The rationale for recanalization therapies in acute ischemic stroke is to preserve brain from the development of ischemic damage by freezing the progression of ongoing irreversible infarct. The paradigm time is brain refers to the fact that shorter time of ischemia is generally related to smaller final infarct volumes. Recent studies have shown that successful early recanalization leads to improved functional outcomes through a reduction in final infarct volumes. The advanced neuroimaging mismatch concept for patient selection for revascularization therapies relies on the possibility of identifying the ischemic brain tissue that may be saved from definitive infarct by means of a timely reperfusion. However, advanced neuroimaging also offers the possibility of identifying on admission the irreversibly damaged brain that will unavoidably develop infarction despite a timely reperfusion. Because final infarct volume is a strong predictor of long-term outcome, we aimed to determine the predictive value of infarct core volume identified on admission as a predictor of final infarct volume whether recanalization is achieved or not. Moreover, we aimed to set the maximal admission lesion volume compatible with favorable outcome (MALCOM) to use it as a selection tool in future endovascular treatment candidates.

Methods
We studied consecutive patients with internal carotid artery/middle cerebral artery occlusion who received at baseline a combination of multiparametric computed tomography/magnetic resonance imaging, who underwent endovascular procedures. Admission infarct core was measured on initial cerebral blood volume–computed tomography perfusion or diffusion weighted imaging–magnetic resonance imaging. We defined percentage of lesion growth (final lesion admission core/admission core) and MALCOM: cutoff admission core volume above which probability of modified Rankin Scale 0 to 2 is <10%. A regression model adjusted for age and recanalization showed that the only predictor of favorable outcome was having admission core lesion below MALCOM (OR: 9.3, 95% CI: 1.9–46.4; P<0.01). Analysis according to imaging modality showed that computed tomography–cerebral blood volume allowed larger MALCOM (42 mL) than magnetic resonance–diffusion weighted imaging (29 mL). In octogenarians, MALCOM (15 mL) was lower in younger patients (40 mL).

Conclusions—Admission lesion core is associated with final infarct volume and is a strong predictor of favorable outcome. MALCOM according to imaging modality and patient age could be set and used on admission to select candidates for endovascular procedures.

Key Words: blood volume ■ endovascular procedures ■ magnetic resonance imaging ■ stroke ■ thrombectomy
Imaging Protocol

Admission core volume was later measured on baseline imaging: cerebral blood volume (CBV) lesion on CT Perfusion (CTP) or diffusion-weighted imaging (DWI) lesion on MRI. MRI was performed on a 1.5 Tesla imaging systems Magnetom Avanto (Siemens, Erlangen, Germany), including axial single-shot Echoplanar DWI (TR: 4300 ms, TE: 109 ms, slice thickness: 5 mm, interslice gap: 1.5 mm, and matrix size: 150x150).

CTP was performed on a Definition AS Siemens (Siemens, Erlangen, Germany) 128-section scanner with the following parameters: collimator of 32x1.5 mm, 80 kVp, and 200 mAs with total coverage of 86 mm. The plane of imaging was parallel to the floor of the anterior cranial fossa starting just above the orbits. Thirty cycles were obtained with a total scan time of 46 s. CTP data were analyzed by Syngo MMWP station (Siemens) using VPCT perfusion software, which based on preset values of cerebral blood flow and CBV automatically calculate the nonviable and penumbra tissue. The anterior cerebral artery was manually used for arterial input function.

Image Analysis

All images were transferred to a separate workstation for analysis using a third party DICOM viewer (Osirix 64-bit; Pixmeo, Geneva, Switzerland). The baseline infarct core volume (mL) was calculated based on MRI–DWI or CTP using a threshold of 1.5 mL/100 mL blood volume on CBV. Final infarct volume on follow-up imaging at 24 to 48 hours was measured on noncontrast CT using a semiautomated lesion outline and segmentation process. Variable window width and center level settings were used for optimal ischemic hypodensity detection with noncontrast CT and DWI images. All images were reviewed by 2 neuroradiologists blinded to clinical information. Absolute infarct growth was calculated as: final infarct volume−admission core volume. Relative infarct growth was defined as: absolute infarct growth/admission core volume×100. No infarct growth was defined by an absolute infarct growth ≥0.

We defined MALCOM as the cutoff admission core volume (CBV or DWI) above which the probability of mRS 0 to 2 is <10%.

Statistical Analysis

Descriptive and frequency statistical analyses were obtained using SPSS 17.0 software. Categorical variables are presented as absolute values and percentages, and the continuous variables are presented as median±SD if normally distributed or median (interquartile intervals) if not normally distributed. Statistical significance for intergroup differences was assessed by Pearson χ² or Fisher exact test for categorical variables and by Student t or Mann–Whitney U test for continuous variables.

Multivariable logistic regression analyses were performed for each group to determine factors that could be considered as independent predictors of favorable outcome.

Variables showing P<0.1 in univariate analysis were included in the multivariate model. A probability value of <0.05 was considered significant for all tests.

Results

Fifty-seven patients were studied (29 MRI and 28 CTP). Patient characteristics are shown in Table. Median time from symptom to imaging, min 268 (120–332). Time from symptom to end procedure 365 (300–450). Complete recanalization was assessed by Pearson χ² or Fisher exact test for categorical variables and by Student t or Mann–Whitney U test for continuous variables.

Variables showing P<0.1 in univariate analysis were included in the multivariate model. A probability value of <0.05 was considered significant for all tests.

Figure 1. Admission infarct core distribution according to 3-month outcome and maximal admission lesion volume compatible with favorable outcome (MALCOM) threshold. Only 10% of patients with admission lesion beyond MALCOM will achieve favorable outcome. mRS indicates modified Rankin Scale.
symptom onset to imaging was 268 minutes (interquartile range, 120–332). After endovascular procedure, the rate of complete recanalization was 77%. Median time from imaging to recanalization was 116 minutes (interquartile range, 67–178). For all patients, mean infarct core volume was 28±22 mL. There were no differences in core volume between patients who achieved further recanalization and those who did not (30.7±24 versus 23.4±19.9 mL; P=0.37). At 24 hours, mean infarct volume was 64±97 mL, absolute lesion growth was 37±92 mL, and relative lesion growth was 25%. The overall rate of favorable outcome at 3 months was 45% (mRS 0–2). In nonrecanalizers, final infarct was larger (136±163 versus 48±59 mL; P=0.01). The absolute infarct growth at 24 hours was substantially smaller if recanalization was achieved (29±77 versus 118±182 mL; P=0.04), and the relative infarct growth was 16.7% if recanalization was achieved versus 198.3% with no recanalization (P<0.01). No infarct growth (≤0 mL) was observed in 18 patients (31.6%), and complete recanalization was achieved in all of them.

Patients with favorable outcome had a smaller final infarct volume (14.1±12.8 versus 109.9±116.5; P>0.01).

Overall, the MALCOM was 39 mL (90% of patients with final mRS 0–2 had a core lesion <39 mL, Figures 1–3). A total of 72.4% of the patients had an admission core within MALCOM. When recanalization was achieved, ≤64% of patients within MALCOM (<39 mL) achieved favorable outcome, whereas despite recanalization only 12% of patients beyond MALCOM (>39 mL) achieved mRS 0 to 2 (P=0.01). A regression model adjusted for age and recanalization showed that the only predictor of favorable outcome was having an admission core lesion below MALCOM (odds ratio, 9.3; 95% confidence interval, 1.9–46.4; P<0.01).

Analysis according to imaging modality showed that CT–CBV allowed larger MALCOM (42 mL) than MR-DWI (29 mL). In octogenarians, MALCOM (15 mL) was lower than in younger patients (40 mL).

**Discussion**

Our study, in line with previous findings, confirms that final infarct volume is a good predictor of long-term outcome. Since final infarct volume can be well predicted on admission by the core lesion in those patients in which recanalization is achieved, we could create and define the concept of MALCOM. Recanalization is becoming a frequent phenomenon with the last generation thrombectomy devices. In our study, 3 of 4 patients achieved a complete recanalization and in these cases the observed admission core lesion barely grew a 16% in the follow-up imaging.

If the admission core volume was below MALCOM (39 mL) and recanalization was achieved, almost 2 of 3 patients achieved a good outcome. However, if the admission core lesion was beyond MALCOM, the chances of recovery were low even if recanalization was achieved. Hypothetically, if all patients receive thrombectomy independently of their core lesion, all potential responders will be treated at the price of treating too many nonresponders. Our study aims to introduce the concept of MALCOM to explore how far can we go reducing the maximal core lesion without substantially denying treatment to potential responders who will regain a good functional outcome after thrombectomy (<10% with the MALCOM definition in this study).

Therefore MALCOM, showed to be a powerful independent predictor of outcome available on admission, can be used as a reliable tool to identify potential responders to thrombectomy. Moreover, the MALCOM concept could be used in the design of future clinical trials, redefining as needed some parameters; that is, for young patient with severe strokes, the MALCOM definition could be reformulated to maximal core
lesion compatible with mRS≤3, leading to a larger acceptable core threshold, and opening the door to optimize the inclusion criteria for thrombectomy according to patient characteristics. In our study, the time from imaging to reperfusion was 116 minutes; recent studies showed that this timeframe can be substantially reduced and may possibly allow to increase the MALCOM threshold.

Previous studies showed that pretreatment noncontrast CT ASPECTS can be used to select those patients who will benefit from endovascular procedures. 11 In a similar approach to the MALCOM concept, this study found that for patients with a baseline ASPECTS score 8 to 10 the probability of achieving a mRS 0 to 2 was 46%. In our study, multimodal admission imaging was able to double the predictive power of good outcome ≤90%. Importantly, this could be performed without discarding a large number of candidate patients because on admission ≤73% of patients presented an infarct core below MALCOM (<39 mL).

Our study also showed that the MALCOM concept can be fine-tuned according to patient characteristics or the imaging method. It is well known that older patients will allow smaller final infarct volumes to achieve a good outcome. In that sense, MALCOM also seemed to be smaller for octogenarians in our study. Also, in our study, CT perfusion techniques seemed to overestimate the initial core volume when compared with MRI. Using a different CTP parameter, such as relative cerebral blood flow, to determine core on admission4–10 may improve accuracy. Final infarct location and topology is also a factor whose influence on outcome was recently described.17 Future larger studies will also have to address whether the predictive power of MALCOM is influenced by CTP parameters, admission core topology, and the advantages of using models combining location and extension of core lesions.

Our present acute stroke neuroimaging protocol includes a complete multiparametric study on admission for all patients; however, initially only patients with unknown or late onset strokes underwent perfusion imaging. Thus, it is possible that patients with a short time from symptom onset are underestimated in this study. This fact should be considered when applying our findings to patients with an early time from symptom onset, especially if CTP is used. It is possible that the thresholds that better identify irreversible core lesion volumes on CTP may change over time, so a specific threshold depending on the time from symptom onset to imaging may be applied for each patient. Finally, the measured core lesion may also vary based on the image processing software used. Further investigations in this sense are being addressed.

Conclusions

Admission lesion core is associated with final infarct volume and is a strong predictor of favorable outcome. MALCOM according to imaging modality and patient age could be set and used on admission to select candidates for endovascular procedures.

Disclosures

None.

References

Maximal Admission Core Lesion Compatible With Favorable Outcome in Acute Stroke Patients Undergoing Endovascular Procedures
Marc Ribo, Alejandro Tomasello, Miguel Lemus, Marta Rubiera, Carla Vert, Alan Flores, Pilar Coscojuela, Jorge Pagola, David Rodriguez-Luna, Sandra Bonet, Marian Muchada, Alex Rovira and Carlos A. Molina

Stroke. 2015;46:2849-2852; originally published online August 20, 2015; doi: 10.1161/STROKEAHA.115.010707
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/46/10/2849

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/