Analysis of the Cost-Effectiveness of Thrombolysis with Alteplase in Stroke

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Abstract

Background: The cerebrovascular accident (CVA) or stroke is the main cause of death in Brazil and little information is available on the cost of treatment.

Objective: To carry out a cost-effectiveness analysis of thrombolysis in stroke, up to three hours after symptom onset, comparing the treatment with alteplase *versus* the conservative treatment, under the perspective of the Brazilian Public Health System (SUS).

Methods: A decision analysis model was developed to compare the two types of treatment. Cycles were considered, during which the patients would go through five stages of disability post-stroke, based on the modified Rankin scale. The probability to present intracranial hemorrhage in the first year was obtained from the NINDS trial. For the subsequent years, one-year cycles were considered to calculate patients' mortality. The outcome was expressed as quality-adjusted life years (QALY). Both direct and indirect costs were considered in the analysis. Costs and outcomes were discounted at 5% a year.

Results: In the first year, the QALY gained was 0.06 for both sexes, with an incremental cost of R$ 2,558 for men and R$ 2,312 for women. The incremental cost-effectiveness ratio (ICER) in one year was R$ 40,539 / QALY (USD 28,956) for men and R$ 36,640 / QALY (USD 26,171) for women. After the second year, the treatment with alteplase reduced the cost of treatment (Purchasing Power Parity index: US$ 1 = R$ 1.4).

Conclusion: The thrombolytic therapy with alteplase within the first three hours following a stroke is cost-effective in the Brazilian Public Health System scenario. (Arq Bras Cardiol. 2010; [online]. ahead print, PP.0-0)

Key words: Health care costs; stroke; tissue plasminogen activator.

Introduction

The cerebrovascular accident (CVA) or stroke is one of the main causes of death among the Brazilian adult population, varying between the first and the third positions, according to the year and state of the Federation[1]. Mortality is only one of the public health measurements of stroke impact, with sequelae being equally important, and, consequently, lack of productivity, loss of quality of life and premature retirement. It is estimated that 85% of the strokes are of ischemic origin and 15% of hemorrhagic origin[2].

The mortality of the ischemic stroke during the first 30 days is approximately 10%, mainly associated with neurological sequelae[3] and can reach 40% at the end of the first year. Among the patients that survive the acute phase of the stroke, most present neurological deficits that require rehabilitation[4]. Around 70% of these individuals will not return to work and 30% will need help to walk.

An epidemiological enquiry carried out the Brazilian Public Health System (SUS)[5] with stroke patients, at the productive age of 20 to 59 years, demonstrated that 80% referred some type of persistent functional disability after the first episode. After the stroke, 70% of the patients became unemployed or retired prematurely.

Up to the last decades, the ischemic stroke outcome was determined by the natural evolution and support measures. In July 1996, the Food and Drug Administration (FDA) approved the use of *recombinant* tissue plasminogen activator (rt-PA) for the treatment of stroke at the acute stage.

In ischemic stroke, the probability of the affected tissue to develop necrosis depends on the residual brain blood flow in the affected region as much as on the duration of ischemia[6]. The main objective of the thrombolytic drugs is to restore blood flow in the affected area as early as possible, with a consequent decrease in ischemia and limitation of the neurological injury[7].

The objective of the present study was to carry out a cost-effectiveness analysis of thrombolysis in stroke up to

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three hours after symptom onset, comparing the treatment strategy with rt-PA with the conservative treatment, under the perspective of the Brazilian Public Health System (SUS).

Methods

The first phase of the study consisted in the review and critical analysis of the literature. The review was carried out by searching the databases Medline, Cochrane and LILACS for all studies published in Portuguese, English or Spanish that had evaluated the use of rt-PA in ischemic stroke treatment during the last ten years, until May 2008. The inclusion criteria were: type of study (randomized clinical trial, review articles, systematic reviews and meta-analyses) and study population (individuals older than 18 years with ischemic stroke). The studies were limited to those carried out with human beings. The main keywords used in the search were: alteplase, rt-PA, stroke, efficacy. After the search had been carried out, their references were analyzed to locate new publications of interest. The search selected, initially, articles according to the title and/or summary and then, the article was read and critically analyzed, if it were relevant to the objective of the study.

The initial search identified 67 articles. Of these, 28 met the inclusion criteria. Sixteen of them were review articles and 10 reported results of controlled clinical trials. A systematic Cochrane[8] review was found on the use of thrombolytic drugs in general, including rt-PA. A summary of this review was published in the *Lancet* in 1997[9]; however, in 2003 this review underwent alterations, and therefore, it was updated.

Four randomized double-blind clinical trials were carried out to assess the effectiveness and safety of rt-PA use in ischemic CVA: National Institute of Neurological Disorders and Stroke (NINDS) trial[10], the first and second European cooperative Acute Stroke Studies (ECASS I[11] e ECASSII[12]) and Alteplase Thrombolysis for Acute Non-interventional Therapy in Ischemic Stroke (ATLANTIS) Study[13].

Cochrane Collaboration performed a systematic review, of which last update was carried out in March 2003, to evaluate the effectiveness and safety of the thrombolytic agents in general, in ischemic stroke. A total of 18 clinical trials were assessed, totaling 5,727 patients assessed, testing urokinase, streptokinase, recombinant tissue plasminogen activator (rt-PA) or recombinant pro-urokinase (r-pro-UK). Approximately half of the data referred to rt-PA.

Table 1 summarizes the results of the clinical trials and the meta-analyses that evaluated the efficacy of rt-PA.

Perspective of the analysis

The estimates of the use of resources and value appraisal were guided by the perspective of the Brazilian Public Health System (SUS).

Target-population

Two groups of patients were analyzed, older than 18 years, of both sexes: the first received treatment with rt-PA and the second received the conservative treatment. Only patients treated within three hours since stroke symptom onset were analyzed.

Model design

The type of analysis selected was the analysis of cost-effectiveness, more specifically, the cost-utility analysis, as the model compared the direct and indirect costs involved in the treatment and follow-up of stroke patients and the health outcome in terms of quality-adjusted life years (QALY).

To estimate the treatment costs and outcomes, a Markov model was created, which simulated the treatment of stroke in the acute phase and the transition of patients between the different levels of severity of post-stroke sequelae, characterized by the different states of Markov. The analysis compared the two treatment strategies considered in the NINDS study[10]: use of rt-PA and placebo, in this case, considered as the conservative treatment. The structure used in the model is shown in Figure 1.

In the present study, the patients were included in the model after an ischemic stroke event. When included in the model, it is assumed that the patient will receive treatment with rt-PA or the conservative treatment. During the treatment, the patient can experience an intracranial bleeding event.

After the stroke treatment, the patients pass through different health stages, according to the degree of sequelae as a consequence of the stroke. In the first year, three-month cycles were considered, at the end of which the patient's status was reassessed and classified according to the modified Rankin scale. The possible states were: R0 (no symptoms), R1 (no significant disability), R2 (minimal disability), R3 (moderate disability), R4 (moderate to severe disability), R5 (severe disability) or death.

After the first year, one-year cycles started to be considered, after which the patients remained at the state they were at the end of the first year or died.

Considered outcomes

The considered health outcome was quality-adjusted life years (QALY). This outcome evaluates the disability caused by the sequelae that impair the quality of life of patients post-stroke. Due to the absence of Brazilian estimates of utility for post-stroke patients, we chose to adopt the utility values of the systematic review created by Post et al[14]. These authors selected 23 articles that measured utilities for the post-stroke health status. Patients that presented risk for stroke reported utilities, with the time trade-off method, of 0.26 (lower limit of 0.11 and upper limit of 0.39) and 0.55 (lower limit of 0.39 and upper limit of 0.75) for major stroke (Rankin scale from 4 to 5) and minor stroke (Rankin scale from 2 to 3), respectively. For the Rankin scale de 0 to 1, a value of 0.75 was considered.

The economic outcomes considered were "direct and indirect costs". Direct costs refer to the resources used for the patient's treatment, such as cost of medication, hospitalization and rehabilitation treatments. These were collected under the perspective of SUS. The indirect costs refer to the onus derived from the loss of productivity of individuals that retire prematurely due to the stroke sequelae.

Both costs and years of life were discounted at a rate of 5% a year. The impact of this percentage on the results of the model was assessed by analysis of sensitivity.

Table 1 - Review of the main studies that assessed the efficacy of rt-PA compared to placebo, in treatment of ischemic CVA

Study	rt-PA Dose	Between sympton onset and treatament	Outcomes	Hemorrhagic Complications	Mortality at the end of the study
ECASS I Clinical Trial Phase III[11]	1.1mg/kg (Máximum 100 mg)	6 hours	Primary (90 days): BI: IT p=0.99; PP=0.16. RMS: IT p=0.41; PP=0.035. Secundary: SSS (90 days): IT p=0.54; PP p=0.03. BI+RMS(90 days): IT e PP p <0.001; NIHSS(24h): IT p=0.02; PP=0.004. NIHSS(90 days): IT=0.1; PP p= 0.01. Time of hospitalization: IT p=0.002; PP p= 0.004 Mortality (30 days): IT p=0.08; PP p=0.36.	Hemorrhagic Infarction: IT: rt-PA= 23.0%; placebo= 30.3% PP: rt-PA: 24.3%; placebo= 29.9% Intraparenchymatous Hemorrhage: IT: rt-PA= 19.8%; placebo= 6.5% PP: rt-PA: 19.4%; placebo= 6.8%	IT: rt-PA= 22.4%; placebo= 15.8%; p= 0.04 PP: rt-PA= 19.4%; placebo= 14.8%; p= 0.17
NINDS trial Clinical Trial Phase III[10]	0.9 mg/kg (Máximum 90 mg)	3 hours	Part A (24h): complete recovery of neurological deficit or improvement > 4 NIHSS: p = 0.2 Parte B (3 months): BI=95-100, NIHSS e RMS < 1, GOS=1: OR=1.7 (IC 95%1.2-2.6); p= 0.008	Asymptomatic hemorrhage within first 36h: similar in the 2 groups Symptomatic hemorrhage within first 36h: rt-PA=6.4% placebo=0.6% p<0.001	rt-PA=17% placebo=21% p=0.30
ECASS II; ClinicalTrial Phase II[12]	0.9 mg/kg (Máximum 90 mg)	6 hours	Primary: RMS 0-1 rt-PA=40.3%; placebo=36.6%; p=0.277 Post-hoc analysis (RMS 0-2): rt-PA=54.3%; placebo=46.0%. Secondary: NIHSS (30 days); BI+RMS;BI(90 days); SSS(90 days); SF-36 (90 days); time of hospitalization. The only secondary outcome with a significant difference between the groups was NIHSS (p=0.023).	Hemorrhagic Infarction: p= NSa Intraparenchymatous Hemorrhage: rt-PA: 11.8% Placebo: 3.1%	rt-PA= 10.5%; placebo=10.7%; p=NSa
ATLANTIS; Clinical Trial Phase III[13]	0.9 mg/kg (Máximum 90 mg)	3-5 hours	Primary: NIHSS < 1 (90 days): IT rt-PA=34.5%; placebo=34.0%; p=0.89 PP rt-PA=34%; placebo=32%; p=0.65 Secondary (30 and 90 days): BI>95: p=NSa RMS=0-1: p=NSa GOS=1: p=NSa	Symptomatic hemorrhage: PP: rt-PA= 7.0%; placebo=1.1%; p<0.001 Asymptomatic hemorrhage: PP: rt-PA= 11.4%; placebo=4.7%; p=0.004	PP : rt-PA= 11.0%; placebo= 6.9%; p=0.09
Cochrane[8] meta analysis	-	-	Death and dependence: OR=0.80 (IC95% 0.69-0.93; p= 0.003)	Intracranial hemorrhage: OR=3.4; IC95% 1.48-7.84	OR=1.17; IC95% 0.95-1.45

[a] Non significant; IT - intention to treat analysis; PP - analysis per protocol; OR - odds ration; IC - confidence interval.

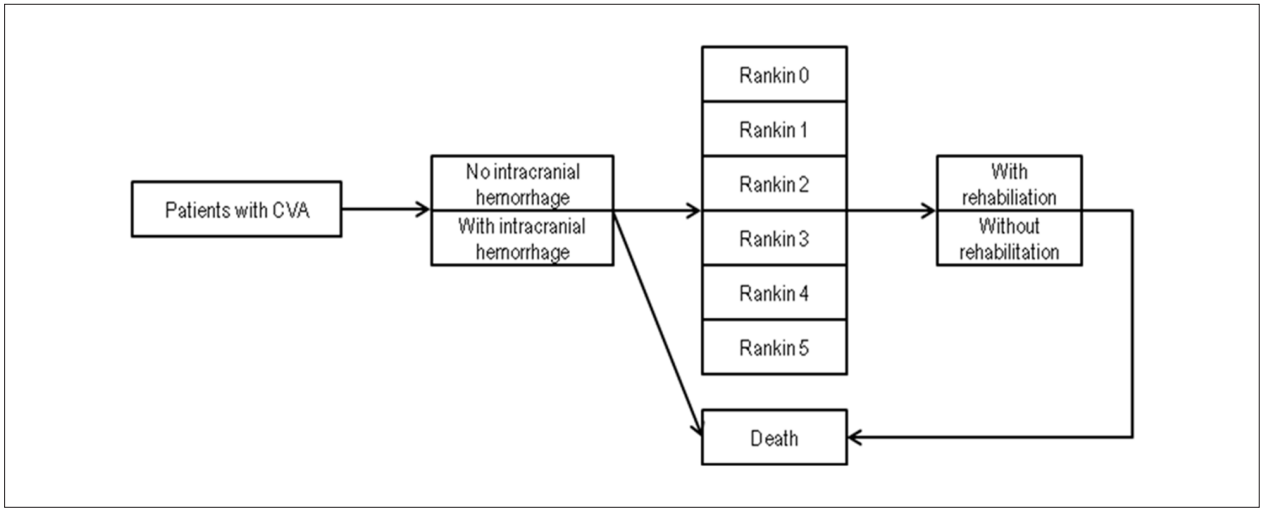

Figure 1 - Structure of Markov´s model.

The results were calculated for different time horizons, varying from 1 to 30 years.

Data collection

Effectiveness Data

The probabilities of transition between the degrees of severity of the post-stroke sequelae every three months were extracted from the NINDS study[10] for the first year of the model, as shown in Table 2. The values for nine months were obtained by interpolating the 6-month and the 12-month data. The choice of the NINDS study was due to the fact that this was the only study that assessed patients who received treatment within three hours after stroke symptom onset, with the approved dose of 0.9 mg/kg.

After this period, the model considered that the patients would remain at the same health status or would die due to other causes at each one-year cycle. The mortality rate due to all causes was extracted from IBGE (The Brazilian Institute of Geography and Statistics) for men[15] and women[16]. The model also considered that, after the stroke, the mortality rate of the patients would be 2.67-fold[17] higher than that of the general population.

After the first year of the model, similar mortality rates were considered for all patients, varying only between men and women, regardless of the degree of severity of the sequelae that the patient presented. Moreover, the probabilities of intracerebral bleeding during the stroke treatment were also obtained from the NINDS study[10], which were 6.40% with rt-PA and 0.60% with the conservative treatment.

The mean age of the patients being treated with rt-PA at the NINDS study[10] was 67 years. Due to the absence of similar studies segmented by age range, the model assumed that the effectiveness obtained at the NINDS study could be extrapolated to other age ranges.

Direct cost data

For the first cycle of the model, the costs of treatment of stroke patients were considered. The use of resources was considered to be equivalent for men and women, except for the amount of rt-PA used. The latter varies according to the patient's weight, as the treatment protocol of 0.9 mg/kg was considered, as well as different mean weights for men and women, 75 kg and 65 kg, respectively. Moreover, the difference between the treatment with rt-PA and the

Table 2 - Results by the modified Rankin scale for pacients that received rt-PA or conservative treatment, after 3, 6, 9 and 12 months

Status	3 months		6 months		9 months		12 months	
	rt-PA	Conservative Treatment	rt-PA	Conservative Treatment	rt-PA	Conservative Treatment	rt-PA	Conservative Treatment
R0	18%	11%	19%	11%	20%	11%	20%	11%
R1	24%	16%	22%	18%	22%	18%	22%	17%
R2	7%	12%	8%	11%	8%	11%	8%	12%
R3	13%	14%	14%	17%	13%	15%	13%	13%
R4	14%	20%	10%	14%	8%	13%	6%	12%
R5	6%	7%	5%	6%	5%	6%	5%	6%
Death	17%	21%	21%	24%	23%	27%	26%	30%

conservative treatment also includes the cost of hospitalization. The NINDS study[10] showed a difference regarding the mean duration of hospitalization of patients undergoing treatment with rt-PA or placebo. However, as the SUS reimbursement is calculated by procedure and not by daily hospitalization cost, this difference could not be incorporated in the model, with conservative results being attained for rt-PA, as the benefit of the decrease in the mean duration of hospitalization in days was not considered.

The costs considered for the treatment of stroke, including the cost of treatment of a bleeding event, using rt-PA or conservative treatment is shown in Table 3.

After the stroke, the patients started the follow-up period, and could be assigned to five different states, classified according to the degree of sequelae, based on the modified Rankin scale, or die. Depending on the post-stroke patient's status, different percentages of patients needed rehabilitation. This percentage was obtained based on a cost-utility study developed under the Canadian perspective[18], which considered the percentage of patients that needed support at a specific structure after the stroke (rehabilitation hospital or long-term care institution) or went back home.

In the current model, we considered that the patient would need or not rehabilitation treatment, but in both cases, he or she would return home. The rehabilitation treatment considered was a daily home visit to assist the patient.

All patients being followed also received treatment with antiaggregants and anti-hypertensive drugs and had a consultation with a neurologist very two months. No differences were considered regarding the use of resources by sex and age range.

Indirect cost data

The indirect costs considered in the model referred to the loss of productivity and early withdrawn of the retirement funds due to the premature retirement of patients, depending on the severity of the stroke sequelae.

In order to do that, we obtained from IBGE[19] the mean rate of unemployment of the population and the mean monthly income of the employed population. Thus, the mean loss of work per year was calculated.

Moreover, a mean monthly retirement of one minimum wage was considered to calculate the additional cost per year of premature retirement.

The model considered, therefore, that, if the patients were younger than the mean age of retirement and were in a state of the Rankin scale ≤ R3 (R3, R4 or R5), the consequence would be the costs caused by the loss of productivity and additional costs concerning the social security. In case of death, only the costs concerning the loss of productivity would apply.

The parameters considered for the calculation of indirect costs are shown in Table 4.

Results

The comparative results of the alternative strategies of treatment were measured by the incremental cost-effectiveness ratio. That is defined, for two specific alternatives of treatment, as the additional cost of treatment divided by the additional health benefit. This "benefit" was expressed in terms of QALY.

The model base case considered a rate of discount of 5% a year and an initial mean age of the patients of 50 years. Additionally, mean retirement ages of 60 and 65 years, for women and men, respectively, were considered.

The one-year results for men and women are shown in Table 5. Table 6 shows the results for different time horizons, from 1 to 30 years.

It can be observed that, for a one-year result, for men, the cost of treatment with rt-PA is higher than the cost of the conservative treatment. This result is mainly directed by the cost of the medication. Part of this additional cost is compensated by the lower cost of rehabilitation and the smaller losses of productivity as early as the two first years, as the patients treated with rt-PA present fewer sequelae than those who receive the conservative treatment.

After the second year post-stroke, for men and women, the treatment with rt-PA starts to present a lower cost when compared to the conservative treatment, when direct and indirect costs are considered. From this time horizon onward, the additional cost of the medication starts to be more than compensated by the smaller losses of productivity and lower social security and patient rehabilitation costs.

The analysis of cost-effectiveness measures the cost in monetary units divided by a non-monetary unit, called the natural unit, for instance, "years of life saved". It allows the estimation of the cost per unit of effectiveness. A healthcare intervention is called cost-effective if it produces a clinical benefit that is justifiable for its cost.

The calculation of how much the additional effectiveness justifies the additional cost is determined by society and depends on social values and the availability of resources. Although the explicit quantification of the acceptable cost for certain effectiveness ("clinical benefit") is difficult to define, valuable levels of reference are the medical interventions that the society chooses to incorporate[20]. The World Health Organization (WHO) recommends a 3-fold value of the Gross Domestic Product (GDP) *per capita* of the country where the analysis was carried out, as the limit of cost-effectiveness justifiable for that context.

Analysis of sensitivity

Univariate analyses of sensitivity were carried out to evaluate the impact of key-parameter variation on the results of the model.

Table 7 presents the results of the variation of the types of costs considered in the analysis. The base results considered in the analysis are the five-year results.

Discussion

Our study suggests that the early intervention in the stroke evolution can be a cost-effective strategy for the Brazilian Public Health System (SUS), using the limits recommended

Table 3 - Cost of the CVA treatment segmented by sex and type of treatment

Costs	Men		Women	
	rt-PA	Conservative treatment	rt-PA	Conservative treatment
Diagnosis				
Skull Computed tomography	R$ 173.52	R$ 173.52	R$ 173.52	R$ 173.52
Etiological Investigation				
Doppler ultrasound of carotid and vertebral arteries	R$ 27.51	R$ 27.51	R$ 27.51	R$ 27.51
Electrocardiogram	R$ 3.22	R$ 3.22	R$ 3.22	R$ 3.22
Chest X ray	R$ 9.50	R$ 9.50	R$ 9.50	R$ 9.50
Transthoracic or transesophageal Echocardiogram with doppler	R$ 20.69	R$ 20.69	R$ 20.69	R$ 20.69
Laboratory assessment				
Complete blood count and platelets	R$ 4.11	R$ 4.11	R$ 4.11	R$ 4.11
Glucose	R$ 1.85	R$ 1.85	R$ 1.85	R$ 1.85
Creatinina	R$ 1.85	R$ 1.85	R$ 1.85	R$ 1.85
Urea	R$ 1.85	R$ 1.85	R$ 1.85	R$ 1.85
Sodium	R$ 1.85	R$ 1.85	R$ 1.85	R$ 1.85
Potassium	R$ 1.85	R$ 1.85	R$ 1.85	R$ 1.85
Arterial gasometry	R$ 15.65	R$ 15.65	R$ 15.65	R$ 15.65
Activated partial thromboplastin time (APTT)	R$ 2.73	R$ 2.73	R$ 2.73	R$ 2.73
Prothrombin Time (PT)	R$ 2.73	R$ 2.73	R$ 2.73	R$ 2.73
Blood typing	R$ 1.37	R$ 1.37	R$ 1.37	R$ 1.37
Total cholesterol and fractions	R$ 12.38	R$ 12.38	R$ 12.38	R$ 12.38
Triglycerides	R$ 3.51	R$ 3.51	R$ 3.51	R$ 3.51
Fibrinogen	R$ 4.60	R$ 4.60	R$ 4.60	R$ 4.60
Hospitalization				
ICU stay	R$ 646.43	R$ 646.43	R$ 646,43	R$ 646.43
Medication and materials				
Aspirin 200mg	R$ 0.02	R$ 0.02	R$ 0.02	R$ 0.02
Captopril 100mg + Hydrochlorothiazide 50mg	R$ 0.10	R$ 0.10	R$ 0.10	R$ 0.10
Propanolol 80mg	R$ 0.02	R$ 0.02	R$ 0.02	R$ 0.02
Actilyse	R$ 2,149.31	R$ -	R$ 1,862.73	R$ -
Infusing pump	R$ 0.97	R$ -	R$ 0.97	R$ -
Intercranial hemorrhage				
Conservative treatment of brain hemorrhage	R$ 81.03	R$ 7.60	R$ 81.03	R$ 7.60
Total	R$ 3,168.65	R$ 944.94	R$ 2,882.07	R$ 944.94

by the WHO. The GDP *per capita* of Brazil in 2007 was US$ 9,700, equivalent to the cost- effectiveness threshold of US$ 29,100 (3x the GDP *per capita*) per QALY.

The NINDS clinical trial showed that patients treated with rt-PA within three hours after symptom onset, when compared to the placebo group, had at least a 30% higher probability of presenting minimal disability or none at all after 3 months. This benefit, although associated with an increased risk of intracranial bleeding, was not related to an increase in mortality.

The treatment of stroke patients implies elevated costs, estimated in 1994 in the United States as 20 billion dollars of direct costs and 46 billion dollars of indirect costs[21]. Therefore, an intervention capable of preventing

the consequent unfavorable stroke outcomes will have an important economic impact.

Christensen et al estimated the cost of the acute treatment of ischemic and hemorrhagic stroke in two Brazilian public hospitals[22]. The authors used a retrospective analysis of medical files and identified 316 patients with a mean hospital stay duration of 12.0±8.8 days for ischemic stroke and 13.3±23.4 days for hemorrhagic stroke. The mean cost of hospitalization for the treatment of ischemic stroke was US$ 1,902. In our study, for the group of hypothetical patients allocated at the alteplase group, it was US$ 2,262 for men and US$ 2,058 for women (Table 3). The same Purchasing Power Parity index: was used: 1 US$ = 1.4 reais[1].

The analysis of cost-effectiveness of thrombolysis in Acute Myocardial Infarction (AMI) has also been recently estimated in our country, in the Public Health System scenario[23]. The researchers concluded that the strategy of pre-hospital thrombolysis of the AMI can save lives and reduce costs related to the treatment of AMI and its complications.

Our study has some limitations, a characteristic of the cost-effectiveness analyses carried out with decision analysis models. The data used in the model are obtained from controlled clinical trials, that is, it refers to efficacy data, instead

[1] http://siteresources.worldbank.org/ICPINT/Resources/summary-tables.pdf

Table 4 - Parameters considered in the calculation of indirect costs

Parameters	Cost	Source
Mean annual income	R$ 13,299.60	Monthly employment research IBGE - july/07
Rate of unemployment	9.45%	Monthly employment research IBGE - jul/07
Mean annual retirement	R$ 4,940.00	12 minimum wages (30/03/07) + 13th salary

Table 5 - Comparative results between rt-PA and the conservative treatment tratamento conservador after one year for men and women

Outcome	Men			Women		
	Treatment with rt-PA	Conservative treatment	Incremental	Treatment with rt-PA	Conservative treatment	Incremental
QALY	0.47	0.41	0.06	0.47	0.41	0.06
Cost	R$ 3,219	R$ 661	R$ 2,558	R$ 2,973	R$ 661	R$ 2,312
RCEI - R$ / QALY salop			R$ 40,539			R$ 36,640

Table 6 - Incremental results over different time horizons

Years	Men			Women		
	Incr years	Incr cost	Cost/QALY	Incr years	Incr cost	RCEI
1	0.03	608	18,765	0.03	363	11,204
2	0.07	(1,233)	(17,539)	0.07	(1,501)	(21,201)
3	0.11	(2,935)	(27,873)	0.11	(3,246)	(30,422)
4	0.14	(4,506)	(32,723)	0.14	(4,878)	(34,768)
5	0.17	(5,951)	(35,550)	0.17	(6,403)	(37,314)
10	0.28	(11,522)	(40,858)	0.30	(12,573)	(42,106)
15	0.35	(14,898)	(42,384)	0.38	(12,855)	(33,511)
20	0.39	(15,024)	(38,582)	0.44	(13,031)	(29,867)
25	0.41	(15,082)	(37,075)	0.47	(13,127)	(28,218)
30	0.41	(15,103)	(36,551)	0.48	(13,170)	(27,541)

Table 7 - Analysis of sensitivity with the impact f the types of costs over the results of the mode

Types	Men			Women		
	Incr years	Incr cost	Cost/QALY	Incr years	Incr cost	Cost/QALY
Direct only	0.03	2,558	78,951	0.03	2,312	71,358
Directs and indirects	0.03	608	18,765	0.03	363	11,204

of effectiveness data that portray the "real world". The result expresses the mean cost of a usual patient, does not portray the cost of patients that present complications and require a long-term hospitalization. No median values were used for the monthly income, as healthcare decision-makers and policy-makers are more familiarized with the use of means for monetary values.

The proposed treatment is based on the guidelines of the Specialty Medical Societies, which does not necessarily express the usual treatment of patients in the Public Health System. The models are probabilistic estimates of the natural history of the disease and their interventions and hardly incorporate all uncertainties inherent to biology and thus, should be always critically analyzed regarding the capacity of generalization for "real-world" patients.

Conclusion

The use of rt-PA thrombolytic therapy within the first three hours of the CVA evolution can change the natural history of the disease. It is noteworthy the fact that this is the only effective intervention available in the current therapeutic arsenal, substituting the conservative and expectant treatment. This intervention can minimize direct costs, by reducing hospitalization time and rehabilitation duration and, especially, it can reduce the indirect costs (loss of productivity, absenteeism, premature death), with a significant socioeconomic impact.

When the loss or gain of productivity can be measured in monetary units, due to a treatment that has been applied, the health policy makers can make more conscious decisions, based on consistent information.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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