Big and bigger data in endovascular stroke therapy

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More than 30 years after initial reports demonstrated the feasibility of intra-arterial or endovascular therapies for the treatment of acute ischemic stroke, big data have finally established requisite evidence for the safety and efficacy of thrombectomy. Cautious enthusiasm for this breakthrough is tempered, as we await the bigger data of these trials to understand the constellation of variables that ensured success. Noninvasive imaging, including multimodal computed tomography and MRI as used in recent endovascular trials, has dramatically advanced since that time, providing snapshots or profiles of the collaterome in a given patient. Data-driven analyses will provide the most potent argument to distinguish comprehensive stroke centers from interventional-ready sites. These trials may provide insight on the future role of telestroke, for intravenous thrombolysis and remote imaging review of multimodal computed tomography or MRI to streamline patient transfer for endovascular therapy. Rather than concluding that recent trials have answered the most important question regarding endovascular therapy, even more data are needed to effectively translate such success and extend such potential benefit to the greatest number of stroke patients encountered on a daily basis.

More than 30 years after initial reports demonstrated the feasibility of intra-arterial or endovascular therapies for the treatment of acute ischemic stroke [1], big data have finally established requisite evidence for the safety and efficacy of thrombectomy. The decisive results of MR CLEAN, a randomized controlled trial of thrombectomy with stent-retriever devices [2], seemingly turned the tide after three large endovascular studies reported negative results only 1 year earlier [3–5]. Numerous critiques had been disseminated to explicate the failures of these landmark trials, focusing on the influence of specific variables such as the presence of proximal arterial occlusion, imaging details, time to treatment and device type, among many other variables in these trial datasets. Such complexity in the heterogeneity of acute ischemic stroke had often been cited as a barrier to developing a standard therapeutic approach that would improve the clinical outcomes of most stroke patients. The relatively simple trial design of MR CLEAN, however, included proximal arterial occlusion yet imaging, time and other variables such as degree of reperfusion did not exclusively substantiate trial success. Within a period of days after the MR CLEAN results were publicized, a succession of ongoing endovascular trials declared lack of equipoise, ethically required for informed consent and randomization of potential subjects. Each of the respective data and safety monitoring boards convened to review interval results, subsequently terminating trial recruitment, with positive results then confirming the superiority of endovascular therapy. Cautious enthusiasm for this breakthrough is tempered, as we await the bigger data of these trials to understand the constellation of variables that ensured success. Interestingly, each of the recent endovascular trials utilized different imaging and other criteria that therefore preclude a harmonized approach to guarantee successful clinical outcome or a panacea across a broad spectrum of stroke patients. Specific lessons, however, may

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be gleaned from these big and bigger data emerging from recent trials.

Successful revascularization with endovascular therapy for acute ischemic stroke is defined by good clinical outcome at 90 days, largely influenced by the baseline pathophysiology or collateral status of a given individual at stroke onset [6]. Such impact of collateral circulation in endovascular stroke therapy was recognized many years ago, by interventional pioneers [7,8]. Noninvasive imaging, including multimodal computed tomography (CT) and MRI as used in recent endovascular trials, has dramatically advanced since that time, providing snapshots or profiles of the collaterome in a given patient [9]. The collaterome is the elaborate neurovascular architecture within the brain that regulates and determines the compensatory ability, response and outcome of cerebrovascular pathophysiology. Imaging selection, defined variably across the trials, is therefore pivotal in triage for endovascular therapy. The relatively small populations recruited in these successful trials compared with their projected sample sizes is likely explained by the use of imaging to enrich patient selection [2,10,11]. Core volumes, mismatch and collateral grade on multimodal CT or MRI may identify ideal candidates and similarly, malignant patterns that portend abysmal outcomes. Implementation of the optimal imaging approach for selection of endovascular therapy candidates may leverage the specific advantages and avoid the logistic difficulties of either multimodal CT or MRI in a particular environment or clinical scenario [12,13]. Ongoing evaluation of wide scale use of these techniques will be important to help advance these imaging goals in the clinical context. Furthermore, a particular imaging technique may not be superior to another as availability and expertise to translate imaging results into medical decision-making are paramount. In sum, the success of an interventional procedure is not defined by the device alone, but by the interaction of the treatment approach with baseline pathophysiology, readily delineated with imaging expertise and indispensible data.

The paradigm or entire approach to endovascular stroke therapy, from prehospital triage to the angiography suite, intensive care unit, rehabilitation and beyond may also encompass essential data elements [14]. Recent endovascular stroke trials have utilized distinct systems of care, processes, integration of various specialists, and timelines. These logistic details now become incredibly important practical aspects for planning wide-scale implementation of endovascular therapy in routine clinical practice. Even before full publication of final trial results, these issues emerge with sundry political implications. Endovascular stroke therapy has been termed 'surgery', eliciting debate regarding the role of various medical specialists. Oddly, neurological expertise in acute stroke management has not been emphasized as the focus has been centered on the interventional procedure rather than the entire process of patient care. The distribution or transfer of stroke patients within a geographic region and role of comprehensive stroke centers has also been raised. Interestingly, these recent trials were not solely conducted at comprehensive stroke centers and numerous questions remain regarding data on the optimal process of care. If experienced interventional specialists are available at a hospital, then why are other components of a comprehensive stroke center required? Data-driven analyses will provide the most potent argument to distinguish comprehensive stroke centers from interventional-ready sites. These trials may provide insight on the future role of telestroke, for intravenous thrombolysis and remote imaging review of multimodal CT or MRI to streamline patient transfer for endovascular therapy. Data from larger scale endovascular registries have revealed that arbitrary time windows are irrational without understanding the degree of collateral status [15–17]. In brief, stroke patients with poor collaterals require rapid triage to endovascular therapy to achieve reasonable outcomes, whereas those patients with robust collaterals may achieve excellent clinical outcomes with endovascular therapy at much later times. These data on collateral status and relative time windows may be leveraged in telestroke models that incorporate expert review of multimodal imaging in sync with patient evaluation at a remote hospital, triaging patients based on collateral status as an important determinant of outcomes after endovascular stroke therapy. Rather than concluding that recent trials have answered the most important question regarding endovascular therapy, even more data are needed to effectively translate such success and extend such potential benefit to the greatest number of stroke patients encountered on a daily basis [2,10,11].

The next phase in endovascular stroke therapy is likely the most critical. Phase IV studies or post-marketing surveillance are important stages of therapeutic development, yet registries are often disparaged. Several endovascular stroke therapy device registries have been launched, but collecting extensive data cannot be underemphasized. We need to understand how the variables described above in recent trials relate to implementation of endovascular stroke therapy in routine clinical practice. Detailed and centrally adjudicated variables regarding process of care, imaging, angiography, diverse patient outcomes and costs are needed to understand the most critical determinants of improved stroke care with endovascular therapy. Specific time intervals in the process of care, such as door-to-imaging versus picture-to-puncture or total procedure time, must be evaluated with respect to impact on ultimate outcomes and importance of data obtained or decision-making during such distinct intervals [18,19]. This data-driven approach mirrors the philosophy of precision medicine revolutionizing healthcare in other disorders [20].

Big and bigger data in endovascular stroke therapy provide momentum that capitalizes on the vast efforts to expand treatment options for stroke patients over the past three decades. Similar to informed consent by our patients, our informed medical therapeutic decision-making in endovascular therapy is contingent on data that are now increasingly available. It is no longer acceptable to reduce extensive datasets to identify singular variables such as time to treatment in disregard for baseline pathophysiology when the potential of big data allows us to refine endovascular therapy based on sophisticated informatics. Further progress in endovascular stroke therapy will emerge from the data science of imaging for patient selection, systems

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engineering and practical implementation of such stroke care across various geographical regions.

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