2)
TICI score		
≤ 2a		7 (11.7%)
≥ 2b		53 (88.3%)
Modified first pass effect TICI≥2b reperfusion		30 (50%)
Maas		
Bad (0)		8 (13.3%)
Moderate (1)		22 (36.7%)
Good (2)		30 (50.0%)
Maas (binary)		
Poor (0)		10 (16.7%)
Good (1,2)		50 (83.3%)
Miteff		
Poor (0)		10 (16.7%)
Moderate (1)		20 (33.3%)
Good (2)		30 (50.0%)
Miteff (binary)		
Poor (0,1)		10 (16.7%)
Good (2)		50 (83.3%)
Tan		
0%		2 (3.3%)
1–50%		11 (18.3%)
> 51–< 100%		32 (53.3%)
100%		15 (25.0%)
Tan (binary)		
Poor (0–50%)		12 (20.0%)
Good (51–100%)		48 (80.0%)
ASITN/SIR		
1		24 (40.0%)
2		16 (26.7%)
3		15 (25.0%)
4		5 (8.3%)
ASITN/SIR (binary)		
Poor (1,2)		40 (66.7%)
Good (3,4)		20 (33.3%)
Final infarct volume at discharge (cc)	60	77.6 (97.3) 34 (106)
Change in NIHSS at 24 h	58	8.8 (8.4) 9 (10)
Hemorrhage on post procedure CT scan		
Yes		13 (21.7%)
No		47 (78.3%)
Early response		
Yes		25 (41.7%)
No		35 (58.3%)
Outcome at 3 months		
Deceased		17 (29.8%)
Poor (mRS > 3)		18 (31.6%)
Good (mRS ≤ 2)		22 (38.6%)
Missing		3

A modified Maas et al. [8] grading system was used to assess pial collaterals on CTA. Pial collaterals were compared between affected and unaffected sides and graded as follows: absent collateral compared to contralateral unaffected side ("absent" score 1), less than compared to contralateral unaffected side ("partial" = score 2), and equal to contralateral unaffected side ("adequate" score = 3). The scores were further dichotomized into good (grade 2 and 3) or poor (grade 1)

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The American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) grading system [11] is a 5-point scale ranging from 0 (no visible collaterals) to 4 (complete and rapid collateral by retrograde perfusion.) As there were no patients with collateral grade 0, we dichotomized this grade into good (grades 2, 3, and 4) and poor (grade 1).

Table 2 Univariate analysis showing the quantification of pial collateral pressure (QPCP) absolute values and QPCP/systemic MAP ratio and association with collateral grades and variables assessed in study

Variable	QPCP Median (IQR)	*p* value	QPCP/systemic MAP Median (IQR)	*p* value
Maas				
Bad (0)	29.5 (18.5)	0.060	0.28 (0.26)	**0.021**
Moderate (1)	36.0 (24.0)		0.38 (0.17)	
Good (2)	42.5 (9.0)		0.46 (0.17)	
Maas (binary, new)				
Poor (0,1)	32.5 (24)	**0.038**	0.35 (0.19)	**0.008**
Adequate (2,3)	42.5 (9)		0.46 (0.17)	
Miteff				
Poor (0)	45.5 (21)	0.291	0.49 (0.27)	0.155
Moderate (1)	35 (19.5)		0.35 (0.17)	
Good (2)	41.5 (18)		0.44 (0.16)	
Tan				
0%	40 (20)	0.997	0.50 (0.31)	0.406
1–50%	38 (19)		0.44 (0.27)	
51–< 100%	42 (25)		0.40 (0.16)	
100%	41 (11)		0.47 (0.15)	
Tan (binary)				
Poor (0–50%)	37 (18)	0.631	0.43 (0.24)	0.890
Good (51–100%)	42 (18)		0.42 (0.17)	
ASITN/SIR				
1	41 (18.5)	0.186	0.40 (0.14)	0.203
2	35.5 (16.5)		0.39 (0.18)	
3	46 (16)		0.49 (0.20)	
4	42 (6)		0.44 (0.18)	
ASITN/SIR (binary)				
Poor (1,2)	39 (17.5)	0.104	0.40 (0.15)	**0.038**
Good (3,4)	45.5 (13)		0.49 (0.19)	
Variable	**QPCP correlation coefficient (*r*)**	***p* value**	**QPCP/systemic MAP correlation coefficient**	***p* value**
CT ASPECTS	0.195	0.136	0.131	0.319
CTA ASPECTS	0.152	0.246	0.072	0.587
Stroke volume	− 0.180	0.168	− 0.160	0.222
NIHSS pre procedure	− 0.037	0.777	− 0.203	0.126
NIHSS post procedure	− 0.180	0.177	0.066	0.625
NIHSS change	0.130	0.330	0.066	0.625
Attempts at thrombectomy	0.027	0.838	0.039	0.769
mRS at 30 days	− 0.294	**0.033**	− 0.149	0.288
Systemic MAP	0.441	**< 0.001**		

Multivariable analysis

With every 10-unit increase in QPCP, the odds of mRS ≤ 2 at 30 days increased by 1.76 (95% CI 1.09, 2.84, $p = 0.019$) when controlling for mRS at presentation (Table 4). A 10-unit increase in systemic MAP was associated with a change in QPCP of 3.82 (95% CI 1.96, 5.67, $p < 0.001$) when controlling for Maas binary collateral grade (Table 5).

Discussion

The brain is supplied by an elaborate network of redundant vessels that can provide collateral blood supply in pathological states [13]. The forms of collateral can be divided into (1) primary, referring to circle of Willis collaterals; (2) secondary, the extracranial to intracranial collateral and pial collateral; and (3) tertiary, indicating the development of neovascularity through angiogenesis within an ischemic territory [14].

Table 3 Univariate associations with mRS at 30 days showing that there are no significant associations between mRS at 30 days and any of the collateral scores

Covariate	Statistics	Level	mRS at 30 days		*p* value
			> 2 *N* = 33	≤ 2 *N* = 20	
Miteff	N (Col %) N (Col %)	Poor Moderate	5 (15.15) 10 (30.3)	3 (15) 8 (40)	0.801
	N (Col %)	Good	18 (54.55)	9 (45)	
Maas	N (Col %) N (Col %)	Bad Moderate	5 (15.15) 14 (42.42)	2 (10) 6 (30)	0.536
	N (Col %)	Good	14 (42.42)	12 (60)	
Maas (binary)	N (Col %) N (Col %)	Poor Good	6 (18.18) 27 (81.82)	3 (15) 17 (85)	1.000
Maas (binary, new)	N (Col %) N (Col %)	Poor Adequate	19 (57.58) 14 (42.42)	8 (40) 12 (60)	0.215
Tan	N (Col %) N (Col %)	0% 1–50%	2 (6.06) 6 (18.18)	0 (0) 2 (10)	0.589
	N (Col %)	51–100%	16 (48.48)	13 (65)	
	N (Col %)	100%	9 (27.27)	5 (25)	
Tan (binary)	N (Col %) N (Col %)	Poor Good	7 (21.21) 26 (78.79)	2 (10) 18 (90)	0.456
ASITN (binary)	N (Col %) N (Col %)	1/2 3/4	24 (72.73) 9 (27.27)	12 (60) 8 (40)	0.336

The form of collateral most relevant to MCA LVO is pial collateral. The pial arteriole connections between the anterior cerebral, posterior cerebral, and middle cerebral territories provide the ability to sustain or promote penumbral flow distal to an occlusion. Many reports have shown that the extent of pial collateral flow directly impacts the volume of the final infarct core [15], and reduced infarct growth [16, 17] and early recanalization by intravenous thrombolysis [18]. The lack of good collateral flow increases the risk of hemorrhagic transformation after endovascular recanalization [19], infarct progression [20], and malignant edema [21]. Based on data from over 20 studies of > 2000 patients with stroke treated with intra-arterial thrombolysis and/or mechanical thrombectomy, with or without prior intravenous thrombolysis, better pretreatment collateral circulation was associated with higher rates of successful recanalization (RR 1.23; 95% CI 1.06, 1.42; $p = 0.006$) and reperfusion (RR 1.28; 95% CI 1.17, 1.40; $p < 0.001$), a lower risk of symptomatic intracranial hemorrhage before discharge (RR 0.59; 95% CI 0.43, 0.81; $p = 0.001$), an increased chance of achieving a favorable functional outcome at 3 months (RR 1.98; 95% CI 1.64, 2.38; $p < 0.001$), and a reduced risk of death at 3 months (RR 0.49; 95% CI 0.38, 0.63; $p < 0.001$) [5, 6, 14, 22–24].

The radiographic identification of pial collateral, via DSA, MR angiography (MRA), CTA, and perfusion technologies, is an area of intense research. However, the widespread clinical applicability of collateral grading has been limited by the complexity of all the various rating systems. A systematic review of pial collateral grading scales in the medical literature identified over 60 different scoring methods [5]. The various collateral grading schemes can be subjective and relatively complex.

DSA is considered to be the gold standard, but it is costly, invasive, and labor intensive. Adequate assessment of pial collaterals may require a complete angiographic examination. The most widely recognized collateral grading scale based on DSA is the ASITN/SIR [11]. This scale has demonstrated positive association with achieving reperfusion, smaller infarct volumes, and better clinical outcomes in the ENDOSTROKE registry and post hoc analyses of Interventional Management of Stroke III (IMS III) and Solitaire FR with the Intention for Thrombectomy [23, 25,

Table 4 Multivariable logistic regression model showing the effect of absolute QPCP on mRS at 30 days

Dependent variable	**Independent variables**	**Adj OR (95% CI)**	***p* value**
mRS at 30 days (≤ 2 vs. > 2)	QPCP (5-unit increase)	1.33 (1.05, 1.69)	**0.019**
	QPCP (10-unit increase)	1.76 (1.09, 2.84)	
	mRS at presentation	0.46 (0.24, 0.88)	**0.018**

Table 5 Linear regression model with the effect of MAP on QPCP while controlling for Maas (binary)

Dependent variable	Independent variables	Beta estimate (95% CI)	*p* value
QPCP	Proximal pressure (5 mmHg)	1.91 (0.98, 2.84)	**< 0.001**
	Proximal pressure (10 mmHg)	3.82 (1.96, 5.67)	
	Maas (good vs. poor)	8.58 (− 0.62, 17.78)	0.067

26]. We utilized the ASITN/SIR collateral grading scale in our cohort and found a statistically significant association with poor ASITN/SIR collateral grades and higher admission MAP. However, there was a non-statistically significant relationship with absolute QPCP measurements and ASITN/SIR collateral grades. Only QPCP/Systemic MAP ratio and a modified binary ASITN/SIR demonstrated statistically significant association ($p = 0.038$). We found that during MER for LVO, a complete angiographic evaluation of the pial circulation cannot always be made by just injecting the ipsilateral ICA proximal to an MCA LVO. Multiple vessels such as the contralateral carotid or the vertebral artery may require evaluation. During MER, generally the interventionalist goes directly to the occluded vessel, often forgoing a complete angiographic evaluation of the pial collateral.

CT-based studies are most commonly used due to their rapid availability and easy accessibility and have been shown to be superior to MRA [14]. We utilized 3 CTA grading scales, including the methods proposed by Maas et al. [8], Miteff et al. [9], and Tan et al. [10]. Good grade collateral status according to the Miteff, Tan, and Maas grading scales has been associated with a mRS 0–2 at 3 months in acute stroke [14]. Poor collateral status on Miteff and Maas grading scales has also been associated with poor functional outcomes 5–6 in the treatment of acute stroke [14]. In a study of 200 patients with acute stroke, only the Miteff collateral grading method was found to be an independent predictor of favorable functional outcome (mRS 0–1) at 3 months (OR, 3.34; 95% CI 1.24, 9.00; $p = 0.01$) when comparing Miteff, Maas, and Tan grading systems [27]. None of these collateral grading systems has been validated in large-scale studies, nor confirmed with physiologic pressure measurements. In our cohort, the Maas collateral grading scale demonstrated a statistically significant relationship with QPCP measurements. However, in our preselected patient cohort of favorable candidates for MER, none of the pretreatment radiographic grading scales were independent predictors of patient outcome.

Currently, there is no consensus on an optimal collateral grading system in ischemic stroke based on imaging modalities [14]. Moreover, not all the grading systems have been assessed for reliability. Given these discrepancies, a quantitative measurement of collaterals by measuring QPCP was performed to gain a better understanding of the physiology. In our series, higher QPCP measurements independently predicted favorable functional outcome.

Sorimachi et al. conducted a similar study evaluating pressures proximal and distal to LVO in patients undergoing intra-arterial thrombolysis of ICA and MCA [28]. They demonstrated that better recanalization was achieved when there was less of a gradient between the pressures proximal and distal to the

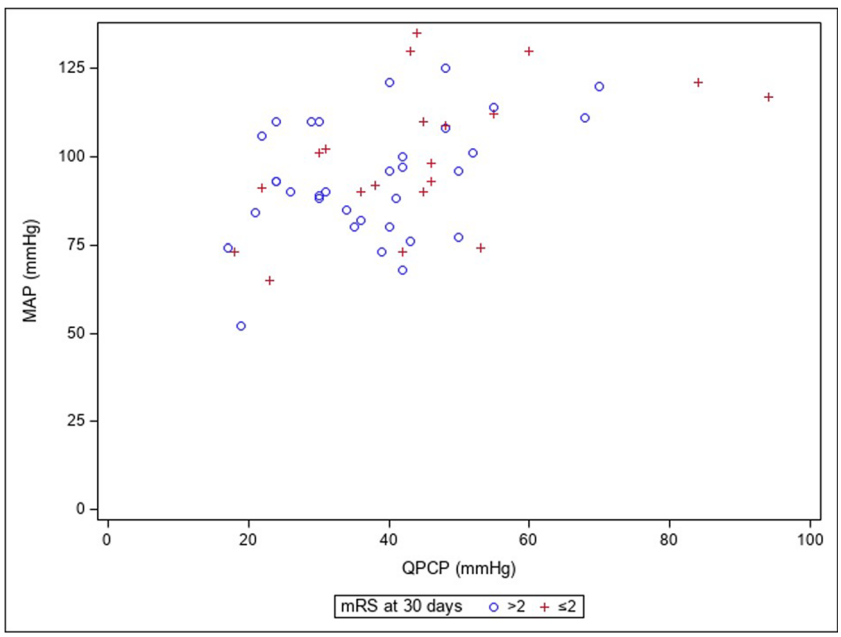

Fig. 4 Scatter plot—this scatter plot demonstrates systemic QPCP (*x*-axis) and systemic MAP (*y*-axis) with good outcomes mRS 0–2, red plus symbol, and bad outcomes mRS 3-6, blue circle symbol

clot. In other words, QPCP/MAP ratios are closer to 1. In addition, patient outcomes were worse when there was a measured decrease 6.7; SD ± 8.5 mmHg ($p = 0.0225$) between the systemic MAP and proximal MAP [28]. In our study, we included patients with only MCA occlusions. We found that QPCP showed a statistically significant relationship with the pretreatment CTA Maas collateral grading scale, and non-statistically significant trends with ASITN/SIRS, Tan, and Miteff grading scales. In addition, higher QPCP was related to better patient outcome mRS 0–2 at 30 days. Although statistically non-significant, subjects with higher QPCP tended to have lower presenting NIHSS scores, higher ASPECT scores, and lower final infarct volumes. In comparison to Sorimachi et al., we also found that higher systemic MAP was associated with higher distal pressure QPCP. We did not find that higher intraprocedural systemic pressures were associated with lower revascularization rates or larger pressure gradients forcing clots more distal and more difficult to retrieve as postulated by Sorimachi [28, 29].

The exact mechanism by which QPCP contributes to a better functional outcome requires further research. We hypothesize that the higher QPCP reflects better pial collateral to perfuse the pressure passive territories distal to an LVO, subsequently reducing infarct volume. Hypotension prior to recanalization is postulated to directly affect the pressure passive system maintaining collateral flow. According to Petersen et al., every 10-mmHg reduction in systemic MAP prior to reperfusion with MER increased the risk of worse outcome by 22% [30]. In their series of 390 patients undergoing thrombectomy, this equated to 4.1-ml increase in infarct volume for every 10-mmHg change in MAP [30]. Other investigators have published that MAPs < 70 mmHg as well as 10% decreases in MAP during MER procedures are associated with poor patient outcomes [30]. Our study did not have the power to provide a discrimination threshold for systemic MAP and clinical outcome. However, it does provide some physiologic evidence to support this concept. When controlling for Maas new binary, a 10-mmHg change in systemic MAP was associated with 3.82-mmHg change in QPCP (95% CI 1.96, 5.67 $p < 0.001$). Procedural systemic MAPs were directly related with QPCP ($p < 0.001$). Higher QPCP were associated with better pretreatment Maas CTA collateral grades ($p = 0.038$) and better overall clinical outcome ($p = 0.033$) (Fig. 4).

Better pial collateral likely promotes improved intrinsic and extrinsic thrombolysis. More favorable back pressures may facilitate dislodgement of the clot and prevent casting of the distal vessels. Our study did not have the power to demonstrate a correlation with reperfusion rates, number of passes, and QPCP. Fifty-three (88%) patients achieved > TICI 2b reperfusion. There likely exists a complex interaction between these hydromechanical forces, thrombus characteristics [31], and vessel wall that likely govern the final revascularization outcome. Better pial collateral also may mitigate ischemia-induced reperfusion injuries, although our study failed to demonstrate a relationship with QPCP and bleeding complications.

Our patient cohort may reflect a selection bias. Only patients that were undergoing MER and met indications for a procedure were included in this study. Perhaps this led to a disproportionate number of patients exhibiting a slow infarct progression, as the fast progressors with poor collaterals may have been excluded [32, 33]. The small sample size also limits conclusions. The prospective nature, the direct physiologic pressure measurements, the comprehensive assessment of confounding variables, and the blinded assessments are the strengths of this study.

Conclusion

Direct pressure measurements distal to an LVO in stroke are feasible and may reflect a real-time objective measure of the pial flow. In our cohort, QPCP measurements were statistically associated with the pretreatment Maas CTA collateral grades. Higher QPCP measurements were associated with more favorable patient outcomes. QPCP also was directly related with proximal systemic MAP providing a quantifiable, yet dynamic variable in the treatment of acute ischemic stroke secondary to LVO. Future studies should be conducted to validate this concept in larger, more diverse groups of patients. This technique may prove useful in forthcoming investigations on the elaborate neurovascular interactions during stroke and provide some insight on patient-specific intraprocedural blood pressure parameters.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent This study was approved by our Institutional Review Board (#11925). Informed consent was obtained from all individual participants included in the study.

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