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Cost-effectiveness analysis of intracranial stent placement versus contemporary medical management in patients with symptomatic intracranial artery stenosis

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Abstract

Background: Intracranial angioplasty and stent placement has been increasingly evaluated as a new method for treatment of symptomatic intracranial stenosis in select patients. The Food and Drug Administration (FDA) has approved intracranial stent treatment of symptomatic atherosclerotic intracranial lesions.

Purpose: To determine the cost-effectiveness of intracranial artery stent placement compared with contemporary medical management for secondary stroke prevention among patients with symptomatic intracranial stenosis.

Methods: Clinical outcome data were obtained from the aspirin treatment arm of the Comparison of Warfarin and Aspirin for Symptomatic Intracranial Disease (WASID) trial (n = 280) and 12 case series (n = 216) of patients who underwent stent placement of symptomatic intracranial stenosis with comparable characteristics. Total cost of procedure and medical management-only was calculated using the rates of major stroke, minor stroke, or death in each group. All costs are expressed in 2010 US$. The quality-adjusted life-year (QALY) of each intervention strategy was estimated using the frequency of the outcomes of major and minor stroke, death, and baseline health. An incremental cost-effectiveness ratio (ICER) was formulated for a 1-year period.

Results: The total rate of stroke at one year was 10.2% (6.1–14.2%) and the rate of all-cause mortality was 3.7% (1.2–6.2%) in the stent group. The corresponding annualized rates of stroke and all-cause mortality in the medical management-only group were 15% (10.8–19.2%) and 2.4% (0.6–4.2%), respectively. The calculated net costs at one year for intracranial stent placement and contemporary medical management were US$16,898 and US$3,468, respectively. Overall, QALYs for the two groups were 0.82 and 0.81 (in a range of 0 to 0.89 corresponding to death and baseline health), respectively. The cost per QALY gained after intracranial stent placement and contemporary medical therapy was US$20,542 and US$4,265, respectively. The corresponding ICER for stent versus medical treatment alone was US$1,416,268.

Conclusion: The reduced risk of stroke following intracranial stent placement is offset by significantly higher procedure-associated net costs. Select procedures in patients with symptomatic stenosis of 70% or greater are more likely to be cost-effective.

Keywords

intracranial stent; cost effectiveness; stroke prevention; intracranial stenosis; intracranial atherosclerosis; WASID

Introduction

Intracranial artery atherosclerosis is attributable for approximately 10% of ischemic stroke in North America [1]. Higher rates have been observed for black, Hispanic, South Asian, and East Asian ethnicities [2–6]. In the Northern Manhattan Stroke Study from 1993 to 1997, the prevalence for strokes secondary to intracranial atherosclerosis was 3, 15, and 13 per 100,000 for whites, African Americans, and Hispanics, respectively

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Table 1.
The demographic and clinical characteristics of patients who underwent medical management or intracranial stent placement

	Medical-Management Only (WASID)	Intracranial Stenting
Number of patients	280	216
Men	60%	79%
Risk factors	(of 280 pts)	(of 204 pts)
HTN	82%	81%
Hyperlipidemia	69%	69%
Diabetes	36%	41%
Smoking	25% (“current”)	64% (“smoking”)
Qualifying event		
TIA	41%	56%
Stroke	59%	44%

[7]. Among patients with ischemic stroke, intracranial atherosclerosis was the etiology for stroke in 9% of whites, 17% of African-Americans, and 15% of Hispanics. Recurrent cerebrovascular events as frequent as 56% have been reported in patients with symptomatic intracranial stenosis [8]. The Comparison of Warfarin and Aspirin for Symptomatic Intracranial Stenosis (WASID) study in 2005 reported a 20.7% rate of ischemic or hemorrhagic stroke during a mean follow-up of 1.8 years on optimal contemporary medical therapy [9]. Intracranial angioplasty and stent placement have increasingly been evaluated as a possible therapeutic option over the past 15 years. Multiple observation studies have found technical success rates greater than 90% and post-intervention stroke rates of 10% or less, although most such trials have not reported events as far as one year [1]. Early data from the SAMMPRIS trial have resulted in a critical evaluation of periprocedural rates of stroke and death [10].

An important component that has not been addressed is the cost effectiveness of the procedure. As the medical community reevaluates the use of intracranial angioplasty and stent placement, further studies should be based on both clinical results and cost effectiveness. We provide the results of this analysis to facilitate such an evaluation.

Methods

Input data sources

Input data was abstracted from multiple sources. Clinical data of 280 patients with symptomaticintracranial disease under medical management on antiplatelet therapy was obtained from the published results of WASID. Comparison clinical data for patients with symptomatic intracranial disease who underwent intracranial stent placement was obtained from 216 patients from 12 different case series [11–22]. Cost data were taken from the Healthcare Cost and Utilization Project (HCUP) and updated via the Medical Care components of the consumer price index [23–25]. Quality-of-life scores for average health, major stroke, and minor stroke were obtained from a published study by Post *et al* [26] and Gore *et al* [27]. Major stroke was defined as a modified Rankin scale (mRS) score of greater than 3. Clinical data abstracted included age, gender, baseline risk factors, and the risk of major stroke, minor stroke, or death by one year. The average age of patients from the antiplatelet therapy arm of WASID was 62.8 years and 60% were men. Patients from the multiple intracranial stent trials were on average 59.5 years of age and 79% were men (Table 1).

Cost calculation

The total cost in each group is the sum of procedure costs (intracranial stent placement), the cost of initial hospital admission and workup, the cost of hospital readmission for stroke during follow-up, the annual cost of disability for major (mRS > 3) and minor stroke, and the cost of death (ICD-9 diagnosis code 434.11 for stroke, procedure code 00.65 for intracranial stent placement) [23–25]. All costs are presented in 2010 US$ and were adjusted for inflation using the Medical Care component of the consumer price index.

Effectiveness

Effectiveness was ascertained via QALY: this translates treatment benefits into life expectancy gained in time of equivalent health status. Published quality of life (QoL) weights vary dependent on the population surveyed. Given that our two patient sources were a mix of those with recent TIA and those with a recent stroke, we derived a weighted average of published QoL weights for average health, minor stroke, and major stroke [26,27]. These QoL scores were 0.89, 0.64, and 0.34, respectively (Table 2).

Cost-effectiveness analysis

The analysis outcome was expressed in terms of an incremental cost-effectiveness ratio (ICER). Asensitivity

Table 2.

Base-case costs and outcome health utility scores

	Costs (2010 USD)
Stent procedure	$1487123
Recurrent stroke admission	$1552623
Disability: major stroke	$1188724
Disability: minor stroke	$320924
Death	$571525
	Utilities
Baseline health	0.8927
Minor stroke	0.6426
Major stroke	0.3426
Death	0

Table 3.

Comparison of mean event rates for the pooled intracranial stent placement group and the antiplatelet arm of WASID (95% confidence interval ranges in parentheses)

	Intracranial stent placement	Medical-management only
Total stroke	10.2% (6.1–14.2%)	15% (10.8–19.2%)
All-cause mortality	3.7% (1.2–6.2%)	2.4% (0.6–4.2%)
Periprocedural stroke	4.6% (1.8–7.4%)	N/A
Major	134	
Minor	202	
Post-discharge stroke (nonperiprocedural)	5.6% (2.5–8.7%)	15% (10.8–19.2%)
Major	0.7% (0–1.8%)	6% (3.2–8.8%)
Minor	4.9% (2–7.7%)	9% (5.7–12.4%)

Table 4.

Outcome of cost-effectiveness analysis

	Intracranial stent placement	Medical-management only
Total cost (2010 USD)	$16,898	$3,468
Total QALY	0.82	0.81
Cost/QALY	$20,542	$4,265
ICER	**$1,416,268**	

analysis was performed evaluating the change in ICER across a range of periprocedural stroke rates within the 95% confidence interval. This analysis was then repeated simulating stroke rates forpatients with >70% symptomatic intracranial stenosis according to outcomes from a WASID pre-specified analysis by Kasner *et al* [28].

Results

The clinical event rates are summarized in Table 3. The total rate of stroke in one year after stent placement was 10.2% (95% confidence interval range 6.1–14.2%) in the pooled stent group, and 15% (10.8–19.2%) in the antiplatelet group of WASID. All-cause mortality was 3.7% (1.2–6.2%) in the stent-treated group compared with 2.4% (0.6–4.2%) for the WASID group. The rate of periprocedural stroke in the stent group was 4.6% (1.8–7.4%), of which half were major strokes. The total cost of treatment with stent placement was US$16,898 per patient compared with US$3,468 per patient with medical management only. The estimated total QALY for patients who underwent stent placement was 0.82 while the QALY for patients on medical-management only was 0.81. The calculated cost per QALY was US $20,542 and US$4265 for stent placement and medical management, respectively. The ICER, which is the additional cost needed for stent placement in order to gain one additional quality-adjusted life year relative to medical management only, was US$1.4 million (Table 4). The ICER was calculated over a range of values between the mean and the least frequent rate within the confidence interval for the observed rate of periprocedural strokes (Figure 1). Assuming a periprocedural stroke rate of 2.5%, the corresponding ICER is reduced to a minimum of US$729,384. This analysis was repeated assuming a total stroke rate of 23% by one year, simulating the rates seen in patients in WASID with a greater than 70% stenosis (Figure 2). The minimum ICER assuming a best-case periprocedural stroke rate of 2.5% is US$238,114.

Discussion

Intracranial stent placement has been increasingly evaluated in the last 15 years in terms of feasibility and prevention of recurrent strokes. This is the first study to analyze the cost effectiveness of this approach relative to medical management. Our analysis shows that based on available data, the costs associated with intracranial stent placement are not outweighed by the consequent

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improved clinical outcome after one year. Although the ICER was approximately halved when the periprocedural stroke rate was reduced to minimum rate of the 95% confidence interval, it remained significantly high (Figure 1). The results of our analysis add to the results of the recently terminated SAMMPRIS trial. The high 1 month rate of stroke and death in patients treated with angioplasty followed by stent placement suggests that broad applicability of this procedure is restricted by limited experience and technology in evolution. As efforts resume in developing new technology, the cost of the procedure needs to be addressed.

Previous analysis of WASID demonstrated a grade-dependent risk of recurrent ischemic stroke in the setting of symptomatic intracranial stenosis [28]. A similar evaluation was not possible with our data due to the fact that several of the larger studies included in the pooled analysis did not stratify post-procedural outcomes according to the pre-procedural degree of stenosis. Notwithstanding this limitation, we simulated the ICER for patients with 70% or greater degree of incident symptomatic intracranial stenosis by assuming the rate of recurrent attributable ischemic stroke by one year in the medical management-only group was the same as that reported by Kasner *et al* [28]. This analysis also assumed that the rate of periprocedural stroke does not significantly vary according to the degree of intracranial stenosis, as has been shown recently by Qureshi *et al* [29]. As a result, the ICER estimate for patients with an incident degree of intracranial stenosis of at least 70% was substantially lower than that for patients with stenosis of at least 50%, although even when the calculation was simulated for the minimum periprocedural stroke rate the ICER remained in excess of US$200,000 (Figure 2). In contrast, the cost-effectiveness of other stroke prevention modalities is notably greater: the reported ICER for carotid stent placement relative to endarterectomy is US $67,891; for warfarin relative to aspirin in patients with nonvalvular atrial fibrillation and additional stroke risk factors the figure is US$8000 [25,30]. In order for intracranial stent placement to be more cost-effective, the cost disparity of stent placement compared to medical management needs to be reduced substantially. Our base case scenario difference in costs between the two treatment strategies was US$13,430. Using these figures, stent placement would need to generate an improvement of at least 0.17 QALYs in order to meet a willingness-to-pay threshold of US$100,000 per QALY gained.

There are several important limitations to this study. Firstly, it is uncertain what proportion of the US$14,871 cost of intracranial stent placement could be partially

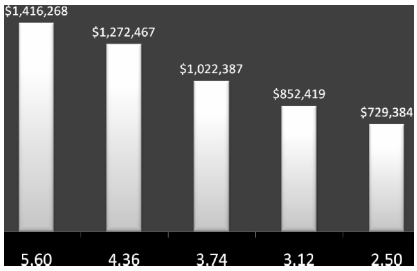

Figure 1. Incremental cost-effectiveness ratio (ICER) across the 95% confidence interval range of periprocedural stroke.

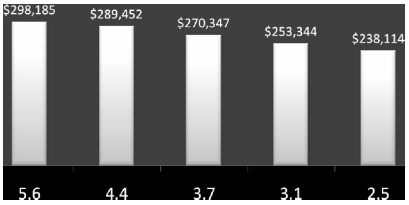

Figure 2. Incremental cost-effectiveness ratio (ICER) across the 95% confidence interval range of periprocedural stroke, assuming a total stroke rate of 23% for patients under medical management alone.

attributed to the costs of hospital admission after the index stroke or TIA. Such an effect would erroneously inflate the relative cost of stent placement; however, given that the majority of intracranial stent placement does not occur during the hospital admission after an initial stroke or TIA this source of bias is likely minimal. Secondly, there are significant points of heterogeneity among the stent trials used in our analysis. Four trials required some period of prolonged dual antiplatelet therapy following stent placement prior to subsequent single antiplatelet therapy: this period was 4 weeks in two studies (Gomez *et al*, Bose *et al*), 6 months in two others (Jiang *et al* 2007, Lee *et al* 2006) and indefinitely in one (Lee *et al* 2005). Patients with a known history of a possible cardioembolic source were not excluded from all trials. Different stent types and delivery systems were utilized, and none of the trials required evidence of operator proficiency or experience with the system used. Thirdly, there was significant variation in the duration between a qualifying ischemic event and stent placement, ranging from within 24 h to almost 3 years. This variation may have obscured the possible additional benefit to early stent placement, as recurrent ischemic events due to intracranial stenosis are significantly more likely to occur within 17 days of the initial event [28].

In conclusion, stent placement for symptomatic intracranial stenosis does not appear to be cost effective. Restricting stent placement to symptomatic stenosis of 70% or greater is more likely to be cost effective; how-

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ever, such evaluation would have to be considered in the light of the final results of the recently completed randomized SAMMPRIS trial.

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