ABSTRACT
Anesthesia for carotid endarterectomy (CEA), general or locoregional, has been an issue of debate in literature ever since the first Cochrane review in 1991. The largest available study on the subject, the GALA trial, has not shown any difference in patient’s outcome – incidence of stroke and 30-day-mortality postsurgery. However, increasing evidence favors regional anesthesia as an independent factor of reduced morbidity after CEA. The advantages and disadvantages of general versus regional anesthesia for CEA have been well established. Cervical plexus blocks (CPBs) are safe and effective anesthetic techniques, but they may also present adverse effects that we must be aware of. Optimal cerebral function monitoring remains a problem to be solved. Cerebral oximetry may prove to be a reliable tool in predicting neurological impairment. This narrative review intends to highlight the latest implemented anesthetic modalities for CEA, including CPB under ultrasound guidance, and to outline the main limitations of general versus regional anesthesia. Following the appropriate anesthetic, modality necessitates a thorough preoperative consultation among the patient, the surgeon, and the anesthetist. The anesthetic plan should be made on an individual basis, taking into consideration patient’s comorbidities and wish.

Key words: Anesthesia; carotid; endarterectomy; general; local

Introduction
Atherosclerotic disease is widespread in the developed world with increasing prevalence in the developing world. Risk factors include smoking, obesity, hypertension, hypercholesteremia, and diabetes mellitus. Atherosclerotic carotid artery disease, in the form of carotid intima-media thickening or luminal stenosis, accounts for 20% of ischemic stroke events.[1,2] Surgery to relieve carotid atherosclerotic disease and to reduce the possibility of ipsilateral stroke due to emboli was first performed at St. Mary’s Hospital, London, in 1954. Since then, evidence for the effectiveness of carotid endarterectomy (CEA) has accumulated, and CEA has been associated with lower stroke/death rates (<3%) compared to carotid artery stenting, although the indications of the latter have expanded the last decade.[3]

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial are both large randomized Class 1 studies that have defined current indications for carotid endarterectomy. NASCET found that, for every six patients treated with CEA, one major stroke would be prevented at 2 years for symptomatic patients with
a 70%–99% stenosis, whereas the European Asymptomatic Carotid Surgery Trial found that asymptomatic patients may also benefit from the procedure but only the group with a high-grade stenosis (>80% stenosis in men and unclear in women).[6,7]

CEA is currently performed routinely under general or regional anesthesia, depending on the local clinical practice and the wish of the patient. As far as regional anesthesia is concerned, blockade of the second, third, and possibly fourth cervical dermatomes is required for the patient to undergo a CEA. This blockade can be achieved in a number of techniques including cervical epidural, superficial, and deep cervical plexus blocks (CPBs) (alone or in combination) or local infiltration by the vascular surgeon. The appropriate anesthetic technique remains controversial and contradicting data are already published.[7,8]

**Background and objectives**

The most common technique to anesthetize patients scheduled for CEA is still general anesthesia.[9] Specific advantages over regional anesthesia include tight arterial carbon dioxide control; cerebral protection afforded by volatile anesthesia and the anesthesiologist preference for general anesthesia because of a secure airway establishment.[9] On the other hand, several benefits of regional over general anesthesia have been suggested: “gold standard” cerebral function monitoring, intact cerebral autoregulation, reducing cardiac- and respiratory-related morbidity, lower shunt insertion rate, shorter hospital stay, and lower cost.[8,10]

The subject of this article is not new, but the main question of which anesthetic technique, general or regional, should be implemented for CEA in terms of patient safety has not been definitely answered. The objective of this article is to re-examine the results of general versus regional anesthesia for CEA in the light of old and new published literature and finally suggest a safe anesthetic plan for the vascular anesthetist. At present, best medical treatment for carotid stenosis is gaining ground against CEA, making the latter’s future role questionable. As there are great risks associated with CEA, patients only benefit from this procedure only when perioperative risks are low, so all possible attempts should be made to minimize risks including the modality of anesthesia.

Accordingly, we will point out the effect of anesthetic technique on patient outcome, especially in terms of morbidity and mortality, and provide evidence regarding the cost-effectiveness of general versus regional anesthesia. We will also communicate special considerations in the light of increasing literature on ultrasound (US)-guided CPB for CEA.

**Methods**

An extensive search of the electronic databases of “PubMed” and “Cochrane Systematic Reviews” was conducted using the phrases “anesthesia,” “general versus local anaesthesia,” “regional anaesthesia” “complications of regional anaesthesia” in combination with keywords “carotid endarterectomy” or “CEA.” Further search also included the keywords “superficial,” “deep,” “combined,” and “intermediate” in combination with “CPB” and “carotid endarterectomy” or “CEA.” Articles included in the results were further examined for possible sources. The search was limited to manuscripts written in English during the period of January 2013 to December 2017.

**What is the ideal anesthetic technique for carotid endarterectomy: General or regional?**

In the past 30 years, a plethora of prospective, randomized, controlled trials have compared regional with general anesthesia and their effects on outcome after CEA. In the literature, it is well established that regional anesthesia improves outcome in certain aspects after surgery, providing better postoperative analgesia than systemic opioid techniques, reduced blood loss, and lower risk of thromboembolic events. Patient factors interact with the type of anesthetic in determining outcome but identifying potential beneficiaries requires further study.[11,12]

Existing literature related to anesthesia for CEA does consistently report the effect of anesthesia type on mortality [Table 1]. The first Cochrane review on the subject was published in 1996 and was last updated in 2013. Neither the latest Cochrane review nor the GALA trial – the single largest trial available – have shown a statistically significant difference in outcomes between general and local anesthesia for CEA, in respect to 30-day incidence of stroke, myocardial infarction (MI), and mortality. These studies report a trend toward lower operative mortality with local anesthetic.[8,10] A subgroup analysis of GALA study also resulted in decreased neurocognitive performance in the group of general anesthesia.[13] However, the GALA trial has certain limitations rendering its results questionable: (a) it is an underpowered study despite the number of patients included and (b) the precise regional anesthetic technique is not tightly controlled.[14]

Nevertheless, increasing data in favor of locoregional compared with general anesthesia have lately emerged. Hussain et al., using the Michigan Surgical Quality Collaborative database, have shown that general anesthesia for CEA is associated with more than two-fold higher mortality compared with regional anesthesia, while Leichtle et al. have demonstrated...
that general anesthesia is an independent risk factor for postoperative MI, particularly in patients with preoperative neurologic symptoms.\textsuperscript{[9,15]} In addition, in 2014, Liu \textit{et al.}\textsuperscript{[16]} demonstrated that patients receiving regional anesthesia had a lower incidence of postoperative unplanned intubation and/or pulmonary resuscitation procedure after CEA. Knappich \textit{et al.}\textsuperscript{[17]} have also shown that local anesthesia is an independent factor associated with lower risk of in-hospital death or stroke, along with shorter clamp time and avoiding shunting.

On the other hand, several authors have focused on the cost-effectiveness of general versus regional anesthesia, suggesting that regional anesthesia for CEA has been associated with shorter anesthesia and operative time and shorter length of hospital stay.\textsuperscript{[18,19]}

### Does regional anesthesia remain “the gold standard” for monitoring cerebral function during carotid endarterectomy?

It has been suggested that performing CEA under regional rather than general anesthesia, may be safer, since the “awake” patient is the “gold standard” of cerebral function monitoring.

However, we must always keep in mind that some patients do not show immediate neurologic deterioration after cross-clamping, which necessitates the existence of a method of cerebral blood flow monitoring even in patients receiving regional anesthesia for CEA.\textsuperscript{[20]} Despite this, regional anesthesia remains a safe method for identifying patients at risk for cross-clamping intolerance.\textsuperscript{[21]}

### Apart from the traditional methods of monitoring cerebral function, is there a novel assay that could improve the outcome?

As already mentioned, CEA necessitates a period of carotid artery cross-clamping. If collateral blood flow through the circle of Willis is insufficient, cross-clamping may cause cerebral ischemia. In these patients, cerebral perfusion is maintained by the use of a surgically inserted shunt to bypass the isolated section of carotid artery. However, literature lacks large randomized controlled trials to support either routine or selective shunting.\textsuperscript{[22]} As avoiding cerebral ischemia is essential, various techniques have been implemented for monitoring cerebral perfusion including electroencephalography, internal carotid artery stump pressure, transcranial Doppler, and somatosensory-evoked potentials.

The potential reliability of cerebral oximetry, using a cutoff of 25% decrease or a cutoff of 20% decrease for >4 min, during CEA under general or under regional anesthesia in combination with “awake” testing, has recently evolved.
However, none of the methods of monitoring cerebral blood flow has been associated with better outcome.\textsuperscript{[23,24]}

**What are the limitations of cervical plexus blocks?**

Regional anesthesia for CEA is considered to be safe and associated with a low rate of conversion to general anesthesia.\textsuperscript{[25]} Possible concerns with regional techniques include remote access to the upper airway, stressful conversion of regional into general anesthesia when necessary, the need for patient cooperation, and the inadvertent subarachnoid or intravascular injection of local anesthetic [Table 2].\textsuperscript{[26]}

Superficial, intermediate, deep, or combined (superficial deep or superficial intermediate) CPBs have been performed in a large number of studies. Older studies advocate the landmark technique, while US guidance, permitting the direct visualization of nerves and other structures, has gained popularity in recent relevant clinical research. US-guided superficial CPB involves injection of local anesthetic just behind the posterior border of the sternocleidomastoid muscle. When performing an US-guided intermediate CPB, local anesthetic is injected at the investing fascia of the neck. Finally, US-guided deep CPB involves injection of local anesthetic under the deep cervical fascia, behind the carotid sheath at the level of carotid artery bifurcation or in close proximity of the posterior tubercle of C4 transverse process.\textsuperscript{[7,27]}

Regarding complications, superficial CPB is associated with the common adverse effects of any nerve block such as inadvertent intravascular injection of local anesthetic and local anesthetic toxicity. In addition to these effects, deep CPB increases the occurrence of complications arising from the placement of the block, including accidental intravascular injection into the vertebral artery, subdural injection resulting in subarachnoid block, large neck hematoma, bilateral recurrent laryngeal nerve palsy, and phrenic nerve palsy.\textsuperscript{[7,27,28]}

Superficial CPB provides a safe, efficient, and easy-to-perform technique, providing adequate surgical analgesia for CEA.\textsuperscript{[29,30]}

Evidence-supporting deep or combined deep CPB technique is controversial. “Deep technique” has been associated, as already mentioned, with higher rate of block-related complications and conversion to general anesthesia.\textsuperscript{[28]}

Evidence from studies using US-guided regional technique does not demonstrate significant differences. The safety and efficacy of US-guided superficial CPB is a mainstay.\textsuperscript{[31]} The same seems to apply to US-guided intermediate CPB.\textsuperscript{[31‑34]}

Sait Kavaklı et al.\textsuperscript{[35]} have also shown that combined cervical versus superficial CPB resulted in less intraoperative use of lidocaine by the surgeon, lower postoperative numerical rating scale values, and higher patient satisfaction.

A major concern is that CPB cannot obviate the possibility of inadequate analgesia, even under US guidance. As a result, it increases patient and surgeon’s discomfort and necessitates combining this method with local infiltration. The problem arises from the anatomical variability of neck structures and nerve and vascular structures. The cervical transverse nerves may cross the body midline and pass to the opposite side, leading to inadequate unilateral block.\textsuperscript{[36]} Another variation is the permanent anastomosis (ansa cervicalis) between the cervical plexus and the ramus colli of the facial nerve.\textsuperscript{[37]}

Hence, it is imperative to know the typical anatomy of each region and be aware of the variation that can occur.

In addition, another problem with respect to CPB is the high risk of unilateral palsy of the vagus nerve, causing hoarseness, difficulty swallowing, or even respiratory distress, which, in most cases, is not clinically significant.\textsuperscript{[36]}

**What is the “gold standard” for peripheral nerve blocks for carotid endarterectomy?**

“Right dose of the right drug placed in the right place” describes the “gold standard” in every peripheral nerve block technique.\textsuperscript{[38]} Ultrasoundography expands toward the gold standard, as it displays in real time the anatomical structures involved.\textsuperscript{[36]} Lidocaine, mepivacaine, bupivacaine, and ropivacaine are all suitable agents for superficial CPB.

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**Table 2: Regional technique for carotid endarterectomy**

| Block type               | Location of local anesthetic administration                              | Approach                  | Complications                                                   | Agents                  |
|--------------------------|------------------------------------------------------------------------|---------------------------|-----------------------------------------------------------------|-------------------------|
| Superficial cervical plexus block | Just posterior to the posterior border of sternocleidomastoid muscle | Classical (landmark) US guidance | Hematoma, Infection, Local anesthetic toxicity, Inadvertent intravascular injection | Lidocaine 1%, Bupivacaine 0.25-0.5%, Ropivacaine 0.25-0.5% |
| Intermediate cervical plexus block | Under the investing layer of the deep fascia of the neck | US guidance               | Accidental intravascular injection, Subdural injection-subarachnoid block, Large neck hematoma, | Ropivacaine 0.25-0.5% |
| Deep cervical plexus block | Under deep cervical fascia                                             |                           | Accidental intravascular injection, Subdural injection-subarachnoid block, | Ropivacaine 0.25-0.5% |

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for CEA. Epinephrine (1:300,000) can be added to local anesthetic solution without any adverse hemodynamic effect.[29] Ropivacaine 0.375% and ropivacaine 0.75% provide similar analgesia, but the former has been associated with lower plasma concentrations.[32]

Are there any other anesthetic modalities for carotid endarterectomy?
The combination of general anesthesia with superficial CPB is an alternative choice that reduces the postoperative analgesic requirements.[39] Better hemodynamics and better postoperative outcome with the combined technique have been reported.[39]

In addition, local infiltration remains an anesthetic option for carotid endarterectomy. However, a sole local infiltration technique has been associated with larger volumes of local anesthetic solution and patient discomfort when compared to CPB.[30] Moreover, Seidel et al. showed that perivascular local anesthetic infiltration in combination with US intermediate CPB confers no benefit and may increase the rate of complications.[40]

Apart of general, regional, or combined general and regional anesthesia for CEA, a fourth option also exists. “General anesthesia with cooperative patient” associated with high patient satisfaction is an anesthetic modality in which anesthesia is induced and maintained with propofol and remifentanil. Immediately before clamping, the doses of drugs are reduced until the patient is awake and able to “cooperate,” thus to obey to verbal commands. This method resembles the “wake-up” test performed during neurosurgical procedures.[41-43]

Who decides what anesthetic modality will be implemented?
No one doubts the value of preoperative consultation, which should aim at identifying the patient who would be unable to tolerate the procedure with the face and the neck covered by surgical drapes. The patient, the surgeon, and the anesthetist should jointly decide what anesthetic technique to follow. The anesthetic plan should be individualized according to concomitant pathology, expected intraoperative technical difficulties and patient’s wish after informed consent is obtained.[8,10,44] At the bottom line, the choice of anesthesia is determined in consultation with the vascular surgeon, taking into account patient’s characteristics.

Conclusion
Regional anesthesia for CEA is still receiving much attention and credit in daily practice and literature reports. It may offer several advantages, but a number of concerns have to be taken into consideration. Evidence-based medicine has its own limitations, and medical questions that cannot be answered by randomized controlled trials do exist.[45]

Optimal planning with surgeon and the patient is of crucial importance. Not all patients and interventions are suitable for a pure regional anesthetic technique. However, locoregional anesthesia should always be an option for the anesthetist for CEA.

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Conflicts of interest
There are no conflicts of interest.

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