

An Examination of Economic Outcomes Associated With Misdiagnosis or Undertreatment of TIA

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Abstract

Transient ischemic attack (TIA) is a common cerebrovascular event that is associated with a high risk for secondary stroke, possibly higher than stroke itself. Nevertheless, a TIA is often described as a “mini-stroke,” implying a less serious event requiring less urgent treatment. In reality, TIA and subsequent secondary stroke are associated with a very high economic burden. Cerebrovascular disease is the most financially costly of all major disease states, while morbidity and mortality risk is highly elevated in TIA patients. TIA is also associated with a very severe quality-of-life burden, which manifests both in terms of diminished functional independence and high rates of depression. Furthermore, TIA is commonly misdiagnosed and underdiagnosed, often leading to inappropriate treatment. More than half of patients who experience TIA are undiagnosed, while those who do receive a diagnosis are often offered neither diagnostic imaging nor hospital admission. Much of the morbidity and mortality associated with TIA and secondary stroke might be avoided by the application of timely and appropriate treatment. Clinical data have shown that accelerated treatment of TIA during its acute phase is associated with an 80% reduction of secondary stroke risk for the following 3 months, the period of greatest risk.

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For author information and disclosures, see end of text.

Introduction

Epidemiology

The incidence of transient ischemic attack (TIA) is estimated to be between 68 and 83 per 100,000 people in the United States.^{1,2} The rate is considerably higher among men and among African Americans, with men overall experiencing TIA at a rate of approximately 101 per 100,000 ($P < .001$ vs women), and African Americans at a rate of approximately 98 per 100,000 ($P < .025$ vs whites).¹ Prevalence rates based on data from the Cardiovascular Health Study, which followed 5201 patients with coronary heart disease (CHD) and stroke, estimated TIA prevalence for women aged 65 to 69 years at 1.6% and women aged 75 to 79 years at 4.1%.³ Men in the group 65 to 69 years of age had an estimated prevalence of 2.7%, and those 75 to 79 years of age 3.6%. In fact, the relationship between TIA prevalence and groups over 65 years of age is not linear: for example, women between 80 and 84 years of age have a rate of 1.7% compared with 3.2% for men in the same age group. There is a strong correlation between TIA occurrence and stroke. A review of 4 European (3 from the United Kingdom) stroke studies showed that 23% of the patients who suffered a stroke had previously experienced a TIA.⁴ Of those patients who experienced TIA before stroke, 17% had a TIA on the same day as the stroke, 9% on the day before, and 43% within the previous 7 days.⁴

TIA Definition

The definition of what constitutes a TIA, making it distinct from stroke or other cerebrovascular events, has evolved over the past 2 decades. In 1990, the National Institute of Neurological Disorders and Stroke defined TIA as an episode of focal loss of brain function with sudden onset and rapid resolution.⁵ It was acknowledged that while episodes lasting less than 24 hours were technically TIAs, this period of time was arbitrarily determined, and the longer the episode, the greater the likelihood of cerebral infarct. A modified definition was proposed in 2002 by the TIA Working Group of Albers et al.⁶ The working group’s definition states that TIA is “a brief episode of neurologic dysfunction caused by a focal brain or retinal ischemia” that lasts less than an hour without evidence of acute infarction. They further note that when clinical signs persist longer or when imaging shows the presence of infarction, then the diagnosis should be that of stroke.

Lamy and colleagues note that more than half of patients with TIA symptoms lasting 60 minutes or longer show lesions based on magnetic resonance diffusion-weighted imaging (DWI), and these patients have a significantly greater chance of experiencing aphasia and/or motor deficit.⁷ Noting that permanent brain injury did indeed occur in a proportion of conventionally defined TIAs, Ovbiagele et al propose a tissue-based definition based on DWI. Such a definition, according to their findings, would result in one third of all TIAs being reclassified as stroke.⁸

Underdiagnosis and Misdiagnosis of TIA

Although stroke is recognizable and a concern to the public at large, TIA is not well understood, although symptoms and clinical events are prevalent. Howard et al studied a group of 18,462 people without a diagnosis of stroke or TIA, many of whom might be expected to have higher than average risk of stroke. The study population was 41% African American, 51% overall were female, and 35% were from the southern and southeastern US “stroke belt.”⁹ They found that stroke/TIA symptoms were surprisingly common among people with no known diagnosis of TIA or stroke. Nearly 18% of those polled described at least 1 stroke/TIA symptom, the most common being “a sudden numbness or dead feeling on one side of the body.”⁹

Additionally, a survey by the National Stroke Association (NSA) of 10,112 US adults in 1999 found that only 8.2% could identify a typical symptom of stroke.¹⁰ A physician diagnosis of TIA had been received by 2.3% of those polled, although an additional 3.2% reported having symptoms consistent with stroke but failed to seek medical attention—suggesting that well over half of people who experience TIA do not actually receive a diagnosis. This is consistent with an earlier study from the United Kingdom, which found that 54% of people who had a TIA had not received medical treatment.¹¹ Furthermore, in the NSA poll, only 64% of people who received a TIA diagnosis had been seen by a doctor within 24 hours of the event.¹⁰

A primary reason for the underdiagnosis of cerebrovascular events associated with high morbidity and mortality is that TIA is widely thought, even by many clinicians, to be a “mini-stroke” and therefore requires a less urgent clinical response.¹²

In fact, TIA should be regarded with a sense of clinical urgency, since the risk of secondary stroke after TIA is at least as great as that following an initial stroke¹³; however, many physicians continue to consider TIA a nonemergency. An audit of 27 primary care practices in 2 separate geographic areas of the United States found that 31% of patients who presented to their primary care physicians with a first-time TIA were neither hospitalized nor had diagnostic studies undertaken for at least 1 month.¹² In addition, emergency departments (EDs) across the United States routinely discharge some TIA patients. A study in Nueces County, Texas, found that patients with TIA who present to the ED have an 88% chance of having brain imaging performed, a 65% chance of being admitted to the hospital, and only a 4% chance of receiving a neurology consult.¹⁴ Moreover, a stroke registry from Canada in 2004 demonstrated that 76% of TIA patients were discharged home from the ED, compared with 11% of those with a confirmed ischemic stroke.¹⁵

Morbidity and Mortality Following TIA

Elevated Post-TIA Risk Persists for 10 to 15 Years

The risk of a major vascular event after TIA is not only high but also long-lasting. With regard to risk of subsequent stroke, Hankey estimated that approximately 15% of strokes are preceded by a TIA.¹⁶ A study by Johnston et al of 16 Kaiser Permanente hospitals in northern California, in which more than 1700 patients had presented with TIA, found that 10.5% of patients returned to the ED within 90 days with stroke, half of them within the first 2 days post-TIA.¹⁷

In the North American Symptomatic Carotid Endarterectomy Trial, patients who had experienced an initial TIA had a 20.1% 90-day risk of secondary stroke, whereas only 2.3% of patients with an initial stroke had secondary stroke during the same time period.¹⁸ Data from the Oxford Vascular Study in the United Kingdom found that the risk of recurrent stroke after TIA was 8.0% at 7 days, 11.5% at 1 month, and 17.3% at 3 months.¹⁹

Over the long term, a study following 290 patients after initial TIA found that the 10-year stroke risk was 18.8%, whereas the risk for myocar-

dial infarction (MI) or death from CHD after TIA was 27.8%.²⁰ Over the 10-year period, patients who had initially experienced a TIA had a 42.8% risk of experiencing a stroke, MI, or vascular death. A recent 3-year study of 183 TIA patients observed a 28% risk of stroke or MI (stroke 19.7%, MI 8.2%) within 36 months of having a TIA or minor ischemic stroke.²¹ Taken together, these data point to a risk of secondary stroke after TIA at least as great as that after initial stroke.

Mortality After TIA

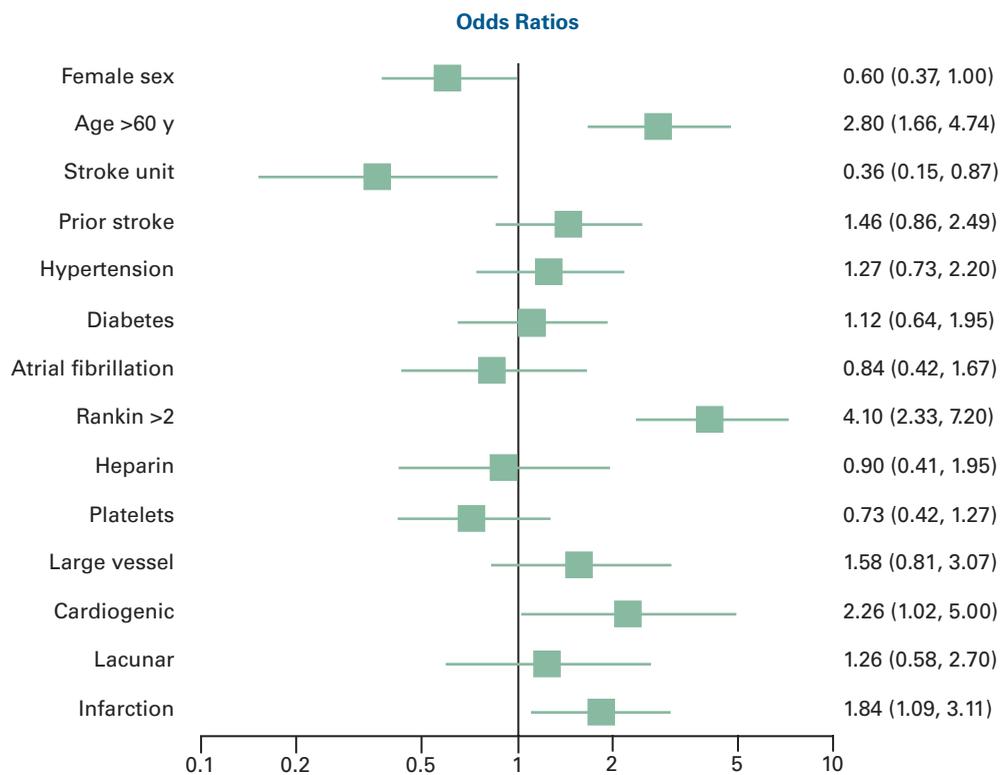
The long-term risks associated with TIA pertain to mortality as well as morbidity. A large observational study from Germany found that the in-hospital mortality risk for TIA patients was 2.2% and an additional 5% over the next 6 months of follow-up, for a total of 7.2% (Figure).¹³ Data regarding the 1-year mortality rate have varied somewhat. According to outcome data collected in Olmsted, Minnesota, 14.8% of patients died within 1 year of experiencing a TIA.²² This study

was based on reliable and trackable Medicare data. Furthermore, a large-scale Japanese study found a 1-year mortality rate of 3.5% in TIA patients; however, it was limited by depending on the return of questionnaires from patients and family members after hospital discharge.²³ In a longer-term study from the Netherlands, post-TIA mortality risk over 10 years was measured at 42.7%.²⁴

Stroke Risk Scoring

Over the course of Johnston et al's study of 16 Kaiser Permanente hospitals, the authors identified 5 independent risk factors for stroke occurring 90 days after TIA: age >60 years, diabetes diagnosis, symptom duration >10 minutes, weakness experienced with the episode, and speech impairment experienced with the episode.¹⁷ The more risk factors, the higher the chance of stroke; having all 5 risk factors conferred a 34% risk of stroke within 90 days.¹⁷ Calculation of stroke risk based on these 5 factors was dubbed the "California Score." The "ABCD Score" was subsequently developed by

■ **Figure.** Multivariate Analysis for Odds Ratio of Death and Dependency at 6-Month Follow-Up for TIA Patients



TIA indicates transient ischemic attack.
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Rothwell and colleagues, based on TIA and stroke data from a UK patient population, for calculating 7-day post-TIA risk of stroke.²⁵ This scoring system is similar to the California Score, with 6 possible points based on 5 risk factors. Four of the risk factors were the same as those used in the California system, the 1 difference being that while the California Score treated diabetes as a risk factor, ABCD replaced it with blood pressure.

The authors of the California and ABCD scores then combined forces to create a new scoring system for acute, 2-day risk of stroke after TIA, as this might be more clinically relevant given the high short-term stroke risk. This system, dubbed ABCD2, added the variables from both systems together, with unilateral weakness and duration of TIA in excess of 60 minutes being given added weight (Table).²⁶ A validation study for ABCD2 found that the 2-day risk for stroke after TIA based on low-, moderate-, and high-risk scoring ranges was 1.0% (0-3 points), 4.1% (4-5 points), and 8.1% (6-7 points).²⁶

Urgent Treatment Leads to Significant Reduction in Secondary Stroke

Considering the substantial morbidity and mortality risk associated with TIA, it is particularly important to note that if there is a greater awareness and recognition of TIA, the sequelae might be considerably less severe. Timely and appropriate treatment of TIA can drastically reduce the risk of secondary stroke. The EXPRESS (Early Use of Existing Preventive Strategies for Stroke) study examined the effect of immediate care compared with delayed care in 1278 TIA and stroke patients,

and found that early initiation of care resulted in an 80% reduction in the 90-day risk of secondary stroke.²⁷ A 2-year French study sought to determine the effect of providing a TIA clinic with 24-hour access (SOS-TIA), the purpose of which was to assess and treat TIA patients as soon after the event as possible. At the end of 2 years, the 90-day stroke risk in more than 1000 TIA patients was 1.24%, which compares to an expected risk rate of 5.96% based on ABCD2 scoring.²⁸

A key element in the armamentarium for acute stroke treatment is tissue plasminogen activator (tPA). Although tPA is not used to explicitly treat TIA, the opportunity to receive tPA increases the likelihood of better clinical and economic outcomes in the event of a secondary stroke immediately following a TIA.^{29,30} Cost efficacy of rapid treatment for TIA was also measured in a randomized trial of 149 TIA patients who were either treated under an accelerated diagnostic protocol (ADP) in the ED or traditional inpatient admission. Whereas the clinical outcomes for the 2 patient groups were comparable, the ADP group had a significantly shorter length of stay versus the inpatient group (25.6 vs 61.2 hours; $P < .001$), and incurred costs were significantly less (\$864 vs \$1528; $P < .001$).³¹

Economic Burden of Stroke

The consequences of stroke secondary to TIA are substantial both in terms of quality of life (QOL) and economically. Lifetime financial costs of stroke may continue to accrue over a period of years, and the indirect costs associated with stroke constitute 58% of the total costs.³² Based on data from strokes that

Table. Risk Factors Employed in the ABCD2 Scoring System for 2-Day Risk of Post-TIA Stroke

Risk Factor	Values	Points
Age	≥60 y	1
Blood pressure elevation (either/or)	Systolic ≥140 mm Hg Diastolic ≥90 mm Hg	1
Clinical features (either/or)	Unilateral weakness	2
	Speech impairment without weakness	1
Duration of TIA	≥60 min	2
	10-59 min	1
Diabetes	Yes/no	1

TIA indicates transient ischemic attack.
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occurred in the United States in 1990, the aggregate lifetime cost associated with an estimated 392,344 “first strokes” in 1990 was \$40.6 billion: \$5.6 billion for subarachnoid hemorrhage (SAH), \$6.0 billion for intracerebral hemorrhage (ICH), and \$29.0 billion for ischemic stroke (ISC).³² Lifetime costs per person of first strokes occurring in 1990 were estimated to be \$228,030 for SAH, \$123,565 for ICH, \$90,981 for ISC, and \$103,576 averaged across all stroke subtypes.³² Nursing home care was estimated to account for 17.5% of lifetime costs, whereas long-term ambulatory care was determined to account for 35.1% of these costs.³²

The overall costs of cerebrovascular disease are not only high, they are greater, by a wide margin, than other major disease states. A 2003 study comparing disease costs in 1997 found that compared with other diseases—including heart disease, cancer, pulmonary illness, and diabetes—cerebrovascular disease was more expensive on a per-person basis by a factor of 3 to 14 times.³³ Approximately two thirds of cerebrovascular disease costs are associated with inpatient care. A Canadian study of nearly 19,000 patients with ISC found that 73% of stroke survivors needed to be hospitalized at least once during the 4.6 years following the index stroke.³⁴ Interestingly, the costs associated with recurrent stroke exceed those of first stroke based on Medicare data.³⁵ Looking forward, the costs associated with stroke are expected to be considerable. The cost of ISC alone from 2005 to 2050 is projected to be \$1.52 trillion for non-Hispanic whites, \$313 billion for Hispanics, and \$379 billion for African Americans.³⁶

QOL Burden From Stroke Is Severe

Stroke survivors can be significantly burdened with a large deleterious effect on QOL. A Spanish study found that 1 year after stroke, disability (measured by the Barthel Index [BI]) was substantially reduced, with 20% of patients being incontinent, 32% requiring assistance for bathing, and 7% entirely dependent for personal hygiene; BI scores in women were significantly lower than in men ($P < .001$) (Figure).³⁷ Depression was also found to be severe, with 67% scoring in the depression range of the Hamilton Rating Scale (women 78% vs men 57%; $P = .014$), and 37.7% scoring in the major depression range.³⁷ It is interesting to note

that only one third of patients were depressed at discharge.³⁷ In fact, while inpatient rehabilitation can improve QOL measures in stroke survivors, a substantial decline in QOL will frequently occur within 6 months of discharge.³⁸

Taking into account the frequency with which individuals with TIA and stroke symptoms fail to receive a TIA or stroke diagnosis, it is perhaps not surprising that a substantial proportion of these undiagnosed individuals also suffer a diminished QOL. A comparison of people with TIA/stroke symptoms, but no diagnosis, with people without symptoms found that the differences on both mental and physical functioning indices were not only significant (both $P < .001$), but that the differences resembled the QOL differences between nonsymptomatic people and those with TIA or stroke.³⁹ The data gave further credence to the notion that a large number of people who experienced TIA and stroke remain undiagnosed and undertreated.

Conclusions

TIA is a serious cerebrovascular event not only commonly misdiagnosed but also frequently underdiagnosed. Although often perceived as a “mini-stroke,” the mortality risk associated with TIA is quite high, and the risk of secondary stroke after TIA is at least as great as an initial stroke. As a consequence of this high rate of post-TIA secondary stroke, there is a substantial economic burden, encompassing high rates of hospitalizations and inpatient rehabilitation. The QOL burden of secondary stroke is also severe and associated with significant mental and physical deterioration. And yet, much of these burdens—both QOL and economic—could be ameliorated with proper diagnosis, a more timely response, and greater awareness of the consequences of TIA.

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