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Title: Automated CTA-Derived Collateral Grading and Morphologic Metrics for Enhanced Prediction of Post-Stroke Outcomes

Running Title: CTA-derived collateral grading in AIS

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Abstract

Background and Purpose: Collateral circulation is a key determinant of treatment response and outcomes in acute ischemic stroke (AIS), yet its assessment in clinical practice remains limited and subjective. While CT perfusion (CTP) offers insight into tissue viability, its restricted availability and susceptibility to artifacts reduce its practical utility, particularly in smaller centers. As an accessible alternative, we developed and validated an automated quantitative collateral index (qCI) derived from CTA using a deep learning U-Net segmentation framework, and evaluated the ability of CTA-based features to predict post-stroke recovery and functional outcomes.

Materials and Methods: We retrospectively analyzed prospectively collected data from 230 AIS patients who underwent endovascular thrombectomy (EVT) between 2019–2023. CTA scans were segmented using a validated neural network–based vascular extraction model to generate 3D vessel networks and compute morphology metrics (vessel length, branching, fractal dimension, tortuosity). A fully automated qCI was derived through hemispheric comparison of vascular features following spatial registration. Agreement of qCI with clinician grading was quantified. Gradient-boosted decision tree models were trained to predict early neurological deterioration (END), early neurological improvement (ENI), and 90-day modified Rankin Scale (mRS) using (i) CTP-only (core, penumbra, mismatch), (ii) CTA-only (qCI + morphology), and (iii) combined CTA+CTP features.

Results: Automated qCI (graded 0–3) showed strong concordance with expert scoring (accuracy 0.863; Pearson $R = 0.880$; Cohen's $\kappa = 0.786$). Dichotomized collateral status achieved 0.938 accuracy (AUROC = 0.945). For 90-day mRS prediction, the CTA-only model outperformed the CTP-only model (AUROC 0.730 vs 0.645) with better calibration (Brier score 0.178 vs 0.295). The combined CTA+CTP model performed best overall (AUROC 0.781), with similar improvements observed for END. CTA-derived features led to significant reclassification gains when added to perfusion-based models.

Conclusions: Automated CTA-derived qCI and cerebrovascular morphology provide rapid, objective, and reproducible collateral assessment with high agreement to expert grading. These features outperform perfusion metrics in several predictive tasks and further enhance prognostic accuracy when combined with CTP. Because CTA is widely available, qCI offers a scalable, clinically practical tool for improving stroke outcome prediction, particularly in settings where CTP is unavailable.

1. Introduction

Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide¹. Rapid and accurate assessment of cerebral perfusion is crucial for determining eligibility for acute reperfusion therapies such as intravenous thrombolysis and endovascular thrombectomy (EVT)². This process typically relies on an integrative assessment of clinical and imaging parameters. Data-driven models for predicting outcomes following acute reperfusion therapies have the potential to support stroke systems of care by optimizing triage, inter-hospital transfer decisions, and informing clinical decision-making for physicians, patients, and their families. As a result, automated and individualized approaches to treatment response and outcome prediction are increasingly being explored and adopted in clinical research and practice³⁻⁵.

Collateral circulation plays a pivotal role in determining final infarct size, treatment response, and functional outcomes in AIS^{6,7}. Robust collateral networks can sustain tissue viability, extend therapeutic windows, and improve prognosis. Traditionally, CT angiography (CTA) is used to visualize the cerebrovascular network and localize the occlusion in AIS patients⁸. Alternatively, CT perfusion (CTP) imaging is typically employed to visualize tissue perfusion and evaluate the ischemic core and penumbra to identify salvageable tissue and guide treatment decisions⁸. CTP-derived assessment of the ischemic core and the ‘tissue-at-risk’ (penumbra) is considered the current gold standard to assess tissue viability, and is often used as a surrogate for collateral flow^{7,9}. However, the clinical application of CTP remains limited by several important drawbacks since CTP requires specialized acquisition protocols and post-processing software that are not uniformly available, particularly in low- and middle-resource settings. The technique is also associated with higher radiation dose, the need for repeated contrast injection, as well as longer scanning and reconstruction times, all of which can delay treatment decisions in hyperacute workflows. Moreover, CTP is highly sensitive to motion and other imaging artifacts, cardiac output, and timing of the contrast bolus, often leading to inconsistent or uninterpretable maps in routine clinical practice. Inter-vendor variability in perfusion thresholds and parameter maps further complicates reproducibility and standardization across institutions¹⁰⁻¹². On the other hand, CTA is universally available and, while rapidly acquired, provides high-resolution visualization of the cerebrovasculature and is integrated into emergent stroke workflows. Its widespread accessibility and simplicity make CTA an ideal platform for quantitative and automated assessment of collateral status and cerebrovascular morphology. Hence, leveraging CTA-derived metrics could represent a practical and scalable approach to collateral evaluation, potentially expanding advanced imaging-based decision-making to settings where CTP is not feasible.

Considering that robust collateral circulation generally lead to improved stroke outcomes, several collateral grading approaches have been developed for CTA imaging^{13,14,15-17}. However, current collateral assessment via CTA often relies on subjective grading based on visual assessment, leading to interobserver variability and delay in interpretation. Hence, developing an automated, rapid, and accurate method of

cerebrovascular collateral assessment with a comprehensive comparative evaluation CTP-based perfusion parameters within the same modeling framework can uniform the value of CTA based collateral assessment and facilitate clinical workflows and improve outcomes. Advancements in machine learning (ML) and medical image processing have paved the way for automated analysis of medical images. Few recent studies have explored automated collateral assessment from CTA images^{18,19} using radiomics, machine- and deep-learning algorithms^{20,21}. Our group has previously pioneered an automated cerebrovascular segmentation algorithm that takes raw angiography scans as input. By combining a probabilistic vessel-enhancing filter with an active-contour-based technique, the algorithm automatically segments and skeletonizes (centerlines) the cerebrovascular tree to extract geometric features and characterize vessel morphology at every point along the centerline²². This model was trained and tested using databases of MR angiography (MRA) scans²³.

Given that CTA is the most common vessel imaging modality obtained during the initial AIS evaluation, we aim to provide an objective, reproducible, and rapid assessment of the brain collateral circulation status using CTA scans. Here, we extend our U-Net based CNN model for vascular segmentation of CTA images, validated on a cohort of AIS patients. We also present a novel morphology-informed approach that uses the segmented vessel networks and their geometric features from CTA scans to automatically evaluate each patient's collateral circulation, expressed as a quantitative collateral index (qCI). We hypothesize that (i) CTA-derived automated qCI strongly correlates with clinically graded CI, and (ii) qCI is a reliable surrogate measure of the penumbra and extent of collateralization and (iii) qCI together with other morphology metrics can enhance outcome prediction in AIS patients, with comparable or even superior accuracy to CTP-derived measures, resulting in an objective, quantitative, and rapid assessment. This could have significant implications for stroke systems of care by optimizing triage, inter-hospital transfer decisions, and informing clinical decision-making for physicians, patients, and their families³⁻⁵.

2. Methods

Using raw CTA imaging, this study presents an automated pipeline for (i) Segmenting cerebral vasculature from CTA scans, (ii) Extracting cerebrovascular morphological features from CTA scans and computing a quantitative collateral index (qCI), (iii) Evaluating the predictive power of the CTA-derived qCI and morphological features for early outcomes as well as 90-day functional outcomes and (iv) Comparing the predictive performance of the quantitative collateral index and vessel morphological metrics derived from CTA against traditional CTP parameters of ischemic core, penumbra and mismatch volume. Figure 1 illustrates the overall workflow and key components of the pipeline.

2.1 Dataset and Study Population

We retrospectively analyzed prospectively collected data from 230 consecutive AIS patients who underwent EVT at the comprehensive stroke center at Inova Fairfax Medical Center (Falls Church, VA) between January 2019 and December 2023. The study was approved by the institutional review boards of Inova Fairfax Medical Center (protocol# INOVA-2024-103) and the University of California, Riverside (Protocol #30175). De-identified data were shared in accordance with the “Data Transfer and Use Agreement” established between the two institutions.

Patients with a confirmed diagnosis of AIS were enrolled in this study: if they (i) had a large or medium vessel occlusion of the anterior circulation, (ii) underwent EVT, (iii) had evaluable non-contrast CT (NCCT) and CTA images at presentation (CTP data was collected when available), (iv) had follow-up neurological assessments at 24-48 hours, and (v) had follow-up functional assessment at the time of hospital discharge and at 90 days post stroke. Exclusion Criteria for this study were incomplete imaging data, severe motion artifacts affecting segmentation, and patients missing functional outcomes. The following patient variables acquired at intake were used to train the outcome prediction model: demographics (age, sex, race, and body mass index); past medical history (smoking status, hypertension, dyslipidemia, diabetes, carotid artery disease, coronary artery disease, heart failure, and atrial fibrillation); systolic and diastolic blood pressure on arrival; the National Institutes of Health Stroke Scale (NIHSS) at presentation, 24-48 hours, and hospital discharge; laboratory data (low density lipoprotein level, blood glucose, platelet count, and neutrophil to lymphocyte ratio on admission); imaging data (side and location of acute vessel occlusion, ASPECTS score of the non-contrast head CT scan, and CTP Core, penumbra, and mismatch volume and ratio at presentation); and acute reperfusion therapy data (intravenous thrombolytics use, post-EVT recanalization status, and door- and onset- to recanalization times). Early neurological deterioration (END) and improvement (ENI) were defined as NIHSS worsening and improvement ≥ 4 points within 24–48 h from initial presentation, respectively.

2.2 Imaging data analysis and qCI estimation

For CTA, the imaging field of view (FOV) was 232mm x 232mm (variable depending on the patient’s head size) with a 512x512 matrix, resulting in 0.45mm x 0.45mm pixel size in X and Y directions (slightly variable per patient) and 1.25mm slice thickness with 0.625mm spacing between slices. Ischemic core and penumbra volumes were obtained from CT perfusion maps automatically generated by RAPID AI²⁴ and Viz.ai²⁵, using each platform’s validated thresholds (ischemic core defined as rCBF < 30% and penumbra as Tmax > 6 seconds). We automatically segmented raw imaging scans using our validated AI-based segmentation model²³. In brief, the segmentation algorithm followed a multi-step process to generate a stack of binary images or a 3D vessel network, which was then skeletonized to extract vessel centerlines and diameters, detecting vessels as small as the imaging resolution. It tracked connected tubular structures in 3D, outperforming other segmentation methods under image acquisition limitations like motion artifacts and inflow effects. After segmentation and vessel skeletonization, branching nodes were used to

compute global geometric features of the 3D vessel tree, such as the total vessel length, average vessel diameter, vascular tortuosity, fractal dimension of the vessel network, average branch length, and total number of branches of the vessel tree.

The extracted quantitative vascular morphology metrics were then utilized to automatically estimate the extent of collateralization of the patient's ipsilateral vascular network. The clinical grading which was utilized for developing and validating our method for automatic estimation of a quantitative collateral index (qCI) was as follows: 0 = ipsilateral collateral supply absent, 1 = ipsilateral collateral supply filling >0% but $\leq$ 50% of contralateral side, 2 = ipsilateral collateral supply filling >50% but <100%, and 3 = ipsilateral collateral supply 100% of contralateral side²⁶. To provide a fast and automatic calculation of the qCI, we spatially registered the CTA scans to a CT template²⁷ and then divided the segmented vascular map into ipsilateral and contralateral hemispheres. We then used the extracted patient-specific vascular geometric features from the vessel tree skeleton to compare the hemispheres. The qCI is derived from a normalized hemispheric ratio framework, where ipsilateral vascular morphologic features relating to vessel density (total vessel length, branch count, fractal complexity) are compared to the contralateral hemisphere following spatial registration. These normalized ratios are then mapped to a continuous collateral score and discretized to match the validated 0–3 grading scale. This estimated qCI was validated against ground truth manual grading by two experienced vascular neurologists. The hemispheric ratio framework reduces sensitivity to global acquisition variability, contrast timing differences, and scanner-dependent intensity variation. Additionally, our previously validated segmentation algorithm has been shown to be robust to acquisition variability and artifact as well as shown to outperform other commonly and publicly available vessel segmentation algorithms for cerebrovascular segmentation.

2.3 Outcome prediction, model comparison & statistical analysis

The modified Rankin Scale (mRS) score is the standard long-term disability outcome measure used in both stroke patient care and clinical trials. The functional status assessment using mRS is typically performed at 90 days post-stroke. The functional outcome was dichotomized into good (mRS $\leq$ 2) and poor (mRS >2) outcome groups. For this multi-feature dataset with cross-correlated predictors, we trained supervised ML models to predict dichotomized mRS outcomes using a structured dataset containing demographic, clinical, laboratory, and imaging variables, including quantitative cerebrovascular features and qCI. The dataset was randomly split into an 80% training set and a 20% blind test set, stratified by outcome class. Within the training set, 5-fold stratified cross-validation was used to generate out-of-fold (OOF) probability estimates for every patient. This provided internal validation that mimics prospective performance while reducing optimism bias. Gradient boosted decision trees (GDBT) were implemented in a Python environment (learning rate = 0.05, maximum iterations = 400, class weight = balanced). To improve probability calibration, models were wrapped with sigmoid calibration.

To evaluate the added value of the CTA-derived qCI and vascular morphological features, we compared the predictive performance of three distinct gradient-boosted tree (GBT)-based models for early neurological deterioration (END), early neurological improvement (ENI), and 90-day functional independence (mRS $\leq$ 2):

- Model A: a CTP-only model incorporating standard perfusion metrics, namely CTP mismatch volume and ratio, CTP hypo-perfusion index and the CTP cerebral blood volume (CBV) index.
- Model B: a CTA-only model incorporating the automatically assessed qCI as well as quantitative morphology metrics, namely vascular tortuosity, vessel network fractality, average diameter, average branch length, maximum branch length, total volume and total length.
- Model C: a combined model integrating both CTA- and CTP-derived features listed in the previous two models.

In addition to the three imaging-based models, we constructed a Clinical-only baseline model incorporating demographic, clinical, laboratory, and conventional imaging covariates without CTP or CTA-derived morphology features. This enabled hierarchical nested comparisons to quantify the incremental predictive value of perfusion metrics and CTA-derived vascular morphology. All models included traditional demographic, clinical, laboratory and imaging covariates as described below in Table 1 and a visualization of the different models and the predictor variables comprising them are included in Supplementary Materials (Supplemental Figure 1).

Model performance was evaluated using discrimination and calibration metrics. The following performance metrics were calculated separately for out-of-fold (OOF) and blind test predictions: discrimination (area under the receiver operating characteristic curve, AUROC), calibration (Brier score and reliability analysis), and standard performance metrics (accuracy, sensitivity, specificity, and F1 scores). Discrimination was quantified with AUROC, while calibration and overall predictive accuracy were assessed using the Brier score. To assess the comparative added value of CTA-derived features, we performed statistical testing on model differences using the DeLong test for correlated ROC curves and constructed bootstrap confidence intervals for performance metrics across 1,000 resamples. Feature importance was quantified using SHAP values to identify which CTA-derived features contributed most to predictive gain. Additionally, we calculated the Net Reclassification Improvement (NRI) to evaluate whether adding CTA-derived features to the CTP model correctly reclassified patients into higher- or lower-risk categories. This framework enabled a rigorous comparative analysis of whether CTA-based metrics alone—or in combination with CTP parameters—could match or surpass traditional perfusion-based models in predicting functional and radiographic outcomes. All analyses were performed using Python (scikit-learn, xgboost, shap, statsmodels) with statistical significance defined as $p < 0.05$.

3. Results

3.1 Segmentation and Feature Extraction

To enable real-time cerebrovascular segmentation from CTA, we developed a convolutional neural network (CNN)–based U-Net model. The model learns to extract the full intracranial arterial tree from pre-processed raw CTA scans using segmentations from our validated algorithm as ground-truth supervision. Its generalization to CTA was specifically evaluated on an independent cohort of 100 CTA studies, representing a key methodological extension beyond our earlier work ²³.

Across all subjects, the mean Dice similarity coefficient (DSC) between CNN-derived and reference vessel masks was 0.91, indicating high spatial overlap and segmentation accuracy. The DSC was first computed per axial slice for each subject and subsequently averaged across the cohort. To ensure that the network preserved morphologic fidelity beyond voxel-level overlap, we compared key vascular geometric features between CNN-derived and reference segmentations. The mean absolute error across all features was below 8%, including total vessel length (5.4%), number of branches (3.9%), total vascular volume (4.2%), and mean vessel diameter (4.1%). These results demonstrate that the model reliably captures both large- and small-caliber vascular structures and maintains geometric consistency with expert-validated segmentations. Table 2 reports the average quantitative metrics extracted from the segmented 3D vessel networks in the 230 AIS patients.

3.2 Collateral Index Estimation

Our CTA-derived qCI estimation method was validated against clinically graded CI for 230 AIS patients from the dataset (Figure 2). The accuracy of estimation was 0.863. The Pearson correlation coefficient (R) and Spearman rho metric were both determined to be 0.880 and 0.877, respectively, and provide a measure of strength and direction of the linear relationship between the manual grading and qCI estimation. Given the metrics have an inherent dependence on inter-rater reliability, in order to correct for chance agreement, the Cohen’s Kappa measure was calculated to be 0.786.

A confusion matrix for the predicted versus ground truth CI is shown in Figure 3. We further dichotomized the collateral index grading into “good” (CI = 2 or 3) and “poor” (CI = 0 or 1) collateral circulation, to evaluate their clinical significance. The accuracy of prediction/estimation of this dichotomized CI grading was 0.938 with a specificity of 0.919, sensitivity of 0.943, F1 score of 0.958, and the AUROC of 0.945.

3.3 Outcome Prediction

Three gradient-boosted tree (GBT)–based models were trained to predict multiple post-stroke outcomes, including END, ENI, and 90-day functional independence (mRS $\leq$ 2). Class distributions for the modeled endpoints were as follows: END occurred in 19.6% (N=44) patients, ENI occurred in 57%% (N=132) and 48% of the patients had a good outcome on the mRS at the 90 day follow up (N=111). Model A and B incorporated only

CTP- and CTA-derived metrics, respectively, with traditional demographic, clinical, and imaging variables. Model C combined both CTA- and CTP-derived measures. Each model was trained using a stratified 80–20 train–test split, with fivefold out-of-fold (OOF) validation to ensure stability and reduce bias. Table 3 lists the model performance metrics for all three models for the mRS end point.

When compared hierarchically, the Clinical-only model demonstrated lower discrimination relative to all imaging-augmented models (PPV 0.61, AUROC 0.6 for mRS). Across outcomes, CTA-only model B consistently achieved moderately higher discriminatory performance than model CTP-only model A, reflected by higher AUROC values and balanced sensitivity–specificity profiles (PPV values reported in Supplemental Table 1). Model B also outperformed Model A in END prediction, indicating that vascular topology provides complementary information beyond perfusion parameters. Both CTP- and CTA-only models performed equally in predicting ENI. Not unexpectedly, Brier scores were lowest for Model C across all outcomes. Brier scores were also lower for model B as compared to model A, reflecting superior calibration and reliability of predicted risk probabilities for worse outcomes (mRS>2). Accuracy and F1-scores also improved modestly with the addition of morphologic and collateral metrics. Pairwise AUROC comparisons between the three models were performed using the DeLong test for correlated ROC curves (Figure 3) on the held-out test set. This nonparametric approach accounts for correlation arising from evaluating the same patient cohort across multiple models. Model C outperformed Model A for outcome prediction ($p < 0.05$ for END, ENI, and 90-day mRS). The prediction accuracy also improved from Model A to Model B. Figure 4 shows the ROC curves of all models for two outcomes – mRS and END as well as a Forest plot to show the DeLong test results.

To evaluate the clinical utility of adding morphology + qCI features, the Net Reclassification Improvement (NRI) metric was computed, reported in Table 4. NRI quantifies how many patients were correctly reclassified into higher- or lower-risk strata when moving from one model to another. Model C demonstrated a positive NRI relative to Model A for all outcomes, indicating that it correctly reclassified a substantial proportion of patients into more appropriate chance of occurrence categories for poor and good outcomes, particularly those with intermediate predicted probabilities under the model with just CTP metrics. Our results show that quantitative CTA-derived qCI and morphology features are comparable and often outperform CTP-based prognostic markers. SHAP feature importance plots for comparing the contribution of CTA and CTP features are included in Supplemental Figure 2.

4. Discussion

It is widely known that brain's collateral circulation status influences AIS outcomes. A better understanding of collateral status can also inform hemodynamic support before, during, and even after EVT. Currently, collateral circulation estimation requires visual

inspection of CTA images by expert clinicians, rendering it a fairly inefficient task within the high-pace stroke triage workflow. On the other hand, for treatment decisions, the salvageable tissue is most commonly estimated by CTP imaging, and attempts have been made for automatic collateral assessment using CTP. However, perfusion data is limited by its availability, acquisition time, and susceptibility to post-processing variability. Consequently, routine collateral assessment remains underutilized in acute stroke workflows, despite its strong association with treatment response and long-term outcomes. CTA is routinely acquired as part of the standard-of-care evaluation for suspected AIS. Beyond simply identifying the site of occlusion, CTA contains rich quantitative information about the vascular network's topology and geometry, which reflects the underlying collateral capacity. Leveraging these widely available datasets enables improved assessment of collateral status.

Prior work has explored automatic collateral assessment, primarily focusing on regional enhancement patterns or automated visual-grade replication. In contrast, our approach quantifies vascular architecture for hemispheric morphologic comparison, generating a structural quantitative collateral index (qCI) derived from vessel topology rather than intensity-based features. Unlike manual grading approaches, the automated qCI computation is fully objective, scalable, and rapid, thereby having the possibility of seamless integration into clinical workflows to aid decision making. Importantly, qCI should be interpreted as a structural surrogate of hemispheric collateral reserve rather than a direct measure of cerebral blood flow. Unlike CTP metrics, which quantify dynamic tissue perfusion, qCI reflects the anatomical density, branching complexity, and geometric integrity of the collateral circulation.

We compared three ML models for outcome prediction, that demonstrate that CTA-derived vascular features can capture physiologically meaningful information about tissue perfusion and viability. The incrementally enhanced outcome prediction performance, accompanied wide availability of CTA, can contribute to democratizing the assessment, particularly in remote areas and low-resource settings. Importantly, in scenarios where CTP imaging is obtained, combining CTA features with perfusion parameters yields superior discrimination and can complement CTP metrics. These findings establish CTA a complementary modality that strengthens prognostic modeling when used alongside CTP and potentially a stand-alone alternative when perfusion imaging is unavailable. Quantitatively, Net Reclassification Improvement (NRI) analysis showed that the combined model more accurately reclassified patients than the CTP-only model, particularly by correctly upgrading true events and downgrading non-events—reflecting meaningful gains in both sensitivity and specificity when qCI and CTA morphology were added. Decomposition of the NRI components confirmed that most of the improvement stemmed from better identification of high-risk patients, indicating that CTA-derived vascular and collateral features capture prognostically relevant information not represented in CTP metrics alone. The positive UpEvt values highlight that patients who ultimately had poor outcomes were more consistently assigned to higher-risk categories by CTA-informed models. Consistent with this, DeLong testing demonstrated statistically significant AUROC improvements for the combined model compared with CTA- or CTP-

only models ($p < 0.05$), confirming that the performance gains were robust and not due to chance.

Given that CTA is already part of standard acute stroke imaging protocols in most institutions, this approach could enable more comprehensive assessment without longer acquisition times or requiring additional contrast. This has significant implications for streamlined imaging workflows, decision-making in low-resource environments, and faster triage where CTP is unavailable or delayed. Furthermore, automating collateral assessment eliminates subjective variability inherent to manual scoring systems and enables standardized, quantitative evaluation across centers and scanner platforms, with potential implications for future multicenter studies. Integrating qCI into AIS workflows can also support other time-sensitive decisions that aligns with existing workflows. An objective collateral assessment can inform individualized hemodynamic management, including the need for blood pressure augmentation in patients with poor collateralization. To our knowledge, this study is the first to demonstrate the feasibility and prognostic power of an automated CTA-derived qCI, benchmarked directly against CTP-based metrics, using rigorous machine learning validation and statistical comparison.

Although collateral status, perfusion metrics, and admission NIHSS are physiologically related, they capture distinct biological constructs. NIHSS reflects clinical deficit, CTP reflects tissue-level hemodynamic compromise, and CTA-derived morphology quantifies structural collateral reserve and vascular architecture – reducing the collinearity or leakage from these features. The hierarchical modeling confirms that CTA-derived features provide additive predictive value beyond these partially overlapping domains. Additionally, GBDT models are relatively robust to multicollinearity and do not assume predictor independence, as splits are selected sequentially based on incremental information gain, thereby the reason for choosing them. Performance evaluation was conducted on a strictly held-out test set, reducing the risk of optimistic bias arising from correlated predictors.

This study has several limitations. This pilot study was limited to retrospective analysis of a smaller database ($n=230$) of patients from a single comprehensive stroke center, which may limit generalizability to broader or more diverse clinical settings. CTA acquisition protocols are standardized at our institution; however, scanner hardware, contrast timing, and reconstruction parameters vary across centers and may influence segmentation performance and morphology measurements. The differences in post-processing algorithms and perfusion thresholds of CTP across commercially available vendors may introduce variability in the comparison models. Future work should focus on external validation across institutions and prospective evaluation of larger patient datasets to confirm the robustness and clinical utility of this approach.

5. Conclusions

This study demonstrates that automated CTA-based cerebrovascular morphology and quantitative collateral index (qCI) provide predictive power comparable to, and in some

cases exceeding, CTP-derived metrics for post-stroke outcome prediction. Integrating these features yields an improvement in model performance, calibration, and risk reclassification. By leveraging readily available CTA data, our approach offers a scalable, time-efficient, and objective framework for assessing collateral status—aiding broader implementation of quantitative collateral imaging in routine stroke care.

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References

1. Go, A. S. *et al.* Heart disease and stroke statistics--2013 update: a report from the American Heart Association. *Circulation* **127**, e6–e245 (2013).
2. Martinez-Gutierrez, J. C. *et al.* Automated Large Vessel Occlusion Detection Software and Thrombectomy Treatment Times: A Cluster Randomized Clinical Trial. *JAMA Neurol* **80**, 1182–1190 (2023).
3. Fang, G., Huang, Z. & Wang, Z. Predicting Ischemic Stroke Outcome Using Deep Learning Approaches. *Front. Genet.* **12**, (2022).
4. Johnston, K. C. *et al.* A Predictive Risk Model for Outcomes of Ischemic Stroke. *Stroke* **31**, 448–455 (2000).
5. Kadyrova, I. A. *et al.* PREDICTION OF OUTCOMES AFTER STROKE: A SYSTEMATIC REVIEW. *Ekologiya cheloveka (Human Ecology)* **22**, 55–64 (2015).

6. Puig, J. *et al.* From 'Time is Brain' to 'Imaging is Brain': A Paradigm Shift in the Management of Acute Ischemic Stroke. *J Neuroimaging* **30**, 562–571 (2020).
7. Jung, S. *et al.* Relevance of the cerebral collateral circulation in ischaemic stroke: time is brain, but collaterals set the pace. *Swiss Med Wkly* **147**, w14538 (2017).
8. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association | Stroke.
<https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000211>.
9. Liebeskind, D. S. Collateral circulation. *Stroke* **34**, 2279–2284 (2003).
10. Peerlings, D. *et al.* Standardizing the estimation of ischemic regions can harmonize CT perfusion stroke imaging. *Eur Radiol* **34**, 797–807 (2024).
11. Peerlings, D. *et al.* Probability maps classify ischemic stroke regions more accurately than CT perfusion summary maps. *Eur Radiol* **32**, 6367–6375 (2022).
12. Demeestere, J., Wouters, A., Christensen, S., Lemmens, R. & Lansberg, M. G. Review of Perfusion Imaging in Acute Ischemic Stroke. *Stroke* **51**, 1017–1024 (2020).
13. Menon, B. K. *et al.* Assessment of Leptomeningeal Collaterals Using Dynamic CT Angiography in Patients with Acute Ischemic Stroke. *J Cereb Blood Flow Metab* **33**, 365–371 (2013).

14. Padhi, R. *et al.* Collateral score as a prognostic marker in acute anterior circulation stroke: A multiphase computed tomography angiography analysis. *JNRP* **16**, 256–263 (2025).
15. Vagal, A. *et al.* Association Between CT Angiogram Collaterals and CT Perfusion in the Interventional Management of Stroke III Trial. *Stroke* **47**, 535–538 (2016).
16. Tan, I. Y. L. *et al.* CT Angiography Clot Burden Score and Collateral Score: Correlation with Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery Infarct. *American Journal of Neuroradiology* **30**, 525–531 (2009).
17. Comparison of Computed Tomography Perfusion and Multiphase Computed Tomography Angiogram in Predicting Clinical Outcomes in Endovascular Thrombectomy | Stroke.
<https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.122.038576>.
18. Aktar, M., Xiao, Y., Tampieri, D., Rivaz, H. & Kersten-Oertel, M. A Radiomics-Based Machine Learning Approach to Assess Collateral Circulation in Ischemic Stroke on Non-contrast Computed Tomography. in *Multimodal Learning for Clinical Decision Support and Clinical Image-Based Procedures* (eds Syeda-Mahmood, T. *et al.*) 24–33 (Springer International Publishing, Cham, 2020). doi:10.1007/978-3-030-60946-7_3.
19. Jiang, J. *et al.* Clot-based radiomics model for cardioembolic stroke prediction with CT imaging before recanalization: a multicenter study. *Eur Radiol* **33**, 970–980 (2023).

20. Automatic Collateral Scoring From 3D CTA Images.
<https://ieeexplore.ieee.org/abstract/document/8960439>.
21. Kim, Y.-C. *et al.* A Deep Learning-Based Automatic Collateral Assessment in Patients with Acute Ischemic Stroke. *Transl. Stroke Res.* **14**, 66–72 (2023).
22. Deshpande, A. *et al.* Automatic segmentation, feature extraction and comparison of healthy and stroke cerebral vasculature. *Neuroimage Clin* **30**, 102573 (2021).
23. Deshpande, A. *et al.* End to end stroke triage using cerebrovascular morphology and machine learning. *Front Neurol* **14**, 1217796 (2023).
24. A benchmarking tool to evaluate computer tomography perfusion infarct core predictions against a DWI standard - Carlo W Cereda, Søren Christensen, Bruce CV Campbell, Nishant K Mishra, Michael Mlynash, Christopher Levi, Matus Straka, Max Wintermark, Roland Bammer, Gregory W Albers, Mark W Parsons, Maarten G Lansberg, 2016. <https://journals.sagepub.com/doi/full/10.1177/0271678X15610586>.
25. Automated detection of intracranial large vessel occlusions using Viz.ai software: Experience in a large, integrated stroke network - Karamchandani - 2023 - Brain and Behavior - Wiley Online Library.
<https://onlinelibrary.wiley.com/doi/full/10.1002/brb3.2808>.
26. Dundamadappa, S., Iyer, K., Agrawal, A. & Choi, D. J. Multiphase CT Angiography: A Useful Technique in Acute Stroke Imaging—Collaterals and Beyond. *American Journal of Neuroradiology* **42**, 221–227 (2021).

27. Muschelli, J. A Publicly Available, High Resolution, Unbiased CT Brain Template. in *Information Processing and Management of Uncertainty in Knowledge-Based Systems* (eds Lesot, M.-J. et al.) 358–366 (Springer International Publishing, Cham, 2020). doi:10.1007/978-3-030-50153-2_27.

Table 1. A comprehensive list of all the demographic, clinical, laboratory, imaging and treatment variables used as predictors in all 3 models.

Demographics, clinical variables and history	Age
	Sex
	RACE
	BMI
	baseline modified Rankin Score
	Baseline TICI score
	Hypertension – y/n
	Diabetes – y/n
	Dyslipidemia – y/n
	Carotid Stenosis – y/n
	CAD/MI – y/n
	Atrial Fibrillation – y/n
	Heart failure – y/n
	Previous stroke – y/n
	Smoking history
	Systolic blood pressure on arrival
	Diastolic blood pressure on arrival
	Mean Arterial Pressure on arrival
	NIHSS on arrival
Laboratory variables	Lipid (LDL)
	Lipid cholesterol
	Blood glucose on admission
	Neutrophil absolute count
	Lymphocyte absolute count
	White Blood Cell count
	Platelet count
	Creatinine at admission
	Troponin at admission
	Sodium at admission
Imaging variables	Location & side of occlusion
	ASPECTS
Acute reperfusion	IV thrombolytics administered
	Final TICI score

therapy - related variables	Door to recanalization time
	Onset to recanalization time
	Drugs administered

Table 2. The quantitative metrics extracted from the segmented 3D vessel networks in the 230 AIS patients.

Global vascular features	Average ± Standard Deviation
Total length (m)	2.09 ± 0.67
Number of branches	153 ± 59
Average branch length (m)	11.29 ± 2.52
Maximum branch length (m)	108.12 ± 8.11
Average diameter (mm)	2.40 ± 0.41
Total volume (ml)	52.12 ± 22.12
Fractal Dimension	1.71 ± 0.29
Vascular Tortuosity (rad/cm)	6.04 ± 2.11

Table 3. Model Performance Metrics for prediction of 90-day functional independence

Model	Accuracy	Sensitivity	Specificity	PPV	AUROC	Brier score	F1 score
A. CTP Perfusion Metrics	0.66	0.59	0.72	0.67	0.645 (95% CI, 0.60-0.68)	0.295	0.61
B. CTA Collateral Index/ morphology	0.76	0.61	0.86	0.80	0.730 (95%CI, 0.69-0.78)	0.203	0.61
C. Combined Model (CTA + CTP)	0.79	0.63	0.88	0.83	0.781 (95% CI, 0.71-0.84)	0.178	0.62

Table 4. Net Reclassification Improvement Scores for model A (CTP) to model C (CTP+A) and for model A to model B (CTA).

NRI →	CTP_to _CTP+A _UpEvt	CTP_to_ CTP+A_ DownEvt	CTP_to_C TP+A_Up NonEvt	CTP_to_CT P+A_Down NonEvt	CTP_to _CTA_ UpEvt	CTP_to_ CTA_Do wnEvt	CTP_to _CTA_U pNonEvt	CTP_to_C TA_Down NonEvt
mRS	0.5909	0.10909	0.289	0.6453	0.6112	0.1982	0.26	0.49
END	0.5555	0.24444	0.368	0.6315	0.8888	0.1111	0.221	0.578
ENI	0.5925	0.40740	0.251	0.5511	0.5555	0.444	0.55	0.45

UpEvt – Upward reclassification for events (poor outcome)

DownEVT – Downward reclassification for events

UpNonEvt – Upwards reclassification for non-events (good outcome)

DownNonEvt – Downward reclassification for non-events

Figure legends:

Figure 1. Overall pipeline summarizing the end-to-end automated process for CTA based collateral quantification, vessel morphology extraction and multivariate outcome prediction, illustrating how the CTA-derived framework was compared against the traditional CTP-based metrics for patient prognostication.

Figure 2. The four varying levels of collateral circulation, measured automatically, shown for visual comparison.

Figure 3. The confusion matrix (*left*) showing the manual collateral grading (ground truth) vs. the estimated qCI derived from CTA based morphology metrics, and the ROC curve of the prediction (*right*).

Figure 4: Receiver operating characteristic (ROC) curves comparing the predictive performance of CTA-based Collateral Index Model, CTP-based Perfusion Model and a combined model with all predictors. The bottom panel shows the Forest plot for the DeLong test performed for model comparison and also includes the Forest plot interpretation guidelines. The outcomes predicted include the dichotomized 90-day mRS, Early Neurological Deterioration (END) and Early Neurological Improvement (ENI).