JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2022; 6: 189-198
https://doi.org/10.30621/jbachs.1013502
RESEARCH ARTICLE

ASSESSMENT OF COST-EFFECTIVENESS OF SURGICAL CLIPPING AND ENDOVASCULAR COIL METHODS IN THE TREATMENT OF UNRUPTURED CEREBRAL ANEURYSMS

Ahmet Kar[1], Ismet Sahin[2], Bayram Sahin[3]

[1] Kirikkale University, Faculty of Health Sciences, Department of Healthcare Management, Kirikkale, Turkey
[2] Lokman Hekim University, Health Services Vocational High School, Department of Healthcare Management, Ankara, Turkey.
[3] Hacettepe University, Faculty of Economics and Administrative Sciences Department of Healthcare Management, Ankara, Turkey.

Address for Correspondence: Ahmet Kar, **E-mail:** ahmetkar@kku.edu.tr
Received: 22.10.2021; **Accepted:** 24.12.2021; **Available Online Date:** 27.01.2022

Cite this article as: Kar A, Sahin I, Sahin B. Assessment of Cost-Effectiveness of Surgical Clipping and Endovascular Coil Methods in The Treatment of Unruptured Cerebral Aneurysms. J Basic Clin Health Sci 2022; 6: 189-198.

ABSTRACT

Purpose: The study aims to assess the cost-effectiveness of endovascular coiling and surgical clipping in the treatment of unruptured cerebral aneurysms.

Material and methods: Patients with ICD 10 I67.1 and treated with one of the two treatment methods performed at the Hacettepe University Hospitals between January 2013 and December 2015 were included in the study. The cost data in the study were obtained by analyzing patient invoices through the automation program of the university hospital. The effectiveness and treatment costs were assessed using the Markov model with the Social Security Institution's (SSI) perspective. To generate the cost input in the model, the lifetime costs obtained based on the expert's opinions were added to the amounts received from patient invoices.

Results: The study results were presented as the incremental cost-effectiveness ratio (ICER). When 3% reduction rate was applied to the costs and effectiveness data, the Quality Adjusted Life Years (QALY) was calculated as 4.39 and 1.84 for the coiling and clipping methods, respectively. Lifetime costs were 66463.40$ and 7900.27$ for the coiling and clipping methods, respectively. The incremental cost-effectiveness rate of endovascular coiling method was 22965.93.

Conclusion: The endovascular coiling method was found to be cost-effective because the ICER score of the process is below the threshold.

Keywords: Cost-effectiveness, coiling, clipping, unruptured cerebral aneurysms

INTRODUCTION

Neurologic diseases are the first leading cause of disability adjusted life years (DALY) and the second leading cause of deaths according to the Global Burden of Disease Study (1). The incidence of unruptured cerebral aneurysms was 3.2% in the systematic review and meta-analysis conducted in 94912 patients from 21 countries (2). In 2016, according to the Turkish Statistical Institute (TSI) data, 9.4% of deaths in Turkey were due to cerebrovascular diseases.

Patients with unruptured intracranial aneurysms (UIA) carry the risk of rupture. Therefore, these patients are treated to prevent subarachnoid

hemorrhage (SAH) (3). Treatment of these aneurysms is essential due to the risk of hemorrhage as most SAH cases arise from ruptured intracranial aneurysms. Management of UIA may vary depending on the natural course of the treatment, morbidity, and mortality of the disease (4).

Surgical clipping of aneurysms had been used as the gold standard until the development of detachable coil technology in the 1990s. However, the endovascular coiling procedure has been used more widely after U.S. Food and Drug Administration (FDA) approval (3).

The cost and value of health services have gradually increasing importance. Despite a large number of cost-effectiveness analyses in some fields of medicine, cost-effectiveness studies about neurosurgery and neurovascular methods are relatively insufficient (5).

This study aims to assess the cost-effectiveness of neurosurgery and neurovascular methods in the treatment of unruptured cerebral aneurysms.

MATERIALS AND METHODS

Cost-utility and budget impact analyses were conducted for comparison of the cost-effectiveness of endovascular coil and surgical clipping procedures, which are the two methods used for the management of unruptured cerebral aneurysms. One-way sensitivity analyses were also conducted concerning various variables.

The study population comprised of patients diagnosed with unruptured cerebral aneurysms with a diagnosis code of ICD 10 I67.1 and those without a diagnosis code of either I60, I61, or I62 in the hospitals of Hacettepe University between January 2013 and December 2015. Patients who were treated and discharged after endovascular coiling or surgical clipping were included in the study. The study was composed of a total of 60 patients (32 in the endovascular treatment group and 28 in the surgical clipping group).

Both endovascular coiling and surgical clipping methods are included in the reimbursement list of the Social Security Institution of Turkey.

No cost-effectiveness studies are available in Turkey investigating the treatment methods of cerebral aneurysms despite the burden of the disease concerning the health service provider, SSI, and community.

The present study is composed of the stages of detecting the costs of the alternative methods, calculation of QALY values and additional cost-effectiveness ratio, and budget impact and sensitivity analysis.

The patients' invoices of the treatment procedure were obtained from the automation program of the hospital to estimate the costs of the alternative

Table 1. Probabilities Used in the Markov Model

	(%) Coiling	(%)Clipping	Reference
Post-operative rupture rate	2	1.8	[10] Wiebers DO, International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362(9378):103-110.
Post-operative mortality rate	0.6	1.7	[11] Brinjikji W, Rabinstein AA, Nasr DM, Lanzini G, Kallmes DF, Cloft HJ. Better outcomes with treatment by coiling relative to clipping of unruptured ıntracranial aneurysms in the United States, 2001–2008. *AJNR Am J Neuroradiol*.2011;32(6): 1071-1075. [12]Kotowski M, Naggara O, Darsaut TE, Nolet S, Gevr G, Kouznetsov E, Raymond J. Safety and occlusion rates of surgical treatment of unruptured intracranial aneurysms: a systematic review and meta-analysis of the literature from 1990 to 2011. *J Neurol Neurosurg Psychiatry*. 2013;84(1):42-48.
Post-operative stroke rate	2.92	6.71	[13]Alshekhlee A, Mehta S, Edgell RC, Vora N, Feen E, Mohammadi A, Kale SP, Flores SC. Hospital mortality and complications of electively clipped or coiled unruptured intracranial aneurysm. *Stroke*. 2010;41(7):1471-1476.
SAH mortality and disability rate	%50 - %15		[4]Takao H, Nojo T, Ohtomo K. Cost-effectiveness of treatment of unruptured intracranial aneurysms in patients with a history of subarachnoid hemorrhage. *Acad Radiol*. 2008;15(9):1126-1132.
Average rupture rate of aneurysm	%0.7		[14]Williams LN, Brown RD. Management of unruptured intracranial aneurysms. *Neurol Clin Pract*. 2013;3(2):99-108.
Mortality rate after stroke	%10		[15]Brønnum-Hansen H, Davidsen M, Thorvaldsen P. Long-term survival and causes of death after stroke. *Stroke*. 2001;32(9):2131-2136.

treatment methods. Then, the invoices were analyzed in detail to reveal the operation, anesthesia, service, medication, surgery, laboratory, materials, imaging, and hospitalization costs.

The expert's opinion was obtained through structured forms considering the postoperative processes and natural course of the disease after the treatment for calculation of lifelong costs of the patients. The extraordinary conditions were simulated as postoperative hemorrhage, stroke, and death in the Markov model. Treatment costs of the patients with stroke were calculated based on the study of Tatar et al. entitled "Direct Treatment Costs of Stroke in Turkey" (6). Costs of post-hemorrhage clipping procedure were calculated based on the study of Aslan entitled "Cost Analysis Based on Transaction Costs, Charges& Billing Diagnostic Related Groups (DRG) at Ankara Training and Research Hospital" (7). When estimating the lifelong cost after discharge, the unit cost of the drugs was calculated from the current price list of the Turkish Medicines and Medical Devices Agency (March 18, 2016), and the unit cost of the other services was estimated from the SSI Health Practice Notificati on. All cost data were used by reducing to the 2015 prices.

The primary effectiveness data are based on the patients' health-related quality of life measurement that was measured through phone interviews using the Turkish version of EQ-5D-5L which was developed by the EuroQol Group Association. Patient health status coefficients for the United Kingdom were used, and the results were tested for the Netherlands and United States coefficients.

Post-discharge cognitive status of the patients was another effectiveness measurement. A cognitive function short form composed of eight questions of the Neuro-QoL (Quality of Life in Neurological Disorders) scale developed for measuring the quality of life in patients with neurologic diseases was used. Coefficients of each patient's health status were converted to QALY values using weights specific for the USA, UK, and Netherlands through the EQ-5D-5L Index Value Calculator. The Markov model was set for the calculation of the cost-effectiveness ratio. It shows the lifelong health status transitions of 1000 hypothetical patients. The patients' health status was reduced to four groups such as "good," "hemorrhage," "stroke," and "death." Transition probabilities obtained from the literature were applied for 1000 hypothetical patients with functional health status, and the cycles ended when all the patients died. The sequences repeated monthly. The total cost for each month was calculated during the lifelong time. Post-discharge expenditures were added to these costs for the patients in both groups and the lifelong total costs were obtained. The patients' lifetime varies depending on the treatment methods, and transition probabilities changed during the sensitivity analyses. First year's cost and quality of life values were not reduced, but for other years the 3% reduction rate that was recommended by the World Health Organization was applied.

The total earned life years and total quality-adjusted life years were calculated for both treatment methods. Then, the incremental cost-effectiveness ratio (ICER) was calculated and compared with the threshold value. The ICER is expressed as the ratio of the difference in costs between two health interventions to the difference in effectiveness. This one-dimensional summary measure can be interpreted as the cost of obtaining an extra unit of effectiveness, and it quantifies the trade-offs between patient

Table 2. Demographic characteristics of the patients

			Method		
			Coiling	Clipping	Total
Sex	Male	n	10	11	21
		%	31.3	39.3	35
	Female	n	22	17	39
		%	68.7	60.7	65
Total		N (%)	32 (100)	28 (100)	60 (100)
Age	< 50 years	n	10	9	19
		%	31.3	32.1	31.7
	≥ 50 years	n	22	19	41
		%	68.8	67.9	68.3
Total		N (%)	32 (100)	28 (100)	60 (100)
		min–max	16–79	26–81	
		mean ± std.dev.	52.75 ± 14.11	51.71 ± 11.3	

Table 3. Size and location of the aneurysms

			Method		Total
			Coiling	Clipping	
Size	<7 mm	n	7	10	17
		%	25.9	41.7	33.3
	7-12 mm	n	14	8	22
		%	51.9	33.3	43.1
	13-24 mm	n	4	5	9
		%	14.8	20.8	17.6
	≥25 mm	n	2	1	3
		%	7.4	4.2	5.9
Total		n(%)	27(100)	24(100)	51(100)
		mean ± std.dev.	10.71 ± 8.66	9.27 ± 5.61	
	PCA	n	3	0	3
		%	9,4	0	5
	MCA	n	9	18	27
		%	28.1	64.3	45
	ICA	n	15	4	19
		%	46.9	14,3	31.7
	BA	n	3	0	3
		%	9.4	0	5
	AcomA	n	2	6	8
		%	6.3	21.4	13.3
Total		n(%)	32(100)	28(100)	60(100)

PCA: Posterior Circulation Aneurysm, MCA: Middle Cerebral Arter Aneurysm ICA: Internal Carotid Arter Aneurysm, BA: Basilar Arter Aneurysm, AcomA: Anterior Communican Arter Aneurysm

outcomes gained and resources spent (8).The threshold value was accepted as the threefold of the national income per capita declared by the TSI for 2015 (27783$) referring to Balçık and Şahin entitled "Cost-effectiveness analysis of pemetrexed and gemcitabine treatment for advanced nonsmall cell lung cancer in Turkey" (9). Transition probabilities used in Markov model are presented in Table 1.

RESULTS

Patient characteristics

The mean duration of hospital stay was 3.28 (± 3.26) days for patients who were treated using the coiling method and 14.46 (± 6.59) days for patients treated with the clipping method.

The demographic characteristics of the patients with unruptured cerebral aneurysm are presented in Table 2. About 35% of the patients were male and 65% were female; 31.7% were below 50 years and 68.3% were 50 years or older. The mean age of the patients treated with the coiling method was higher than those treated with the clipping method (52.75 vs. 51.71). Patients' aneurysm size and location are presented in Table 3. The data on the size of the aneurysm were available in 51 patients while the data of 9 patients could not be identified. Almost half of the patients treated with the coiling method (51.9%) had an aneurysm measuring 7–12 mm; however, most of the patients treated with the clipping method (41.7%) had an aneurysm smaller than 7 mm. While most patients (46.9%) treated with the coiling method had internal carotid artery aneurysm (ICA), the patient treated with the clipping method had middle cerebral artery aneurysm (MCA).

Costs

Cost of the patients who were treated with endovascular coil method are presented in Table 4.

The average total invoice amount of the patients treated with endovascular coiling was 14906.77$.

Table 4. Cost of the patients who were treated with endovascular coiling and clipping

Invoice Items	Coiling			Clipping		
	Mean $	Standard Deviation $	%	Mean $	Standard Deviation $	%
Surgery	0.00	0	0	535.78	323.70	21.22
Anesthesia	113.25	82.18	0.76	112.00	80.33	4.43
Services	42.89	65.27	0.29	251.08	239.22	9.94
Medication	278.88	177.86	1.87	302.27	302.31	11.97
Consultation	0.28	0.74	0	6.27	4.12	0.25
Laboratory	35.36	22.04	0.24	135.15	141.62	5.35
Materials	13881.83	5431.28	93.12	863.48	871.93	34.19
İmaging	498.58	152.06	3.34	118.18	103.19	4.68
Hospitalization	55.70	33.34	0.37	201.20	130.57	7.97
Total	14906.77		100	2525.41		100

Table 5. Cognitive function and quality of life scores of the patients

		n	Minimum	Maximum	Mean	Standard Deviation
Coiling	QALY (UK)	27	0.24	1	0.76	0.18
	QALY (Holland)	27	0.47	1	0.80	0.15
	QALY (US)	27	0.42	1	0.81	0.13
	Cognitive Function	27	16	40	34.26	8.52
Clipping	QALY (UK)	26	0	0.88	0.59	0.28
	QALY (Holland)	26	0	0.87	0.61	0.28
	QALY (US)	26	0	0.88	0.66	0.27
	Cognitive Function	26	8	40	27.46	12.25

The item "operation" is not included in the invoices of these patients as the procedure is performed in the Department of Interventional Radiology and not evaluated as a surgical procedure. The percentage of the materials in the invoice items accounts for 93.12% of the total invoice amount. The average cost of consultation is low because of some patients had no consultation fee in their invoice.

When the invoices of the patients treated with surgical clipping were analyzed, the equipment cost accounted for the vast majority of the invoice, as in endovascular treatment. However, this ratio was 34.19% for surgical clipping. The average materials costs were 863.48$. The second leading high cost was 21.22% for the operation (average, 535.78$) and the average total invoice amount was 2525.41$

The potential costs after discharge were modeled considering the treatment protocols and patient follow-up processes by obtaining the expert's opinions.

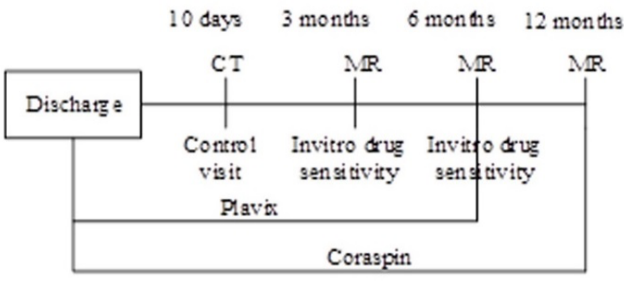

Figure 1. 12 months of follow up costs of the patients who were discharged after endovascular coil treatment

The costs derived from the procedure shown in Figure 1 are as follows:
Consultation: 16.54$
Imaging: 60.66 + 71.69 + 71.69 + 71.69 = 275.73$
Medication: 73.14 + 16.72 = 89.86$
Laboratory: 70.22 + 70.22 = 140.44$
Total: 522.57$

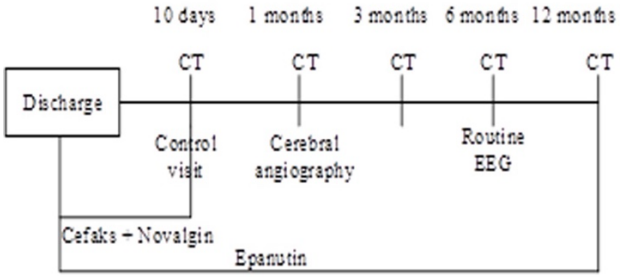

Figure 2. 12 months of follow up costs of the patients who were discharged after surgical clipping treatment

The costs derived from the procedure shown in Figure 2 are as follows:
Consultation: 16.54$
Imaging: 60.66$ + 60.66$ + 577,94$ + 60.66$ + 60.66$ + 60.66$ = 881.24$
Medication: 7.83$ + 1.28$ + 35.18$ = 44.29$
Total: 942.07$

The total cost input that would be used in the Markov model was obtained by adding the costs in Figures 1 and 2 to the costs illustrated in Table 4. Lifetime cost of coiling and clipping groups were found respectively 66463.40$ as a result of 460 months markov cycle and 7900.27$ as a result of 210 months markov cycle.

Effectiveness and cost-effectiveness

Cognitive function and quality of life scores of the patients are presented in Table 5.

Thirty-two patients who treated with coiling and 28 patients who treated with clipping were called; however, a total of 53 patients could be interviewed, and the EQ-5D scale was applied. The cognitive function short form of the Neuro-Qol scale was used as the effectiveness indicator, aside from the QALY values used in the Markov model.

Quality of life scores were marked as zero for patients in the clipping group who died after discharge. The maximum cognitive functioning score is 40. The mean quality of life and cognitive conditions of the patients in the coiling method group were higher than in the clipping method group.

Sensitivity analysis

How the results of the cost-effectiveness analysis were changed by the reduction in the costs of the coiling method, using weights specific for Netherlands and the US, and taking time cycle as 393 months when not all but 99% of the patients died are tested using the sensitivity analysis.

The ICER stayed between 9799.05 and 18128.78 in all sensitivity analyses and continued to be below the cost-effectiveness threshold. In order for ICER score to be equal to national income per capita (9261$), the cost of coil material should be reduced by 52%.

Table 6. One-way sensitivity analysis

Variable	Variation	ICER ($/QALY)
Material Cost of Coiling	Decreased 10%	18128
	Decreased 20%	13895
	Decreased 30%	11841
	Decreased 40%	9799
Reduction rate	5%	25925
Effectiveness data	Weighted according to Holland	23709
	Weighted according to US	23425
Time period	Life time of 99% of cohort died	23602

Budget impact analysis

Budget impact analysis was conducted to investigate the burden and affordability of these treatment methods. The patient population with cerebral aneurysm in Turkey was used in the budget impact analysis.

The prevalence of unruptured cerebral aneurysm was 3.2% in the systematic review and meta-analysis of Vlak et al conducted in 94912 patients from 21 countries (2). The TSI reported that the population of Turkey reached to 78741053 by December 31, 2015. So, the target population was 2519714 individuals.

Despite the absence of a consensus about the management of unruptured cerebral aneurysms, the size of an aneurysm is an essential parameter for making a decision on which aneurysms should be treated. Wang et al. propose that patients with small asymptomatic aneurysms should be followed-up instead of being treated (15). About 65–85% of UIA are in the small size class (< 7 mm) (16). Two different budget impact analyses were performed with the assumption that 35% and 15% of the target population would be treated.

Table 7. Budget impact analysis

	Budget impact	
	15%	35%
Coiling	5634124587.39$	13146287272.55$
Clipping	954518150.11$	2227209016.93$

The coiling method in the treatment of unruptured cerebral aneurysms exhibited an impact valued at a minimum of 5634124587.39$ and the budgetary impact of clipping has been calculated as minimum 954518150.11$.

DISCUSSION

With the developing technologies, treatment paradigms for cerebral aneurysms shifted from open surgical clipping to endovascular embolization as primary therapy in most cases. Luther et al. created time trend series and utilized linear and logistic regressions to quantify treatment changes (17). Unruptured intracranial aneurysms with a treatment of surgical clipping or endovascular coiling from 2004 to 2014 were identified. Result of the study show that the annual caseload for surgical clipping remained stable but increased for endovascular treatment (+615/year, p<0.0001). Similarly, Lin et al. conducted retrospective cohort study, data from the national inpatient sample were used to investigate trends in aneurysm treatment patterns in the USA (18). Results showed that the use of endovascular coiling increased at least twofold for patient (p<0.001) with the majority of unruptured aneurysms treated with coiling from 1998 to 2007. Hoh et al. compared the clipping and coiling procedures concerning the duration of hospital stay and total hospital costs in adult patients with ruptured and unruptured aneurysms (19). A total of 9635 patients with ruptured aneurysms (6019 clipping, 3616 coiling) and 9399 patients with unruptured aneurysms (4700 clipping, 4699 coiling) was included in the study. The authors have detected that the clipping procedure has led to longer duration of hospital stay (p < 0.0001) and higher overall hospital costs (p = 0.0002). Similar results were obtained in patients with unruptured aneurysms. Kang et al. analyzed the efficacy of endovascular coiling compared with surgical clipping in patients with unruptured cerebral aneurysms (20). After a systematic search they found that endovascular coiling was associated with a shorter length of and a lower incidence of short-term complications compared with surgical clipping.

In a cost-effectiveness analysis conducted in Korea, Chang et al. have detected that clipping procedure has led to lower hospital costs. The mean duration of hospital stay was 8.6 days for the coiling method and 15 days for the clipping method (21).

Duan et al. have analyzed the short-term total hospital costs and primary cost drivers of the coiling and clipping procedures for UIA (22). They found that the overall hospital costs were 24.574 $ for the clipping and 31.371 $ for the coiling procedure.

Yentur et al. have analyzed the cost-effectiveness of the clipping and coiling procedures of intracerebral aneurysms (23). Although the coiling method had a shorter duration of hospital stay and fewer complication rates, the total cost of this procedure is higher than the clipping method due to the expensive disposable medical devices like the coil or catheter. Similarly, we found that the material cost accounts for 92% of the total invoice amount of the coiling method. The coil material used to fill the aneurysm is expensive and imported.

Molyneux et al. have investigated the differences between these two methods concerning re-hemorrhage of the treated aneurysm, quality of life, epilepsy, cost-effectiveness, and neuropsychological outcomes. The authors have found that endovascular treatment method is more advantageous in all respects (24).

King et al. had investigated the cost-effectiveness of the surgical intervention for asymptomatic UIA when endovascular coiling method was started to be used (25). According to the result of the study, the endovascular coil method provided an additional 0.88 QALY, and the ICER value was 24200 $ per QALY.

Takao et al. have analyzed the cost-effectiveness in patients with an unruptured aneurysm who had a history of SAH (4). The cost-effectiveness results varied depending on the location and the size of the aneurysm. While surgical clipping was found to be cost-effective for aneurysms measuring 25 mm or larger, the coiling method was found to be cost-effective for those measuring 7 mm or smaller posterior circulation aneurysms.

Maud et al. found that the QALY of the coiling method was 0.69 in the treatment of ruptured aneurysms, this value was 0.64 for the clipping method in the cost-effectiveness study (26). The cost per QALY of the endovascular method was 65424 $ while the surgical approach was 64824 $.

According to the results of the present study, the duration of hospital stay was shorter and the quality of life was better in patients treated with coiling. Lifelong cost of the coiling method was higher than the clipping method. Although the cost of incremental QALY is higher compared to the clipping method, the coiling method is cost-effective as it has a score below the threshold value. Ben-Israel et al. investigated that at which price or efficacy are new technologies cost-effective in unruptured intracranial aneurysms (27). They showed that cost-effectiveness does not appear to be a barrier to innovation in reducing the recanalization rate of unruptured cerebral aneurysm treated by endovascular coil embolization.

Multiple studies have been performed with mixed results. Some studies suggest that endovascular treatment produces better clinical outcomes, but is associated with increased need for retreatment. Other studies report increased durability in aneurysms treated with microsurgical clipping, but that clipping may be associated with worse functional outcomes in some cases. Moreover, studies present different cost results associated with different treatment modalities, including country-dependent cost differences (28).

CONCLUSION

Although there is no consensus on the management of cerebral aneurysms, endovascular coil technique and surgical clipping are two alternative treatment options. In this study, cost effectiveness of these two health interventions is assessed and the endovascular coiling method was found to be cost effective compared to surgical clipping.

In our study costs were calculated based only on the expenditures reported to SSI as the study was conducted with the perspective of the reimbursement institution. If the study would be conducted with the social aspect, the coiling method is estimated to cause lower cost per QALY because the wage loss and cost of pain are higher for the clipping method. The material cost is the most critical parameter for coiling. Providing a coil material with a lower cost would significantly improve the cost effectiveness of the method.

Limitations

This is a single center study which is conducted in a tertiary teaching hospital. Therefore, this should be taken into account when generalizing the results of the study.

Acknowledgments: This study is derived from corresponding author's PhD thesis.

Author contributions: Ahmet Kar contributed to conception, design, supervision, data collection, analysis, literatüre review, writing and critical review. İsmet Şahin contributed to conception, design, supervision, analysis, literatüre review, writing and critical review. Bayram Şahin contributed to conception, design, supervision, analysis, literatüre review, writing and critical review.

Conflicts of Interest: There is no conflicts of interest associated with this publication.

Ethical approval: Ethical approval was obtained from Hacettepe University Non-Interventional Clinical Research Ethics Committee (No:76000869/433-852).

Funding: There has been no significant financial support for this work that could have influenced its outcome.

Peer review: Externally peer reviewed.

REFERENCES

1. Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Neurology. https://www.sciencedirect.com/science/article/pii/S1474442217302995. Published September 17, 2017. Accessed May 20, 2018.
2. Vlak MHM, Algra A, Brandenburg R, Rinkel GJE. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and period: a systematic review and meta-analysis. Neurology. 2011;10(7):626-636.
3. Hwang JS, Hyun MK, Lee HJ, Choi HJ, Kim JH, Lee NR, Kwon JK, Lee EJ. Endovascular coiling versus neurosurgical clipping in patients with unruptured intracranial aneurysm: a systematic review. BMC Neurol. 2012;12(1):2-7.
4. Takao H, Nojo T, Ohtomo K. Cost-effectiveness of treatment of unruptured intracranial aneurysms in patients with a history of subarachnoid hemorrhage. Acad Radiol. 2008;15(9):1126-1132.
5. Zygourakis CC, Kahn JG. Cost-effectiveness research in neurosurgery. Neurosurg Clin N Am. 2015;26(2):189-196.
6. Tatar M, Senturk A, Tuna E, Karabulut E, Caliskan Z, Arsava EM, Topcuoglu MA. Direct treatment costs of stroke in Turkey. Value in Health. 2015;18(7):A388.
7. Aslan H. Cost Analysis Based on Transaction Costs, Charges& Billing Diagnostic Related Groups (DRG) at Ankara Training and Research

Hospital. [master thesis]. Ankara, Türkiye: Hacettepe University; 2015.
8. Bang H, Zhao H. Median-based incremental cost-effectiveness ratio (ICER). Journal of Statistical Theory and Practice. 2012;6:428-442.
9. Balçık PY, Şahin B. Cost-effectiveness analysis of pemetrexed and gemcitabine treatment for advanced nonsmall cell lung cancer in Turkey. Turk J Med Sci. 2016;46(1):152-158.
10. Wiebers DO, International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet. 2003;362(9378):103-110.
11. Brinjikji W, Rabinstein AA, Nasr DM, Lanzini G, Kallmes DF, Cloft HJ. Better outcomes with treatment by coiling relative to clipping of unruptured ıntracranial aneurysms in the United States, 2001–2008. AJNR Am J Neuroradiol.2011;32(6): 1071-1075.
12. Kotowski M, Naggara O, Darsaut TE, Nolet S, Gevr G, Kouznetsov E, Raymond J. Safety and occlusion rates of surgical treatment of unruptured intracranial aneurysms: a systematic review and meta-analysis of the literature from 1990 to 2011. J Neurol Neurosurg Psychiatry. 2013;84(1):42-48.
13. Alshekhlee A, Mehta S, Edgell RC, Vora N, Feen E, Mohammadi A, Kale SP, Flores SC. Hospital mortality and complications of electively clipped or coiled unruptured intracranial aneurysm. Stroke. 2010;41(7):1471-1476.
14. Williams LN, Brown RD. Management of unruptured intracranial aneurysms. Neurol Clin Pract. 2013;3(2):99-108.
15. Brønnum-Hansen H, Davidsen M, Thorvaldsen P. Long-term survival and causes of death after stroke. Stroke. 2001;32(9):2131-2136.
16. Wang DZ, Wang H, Fraser K, Lanzino G. Treatment options for unruptured cerebral aneurysm. Cerebrovasc Dis. 2004;6(6):451-458.
17. Luther E, McCarthy D.J., Brunet M.C., Sur S., Chen S.H., Sheinberg D., ... Starke R.M. Treatment and diagnosis of cerebral aneurysms in the post-International Subarachnoid Aneurysm Trial (ISAT) era: trends and outcomes. Journal of Neurointerventional Surgery. 2020;12(7), 682-687.
18. Lin N. Cahill KS, Frerichs KU, Friedlander RM., Claus EB. Treatment of ruptured and unruptured cerebral aneurysms in the USA: a paradigm shift. Journal of Neurointerventional Surgery. 2018;10(1):69-76.
19. Hoh BL, Chi YY, Lawson MF, Mocco J, Barker FG. Length of stay and total hospital charges of clipping versus coiling for ruptured and unruptured adult cerebral aneurysms in the nationwide ınpatient sample database 2002 to 2006. Stroke. 2010;41(2):337-342.
20. Kang XK, Guo SF, Lei Y, Wei W, Liu HX, Huang LL, Jiang QL. Endovascular coiling versus surgical clipping for the treatment of unruptured cerebral aneurysms: Direct comparison of procedure-related complications. Medicine. 2020;99(13).
21. Chang HW, Shin HS, Suh SH, Kim B, Rho MH. Cost-effectiveness analysis of endovascular coiling versus neurosurgical clipping for ıntracranial aneurysms in the Republic of Korea. Neurointervention. 2016;11(2): 6-91.
22. Duan Y, Blackham K, Nelson J, Selman W, Bambakidis N. Analysis of short-term total hospital costs and current primary cost drivers of coiling versus clipping for unruptured intracranial aneurysms. J Neurointerv Surg. 2015;7(8):614-618.
23. Yentur E, Gurbuz S, Tanriverdi T, Kaynar MY, Kocer N, Islak C. Clipping and coiling of ıntracerebral aneurysms, a cost analysis from a developing country. Neurosurg Q. 2004;14(3):127-132.
24. Molyneux A, Kerr RSC, Yu LM, Clarke M, Sneade M, Yamold JA, Sandercock P. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. Lancet. 2005;366(9488);809-817.
25. King JT, Glick HA, Mason TJ, Flamm ES. Elective surgery for asymptomatic, unruptured, intracranial aneurysms: a cost-effectiveness analysis. J Neurosurg. 1995;83(3):403-412.
26. Maud A, Lakshminarayan K, Suri MFK, Vazquez G, Lanzino G, Qureshi AI. Cost-effectiveness analysis of endovascular versus neurosurgical treatment for ruptured intracranial aneurysms in the United States. J Neurosurg. 2009;110(5):880-886.
27. Ben-Israel D, Belanger B.L, Adibi A, Eesa M, Mitha AP, Spackman E. Innovation in unruptured

intracranial aneurysm coiling: At which price or efficacy are new technologies cost-effective?. Plos One. 2021;16(8), 1-14.
28. Abecassis I.J, Zeeshan Q, Ghodke BV, Levitt MR, Ellenbogen RG, Sekhar LN. Surgical versus endovascular management of ruptured and unruptured intracranial aneurysms: emergent issues and future directions. World Neurosurgery. 2020;136,17-27.