



## Cost-effectiveness of Carotid Bifurcation Resection and Interposition of a Polytetrafluoroethylene Graft versus Carotid Endarterectomy in Belgium: A Preliminary Study

Philippe De Vleeschauer<sup>1\*</sup>, Ian Diebels<sup>1,2</sup> and Marc Dubois<sup>1</sup>

<sup>1</sup>Department of Thoracic and Vascular Surgery, Heilig-Hartziekenhuis, Belgium

<sup>2</sup>Department of Medicine and Health Sciences, University of Antwerp, Belgium

### Abstract

**Introduction:** Cerebrovascular disease is an important global health problem. The economic burden of stroke involves the direct hospital cost and the indirect long-term cost. In Europe the cost of ischemic stroke during the acute phase (first year) has been estimated to be 18,000-20,000 Euros. Moreover, the lifetime cost of stroke is approximately 50,000 Euros. If the stroke is due to significant carotid artery disease, different treatments are available. We present our preliminary results on the cost-effectiveness of Carotid Bifurcation Resection and Interposition of a Polytetrafluoroethylene Graft (BRIG) versus Carotid Endarterectomy (CEA).

**Methods:** A total of 60 patients were included, 30 BRIG and 30 Carotid endarterectomies (CEA). All CEA were performed by one surgeon, Dubois M. All BRIG procedures were performed by a single surgeon, Ph. De Vleeschauer. Analysed costs were divided in total cost of hospital stay, the resource cost and pharmaceutical cost.

**Results:** The results show that the total cost of hospital stay was similar in both groups: 3,124.90 for CEA vs. 3,178.46 for BRIG (p=0.81). The total hospital stay cost of the BRIG group was 53.56 Euros (1.7%) more than in the CEA group; however this result was statistically not significant. Nevertheless in Belgium we have to make a distinction in the choice of room namely between a single and twin room. If this single room group is ignored, the total hospital stay cost of the BRIG group is 480.92 Euro (19%) more expensive than the CEA group. There was a significant difference in material cost both as regards to the total cost as the cost for the patient and the national health insurance (150.64 Euro vs. 600.62 Euro, p< 0.01). On the other hand, the pharmaceutical expenses in the CEA group were 15.34 euro (11%, p=0.01) significantly higher compared to the BRIG group.

**Conclusion:** The BRIG procedure has a higher overall cost, mainly due to the more expensive graft. However, the lower hospital morbidity and mortality as compared to the CEA are promising and suggest an overall cost reduction concerning stroke prevention. These preliminary results justify further research of the BRIG procedure.

### Introduction

Cerebrovascular disease is the fourth most common cause of death in the USA [1]. The annual incidence of stroke rises with age, however the incidence in the high income countries shows an overall decrease [2]. The economic burden of stroke includes direct and indirect costs (Table 1). The median proportion of indirect cost was 32% of the total stroke cost as shown in the systematic review by Joo et al. [3]. The direct cost of stroke is largely determined by the length of hospital stay which in turn is significantly determined by medical complications [4]. In Belgium, the cost of stroke during the acute phase has been estimated to be 44.600 euro [5]. This is not confirmed in other studies.

About 85 percent of strokes are ischemic strokes caused by progressive stenosis of the cerebral arteries. Nevertheless strokes are to be avoided. Carotid surgery is one of the possibilities if the significant carotid artery disease has been identified.

Since 1953 carotid endarterectomy (CEA) is considered the golden standard. The first case in the medical literature was published in The Lancet in 1954. The surgeon was Felix Eastcott [6]. However,

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#### \*Correspondence:

Philippe De Vleeschauer, Department of Thoracic and Vascular Surgery, Heilig-Hartziekenhuis, Mechelsestraat 24, Lier 2500, Belgium, Tel: +32 3 491 28 66, +32 4 77 61 04 91; Fax: +32 3 491 28 09;

E-mail: drpdv@icloud.com

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**Table 1:** Cause-cost relation for stroke.

Cost	Cause
Direct	Acute hospitalization
	Rehabilitation
	Subsequent medical complication
Indirect	Lost productivity
	Caregiver burden

since 10 years we are performing an alternative surgical technique to CEA namely carotid bifurcation resection and interposition of a PTFE graft (BRIG). Primary outcome results are promising and have been published previously [7,8].

In this study, we evaluated the cost and effectiveness of the BRIG technique versus the CEA technique in our hospital.

## Methods

A total of 60 patients undergoing elective CEA (n =30) or BRIG (n=30) for the treatment of significant carotid artery stenosis were included. All preoperative examinations were performed in an ambulatory setting including: clinical laboratory examinations, Duplex ultrasound, CT- or MRI-angiography and cardiologic diagnostic examinations. These pre-procedure costs were the same for both groups. The day prior to surgery, the patient was admitted to the hospital and seen by the anaesthesiologist.

Significant stenosis was defined as more than 70% luminal narrowing as assessed by duplex-ultrasound examination and confirmed by CT-angiography. A magnetic resonance imaging (MRI) was only performed in patients with an iodine contrast allergy.

At our hospital, 2 fulltime vascular surgeons are part of the Department. Either has chosen in the meantime the BRIG technique as a standard procedure [7]. The other vascular surgeon used only the CEA technique.

All CEA procedures were performed under general anaesthesia and continuous blood pressure monitoring. After dissection of the carotid bifurcation, 7500 IU systemic heparin was administered after which the common, internal and external carotid arteries were clamped. During the CEA, a shunt was never used. After the endarterectomy, the distal intima was fixed by interrupted 6/0 polydioxanone (PDS) sutures. The arteriotomy was closed with a Dacron patch using a running 6/0 polypropylene (Prolene) suture. On the first postoperative day, 100 mg acetylsalicylic acid was started once a day.

All BRIG procedures were also performed by a single surgeon. Anaesthesia and blood pressure monitoring were the same as with the CEA. Dissection of the carotid bifurcation was performed via a CEA approach. However, after systemic heparinization with 7500 IU, the carotid arteries were clamped and the carotid bifurcation (common, internal and external carotid artery) was resected. An interposition of a 6 mm polytetrafluoroethylene graft was created between the common and internal carotid artery after ligation of the external carotid artery. Surgical details of the BRIG procedure have been described previously [7]. On the first postoperative, 100 mg acetylsalicylic acid was also started once a day.

The complete invoice of all included patients was collected. Hospital costs were divided in three parts: total cost of stay, the resource cost and pharmaceutical cost.

On the one hand, it's important to know how much the total cost of the hospital stay is and on the other hand to find out which part is paid by the patient and the national health insurance. The resource cost included the cost of the prosthesis and surgical material. The pre-procedure costs were the same for both groups and were therefore not considered to be important. In Belgium a distinction must be made between patients who choose explicitly for a single room and those who do not. In the case of a single person room, both the surgeon and the anaesthesiologist charge mostly a 100% extra fee on their

**Table 2:** Total hospital stay cost.

Surgery type	Room type	Fee	N	Averagecost (euro)	Minimum cost (euro)	Maximum cost (euro)	
CEA	Total	Total	30	3,124.90	2,373.35	4,495.54	
		Patient	30	780.46	55.54	2,013.42	
		Insurance	30	2,344.44	2,172.10	2,650.78	
	1 person	Total	11	4,085.67	3,896.48	4,495.54	
		Patient	11	1,785.61	1,609.00	2,013.42	
		Insurance	11	2,300.06	2,172.10	2,482.12	
	≥2 persons	Total	19	2,550.24	2,373.35	2,923.84	
		Patient	19	177.36	55.54	273.06	
		Insurance	19	2,372.87	2,191.40	2,650.78	
	BRIG	Total	Total	30	3,178.46	2,798.18	4,503.81
			Patient	30	373.27	138.52	1,827.95
			Insurance	30	2,805.19	2,614.50	3,097.86
1 Person		Total	3	4,430.50	4,357.50	4,503.81	
		Patient	3	1,710.39	1,592.84	1,827.95	
		Insurance	3	2,720.11	2,675.86	2,764.66	
≥2 persons		Total	27	3,031.16	2,798.18	3,323.77	
		Patient	27	215.98	138.52	312.8	
		Insurance	27	2,815.18	2,614.50	3,097.86	

**Table 3:** Farmaceutic cost.

Surgery type	Room type	Fee	N	Averagecost (euro)	Minimum cost (euro)	Maximum cost (euro)
CEA	Total	Total	30	155.33	130.05	190.14
		Patient	30	53.12	31.66	81.97
		Insurance	30	102.21	90.51	124.41
	1 person	Total	11	154.41	130.05	190.14
		Patient	11	51.43	31.66	70.07
		Insurance	11	102.98	90.51	118.75
	≥ 2 persons	Total	19	155.88	130.05	190.14
		Patient	19	54.13	32.36	61.73
		Insurance	19	101.75	96.18	117.41
BRIG	Total	Total	30	141.49	106.78	187.57
		Patient	30	44.43	14.26	84.93
		Insurance	30	97.06	84.04	109.00
	1 Person	Total	3	137.64	135.72	139.58
		Patient	3	38.20	36.80	39.61
		Insurance	3	99.44	98.92	99.97
	≥ 2 persons	Total	27	140.07	106.78	99.97
		Patient	27	43.28	14.26	84.93
		Insurance	27	96.79	84.04	109.00

**Table 4:** Resource cost.

Surgery	Fee	Cost (euro)
CEA	Total	165.65
	Patient	15.01
	Insurance	150.64
BRIG	Total	660.67
	Patient	60.06
	Insurance	600.62

provided medical service. This extra fee is not covered by the national health insurance. Neither follow-up cost after discharge nor total one year cost were included because these data are almost impossible to obtain in Belgium.

### Statistical methods

Variables were divided in continuous and categorical. Continuous variables were expressed as mean with a minimum and maximum range value and were analysed with the student's T-test. Categorical values were expressed in absolute numbers and percentages. A p-value  $\leq 0.05$  was considered to be statistically significant, a p-value  $< 0.1$  as marginally significant.

## Results

There was no significant difference in the average hospital stay for the BRIG group and CEA group, which was respectively 4, 82 and 5 days (p-value 0.48). The total hospital stay cost and pharmaceutical cost are summarized in Table 2 and 3. The costs were divided according to the room choice and to whom (the patient or national health insurance) the costs were charged.

The resource cost was mainly determined by the use of a Dacron patch (CEA) or PTFE 6 mm graft (BRIG), and was the same in every patient. The cost for a Dacron patch and PTFE graft was respectively 165.16 euro and 660.67 euro. The patient was charged 9.1% (15.01

**Table 5:** Significant cost-difference.

Cost	Room type	Fee	p-value	Significantly different
Hospital cost	Total	Total	0.81	No
		Patient	0.10	Marginal
		Insurance	$< 0.01$	Yes
	1 person	Total	0.07	Marginal
		Patient	0.53	Marginal
		Insurance	$< 0.01$	Yes
	≥ 2 persons	Total	$< 0.01$	Yes
		Patient	0.6	No
		Insurance	0.04	Yes
Farmaceutic cost	Total	Total	0.01	Yes
		Patient	0.10	Marginal
		Insurance	0.10	Marginal
	1 Person	Total	0.12	No
		Patient	0.09	Marginal
		Insurance	0.58	No
	≥ 2 persons	Total	0.06	Marginal
		Patient	0.13	No
		Insurance	0.11	No
Resource cost	Total	$< 0.01$	Yes	
	Patient	$< 0.01$	Yes	
	Insurance	$< 0.01$	yes	

euro for the patch and 60.06 euro for the graft), the remaining cost respectively 150.64 euro (patch) and 600.62 euro (graft) was reimbursed by the national health insurance (Table 4). There was a significant difference in material cost both with regard to the total cost on the one hand and the cost for the patient and the national health insurance on the other hand (p  $< 0.01$ ) (Table 5).

**Table 6:** Average cost in the first year after ischemic stroke.

Country, Year	Cost	Comments
France, 2013	16,686 euro	
Germany, 2005	18,517 euro	Ischemic
Sweden, 1994	21,975 USD	
Netherlands, 2006	16,598 – 22,448 euro	Dependant on age and gender
Australia, 2014	19,992 USD	Ischemic

**Table 7:** Lifetime cost of stroke.

Country, year	Cost	Comments
Germany, 2005	50,507 euro	Men: 54,552 euro Women: 47,596 euro
Australia, 2014	68,769 USD	
USA, 1996	90,981 USD	
England, 1996	2,000 – 62,000 pounds	Wide difference between average cost of cases

**Table 8:** Results of large randomised controlled trials comparing carotid endarterectomy to carotid artery stenting and our results with the BRIG produce.

Procedure	Randomised controlled trials	30-day stroke (%)	30-day mortality (%)	Cumulative $\geq$ 70 Restenosis (%)
CEA	CREST, 2010 [20]	2.3	0.3	6.3 (2 yr)
	SPACE, 2008 [21,22]	6.3*		4.6 (2 yr)
	EVA-3S, 2006 [23,24]	3.9**		2.8 (3 yr)
	SAPPHIRE, 2004 [25]	9.9***		NA
	CAVATAS, 2001 [26,27]	9.8**		5.2 (1 yr)
CAS	CREST (2010)	4.1	0.7	6.0 (2 yr)
	SPACE (2008)	6.8*		10.7 (2 yr)
	EVA-3S (2006)	9.6**		3.3 (3 yr)
	SAPPHIRE (2004)	4.4***		NA
	CAVATAS (2001)	9.9**		22.0 (1 yr)
BRIG [7,8] N=103		Minor: 1.9 Major: 0	1.0	1.4 (4 yr)

NA: Not Available; CEA: Carotid Endarterectomy; CAS: Carotid Artery Stenting; BRIG: Carotid Bifurcation Resection and Interposition of a polytetrafluoroethylene Graft

\*Cumulative endpoint of ipsilateral stroke or death

\*\*Cumulative endpoint of any stroke or death

\*\*\*Cumulative endpoint of ipsilateral stroke, myocardial infarction or death

**Table 9:** Results of different prosthetic graft materials.

Material	Hospital mortality (%)	Hospital morbidity (%)	Restenosis rate
PTFE (n=103)	1.0	Minor stroke: 1.9 Major stroke: 0 Graft infection: 0	Prox. anastom: 1.4 (4 years) Distal. anastom: 0
Dacron (n=292)	1.8	Ischemic stroke: 6.5 hemorrhagic stroke: 5.8 Early graft thrombosis: 1 Graft infection: 1.4	Prox. Anastom: 3.4 (2.5 years) Distal anastom: 0.7

The results show that the total cost of hospital stay was similar in both groups: 3,124.90 euro for CEA group vs. 3,178.46 Euro for the BRIG group ( $p=0.81$ ). The total hospital stay cost of the BRIG group was 53.56 Euros (1.7%) more than in the CEA group; however this result was statistically not significant at present.

Nevertheless in Belgium we have to make a distinction in the choice of room namely between a single and twin room. In a single room, the total hospital stay cost for respectively CEA and the BRIG group was 1,535.43 Euro (60%) and 1,400.00 Euro (46%) more expensive than in a twin room. The extra cost is mainly due to the additional fees for the surgeon and anaesthesiologist as mentioned previously.

If this single room group is ignored, the total hospital stay cost of the BRIG group was 480.92 Euro (19%) more expensive than the

CEA group. This additional cost (495,51 Euro) was mainly due to the higher PTFE graft cost.

On the other hand, the pharmaceutical expenses in the CEA group were 15,34 Euro (11%,  $p=0.01$ ) significantly higher compared to the BRIG group. It is striking that for the CEA group – BRIG group resp. 31%-34% of the total cost of pharmaceutical specialties, must be paid by the patient and resp. 71%-90% of those cost are due to only 2 specialties namely phenylephrine 1% (30 Euro) and protamine (8 Euro).

## Discussion

Stroke is an important cause of disease burden and health expenditure. The average cost first year after stroke and the lifetime cost of stroke are similar for different countries and continents (Table 6 and 7) [9-14].

In Europe, the cost of hospitalization represents about 25% to 45% of the sum spent during the first year after stroke [5]. The average cost of hospitalization for stroke related disorders in 2007 amounted 6,188 Euro in Belgium. Preventing strokes is therefore financially very important. Among the ischemic strokes, patients with significant carotid artery stenosis suffer from rates of disabling or fatal stroke that are twice that of the general population.

Since the introduction of CEA in 1954 for the treatment of carotid artery stenosis, CEA is considered as the golden standard for the treatment of symptomatic or significant asymptomatic carotid stenosis. Condition is that the surgical centre has a low hospital morbidity and mortality. For example in 2002 the Dutch Stroke Guidelines of The Dutch Institute of Healthcare Improvement (CBO) for CEA of carotid stenosis are as follows:

1. Combined operative morbidity and mortality less than 5%-7% for CEA of 70%-99% symptomatic carotid stenosis.
2. 2% morbidity and mortality for CEA of 50%-70% symptomatic carotid stenosis.
3. <2% morbidity and mortality for CEA of >50% asymptomatic stenosis [9]. The guidelines for CEA in the USA are similar [15].

Surgical morbidity and mortality less than 6% in symptomatic carotid stenosis of good-risk patients and less than 3% in asymptomatic carotid stenosis of good-risk patients.

The last decade stenting of the carotid arteries (CAS) becomes more and more popular especially among the radiologist but the results are still not convincing. Ciccone MM et al. [16] argue that carotid artery stenting constitutes a good alternative to CEA in carotid revascularization when the procedures are selected based on patient-specific risk factors.

However, more important data (>1,500,000 procedures) from contemporary administrative dataset registries suggest that stroke/death rates following CAS remain significantly higher than after CEA and often exceed accepted AHA (American Heart Association) thresholds. There was no evidence of a sustained decline in procedural risk after CAS [17].

Further a study in South Korea showed that the cost from procedure onset to discharge including the resource cost was significantly lower in the group of CEA compared to CAS [18]. The cost was higher in the CAS group because the resource cost was approximately three times higher in the CAS group than in the CEA group. In another multicentre study by McDonald et al. used data from the National Inpatient Sample to estimate hospital costs for nearly 200,000 patients who underwent either CAS or CEA between 2001 and 2008 [19]. They found that hospital costs were nearly \$5,000/patient higher with CAS than CEA but their study did not consider physician costs, which are substantially higher with CEA (due to anaesthesiology services).

Therefore, the authors of this article consider the CAS technique so far as no acceptable alternative for the treatment of carotid stenosis.

10 years ago we started with the BRIG procedure at our department. At the beginning the BRIG technique was only used for symptomatic restenosis and pseudoaneurysm after previous CEA. At this time, it has become a routine procedure in the treatment of carotid artery disease for this surgeon. Meanwhile, he has treated more than 144 cases and he still has no major stroke with the BRIG

technique, furthermore only 2 cases with minor stroke and 1 death (unpublished results).

If one wants to compare these two surgical techniques (BRIG and CEA), then two things are of particular importance. Firstly the hospital morbidity and mortality and secondly the restenosis rate at medium-long term. As to the cost of the surgical procedure, the hospital morbidity is especially important, and above all the stroke rate. The BRIG technique scored up till now clearly better than the CEA technique both in terms of hospital morbidity-mortality as the restenosis rate [8]. It should however be noted that the groups strongly differ in number.

Up till now we did not observe any major stroke in the BRIG group, whose total cost in comparison to CEA group is 481 Euro higher. This additional cost is mainly due to the difference in cost between a Dacron patch (CEA) and PTFE graft (BRIG). Consequently, the extra cost for 100 patients treated by the BRIG technique, is about 48,000 Euros, or 42,000 Euros paid by the national health insurance. If you can avoid 1 stroke in 100 patients, treated with a different technique, one can at least save the first year after stroke about 16,000 Euros and roughly 50,000 Euros lifetime cost after stroke. On the basis of these data, the hospital morbidity of the BRIG technique must be at least 1% lower than the CEA in order to have true financial benefit. So far our, although limited experience with the BRIG technique shows a more than 1% lower hospital morbidity than the CEA technique and justifies to collect more data also from other countries (Table 8). But are randomized studies always necessary for this purpose? In 2005, following correspondence from John Wu was published in *The Lancet*: "In this 100<sup>th</sup> year of celebration of Albert Einstein, I have been thinking about his papers on theoretical physics, done purely by deduction, and how they changed our view of the world. His way of thinking is in sharp contrast to that of evidence-based medicine, which has become almost a dogma in some medical circles. Yet if everything has to be double-blinded, randomised, and evidence-based, where does that leave new ideas? I do worry that if evidence-based medicine becomes the dominant thinking, it could impede advances in medicine" [28].

However, it makes sense to collect at least larger numbers of the BRIG technique.

In our BRIG technique, a PTFE graft is used. Different materials have been proposed. The use of autologous material led to an increased restenosis rate and total occlusion [29]. The prosthetic materials show a favourable outcome. A recent study on carotid replacement with Dacron grafts showed a worse result than PTFE grafts as listed in Table 9 [7,30]. Both studies show that the restenoses occur mainly at the level of the proximal anastomosis. The infection risk is low and only led to the replacement of the graft by an autologous greater saphenous vein in the Dacron group.

The BRIG procedure shows a lower incidence of restenosis than CEA, despite the small amount of cases (Table 8). The extent, to which redo surgery and additional costs can be avoided, remains though unclear because there is currently no gold standard for the approach to carotid restenosis.

It is generally accepted that symptomatic restenosis needs surgery but the incidence remains very low. In a multicentre regional registry, Goodney P et al. [31] reported that restenosis occurred in 10% of the patients and patients with 50-99% restenosis were asymptomatic in most cases. Only 3 patients (1%) of 288 with restenosis were



symptomatic. In our department, only symptomatic restenosis were treated by surgery.

The problem of asymptomatic significant restenosis is much more complex. Indeed, it is very difficult to predict if and when such restenosis becomes symptomatic. Therefore it is still quite difficult to prove that the BRIG technique is cost-effective on the long term with regard to symptomatic restenosis and redo surgery.

## Conclusion

The BRIG procedure has a higher overall cost, mainly due to the more expensive graft. However, the lower hospital morbidity and mortality as compared to the CEA are promising and suggest an overall cost reduction with regard to the prevention of stroke. It is still very difficult to prove that the BRIG technique is cost-effective on the long term concerning symptomatic restenosis and redo surgery. The results of the BRIG technique require confirmation and justify further research of this procedure.

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