What Is Meant by “TICI”?  
J.E. Fugate, A.M. Klunder, and D.F. Kallmes

ABSTRACT

BACKGROUND: In 2003, Higashida et al proposed the Thrombolysis In Cerebral Infarction scale to evaluate angiographic intracranial flow. Our aim is to review how subsequently published studies define TICI.

MATERIALS AND METHODS: We used the ISI Web of Knowledge and SciVerse Scopus databases to search for “TICI” and “thrombolysis in cerebral infarction” and for articles that cited the original TICI paper from January 2004 through May 2012. Articles were categorized according to their definition of the TICI categories, typically grades 0–4, with grade 2 (partial reperfusion) subdivided into 2a and 2b, and rate of contrast entry to the perfused area. In addition, we catalogued the type of redefinitions of TICI subcategory 2 and additions of new categories.

RESULTS: Of 236 articles screened, 74 were included. Eight (11%) explicitly followed the TICI scale as originally defined. Thirty-seven (50%) cited Higashida but did not define their scale. Fifteen (21%) used and explained modified scales. Thirteen (18%) used the term TICI, but did not define the scale and did not cite Higashida. Eighteen (24%) specified a 2a subcategory. Nine defined grade 2a as <50% filling, 6 defined it as <67%, and 3 did not offer a percentage. Two studies added a 2c subcategory. Fifty-two (70%) used a cutoff level to define “successful reperfusion.” Of these, 65% used TICI ≥2, 33% used TICI ≥2b, and 2% used TICI = 3.

CONCLUSIONS: There is substantial variability in the definition and/or application of the TICI scale in the literature. This variability could considerably impact our understanding of results of revascularization studies.

ABBREVIATIONS: TICI = Thrombolysis in Cerebral Infarction; TIMI = Thrombolysis in Myocardial Infarction

The Thrombolysis in Myocardial Infarction scale is a widely applied, graded response scale for assessment of treatment outcome in the coronary arteries.1 In 2003, Higashida et al2 proposed a seemingly simple modification of the TIMI scale to evaluate intracranial perfusion assessed in cerebral angiography. This new scale, the Thrombolysis in Cerebral Infarction scale, was intended to standardize the grading of angiographic outcomes, particularly for trials of endovascular treatment of acute ischemic stroke (Table 1). As originally described, TICI categories span from no perfusion (grade 0) to complete perfusion (grade 3). The “partial perfusion” category (grade 2) is defined as cases in which contrast passes the obstruction but with rates of entry and washout slower than normal and is subdivided into 2 subcategories, 2a and 2b. Although the TICI scale has achieved fairly rapid acceptance into the medical literature, the scale was somewhat arbitrarily created and has not been validated or tested systematically.

Although the TICI scale has been criticized because of confusing internal inconsistencies,3 it is still widely used in the literature.4 Modifications of the TICI scale have been subsequently proposed, such as a change in the definition of the 2a subcategory (to indicate <50% filling of the vascular territory) or by the addition of a 2c subcategory.5 Our current aim is to review published studies that use the TICI scale to describe how the TICI scale is defined and utilized across studies.

MATERIALS AND METHODS

We performed a search of the medical literature by using the ISI Web of Knowledge and SciVerse Scopus databases. We searched for the terms “TICI” and “thrombolysis in cerebral infarction.” We also used these databases to search for all articles from January 2004 through May 2012 that cited the original TICI paper. In addition, we reviewed the reference list from all identified articles to identify other papers by using graded response scales for cere-
bral perfusion, whether or not these papers referenced or utilized the original TICI paper.

In the initial description of the TICI scale in 2003, grade 0 indicates no perfusion as evidenced by no antegrade flow beyond the point of arterial occlusion. Grade 1 is defined as penetration with minimal perfusion and applies when the “contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction.” Grade 2 is broadly defined as partial perfusion, which occurs when the contrast material passes beyond the obstruction, opacifies the distal arterial bed, but the rate of entry of contrast and/or its rate of clearance from the vascular bed are slower than comparable areas not perfused by the previously occluded vessel. The opposite cerebral artery or the arterial bed proximal to the occlusion can be used for comparison rates. Grade 2 is subdivided into 2a and 2b. A grade of 2a indicates partial filling (less than two-thirds) of the entire vascular territory and 2b indicates complete filling of the expected vascular territory, but with a perceptibly slower filling rate than normal. Finally, grade 3 is defined as complete perfusion and applies when antegrade flow into the bed distal to the obstruction occurs as promptly as into the involved bed and clearance of contrast material from the involved bed is as rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.

### Table 1: The original Thrombolysis in Cerebral Infarction perfusion scale

<table>
<thead>
<tr>
<th>Category</th>
<th>Title</th>
<th>Description</th>
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<tbody>
<tr>
<td>Grade 0</td>
<td>No Perfusion</td>
<td>No antegrade flow beyond the point of occlusion.</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Penetration with Minimal Perfusion</td>
<td>The contrast material passes beyond the area of obstruction but fails to opacify the entire cerebral bed distal to the obstruction.</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Partial Perfusion</td>
<td>The contrast material passes beyond the obstruction and opacifies the arterial bed distal to the obstruction. However, the rate of entry of contrast into the vessel distal to the obstruction and/or its rate of clearance from the distal bed are perceptibly slower than its entry into and/or clearance from comparable areas not perfused by the previously occluded vessel.</td>
</tr>
<tr>
<td>Grade 2a</td>
<td>Only partial filling (less than two-thirds) of the entire vascular territory is visualized.</td>
<td></td>
</tr>
<tr>
<td>Grade 2b</td>
<td>Complete filling of all of the expected vascular territory is visualized but the filling is slower than normal.</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>Complete Perfusion</td>
<td>Antegrade flow into the bed distal to the obstruction occurs as promptly as into the obstruction and clearance of contrast material from the involved bed is as rapid as from an uninvolved other bed of the same vessel or the opposite cerebral artery.</td>
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</table>

### RESULTS

Of 74 total included articles, 8 (11%) followed the original TICI scale completely and explicitly stated the categories.6–13 One article claimed to have followed the scale completely but did not state the categories.14 Thirty-seven (50%) articles did not explicitly define the scale but still cited the original paper by Higashida et al.15–31 Modifications of the TICI scale were used in 15 (20%) articles.4,5,21–65 Of these, 8 cited only the original TICI paper, 4 cited the original TICI paper and other papers, and 3 cited only other papers. Thirteen (18%) articles used TICI but did not define the scale and did not cite the original TICI paper.13,30,56,66–75 These results are depicted in Fig 1.

Eighteen (24%) of articles mentioned the rate of contrast filling in their use of TICI. Most modifications of TICI eliminated the subcategories of 2a and 2b. Only 18 (24%) articles specified a 2a subcategory. Of these, 9 defined 2a as filling of <67% of the affected vascular territory (compatible with the original TICI) and 6 defined 2a as filling of <50% of the affected vascular territory. A 2c subcategory was added in 2 articles, and a category 4 was added in 1 article. Examples of the variability in definitions of TICI categories are detailed in Table 2.

Most articles (n = 52, 70%) defined a threshold within the TICI scale that indicated “successful revascularization” as one of the study end points. Of these, 34 (65%) used TICI ≥2, 17 (33%) used TICI ≥2b (although only 1 of these studies defined a precise
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the term “TICI” when reporting outcomes after revascularization,
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in the recent English literature. Far from being a consistent and uni-
context run-off
Grade 3 Full perfusion with filling of all distal branches, including M3, M4
Normal flow
Partial recanalization with >50% reperfusion
Full perfusion with normal filling of distal branches in a normal hemodynamic
fashion
Grade 4 Complete recanalization/reperfusion
cutoff for 2b; 67% filling of the vascular territory), and 1 used
TICI = 3. These thresholds for successful angiographic revascu-
larization were prespecified in the methods in 40 (77%) of these
articles.

DISCUSSION
The term “TICI” connotes a standard and widely accepted metric of
revascularization, analogous to the ubiquitous TIMI outcome for
coronary revascularization. In the current study, we found substan-
tial variability in how the term “TICI” scale is both defined and used
in the recent English literature. Far from being a consistent and uni-
versal scale, we noted that only a small minority of studies, by use of
the term “TICI” when reporting outcomes after revascularization,
actually used the original TICI scale. Furthermore, many studies
failed to provide sufficient detail to allow the reader to understand
exactly what categories were used. Finally, the definition of successful
revascularization varied widely among studies. These current find-
ings are relevant for several reasons.

First, our understanding of the current literature has the poten-
tial to be greatly affected by these findings. The modification
that changed the cutoff point between TICI subcategories 2a and
2b has particular relevance because a grade on the TICI scale ≥2b
was used as an end point to define successful reperfusion in
one-third of the articles that specified this end point in our study.
Second, the definition of TICI will affect study design for future
trials of endovascular therapy for acute ischemic stroke. The TICI
grading scale is increasingly used to define
end points of revascularization success in
studies. If we define success as achieving a
certain grade of TICI (eg, TICI 2b) but we
do not have consistent grading systems, we
cannot compare or combine results of clin-
ic studies. To achieve enough patients for
studies to be powered adequately, it is nec-
essary for investigators from different cen-
ters to collaborate together. Without a stan-
dardized grading scale, this will not be
possible. It is essential that we communi-
cate clearly with consistent terminology.

To our knowledge, our study is the first
to specifically describe the varying defini-
tions of the TICI scale as it is reported in the
literature. Others, however, have previ-
ously called attention to the confusion sur-
rrounding the TICI scale.3 In 2007, Tom-
sick76 acknowledged confusion about the
different revascularization scales. He noted
the inconsistent descriptions and applica-
tions in the literature; some focus on recan-
alization, some focus on reperfusion, and
others confusingly (and erroneously) use
the terms interchangeably. Letters denoting
acronyms for different scales are littered
throughout the literature and include the
TICI, TIMI, TIBI (Thrombolysis in Brain Ischemia), and AOL (Arterial Occlusive Le-
sion) scales. In a previous review of the
TICI scale, the inherent inconsistencies within the original TICI
scale itself were identified.1 For example, there is no applicable
TICI grade for a case in which greater than two-thirds but less
than “complete” filling of the vascular territory is visualized. In
addition, there is no applicable TICI grade for a partially revascu-
larized territory with normal rate of distal opacification, a sce-
nario not uncommonly encountered.3

The TIMI scale—unlike the TICI scale—has not been the sub-
ject of frequent modifications. The definition of the TIMI scale
throughout the abundant cardiology literature has not been sys-
temically evaluated, but there is general consensus that when used
for the evaluation of myocardial perfusion before and after coro-
nary reperfusion therapies, it is used consistently. In the mid1990s, a quantitative assessment of coronary flow called the
corrected TIMI Frame Count (CTFC) was reported in an attempt
to standardize the scale,77 but the original semiqualitative TIMI
scale has continued to be the standard used by interventional
cardiologists. However, the TIMI scale cannot be easily applied to
the more complex cerebral arteries. One review found that 7 dif-
ferent operationalized versions of the TIMI scale have been used
in major stroke trials, emphasizing again the need for a single,
uniform, consistent scale for grading of perfusion in cerebral
arteries.78

This study has several limitations. Some articles from our lit-
erature search were not reviewed because of a lack of accessibility
of full-length articles or because they were written in languages

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Grade 0</td>
<td>No flow&lt;br&gt;No canalization&lt;br&gt;Complete occlusion&lt;br&gt;No recanalization/reperfusion</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Minimal recanalization (&lt;20%)&lt;br&gt;Minimal flow (very slow) without significant flow distal to the occlusion site&lt;br&gt;Limited or no reperfusion&lt;br&gt;Distal movement of thrombus without reperfusion&lt;br&gt;Perfusion past initial occlusion, but limited distal branch filling</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Partial recanalization—recanalization of some but not all of the occluded arteries&lt;br&gt;Incomplete recanalization/reperfusion&lt;br&gt;Near-normal flow, with flow distal to the occlusion but not filling the distal branches normally</td>
</tr>
<tr>
<td>Grade 2a</td>
<td>Perfusion of &lt;50% of the MCA distribution&lt;br&gt;Partial filling of the entire vascular territory</td>
</tr>
<tr>
<td>Grade 2b</td>
<td>Partial perfusion with incomplete distal filling of &lt;50% of expected territory&lt;br&gt;Partial filling of the entire vascular territory</td>
</tr>
<tr>
<td>Grade 2c</td>
<td>Partial perfusion with incomplete distal branch filling of ≥50–99% of the expected territory&lt;br&gt;Complete filling, but the filling is slower than normal&lt;br&gt;Perfusion of half or greater of the vascular distribution of the occluded artery</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Near-complete perfusion without clearly visible thrombus but with delay in contrast run-off</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Full perfusion with filling of all distal branches, including M3, M4&lt;br&gt;Normal flow&lt;br&gt;Partial recanalization with &gt;50% reperfusion&lt;br&gt;Full perfusion with normal filling of distal branches in a normal hemodynamic fashion</td>
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Table 2: Varying definitions of TICI grades in the literature
other than English, creating a selection bias. However, increasing the number of studies we reviewed may have increased the observed variability in TICI definitions. Also, the categories into which articles were divided were subjectively chosen and were evaluated by only 2 investigators.

Further opportunities to refine our grading scales and further our understanding of brain reperfusion abound. Weaknesses in current grading scales for cerebral perfusion are not limited to confusing terminology. Vessel recanalization in the treatment of acute ischemic stroke has been shown to be associated with favorable clinical functional outcomes, but when reperfusion is only partial, the clinical relevance of the use of different TICI grade 2 subdivisions is not known. Furthermore, there are few data regarding the intra-observer and interobserver variability when applying the TICI scale to angiography results. It also remains unclear whether it is appropriate to apply TICI to the posterior circulation and whether the degree of collateral flow—particularly in cases with distal M3–4 occlusions—modifies the effect of revascularization (as measured by TICI) on clinical outcomes.

Scales are designed to aid in the objective description of angiographic results, standardize data for research studies, and assist in outcome prediction. We hope that by clarifying what we mean by "TICI," we will be better able to evaluate the efficacy of revascularization therapies for acute ischemic stroke in the future.

CONCLUSIONS

There is substantial variability in how the TICI scale is defined and applied in the cerebrovascular literature. Few studies provide sufficient detail for readers to understand what is meant by each TICI grade. Because TICI score is increasingly used as an outcome measure in studies of revascularization therapies in acute ischemic stroke, this variability has the potential to considerably impact results and our understanding of these therapies.

disclosures: David Kallmes—UNRELATED: Consultancy; ev3,* Grants/Grants Pending: MicroVention,* Sequent Medical,* ev3,* Benvemere Medical,* Travel/Accommodations/Meeting Expenses Unrelated to Activities Listed: Cadman* (*money paid to institution).

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