Assessment Of Collateral Pathways In Acute Ischemic Cerebrovascular Stroke Using A Mansour Grading Scale; A New Scale, A Pilot Study

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Citation
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Abstract
Objective:
The purpose of this study was to assess collateral pathways in acute ischemic stroke using a new grading scale (Mansour Scale) and correlating the findings with different risk factors, clinical outcome and recanalization rate with endovascular management.

Cerebral collateral circulation is an indirect pathway for restoration of blood flow to ischemic areas in case of obstruction of their primary blood supply. Assessment of cerebral collaterals is of utmost importance in the setting of acute stroke as it carries diagnostic, therapeutic and prognostic values. Our study aimed at assessing collaterals in acute ischemic stroke using a new grading scale (Mansour Scale) developed in our department and correlating the angiographic findings with different stroke risk factors and with clinical outcome. The new scale assesses collaterals regarding their type, pattern, site of occlusion, robustness and functionality and outcome is assessed using NIHSS scale.

Conclusion:
We concluded that better collateralization by our new scale is associated with better recanalization and better clinical outcome. We found no effect of different stroke risk factors studied on collateral development.

INTRODUCTION
The cerebral collateral circulation refers to the subsidiary network of vascular channels that stabilize cerebral blood flow when principal conduits fail. Restriction of the blood flow is the major cause of recruitment of these collaterals in acute ischemic stroke. Effective perfusion to the ischemic area results from the net balance between residual anterograde flow across the obstructive lesion and the flow through collateral routes—often using retrograde flow via auxiliary vessels (1).

Three principal pathways constitute cerebral collaterals; Circle of Willis, Leptomeningeal Collaterals and Extracranial-Intracranial anastomosis. Several techniques can provide insight into collateral flow in patients with ischemic stroke using different imaging modalities, but conventional angiography is superior in many aspects regarding spatial and temporal resolution and is the only modality that illustrates retrograde leptomeningeal collateral flow reliably and in detailed fashion (2).

In the literature, there are over eighty publications describing 63 methods for grading collateral flow on the basis of conventional angiography. However, these methods measure the general status of collaterals and not actual anatomical connections and most of them are unvalidated and contain many flaws. The need for a reliable grading scale for proper assessment of collaterals is mandatory. In this study we aimed at assessing collateral pathway in acute stroke using a newly invented classification/ grading scale (Mansour Scale) and correlating the findings with different risk factors, recanalization and clinical outcome (3).

SUBJECTS AND METHODS
We conducted a prospective study that enrolled 30 patients with acute ischemic insults (stroke or transient ischemic attacks) with different neurological symptoms, severity and risk factors who presented to different stroke centers in Alexandria and Tanta. All our patients underwent a complete history taking, thorough general and neurological examination, assessment of severity using National Institutes of Health Stroke Scale (NIHSS) scale, routine laboratory
investigations and different neuroimaging modalities (CT or MRI). An informed consent was taken from all patients. All our patients underwent catheter angiography either as a primary endovascular intervention for recanalization (IA-rtPA injection or mechanical thrombectomy) or as a secondary preventive measure (angioplasty or stenting). Collateral status was assessed according to a Mansour Scale (Appendix) and a grading score was given to each type of collaterals according to the next table (Table 1). Collaterals were correlated with different risk factors, recanalization rate and clinical outcome. Our new grading scale assessed collaterals regarding their type, pattern, site of occlusion, robustness and functionality.

**Table 1**

Mansour Scale for collaterals grading

<table>
<thead>
<tr>
<th>Mansour Collaterals Grading Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- Recruitment of collaterals:</td>
</tr>
<tr>
<td>No collaterals</td>
</tr>
<tr>
<td>One branch recruited</td>
</tr>
<tr>
<td>More than one branch recruited</td>
</tr>
<tr>
<td>2- Extension of filling:</td>
</tr>
<tr>
<td>No filling</td>
</tr>
<tr>
<td>One distal branch filled</td>
</tr>
<tr>
<td>More than one distal branch filled</td>
</tr>
<tr>
<td>No area of capillary free zone</td>
</tr>
<tr>
<td>3- Laterality:</td>
</tr>
<tr>
<td>No supply</td>
</tr>
<tr>
<td>Unilateral supply</td>
</tr>
<tr>
<td>Bilateral supply</td>
</tr>
<tr>
<td>4- Source of supply:</td>
</tr>
<tr>
<td>No source for supply</td>
</tr>
<tr>
<td>Externally Dependent</td>
</tr>
<tr>
<td>Internally Dependent</td>
</tr>
<tr>
<td>Leptomeningeal supply</td>
</tr>
<tr>
<td>Willian supply</td>
</tr>
<tr>
<td>Mixed Dependence (External + Leptomeningeal or Willian)</td>
</tr>
<tr>
<td>Mixed Dependence (External + Leptomeningeal + Willian)</td>
</tr>
<tr>
<td>5- Modified items:</td>
</tr>
<tr>
<td>a- Presence of impending pathology in the way of collaterals:</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>b- Presence of low perfusion state by neuro-imaging:</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

CT-angiography revealed a marked stenosis of the left middle cerebral artery with a length of 10 mm (Figure 2).

**Figure 2**

CTA-SI (axial view) showing severe stenosis of left MCA (10 mm length)

IA thrombolysis was considered, but the symptoms rapidly decreased and after two hours (during the DSA) there was only slight dysphasia remaining. The initially considered thrombolysis was not carried out and the patient was put on aspirin.
36 hours after admission the patient again developed dysphasia and facial paresis. NECT showed no signs of infarction and CT-angiography showed increased stenosis. CTP showed slightly increased CBV in the left middle cerebral artery (MCA) territory and reduction of CBF in the border-zone mainly between the anterior cerebral artery (ACA)/MCA and the posterior cerebral artery (PCA)/MCA territories on the left side. MTT was prolonged in the entire distribution area of the MCA (Figure 3).

**Figure 3**
CTP showing slightly increased CBV in the left middle cerebral artery (MCA) territory (A) and reduction of CBF in the border-zone mainly between the anterior cerebral artery (ACA)/MCA and the posterior cerebral artery (PCA)/MCA territories on the left side (B). MTT was prolonged in the entire distribution area of the MCA (C).

DWI showed small acute infarcts with a rosary-like distribution in the deep white matter along the lateral ventricle on the left side (Figure 4).

**Figure 4**
DWI showing multiple hyperintensities in a rosary-like distribution involving deep white matter along the lateral ventricle on the left side.

Because of increasing symptoms on the following day, a successful balloon dilatation of the stenosis was carried. After treatment the patient rapidly improved. MR-Perfusion performed three days after treatment showed normalized perfusion (Figure 5).

**Figure 5**
Serial DSA images showing severe stenosis of left MCA (a), balloon angioplasty (b-e) and successful recanalization (f).

Collaterals:
(A) ACA-MCA Leptomeningeal collaterals
Left internal carotid angiogram, AP oblique view, demonstrates severe stenosis of the Lt MCA. Note distal ACA surface collaterals retrogradely filling the distal MCA circulation (Figure 6).
Figure 6
DSA (AP oblique view) Lt ICA injection showing severe stenosis (black arrow) of the Lt MCA with ACA-MCA leptomeningeal collaterals

(B) PCA-MCA Leptomeningeal collaterals
Left vertebral injection, AP view, demonstrates distal left PCA collaterals retrogradely filling left MCA branches, as well as left posterior temporal collaterals to the Lt anterior temporal circulation (Figure 7).

Figure 7
DSA (AP view) showing distal Lt PCA - MCA collaterals, as well as left posterior temporal collaterals to the Lt anterior temporal circulation

Collaterals types, patterns, robustness and grading:
1-Type and pattern:
Internally dependent
2-Robustness and strength:
- Recruitment of collaterals: More than one branch recruited
- Extension of filling: More than one distal branch filled
- Laterality: Unilateral supply
- Source of supply: Leptomeningeal supply
3- Collaterals Score: 8.5 – 1 (due to presence of low perfusion state by neuroimaging) = 7.5

Case (2)
A 55-year-old male patient presented with recurrent right sided TIAs.
(A) MRI (DWI) shows acute infarcts in the left MCA territory (Figure 8).
Figure 8
MR DWI showing hyperintense lesions involving Lt MCA territory

(B) DSA of Left CCA shows critical stenosis of left ICA and (c) poor antegrade flow in the cerebral circulation (Figure 9).

Figure 9
DSA of Lt CCA showing severe stenosis of Lt ICA

(C) Post-procedure left CCA angiogram reveals the patent stented segment with good antegrade flow in cerebral circulation (Figure 10).

Figure 10
DSA of Lt ICA post stenting showing patent stented segment with good flow in cerebral circulation (a-d).

Collaterals:
(A) Willisian collaterals (Figure 11).
Assessment Of Collateral Pathways In Acute Ischemic Cerebrovascular Stroke Using A Mansour Grading Scale; A New Scale, A Pilot Study

Figure 11
Right vertebral angiogram, AP view, demonstrates filling of bilateral posterior communicating arteries, Circle of Willis collaterals. Subsequent filling of the bilateral anterior and middle cerebral circulations is seen.

(B) Leptomeningeal collaterals (Figure 12, 13).

Figure 12
Right vertebral angiogram, lateral view, demonstrates a prominent splenial artery (arrow) serving as a pial collateral to the pericallosal branch of the anterior cerebral artery (ACA). Conspicuous posterior temporal branches of the posterior cerebral artery (PCA) are noted.

Collaterals types, patterns, robustness and grading:
1-Type and pattern:
Internally dependent
2-Robustness and strength:
- Recruitment of collaterals:
One branch recruited
- Extension of filling:
More than one distal branch filled
- Laterality:
Unilateral supply
- Source of supply:
Internally dependent
3- Collaterals Score: 7

RESULTS
30 patients were enrolled; 19 patients (63.3 %) were males, mean age was 57.73 ± 11.92 ranging from (19-81). 23 patients (76.7%) were hypertensive, 15 patients (50.0%) were diabetic, 12 patients (40.0%) had history of TIA, 17 patients (56.7%) were hyperlipidemic and 15 patients (50.0%) were smokers.

On initial assessment of the patients on presentation using NIHSS; 7 patients were classified as Minor (1-4) (23.3%), 19 patients were Moderate (5-12) (63.3%) and 4 patients were Severe (>12) (13.3%). On follow up assessment upon discharge with the same scale; 4 patients (13.3%) scored 0 (Complete Recovery), 9 patients were Minor (30.0%), 14 patients were Moderate (50.0%) and only 3 patients were
Severe (6.7%). Outcome of the patients was grouped into 3 groups (Improved – Stationary – Worsened) based on assessment of NIHSS upon admission and discharge as change of stroke severity by 4 points or more. We found that 14 patients (46.7%) showed improvement, 15 (50.0%) patients with a stationary course and only 1 patient (3.3 %) worsened on follow up. Mean period for follow up was 6.93 ± 2.90 day, ranging from (2-15 days).

Analysis of the collaterals on DSA in the studied group showed 23 patients (76.7%) with collaterals and 7 patients (23.3%) with no collaterals. Of those 23 patients, one patient (3.3%) had only Externally dependent collaterals, 10 patients (33.3%) had only Internally dependent collaterals and 12 patients (40.0%) had Mixed dependence (both External and Internal). Further analysis of the group showed that a functioning Circle of Willis was present in 14 patients (63.3%) and Leptomeningeal collaterals were present in 8 patients (36.4%).

Data analysis showed no statistically significant effect of the different selected stroke risk factors on collateral development using Fisher Exact test (Table 2).

We found a statistically significant effect of collaterals development on favorable clinical outcome with p value: 0.043 using Monte Carlo test and statistical significance at p ≤ 0.05 (Table 3).

### Table 2
Relation between different risk factors and collateral development

<table>
<thead>
<tr>
<th></th>
<th>Collaterals (n = 23)</th>
<th>No collaterals (n = 7)</th>
<th>TEp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>5 21.7</td>
<td>2 28.6</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>18 78.3</td>
<td>5 71.4</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 52.2</td>
<td>3 42.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>11 47.8</td>
<td>4 57.1</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13 56.5</td>
<td>5 71.4</td>
<td>0.669</td>
</tr>
<tr>
<td>Yes</td>
<td>10 43.5</td>
<td>2 28.6</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10 43.5</td>
<td>3 42.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>13 56.5</td>
<td>4 57.1</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>12 52.2</td>
<td>3 42.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>11 47.8</td>
<td>4 57.1</td>
<td></td>
</tr>
</tbody>
</table>

We found a statistically significant effect of collaterals development on favorable clinical outcome with p value: 0.043 using Monte Carlo test and statistical significance at p ≤ 0.05 (Table 3).

### Table 3
Relation between collateral development and clinical outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Collaterals (n = 23)</th>
<th>No collaterals (n = 7)</th>
<th>Mcp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>13 56.5</td>
<td>1 14.3</td>
<td>0.043*</td>
</tr>
<tr>
<td>Stationary</td>
<td>10 43.5</td>
<td>5 71.4</td>
<td></td>
</tr>
<tr>
<td>Worsened</td>
<td>0 0.0</td>
<td>1 14.3</td>
<td></td>
</tr>
</tbody>
</table>
Grading of collaterals was done by Mansour Scale for all cases. We found a statistically significant association between the mean rating score of collaterals grading and improvement of the clinical outcome with p value <0.0001 (Table 4)

**Table 4**
The mean rating score of collaterals grading and clinical outcome

<table>
<thead>
<tr>
<th></th>
<th>Improved (n=13)</th>
<th>Stationary (n=10)</th>
<th>p value</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean value</td>
<td>8.615385</td>
<td>6.05</td>
<td>&lt;0.0001</td>
<td>6.4872</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.983593</td>
<td>0.87892</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Robustness of collaterals to the ischemic area was assessed using the new grading scale and was correlated to clinical outcome. There was a statistically significant difference with p value (0.027) for Recruitment of collaterals, p value (0.011) for Extension of filling and p value (0.048) for Laterality. Patients with more than one branch recruited, extension of filling for one or more than one distal branch and patients with bilateral collaterals showed significant improvement of their clinical condition (Table 5).

**Table 5**
Relation between clinical outcome and different grading scale parameters

In our study, 11 patients received intra-arterial intervention in the setting of acute stroke; 8 patients received IA-rtPA and 3 patients had mechanical thrombectomy. Recanalization rate in both mechanical thrombectomy and intra-arterial thrombolysis patients was correlated with the mean score rating of collaterals grading system. We found a statistically significant association between higher mean score and good recanalization with p value 0.0002 (Table 6)

**Table 6**
Recanalization rate and the mean score rating of collaterals grading system

<table>
<thead>
<tr>
<th></th>
<th>TIMI score (0-1)</th>
<th>TIMI score (2-3)</th>
<th>p value</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>3.2</td>
<td>8.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard deviation</td>
<td>1.720465</td>
<td>0.989529</td>
<td>0.0002</td>
<td>6.1158</td>
</tr>
</tbody>
</table>

**DISCUSSION**
Our study suggests no association between the studied stroke risk factors and the development of collaterals in the setting of acute ischemic stroke.

Regarding hypertension; a positive relation between high blood pressure and collateral formation was described by Kyriakides in 1991(4), but Koerselman et al. (5) stated exactly the opposite in 2005 describing a deleterious effect of hypertension on collateral development. Further studies with large sample are still needed.

Regarding Diabetes Mellitus; our study agrees with Lazzaro et al (6), who studied the effect of DM on pial collaterals in a 104 patients and concluded that there is no association between diabetes and the extent of pial collaterals in ischemic stroke patients although this finding is contrary to observations of collateral circulation in other organs where diabetes stimulates angiogenesis (e.g. retina). This could be due to the effect of blood brain barrier in resisting the glucose influx except in cases of inflammation. The impact of diabetes on the cerebral vasculature, as measured by angiography, has not previously been described.

Regarding a history of TIA; no study, to our knowledge has assessed the direct association between prior TIA and the development of collaterals though indirectly multiple studies assessed the link between prior TIAs and less infarction size and good outcome suggesting a role in increasing blood to penumbra through ischemic preconditioning and through collateral development. Further studies with large sample are still needed (7).

Regarding hyperlipidemia; our study does not agree with multiple studies in animal models suggesting that hyperlipidaemia may retard collateral remodelling. Murine models of both dietary and genetic hypercholesterolaemia have demonstrated reduced collateralization in several ways (8).Couffinhal et al, Duan et al and Tirziu et al found that hyperlipidemia adversely affects native collateral development in animal models (9).

Regarding cigarette smoking; the relation between smoking
as a risk factor and collaterals development is scarce and controversial throughout literature. Some studies suggest that smoking increases collaterals through causing chronic mild hypoperfusion and stimulating angiogenesis while other studies suggest that smoking decrease angiogenesis by causing endothelial dysfunction (reduced endothelial progenitor cell numbers and function). Currently, clinical studies do not show a consistent relation between collateralization and smoking and further trials are still needed (10,11). We found a statistically significant association between favorable clinical outcome and collateral development. We also found a strong statistically significant effect of robustness of collaterals as assessed by our new grading scale and good outcome.

The link between positive clinical outcome of stroke and collateral status is strong among literature. Multiple studies demonstrated that strong link with the use of different imaging modalities (12,13,14) . Our study agrees with Kucinski et al (15), who found that collateralization is the only independent predictor of favorable outcome in a multivariate analysis of radiological predictors after angiographically controlled thrombolytic therapy. Our study also agrees with the recent study of Bang et al (16) who concluded that pretreatment angiographic collateral grade using (Thrombolysis In Myocardial Ischemia [TIMI] scale) determines the recanalization rate after endovascular revascularization therapy.

**CONCLUSION**

In agreement with most studies to our knowledge, our study suggests that the presence of collaterals is a strong predictor of good clinical outcome regardless of its type and pattern. Also patients with collaterals showed higher rate of recanalization with acute endovascular management.

**References**

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