Impact of Clinical Trials on Neurosurgical Practice: An Assessment of Case Volume

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■ OBJECTIVE: **To evaluate the effect of important trials on the practice of neurosurgery.**

■ METHODS: **We hypothesized that evidence from trials addressing the management of intracranial aneurysms (International Subarachnoid Aneurysm Trial [ISAT]) and nontraumatic intracerebral hemorrhages (Surgical Trial in Intracerebral Hemorrhage [STICH]) and vertebral augmentation for osteoporotic vertebral body fractures had a significant impact on the frequency of the corresponding neurosurgical procedures. A Medicare administrative database was queried for corresponding Common Procedural Terminology codes and units billed per calendar year. The effects of ISAT and STICH were evaluated using a generalized linear model. The effect of the vertebral augmentation study was evaluated using a *t* test.**

■ RESULTS: **After publication of ISAT in 2002, the rate of increase in proportion of cerebral aneurysms that were treated with embolization (Common Procedural Terminology code 61624) per year increased from 3.9% to 5.5% ($P = 0.01$). After publication of STICH in 2005, the number of craniotomies performed for intracerebral hematoma decreased from 2341 in 2002 to 1646 in 2011 ($P = 0.03$). After 2 publications in 2009, performance of vertebral augmentation decreased from a high of 99,961 in 2009 per year to 77,108 in 2013 ($P = 0.002$).**

■ CONCLUSIONS: **Randomized clinical trials remain the gold standard in the medical community to demonstrate efficacy, but their true impact relies on rapid and extensive assimilation into everyday medical practice. However, the described methodology establishes a temporal relationship only and does not prove causation. Nonetheless, trends in procedural volume suggest that the results of these select randomized clinical trials had a significant effect on neurosurgical practice affecting Medicare patients within an interval of a few years.**

INTRODUCTION

The randomized clinical trial has become the de facto gold standard for establishing the efficacy of a clinical intervention. These trials are often critiqued on their design, their statistical methodology, and the power of their results, but the true impact is how an individual trial (or group of trials) affects clinical practice. Data on assimilation of trial results into daily medical practice suggest that a multitude of factors influence when, if, and how these results enter the clinical realms (8-11). The Institute of Medicine identified a quality chasm (2) and has spent more than a decade fostering improvement of health care quality through the application of best scientific knowledge (8). This situation has motivated the development of strategies for linking findings from clinical trials with treatment implementation as well as strategies for knowledge dissemination (20).

Since the 1970s, there have been several landmark trials pertaining to numerous neurosurgical conditions, including, but not limited to, nontraumatic hemorrhagic stroke, nontraumatic vertebral body fractures, and intracranial aneurysms (4, 17, 24). The impact of these trials on neurosurgical practice has not been

Key words
- Aneurysm
- Cerebellar hematoma
- Neurosurgery
- Randomized trial
- Vertebral augmentation

Abbreviations and Acronyms
COSS: Carotid Occlusion Surgery Study
CPT: Common Procedural Terminology
HAMLET: Hemicraniectomy After Middle Cerebral Artery Infarction with Life-Threatening Edema Trial
ISAT: International Subarachnoid Aneurysm Trial
RCT: Randomized controlled trial
SAMMPRIS: Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis
SAVE: Survival and Ventricular Enlargement
STICH: Surgical Trial in Intracerebral Hemorrhage

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formally studied. The International Subarachnoid Aneurysm Trial (ISAT) evaluated the short-term to medium-term outcomes of endovascular coil embolization versus surgical clipping of patients with ruptured intracranial aneurysms (24). The Surgical Trial in Intracerebral Hemorrhage (STICH) reported on the outcome of medical management alone versus medical management combined with surgical hematoma evacuation for patients with spontaneous supratentorial intracerebral hemorrhage (18). Trials reported by Kallmes et al. (17) and Buchbinder et al. (4) reported on the efficacy of vertebroplasty for nontraumatic osteoporotic vertebral body fractures compared with sham surgery.

Using a population-based database, we sought to evaluate the impact of the above-mentioned pivotal neurosurgical trials on real-life clinical practice. We hypothesized that an increase or decrease in procedural volume would follow the results of positive or negative results, respectively, and would indicate as a surrogate marker the widespread acceptance of the premise and outcome of a trial in daily neurosurgical practice. We especially wanted to evaluate this effect in instances where the outcome of the trial supported the prevailing practice at the time the trial was conducted.

MATERIALS AND METHODS

Database Review

We retrospectively reviewed the administrative Medicare database, which records the number of procedures performed each year and may be queried using Common Procedural Terminology (CPT) codes. Data were taken from the most recent version of the Centers for Medicare and Medicaid Services Physician/Supplier Procedure Summary Master File, which is a 100% summary of all Part B Carrier and Durable Medical Equipment Regional Carrier claims processed through the Common Working File and stored in the National Claims History Repository (6).

The patient population studied comprises all Medicare patients in the United States. Most Medicare patients are $\geq$65 years old, but a smaller proportion are patients $<$65 years old with disability.

Data Analysis and Statistical Methodology

ISAT. To examine the impact of ISAT, we retrospectively reviewed the Medicare database for the 11-year period 1996–2011. We began with 1996 data because Gugliemi detachable coils were approved by the U.S. Food and Drug Administration in 1995, making 1996 the first full year this device was available in the United States for use in endovascular embolization. The last year recorded was 2011. After this year, the percentage of clipping versus coiling has remained stable. The CPT codes used for aneurysm clipping were 61697, 61698, 61700, and 61702.

Embolization of intracranial aneurysm is coded 61624, transcatheter permanent occlusion or embolization (e.g., for tumor destruction, to achieve hemostasis, to occlude a vascular malformation), percutaneous, any method, central nervous system (intracranial, spinal cord). This code applies to more than just aneurysm coiling, but it is the code most commonly used for aneurysm coiling. The general nature of this code makes it difficult to determine the absolute number of aneurysm coiling procedures in a given year. However, it does allow for generalization or identification of trends in the number of intracranial embolization procedures performed. Similarly, a few open surgical aneurysm clipping procedures that may have been coded using skull base–specific codes are not represented here.

To determine if changes in numbers could be attributed to random chance, a regression line was fit on "proportion of coiling." Because the proportion of coiling is a proportion, the "generalized linear model (glm) with logit link" was used with "coiling+clipping" as the weight, weighting years with more data more heavily. The change in slope in the years before and after the trial was compared for significant change.

STICH. For craniotomy for evacuation of hematoma, we evaluated CPT code 61313 for the years 2002–2011, with 2011 the most recent year available. A linear regression was fit to the data for the years 2002–2005 and compared with 2006–2013.

Vertebral Augmentation. For vertebral augmentation, we retrospectively reviewed the Medicare database for the 5-year period 2006–2013. The year 2007 was the first year that separate codes were used for vertebroplasty and kyphoplasty. The following CPT codes were examined, covering vertebroplasty and kyphoplasty: 22520, 22521, 22522, 22523, 22524, and 22525. There are not enough data points for meaningful linear regression modeling. A t test was used to compare the number of procedures performed in the years before publication, 2006–2009, with the number of procedures performed after publication, 2010–2013.

RESULTS

ISAT

The number of coiling procedures increased from 808 in 1997 to 5830 in 2011, whereas craniotomies decreased from 3204 to 1565 per year over the same period. The increase in the percentage of cerebral aneurysms treated endovascularly began to level out in 2007 at roughly 70% but was still incrementally increasing. The annual rate of increase in percentage of cerebral aneurysms treated endovascularly before publication of ISAT was 3.8% and after publication was 5.5% using 2007 as the endpoint ($P = 0.01$) (**Figure 1**). After 2007, the change per year leveled off, and the percentage of coiling versus clipping has remained 70:30.

STICH

The total number of craniotomy procedures performed for removal of intracerebral hematoma decreased each year from 2341 in 2002 to 1646 in 2011 ($P = 0.03$) (**Figure 2**). Limited data are available from the time period before the publication of the STICH trial, and information about the outcome of the trial was available at least 1 year before formal publication (9).

Vertebral Augmentation. For vertebral augmentation, the number of procedures coded increased from 18,704 in 2002 to 90,570 in 2007, the first year vertebroplasty and kyphoplasty codes were available and approved for use by the Centers for Medicare and Medicaid Services. In 2009, the year the studies by Kallmes et al. and Buchbinder et al. were published, the largest number of procedures, 99,961, was coded; this decreased to 77,108 in 2013, the most recent year data were available. The number of kyphoplasty procedures performed in 2010–2013 (86,821, 83,278, 79,801, and 77,108) was significantly lower than the number of procedures