The Value of Quality of Life Research in Stroke

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See related article, pages 2081–2085.

This issue of *Stroke* contains an excellent article by Williams et al that deals with an important area of outcomes research: health-related quality of life (HRQOL). Williams and colleagues have previously created and validated the Stroke Specific Quality of Life scale (SSQOL), which is now being used as a secondary outcome measure in many ongoing stroke clinical trials. In this article, they measure the validity of obtaining the SSQOL from a family proxy.

For many among the readership of *Stroke*, outcomes research may not be as stimulating as other topics, such as the results of clinical trials or epidemiological studies. Most who pick up this issue will not (or did not) immediately focus on the Williams article and read it first. And yet, research with regard to outcomes such as HRQOL is of increasing importance, especially for clinical trialists.

Stroke clinical trials in general have used “crude” ordinal scales such as the modified Rankin (mRS) to measure functional poststroke outcomes. The mRS is clinically meaningful in that it is a measure of poststroke independence, and independence is an important outcome for our patients. As such, it is an appropriate outcome measure and describing it as “crude” is not intended to criticize studies that have used it. However, measures like the mRS or the Barthel Index are relatively insensitive to change over time (especially if dichotomized in analysis), can exhibit ceiling or floor effects in a given study population, and may poorly represent the impact of stroke on a patient’s subsequent life. For example, with regard to the last point, in some trials an optimal poststroke outcome is defined as a mRS of 0 to 2. A patient with a NIHSS score of 2 for a visual field cut might live independently and be considered an optimal outcome on the mRS, but may still feel greatly impaired by their deficit and be unable to drive or work in their previous occupation.

Let us look at how outcomes were measured in one of the major acute stroke clinical trials performed to date: the NINDS tPA trial. In this trial comparing a successful treatment to placebo, a large effect size was found across 4 relatively “crude” end points and a combined measure of all 4. Subsequent trials do not have the luxury of a placebo group, and results will not likely exhibit so robust of an effect size. To determine whether new investigational methods or treatments being tested are clinically meaningful, investigators must either increase the sample size or find more sensitive measures that will allow detection of a clinically meaningful but smaller between-groups effect size. In the recent SAINT I study, for example, the investigators analyzed the full range of mRS outcomes using the Cochran-Mantel-Haenszel test for their primary outcome and found a statistically significant between-groups difference in favor of treatment with NXY-059. A 3-level categorization of mRS was also significant, but several other separate dichotomizations were not. The choice of outcome measures and analysis is obviously critical to optimal clinical trials, especially in the current environment where enrollment in stroke clinical trials is often slower than expected, making the option of mega-trials with larger sample size unlikely.

Quality of life scales may at first seem like a “soft science” to some. However, several validated scales exist and data are accumulating that these scales (or subscales within them) are very useful outcome measures. Because poststroke quality of life is highly correlated with disability and motor function, these scores (or subscores) can be used as functional outcomes, and are highly correlated with traditional functional outcome measures. Some contain additional items that measure domains of poststroke care that are relevant to stroke patients and family members, such as vision or language impairments. The best of these HRQOL scales avoid ceiling and floor effects, and are sensitive to the poststroke changes over time that are of clinical significance to patients and families. As such, they may one day be primary outcome measures in clinical trials rather than secondary outcome measures. The day of HRQOL measures as primary outcome has not yet arrived, however. It should be noted that in the SAINT I trial, the Stroke Impact Scale and the EuroQol EQ-5D were both used as secondary outcome measures, and trended toward but did not reach significance (with the exception of the EQ-5D visual analogue scale, which reached statistical significance at the 0.05 level).

It is critical that a scientific approach to HRQOL research be continued so that we may discover the proper role of QOL scales in stroke clinical research. In this issue, Williams et al describe the relationship between patient and proxy scores on the SSQOL, showing that proxy scores are systematically lower. They demonstrate that patient depression and proxy perception of burden are important factors that influence agreement between patients and proxies. Proxy interviews are a necessary part of stroke research because language is often impaired in stroke survivors. Thus, the information provided herein by Williams and colleagues will be of great importance to those who will use the SSQOL or other HRQOL scales in ongoing clinical trials and in the future.

Disclosure

None.

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References


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