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## Haemodynamic depression during carotid angioplasty and stenting

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### Summary

Haemodynamic depression is commonly defined as a change in arterial pressure (hypotension with systolic pressure values of less than 90 mmHg) and heart rate (bradycardia, heart rate of less than 60 beats per minute). Carotid angioplasty and stenting (CAS) can result in many complications, particularly in the perioperative period. Apart from the most serious complications, such as stroke and temporary ischaemic attack (TIA), as well as local complications (related to the puncture of the femoral artery), the researchers are especially interested in haemodynamic depression. It is closely related to the interventional treatment area. The region of the common carotid artery bifurcation and the initial section of the internal carotid artery are abundant in baroreceptors and mechanoreceptors. Various prophylactic measures were introduced to clinical practice due to possible complications, such as hypotension and perioperative bradycardia. They include preoperative fluid infusion, atropine administration, infusion of 'pressor' amines and provision of an intracardiac electrode for the time of the procedure.

**Key words:** haemodynamic depression • carotid angioplasty and stenting • perioperative bradycardia

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### Background

Haemodynamic depression is defined by many researchers as changes of the arterial pressure (hypotension with systolic pressure values of less than 90 mmHg) and of the heart rate (bradycardia, heart rate of less than 60 beats per minute) [1–3]. According to different reports, its incidence in the perioperative period of carotid angioplasties reaches 68% [1,4,5].

Transcutaneous techniques belong to a group of dynamically developing surgical techniques. With their increasing application in the clinical practice, they may become an alternative of traditional surgical options. As shown in many publications (including such randomised studies as SAPHIRE and CARESS), in the group of patients with the highest surgical risk, CAS procedures (carotid angioplasty and stenting) with neuroprotection are connected with much more advantageous results than the CEA surgeries (carotid endarterectomy) [6–11].

Although CEA still remains a golden standard of treatment of carotid artery stenosis, CAS may be less distressing for the patients if carried out only in selected clinical

situations and by experienced operators [12,13]. They often require a shorter hospitalisation time if performed from a vascular approach, with neuroprotection of the CNS ensured by neuroprotective devices. In case of a concomitant ischaemic heart disease, they allow for a simultaneous angioplasty of coronary arteries and of the carotid artery.

### Qualification for Surgical Treatment (Transcutaneous Carotid Angioplasty)

Brain stroke is the third most common cause of death in the whole world. It is estimated that more than 30 000 Poles die of stroke every year. Further 40 000 survive but their neurological deficits frequently lead to disability of different degree [14,15]. The risk of a repeated stroke in the period of one year amounts to 6–12%, and to as much as 40–50% within the period of 5 years [16,17]. That is why prevention of atherosclerosis as the main cause of stroke, secondary prophylaxis and treatment of atherosclerotic lesions in carotid arteries are so important.

Surgeries (carotid endarterectomy and transcutaneous operations basing on carotid artery catheterisation) are

carried out in patients with the most advanced, haemodynamically significant lesions, with carotid stenosis of more than 70%, even if asymptomatic. Treatment of stenosis of 60% is also considered, if accompanied by symptoms of insufficient blood supply to the cerebral circulation.

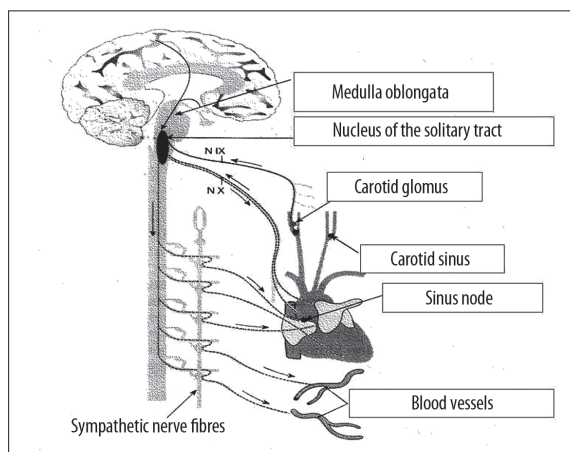
In Europe, it is advised to perform surgery when the stenosis reaches  $\geq 80\%$  ( $\geq 90\%$  in women), as indicated by the results of the ECST study (*European Carotid Surgery Trial*). In North America, it was decided on the basis of the NASCET study (*North American Symptomatic Carotid Endarterectomy Trial*) that the surgical treatment of internal carotid artery should be introduced with stenosis amounting to  $\geq 50\%$ . Differences in these studies are most probably a result of using different diagnostic methods of stenosis measurement in the internal carotid artery and different definitions of end points [18–20].

The largest randomised study (CREST) compared CAS procedures including neuroprotection with a classical endarterectomy. Preliminary results showed that the efficacy and safety of carotid artery treatment are not significantly different in both study groups [21]. The decision concerning the type of surgery should always be made individually in every case. In some clinical situations, such as: high risk connected with endarterectomy (mostly due to the advanced age or the presence of coronary disease), recurrent postoperative stenoses, stenosis resulting from radiotherapy, occlusion of contralateral internal carotid artery or a high bifurcation of the common carotid artery (C2–C3), the transcutaneous techniques seem to be more advantageous. However, in case of antithrombotic treatment intolerance, coexisting renal disease, or unstable atheromatous plaque, it is advisable to qualify the patient to surgical endarterectomy [12]. Patients' preferences are also important, as those who may choose, decide on less invasive procedures.

CAS happens to be a cause of many complications, especially in the perioperative period. Only the introduction of neuroprotective devices, protecting the brain from potential embolism with material released from ruptured atherosclerotic plaques, allowed for a reduction of the most serious complications (stroke, death) and their more common application in the clinical practice [4,5,22,23].

Apart from the most feared complications of CAS, including brain stroke, TIA (temporary ischemic attack) and local complications connected with puncture of the femoral artery, the researchers are especially interested in the haemodynamic depression in the peri- and postoperative period. It is closely connected with the area of interventional treatment [23,24]. The region of common carotid artery bifurcation and the initial segment of the internal carotid artery belong to locations abundant in baroreceptors – biological sensors of haemodynamic balance. They belong to a group of mechanoreceptors and react both to vessel dilation due to absolute BP values and to dynamics of their changes [25].

As opposed to CAS surgery, CEA as a classical operation method in the treatment of carotid artery stenosis, allows for a better control of haemodynamic changes connected with reflexes from baroreceptors. According to Park BD



**Figure 1.** Baroreceptor reflex.

et al., a clinically significant hypotension was found considerably more often in the group of patients subjected to CAS (35% in the group of CAS vs 12.6% in the group of CEA) and was connected with a higher risk of heart attack, increased mortality, and longer hospitalisation time [26]. A typical procedure during CEA is to increase the BP initially by 20–30 mmHg. Moreover, some operators inject the region of the carotid glomus with an anaesthetic, which is supposed to prevent the release of stimuli from this area [27].

### Reflexes from Baroreceptors

Stimulation of baroreceptors of the carotid sinus by dilation of the artery, or their decompression on decrease of the arterial wall tone, activates a reflex reaction. Its effect is both on the heart rate and on the vascular muscle tone (Figure 1). It is supposed to counteract changes, which is in accordance with the negative feedback mechanism. A dynamic balance between the tone of the parasympathetic system and the sympathetic system allows for a rapid reaction to the changing haemodynamic conditions and guarantees normal values of BP. It is also worth underscoring that the reactivity of baroreceptors decreases with age. That is why these are mainly the older patients that (due to a high surgical risk and presence of comorbidities) are subjected to transcutaneous CAS procedures.

The region of the carotid sinus gives rise to afferent fibres of the Hering's nerve that convey signals on current haemodynamic conditions to the afferent fibres of the glossopharyngeal nerve, and to the centre of haemodynamic regulation in the medulla oblongata, and then to motor nuclei of the vagus nerve [28,29]. After integration with the stimuli from higher anatomical structures of the nervous system, there follows a decrease in the tone of the sympathetic system and increase in the activity of the parasympathetic system. This leads to a slower heart rate, decreased peripheral resistance, and decrease in BP values. Intracardial afferent fibres of the vagus nerve lead to both atria of the heart, nodes (sinoatrial, atrioventricular) and the initial segment of the electrical conduction system of the ventricles. However, there is also some asymmetry: the right vagus nerve innervates the sinoatrial node, while the intracardial fibres of the left vagus nerve supply the atrioventricular node. A similar asymmetry in innervation

is also found in the sympathetic system. Fibres of the right stellate ganglion are responsible for stimulation of the sino-atrial node – positive chronotropic effect, while the fibres of the left ganglion innervate the muscle of the ventricles mainly – positive inotropic effect [28,30,31].

### **Risk Factors of Haemodynamic Depression**

Implantation of a stent and pressure used for its deployment during CAS procedures are the stimuli that initiate the above presented cascade of reactions. Experimental animal model studies have accounted for the cause of hypotension after carotid angioplasties – a constant centrifugal mechanical force exerted by a stent on the wall of the carotid sinus, leading to a continuous activation of the reflexes from baroreceptors [32].

Currently, attempts are made to find factors that would allow us to indicate patients with the most pronounced reflex, BP decrease, and HR slowdown. Relatively well recognised risk factors of haemodynamic depression in the peri- and postoperative period include the history of previous surgeries (CEA) of the artery subjected to angioplasty, and chronic smoking habit. Patient's age, history of diabetes and ischaemic heart disease, EF value, location of the atherosclerotic plaque and its structure are of importance as well. Moreover, the type of the implanted stent, its length, material used for its construction, as well as the use of postdilatation in order to recreate the lumen of the artery after its release are also important.

The protective significance of the previous procedure of carotid endarterectomy (CEA) is connected with a lower number of baroreceptors in the wall of artery (due to a mechanical removal of the atherosclerotic plaque) and with a presence of some kind of scar which reduces the sensitivity of baroreceptors to BP changes. Higher BP values are needed to activate these receptors than in patients without a history of previous endarterectomy [33].

Smoking, connected with an increased release of such mediators as noradrenaline or adrenaline, increases the tone of the sympathetic nervous system, leading to a higher heart rate and higher BP values in smokers. At the same time, the sensitivity of baroreceptors to mechanical stimuli is decreased and the patient is 'protected' from haemodynamic depression connected with CAS surgeries [34,35].

One of the complications of diabetes is neuropathy, which involves the autonomic system as well. It leads to a dysfunction of all body systems [36]. As far as the circulatory system is concerned, the regulation of the heart rate is disturbed, showing a decrease in its 24-hour variability. As far as the blood pressure is concerned, there is no physiological decrease of its value in the night and no paradoxal hypertension in lying position [37,38]. Therefore, a deficient response of baroreceptors to pressures used during stent implantation and to inflation of a balloon used for stent deployment, as well as the lack of haemodynamic depression in patients with diabetes, seem obvious [1].

One more factor that allows us to predict haemodynamic instability is the structure of the atherosclerotic plaque.

In classical surgeries (CEA), a higher risk of death or serious cardiovascular incidents (brain strokes, heart infarcts) appeared when the removed atherosclerotic plaque was ulcerous and soft. It was explained by the fact that hard, strongly calcified plaques are more stable and less susceptible to ruptures, and thus the embolisation of the cerebral circulation with a released material is less frequent. Transcatheter procedures (CAS) were connected with a reverse tendency, i.e. the calcified plaques predisposed to haemodynamic instability and to complications in the form of prolonged hypotension and bradycardia in the postsurgical period more often. The difference could be explained by much higher values of pressure used to widen the calcified stenoses during stent implantation and a more frequent deployment of stents in order to optimise the procedure [39–41].

It was also proved that coexisting coronary disease [40–42], and especially the reduction of EF below 25%, is significantly more often connected with haemodynamic instability in the perioperative period and after CAS procedures [39,40,43]. Heart ischaemia, both acute and chronic one, may stimulate receptors of the atrioventricular node and increase the tone of the vagus nerve. This increases the sensitivity of carotid baroreceptors and leads to their excessive reflex [44]. This is especially true in patients aged over 78 years [40,41,43].

As it was shown, haemodynamic instability during CAS procedures is influenced by both the type of the procedure (the highest BP decreases observed during stent deployment, as compared to stent's self-expanding) and the type of the implanted stent [24,25]. According to Diehm et al., from among self-expanding stents, the ones made of nickel titanium are connected with a higher risk of perioperative hypotension than the Egiloy ones [45].

The available literature includes no data concerning the influence of neuroprotection on the incidence of haemodynamic depression. However, there appeared articles on intolerance to neuroprotective devices, leading to a spasm of the internal carotid artery on device elements [46]. However, despite all the above mentioned facts, the role of neuroprotective devices in the reduction of thromboembolic complications of CAS procedures seems priceless. In the light of the recent studies, it is recommended to perform CAS with neuroprotection only [4,7,22,23].

### **Perioperative Prophylaxis**

Due to possible complications: hypotension and perioperative bradycardia during CAS procedures, prophylactic methods were introduced to the clinical practice. They include fluid infusion in the preoperative period, atropine administration during every procedure or only in case of bradycardia, infusion of 'pressor' amines, and provision of an intracardiac electrode for the time of the procedure [42,46,47]. It was proved that they have a significant influence on the incidence of persistent haemodynamic depression and significantly decrease the cardiovascular mortality in the perioperative period. This is especially true in the group of patients with primary lesions not subjected to previous surgical endarterectomy [47].

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