Assessment and Improvement of Figures to Visually Convey Benefit and Risk of Stroke Thrombolysis

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Background and Purpose—Deciding whether to use intravenous fibrinolytic therapy for acute cerebral ischemia within 3 hours of onset is challenging for patients, family members, and health care providers. Visual displays can permit individuals to rapidly understand response patterns to therapy. This study sought to evaluate, refine, and improve existing visual aids for stroke fibrinolytic decision-making.

Methods—Existing visual aids were identified by Medline search and querying of national guideline organizations, pharmaceutical manufacturers, and stroke specialists, and were rated on a formal 8-point quality rating scale (0, lowest; 8, highest). Based on available instruments, new visual displays were developed to improve informed decision-making in routine practice.

Results—Two existing visual aids were identified, one from an emergency medicine society and one from a pharmaceutical company. Both were comparison visual displays of outcomes with and without treatment; no decision matrix visual aid was found. Both scored 4.0 on the quality scale, showing defects of effect size distortion, privileging less salient outcomes, dissimilar representation by treatment group, and limited stakeholder participation in generation. Revised versions of these graphics were developed with higher quality scores (6.75 and 7.75). In addition, a new decision matrix display with quality score 8.0 was developed that complements the numeric text of a national patient education tool developed jointly by US neurology, emergency medicine, and stroke patient organizations.

Conclusion—Existing visual aids for stroke fibrinolysis decision-making have deficiencies. New visual displays are now available to convey the health benefits and risks of fibrinolytic stroke therapy efficiently and informatively to patients and family members. (Stroke. 2010;41:300-306.)

Key Words: acute stroke ■ cerebral infarction ■ decision-making ■ thrombolysis ■ treatment

Deciding whether to use intravenous fibrinolytic therapy for acute cerebral ischemia within 3 hours of onset is challenging for patients, family members, and health care providers. Lay individuals must rapidly agree to or decline an interventional that has substantial potential benefits, but also substantial potential risks, for a condition that often first suddenly and unexpectedly appeared only tens of minutes earlier. Lengthy and iterative discussions, appropriate in nonacute settings, are potentially dangerous in acute stroke because of the high neuronal cost of deliberation. For every 1 minute that therapy is delayed in the typical large artery ischemic stroke, 2 million more brain cells die. For every 10 minutes that therapy is delayed, 1 less patient of every 100 treated experiences a benefit from treatment.¹ For this reason, the national target for the time interval from patient arrival in the emergency department to start of therapy is 60 minutes,² and much of that time is consumed by diagnostic and initial stabilizing care, leaving only a brief interval for treatment decision counseling.

Graphical displays can permit individuals to rapidly understand response patterns to therapy.³ Although understanding of quantitative risk is critical for informed consent and shared decision-making, lay individuals often fail to comprehend key aspects of numeric information that is presented simply as text. Universal human cognitive limitations cause biases in interpreting numeric probabilities that affect all individuals.³⁻⁵ Moreover, many patients have limited numeracy skills, discomfort with numeric expressions of risk, and analytic reasoning processes are impaired by age and by the stroke itself. Graphs are an appealing complement to numbers because they are visually interesting and exploit rapid, automatic visual perception skills. A well-designed visual display can reduce the amount of mental computation by replacing it with automatic visual perception and help patients to personalize health risk information, appreciate the scientific uncertainties inherent in the treatment choice, clarify the personal value or desirability of potential benefits relative to potential harms, and communicate their values to their practitioners. Because of the extreme time
urgency in acute stroke decision-making, graphic decision aids can play a critical role in facilitating informed consent and empowering patients and family to participate in shared decision-making.

However, the power of graphical decision aids to inform inevitably is accompanied by an equal power to mislead. The quality of graphical decision aids can vary. Presentational biases, including framing, axis distortion, and relative rather than absolute comparison, may distort the decision-making process and prevent patients and families from reaching an accurate appraisal of health risks and a well-informed selection of their therapy. The quality of graphical decision aids for intravenous fibrinolytic therapy in acute stroke has not previously been formally investigated.

**Materials and Methods**

Existing visual aids for fibrinolytic stroke therapy decision-making were identified by Medline search and querying of national guideline organizations, pharmaceutical manufacturers, and stroke specialists (see Appendix for search strategy). The inclusion criterion was decision support graphic focused on benefits and risks of thrombolytic stroke therapy. Exclusion criteria were: (1) illustration focused on pathophysiology or mechanism of action and (2) nonfigural (verbal or numeric) decision support instrument. One stroke neurologist (J.L.S.) identified suitable retrieved publications and extracted the data.

Using a modified Delphi process, we constructed a formal rating scale to assess the quality of the visual displays. Scale items were drawn from best-practice recommendations regarding construction of visual figures to convey health benefits and risks in medical decision-making, including relevant elements of the International Patient Decision Aid Standards Collaboration quality checklist.3,5–7 The resulting Quality Scale for Emergency Clinical Decision Aid Graphics has 8 items and total score (Table). Individual items address graph type, depiction of benefits and risks, uniform depiction of outcomes across treatment groups, effect size distortion, proportionality of display elements to underlying data, absolute rather than relative risk ratios, figural emphasis of noncomparable outcomes according to salience to patients, data sources, and stakeholder and patient participation in graph generation. In addition, when display elements were disproportionate to the quantities they depicted, the degree of distortion was quantified using the Tufted lie factor (LF): LF = size of effect shown in graphic/size of effect in data.6 As recommended by Tufted, values >1.05 or <0.95 were considered to indicate substantial distortion. Quality scale scoring was performed by 2 senior investigators (J.L.S., B.O.). Concurrence at the total score level was assessed by correlation coefficient and at component item level by the kappa statistic. Discrepant total scores, should any have occurred, were to be handled by averaging.

If deficiencies were noted in available graphic displays, revised displays were constructed, removing the deficiencies to the extent possible within the original general framework of the figure. The revised displays were then rescoring on the quality scale.

**Results**

Two existing visual aids were identified. Both were comparison visual displays of outcomes with and without treatment.

One display, from the American Academy of Emergency Medicine (AAEM), scored 4.0 on the quality rating scale (Figure 1A).12 Defects included distortion, visual misprivileging, dissimilar representation by treatment group, and no indication of inclusion of multiple specialties, methodologists, and lay individuals in figure generation.

**Effect Size Distortion**

The placebo good recovery rate is displayed as 6 of 18 (33%), but the actual average of good outcomes on all 4 end-point scales is 29%.9 The resulting Tufted LF is 1.14 (33/29), indicating overestimation of the rate of good outcomes without treatment.

**Visual Misprivileging**

The figure hues give the greatest color emphasis to the single black circle (strong figure/ground psychophysical relationship), but the black color represents a less important short-term outcome (bleeding with early worsening) than the red–green final functional outcomes, which is the end point that is of greatest importance to patients and families.

**Dissimilar Representation by Treatment Group**

The figure shows deaths only in relation to symptomatic hemorrhage in the treatment group and not all-cause mortality across both treatment groups. In the NINDS study, there actually was no statistically significant between-group differences in the death rate, and deaths were numerically more frequent in the placebo than in the tissue plasminogen activator (TPA) group.
Participants in Figure Generation
The AAEM website does not indicate who participated in figure generation. Besides emergency physicians, who were presumably involved, it is not clear if physicians from other specialties, stroke disease experts, health methodologists, or patients/lay individuals participated.

A revised figure was produced that corrected the visual misprivileging and dissimilar representation by treatment group, but did not alter the distortion, with a resulting quality score of 6.75 (Figure 1B).

The other display, from Genentech, the US manufacturer of TPA, scored 4.0 on the quality rating scale (Figure 2A). Defects included distortion, visual misprivileging, dissimilar representation by treatment group, and no indication of inclusion of multiple specialties, methodologists, and lay individuals in figure generation.

Effect Size Distortion
Several graphic elements are not proportionate to the quantities they depict, including 4 cells with Tuft LF departing from 1.0 by 10% or more. For the TPA group, the rate of death is overestimated (LF, 1.10), whereas for the placebo group the rate of death is underestimated (LF, 0.89). Also, for the TPA group, the rates of moderate and severely disabled outcomes are underestimated (LF, 0.89).

Visual Misprivileging
The figure hues give the greatest color emphasis to the single red person in the figure (strong figure/ground psychophysical relationship), but the red color represents a less important short-term outcome (bleeding with early worsening) than the blue–gray final functional outcome, which is the end point that is of greatest importance to patients and families.

Dissimilar Representation by Treatment Group
The figure shows similar outcomes with an attractive blue color for TPA-treated patients vs a dull gray for placebo-treated patients.

Participants in Figure Generation
The web site on which the figure is displayed does not indicate who participated in figure generation. It is not clear if physicians from multiple specialties, stroke disease experts, health methodologists, or patients/lay individuals participated.

A revised figure was produced that corrected the visual misprivileging and dissimilar representation by treatment group, reduced the distortion of effect size, and partially corrected limited inclusiveness in stakeholder participation, with a resulting quality score of 7.75 (Figure 2B). Only 1 element had a Tuft LF departing from 1.0 by 10% or more—an overestimate in the TPA group of the rate of severe disability (LF 1.11).

The literature review identified no existing choice consequence matrix graphic displays. Accordingly, our panel developed several. The version shown in Figure 3 was selected for general distribution because it complemented the all-text decision aid that has been jointly developed and endorsed by the American Academy of Neurology, the American College of Emergency Physicians, and the American Heart Association/American Stroke Association. The American Academy of Neurology, American College of Emergency Physicians, and the American Heart Association/American Stroke Association patient guide has no graphical depiction of benefits and risks, but the text does frame numeric statements of benefits and risks in a choice consequence manner, eg, that 1 in 3 patients who receive TPA improve as a result and 6 of 100 have bleeding, among whom 1 has death or serious disability as a result. The Figure 3 icon

Figure 1. A, Figure from an emergency medicine society shows defects of effect size distortion, privileging less salient outcomes, and dissimilar representation by treatment group. B, Replacement of the black circle with a red double minus circle corrects the privileging of less salient outcomes and dissimilar representation by treatment group. However, the effect size distortion is not corrected. Figure published with permission of UCLA Stroke Center.
array graphically depicts the same information conveyed textually in the American Academy of Neurology, American College of Emergency Physicians, and the American Heart Association/American Stroke Association education sheet. The display scored 8.0 on the quality checklist and had no graphical element with a Tufte LF departing from 1.0 by 5% or more.

Additional choice consequence array options that were developed are shown in Supplemental Figure I (A1 and A2), available online at http://stroke.ahajournals.org. Supplemental Figure I (A2), is noteworthy because it is the figure that patient informants in the study generally preferred. Most stroke patients placed great emphasis on the figure showing a clear depiction of final outcome and considered the simultaneous depiction of intermediate events, such as early symptomatic hemorrhage or early recanalization, to be distracting and less desirable. However, because of concerns in the physician community, the early symptomatic hemorrhage depiction was retained in Figure 3.

Inter-rater agreement on the quality scale ratings for the 5 rated figures was substantial. The total scores for each of the 5 figures were 100% concordant ($r=1.0$). Across the 40 total individual line-item ratings, interobserver agreement was 90% and kappa value was 0.71 (95% CI, 0.45–0.98), indicating substantial agreement.

**Discussion**

Evidence describing the effectiveness and feasibility of patient decision aids is substantial.5–8 Trials indicate that decision aids are superior to standard counseling in improving patients’ knowledge and realistic expectations about the results of treatments and other procedure. Decision aids are particularly important for emergency decision-making. This study identified deficiencies in existing visual aids for acute stroke fibrinolysis decision-making and developed corrected and new displays that convey the benefits and risks of therapy efficiently and more accurately to patients, family members, and practitioners.

The errors in existing graphics largely were in the direction to be expected given the competing interests of the stakeholders generating them. The AAEM graphic arose from a position statement process whose stated goal was to protect emergency physicians from medicolegal risk, not to facilitate patient decision-making.15 Accordingly, it is not surprising that the resulting graphic by color unduly visually highlighted therapy risks that might lead to medicolegal suits and by element size underestimated the net benefit of therapy (if neither treatment arm is superior, then the physician cannot be sued no matter what treatment is pursued). The Genentech graphic arose from a for-profit pharmaceutical company. As a result, it is not surprising that the figure by color unduly visually emphasized as desirable outcomes in the treatment group that were not actually different from outcomes in the placebo group. Perhaps somewhat unexpected was that the Genentech figure by element size underestimated, rather than overestimated, the benefit of therapy. This underestimate may have reflected self-interested caution in advancing therapeu-
tic claims, even when justified, in the face of skepticism from some members of the physician audience.

The elementary deficiencies identified in both graphics by the formal rating scale are not the only liabilities of these figures. An additional defect we noted in both the AAEM and Genentech figures was misapplication of the global statistic. Both figures state that they depict “disability” outcomes. However, neither figure is actually based on just the measures of disability used in the 2 NINDS-TPA trials. Although neither graphic is presented with an explanation of the derivation of the numeric values that the icon arrays represent (an additional, substantial weakness of the decision aids), internal evidence (AAEM) and personal communication (Genentech) indicate that both derived their underlying rates of disability numeric values by an application to individual patients of the global statistic test that was the primary outcome measure of the trials. In the NINDS Study, the effect of treatment in improving outcome was assessed on 4 different outcome scales measuring neurological deficit (NIH Stroke Scale), instrumental activities of daily living (Barthel Index), and global disability (modified Rankin Scale and Glasgow Outcome Scale). An inherent defect of the global statistic is that the vector effect in populations that it assesses is not directly translatable into impact on individual patients.16,17 Despite this established, formal barrier, the AAEM and Genentech figure designers apparently simply averaged together the disability and the nondisability scales without regard for their divergent appearance in individual patients.

We created corrected versions of the figures. In these versions, visual misprivileging and dissimilar representation by treatment group are removed and the breadth of stakeholders participating in figure creation increased. The corrected Genentech figure, although not the corrected AAEM figure, is based on an actual measure of individual patient disability (the modified Rankin Scale) rather than a misapplication of the global statistic. These corrected figures can be considered for use in patient counseling when a graphic that compares visual displays of outcomes with and without treatment is desired. A remaining drawback of these figures is that they visually depict the net effect of treatment at only 1 (AAEM)
or 3 (Genentech) transitions in disability state, rather than all 6 transitions measured by the modified Rankin Scale or all 7 transitions recognized by the World Health Organization. As a result, they substantially underestimate the net benefit conveyed by therapy.

We also created a choice consequence figure that scores well on the quality scale. Advantages of choice consequence displays compared with outcome comparison displays include focusing reader attention directly on the outcomes affected by treatment selection and disambiguation of the beneficial and harmful effects of therapy. Disadvantages include showing only alterations in outcome, not the full array of outcomes that result from each treatment option. Choice consequence displays are frequently used in formal standard gamble studies eliciting patient preferences about therapies and outcomes. The choice consequence figure we derived has the added advantage of being the visual correlate of the numeric text statement of treatment benefits and risks issued jointly by the American Academy of Neurology, the American College of Emergency Physicians, and the American Heart Association/American Stroke Association and the leading US neurological, emergency medicine, and stroke patient support societies.

The choice consequence figure we derived does have a drawback of overemphasizing harms of TPA therapy. The rate of symptomatic intracerebral hemorrhage shown is derived from the NINDS trials definition of symptomatic intracerebral hemorrhage. This definition is now generally recognized to be overly inclusive, encompassing asymptomatic as well as truly symptomatic hemorrhages. The more modern definitions of symptomatic intracerebral hemorrhage used in the ECASS 3 and SITS-MOST trials would provide patients with a more accurate understanding of risk, but we retained the NINDS definition rates because they are incorporated in the American Academy of Neurology, the American College of Emergency Physicians, and the American Heart Association/American Stroke Association statement and are still most familiar to clinicians. In addition, although the graphic shows both beneficial and harmful effects of therapy on final outcome, it displays only harmful short-term effects of therapy. A balanced figure would show a beneficial short-term outcome analogous to the displayed harmful symptomatic intracerebral hemorrhage outcome, such as therapy-related increase in the rate of early recanalization associated with early clinical improvement or in the rate of dramatic early recovery. We did generate and test such graphics, but the additional outcome made the figure too complex for rapid comprehension by some lay informants. Alternatively, a balanced figure can be created by removing all short-term outcomes and showing only the effect of treatment on final outcome, as shown in Supplemental Figure I (A2). This approach was favored by several lay informants, because it made the figure even more rapidly comprehensible and allowed them to focus on the outcome of greatest salience—final functional state. Practitioners who want to use the decision aid that appeared most supported by patients may prefer this figure.

Our study has additional limitations. We focused on visual decision aids. Numeric and verbal formats are also important means of conveying for presenting outcome information to decision-makers. Important work in this area in relation to stroke thrombolytic therapy has been performed. The figure development process involved physicians and nurses from multiple specialties and stroke survivors, but not healthy individuals at risk for stroke or family members of stroke survivors. We searched Medline, but not other large bibliographic databases such as EMBASE, and the search was performed by only 1 experienced investigator, so we may not have identified all published figural aids, especially those published in non-English languages. This study assessed existing and developed new visuals assessed based on formal ratings scales and input from stakeholders, but it did not test visual aid performance in a large group of patients or in the acute stroke settings. Future studies should analyze formally if patients and their surrogate decision-makers find the figure helpful in real-time decision-making and how well the figure leads patients and proxies to reach decisions that accord with the patient’s underlying values.

The benefit and risk display approaches developed in this study have general applicability to a variety of acute stroke treatments. In addition to aiding patient and clinician decision-making regarding intravenous TPA in the <3-hour window, these graphic templates can be applied to facilitate treatment decisions regarding intravenous TPA in the 3- to 4.5-hour window, intra-arterial fibrinolysis <6 hours, mechanical embolectomy <8 hours, organized supportive care on a stroke unit, aspirin therapy within the first 48 hours, and hemispherectomy for massive cerebral infarction.

Conclusion

The visual displays presented here are intended to support intravenous TPA decision-making and supplement, rather than replace, patient–practitioner discussions. In the brief time period available for brain resuscitation interventions in acute cerebral ischemia, they can help to convey the health benefits and risks of fibrinolytic stroke therapy efficiently and informatively to patients, family members, and clinicians.

Appendix

Text and Search Strategy

The Medline search for articles from January 1996 to June 2009 used the following combination of key words: <stroke OR cerebral ischemia OR brain ischemia OR cerebral infarct> AND <thrombolysis OR fibrinolysis OR acute treatment OR revascularization OR recanalization OR thrombolytic OR fibrinolytic OR TPA OR tissue plasminogen activator> AND <visual OR decision OR risks OR benefits OR consent OR graphical OR graphic OR guideline OR guide OR guidance OR aid OR number needed to treat OR framing OR presentation OR format>.

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Disclosures

Dr Gadhia is an employee of the University of California, which holds a patent on retrieval device therapies for acute stroke. Dr
Starkman is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, has served as a site investigator in a multicenter trials run by Vernalis, Paion, Lundbeck, and NTI, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, has served as an unpaid site investigator in a multicenter trials run by Vernalis, Paion, Lundbeck, and NTI, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, and is an employee of the University of California, which holds a patent on retriever devices for stroke; and is funded by NIH-NINDS Awards P50 NS044378 and U01 NS 44364. Dr Ovbiagele is a site investigator in multicenter trials sponsored by AGA Medical, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled; is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, administers stroke thrombolytic therapy in his practice (<5% of effort); is an employee of the University of California, which holds a patent on retriever devices for stroke; and is funded by NIH-NINDS Awards P50 NS044378 and U01 NS 44364. Dr Ovbiagele is a site investigator in multicenter trials sponsored by AGA Medical, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled; is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, administers stroke thrombolytic therapy in his practice (<5% of effort); and is an employee of the University of California, which holds a patent on retriever devices for stroke. Dr Ali is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled; has served as an unpaid site investigator in a multicenter trials run by Vernalis, Paion, Lundbeck, and NTI, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, and is funded by NIH-NINDS Awards P50 NS044378 and U01 NS 44364. Dr Saver is a scientific consultant regarding trial design and conduct to CoAxia, Concentric Medical, Brainsgate (all modest); has served as an unpaid site investigator in a multicenter trials run by Vernalis, Paion, Lundbeck, and NTI, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled; is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, administers stroke thrombolytic therapy in his practice (<5% of effort); is an employee of the University of California, which holds a patent on retriever devices for stroke; and is funded by NIH-NINDS Awards P50 NS044378 and U01 NS 44364. Dr Saver is a scientific consultant regarding trial design and conduct to CoAxia, Concentric Medical, Brainsgate (all modest); has served as an unpaid site investigator in a multicenter trials run by Vernalis, Paion, Lundbeck, and NTI, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled; is a site investigator in the NIH CLEAR-ER, IMS 2, IMS 3, and MR RESCUE multicenter clinical trials, for which the UC Regents received payments based on the clinical trial contracts for the number of subjects enrolled, administers stroke thrombolytic therapy in his practice (<5% of effort); and is an employee of the University of California, which holds a patent on retriever devices for stroke; and is funded by NIH-NINDS Awards P50 NS044378 and U01 NS 44364.
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