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The cost effectiveness analysis of mechanical thrombectomy with venous thrombolytic compared with venous thrombolytic alone in patients with an acute stroke in Iran

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Background: **Stroke is the most common cause of mortality and illness among neurological patients. In recent years, novel significant technologies have been developed to improve the treatment of patients with stroke, such as mechanical thrombectomy or arterial thrombolytics along with intravenous thrombolytics. However, its economic impact in developing countries has not yet been assessed.** ***Objective:*** **The aim of this study is to put forward a piece of academic research on the cost-effectiveness of the two above-mentioned therapeutic methods in patients with severe stroke in Iran.** ***Method:*** **The Markov model contained three modes for the evaluation of the cost-effectiveness analysis of mechanical thrombectomy with intravenous thrombolytics compared with intravenous thrombolytics alone in patients with an acute stroke in Iran. The cycle was a one-year study and life time frame. The input data of the model included clinical, epidemiological and cost data. A series of patients with stroke who referred to a referral cardiac hospital in Tehran during one month period were used as sample. The cost of these patients was extracted by referring to their medical records. One-way sensitivity analysis and Tournado were exerted to measure the impacts of uncertainty inputs of the model. A discount rate of 5% was used. Ethics approval was obtained from the local institutional review board.** ***Results:*** **A total of 50 patients with acute stroke were enrolled who referred to the referral hospital. Despite the fact that the thrombectomy therapy with intravenous thrombolytics costs 320565 dollars, the additional cost could be justified in terms of benefits that participant would receive of 2.43 QALY. In addition, in the intravenous thrombolytics group, 1,441 QALY is generated in the value of 270,410 dollars. The incremental cost-effectiveness to gain a QALY was 49171 dollars. Taking all evidence into account, the variables of thrombectomy efficacy, discount rate, and thrombectomy cost should have the most impact on cost-effectiveness outcome.** ***Conclusion:*** **Thrombectomy therapy with intravenous thrombolytics is a cost-effective measure for patients with acute stroke. National research and cultivation in this area can greatly reduce the burden of stroke.**

INTRODUCTION

Stroke is one of the common cause of death and illness among neurological patients (1). It is the number one cardiovascular disorder in the United States and in the world and it is the fourth leading cause of death in the world after heart disease and cancer (2). Evidence suggests that the burden of disease from stroke in developing countries, and low incomes and middle incomes are increasing, as it is estimated that a large volume of stroke will occur in poorer countries in the coming years (3, 4).

In recent years, there has been a lot of progress in the clinical management of patients with stroke and significant specialized interventions have been developed. The production of anticlot drugs as one of these achievements in the form of injections in less than 4 hours from the onset of symptoms has had a dramatic effect on the reduction of morbidity and inability of patients. However, the patient may not receive the medication over time, in which different methods may be used simultaneously.

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One of them is using mechanical thrombectomy alongside of intravenous thrombolytics therapy, which scientific evidence approve that there are significant clinical improvements compared with the separate presentation of intravenous thrombolytics (5-7).

However, the decision to develop these new service trends in all countries requires an examination of the financial and economic impacts that if utilized by these new technologies, regardless of the size of the allocation of resources and the financial situation of these countries, can have potentially beneficial effects (8, 9). It reduces the use of these expensive technologies and increases inefficiencies in allocating limited resources to stroke management (10).

Iran is one of the developing countries which is ranked among the middle income countries. In Iran, stroke causes several thousand deaths and also results in major physical disabilities such as walking and performing self-care (11-13). Scientific evidence suggests that a significant amount of this disease can be reduced by developing stroke units and applying new technologies to stroke (14, 15). However, financial constraints on this path have led to the development of technologies that have the greatest clinical advantage over increased fiscal costs. So, the implementation of this recommendation across Iran requires more resource allocation and ensuring that value for money is essential in this decision (16-18).

The recommendation to use thrombectomy plus intravenous thrombolytics has recently been included in the current protocol for managing stroke patients in Iran without analyzing value-for money and taking into account its economic impacts (19, 20). The aim of this study was to evaluate the cost-effectiveness of performing thrombectomy with intravenous thrombolytics versus the presentation of only intravenous thrombolytic therapy in patients with acute stroke in Iran.

METHOD

The data related to the cost of using interventions collected through access to medical records of patients referring to Shahid Rajaee Heart Hospital, a refarral hospital in Iran. Shahid Rajaee Hospital is one of two specialized hospitals for the treatment of patients with vascular problems that is located in Tehran. The hospital is known as a reflexology center that refers patients with complex cardiovascular problems from nearby provinces to the hospital. New technologies for stroke treatment are being used in this hospital before being widely used in centers around the country. Therefore, this hospital can be a good reference for extracting cost data from patients and generalizations to the whole country.

In order to evaluate the long-term economic and clinical effects of mechanical thrombectomy with intravenous thrombolytic versus intravenous thrombolytics, a Markov model developed by Health Quality Ontorio was applied (21). Due to the difference in epidemiological data and cost data in Iran, the model was adjusted.

For cost-effectiveness analysis, clinical outcome selected for the effectiveness of this model is QALY all of which have been extracted from published studies (15, 19, 21). Costs and interpretation of evidence are considered from the payer's perspective. As mentioned above, the input of the model was patients with severe stroke that obstruction is confirmed by diagnostic tests and of whom previously there were not any disability.

To extract costs, the medical records of those patients aged 60 to 65 years collected. Patients who died before medical interventions were removed from the sampling. Sexual differences were not applied between patients at the time of data extraction. For cost-effectiveness analysis, the Markov model selected which has been developed by the Ontario Institutes of Health's Health Technology Assessment Group (21). The discount rate of five percent was applied to the consequences and costs. The length of each period was one year and the time frame of this model was up to the end of the patients 'lives, which was adjusted to the patients' life expectancy. The model consists of three modes of health: able patients with severe stroke (mRS ranging from 0 to 2), disable patients with stroke (mRS ranging from 3 to 5) and patient death (mRS is 6). Patients will receive either a thrombectomy with intravenous or in another strategy only receive intravenous thrombolytic therapy. Patients after receiving interventions, either remain abled, or have a disability and continue or die, and end with death. The schematic diagram of the model is as shown in Figure 1.

After meeting the clinical specialists of the project and reading the case files of patients with severe stroke, cost items related to the implementation of any of the interventions strategies under study were extracted. These costs include the cost of clinical interventions, laboratory tests, nursing care, hospital accommodation, visits by clinicians and costs associated with patient admissions. As stated, these costs were extracted by referring to the patients' medical record.

Then, the number of times every cost item used in patients in each of the study strategies is clearly determined. The cost of carrying out the application was obtained by inquiry from the Ministry of Health's Medical Tariff Department and the relative value book approved by the government in 2017. Ethics approval was obtained from the local institutional review board.

Ethics approval and consent to participate

Informed consent forms were obtained from all subjects participated in the study. The Ethics Committee of Iran University of Medical Sciences concurred with the study protocol (IR.IUMS.REC.1395. 9221504205).

RESULTS

The largest difference in the cost of staying in the strategy of thrombectomy plus intravenous thrombotic was the drug consumption. The cost of tracking disabling patients was about 60% higher than that of independent patients. Table 1 shows the cost per item cost in the study guidelines.

The results of the cohort simulation show that the mechanical thrombectomy strategy along with intravenous thrombolytic can bring 2.43 units of QALY with a cost of 320565 dollars per patient and 0.64 of inabilities. In the strategy of conducting intravenous thrombolytics can provide 1.41 units of QALY and the cost of 270410 dollars per patient and 1.6 times of physical disabilities. In fact, the mechanical thrombectomy strategy along with intravenous thrombolytics can gain of 1.02 more QALY and a 0.96 decrease in the incidence of disability, imposes an additional cost of 50155 dollars on the health system. Therefore, the cost per each earned QALY is 49171 dollars and the cost per disablement is 52244 dollars. These findings are shown in Table 2.

Considering the threshold of three times of per capita GDP, which is $16,328 dollars in 2017, mechanical thrombectomy with intravenous thrombolytics in patients with acute stroke can be justified to be cost-effective strategy. Figure 2 shows the cost-effectiveness map.

Sensitivity analysis of important variables

We used sensitivity analysis to investigate the effects of uncertainty on input data. In this analysis, the effects of the change in input data on the calculation result are examined. The findings of the sensitivity analysis show that the variables of the desirable variables of patients with mechanical thrombectomy with intravenous thrombolytics incidence and

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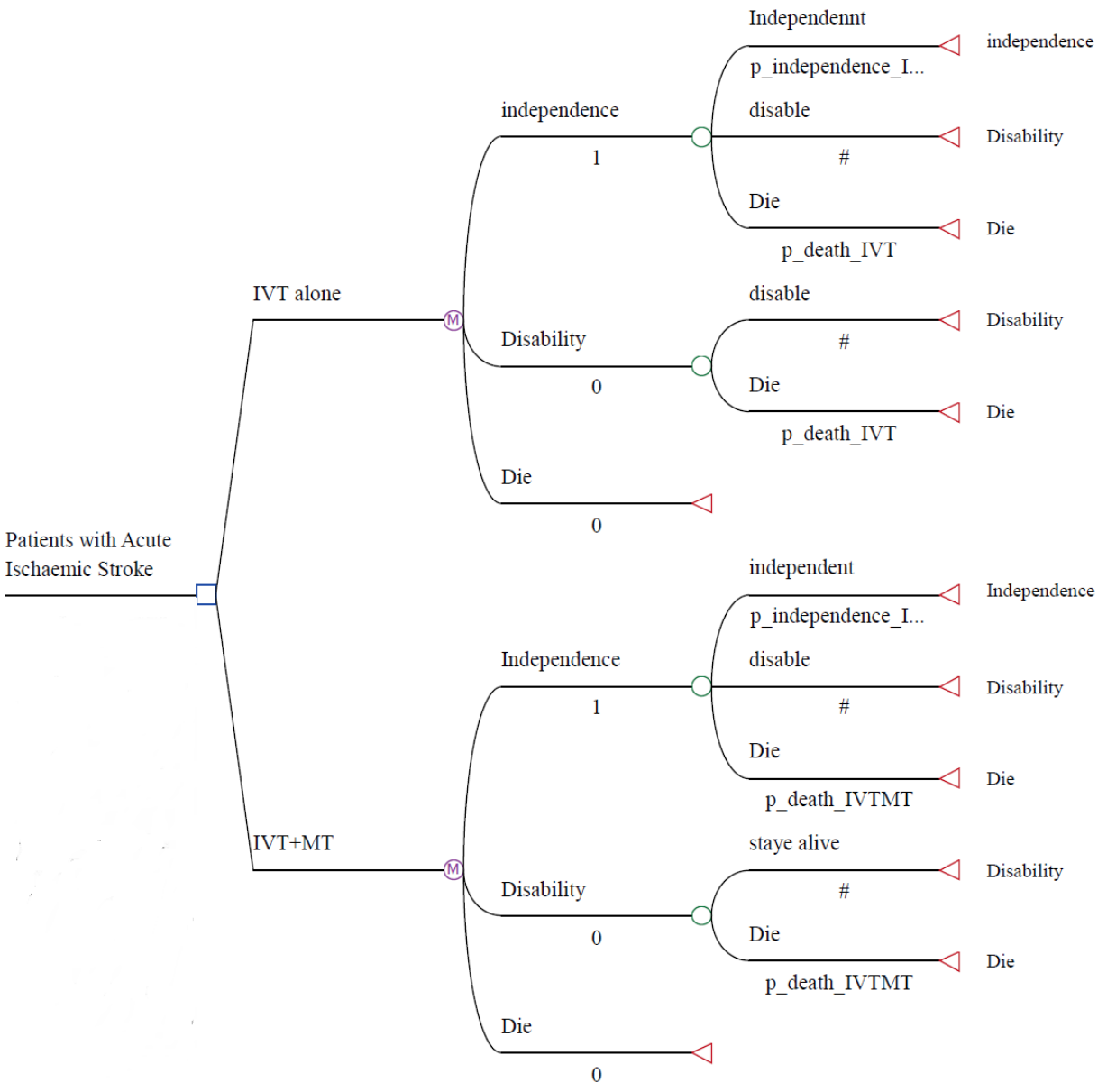

Figure 1 Extended Markov model (IVT: strategy of conducting venous thrombolytic & IVT+MT: The strategy of thrombectomy with venous thrombolytic)

disability were the probability of maintaining the patient's independence in performing daily functions in a group with mechanical thrombectomy accompanied by intravenous thrombolytics And also the variable cost of patients who had the ability to perform daily functions and received intravenous thrombolytics had the most effect on the findings of economic evaluation. In Figure 3, we can see the findings of the Tornado sensitivity analysis.

DISCUSSION

New treatments for patients with stroke impose high costs on the health system while reducing mortality and disability in patients. Considering the economic impacts of these new medical technologies can help policymakers to better use the limited resources of health and make a best decision.

This study evaluates the clinical and economic effects of the simultaneous presentation of mechanical thrombectomy and intra-intravenous thrombectomy compared with intra-intravenous thrombolytics alone in patients with an acute stroke in Iran. According to the findings, mechanical thrombectomy therapy with intra-intravenous thrombectomy can lead to the better quality and quantity of life and to assuage the pain and disability severity compared with intra-intravenous thrombolytics alone. Taking all the evidence into account, the modeling recommend that the mechanical thrombectomy therapy with intra-intravenous thrombolytics can provide a unit of QALY for an additional cost of nearly 50,000 dollars compared with intravenous thrombolytics per se. This amount of cost per unit of QALY, based on the domestic threshold of a figure of nearly 16,000 $, is a cost effective strategy. The concurrent application leading to the alleviation of the

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Table 1 The cost of interventions in two senarios

	strategy of conducting venous thrombolytic	The strategy of thrombectomy with venous thrombolytic
Laboratory tests	**4655309**	**5371511**
Drug intake section	**8470691**	**9773875**
Visit the doctor	**10982540**	**11827351**
Consumer goods	**4721050**	**544366**
Diagnostic imaging	**8709770**	**10049734**
Cost of stay in the hospital	**45362959**	**52341876**
The cost of the rtPA drug	**25440000**	**25440000**
The cost of conducting thrombolysis	**3006007**	**3006007**
Fee for mechanical thrombectomy	----------	**40000000-21000000**
Other costs	**5871716**	**6323387**
Costs of therapeutic management of the strategy	**117220042**	**158978107**
Cost tracking patient with stroke and disability		**48000000**
Cost tracking patient with stroke and independent		**30000000**

Table 2 Results from simulation and cost-effectiveness analysis

	strategy of conducting venous thrombolytic	The strategy of thrombectomy with venous thrombolytic	Incremental rate
cost	270410000	320565000	50155000
QALY	1.41 (0.65)	2.43 (1.19)	1.02
The number of disabilities	1.6	0.64	-0.96
Cost per each QALY	49171568		
Cots per each disability prevented	52244791		

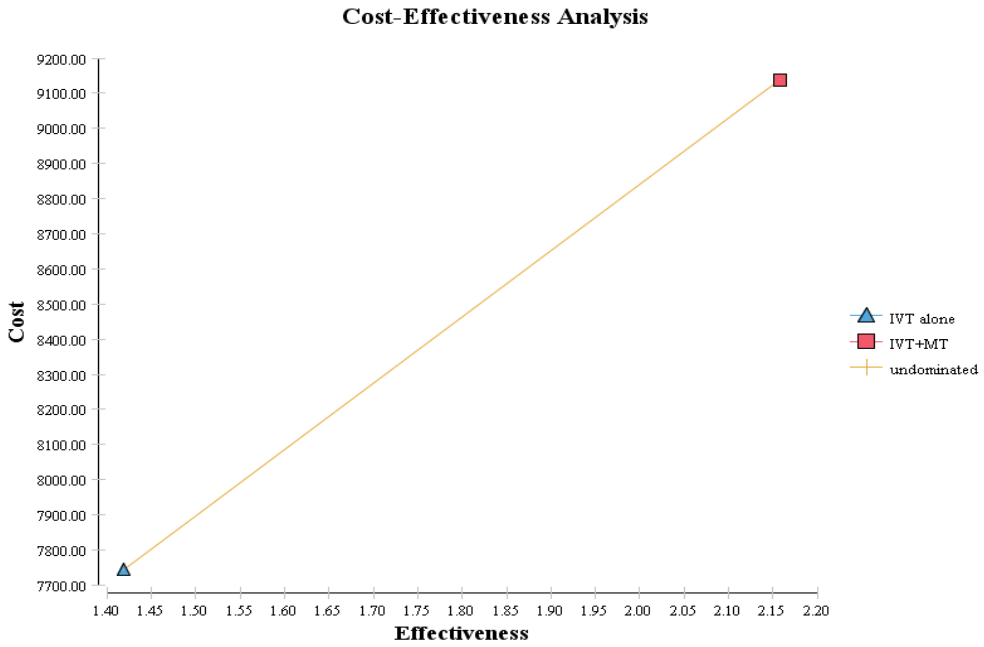

Figure 2 Cost effectiveness map

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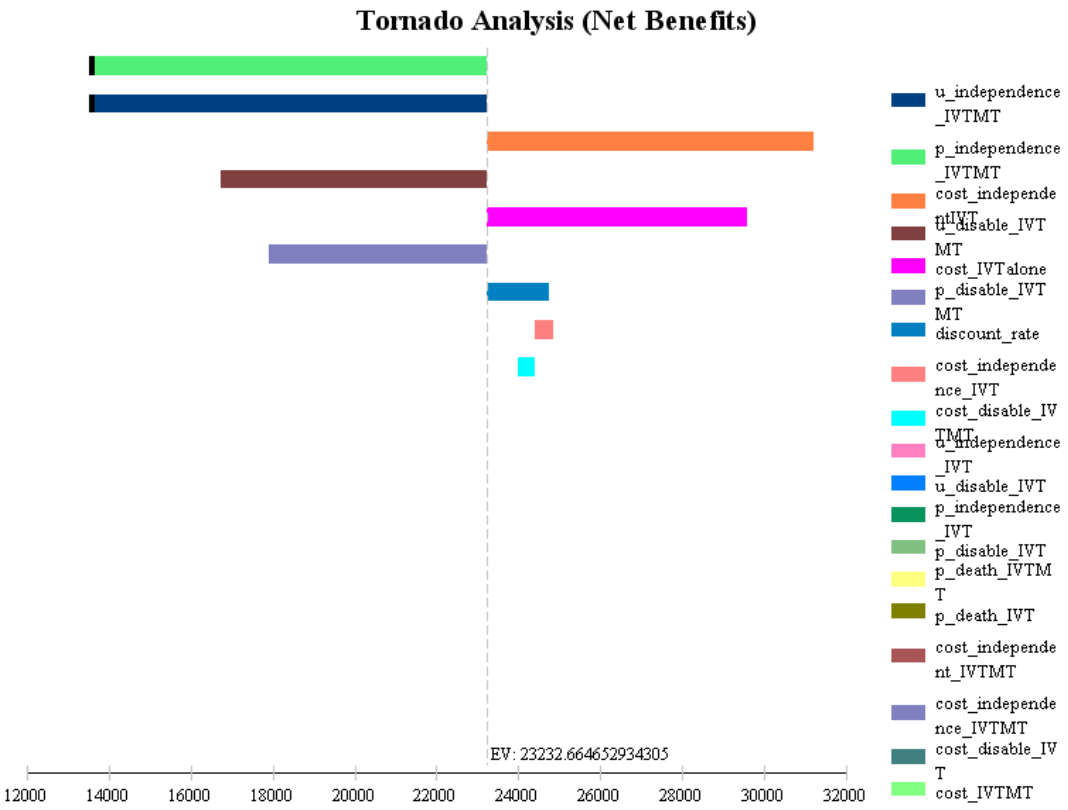

Figure 3 Tornado Sensitivity Analysis Chart

disabilities emanating from an acute stroke is so cost effective that the saved cost per each disability prevented had been for a modest 52244 $.

Various studies have so far addressed the cost-effectiveness of the interventions under this study. In a study by Kin and his colleagues in 2011, increased cost and QALY of mechanical thrombectomy with intravenous thrombolytics and intravenous thrombolytics alone was presented separately in the United States (22). The results of this study showed that mechanical thrombectomy with intravenous thrombolytics provided 0.68 QALY units with a cost of 1,600 dollars, considering the sensitivity analysis showed that in more than 97% of cases it would be an effective cost-effective intervention for patients with cerebrovascular accidents in large vessels. Guen Hun et al., also found that mechanical thrombectomy along with drug therapy resulted in an increase of 0.82 QALY and an increase of 7718 dollars per patient in united states setting (23). The researchers found that the incremental cost-effectiveness of this intervention was $ 9386 per unit QALY. In a study in Canada, Xie and his colleagues found that ICER of providing mechanical thrombectomy plus intravenous thrombolytics compared with thrombolysis alone was 11990 dollars (24). The researchers found that in most cases, the sensitivity analysis the intervention was a cost-effective measure. Having outlined the studies in general terms, the simultaneous use of mechanical and intravenous thrombotic thromboembolism in patients with acute stroke has been cost effective. The increase in QALY in this study was 1.02 units, while in other studies, it was the less. The greater effects of the simultaneous use of mechanical thrombolytics with intravenous thrombectomy in Iran could be due to the difference in the mortality rate of patients with acute cerebral stroke and a significant incidence of inability in these patients in Iran compared to developed countries that studied above. Therefore, it can be expected that simultaneous presentation of mechanical thrombectomy with intravenous thrombolytics can be more effective. This paper is the first cost-effectiveness study of mechanical thrombotic with intravenous thromboembolism compared to intravenous thrombolytics in developing countries. Obviously, the study was confronted with limitations.

Patients in the study were in the age group of 60 to 65 who were referred to the hospital personally, while the findings of this study may not be generalizable for patients with elder age of incidence in stroke. Despite the fact that the hospital under study is one of the most important refractory hospitals in the country regarding cardiovascular problems, the process of providing care in different hospitals is different. In fact, in deprived hospitals, where patients have limited access to health care than developed areas, they may not receive medical treatment during a golden time. This can affect the outcome of this study.

In addition valid clinical studies on patients with acute stroke in Iran to assess the clinical effects of interventions and the calculation of quality of life have led to the use of international evidence. While some cost data were extracted in consultation with clinical experts, the sensitivity analysis shows the strength of the cost-effective findings. Hence, the study would urge to give these recommendations serious consideration that new clinical guidelines can be issued on the contemporaneous indication of the both therapy as not only it would be of benefit to the patients with a stroke in terms of clinical effect, but also it would be cost effective procedure.

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CONCLUSION

Considering the vast majority of studies, the strategy of mechanical thrombectomy with intravenous thrombolytics in the treatment of people with an acute stroke is a cost-effective clinical practice that maintains the value of money in the health system. To add, patients who are not candidates for intra-intravenous thrombolytics due to delays at the time of the referral to the treatment centers can also take this strategy with due consideration for the correct choice of the patient.

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