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## *Μεταπτυχιακή Διπλωματική Εργασία*

*"Completion imaging after carotid endarterectomy; a  
systematic review of the literature"*

υπό

**ΚΩΝΣΤΑΝΤΙΝΟΥ ΣΠΑΝΟΥ**

Αγγειοχειρουργού

Υπεβλήθη για την εκπλήρωση μέρους των  
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## Abstract

Completion imaging has been suggested in order to assess the quality of the outcome in terms of technical success in carotid endarterectomy. This allows for the on-table correction of any defect and subsequently may improve the clinical outcome. The aim of this study was to present existing evidence of different completion imaging techniques after carotid endarterectomy and their role on clinical outcome. A systematic review of the literature was undertaken (Preferred Reporting Items for Systematic reviews and Meta-Analyses) searching in MEDLINE, CENTRAL, and Cochrane databases including studies reporting on completion imaging techniques after carotid endarterectomy. A total of 12,378 patients (in 35 studies; 20 retrospective and 15 prospective) underwent a completion imaging technique (n=13,307) after carotid endarterectomy; arteriography in 19 studies with 5,340 patients, angioscopy in 5 studies with 2,095 patients, DUS in 21 studies with 5,722 patients and TCD in 2 studies with 150 patients. Ten studies assessed > 1 imaging technique. The mean age was 67±7 years old (69% males) with the most common comorbidities to be hypertension in 74%, smoking in 64% and hyperlipidemia in 54% of the patients. Almost half of the patients (4949; 44%) were treated for symptomatic disease. In 1,104 (9.7%) patients a major defect or pathological finding was identified intra-operatively, while in 329 (2.9%) a minor defect. Common pathological findings were the presence of mural thrombus, carotid dissection, residual stenosis and intimal flaps. An immediate re-intervention was undertaken in 75% (790/1053) of the patients to treat a major defect. In patients with re-intervention, only 2.3% (14/609) had an intra-operative stroke and 0.8% (5/609) a transient ischemic attack (TIA), while only 1.4% (8/575) had a stroke and 0.2% a TIA (1/575) during 30-day post-operative period. No intra-operatively death was reported. During the first post-operative 30-

days, the restenosis rate of internal carotid was 0.5% (3/575) and of common carotid artery 0.2% (1/575). Completion imaging techniques can detect defects that may lead to immediate intra-operative surgical revision in almost 10% of patients with low intra-operative stroke/TIA rate, and low early carotid restenosis. During the 30-day follow up period, in those patients the incidence of stroke/TIA may be low but present. This review cannot prove whether completion imaging techniques improve outcomes because of the absence of a randomized control study.

## **Chapter 1**

### **1. Introduction**

#### **1.1 Atheromatosis**

Atheromatosis is a disease that allocated in arterial tree, the so called ‘Atherosclerotic cardiovascular disease (CVD)’ which remains the most important reason for premature death worldwide.<sup>1</sup> In fact, CVD is responsible for the death of 17.5 million people in 2012, which translates into 3 in every 10 deaths. Of these, almost half died from stroke.<sup>2</sup> A recent study, the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD 2010) reported that stroke was the second cause of death and the third one of disability-adjusted life-years (DALYs) worldwide in 2010.<sup>3</sup>

#### **1.2 Definition of stroke**

As it was highlighted, one of the clinical presentations of atheromatosis is stroke. The recent definition of stroke from American Heart Association is defined as an episode of neurologic dysfunction caused by focal cerebral or retinal infarction, where infarction is defined as brain or retinal cell death, attributable to ischemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury.<sup>4</sup> They have also suggested the definition of transient ischemic attack (TIA) as a brief episode of neurological dysfunction as a result of a focal temporary cerebral ischemia which is not associated to acute infraction.<sup>4</sup>

The etiology of stroke can be classified to the events deriving from carotid artery disease (internal carotid artery; ICA) (25%), the small intracranial arteries (25%), cardiac embolism (20%), or other rarer causes (5%), and of course in a 25% of

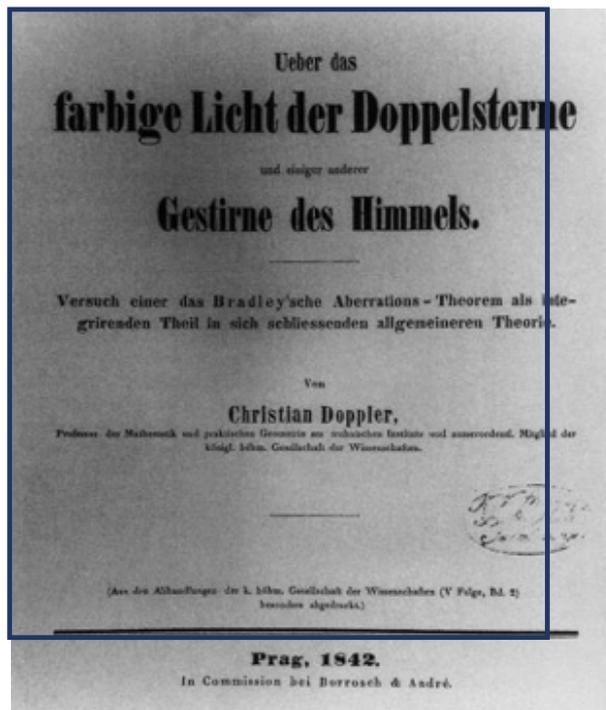


closure , showed superiority of patch technique in terms of decreasing the risk of early and late cerebrovascular event. The risk of carotid artery thrombosis was also decreased along with the restenosis rate in patients treated with patch closure.<sup>9</sup> Another study comparing all three types of carotid endarterectomy (patch, primary closure and eversion CEA), showed that the early rate of cerebrovascular events was 0.8% after eversion CEA, 1.0% after primary closure, and 2.8% after CEA-patch without any significant differences. However, the restenosis rate was lower in eversion technique.<sup>10</sup> However, specific factors have not been identified that give an explanation why one technique might be better than the other.

## **1.4 Diagnosis**

### **1.4.1 Colored Duplex scan**

Colored duplex scan has been broadly used in the diagnosis algorithm of ACS. The history of this techniques goes back to 1843, when Christian Doppler published his work on the so called ‘Doppler effect’ or Doppler phenomenon which was defined as ‘the observed changes in the frequency of transmitted waves when relative motion exists between the source of the wave and observer’.<sup>11</sup>



However, only in 50s' a physician from Osaka, Satomura developed the first doppler ultrasound device.<sup>11</sup> Already, in 1976 the directional Doppler cerebrovascular examinations was considered as an adjunctive method of preselection of candidates for diagnostic arteriography.<sup>12</sup> In 1983 a Japanese group first reported the use of a colored model. Since then, many novelties have followed the colored duplex devices in order to produce accurate results.<sup>12</sup> In a recent systematic review of the literature and meta-analysis the sensitivity and specificity for the diagnosis of angiographic stenosis of >70%, was 90% and 94%, respectively.<sup>13</sup>

Thus, ESVS guidelines recommend the Duplex ultrasound as a first-line examination (class I, level A). In particular, when a patient is a candidate for CEA, it is recommended that the use of Duplex scan for the measurement of the stenosis may be enhanced by computed tomographic angiography (CTA) or magnetic resonance angiography (MRA), or by a second Duplex scan from another physician (class I, level A).<sup>7</sup>

Duplex ultrasound (DUS) has a low cost and good accessibility. Duplex scan criteria for assessing the degree of the stenosis includes peak systolic velocity (PSV), end-diastolic velocity (EDV) and their ratios in the ICA and common carotid artery (CCA). Additionally, since late 80s' colored duplex scan started to be used intra-operatively as a completion imaging method.<sup>14</sup>

#### **1.4.2 Digital subtractive angiography (DSA); 'angiogram'**

Ninety-two years ago, Dr. Egas Moniz was the pioneer who first introduced the cerebral angiography. This imaging examination, the so called 'angiogram' was the gold standard for many years for the diagnosis of cerebral arteries pathology, extra-cranially and intra-cranially. He has received three nominations for the Nobel Prize for the discovery of cerebral angiography, however he had not acquired it for that reason.<sup>15</sup>

Many studies followed giving prominence to the important diagnostic role of DSA in carotid disease. In 1984 Foley, et al.<sup>16</sup> reported one of the first studies in which they performed a selective carotid arteriography in patients prior to carotid surgery, and they suggested that intravenous DSA is a valuable screening test and can be used to device for the treatment of most patients with symptomatic carotid disease.

The two most known randomized control trials on carotids of the previous century are The European Carotid Surgery Trial (ECST)<sup>17</sup> and the North American Symptomatic Carotid Endarterectomy Trial (NASCET).<sup>18</sup> Although they reported different methods for measuring the severity of the stenosis, both were randomizing patients who had to undergo an intra-arterial angiography. In both methods you have to estimate the percentage of the stenosis having as a numerator the minimum luminal

diameter of the ICA, but as a denominator in ECST (European Carotid Surgery Trial) the estimated artery diameter in the level of the carotid bulb was used, and in NASCET the diameter of the distal from the stenosis segment of ICA which was normal was used. Thus, there were cases that the ECST type of measuring was overestimating the degree of the stenosis in comparison to NASCET. Even today, this type of measuring especially the NASCET way has some application in daily practice. Since then for many years, diagnosis on asymptomatic and symptomatic disease was based on digital subtractive angiography.

However, in another RCT; the Asymptomatic Carotid Atherosclerosis Study (ACAS),<sup>19</sup> that patients underwent DSA, the rate of intra-procedural events were high, thus 1.2% of the strokes were angiographic related. After that, the DSA as a diagnostic mean has been abandoned and duplex ultrasound, along with CTA and MRA has taken over.<sup>19</sup> In the recent ESVS guidelines, it is in the recommendations that DSA should not be a diagnostic tool in patients being considered for revascularization, unless there are significant discrepancies on non-invasive imaging (Class III, Level A).<sup>7</sup>

### **1.4.3 Angioscopy**

Angioscopy is a catheter-based technologies aimed at identifying arterial wall. Since early 40s' the angioscopy was developed as device, but it was tested mainly in animals and human cadavers. The first vascular endoscopy was performed by Vollmar and Storz in 1968, using a rigid endoscope in order to assess the outcome of a semi-closed loop endarterectomy.<sup>20</sup> Since then Angioscopy, has been used mainly in coronary artery disease diagnosis and intervention.<sup>21</sup>

#### **1.4.4 Transcranial Doppler**

Rune Aaslid, in 1982, introduced the TCD for detecting blood flow in the basal intracerebral arteries.<sup>22</sup> In the anatomy of the human skull, there are areas in which are relatively less thick and offer sufficient imaging- acoustic window. The 4 commonly available acoustic windows in adults are - temporal, orbital, suboccipital, and submandibular. Through the transtemporal window, the flow velocities in middle cerebral artery, anterior cerebral artery (ACA), posterior cerebral artery (PCA), and posterior communicating artery PCOM can be obtained. The ophthalmic artery (OA) and ICA siphons are insonated through the transorbital window.<sup>23</sup> Intraoperative TCD monitoring has been used for assessing the results of carotid endarterectomy.<sup>24</sup>

#### **1.5 Peri-operative cerebrovascular events of carotid endarterectomy**

The main reason for CEA is the prevention of a cerebrovascular event due to carotid artery stenosis. Thus, the peri-operative event rate of CEA should also be low, especially in asymptomatic patients. Recently in a study from Vascular Quality Initiative, including >30,000 patients treated for asymptomatic carotid artery stenosis, the peri-operative stroke rate was <1%.<sup>25</sup> In other real world experience studies, the peri-operative stroke rate was also ranging from 0.9% to 1.1% including >2000 patients that underwent CEA.<sup>26,27</sup> However, in symptomatic patients the risk of a peri-operative stroke has been higher ranging from 3.2% to 6.2% in RCTs.<sup>28-31</sup> Taking into account the event rates, many have suggested that there is no need for further

assessment of the CEA technique, especially during the completion of the operation, thus, the role of completion imaging techniques is still debatable.

## **1.6 Imaging techniques for the assessment of carotid endarterectomy**

Completion imaging after carotid endarterectomy has been applied for the last 40 years. Although, many studies have been published on the role of completion imaging techniques, this adjunctive procedure has not been broadly used world widely. In particular, there is no any strong recommendation on the role and clinical importance of completion imaging techniques. The ESVS guidelines<sup>7</sup> suggested that ‘targeted monitoring and quality control strategies may be considered to reduce the risk of perioperative stroke.’ This is the confirmation that completion imaging after carotid endarterectomy has found a spot in carotid disease treatment. It is apparent that the use of loco-regional anesthesia in carotid endarterectomy will protect patients from strokes due to hemodynamic issue during the clamping time of carotids, but will not prevent adverse events because of the distal embolization of retained thrombus or the presence of a flap. This would mandate the intra-operative assessment of the outcome such as angiography, DUS, angioscopy or TCD.

Intra-operative duplex scanning may be undertaken either with a classic transducer for the carotids ranging from 7.5MHz to 10MHz<sup>14,32,33</sup> or with a specific probe like a ‘hockey stick’ which is an intra-operative transducer of either 5MHz or 7MHz.<sup>34</sup> The examination can be performed with ultrasonic gel being applied and covered by a plastic sleeve. Following endarterectomy and restoration of blood flow, saline solution was used to fill the wound to assure acoustic coupling. The transducer was kept close to the exposed artery but not directly on it. In case of the ‘hockey

stick' transducer, it can be positioned directly on the artery. Any irregularities of the vessel wall, such as intimal ridges, flaps, as well as kinking and diameter changes can be measured and recorded. After arterial imaging, power and pulsed Doppler flow velocity patterns were routinely recorded from the CCA, ICA and the ECA. The pulsed wave Doppler sample volume can be positioned mid-stream of the flow and the Doppler beam angle was kept at 60 ° to the vessel axis. The parameters that are being evaluated are peak systolic velocity (PSV), end diastolic velocity (EDV) and degree of spectral broadening.<sup>35,36</sup> The measurements can be repeated after approximately 15 to 20 minutes in cases that there is evidence on a potential defect. Generally, PSV >120-150 are considered suspicious for a presence of a stenosis, while presence of a flap >2-3mm is also considered pathological defect.

De Backey who is considered to be the first one ever performing a carotid endarterectomy, in his letter describing the steps of the procedure, in the end he is reporting that he performed an 'arteriogram' to evaluate the result of the procedure, thus the first completion imaging took place in the first ever endarterectomy.<sup>12</sup> Since then, many studies have highlighted the use of intra-operative DSA at the end of endarterectomy for the assessment of the outcome of the operation. There is no specific protocol for the intra-operative DSA; and in most studies, after the completion of the CEA, a direct puncture of the proximal part of the CCA is undertaken with a needle (19-23 gauge) and the insertion of contrast.<sup>37-40</sup> Commonly in asymptomatic patients underwent biplanar (anteroposterior and 30-degree lateral position) extracranial reconstruction is being undertaken, while symptomatic also received a biplanar intracranial angiography. The pathological findings are based on morphological defects and the percentage of a stenosis.

Angioscopy has been also applied in completion imaging of carotid endarterectomy having a lot of advantages such as the detection of thrombus, plaque disruption or restenosis, while giving the opportunity to the Vascular Surgeon to treat any complication.<sup>41</sup> The lumen of the CEA area can be investigated with a flexible hysteroscope which is inserted through the remaining, unsutured, gap between patch and arterial wall into the artery. The distal endarterectomy site can be visualized first, followed by the midpoint and finally the proximal endarterectomy site and common carotid artery. Generally, all intimal flaps >3 mm should be repaired and in case of thrombus presentation, this should be aspirated (in any size) from the lumen. After the angioscopy, the patch or the arteriotomy is concluded and the flow is restored first up the ECA (with a temporal occlusion of the proximal part of the ICA) and then up the ICA.<sup>24,41,42</sup>

The use of TCD does not represent an actual mean of completion imaging assessment technique after CEA, however, it can be used simultaneously with the other techniques for better outcome evaluation. Normally, the ipsilateral MCA is insonated through the transtemporal window and the transducer is positioned in place, monitoring the flow of the artery from the beginning of the anesthesia to 30 minutes after the declamping of the carotid artery.<sup>24</sup> Many physicians are basing their decision on the shunt use on the arterial flow decrease during the procedure in the TCD. Additionally, some indirect findings might raise the suspicion of a stenosis in the CEA area after the completion of a CEA: a waveform with a delayed systolic flow acceleration, flattened systolic upstroke, and slow diastolic deceleration with the end diastolic velocity being >50% of the PSV. Recently, Zhao et al.<sup>43</sup> suggested criteria

for the use of TCD for intracranial stenosis  $\geq 70\%$  assessment by defining stenotic / pre-stenotic ratio  $\geq 3$  on TCD that improved sensitivity and showed good agreement with invasive angiography.

## **Chapter 2**

### **2.1 Aim**

Completion imaging has been suggested in order to assess the quality of the outcome in terms of technical success in carotid endarterectomy, thus you can immediately repair any lesion derived from the operation and subsequently improve the clinical outcome. The aim of this study was to present existing evidence of different completion imaging techniques after carotid endarterectomy and their role on clinical outcome.

### **2.2 Methods**

#### **2.2.1 Search strategy**

We searched the literature electronically including the databases MEDLINE (database provider PubMed), EMBASE (database provider Ovid), and Cochrane Central Register of Controlled Trials from 1980-2019. The P.I.C.O. (patient; intervention; comparison; outcome) model (Table 1) was used to define the clinical questions and find the clinically relevant evidence in the literature.<sup>44</sup> In order to isolate associated studies, the following search terms were combined: in the Expanded Medical Subject Headings (MeSH) and key word searches for “completion imaging”

and “carotid endarterectomy” or “ Intraoperative Completion Studies” and “carotid endarterectomy” or “ Intra-operative Duplex” or ‘intra-operative angiogram’ or intraoperative angioscopy’. We have primarily selected all the associated studies basing on the title and abstract, whereas a secondary selection was undertaken taking into account the full text of publications. A manual screening of the reference lists of selected articles identified through the electronic search was also undertaken.

|   |  |   |
|---|--|---|
| P | Patient, Population, or Problem              | Patients with carotid disease   |
| I | Intervention, Prognostic Factor, or Exposure | Completion imaging after carotid endarterectomy   |
| C | Comparison or Intervention (if appropriate)  | Among the imaging techniques when available   |
| O | Outcome you would like to measure or achieve | Minor and major findings from the completion imaging technique, the clinical presentation and the re-intervention. During follow up, the clinical events were also assessed as a secondary outcome. |
|   | What type of question are you asking?        | Is completion imaging after carotid endarterectomy a safe procedure? Does this allow the correction of the defect?  |
|   | Type of study you want to find               | Any study reporting on a completion imaging technique after carotid endarterectomy treatment  |

**Table 1.** P.I.C.O. model.

### **2.2.2 Study selection**

All included articles was in English. The major eligibility criterion was to report on a completion imaging techniques after carotid endarterectomy treatment. Articles were excluded if they had <30 patients or if they did not describe their imaging technique.

Two authors (K.S. and P.N.) have independently evaluated all articles of the initial search strategy and any differences were resolved by a senior physician (A.G.). Selected abstracts were subsequently reviewed to see if they meet the eligibility criteria. To avoid the inclusion of duplicate publications of the same data, the data were examined for similarities (e.g. identical start and end dates), and if necessary, the authors were contacted for clarification.

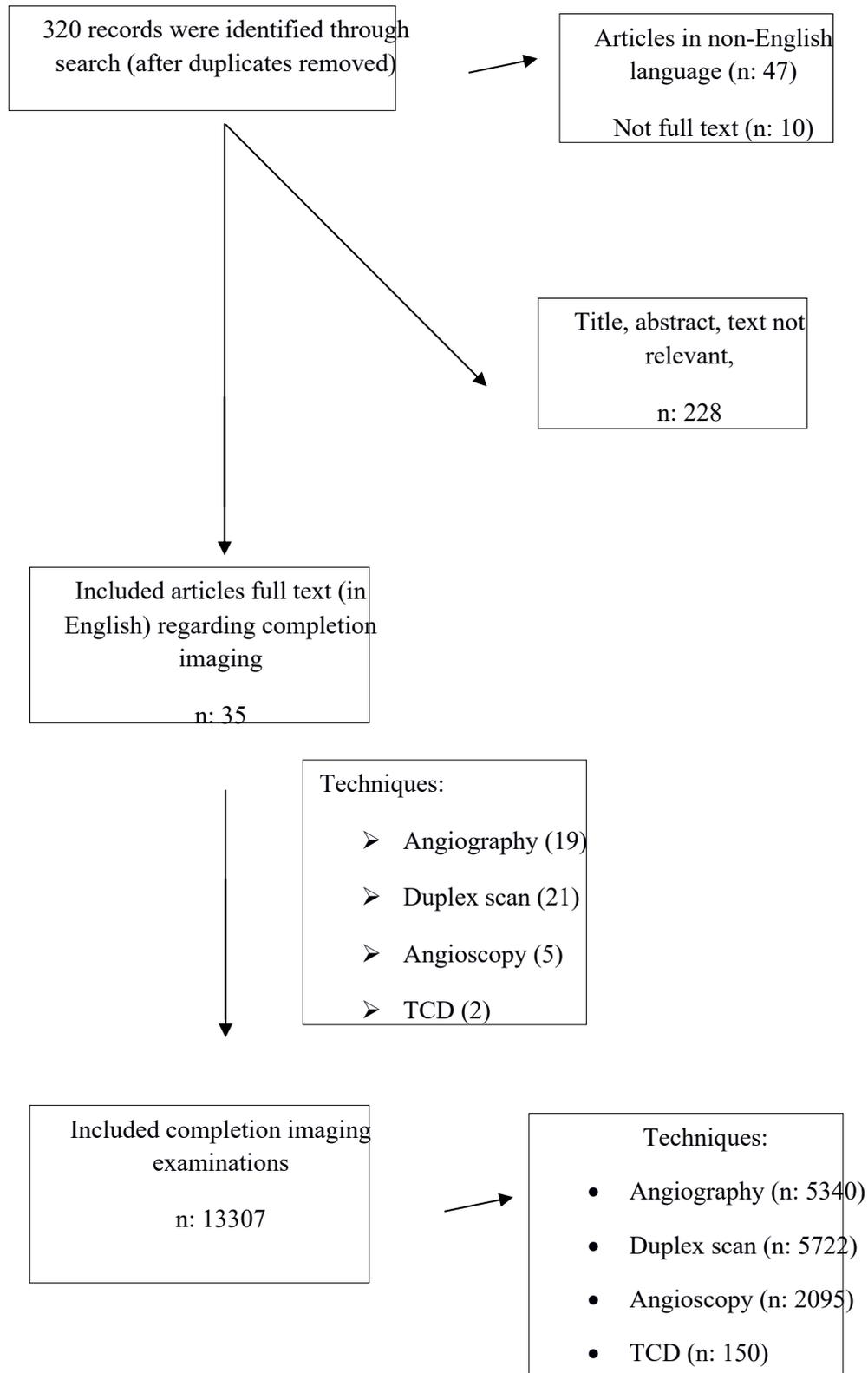
### **2.2.3 Extraction of data**

All data were extracted from the text and tables; any missing data were not available from the corresponding authors. An Excel file was used in order to fill all the details. Data included the characteristics of the studies such as journal type, date of publication, study design, country origin of the center, corresponding authors, period of the study and the treatment endograft details. Additionally, demographics (age, sex), and the comorbidities of each patient such as hypertension (HT), smoking, diabetes mellitus (DM), coronary artery disease (CAD), chronic renal insufficiency, chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), peripheral arterial disease (PAD) were also recorded. The clinical presentation either symptomatic (stroke, TIA, amaurosis fugax) or asymptomatic, type of anesthesia and

the use of shunt were also recorded. The protocol of each completion imaging technique was also assessed.

Primary outcome was defined as the minor and major findings from the completion imaging technique, their clinical presentation and the re-intervention that was mandatory in order to treat those lesions. During follow up, the clinical events were also assessed as a secondary outcome.

The systematic review protocol, the selection process, and reporting were based on the 2009 PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement<sup>45</sup> (Figure 1).



**Figure 1.** PRISMA reporting system.

#### **2.2.4 Statistical analysis**

Only data that are descriptive were presented because this systematic review does not aim to the comparison of any techniques and most studies were case series.

### **Chapter 3**

#### **3.1 Results**

A total of 12378 patients (in 35 studies; 20 retrospective and 15 prospective) underwent a completion imaging technique (n=13307) after carotid endarterectomy; in 19 studies 5340 patients underwent arteriography, in 5 studies 2095 angioscopy, in 21 studies 5722 DUS and in 2 studies 150 patients underwent TCD. Ten studies assessed > 1 imaging technique. (Table 2)

| Author                            | Journal                                    | Date | Study                         | Patients | Methods  |
|-----------------------------------|--|------|-------------------------------|----------|--|
| Wieker et al. <sup>37</sup>       | JVS  | 2018 | Retrospective                 | 770      | Arteriography  |
| Yuan et al. <sup>46</sup>         | World of Neurosurgery                      | 2014 | Retrospective                 | 225      | Duplex scan  |
| Lanceveve et al. <sup>38</sup>    | Ann Vasc Surg                              | 2013 | Retrospective                 | 179      | Arteriography  |
| Sharpe et al. <sup>41</sup>       | EJVES                                      | 2012 | Retrospective                 | 1600     | Angioscopy in 1483                                       |
| Wallaert et al. <sup>32</sup>     | JVS  | 2011 | Retrospective                 | 2033     | DUS imaging in 1919, arteriography in 94, and both in 20 |
| Ricco et al. <sup>47</sup>        | EJVES                                      | 2011 | Prospective                   | 1055     | Arteriography  |
| Schanzer et al. <sup>33</sup>     | Vascular and Endovascular Surgery          | 2007 | Retrospective                 | 399      | Duplex scan  |
| Pratesi et al. <sup>48</sup>      | EJVES                                      | 2006 | Prospective                   | 430      | Arteriography  |
| Ascher et al. <sup>34</sup>       | J Vasc Surg                                | 2004 | Retrospective                 | 590      | Duplex scan  |
| Mullenix et al. <sup>49</sup>     | American Journal of Surgery                | 2003 | Prospective                   | 100      | Duplex scan  |
| Valenti et al. <sup>50</sup>      | Cardiovascular Surgery,                    | 2003 | Retrospective                 | 138      | Duplex scan and Arteriography                            |
| Woelfle et al. <sup>51</sup>      | CARDIOVASCULAR SURGERY                     | 2002 | Prospective                   | 111      | Arteriography  |
| Pross et al. <sup>39</sup>        | JVS  | 2001 | retrospective                 | 338      | 333 Arteriography, 26 duplex scans, and 21 both          |
| Osman et al. <sup>52</sup>        | Annals of Royal College of Surgeon England | 2001 | Retrospective                 | 110      | Angioscopy   |
| May et al. <sup>53</sup>          | Archives of Surgery                        | 2000 | Prospective                   | 96       | Duplex scan  |
| Mansour et al. <sup>54</sup>      | JVS  | 1999 | Retrospective                 | 560      | Duplex scan  |
| Seelig et al. <sup>55</sup>       | Mayo Clin Proceedings                      | 1999 | Retrospective                 | 102      | Duplex scan  |
| Zannetti et al. <sup>42</sup>     | EJVES                                      | 1999 | prospective multicentre study | 1303     | Arteriography in 1004; angioscopy in 299; 2 duplex scan  |
| Steinmetz et al. <sup>56</sup>    | EJVES                                      | 1998 | Prospective                   | 100      | Duplex scan  |
| Westerband et al. <sup>57</sup>   | Ann Vasc Surg                              | 1997 | Retrospective                 | 138      | Arteriography  |
| Walker et al. <sup>36</sup>       | EJVES                                      | 1996 | Prospective                   | 50       | Duplex scan and transcranial Doppler (TCD)               |
| Papanicolaou et al. <sup>58</sup> | JVS  | 1996 | Prospective                   | 78       | Duplex scan + 26 duplex scan with Arteriography          |
| Gaunt et al. <sup>24</sup>        | EJVES                                      | 1996 | Prospective                   | 100      | TCD and angioscopy and duplex scan                       |
| Lohr et al. <sup>59</sup>         | CARDIOVASCULAR SURGERY                     | 1995 | Retrospective                 | 168      | Arteriography  |
| Lingenfelter et al. <sup>60</sup> | Ann Vasc Surg                              | 1995 | Prospective                   | 50       | Duplex scan and Arteriography                            |
| Branchereau et al. <sup>61</sup>  | Ann Vasc Surg                              | 1995 | Prospective                   | 96       | Angioscopy   |

|                                       |                   |           |               |       |  |
|---------------------------------------|-------------------|-----------|---------------|-------|--|
| <b>Hoff et al.<sup>35</sup></b>       | EJVES             | 1994      | Prospective   | 44    | Duplex scan and Arteriography  |
| <b>Baker et al.<sup>62</sup></b>      | JVS               | 1994      | Retrospective | 283   | Duplex scan  |
| <b>Kinney et al.<sup>63</sup></b>     | JVS               | 1993      | Prospective   | 430   | Duplex scan (142), duplex scan and arteriography (268), or clinical inspection (51)  |
| <b>Donaldson et al.<sup>64</sup></b>  | ANNALS OF SURGERY | 1992      | Retrospective | 410   | Arteriography  |
| <b>Sawchuk et al.<sup>65</sup></b>    | JVS               | 1989      | Retrospective | 80    | Duplex scan  |
| <b>Bredenberg et al.<sup>66</sup></b> | JVS               | 1989      | Retrospective | 50    | Arteriography  |
| <b>Schwartz<sup>14</sup></b>          | JVS               | 1988      | Prospective   | 76    | Duplex scan  |
| <b>Alpert et al.<sup>40</sup></b>     | JVS               | 1984      | Retrospective | 40    | Arteriography  |
| <b>Holder et al.<sup>67</sup></b>     | AJNR              | 1981      | Retrospective | 55    | Arteriography  |
| <b>Total</b>                          |                   | 1981-2018 |               | 12387 | 19 studies, 5340 patients with arteriography; 5 studies, 2095 with angioscopy; 21 studies, 5722 with DUS and in 2 studies 150 with TCD |

**Table 2.** Details of the included studies. (JVS: Journal of Vascular Surgery; Ann Vasc Surg: Annals of Vascular Surgery; EJVES: European Journal of Vascular and Endovascular Surgery; AJNR: American Journal of Neuroradiology)

The mean age was  $67 \pm 7$  years old (69% males) with the most common comorbidities to be hypertension in 74%, smoking in 64% and hyperlipidemia in 54% of the patients. (Table 3).

| Author                            | Age  | Gender | Smoking | HT   | HL  | CAD | COPD | DM  | CRD | PAD |
|-----------------------------------|------|--------|---------|------|-----|-----|------|-----|-----|-----|
| Wieker et al. <sup>37</sup>       | 70.6 | 602    | 425     | 748  | 699 | 464 | Na   | 278 | 77  | 165 |
| Yuan et al. <sup>46</sup>         | -    | -      | -       | -    | -   | -   | -    | -   | -   | -   |
| Lancelevec et al. <sup>38</sup>   | 72   | 160    | -       | 80   | 79  | 38  | Na   | 34  | 46  | -   |
| Sharpe et al. <sup>41</sup>       | -    | 1107   | -       | -    | -   | -   | -    | -   | -   | -   |
| Wallaert et al. <sup>32</sup>     | -    | 1254   | 1618    | 1807 | -   | 683 | -    | 598 | 103 | -   |
| Ricco et al. <sup>47</sup>        | -    | 728    | 696     | 685  | -   | 221 | -    | 232 | 57  | 295 |
| Schanzer et al. <sup>33</sup>     | 70   | 309    | -       | 149  | 136 | -   | -    | -   | -   | -   |
| Pratesi et al. <sup>48</sup>      | 70.5 | 300    | 285     | 290  | 195 | 97  | -    | 106 | -   | -   |
| Ascher et al. <sup>34</sup>       | -    | 355    | -       | -    | -   | -   | -    | -   | -   | -   |
| Mullenix et al. <sup>49</sup>     | 70   | -      | 77      | 86   | 69  | 62  | -    | 27  | -   | 53  |
| Valenti et al. <sup>50</sup>      | 69   | 107    | -       | -    | -   | -   | -    | -   | -   | -   |
| Woelfle et al. <sup>51</sup>      | 70.1 | 81     | 25      | 82   | 64  | -   | 13   | 26  | -   | -   |
| Pross et al. <sup>39</sup>        | 70.4 | 240    | -       | -    | -   | -   | -    | -   | -   | -   |
| Osman et al. <sup>52</sup>        | -    | -      | 81      | 21   | 41  | 47  | -    | 14  | 6   | 27  |
| May et al. <sup>53</sup>          | -    | 60     | -       | -    | -   | -   | -    | -   | -   | -   |
| Mansour et al. <sup>54</sup>      | 69   | 72     | 43      | 71   | 15  | 63  | -    | 26  | Na  | 17  |
| Seelig et al. <sup>55</sup>       | -    | 325    | -       | -    | -   | -   | -    | -   | -   | -   |
| Zannetti et al. <sup>42</sup>     | 72.4 | 65     | 67      | 77   | 59  | -   | -    | 28  | -   | -   |
| Steinmetz et al. <sup>56</sup>    | 69.3 | 961    | 691     | 910  | 665 | 381 | -    | 242 | -   | 414 |
| Westerband et al. <sup>57</sup>   | 68   | 109    | 72      | 83   | -   | 75  | -    | 27  | 7   | 69  |
| Walker et al. <sup>36</sup>       | 69   | 39     | 15      | 24   | -   | -   | -    | 15  | -   | -   |
| Papanicolaou et al. <sup>58</sup> | 65   | 43     | 56      | 64   | 29  | -   | -    | 37  | -   | -   |
| Gaunt et al. <sup>24</sup>        | -    | -      | -       | -    | -   | -   | -    | -   | -   | -   |
| Lohr et al. <sup>59</sup>         | 68.9 | 89     | 79      | 115  | 68  | -   | -    | 39  | -   | -   |
| Lingenfelter et al. <sup>60</sup> | -    | 30     | 34      | 37   | 26  | -   | -    | 13  | -   | -   |
| Branchereau et al. <sup>61</sup>  | 69.3 | 82     | 69      | 58   | 31  | -   | -    | 20  | -   | -   |
| Hoff et al. <sup>35</sup>         | 64   | 30     | 19      | 21   | -   | 20  | -    | 5   | -   | -   |
| Baker et al. <sup>62</sup>        | 66   | 212    | Na      | Na   | -   | Na  | -    | -   | -   | -   |
| Kinney et al. <sup>63</sup>       | 64.7 | 387    | 254     | 414  | -   | 271 | 125  | 47  | 56  | -   |
| Donaldson et al. <sup>64</sup>    | 67   | 254    | 188     | 238  | -   | 184 | 50   | 72  | 14  | -   |
| Sawchuk et al. <sup>65</sup>      | -    | -      | -       | -    | -   | -   | -    | -   | -   | -   |
| Bredenberg et al. <sup>66</sup>   | -    | -      | -       | -    | -   | -   | -    | -   | -   | -   |

|                             |      |           |     |     |     |     |     |     |    |     |
|-----------------------------|------|-----------|-----|-----|-----|-----|-----|-----|----|-----|
| Schwartz <sup>14</sup>      | 64   | -         | -   | -   | -   | -   | -   | -   | -  | -   |
| Alpert et al. <sup>40</sup> | Na   | -         | -   | -   | -   | -   | -   | -   | -  | -   |
| Holder et al. <sup>67</sup> | 60.5 | 55        | Na  | Na  | 2   | Na  | Na  | 2   | Na | Na  |
| <b>Total</b>                | 67±7 | 69% males | 64% | 74% | 54% | 37% | 20% | 24% | 7% | 29% |

**Table 3.** Demographics and co-morbidities of the patients.

Almost half of the patients (4949; 44%) were treated for symptomatic disease.

In Table 4, the type of carotid endarterectomy is described. Most of the patients were treated under general anesthesia (64%; 4309/6724). Shunt was used in 37% (2627/7057).

| Author                        | Surgery   | TIA | Stroke | Amaurosis fugax | Asymptomatic | Anesthesia                | Shunt |
|-------------------------------|---|-----|--------|-----------------|--------------|---------------------------|-------|
| Wicker et al. <sup>37</sup>   | 426 patch, 393 eversion, and 8 other                  | 126 | 201    | -               | 473          | GA 139; 688 locoregional  | -     |
| Yuan et al. <sup>46</sup>     | -   | -   | -      | -               | -            | GA                        | -     |
| Lancevee et al. <sup>38</sup> | Patch   | 12  | 16     | 5               | 67           | -                         | -     |
| Sharpe et al. <sup>41</sup>   | -   | 960 | 396    | -               | 232          | -                         | -     |
| Wallaert et al. <sup>32</sup> | 1641 patch; 334 eversion; 58 primary                  | -   | -      | -               | 1704         | 1861 GA; 883 locoregional | 1175  |
| Ricco et al. <sup>47</sup>    | 1107 patch; 11 primary; 61 eversion                   | 318 | 185    | -               | 552          | -                         | 283   |
| Schanzer et al. <sup>33</sup> | Patch   | -   | -      | -               | -            | -                         | 60    |
| Pratesi et al. <sup>48</sup>  | 312 patch   | -   | -      | -               | 276          | -                         | 44    |
| Ascher et al. <sup>34</sup>   | 644 patch   | -   | -      | -               | 464          | GA                        | -     |
| Mullenix et al. <sup>49</sup> | -   | 14  | 11     | 13              | 62           | -                         | -     |
| Valenti et al. <sup>50</sup>  | Primary in 80 cases, an eversion in 53 and patch in 8 | -   | -      | -               | 41           | GA                        | -     |
| Woelfle et al. <sup>51</sup>  | -   | 47  | 16     | -               | 52           | -                         | -     |
| Pross et al. <sup>39</sup>    | Primary in 63 cases. Patch in 317 cases,              | 54  | 50     | 94              | 180          | GA 377; 3 local           | 127   |
| Osman et al. <sup>52</sup>    | 56 eversion, 54 primary                               | 15  | 26     | 10              | 28           | -                         | -     |
| May et al. <sup>53</sup>      | 70 patch  | -   | -      | -               | -            | -                         | 86    |
| Mansour et                    | -   | 23  | 30     | 18              | 29           | -                         | -     |

|                                   |   |      |     |    |      |                    |                 |
|-----------------------------------|---|------|-----|----|------|--------------------|-----------------|
| al. <sup>54</sup>                 |   |      |     |    |      |                    |                 |
| Seelig et al. <sup>55</sup>       | -                                       | -    | -   | -  | -    | -                  | -               |
| Zannetti et al. <sup>42</sup>     | Patch                                   | 15   | 13  | 6  | 60   | -                  | -               |
| Steinmetz et al. <sup>56</sup>    | 50% eversion vs primary                 | -    | -   | -  | -    | 841 local          | 170             |
| Westerband et al. <sup>57</sup>   | 39 primary; 115 patch                   | 49   | -   | 31 | -    | -                  | 69              |
| Walker et al. <sup>36</sup>       | -                                       | 28   | -   | 20 | 2    | -                  | -               |
| Papanicolaou et al. <sup>58</sup> | -                                       | 10   | 25  | 2  | -    | -                  | -               |
| Gaunt et al. <sup>24</sup>        | -                                       | -    | -   | -  | -    | -                  | -               |
| Lohr et al. <sup>59</sup>         | -                                       | 39   | 25  | 63 | -    | -                  | -               |
| Lingenfelter et al. <sup>60</sup> | 50 patch                                | 25   | 7   | -  | 21   | GA                 | 46              |
| Branchereau et al. <sup>61</sup>  | -                                       | -    | -   | -  | 49   | -                  | 29              |
| Hoff et al. <sup>35</sup>         | 38 patch                                | 17   | 7   | 12 | 3    | -                  | 40              |
| Baker et al. <sup>62</sup>        | -                                       | -    | -   | -  | -    | -                  | -               |
| Kinney et al. <sup>63</sup>       | 264 patch                               | 184  | 106 | 74 | 97   | GA                 | 420             |
| Donaldson et al. <sup>64</sup>    | -                                       | 167  | 41  | 79 | -    | GA                 | 78              |
| Sawchuk et al. <sup>65</sup>      | -                                       | -    | -   | -  | -    | -                  | -               |
| Bredenberg et al. <sup>66</sup>   | 25 patch - 25 primary                   | 41   | 5   | -  | 4    | GA                 | -               |
| Schwartz <sup>14</sup>            | 71 primary                              | 36   | 11  | -  | 11   | 81% local          | -               |
| Alpert et al. <sup>40</sup>       | 26 primary; 14 patch                    | -    | -   | -  | -    | -                  | -               |
| Holder et al. <sup>67</sup>       | -                                       | 39   | 16  | -  | -    | GA                 | -               |
| <b>Total</b>                      | 5732 patch; 1152 primary; 1547 eversion | 4949 |     |    | 4407 | GA: 64%; 4309/6724 | 37% (2627/7057) |

**Table 4.** Description of carotid endarterectomy type and the clinical presentation.

**Table 5** describes the techniques of completion imaging and the criteria of re-intervention that were used for each study.

| Author                      | Techniques   | Criteria for intervention |
|-----------------------------|--|---------------------------|
| Wieker et al. <sup>37</sup> | Angiography needle (22-gauge) in the CCA; biplanar (anteroposterior and 30-degree lateral position) extracranial reconstruction in ACS intracranial one in symptomatic | -                         |

|                                       |  |   |
|---------------------------------------|--|---|
| <b>Yuan et al.</b> <sup>46</sup>      | -  | (i) non-stenotic on DUS imaging; (ii) the Doppler PSV was <120 cm/second, corresponding to 0-40% diameter stenosis; and (iii) spectral Doppler waveforms appeared laminar without spectral broadening   |
| <b>Lanceveve et al.</b> <sup>38</sup> | Retrograde direct puncture of the common carotid with a 21-gauge needle                                | -   |
| <b>Sharpe et al.</b> <sup>41</sup>    | The lumen of the endarterectomy zone was then inspected with a flexible hysteroscope (Olympus 1070-48) | Repair all intimal flaps >3 mm and to aspirate any residual thrombi (irrespective of size) from the lumen   |
| <b>Wallaert et al.</b> <sup>32</sup>  | -  | -   |
| <b>Ricco et al.</b> <sup>47</sup>     | Direct needle puncture and retrograde catheterization of the CCA                                       | One frontal and one 45 oblique view to avoid the superposition of the ICA and ECA. A third angle was obtained to analyze the cerebral vessels   |
| <b>Schanzer et al.</b> <sup>33</sup>  | ICA were all evaluated with B-mode ultrasound, and Doppler waveforms were obtained                     | A visualized abnormality (mobile plaque >2 mm) or flow disturbance (peak systolic velocity >125 cm/s)   |
| <b>Pratesi et al.</b> <sup>48</sup>   | A 21 gauge needle in the CCA   | -   |
| <b>Ascher et al.</b> <sup>34</sup>    | An intraoperative “hockey stick” transducer inserted in a sterile latex cover filled with acoustic gel | Imaging abnormalities were mobile flap 2 mm or greater in length in the ICA, flap 3 mm or greater in the CCA, and technical defects causing greater than 30% luminal diameter reduction   |
| <b>Mullenix et al.</b> <sup>49</sup>  | -  | Proposed completion duplex criteria: ICA PSV 125 cm/sec; ICA/CCA velocity ratio 2.0; Spectral broadening; Throughout systole ICA B-mode flap 2 mm; Major anatomic problem   |
| <b>Valenti et al.</b> <sup>50</sup>   | -  | Presence of residual stenosis >50%, intimal flaps >3 mm and hemodynamically kinkings (>45°) CCA, ECA and ICA as major technical defects; the presence of residual stenosis >30%, intimal flaps >1.5 mm and kinkings >45° as minor technical defects |
| <b>Woelfle et al.</b> <sup>51</sup>   | A 21 gauge needle in the CCA   | -   |
| <b>Pross et al.</b> <sup>39</sup>     | A 20-22 gauge needle in the CCA  | -   |
| <b>Osman et al.</b> <sup>52</sup>     | A choledochoscope  | -   |
| <b>May et al.</b> <sup>53</sup>       | -  | Intraoperative velocity spectra of the ICA: (1) normal laminar flow (<100 cm/s), (2) mild or moderate flow disturbance (100-150 cm/s), and (3) severe flow disturbance (>150 cm/s). Defects that need revision >2mm                                 |

|  |   |  |
|--|---|--|
| <b>Mansour et al.</b> <sup>54</sup>      | -   | Six categories: (A) none, (B) 1%-15% diameter reduction, (C) 16%-49% diameter reduction, (D) 50%-79% diameter reduction, (D+) 80%-99% diameter reduction, and (E) complete occlusion   |
| <b>Seelig et al.</b> <sup>55</sup>       | Duplex scan   | Increased velocity and turbulence, retained proximal or distal atheroma, flaps, or fronds  |
| <b>Zannetti et al.</b> <sup>42</sup>     | -   | Peak systolic velocity >229 cm/s or no flow could be detected, or an anatomic defect such as an intimal flap, a residual plaque, or a dissection   |
| <b>Steinmetz et al.</b> <sup>56</sup>    | A 21 gauge needle in the CCA  | -  |
| <b>Westerband et al.</b> <sup>57</sup>   | A19 gauge butterfly in CCA  | -  |
| <b>Walker et al.</b> <sup>36</sup>       | -   | -  |
| <b>Papanicolaou et al.</b> <sup>58</sup> | A 21 gauge needle in the CCA  | -  |
| <b>Gaunt et al.</b> <sup>24</sup>        | TCD monitoring was performed using a Scimed PcDop 842 2MHz TCD. -                           | -  |
| <b>Lohr et al.</b> <sup>59</sup>         | A 20 gauge needle in the CCA  | (1) stenosis >30%; (2) intimal flap > 2mm; (3) intraluminal filling defect; and (4) any significant kink or angulation   |
| <b>Lingenfelter et al.</b> <sup>60</sup> | A 19 pediatric gauge needle in the CCA  | -  |
| <b>Branchereau et al.</b> <sup>61</sup>  | Angioscope through a 5mm cease between sutures of endarterectomy site                       | -  |
| <b>Hoff et al.</b> <sup>35</sup>         | A needle in the CCA and DUS   | Five categories: (a) normal, PSV <125 cm/s, no spectral broadening; (b) 1 to 16% stenosis, PSV <125cm/s, spectral broadening in deceleration phase of the systole; (c) 16 to 49% stenosis, PSV <125cm/s, spectral broadening obliterating the systolic window; (d) 50-99% stenosis, PSV >125cm/s, marked spectral broadening throughout the systole; and (e) total occlusion. Any irregularities of the vessel wall, such as intimal ridges, flaps, as well as kinking and diameter changes were measured and recorded |
| <b>Baker et al.</b> <sup>62</sup>        | A 10 MHz probe was encased in a sterile plastic covering and passed onto the surgical field | -  |

|  |   |  |
|--|---|--|
| <b>Kinney et al.</b> <sup>63</sup>     | -   | 3 categories: (1) normal, (2) wall irregularity, less than 10% ICA stenosis, and (3) 10% to 30% ICA residual stenosis.<br><br>Normal (0%-15%); Systolic peak flow velocity < 100 cm/sec. Mild (16%-49%); Systolic peak flow velocity 100-125 cm/sec; Moderate (50%-75%); Systolic peak flow velocity 126-150 cm/sec; Severe (> 75%); Systolic peak flow velocity > 150 cm/sec; diastolic frequency >125 cm/sec |
| <b>Donaldson et al.</b> <sup>64</sup>  | A needle in the CCA   | -  |
| <b>Sawchuk et al.</b> <sup>65</sup>    | -   | Minor technical defects were considered to be intimal flaps less than 3 mm in length and stenosis less than 50% in diameter. All larger defects were considered major. The degree of recurrent stenosis was classified as the presence of any identifiable plaque, 25% to 49% stenosis, 50% to 74% stenosis, 75% to 99% stenosis, or complete occlusion  |
| <b>Bredenberg et al.</b> <sup>66</sup> | A 21 gauge needle in the CCA  | -  |
| <b>Schwartz</b> <sup>14</sup>          | Completion duplex ultrasonography was accomplished with a 10MHz high-resolution ultrasound imaging transducer coupled with a 7.5 MHz pulse-gated Doppler transducer | -  |
| <b>Alpert et al.</b> <sup>40</sup>     | A 23 gauge needle in the CCA  | -  |
| <b>Holder et al.</b> <sup>67</sup>     | A needle in the CCA   | -  |

In 1104 (9.7%) patients a major defect or pathological finding was identified intra-operatively, while in 329 (2.9%) a minor defect. Common pathological findings

were the presence of mural thrombus, carotid dissection, residual stenosis and intimal flaps. (Table 6).

| Author                            | major | minor | Findings   |
|-----------------------------------|-------|-------|--|
| Wiekert et al. <sup>37</sup>      | 57    | -     | ICA: mural thrombus in 4, dissections in 4, residual stenosis in 5, and intimal flaps 1. Six combined ICA and external carotid artery (ECA) lesions, 35 ECA lesions          |
| Yuan et al. <sup>46</sup>         | 27    | -     | Kinking  |
| Lancelevee et al. <sup>38</sup>   | 13    | -     | 3 stenosis ECA, 2 ECA thrombosis, 5 flap ICA, 2 ICA stenosis, CCA stenosis   |
| Sharpe et al. <sup>41</sup>       | 135   | -     | 104 intraluminal thrombus; 31 intima flap  |
| Wallaert et al. <sup>32</sup>     | 88    | -     | Flap/debris/ plaque in 67. Dissection- thrombosis- velocity in 9. In 10 a false positive   |
| Ricco et al. <sup>47</sup>        | 72    | -     | Revision for ECA flap (30), thrombus in contact with the patch (7), distal ICA flap or stenosis (20) and CCA flap or residual plaque (15)                                    |
| Schanzer et al. <sup>33</sup>     | 18    | -     | -  |
| Pratesi et al. <sup>48</sup>      | 5     | -     | -  |
| Ascher et al. <sup>34</sup>       | 15    | -     | 7 intimal flaps, 4 free-floating clots, 2 ICA stenoses, 1 ICA pseudoaneurysm, and 1 retrograde CCA dissection  |
| Mullenix et al. <sup>49</sup>     | 34    | -     | 24 were B-mode flap CCA, ICA, ECA  |
| Valenti et al. <sup>50</sup>      | 4     | 32    | Angiography identified 4 kinkings not found with CDS   |
| Woelfle et al. <sup>51</sup>      | 5     | 11    | dilatation of severe ICA spasm 1; re-exploration of distal ICA occlusion 1; reopening of occluded ECA 3  |
| Pross et al. <sup>39</sup>        | 28    | -     | 14 abnormal internal carotid arteries (ICAs) and 14 ECAs   |
| Osman et al. <sup>52</sup>        | 10    | -     | 9 intimal flaps, 1 flap plus thrombus  |
| May et al. <sup>53</sup>          | 33    | -     | -  |
| Mansour et al. <sup>54</sup>      | 13    | -     | 13 ICA spasm (n=9); II, high distal resistance flow (n=2); III, high grade residual stenosis (n= 1); IV, intraluminal thrombosis (n= 1).                                     |
| Seelig et al. <sup>55</sup>       | 20    | 146   | 20 major defect that required revision for fronds or flaps (n = 11), retained atheroma (n = 5), low flow (n = 2), high velocity or turbulence (n = 1), or dissection (n = 1) |
| Zannetti et al. <sup>42</sup>     | 29    | -     | -  |
| Steinmetz et al. <sup>56</sup>    | 112   | -     | -  |
| Westerband et al. <sup>57</sup>   | 29    | 56    | -  |
| Walker et al. <sup>36</sup>       | 3     | 21    | -  |
| Papanicolaou et al. <sup>58</sup> | 10    | 10    | 7, intimal flap in the ICA with or without platelet thrombus were confirmed by direct examination, 3 ECA   |
| Gaunt et al. <sup>24</sup>        | 30    | -     | 23 TCD embolization; angiography 27 patients in the ICA and CCA: 4 intimal flaps (> 3mm), 15 minor thrombi (< 3mm) and 8 major thrombi (> 3mm); 3 major stenosis             |
| Lohr et al. <sup>59</sup>         | 37    | -     | -  |
| Lingenfelter et al. <sup>60</sup> | 15    | -     | 4 ICA stenosis or kink; 2 ECA plaque   |
| Branchereau et al. <sup>61</sup>  | 36    | -     | 36 angiography: The defect was an intimal flap in 26 cases, detachment of the distal plaque in seven cases, and an intimal wedge in five cases                               |
| Hoff et al. <sup>35</sup>         | 17    | -     | 2 minor DSA; 3 ECA occ, Kinking DSA, 11 in duplex scan   |
| Baker et al. <sup>62</sup>        | 9     | 53    | 62 (53 minor: atheroma in CCA 35, ICA 5, ECA 2, small frond in the bulb 2, thickened wall of the vein patch 2, ICA kink 7, 2 retained atheroma) 9 major                      |
| Kinney et al. <sup>63</sup>       | 26    | -     | 26   |
| Donaldson et al. <sup>145</sup>   | 130   | -     | -  |

|                                       |                |               |   |
|---------------------------------------|----------------|---------------|---|
| <b>Sawchuk et al.<sup>65</sup></b>    | 21             | -             | The 21 minor defects consisted of four internal carotid artery lesions, nine common carotid artery lesions, and eight external carotid artery lesions, 19 had 1 to 3 mm intimal flaps, and two had small stenosis |
| <b>Bredenberg et al.<sup>66</sup></b> | 14             | -             | 3 had a lumen that was compromised by suture; 3 had a small discrete platelet thrombus 2 had major defects in ECA   |
| <b>Schwartz<sup>14</sup></b>          | 17             | -             | 17 (6 residual ICA stenoses, 3 by "kinked" ICA, 8 debris or intimal flaps in their ECA, and 1 occ ECA   |
| <b>Alpert et al.<sup>40</sup></b>     | 17             | -             | External carotid occlusion 2, External carotid irregularity 7, Internal carotid stenosis 1, Internal carotid irregularities 6, Platelet debris 1  |
| <b>Holder et al.<sup>67</sup></b>     | 34             | -             | -   |
| <b>Total</b>                          | 1104<br>(9.7%) | 329<br>(2.9%) |   |

**Table 6.** Intra-operative pathological findings

An immediate re-intervention was undertaken in 75% (790/1053) of the patients to treat a major intra-operative imaging finding. In patients with re-intervention, only 2.3% (14/609) had an intra-operative stroke, and 0.8% (5/609) a transient ischemic attack (TIA), while only 1.4% (8/575) had a stroke and 0.3% a TIA (2/575) during 30-day post-operative period. No intra-operatively death was reported. During the first 30 post-operative days, the restenosis rate of ICA was 0.5% (3/575) and 0.2% (1/575) of common carotid artery. (Table 7).

| Author                               | Re-intervention  | Clinical presentation | Restenosis at 30 days | CVD event at 30 days |
|--------------------------------------|--|-----------------------|-----------------------|----------------------|
| <b>Wieker et al.<sup>37</sup></b>    | 57   | 0 stroke              | 1                     | 0                    |
| <b>Yuan et al.<sup>46</sup></b>      | 11   | 0 stroke              | 0                     | 0                    |
| <b>Lanceveve et al.<sup>38</sup></b> | 8: residual plaque resection (4),<br>endarterectomy fixation (4) | 0 stroke              | -                     | 0                    |
| <b>Sharpe et al.<sup>41</sup></b>    | Aspiration (104) and exploration<br>(31)                         | 0 stroke              | 0                     | 0                    |
| <b>Wallaert et al.<sup>32</sup></b>  | 88   | -                     | -                     | -                    |

|  |   |                     |   |          |
|--|---|---------------------|---|----------|
| <b>Ricco et al.</b> <sup>47</sup>        | 72  | 2 strokes,<br>4 TIA |   |          |
| <b>Schanzer et al.</b> <sup>33</sup>     | ECA (8), proximal ICA (6), distal ICA (2), site endarterectomy (2)  | -                   | 0 | 0        |
| <b>Pratesi et al.</b> <sup>48</sup>      | 5   | -                   | - | 5 stroke |
| <b>Ascher et al.</b> <sup>34</sup>       | 15  | 0 stroke            | - | -        |
| <b>Mullenix et al.</b> <sup>49</sup>     | 7: ICA flap>2mm (4), kink (1), dissection (1), spasm (1)  | 0 stroke            | - | -        |
| <b>Valenti et al.</b> <sup>50</sup>      | 4   | -                   | - | -        |
| <b>Woelfle et al.</b> <sup>51</sup>      | 5   | 0 stroke            | - | 3 stroke |
| <b>Pross et al.</b> <sup>39</sup>        | 24  | 0 stroke            | - | -        |
| <b>Osman et al.</b> <sup>52</sup>        | intimal flaps excision (6) and tacking sutures (4)  | 0 stroke            | 0 | 0        |
| <b>May et al.</b> <sup>53</sup>          | CCA flaps (5), ICA flaps (5), ECA (11: 9 flaps, 1 occlusion, 1 debris)  | 0 stroke            | 2 | 0        |
| <b>Mansour et al.</b> <sup>54</sup>      | Stenosis (1) and thrombus (1)   | 0 stroke            | 0 | 0        |
| <b>Seelig et al.</b> <sup>55</sup>       | Intima flaps (11), retained atheroma (5), low flow (2), high velocity or turbulence (1), dissection (1)   | 0 stroke            | 0 | 0        |
| <b>Zannetti et al.</b> <sup>42</sup>     | 14: ECA (11), ICA(3)  | 0 stroke            | - | -        |
| <b>Steinmetz et al.</b> <sup>56</sup>    | ICA-CCA (35): flaps (19), occlusion (1), residuals lesions in ICA (10), lesions in CCA(3); ECA lesions (13)   | 5 stroke            | - | -        |
| <b>Westerband et al.</b> <sup>57</sup>   | 32 defects in 29pt: ICA defects (10), endpoint flaps (7), kinks (2), dissection (1); ECA defects (16), severe endpoint defects (10), total occlusions (6); CCA defects (6), irregular proximal shelves (5), web (1) | 1 stroke            | 1 | -        |
| <b>Walker et al.</b> <sup>36</sup>       | 3: 2 kinking at the distal endarterectomy site requiring patch-plasty and the third a large mass of intramural thrombus.  | 0 stroke            | - | -        |
| <b>Papanicolaou et al.</b> <sup>58</sup> | 10  | 0 stroke            | 0 | 0        |
| <b>Gaunt et al.</b> <sup>24</sup>        | Angioscopy (27); Stenosis (2)   | 0 stroke            | - | -        |
| <b>Lohr et al.</b> <sup>59</sup>         | 23: stenosis CCA (4), intinma flap (1); ECA flaps (6), stenosis (1), no flow (1); intima flap ICA (5), spasm (1), no flow (1), kink (3)   | 0 stroke            | - | -        |

|   |   |   |  |  |
|---|---|---|--|--|
| <b>Lingenfelter et al.<sup>60</sup></b> | 6   | 0 stroke  | 0  | 0  |
| <b>Branchereau et al.<sup>61</sup></b>  | 5: intima flaps (4), intimal fragment(1)  | 0 stroke  | -  |  |
| <b>Hoff et al.<sup>35</sup></b>         | Occluded ECA (3), kink (1)  | 0 stroke  | 0  | 0  |
| <b>Baker et al.<sup>62</sup></b>        | 9: intima flaps (7), residual plaque (1), turbulent flow alone (1)  | 1 stroke  | -  | 0  |
| <b>Kinney et al.<sup>63</sup></b>       | 26 carotid endarterectomy sites were revised based on intraoperative study results  | 0 stroke  | -  | 0  |
| <b>Donaldson et al.<sup>64</sup></b>    | 66 cases, including kinks (23), external carotid flaps (18), common carotid plaque (10), thrombus (10), distal internal carotid stenosis (8), intracranial occlusion (1), and spasm (1) | -   | -  | 2 TIA  |
| <b>Sawchuk et al.<sup>65</sup></b>      | 0   | 0 stroke  | -  | 0  |
| <b>Bredenberg et al.<sup>66</sup></b>   | 8   | 0 stroke  | -  | 0  |
| <b>Schwartz<sup>14</sup></b>            | 8; intraluminal thrombus (4) and excessive elongation (kinking) after plaque removal (3), stenosis (1)  | 0 stroke  | -  | 0  |
| <b>Alpert et al.<sup>40</sup></b>       | -   | 1 TIA   | -  | -  |
| <b>Holder et al.<sup>67</sup></b>       | -   | 5 poor clinical result                                  | -  | -  |
| <b>Total</b>                            | 75% (790/1053)  | Stroke:<br>2.3%<br>(14/609);<br>TIA:<br>0.8%<br>(5/609) | ICA: 0.5%<br>(3/575);<br>CCA:<br>0.2%<br>(1/575) | Stroke:<br>1.4%<br>(8/575);<br>TIA 0.3%<br>(2/575) |

**Table 7.** Re-intervention and morbidity (restenosis and stroke) during early period.

## Chapter 4

### 4.1 Discussion

This systematic review, has demonstrated that completion imaging techniques have been already applied in > 12000 patients. The most common imaging techniques were in arteriography (n=5340), DUS (n=5722) and angioscopy (2095). In arteriography, commonly the CCA was punctured with a small caliber needle (19-23 gauge) and a multi-planar reconstruction was achieved; the important benefit of this technique is the not only extracranial but also intracranial circulation can be assessed. Additionally, the presence of flap or insufficient endarterectomy in the distal part of the site of endarterectomy in patients with high bifurcation or the presence of a kink can be better assessed with angiography.<sup>37-40</sup> In DUS technique, the benefit is that not only morphological but also hemodynamic residual stenosis can be assessed. On the other hand, angioscopy's main advantage is that can identify and aspirate even small thrombi, particularly those that are produced from the bleeding of the transected vasa vasorum onto the site of CEA. Sharpe et al.<sup>41</sup> highlighted that in 7% of the patients, a thrombus was aspirated prior release of the arterial flow. It is unlikely that any physician would suggest ignoring the thrombi if they could identify them immediately post-operatively. In this study, it was also demonstrated that the experience of the surgeon did not play any role in the presence of thrombus before the release of the arterial flow.

In this review, it was shown that completion imaging techniques have been used in both symptomatic and ACS, and in different types of carotid endarterectomy techniques such as eversion, primary closure and patch closure with or without shunt. The main criteria that have been used in order to assess the presence of major or

minor defect were according to the imaging technique. Thus, in angiography 3 categories were identified: normal, irregular wall, < 10% ICA stenosis, and 10% - 30% ICA residual stenosis.<sup>63</sup> In DUS, the defects were categorized either according to morphology; classified into six categories: none, 1%-15% residual stenosis, 16%-49%, 50%-79%, 80%-99% residual stenosis and complete occlusion,<sup>54</sup> or according to hemodynamical criteria; five categories: normal, PSV <125 cm/s, no spectral broadening; 1-16% stenosis, PSV <125cm/s, spectral broadening in deceleration phase of the systole; 16-49% stenosis, PSV <125cm/s, spectral broadening obliterating the systolic window; 50-99% stenosis, PSV >125cm/s, marked spectral broadening throughout the systole; and total occlusion.<sup>35</sup> Generally, PSV >100-150cm/sec would illustrate a residual stenosis. Another study proposed also the ICA/CCA velocity ratio >2.0 as a meter of residual stenosis.<sup>49</sup> The presence of irregular wall such as intimal flaps or insufficient endarterectomy, as well as the artery kinking were measured and recorded. The limit that a defect needed revision was commonly >2mm either in angiography, angioscopy or DUS.

The main risk of endarterectomy either in asymptomatic or symptomatic patients is the event of an intra-/ peri- operative stroke, thus medical treatment and various techniques have been applied to reduce this risk. Immediate post-operative occlusion of the ICA due to thrombus, or distal embolization, is the most common reason of intra-operative cerebrovascular event. Those adverse events are commonly associated to technical failure in CEA site such as residual atheromatic plaque, intimal flaps, thrombus, and residual stenosis, which may mandate imminent intervention. It has been previously shown that the identification of a major defect may be upto almost 100%.<sup>50</sup> In this review, the incidence of minor and major defect was 2.9% and 9.7%, respectively. If you interpret that into clinical practice that would translate that

almost 1 out of 10 patients that has a carotid endarterectomy might have a major defect after the procedure. However, not all patients were treated for this imaging lesion; 75% of the patients with a major defect had an immediate intervention to correct it. The incidence of stroke and TIA in those patients that have a correction of their imaging defect was 2.3% and 0.8%, respectively, while the 30-day incidence of stroke and TIA was 1.4% and 0.3%, respectively. No death was noted in this category of patients. Along this line, a recent systematic review of the literature included 9 RCTs reporting on 3709 patients who underwent CEA demonstrating a stroke rate at 30 days of 1.82%.<sup>68</sup>

However, the EVEREST study<sup>42</sup> suggested that the patients with the diagnosis of major defects in CEA site that need an immediate re-intervention, have a poor early clinical prognosis. Thus, completion imaging protocol, did not offer to those patients better and favorable outcomes after CEA. For that reason, the excellent technical success and meticulous technique are needed in order to have the best outcomes in CEA. Data from the New York Carotid Artery Surgery (NYCAS) study also demonstrated that the incidence rates of stroke were similar in patients having a completion imaging strategy (2.8%) vs the patients without one (2.4%).<sup>69</sup>

Restenosis after carotid endarterectomy ranges up to 5.53% after the 1 post-operative year.<sup>70</sup> In the current systematic review, the incidence of ICA and CCA restenosis at 30 days was 0.5% and 0.2%, respectively. This shows that immediate intervention can actually minimize the complication of restenosis after CEA. Many factors have been associated with restenosis after CEA such as DM, HL, female gender, CRD, HT, and tobacco use.<sup>71</sup> Potentially, the residual thrombi or other flaps and defects may also be factors for an early restenosis. It is apparent that the most of

the physician that intervene in carotids with CEA, do not usually apply any type of completion imaging technique during the procedure other than clinical assessment of the endarterectomy site.

However, the presence of specialty such as being a Vascular surgeons and the higher experience (high-volume centers) have been associated to higher chance of using a completion imaging technique during CEA.<sup>69</sup> The recent ESVS guidelines<sup>7</sup> highlighted that targeted monitoring and quality control strategies may be considered to reduce the risk of perioperative stroke. Evidence of this study, show that the incidence of a major defect is not negligible, the event rates during the immediate re-intervention were low and the 30-day outcomes in terms of restenosis and CVD are also excellent. If someone takes into consideration that more than half of the studies were undertaken before and around early 2000s' that best medical treatment was not so intensive as recently, the outcomes might be even better.

The main limitation of the study was the absence of any randomized control trial. Most of the studies were of retrospective nature. The heterogeneity was apparent in terms of the patients' population, carotid endarterectomy techniques and completion imaging techniques. However, the accumulative outcomes seem promising, and future RCTs may evaluate the role of the completion imaging techniques in carotid endarterectomy.

## **Chapter 5**

### **5.1 Conclusion**

Completion imaging techniques can detect defects that may lead to immediate intra-operative surgical revision in almost 10% of patients with low intra-operative stroke/TIA rate, and low early carotid restenosis. During the 30-day follow up period, in those patients the incidence of stroke/TIA may be low but present. This review did not extract any evidence on which completion imaging technique provides the best outcomes. Additionally, this review cannot prove sufficiently whether completion imaging techniques improve outcomes because of the absence of a randomized control study.

## Chapter 6

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