New Interventional Neuroradiological Procedures in Serbia - The Direct Costs of Classical Neurosurgical Intervention in Relation to the Endovascular Treatment of Intracranial Aneurysms

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SUMMARY

Introduction: Intracranial aneurysms are one of the major causes of the neurosurgical morbidity and mortality. Each new therapeutic method, in relation to the standard one, generates high medical costs, as a rule. There have not been estimate of costs of treatment of intracranial aneurysms in Serbia.

Objective: The aim of this study was to compare direct medical costs of clipping the neck of the aneurysm in relation to the new neuroradiological technique based on filling the aneurysmal sack with platinum coils and/or stenting the neck of the aneurysm.

Methods: In a study approved by the Ethics committee of the Belgrade School of Medicine, we retrospectively measured the direct costs of treatment of bleeding and non-bleeding aneurysms at the Clinic of Neurosurgery, Clinical Centre of Serbia (CCS) in 2010. The study included a total of 300 patients divided in two groups: 1) study group included 99 patients with embolized aneurysms and 2) control group included 201 patients who were operated on by classical neurosurgical technique. Direct medical costs were calculated by the methodology of the State Health Care Insurance Fund. Analysis of results was performed using a software package SPSS.

Results: Endovascular treatment was associated with 3% of adverse effects, lower mortality (2% vs. 2.9%), significantly shorter length of hospital stay (Z = - 8.566; p < 0.01), longer duration of anesthesia (226.7 to 195.2 minutes) and significantly higher costs (Z = - 12.475; p < 0.01) compared to neurosurgical treatment. A significant difference in costs was determined mainly by the price of embolization material, 328,169 RSD per patient (3,111€), and the number of resolved aneurysms (more than one, when the multiple aneurysms were treated).

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**Conclusion:** The procedural costs of embolization technique are high, as opposed to small number of hospital days. The readiness of the State Health Care Insurance Fund to pay for the costs of embolization should be approved following cost-utility analysis of both modalities, for the longer period of time.

**Keywords:** intracranial aneurysms, embolization, neurosurgery, direct costs

**INTRODUCTION**

The development of neurosurgery, neurology, and neuroradiology techniques has contributed to the quality of interventional neuroradiological procedures (INRP). Neuroradiological techniques include: computerized tomography (CT), CT angiography (CTA), magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA).

INRP includes: preoperative intravascular embolization of hypervascular tumors of skull base, head and neck (angiomas, glomus, and meningeomas), spinal and paraspinal tumors and treatment of aneurysms, arteriovenous malformations (AVM), arteriovenous dural fistulas (dAVF) – cranial and spinal. In the multidisciplinary treatment of diseases, anesthesia – as a key factor of clinical support – enabled the performance of diagnostic and therapeutic INRP [1, 2].

Clinical Centre of Serbia (CCS) is the largest health facility of tertiary level of care in Serbia. At the Clinic of Neurosurgery, the Section for interventional and invasive neuroradiology has been conducted more than 500 INRP during past decade [3]. The method has been also applied in Military Medical Academy and Clinical Centers of Kragujevac, Nis and Novi Sad. Amongst all INRPs, since 2007, aneurysm embolization is often the most accomplished [3].

According to the statistical data, cerebral aneurysms may be expected in 5% of the population, and 1 – 2% among them will have their aneurysm ruptured with a dramatic clinical picture and consequences [4, 5, and 6]. Today it has been assumed that endovascular treatment, compared to neurosurgical treatment, is better, more modern and less aggressive therapy, associated with low rate of complications, lower mortality, shorter length of hospitalization and lower costs of treatment. From the point of lower costs neurosurgical therapy is preferred over the neuroradiological procedures, and as a rule, newer, more sophisticated methods are more expensive than the standard ones, but the quality of life of patients with aneurysmal SAH is better after embolization [7, 8, 9, and 10].

The incidence of subarachnoid hemorrhage (SAH) after rupture of cerebral aneurysm is 10 – 14 per 100,000 inhabitants – for one-year period. It is estimated that during the life span, 15 – 20% of all aneurysms will be ruptured. The results show that SAH is the cause of death in 30% of younger patients (mean age 52), in the first 24 hours. Aneurysmal re-bleeding, in the next 4 weeks, without treatment, may be expected in 25 – 30% of all patients [4]. The mortality rate is 3% for aneurysms embolized after acute bleeding. It is lower than in untreated acute bleeding aneurysms [11].

Under the conditions of market economy, each new treatment method has been verified in relation to the previous standard one, testing its utility for the society and availability for patients. Will the new method replace the previous one depends on the health policy makers, their determination, readiness and the limits of resources? There are published economic studies dealing with direct medical costs of the INRP, but in Serbia there were not done before. Economic evaluations of the total cost of illness include direct medical costs: preclinical, diagnostic, therapeutic (embolization or neurosurgical costs) and of rehabilitation, but ignore personnel costs (salaries of doctors and nurses), the costs of treating complications, re-interventions, control examinations (CT, DSA, MRA) and consumption of medications. Indirect costs to society, resulting from the loss of working contribution, during and after treatment (disability, retirement, or a lethal outcome), rarely or never have been calculated. The effectiveness of therapy and effectiveness of procedures (utility) is measured by extending the life span. Adjusted years of life, in relation to quality (quality-adjusted life-years – QALY), has been the most commonly used measure of the useful effect of therapy (cost utility analysis – CUA). Contemporary endovascular treatment of aneurysms was introduced in 1991 (platinum coil) and, since 1995, has increasingly been applied in Euro-
At the Clinic of Neurosurgery clipping of the aneurysmal neck was the single therapeutical method available until 1985, but since 2006 increasingly more patients have been treated with endovascular treatment of aneurysms – particularly the complex inoperable aneurysms. Today, there have been two trained teams who exert embolization in the neuroradiological section of the Clinic of neurosurgery.

### RESULTS

There have been more female patients, mean age 54.02 ± 10.74 y/o, than male ones, mean age 49.02 ± 12.34, and it has been proven statistically significant \( p < 0.01 \) by T-test.

Clinical variables of patients in the study are shown in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Investigated group</th>
<th>Control group</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of intervention (Minutes)</td>
<td>226.72 ± 85.34</td>
<td>195.22 ± 48.87</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Length of hospitalization (patient days)</td>
<td>10.84 ± 7.42</td>
<td>19.41 ± 9.44</td>
<td>&lt; 0.01</td>
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</table>

### OBJECTIVE

The main objective of this study was to compare the relationship of direct medical costs between aneurysmal neck clipping and the INRP, i.e. embolization with coils and/or stents.

### METHODS

In the academic, retrospective, non-commercial study, approved by the Ethics committee of the Faculty of Medicine, University of Belgrade – the document number 470/IV7, we measured the direct costs of treatment of bleeding and non-bleeding aneurysms at the Clinic of Neurosurgery in the CCS. The study included a total of 300 patients divided in two groups: 1) study group included 99 patients with embolized aneurysms, and 2) control group included 201 patients who were operated on by classical neurosurgical technique. Direct medical costs were calculated by the methodology of the State Health Care Insurance Fund. Both procedures were performed under general endotracheal anesthesia (GETA). The time of anesthesia registered in anesthesia protocols represents the period of time during that the anesthesiologist is responsible for the patient’s vital functions in the angiography theatre. Anesthesia during the intervention includes: introduction, maintaining of anesthesia and emergence from anesthesia. Neuroradiological and surgical time mean the time from the puncture of an artery (mostly right femoral artery), or surgical incision, until definite hemostasis of the puncture place or the last stitch of the scalp. Radiological protocols, among other data, record the amount of exposition to radiation, what is significant in terms of radiation exposure of patient and the team performing the intervention.

Analysis of results was performed using a commercial software package SPSS.

### RESULTS

<table>
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</thead>
<tbody>
<tr>
<td>Direct costs RSD</td>
<td>1,245,331 ± 621,468.44</td>
<td>351,176.80 ± 174,281.80</td>
<td>( p &lt; 0.01 )</td>
</tr>
<tr>
<td>Direct costs €</td>
<td>12,001.65 ± 5,852.02</td>
<td>3,328.71 ± 1,651.97</td>
<td>( p &lt; 0.01 )</td>
</tr>
</tbody>
</table>
and prognosis, patients of both groups were comparable for anesthetic risk (ASA) and the clinical grading of subarachnoid hemorrhage (Hunt-Hess modified scale). The localization of aneurysms, 48% ACI in the study group, and 42% ACM in the control group, showed a significant difference, in accordance with generally accepted areas of indication. There were 14% of acute bleeding aneurysms, resolved by neurosurgical treatment, and 11% were resolved by endovascular interventions. The complications during the endovascular procedure were presented in 14% of patients (spasm, ischemia, aneurysmal rupture), and amongst them 3% were more severe (thrombosis, dissection of aneurysm) and produced remaining neurological deficit. We have no relevant information about complications left behind the clipping of the neck of aneurysms. In the postoperative time, at the Intensive Care Unit, the mortality was 2% (n = 2) for the investigated group, and 2.9% (n = 6) for control group.

Forasmuch as there is a difference in the length of procedure between anesthetic and surgical protocols. In Table 2, the data were presented, and calculated from the anesthetic protocols and the number of patient days in the disease history.

There has been difference in the duration of INRP in relation to the neurosurgical intervention, and it has been proven statistically significant (p < 0.0001) by T-test.

Mann-Whitney test demonstrated that there was a statistically significant difference in the number of patient days in favor of the control group, where hospitalization was longer by almost 9 days (Z = - 8.566, p < 0.01).

Single price of neurosurgical service was 20,810.82 RSD, and the price of clip 14,800 RSD [12]. Average cost of standard therapy (Table 3.) was: 298,521.00 RSD Mediana (range: 140,062.00 to 1,032,234 RSD), but the cost of general anesthesia was not counted. The average cost of general anesthesia was 20,123.29 RSD.

Single price of neuroradiological service, for the socially insured patient, was 56,088.40 RSD (n = 69), and 3,000 € for foreign citizens (n = 30) [13]. The total invoiced value of the material for embolization was: 71,643,481.31 RSD (n = 69), and 28,394,952, 35 RSD (n = 30), or 100,038,433.66 RSD (n = 99) in total. For the group of embolized patients, the average cost of the procedure, where the cost of general anesthesia wasn’t included, has been: Median – 1,146,523.00 (range: 194,059.00 to 3,854,595.00) RSD. Cost of general anesthesia was 35,277.58 RSD.

Mann-Whitney test demonstrated that there was a statistically significant difference in the cost of the intervention, in RSD, between two groups of patients. Z = - 12.348; p < 0.01.

Average costs for the standard group were 3,328.71 ± 1,651.97 €, Median: 2,830 € (1,328 € minimum value; 9,784 € maximum value).

Average costs for the study group were 12,001.65 ± 5,852.02 €, or Median: 11,680 € (range: 1,840 – 36,536 €).

Mann-Whitney test demonstrated that there was a statistically significant difference in costs between the two groups of patients, in €: Z = - 12.475, p < 0.01.

**DISCUSSION**

Anthropological variables of the patients agree with other studies where the conclusion postulated that females get aneurysmal SAH more often than male, middle-aged patients [5. 14]. Patients in both groups were 2 – 5 years older than patients in these studies, in our opinion according to the better standard of life which postpone the onset of first SAH.

When an aneurysm is diagnosed, by digital subtraction angiography (DSA), the anatomical characteristics of it have to be assessed and a decision is made of the modality of treatment. In the case of acute aneurysm, urgent therapeutic decision has to be made, because the time is an important factor, given the tendency of cerebral arteries vasospasm, increased blood coagulation and further complications. In our study, acute aneurysms were resolved more often by neurosurgical treatment (14% vs. 11%), in relation to embolization, which has been explained by the deficiency of embolization material (stent, coil), regarding the restricted and small health budget.

Endovascular treatment was associated with nearly 3% of adverse complications, lower mortality (2% vs. 2.9%), shorter length of hospital stay, for more than 8 days (10.84 vs. 19.41) and longer duration of anesthesia (226.72 vs. 195.22 minutes). The data on mortality and difference in length of hospital stay (8.5 days) are consistent with other studies.
from European Union countries, in spite of the fact that the average number of hospital days is smaller (4.5 vs. 7.4 days; and 3.4 vs. 10.5 days) [12, 16, 17].

Costs of single service associated with the INRP are higher for the socially insured patient, more than 2.5 times in relation to the neurosurgical treatment (20,810.82 RSD vs. 56,088.40 RSD). The cost is even less favorable for foreign citizens with health insurance. Embolization material participated 88% in total costs. Average, direct costs of aneurysm embolization were 1,245,331 RSD (12,002 €) vs. 351,177 RSD (3,329 €) for neurosurgical treatment. A statistically significant difference was determined mainly by the price of embolization material, approximately 328,169 RSD (3,111 €) per patient, and the number of resolved aneurysms (more than one, when the multiple aneurysms were treated). Costs of neurosurgical treatment generally were increased by the cost of treatment in ICU and the number of hospital days. Other studies approximately indicate the same expenditure of funds [17, 18].

If the cost of general endotracheal anesthesia (GETA) would have been calculated, the total cost of endovascular treatment would be increased by further 3%, and neurosurgical treatment by 20%, in accordance to a greater number of GETA (99 vs. 201). According to a study in CCS and our previous studies, the cost of GETA increase costs by 10 – 20 % [19, 20, 21].

Multicenter study comparing coiling and clipping of aneurysmal neck, on 2,143 patients, demonstrated that endovascular procedure was better in terms of preventing re-bleeding after aneurysmal rupture, with significantly lower morbidity and mortality in relation to the surgical approach [22]. Feasibility study of preventive embolization of unruptured aneurysms made the conclusion that for the 50 y/o patients, treatment of aneurysms was cost effective regarding both modalities, for all simulations of rupture ranging from 0.3 – 5 % per year [6]. Regarding the 70 y/o patients, the embolization was not cost-effective if the simulated frequency of aneurysmal rupture was less than 1% for male patients, and ≤ 0.5 % for females, per year. The risk of formation of new aneurysms had no corresponding effect on the study.

Our current analysis demonstrated that the direct costs of the treatment of bleeding and non-bleeding aneurysms, resolved by endovascular procedure, were larger in relation to the standard neurosurgical procedure – for the period of hospitalization.

In the economic assessment, the question whether the embolization is more useful, in relation to neurosurgical treatment, if the same amount of resources would be spent? The effectiveness of both modalities of treatment has to be demonstrated by the saved years of life, and that would help us in assessing the cost-effectiveness, which we intend to do in our next study. Endovascular treatment is being developing faster than neurosurgical treatment of cerebral aneurysms. Assessment of endovascular treatment efficiency is based on the relative utility and cost-effectiveness.

**CONCLUSION**

Endovascular therapy, compared to neurosurgical treatment, has been associated with lower morbidity, mortality and higher price of embolization material, for all ruptured and unruptured aneurysms. High procedural costs stand opposite to fewer hospital days. Endovascular treatment, as an alternative to neurosurgical treatment, should be offered to all patients as a viable therapeutic option, given specially the treatment of unruptured aneurysms of posterior cerebral circulation. Which strategy would be selected depends on aneurysmal location, its size, relationship of fundus and neck, as well as by the age of patients, their comorbidity, and the technical characteristics of available embolization material. The readiness of State Health Care Insurance Fund to bear the costs of new INRP should be confirmed by the new feasibility study (CUA) of both modalities, for the multi-year period.

**REFERENCES**

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Direktni troškovi klasične neurohirurške intervincije u odnosu na endovaskularni tretman intrakranijalnih aneurizmi

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KRATAK SADRŽAJ

Uvod: Intrakranijalne aneurizme su uzrok velikog morbiditeta i mortaliteta. Svaka nova metoda, u odnosu na standardnu, po pravilu generiše visoke medicinske troškove. Do sada nije bilo procene troškova lečenja intrakranijalnih aneurizmi u Srbiji.

Cij rada: Cilj istraživanja je bio da se uporedi odnos direktnih medicinskih troškova klipsovanja vrata aneurizme u odnosu na novu neuroradiološku tehniku embolizacije aneurizme koilom i/ili stentom.

Metod: Retrospektivno, u nekomercijalnoj studiji, izmerili smo direktnе troškove lečenja krvarečih i nekrvarečih aneurizmi u Klinici za Neurohirurgiju Kliničkog centra Srbije (KCS), tokom 2010 godine. U istraživanje je uključeno ukupno 300 bolesnika, podeljenih u dve grupe: 1) ispitivanu grupu, u koju je svrstano 99 bolesnika sa embolizom aneurizma, i 2) kontrolnu grupu, u kojoj je 201 bolesnik, operisani klasičnom neurohirurškom tehnikom. Direktni troškovi lečenja su računati iz perspektive Republičkог fonda za zdravstveno osiguranje (RFZO). Obrada rezultata vršena je pomoću komercijalnog, statističkог programskог paketa SPSS.

Rezultati: Endovaskularni tretman bio je povezan sa 3% neželjenih efekata, manjim mortalitetom (2 % prema 2.9 %), statistički značajno kraćom dužinom bolničkог boravka (Z = - 8.566, p < 0.01), dužim trajanjem anestezije (226.7 prema 195.2 minuta) i statistički značajno većim troškovima (Z = -12.475, p < 0.01) u odnosu na neurohirurški tretman. Statistički značajna razlika uglavnom je određena cenom embolizacionog materijala, 328,169 RSD (3,111 €) i brojem rešenih aneurizmi (više od jedne, kada su rešavane multiple aneurizme).


Ključне rečи: intrakranijalne aneurizme, embolizacija, neurohirurgija, direktni troskovi

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