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Cost-effectiveness Analysis of AngioJet and CDT for Lower Extremity Deep Vein Thrombosis Among Chinese Population

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Abstract

AngioJet has sufficient safety and efficacy in the treatment of acute and subacute lower extremity deep vein thrombosis (LEDVT). But the price of consumables used by AngioJet is relatively high and there is a lack of relevant research on health economics to measure the benefits to patients. Objective of this study is to estimate the cost effectiveness of AngioJet compared with catheter-directed thrombolysis (CDT) among Chinese population. Using a Markov decision model, we compared the 2 treatment strategies in patients with LEDVT. The model captured the development of post-thrombotic syndrome (PTS), recurrent venous thromboembolism, and treatment-related adverse events within a lifetime horizon and the perspective of a third-party payer. Model uncertainty was assessed with one-way and Monte Carl sensitivity analyses. The clinical inputs were obtained from the literature. Costs obtained from the hospital accounts and the literature are expressed in US dollars ($). Utilities were defined as quality adjusted life years (QALY). In cost-effectiveness analysis, AngioJet accumulated $1064.6445/QALY compared with $2080.1561/QALY after CDT treatment alone. AngioJet has higher long-term cost-effectiveness than CDT at a willingness to pay threshold of $11 233.52. One-way sensitivity analysis showed that the utilities of PTS and post-LEDVT state had significant influence on the results and the model maintained a strong stability under ± 10% fluctuation of utilities. Monte Carl sensitivity analysis shows that AngioJet model has strong stability and AngioJet has higher long-term cost-effectiveness than CDT. AngioJet is likely to be a cost-effective alternative to the CDT for patients with LEDVT.

Keywords

lower extremity deep venous thrombosis, catheter-directed thrombolysis, percutaneous mechanical thrombectomy, cost-effectiveness analysis

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Introduction

Lower extremity deep vein thrombosis (LEDVT) and pulmonary embolism (PE) are the most common venous thromboembolism (VTE) in clinical practice and the incidence of VTE can reach 0.1% to 0.2% per year.[1,2] At present, anticoagulation has been established as the standard treatment for LEDVT. Anticoagulation effectively prevents thrombus extension, PE, death, and recurrence in patients with LEDVT.[3] However, about 20% to 50% of patients with anticoagulation still develop post-thrombotic syndrome (PTS).[4] Therefore, the effective elimination of thrombus and reduction of complication incidence are the key to LEDVT treatment.[5]

Catheter-directed thrombolysis (CDT) is the recommended treatment in current guidelines and percutaneous mechanical thrombectomy (PMT) is a relatively new intervention for the treatment of LEDVT recommended by the US FDA in 2006.[6,7] AngioJet is the most widely used among all hydrodynamic PMT devices, with simple operation, high treatment efficiency, and no serious damage to vein wall and valve.[8] In

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addition to reducing the risk of PTS, the advanced therapies (CDT or Mechanical thrombectomy) can also reduce the hospital stay and the occurrence of complications such as bleeding.[9]

Markov model was developed by mathematician Andrei Markov. It was first applied in the selection of therapies by Beck in 1983.[10] With the improvement and development of the model, Markov is widely used in clinical decision and has become the main method of health economics evaluation.[11] Markov model determines different states according to different situations, and assumes that the patient is always in a certain state. All events are represented as transitions between states, and each state is assigned a utility. By simulating a random process, it can calculate the probability of disease outcome and evaluate the outcome and cost of various schemes.[12]

Current studies have shown that AngioJet has sufficient safety in the treatment of acute and subacute LEDVT, which can effectively clear thrombus, reduce the operation time and complications.[13,14]The therapeutic effect of AngioJet is also better than CDT.[15,16] But its indications are still controversial. In addition, the price of consumables used by AngioJet is relatively high and there is a lack of relevant research on health economics to measure the benefits to patients. Therefore, the treatment methods are mostly chosen according to doctors' experience and patients' wishes rather than consensus. This study aims to build a Markov model to predict the long-term cost of the 2 treatment methods and give clinicians suggestions on the choice of treatment methods. So that patients can get the maximum benefit in terms of efficacy, life, and economy.

Materials and Methods

Decision Model

In this study, we developed a Markov model with the perspective of a third-party payer and a lifetime horizon to compare 2 treatment strategies for the patients with LEDVT. Model uncertainty was assessed with one-way and Monte Carl sensitivity analyses. The 2 strategies were standard treatment with anticoagulation and elastic compression stockings, with CDT or AngioJet in addition to standard treatment. We expressed the results in monetary costs ($), quality adjusted life years (QALYs), and an incremental cost-effectiveness ratio (ICER). This study was approved by the Regional Committee for Medical and Health Research Ethics. To build the model, we made the following assumptions:

1. All patients entered the model in an LEDVT state, that is the first cycle. The decision tree was established according to the therapy (AngioJet or CDT).
2. The subsequent cycles represented the long-term phase where the mutually exclusive health states were: (a) post-LEDVT, (b) PTS, (c) permanently disabled from complications, and (d) dead.
3. Disabled complications were defined as intracranial bleeding and the occurrence of intracranial hemorrhage was classified as fatal and disabling. Patients who were permanently disabled from an intracranial bleed remained in this state until death. Any non-disabling major bleeding was modeled as a temporary health state for the remainder of the cycle.
4. Unless experiencing a fatal or disabling complication, all patients received 3 months anticoagulation after surgery and no additional surgical intervention was performed. Patients need long-term anticoagulation, if the PTS or thrombus recurrence occurred and discontinue anticoagulation when there was a disabling complication. After a recurrent VTE with resumption or adjustment of anticoagulation, any decrement in utility was assumed to be transient and without significant impact on long-term utility. Long-term anticoagulation was defined as oral rivaroxaban.
5. The cost of each operation in this study included the inferior lumen filter, so PE was not included in the model.
6. Determine 20 cycle periods, and the Markov state can be transferred to other states in each period. The utilities were defined as QALYs.
7. The fee was settled in US dollars with an exchange rate of 6.46.
8. For model construction and analyses we used Tree Age Pro Suite 2011 (Tree Age Software, Williamstown, MA, USA) and Microsoft Excel 2010 (Microsoft, Redmond, WA, USA).

Table 1. Markov Model Parameters.

		AngioJet	CDT
Probabilities	PTS	0.2159	0.411[15]
	Disabling complications	0.0016	0.0021[16]
	Death	0.0016	0.0042[16]
	Recurrent VTE	0.0317	0.033[17]
	Anticoagulation related disabling complications	0.0136[18]	
	Death of complications	0.458[18]	
Utilities (QALY)	Post-LEDVT	0.8628[15]	
	PTS	0.7745[17]	
	Disabling complications	0.32[19]	
	Death	0	
Cost ($)	Hospitalization costs	11 957.95	10 198.07
	Post DVT and on long-term anticoagulation	3108.8	
	Disabling complications	2243.72[20]	
	PTS	754.21[15]	

Parameter Determination

As shown in Table 1, the probabilities and utilities in the mode were derived from the literature search and meta-analysis. Hospitalization costs were obtained from the hospital accounting system, and costs for PTS and disabling complications were obtained from the literature. At present, there is a lack of relevant systematic review about AngioJet, so the probabilities of AngioJet were retrieved from literature. Warfarin requires regular review of INR to adjust dosage. The cost includes transportation cost, absenteeism cost, inspection cost, and so on. The cost variation among individuals was too large for statistical analysis. Therefore, long-term anticoagulation was defined as rivaroxaban 20 mg ($8.54) per day.

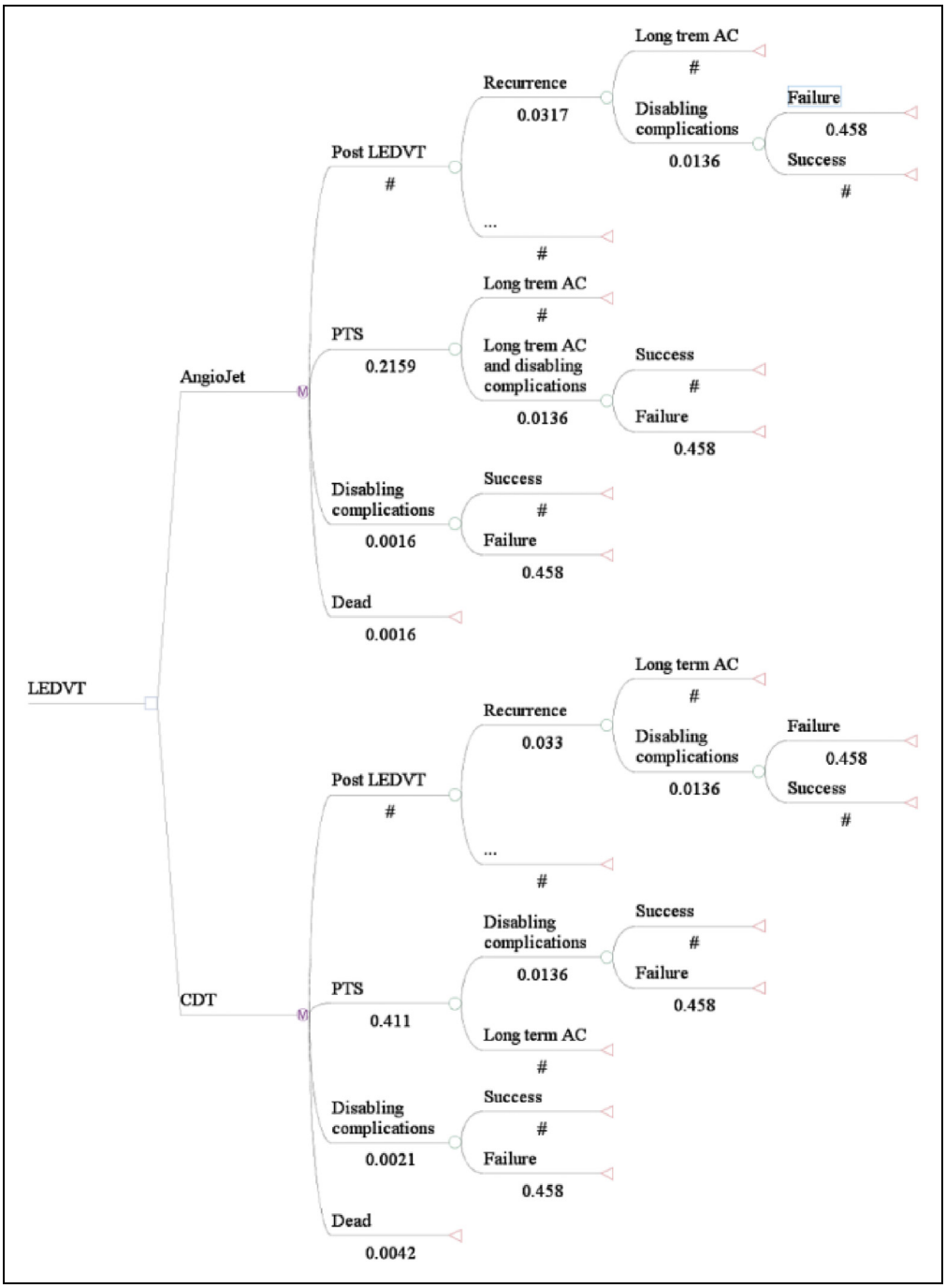

Figure 1. Markov model decision tree construction.

Table 2. The Results of Model.

		AngioJet	CDT
Probability	Post-LEDVT	0.41001	0.29783
	PTS	0.48173	0.55629
	Disabling complications	0.00772	0.00902
	Dead	0.10055	0.13686
Cost		24 018.38	49 570.12
Eff		22.56	23.83
C/E		1064.6445	2080.1561

Ethical approval to report this case series was obtained from ETHICS COMMITTEE (APPROVAL NUMBER:2021ky085) *. Verbal informed consent was obtained from the patients for their anonymized information to be published in this article.

Results

Cost-Effectiveness Analysis

The decision tree construction was shown in Figure 1. WTO defines the results of the cost-effectiveness study by ICER and

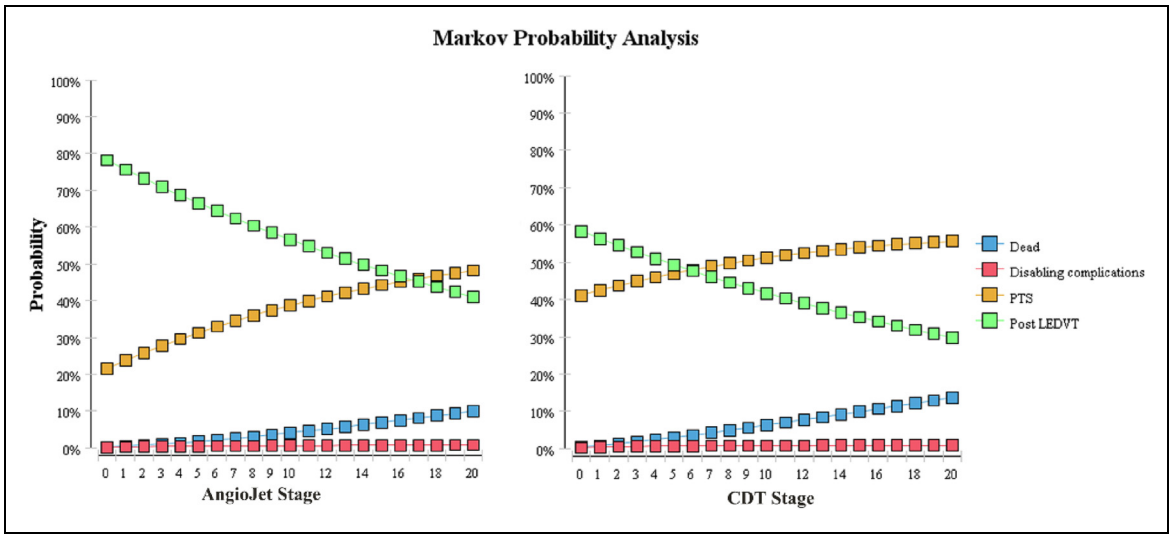

Figure 2. Markov probability analysis.

per capita GDP. The highly cost-effective was defined when ICER is less than per capita GDP. Chinese per capita GDP in 2020 is $11 219.01, which is taken as the Willingness to pay (WTP) in this study.

As shown in Table 2, the post-LEDVT state is the ideal state after surgical treatment. After 20 cycles, the probability of the post-LEDVT state in AngioJet group was 0.353, and 0.2570 in CDT group. Patients in AngioJet group had a high probability of being in an ideal state. The PTS probability of CDT group was 0.4308, which was higher than that of AngioJet group. Because the outcome tends to go in the direction of higher utility so the probability of disabling complications was small in both groups, with the AngioJet group being 0.0077 and the CDT group being 0.0090. The probability of death in the 2 groups after 20 cycles was 0.1006 and 0.1369.

As shown in Figure 2, the probability of post-LEDVT state in the 2 groups gradually decreased, the probability of PTS increased greatly, and the probability of death and disabling complication increased slightly with the progress of circulation, which was the same as the outcome of disease.

AngioJet treatment was associated with an effectiveness of 22.56 QALYs and the cost of $24 018.38. Patients receiving CDT accumulated 23.83 QALYs and the cost of $49 570.12. Hence, under base-case conditions the C/E of AngioJet and CDT were $1064.6445/QALY and $2080.1561/QALY (Figure 3 and Table 2).

One-way Sensitivity Analyses

There may be some bias because of the data related to surgery and drug prices were obtained from only 1 hospital, and the relevant parameters were all derived from literature. The influence of variables on the cost-effectiveness analysis was determined by Tornado analysis. The utilities float is $\pm 10\%$, and the cost discount rate is $\pm 5\%$.

As shown in Tornado graph, each parameter in the order of influence degree from high to low was: utilities of PTS (u_PTS), utilities of post-LEDVT state (u_Post-LEDVT), long-term anticoagulative cost, CDT cost, AngioJet cost, PTS cost, utilities of disabling complication, disabling complication cost. Among them, u_PTS and u_Post-LEDVT had a greater influence on the results, and one-way sensitivity analysis was conducted for them (Table 3).C/E in AngioJet group is better than that in CDT group when the effect value changes, indicating that the research model has a strong stability (Figure 4).

Monte Carl Sensitivity Analyses

The Monte Carl sensitivity analyses were used to verify the Markov model. The model was simulated several times and all the simulation results were concentrated together. The ICER of the comparison of 2 groups was finally calculated.

As shown in scatter plot, the cost and effect of the 2 components are significantly different, which is the same as the result of cost-effectiveness analysis. The scattered points are relatively concentrated, indicating that the model is stable (Figure 5). In the ICER scatter plot, the oblique line in the figure is WTP. The simulation results are below WTP and all of them are in the third quadrant. The incremental cost is positively correlated with the incremental effect, indicating that AngioJet is more cost-effective than CDT within the range of WTP. Moreover, the scattered points are distributed in the ellipse, which indicates that the results of the model are relatively stable (Figure 6).

The cost-effectiveness acceptable curve and net monetary benefit yield curve consider the influence of cost, effect and WTP, and can compare the decision from multiple aspects, so that the analysis results are more accurate.

After simulation, the net monetary yield curve (Figure 7) was obtained: the curve of AngioJet was always above that of

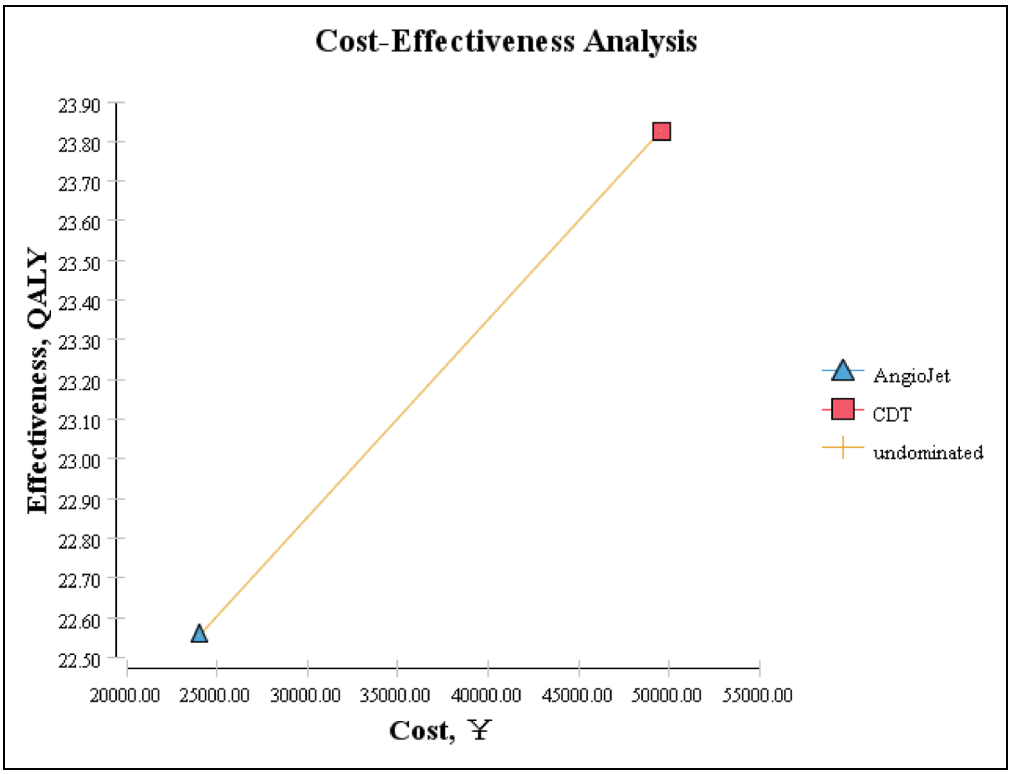

Figure 3. Cost-effectiveness analysis.

CDT. It indicates that under the same WTP, AngioJet's income is higher than CDT. The net monetary income of the 2 groups increases with the increase of WTP. However, CDT curve has a high slope, which means it will be dominant after WTP reaches a certain value.

Figure 8 shows the cost-effectiveness acceptance curve, which indicates that the acceptance rate of AngioJet is higher than CDT within the range of WTP = 11 219. When the WTP reached $13436, the acceptance rate of the 2 groups began to change. When the WTP reached $22394, the acceptance rate of the 2 groups was equal. It shows that CDT can obtain higher willingness to accept with the increase of WTP, but within the range of WTP, AngioJet has obvious advantages. The result is the same as the result of the net monetary yield curve.

Table 3. One-way Sensitivity Analyses

	Variable	Strategy	Cost	Eff	CE
u_PTS	0.69705	AngioJet	24 018.381	21.36	1124.54
		CDT	49 570.122	22.23	2230.25
	0.73577	AngioJet	24 018.381	21.96	1093.88
		CDT	49 570.122	23.03	2152.77
	0.7745	AngioJet	24 018.381	22.56	1064.85
		CDT	49 570.122	23.83	2080.48
	0.81322	AngioJet	24 018.381	23.15	1037.33
		CDT	49 570.122	24.63	2012.90
	0.85195	AngioJet	24 018.381	23.75	1011.19
		CDT	49 570.122	25.43	1949.57
u_Post-LEDVT	0.77652	AngioJet	24 018.381	21.50	1117.11
		CDT	49 570.122	23.06	2150.01
	0.81966	AngioJet	24 018.381	22.03	1090.36
		CDT	49 570.122	23.44	2114.68
	0.8628	AngioJet	24 018.381	22.56	1064.85
		CDT	49 570.122	23.83	2080.48
	0.90594	AngioJet	24 018.381	23.08	1040.52
			49 570.122	24.21	2047.38
	0.94908	AngioJet	24 018.381	23.61	1017.27
		CDT	49 570.122	24.6	2015.31

Discussion

DVT has become the third most common vascular disease with the increase of age and risk factors. Although traditional anticoagulant strategies can reduce the incidence of PE and PTS, they are inefficient at removing thrombus. The incidence of PTS in 2 years is as high as 40%[17] which seriously affects the quality of patients' life and brings a heavy burden to the family and society.[18] Therefore, rapid recovery of venous access is the key to the clinical treatment of LEDVT. People's concept of treatment for LEDVT is changing constantly with the accumulation of clinical experience and the development of scientific and technological devices. At present, the treatment of LEDVT is interventional therapy on the basis of traditional anticoagulation, so as to achieve the goal of rapid removal of thrombus.

CDT is the most widely used thrombolytic method with an effective rate of 85% to 90%.[19] Because it can quickly clear the thrombosis, and doesn't damage the valve and venous wall, which reduce the occurrence of complications. CDT has gradually become the preferred treatment method for clinicians.

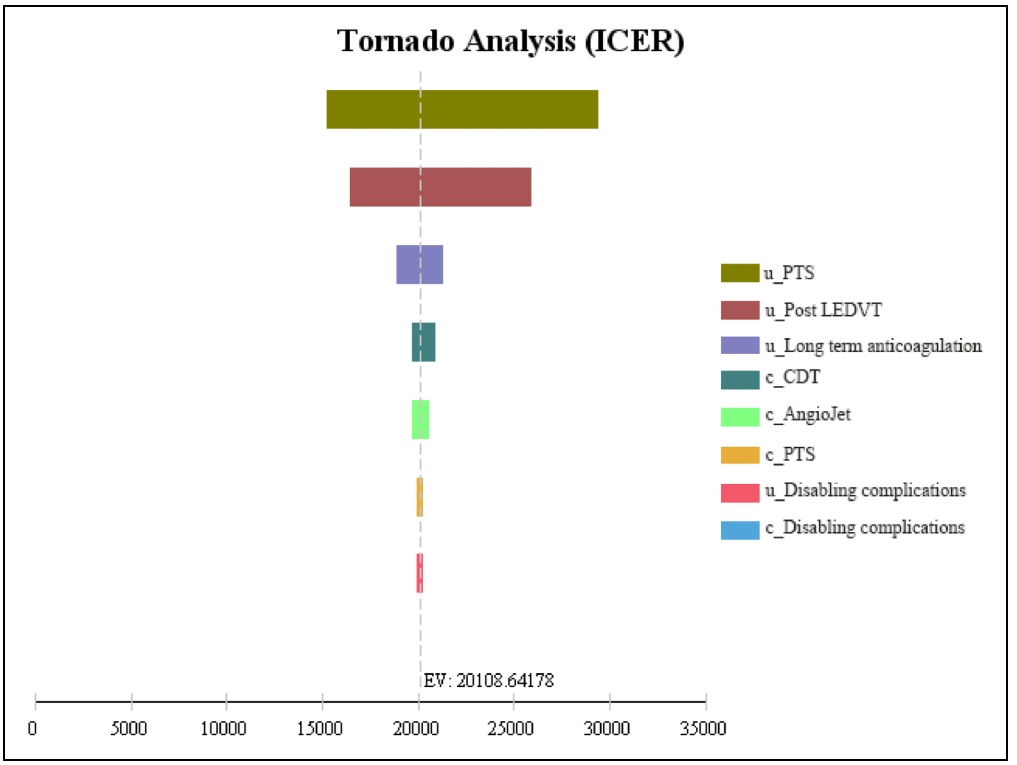

Figure 4. Tornado analysis.

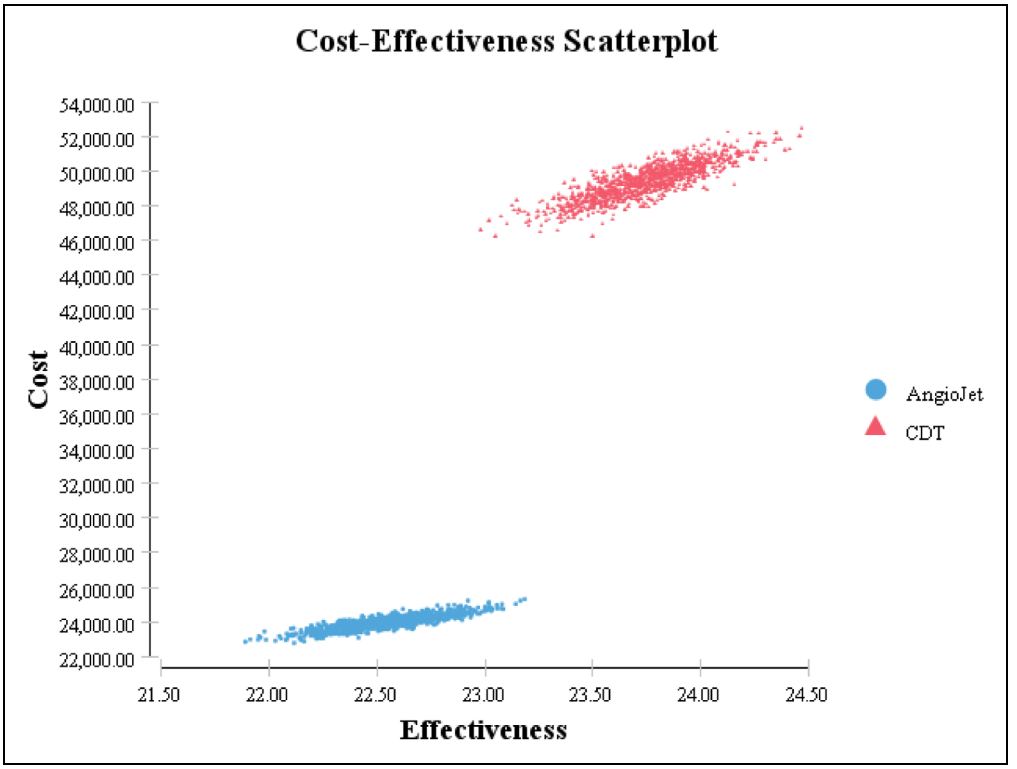

Figure 5. Cost-effectiveness scatter plot.

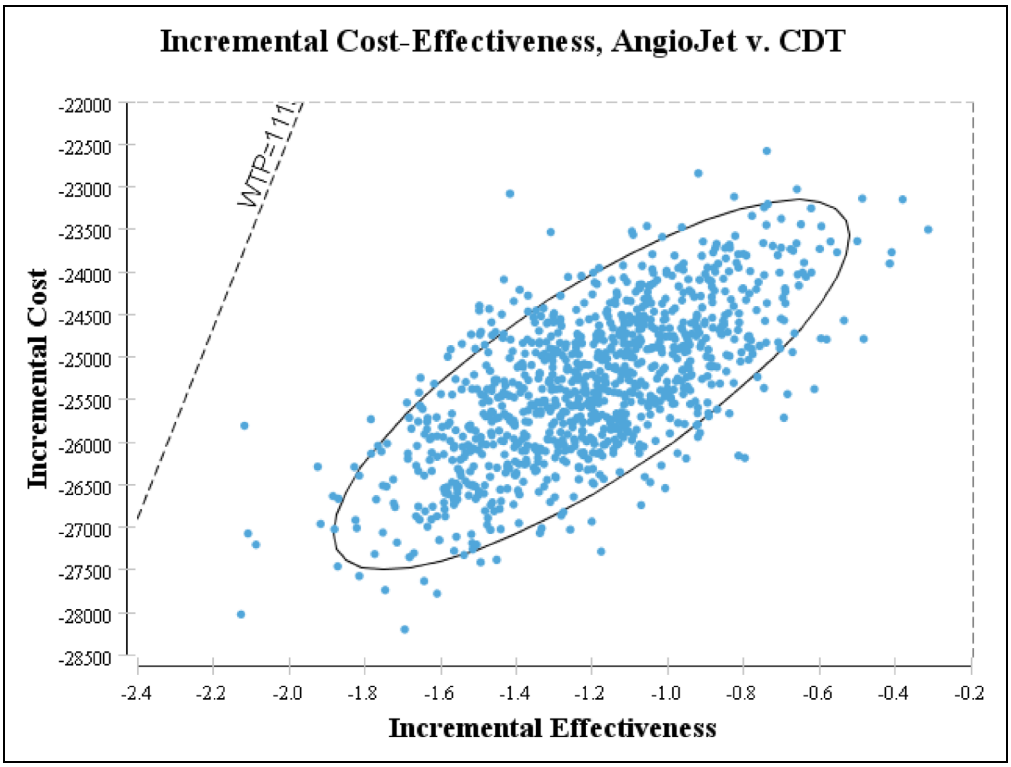

Figure 6. Incremental cost-effectiveness.

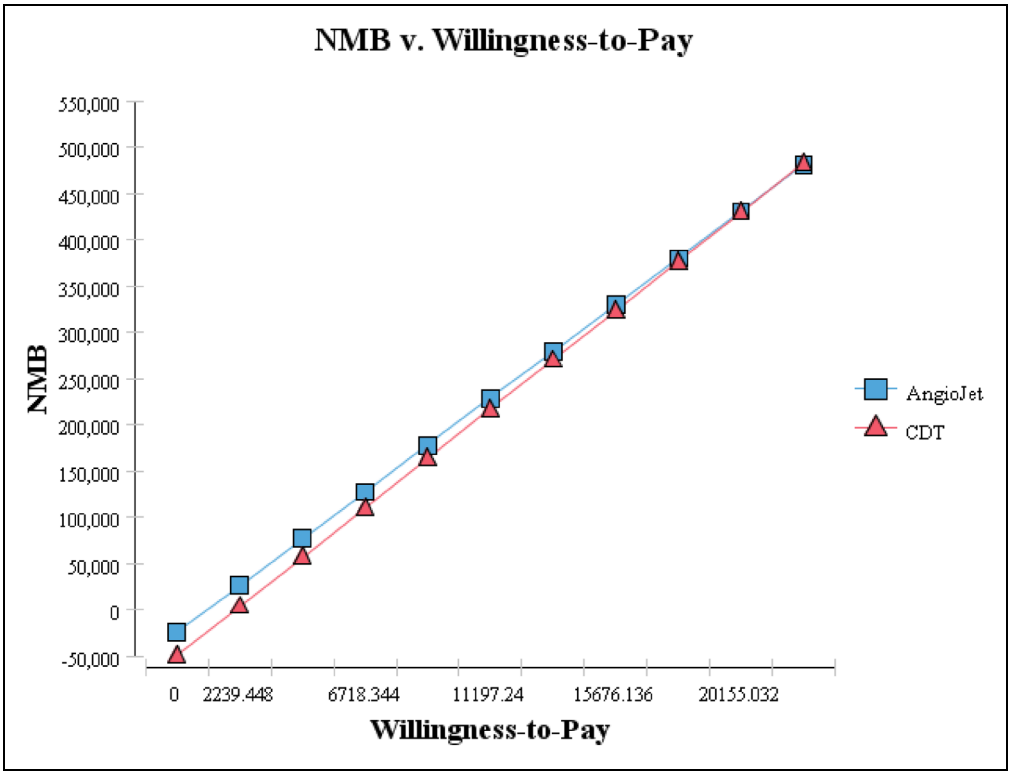

Figure 7. Net monetary benefit yield curve.

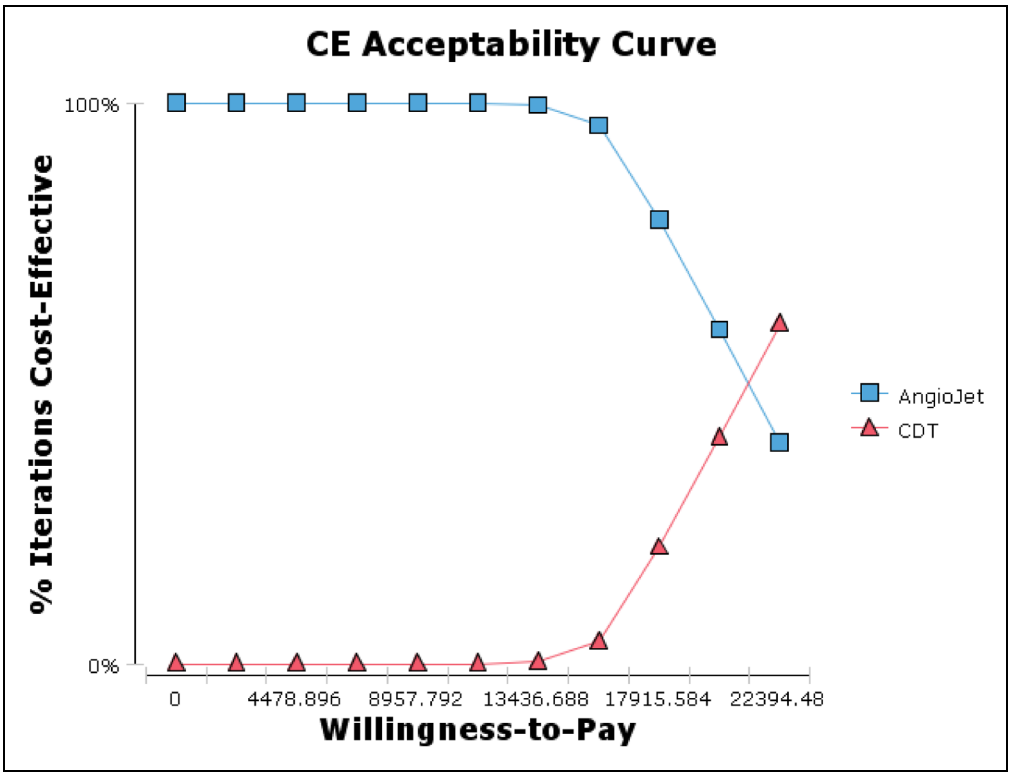

Figure 8. CE acceptability curve.

Xu, Y. et al. treated 238 acute LEDVT patients with CDT, among which 198 patients (83.91%) had a thrombolysis rate above Grade II, and only 23 patients (9.66%) had bleeding complications, without fatal complications.[20] Jun Zhu et al. treated 33 patients with LEDVT and found that the majority of patients with thrombus dissolution was up to 97%.[21] Current guidelines recommend CDT as one of the treatment methods for LEDVT,[22] indicating that CDT has high safety and effectiveness in the treatment of LEDVT. However, its clinical application still has certain limitations. In the treatment process, patients need to undergo multiple angiography examinations to clarify the effect of thrombolysis, which increases the x-ray exposure of patients and operators, and the use of long-term urokinase also increases the risk of bleeding in patients.[23]

AngioJet is widely used. The device mode can be divided into pulse mode and thrombectomy mode. The pulse mode can segment thrombus, make thrombolytic drugs fully contact with thrombus, shorten thrombolytic time and reduce the use of thrombolytic drugs. Thrombectomy mode can quickly clear the thrombus and restore venous access. The operation is simple and efficient, and will not cause serious damage to the vein wall and valve.

However, bradycardia and hemoglobinuria may be caused due to the destruction of red blood cells by saline high-pressure injection, and the degree of hemolysis increases with the extension of operation time, leading to renal function injury in severe cases. Current studies have shown that AngioJet has sufficient safety in the treatment of acute and subacute LEDVT, which can effectively remove thrombus and reduce the operation time and complications.[13,14] Liu used AngioJet combined with CDT to treat 38 patients with extensive LEDVT, and the technical success rate was 100%. During the average follow-up period of 20 months, the incidence of PTS was 17%,[24] which was similar to the conclusion reached by foreign scholars.[25]

Although many of the above studies have confirmed the advantages of AngioJet in LEDVT treatment, there are also many controversies about the advantages and disadvantages of the 2 methods. AngioJet does not show its advantages in terms of short-term efficacy and long-term complications, and there are also controversies in terms of cost-effectiveness.[26]

Although AngioJet treatment for LEDVT in China has good short-term efficacy, the cost is often high. Due to the complexity of the etiology of LEDVT and confiding factors, it is necessary to study the clinical value and cost-effectiveness of AngioJet or CDT in the treatment of this kind of disease. Based on the Markov model, this paper analyzes the costs and benefits of the 2 treatment methods in 20 cycles from the perspective of patients, so as to judge their merits and demerits. The benefit of patients was evaluated by QALY in this study. This method takes into account the effect of the treatment methods on the quality of life of the patients and allows a more comprehensive evaluation of the post-operative status of the patients. According to the data obtained from the survey and relevant literature, the discount rate is included in the study to make the conclusion closer to the society.

The results show that AngioJet has more advantages over CDT in cost-benefit comparison. Univariate sensitivity analysis showed that AngioJet still showed a strong advantage when PTS effect value and post-thrombosis effect value, 2 variables

that had a greater influence on the model, were within a 10% fluctuation range. Probability sensitivity analysis shows that the model has strong stability, and AngioJet has obvious advantages in the WTP range. The conclusion of this study is reliable and consistent with the clinical conclusion. However, this study is the first time to establish the Markov model of AngioJet and CDT in the treatment of LEDVT on the decision analysis software. And the data can only be obtained through database retrieval. Moreover, researches are mostly retrospective at present, which may have large bias, and long-term clinical follow-up investigation is still needed.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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