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SYSTEMATIC REVIEW

Editor's Choice — Predictors of New Ischaemic Brain Lesions on Diffusion Weighted Imaging After Carotid Stenting and Endarterectomy: A Systematic Review

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WHAT THIS STUDY ADDS

This systematic review presents an overview of the available evidence on patient related features associated with an increased susceptibility to the development of new ischaemic brain lesions on magnetic resonance diffusion weighted imaging after carotid endarterectomy and carotid artery stenting. These demographic, radiological, and biochemical predictors may be helpful in decision making on patient selection for medical intervention, carotid stenting, or endarterectomy.

Objectives: Peri-procedural ischaemic brain lesions on diffusion weighted imaging (DWI) after carotid endarterectomy (CEA) and carotid artery stenting (CAS) have been related to a higher chance of recurrent cerebrovascular events. This systematic review provides an overview of patient characteristics associated with increased risk of new DWI lesions.

Methods: MEDLINE, EMBASE, and Cochrane library databases were systematically searched (update November 2018) for studies reporting post-procedural DWI lesions after CEA or CAS. Data derived from both procedures were analysed separately. Studies reporting predictive features that were present prior to intervention were assigned to 10 categories: age, gender, cardiovascular risk factors, symptomatology, plaque vulnerability, atherosclerotic burden, cerebrovascular haemodynamics, carotid/arch anatomy, inflammatory markers, and markers of coagulation. A semi-quantitative analysis was performed by plotting studies that found an association between the investigated features and DWI lesions against those that did not find an association.

Results: Forty-six studies (5018 patients) were included: 10 reported only CEA, 33 CAS, and three both interventions. 68.0% of 1873 CEA patients and 55.9% of 3145 CAS patients were symptomatic. The weighted prevalence of DWI lesions was 18.1% (95% CI 14.0—22.7%) in CEA patients compared with 40.5% (95% CI 35.4—45.7%) in CAS patients. Studies reporting on CEA patients predominantly found an increased risk in symptomatic patients (two of seven studies, including 848/1661 patients), those with impaired haemodynamics (five of five studies), and increased inflammatory markers (two of three studies). Studies reporting on CAS patients often found a positive association with age (10/26 studies), high plaque vulnerability (25/34 studies), or complex carotid/arch anatomy (three out of five studies).

Conclusions: For patients undergoing CEA, symptomatic status, impeded cerebral haemodynamics, and increased inflammatory markers are associated with increased susceptibility to peri-operative DWI lesions. In CAS patients, higher age, plaque vulnerability and complex carotid/aortic arch anatomy were identified as risk factors. These clinical predictors may assist with decision making on patient selection for medical treatment, CEA or CAS.

Keywords: Carotid endarterectomy, Carotid artery stenting, Magnetic resonance diffusion weighted imaging, Ischaemic brain lesions
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INTRODUCTION

The occurrence of peri-procedural ischaemic brain lesions on magnetic resonance imaging (MRI) after treatment of the carotid artery has been a topic of increasing interest.[1—3]

A considerably high incidence of these so called diffusion weighted imaging (DWI) lesions are reported after both carotid artery stenting (CAS; 37—50%) and carotid endarterectomy (CEA; 10—17%).[1–3] DWI lesions are associated with a higher risk of recurrent cerebrovascular events.[4,5] In the MRI substudy of the ICSS (International Carotid Stenting Study) it was demonstrated that recurrent stroke or transient ischaemic attack (TIA) was more likely to occur in DWI positive patients than in DWI negative patients (hazard ratio 2.85).[4] DWI positive patients are also more likely to develop definite brain infarction on follow up MRI than DWI negative patients.[5] Furthermore, the presence of silent ischaemic lesions may lead to early onset cognitive decline and dementia.[6] These results suggest that peri-procedural DWI lesions may be used as a surrogate and clinically relevant marker for cerebral ischaemia.

DWI lesions on MRI reflect intracellular movement of water resulting in cytotoxic oedema; they are considered reminiscent of early pathological changes resulting from acute ischaemia.[7] Different theories regarding the aetiology of these lesions exist. During and after CAS or CEA, dislodgement of thrombotic material or atherosclerotic debris of vulnerable plaques can lead to cerebral embolisation.[3] A second hypothesis is that haemodynamic and embolic mechanisms interact in development of new (silent) ischaemic lesions as a result of "impaired clearance of emboli".[8]

Over the last few years several studies have been performed investigating the occurrence of new DWI lesions in relation to procedural features and patient characteristics. Besides optimising interventional techniques and improving peri-procedural antiplatelet therapies, identification of patients at risk of peri-procedural DWI lesions can be helpful in determining the optimal treatment strategy, ranging from CEA and CAS to best medical treatment (BMT). Novel insights supporting clinicians in decision making based on individual patient characteristics are needed. The aim of this study was to provide an overview of predictive features, based on patient characteristics, for the development of new DWI lesions following treatment of the carotid artery.

MATERIALS AND METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9]

Search strategy

A systematic search was performed in the MEDLINE, EMBASE, and Cochrane databases in February 2018, updated in November 2018. The Medical Subject Headings (MeSH) terms "diffusion magnetic resonance imaging", "endarterectomy", and "stents" were combined using various synonyms for DWI lesions and carotid artery stenting and endarterectomy. The full search strategy can be found in Supplementary material (I).

Original studies that reported patients undergoing CEA or CAS and performed both a pre- and post-procedural MR-DWI scan were included. Exclusion criteria were case reports, case series of $<$ 10 patients, animal studies, and reviews. Investigated parameters had to be based on pre-operative data, studies that only involved intra- or post-operative measurements were excluded. Articles in English, Dutch, German, and French were considered.

Duplicates were removed and studies published in languages other than those mentioned above were excluded. Two authors (M.L.R., A.J.A.M.) independently assessed full text eligibility based on title and abstract screening. Discordant judgements were addressed by consulting a third author (G.J.B.). The reference lists of all included papers were searched manually to identify missed but potentially relevant studies.

Data processing and assessment of methodological quality

Data derived from CEA and CAS were analysed separately to account for inherent differences in type of patients selected for each procedure and the procedure itself. If quantitative or separated CEA/CAS data were not provided, corresponding authors were contacted. If there was no response the article was excluded. The Newcastle—Ottawa Scale (NOS) was used to assess quality of cohort studies based on selection and comparability of study groups and ascertainment of the outcome of interest (average quality was defined as 6—7 points out of 9, good quality was defined as 8—9 points out of 9). For randomised controlled trials (RCTs), the Cochrane Collaboration's risk of bias tool was used for assessment of random sequence generation, allocation concealment, selective reporting, blinding, and missing data.[10,11] Two authors (M.L.R., A.J.A.M.) independently assessed methodological quality and carried out data extraction from the individual papers.

Statistical analysis

All reported predictive parameters were collected and subsequently assigned to different categories (Table 1). Categories were as follows: age, gender, cardiovascular risk factors, symptomatology, (ipsilateral) plaque burden or vulnerability, atherosclerotic burden, impaired cerebrovascular haemodynamics, difficult arch/carotid anatomy, increased inflammatory markers, and increased markers of coagulation. When a category was reported on in fewer than three articles, this category was excluded from further analysis. A semi-quantitative analysis was performed for each of the above mentioned categories, comparing features significantly associated with an increased risk of post-procedural DWI lesions to those for which no significant association was found. The results with total number of investigated patients were shown in radar graphs.

The prevalence of DWI was estimated using a random effects model with double arcsine transformation.[12] Weighted means with 95% confidence interval (CI) of the proportion of patients with new post-procedural DWI lesions were calculated for CEA and CAS patients; subgroup analyses were performed for different MR field strengths. Symptomatic and asymptomatic patients were analysed together. Funnel plots were used to assess publication bias.

Table 1. List of the predictive categories for post-procedural diffusion weighted imaging lesions after carotid endarterectomy or carotid artery stenting with the assigned parameters as reported by the included studies

Category	Reported pre-procedural predictive parameters
Age	Age
Gender	Gender
Cardiovascular risk factors	Hypertension; DM; hypercholesterolaemia; HDL cholesterol, LDL cholesterol; currently smoking; history of smoking; high BMI
Symptomatology	Symptomatic status (ischaemic stroke; TIA or monocular vision loss in ipsilateral carotid territory <6 months); pre-operative stroke <14 days
Plaque burden/vulnerability	High degree of stenosis; longer lesion; large plaque volume; jellyfish sign; plaque ulceration; plaque calcification (proximal/distal); intraplaque haemorrhage; atheromatous plaque; fibrolipid plaque, large necrotic core; high intima media thickness; high intensity signal plaque; high signal intensity (ratio); high plaque muscle intensity ratio; plaque echolucency; high extensive remodelling ratio; enhancement vasa vasorum; eccentric lesion; plaque surface irregularity; floating plaque
Atherosclerotic burden	Contralateral carotid lesion; CAD; PAOD; aortic plaques
Cerebrovascular haemodynamics	Impeded cerebrovascular reactivity to acetazolamide; high CBRBP/CBF asymmetry; haemodynamic tandem intracranial lesion, reduced MCA signal intensity; high CBL / MCA asymmetry; collateral flow; increased ICA PSV; increased ICA EDV
Arch/carotid anatomy	Type II/III aortic arch; CCA or ICA tortuosity (index); arch elongation; large ICA angle; high CCA/ICA angle ratio; high expert score for anatomical suitability
Inflammatory markers	Increased CRP; increased hsCRP; increased TNF-α
Markers of coagulation	High fibrinogen; high platelet count

DM = diabetes mellitus; BMI = body mass index; CAD = coronary artery disease; PAOD = peripheral arterial occlusive disease; MCA = middle cerebral artery; CBL = cerebellar hemispheric; CBRBP = central benzodiazepine receptor binding potential; CBF = cerebral blood flow; ICA = internal carotid artery; PSV = peak systolic velocity; EDV = end diastolic velocity; CRP = C reactive protein; hsCRP = high sensitivity C reactive protein. TNF = tumour necrosis factor; HDL = high density lipoprotein; LDL = low density lipoprotein; TIA = transient ischaemic attack; CCA = common carotid artery. Plaque burden/vulnerability refers to the ipsilateral carotid artery.

MetaXL 5.3 (Epigear International Pty Lts) was used for statistical analysis.

RESULTS

Study selection

The search yielded 850 articles. After removal of duplicates, 695 articles were left of which 46 studies reporting on predictive features for development of DWI met the inclusion criteria (Fig. 1). An overview of the included studies is provided in Table 2. Two substudies of randomised trials were included, other studies were prospective (n = 29) and retrospective (n = 15) cohort studies. The methodological quality of the included studies was high since all but one cohort study reached a NOS score of 7 or higher out of 9, and risk of bias was low for the two RCT substudies (Table 2).

Study sample. A total of 5018 unique patients were included from 46 studies, of which 10 reported only CEA patients, 33 only patients that had CAS, and three both patient categories. For both CEA and CAS patients the same 10 investigated features were described. A total of 1873 CEA patients from 13 studies (68% symptomatic) and 3145 CAS patients from 36 studies (55.9% symptomatic) were included. A weighted mean of 18.1% (95% CI 14.0—22.7%) new post-procedural DWI lesions in CEA patients was significantly lower than 40.5% (95% CI 35.4—45.7% in CAS patients. There was no evidence of publication bias based on funnel plots.

Most studies (n = 28) used solely 1.5 T MRI, some used 3 T or a combination of 1.5 T and 3 T (n = 10 and n = 2 respectively), while six studies did not report the field strength used. Pooled prevalence of new DWI lesions after CEA in studies using 1.5 T was 15.3% (95% CI 10.2—21.2%) compared with 14.1% (95% CI 9.09—20.0%) with 3 T MRI and 30.3% (95% CI 21.8—39.5%) in combined studies. The reported pooled prevalence of new DWI lesions after CAS was 38.0% (95% CI 32.4—43.7%) in studies using 1.5 T MRI, compared with 38.7% (95% CI 27.8—50.3%) with 3 T and 48.1% (95% CI 27.0—69.5%) in combined studies.

CEA. An overview of the reported predictive features is provided in Table 3, more detailed information on the individual study results can be found in Supplementary material (III). None of the investigated features was negatively associated with new DWI lesions. All studies described either a positive association or found no association. To illustrate the relationship between studies finding a positive association between the investigated parameter and the presence of new DWI lesions and studies not finding a significant association, the results are plotted in Fig. 2A. Nine of 13 included articles reporting CEA patients investigated age, of which none reported a significantly higher chance of new DWI lesions with increasing age. None of the 10 studies reporting gender found a significant association (1696 patients).[13] Symptomatic status (*e.g.* symptomatic *vs.* asymptomatic) or recent stroke (< 14 days from intervention) was associated with an increased risk of new DWI

Table 2. List of the studies reporting post-procedural diffusion weighted imaging (DWI) lesions after carotid endarterectomy or carotid artery stenting included in the review

Author	Type of study	Definition outcome	Patients *n*	Symptomatic lesions %	New DWI lesions %	MRI field strength	NOS/ Cochrane
Carotid endarterectomy							
Gwon 2017[18]	Retrospective cohort	≥1 new lesion	556	50	14	Unknown	8
Lee 2016[13]	Retrospective cohort	≥1 new lesion	292	100	28	1.5 T	8
Heider 2007[23]	Prospective cohort	≥1 new lesion	183	50	22	1.5 T	9
Aso 2009[44]	Prospective cohort	≥1 new lesion	150	74	17	1.5 T	8
Sato 2011[21]	Prospective cohort	≥1 new ipsilateral lesion	112	67	8	1.5 T	8
Suzuki 2009[22]	Prospective cohort	≥1 new ipsilateral lesion	106	74	13	3 T	8
Oikawa 2013[20]	Prospective cohort	≥1 new ipsilateral lesion	101	100	9	1.5 T	8
Lee 2014[55]	Prospective cohort	≥1 new lesion	94	77	25	1.5 T/3 T	8
Muller 2017[60,a]	RCT substudy	≥1 new lesion	87	100	16	1.5 T/3 T	High
Sfyroeras 2013[64]	Prospective cohort	≥1 new lesion	66	17	8.9	1.5 T	7
Maruyama 2015[58,a]	Retrospective cohort	≥1 new ipsilateral lesion	51	55	8	3 T	9
Akpinar 2015[43]	Prospective cohort	≥1 new lesion	51	55	16	1.5 T	7
Burow 2014[45,a]	RCT substudy	≥1 new lesion	24	100	8	1.5 T/3 T	High
Weighted mean				68.0	18.1 (95% CI 14.0–22.7)		
Carotid artery stenting							
Bijuklic 2013[14]	Retrospective cohort	≥1 new lesion	728	29	33	1.5 T	8
Groschel 2008[47]	Prospective cohort	≥1 new lesion	176	51	51	1.5 T	8
Rosenkranz 2010[62]	Prospective cohort	≥1 new lesion	147	100	29	1.5 T	8
Lin 2018[56]	Prospective cohort	≥1 new lesion	128	52	50	3 T	8
Russjan 2011[63]	Prospective cohort	≥1 new lesion	127	100	21	1.5 T	8
Huang 2014[49]	Retrospective cohort	≥1 new lesion	126	37	26	1.5 T	8
Yoshimura 2011[75]	Prospective cohort	≥1 new ipsilateral lesion	112	57	41	1.5 T	8
Sakamoto 2016[29]	Retrospective cohort	≥1 new lesion	110	50	18	3 T	7
Ichinose 2017[15]	Prospective cohort	≥1 new lesion	104	42	42	3 T	9
Abiko 2018[42]	Retrospective cohort	≥1 new lesion	98	58	19	Unknown	7
Muller 2017[60,a]	RCT substudy	≥1 new lesion	97	100	51	1.5 T/3 T	High
Chung 2016[46]	Prospective cohort	≥1 new ipsilateral lesion	94	43	27	3 T	7
Kashiwazaki 2017[51]	Retrospective cohort	≥1 new lesion	82	Unknown	18	1.5 T	7
Krapf 2006[54]	Prospective cohort	≥1 new lesion	77	58	45	1.5 T	8
Song 2013[65]	Retrospective cohort	≥1 new lesion	76	75	59	3 T	8
Zhou 2011[76]	Retrospective cohort	≥1 new lesion	67	52	46	1.5 T	9
Kastrup 2016[52]	Retrospective cohort	≥1 new lesion	62	100	55	1.5 T	8
Mizobe 2018[36]	Prospective cohort	≥1 new lesion	60	100	28	3 T	8
Yamada 2011[73]	Retrospective cohort	≥1 new lesion	52	58	40	1.5 T	8
Gunduz 2014[48]	Prospective cohort	≥1 new lesion	52	75	56	1.5 T	8
Yamada 2010[74]	Prospective cohort	≥1 new lesion	50	52	38	1.5 T	7
Stojanov 2012[66]	Prospective cohort	≥1 new lesion	50	74	14.9	1.5 T	9
Tanemura 2013[16]	Retrospective cohort	≥1 new ipsilateral lesion	48	49	70	3 T	8
Maggio 2017[57]	Retrospective cohort	≥1 new lesion	47	Unknown	36	1.5 T	8
Koyanagi 2016[53]	Prospective cohort	≥1 new lesion	46	48	23	1.5 T	8
Jongen 2010[50]	Prospective cohort	≥1 new ipsilateral lesion	45	100	27	1.5 T/3 T	8
Maruyama 2015[58,a]	Retrospective cohort	≥1 new ipsilateral lesion	37	46	27	3 T	9
Matsukawa 2015[59]	Prospective cohort	≥1 new lesion	36	67	31	3 T	7
Takemoto 2012[67]	Prospective cohort	≥1 new ipsilateral lesion in ICA territory	36	56	19	1.5 T	8
Varetto 2015[72]	Prospective cohort	≥1 new lesion	35	8	54	1.5 T	7
Tulip 2012[70]	Prospective cohort	≥1 new lesion	34	43	50	1.5 T	6
Burow 2014[45,a]	RCT substudy	≥1 new lesion	26	100	69	1.5 T/3 T	High
Timaran 2010[69]	Prospective cohort	≥1 new lesion	24	42	71	1.5 T	7
Pini 2013[61]	Prospective cohort	High lesion number (>5) or volume (≥100 mm^3)	20	65	90	Unknown	8
Uchiyama 2012[71]	Prospective cohort	≥1 new ipsilateral lesion	19	100	79	Unknown	7
Tanabe 2016[68]	Retrospective cohort	≥1 new lesion	18	78	61	1.5 T	7
Weighted mean				55.9%	40.5 (95% CI 35.4–45.7)		

CI = confidence interval; RCT = randomised clinical trial; DWI = diffusion weighted imaging; MRI = magnetic resonance imaging; NOS = Newcastle–Ottawa scale; ICA = internal carotid artery.

[a] Study included both carotid endarterectomy and carotid artery stenting patients. Prevalence of DWI lesions was calculated using random effects model with double arcsine transformation.

lesions in only two out of nine studies. However, these two studies represented a relatively large number of patients (848 out of 1661) (Fig. 2A). Cardiovascular risk factors and atherosclerotic burden (excluding ipsilateral carotid atherosclerosis) were never found to be significant predictors (respectively nine and six reporting articles). Eleven studies reported various measures of plaque characteristics, two of them found a significant increased risk of development of new DWI lesions in case of high plaque vulnerability/high plaque burden (386 out of 1672 patients). All five articles investigating measures for cerebral haemodynamics, found an increased risk of new DWI lesions in cases of preoperatively impaired cerebral haemodynamics (761 patients). Aortic arch and carotid anatomy was investigated in one study and was not associated with increased predisposition to new DWI lesions in CEA patients. Three studies reported markers of inflammation (high sensitivity C reactive protein [hsCRP] or CRP), of which two were found to be independently associated with new DWI lesions (475 out of 526 patients). A marker of coagulation (fibrinogen) was reported once and was found to be associated with an increased chance of new DWI lesions (183 patients).

CAS. An overview of the reported predictive features and 36 articles reporting CAS is given in Table 4 and graphically represented in Fig. 2B. More detailed information can be found in Supplementary material (III). Twenty-six studies (on 2849 patients) reported age as a predictive feature and 10 (1725 patients) described a significantly increased chance of new post-procedural DWI lesion in older patients. Of the 22 studies reporting gender, only one study ($n = 20$) described a negative association between male gender and the incidence of new lesions; others did not show a significant association. Symptomatic status was associated with an increased risk in four ($n = 409$) of 22 studies investigating reporting on this topic ($n = 2298$). Cardiovascular risk factors were reported in 24 articles and were only associated with new DWI lesions in three studies (significant association with hypertension in one study, $n = 728$[14] and significant association with low density lipoprotein cholesterol in two studies, $n = 152$[15,16]). Increased ipsilateral plaque burden or plaque vulnerability was often investigated ($n = 3114$) and frequently showed an increased chance of new DWI lesions ($n = 2130$). Within this category, signal intensity (ratio) and plaque volume/area were most often found to be predictive of new DWI lesions. Features representative of atherosclerotic burden (other than ipsilateral carotid atherosclerosis) were investigated in 20 studies ($n = 1467$) and were found to be predictive of development of a new lesion in three of them ($n = 349$).

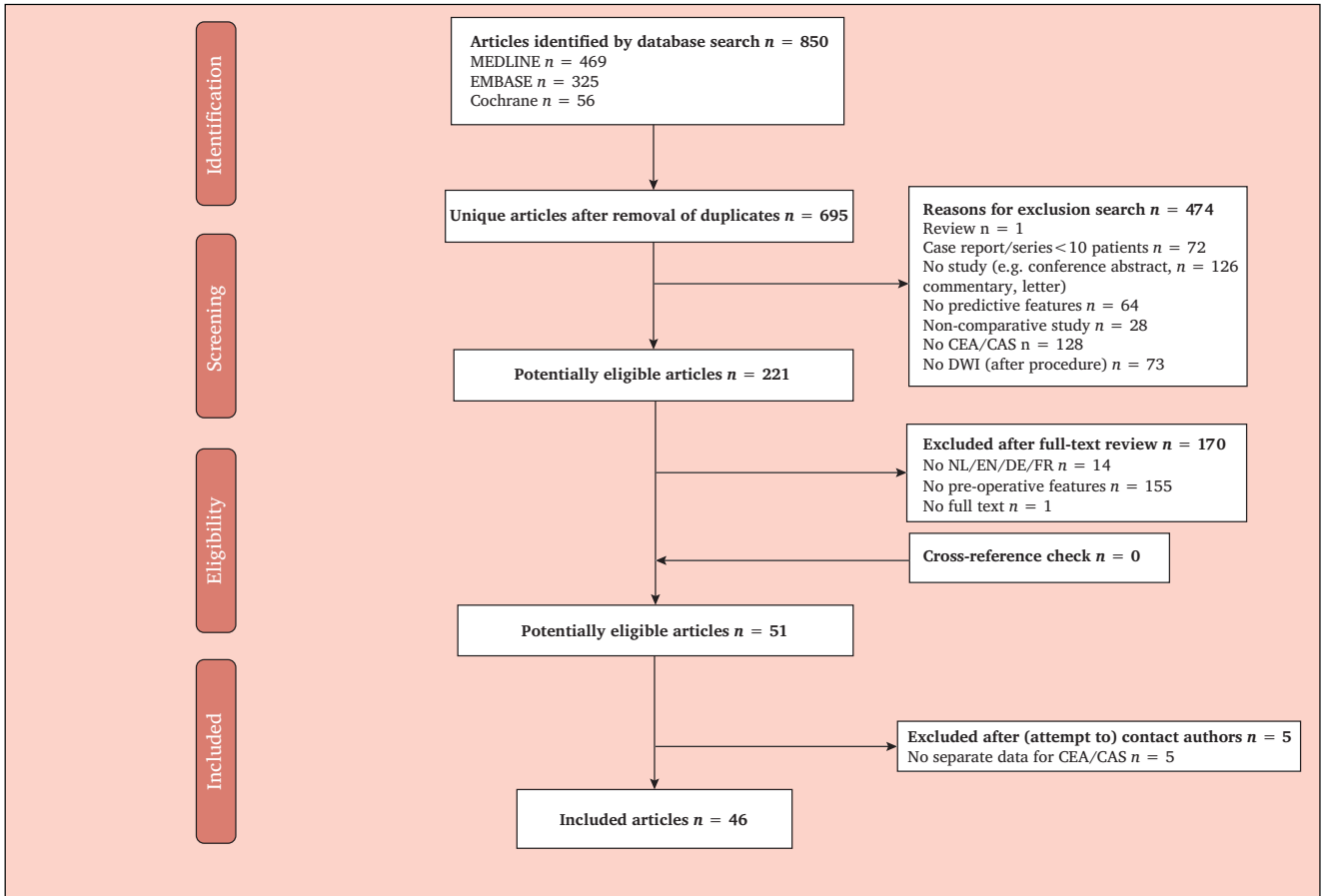

Figure 1. Flowchart showing selection of articles reporting post-procedural diffusion weighted imaging (DWI) lesions after carotid endarterectomy (CEA) or carotid artery stenting (CAS) for review. CAS = carotid artery stenting; CEA = carotid endarterectomy; DWI = diffusion weighted imaging; NL = Dutch; EN = English; DE = German; FR = French.

Table 3. Results of investigated predictive features for development of post-procedural diffusion weighted imaging (DWI) lesions after carotid endarterectomy (CEA), sorted in descending order by number of included patients

Study on CEA	Patients *n*	Higher age	Male gender	Presence of symptoms	Cardiovascular risk factors	Plaque burden and characteristics	Atherosclerotic burden (excl ipsilateral carotid artery)	Impeded cerebral haemo dynamics	Difficult arch/ Carotid anatomy	Markers of inflammation	Markers of coagulation
Gwon 2017[18]	556	NS	NS	+	NS	NS	NS				
Lee 2016[19]	292	NS	NS	+	NS	NS / +[a]	NS	+		+	
Heider 2007[23]	183	NS	NS	NS	NS	NS	NS			+	+
Aso 2009[44]	150	NS	NS	NS	NS			+			
Sato 2011[21]	112	NS	NS	NS	NS	NS		+			
Suzuki 2009[22]	106	NS	NS	NS	NS	NS	NS	+			
Oikawa 2013[20]	101	NS	NS		NS	NS		+			
Lee 2014[55]	94	NS	NS	NS		NS / +[a]					
Muller 2017[60,b]	87					NS			NS		
Sfyroeras 2013[64]	66			NS	NS	NS					
Akpinar 2015[43]	51		NS	NS	NS		NS				
Maruyama 2015[58,b]	51	NS	NS	NS	NS	NS	NS			NS	
Burow 2014[45,b]	24					NS					

CEA = carotid endarterectomy; DWI = diffusion weighted imaging.
+ = Feature significantly associated with an increased risk of post-procedural DWI lesions; NS = no significant association with DWI lesions or no negative associations.
Cells are blank when a specific feature was not described by the study.
[a] Multiple features were investigated within one category resulting in both significant as well as insignificant associations.
[b] Study included both CEA and carotid artery stenting patients.

Impaired cerebral haemodynamics was found to be a risk factor for peri-procedural DWI lesions in three ($n = 143$) of five ($n = 307$) studies. Difficult carotid (large internal carotid artery angle) or arch anatomy (types II or III aortic arch configuration) was associated with new lesions in three ($n = 887$) of a total of five studies ($n = 957$). Markers of inflammation and markers of coagulation were investigated less frequently and were found to have a significant association with the presence of new DWI lesions in respectively three of eight and one of two studies.

DISCUSSION

In this review a systematic overview of the available evidence on predictive features for development of post-procedural DWI lesions after CEA (13 studies, 1873 patients) and CAS (36 studies, 3145 patients) has been provided. For both CEA and CAS age, gender, cardiovascular risk factors, symptomatology, plaque burden/vulnerability, atherosclerotic burden, cerebrovascular haemodynamics, arch/carotid anatomy, inflammatory markers, and markers of coagulation were investigated as potential predictive features. Factors associated with the development of new DWI lesions were pre-procedural symptoms, impeded cerebral haemodynamics and increased inflammatory markers in CEA patients and age, plaque vulnerability and difficult vascular anatomy in CAS patients.

Symptomatic patients are known to have a higher risk of post-procedural events than asymptomatic patients.[17] It is therefore not unexpected that a risk benefit for asymptomatic patients applies for development of DWI lesions as well.[18,19] CEA patients with impeded pre-procedural haemodynamics may be at risk during clamping of the carotid artery, since it may cause a critical reduction in cerebral perfusion. Only one of the included studies reporting cerebral haemodynamics used routine intraluminal shunting;[19] others stated that no shunt was used.[20–22] It is unclear whether these studies used electrophysiological neuromonitoring to determine maintenance of sufficient cerebral perfusion after carotid artery cross clamping. Patients with an inadequate collateral blood flow may be more at risk of ischaemic complications due to the impaired clearance of emboli theory. According to this concept, haemodynamic impairment may facilitate onset of ischaemia due to emboli generated from a proximal lesion.[8] Studies finding a positive association between increased inflammatory markers and new lesions used CRP or hsCRP as an inflammatory marker.[19,23] These studies advocate that inflammation may be related to the presence of macrophages and T lymphocytes in the plaque, which is associated with plaque instability. This hypothesis is strengthened by studies finding differences in levels of inflammatory markers between symptomatic and asymptomatic patients.[24] Nevertheless, according to the results, investigated features of plaque instability in CEA patients were often found not to be associated with new DWI lesions.

Higher age as a peri-procedural risk factor in CAS patients corresponds to the literature describing increased risk of stroke after CAS with age acting as an effect modifier for outcome.[25,26] Furthermore, biobank studies have revealed that increased age is related to increased plaque vulnerability.[27] This review has shown that high plaque vulnerability was associated with new DWI lesions in CAS patients.

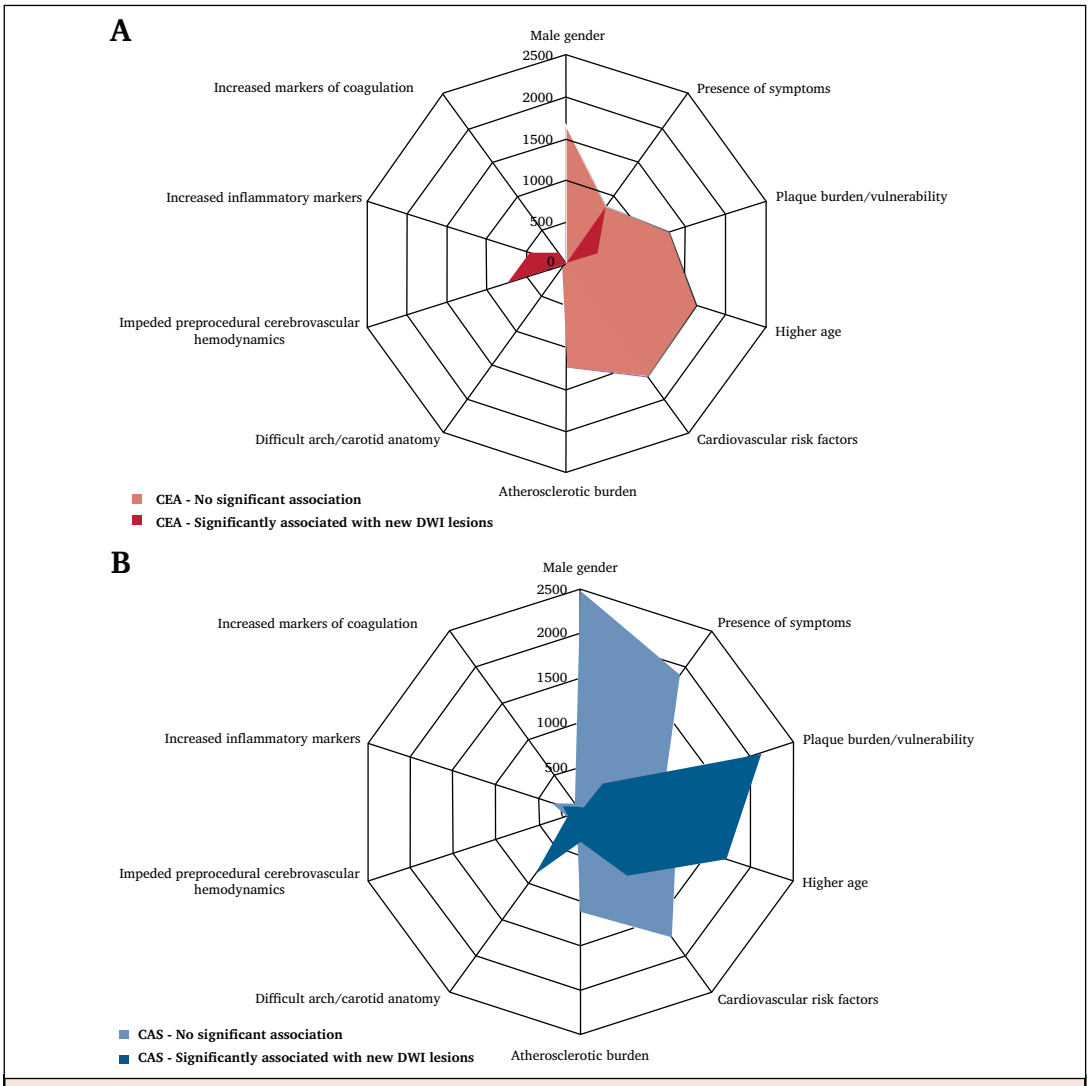

Figure 2. Radar graphs of the included prognostic features for carotid endarterectomy (CEA; A) and carotid artery stenting (CAS; B) in studies reporting post-procedural diffusion weighted imaging (DWI) lesions after CEA (13 studies) or CAS (36 studies). Studies that found a significant association (dark coloured) were plotted against studies not finding a significant association (light coloured). The *y* axis represents the cumulative number of patients from the studies; each axis of the circular radar graph represents one prognostic category. CAS = carotid artery stenting; CEA = carotid endarterectomy; DWI = diffusion weighted imaging.

Vulnerable plaques, identified by the presence of intraplaque haemorrhage, lipid rich necrotic core, and rupture of the fibrous cap are known to cause more ischaemic strokes or TIAs in carotid stenosis patients.[28] They are also thought to be risk factors for embolic complications after CAS, by distal embolism into intracranial arteries as a result of debris migration during the procedure.[29] The same mechanism may apply for development of DWI lesions in CAS patients. Increased tortuosity of the supra-aortic arteries has been associated with a higher risk of stroke/death within 30 days of CAS;[30] however randomised trial evidence comparing CEA and CAS in terms of clinical outcome is lacking. Complex anatomy of the supra-aortic arteries increases technical challenges during stenting procedure and repeated attempts to advance the catheter and guidewire may cause dislodgement of thrombotic material. An ICSS substudy also included in this review demonstrated that patients with a complex configuration of the aortic arch and internal carotid artery (ICA) tortuosity increase the risk of DWI lesions in CAS, but not CEA.[31]

The pooled prevalence of 18.1% new DWI lesions in CEA patients as described in Table 2 is equivalent to that described in two RCTs comparing CEA and CAS for prevalence of new DWI lesions (18—25%).[3,32] The pooled prevalence of 40.5% in CAS patients, however, seems to be lower than reported in both trials (50% and 49%). This may be partly explained by the fact that the study sample in one of these trials involved only symptomatic patients[3] whereas in the current review studies on both symptomatic and asymptomatic patients were included. Another possible explanation for the differences in prevalence is the change over time in stent design and type of cerebral protection device as well as changes in antithrombotic and lipid lowering therapy.[33—36] Moreover, patients with a deemed

Table 4. Results of investigated predictive features for development of post-procedural diffusion weighted imaging lesions after carotid artery stenting (CAS), sorted in descending order by number of included patients

Study on CAS	Patients *n*	Higher age	Male gender	Presence of symptoms	Cardiovascular risk factors	Plaque burden and characteristics	Atherosclerotic burden (excl ipsilateral carotid artery)	Impeded cerebral haemo dynamics	Difficult arch/ carotid anatomy	Markers of inflammation	Markers of coagulation
Bijuklic 2013[14]	728	+	NS	NS	NS/+[a]	NS/+[a]			NS/+[a]		
Groschel 2008[47]	176	+	NS	NS	NS	NS/+[a]	NS/+[a]				
Rosenkranz 2010[62]	147	+	NS		NS	NS/+[a]					
Lin 2018[56]	128	+	NS	NS	NS	NS/+[a]	NS			+	
Russjan 2011[63]	127	+	NS		NS	NS/+[a]					
Huang 2014[49]	126	NS	NS	NS	NS	NS	NS/+[a]				
Yoshimura 2011[75]	112	NS	NS	+	NS	NS/+[a]	NS			NS	
Sakamoto 2016[29]	110					NS					
Ichinose 2017[15]	104	NS	NS	NS	NS/+[a]	NS/+[a]		NS		NS	NS
Abiko 2018[42]	98	NS									
Muller 2017[60,b]	97					NS			NS/+[a]		
Chung 2016[46]	94			+		NS					
Kashiwazaki 2017[51]	82	NS	NS		NS	NS					
Krapf 2006[54]	77	NS			NS	NS/+[a]	NS				
Song 2013[65]	76	NS	NS	NS	NS	NS	NS				NS/+[a]
Zhou 2011[76]	67	+	NS	NS/+[a]	NS	NS	NS				
Kastrup 2016 [52]	62	+	NS	NS	NS	NS/+[a]	NS		NS/+[a]		
Mizobe 2018[36]	60	NS	NS	NS	NS	NS	NS	NS			
Gunduz 2014[48]	52	NS			NS	+	NS	+			
Yamada 2011[73]	52	NS	NS	NS	NS	NS/+[a]	NS			NS	
Stojanov 2012[66]	50	NS	NS	NS	NS	NS/+[a]	NS		NS		
Yamada 2010[74]	50	NS	NS	NS	NS	NS/+[a]	NS			+	
Tanemura 2013[16]	48	NS	NS	NS	NS/+	NS/+[a]	NS			NS	
Maggio 2017[57]	47	+	NS	NS	NS	NS	+				
Koyanagi 2016[53]	46	+	NS	NS	NS	NS/+[a]	NS	+			
Jongen 2010[50]	45	NS	NS	NS	NS	NS	NS	+			
Maruyama 2015[58,b]	37	NS	NS	NS	NS	NS/+[a]	NS			NS	
Matsukawa 2015[59]	36	NS		+		NS					
Takemoto 2012[67]	36					+	NS				
Varetto 2015[72]	35					+					
Tulip 2012[70]	34			NS							
Burow 2014[45,b]	26					NS/+[a]					
Timaran 2010[69]	24					NS					
Pini 2013[61]	20	NS	−	NS	NS	NS	NS		NS	+	
Uchiyama 2012[71]	19					+					
Tanabe 2016[68]	18					+					

CAS = carotid artery stenting.
+ = Feature significantly associated with an increased risk of post-procedural DWI lesions; − = significantly associated with a decreased risk at post-procedural DWI lesions; NS = no significant association with DWI lesions found.
Cells are blank when a specific feature was not described by the study.
[a] multiple features were investigated within one category resulting in both significant as well as insignificant associations.
[b] Study included both CEA and CAS patients.

high risk anatomy were more likely to be treated conservatively over the more recent years, resulting in a shift of patient selection. In light of evidence suggesting that very urgent intervention may increase procedural risk due to presumed plaque vulnerability, procedural timing has to be planned more carefully.[37,38]

In previous studies the advantage of CEA over CAS with respect to prevention of new DWI lesions has already been demonstrated.[2,3] Although a meta-analysis of European RCT data showed that CAS was associated with a significantly higher risk of procedural death/stroke risk after 30 days than CEA, follow up results of these RCTs show that CAS appears to be as durable as CEA after the first 30 days.[39] Ongoing advances in stenting technology and safety may lead to a point where CAS is an equivalent treatment option compared with CEA in terms of major adverse events. The risk of peri-operative DWI lesions has become increasingly important since these lesions are associated with a higher risk of recurrent cerebrovascular events.[4,5] As peri-operative stroke risk has gradually decreased over the years, the necessity for a surrogate marker to assess possible effects of changes in treatment is growing. Subtle peri-operative events such as micro-embolism or a minor decrease in cerebral perfusion may not be enough to cause

stroke but can lead to silent ischaemic lesions. Decision making on type of intervention may be supported by patient profiling based on the investigated features. Secondly, as secondary stroke prevention has changed considerably (widespread use of statins and lower blood pressure targets), the discussion on invasive treatment vs. BMT has re-emerged, especially in patients with a low risk of future cerebrovascular events. In the light of this debate, the risk of development of peri-procedural DWI lesions may contribute to an individualised risk benefit assessment.

This review focused on pre-procedural risk assessment for development of DWI lesions. Naturally, treatment type and procedural conditions influence the likelihood of new DWI lesions greatly and the possible effect of choice of interventional techniques and medication on the risk of new DWI lesions must be emphasised. A recent review of cerebral protection described several studies reporting a higher prevalence of DWI lesions in patients treated with cerebral protection than in those treated without cerebral protection. Extensive comparison of type of protection strategy (proximal occlusion, distal occlusion, and filter type) did not lead to any convincing evidence of a superiority of one of these protection devices in terms of DWI lesions.[34] A meta-analysis investigating stent design found no differences in terms of major adverse events but found an increased risk of development of peri-procedural DWI lesions in patients treated with open cell stenting.[40] Administration of additional pre-procedural anticoagulants and additional lipid lowering therapy may be protective for development of new DWI lesions.[35,36,41] Another topic of interest is procedural timing in symptomatic patients.[37] As cerebrovascular events are more likely to occur in patients with unstable plaque, one could rationalise that timing of the procedure in symptomatic patients may influence the chance of dislodgement of plaque debris and therefore new DWI lesions, in line with research suggesting increased stroke risk after very urgent CEA.[38] Future research on intervention timing should incorporate presence of DWI lesions as one of the secondary outcome measures.

Limitations

Most of the included studies were retrospective or prospective cohort studies in which the reason for selection for either one of the interventions (CEA or CAS) varied and may have been based on patient characteristics such as age and comorbidities or the physician's preference, introducing selection bias. To account for inherit differences no direct comparisons between the groups were made. Future research should focus on identifying risk factors for DWI lesions after both CEA and CAS in patients with comparable characteristics.

There's a wide heterogeneity in the investigated parameters, even within one type of predictive category. Few studies investigated the same parameter using consistent imaging modalities when evaluating for example plaque instability or cerebral haemodynamics. Although both of these investigated categories appear promising tools for identification of patients at risk of developing new DWI lesions, one specific instrument could not be selected for risk assessment for heterogeneous data collection and quantifying the risk. Moreover, symptomatic and asymptomatic patients could not be analysed separately as these data were generally not provided by the included studies. As the optimal treatment strategy for asymptomatic patients has yet to be determined, assessment of predictive parameters for DWI lesions in this specific category could be especially helpful. Future research should focus on development of a risk prediction model to assist decision making on type of revascularisation.

Included studies used 1.5 T, 3 T, or a mix of both MR field strengths. A previous study has shown differences in DWI lesion detection rates after CEA/CAS of the carotid artery between field strengths.[3] As most studies used only one type of field strength, this is not likely to have caused a bias in the results of the individual studies. Reasonably, studies using 1.5 T may have underreported silent ischaemic lesions, although pooling of studies based on MRI field strength did not result in a lower prevalence of DWI lesions in these studies than studies using 3 T MRI.

The majority of studies used the presence of new DWI lesions as their primary endpoint; however, some mentioned DWI only as a secondary outcome measure. These studies were likely to be underpowered to detect a statistically significant difference in DWI lesions for the investigated feature. In particular CEA studies in which the prevalence of DWI is lower may have suffered from this statistical problem. Pooling of data by performing an individual patient data meta-analysis may offer a solution to this problem; unfortunately this was not feasible due to the large heterogeneity of the investigated predictive features.

CONCLUSION

Risk factors associated with the development of new DWI lesions after carotid stenting or endarterectomy are heterogeneous. For CEA patients, assessment of symptom status, pre-procedural cerebral haemodynamics, and inflammatory parameters may help to identify those at risk of new DWI lesions. In CAS patients, age and imaging of plaque characteristics and anatomy of supra-aortic arteries provide information on susceptibility to new DWI lesions. These predictive features may assist in risk assessment to determine the indication for and optimal type of treatment being either medical intervention, carotid artery stenting, or endarterectomy as revascularisation strategy.

CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2019.04.016.

REFERENCES

1 Schnaudigel S, Gröschel K, Pilgram SM, Kastrup A. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke* 2008;**39**:1911–9.
2 Gensicke H, Zumbrunn T, Jongen LM, Nederkoorn PJ, MacDonald S, Gaines PA, et al. Characteristics of ischemic brain lesions after stenting or endarterectomy for symptomatic carotid artery stenosis: results from the international carotid stenting study-magnetic resonance imaging substudy. *Stroke* 2013;**44**:80–6.
3 Bonati LH, Jongen LM, Haller S, Flach HZ, Dobson J, Nederkoorn PJ, et al. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). *Lancet Neurol* 2010;**9**:353–62.
4 Gensicke H, van der Worp HB, Nederkoorn PJ, Macdonald S, Gaines PA, Van Der Lugt A, et al. Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk. *J Am Coll Cardiol* 2015;**65**:521–9.
5 Wolf O, Heider P, Heinz M, Poppert H, Schmidt-Thieme T, Sander D, et al. Frequency, clinical significance and course of cerebral ischemic events after carotid endarterectomy evaluated by serial diffusion weighted imaging. *Eur J Vasc Endovasc Surg* 2004;**27**:167–71.
6 Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol* 2009;**8**:1006–18.
7 Gray WA. Flights from wonder: the search for meaning in diffusion-weighted brain lesions. *J Am Coll Cardiol* 2015;**65**:530–2.
8 Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch Neurol* 1998;**55**:1475–82.
9 Moher D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred reporting Items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;**6**:1–6.
10 Ottawa Hospital Research. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses.
11 Higgins J, Altman D, Gotzsche P, Juni P, Moher D, Oxman AD. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;**343**:d5928.
12 Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. *J Epidemiol Commun Health* 2013;**67**:974–8.
13 Lee C-Y, Kim H-W, Kim HR, Kim J-H, Seo J-H. Isolated central retinal artery occlusion (CRAO) without other thromboembolic event after carotid artery stenting (CAS). *Interv Neuroradiol* 2016;**22**:24.
14 Bijuklic K, Wandler A, Varnakov Y, Tuebler T, Schofer J. Risk factors for cerebral embolization after carotid artery stenting with embolic protection: a diffusion-weighted magnetic resonance imaging study in 837 consecutive patients. *Circ Cardiovasc Interv* 2013 Jun;**6**:311–6.
15 Ichinose N, Hama S, Tsuji T, Soh Z, Hayashi H, Kiura Y, et al. Predicting ischemic stroke after carotid artery stenting based on proximal calcification and the jellyfish sign. *J Neurosurg* 2017 Jul;**128**(5):1280–8.
16 Tanemura H, Maeda M, Ichikawa N, Miura Y, Umeda Y, Hatazaki S, et al. High-risk plaque for carotid artery stenting evaluated with 3-dimensional T1-weighted gradient echo sequence. *Stroke* 2013 Jan;**44**:105–10.
17 Lokuge K, de Waard DD, Halliday A, Gray A, Bulbulia R, Mihaylova B. Meta-analysis of the procedural risks of carotid endarterectomy and carotid artery stenting over time. *Br J Surg* 2018;**105**:26–36.
18 Gwon JG, Kwon TW, Cho YP, Kang DW, Han Y, Noh M. Analysis of risk factors for cerebral microinfarcts after carotid endarterectomy and the relevance of delayed cerebral infarction. *J Clin Neurol* 2017 Jan;**13**:32–7.
19 Lee E-J, Cho Y-P, Lee S-H, Lee JS, Nam HJ, Kim BJ, et al. Hemodynamic tandem intracranial lesions on magnetic resonance angiography in patients undergoing carotid endarterectomy. *J Am Heart Assoc* 2016 Oct;**5**(10):e004153.
20 Oikawa K, Ogasawara K, Saito H, Yoshida K, Saura H, Sato Y, et al. Combined measurement of cerebral and cerebellar blood flow on preoperative brain perfusion SPECT imaging predicts development of new cerebral ischemic events after endarterectomy for symptomatic unilateral cervical carotid stenosis. *Clin Nucl Med* 2013 Dec;**38**:957–61.
21 Sato Y, Ogasawara K, Kuroda H, Suzuki T, Chida K, Fujiwara S, et al. Preoperative central benzodiazepine receptor binding potential and cerebral blood flow images on SPECT predict development of new cerebral ischemic events and cerebral hyperperfusion after carotid endarterectomy. *J Nucl Med* 2011 Sep;**52**:1400–7.
22 Suzuki T, Ogasawara K, Hirooka R, Sasaki M, Kobayashi M, Ishigaki D, et al. Preoperative single-slab 3D time-of-flight magnetic resonance angiography predicts development of new cerebral ischemic events after carotid endarterectomy. Clinical article. *J Neurosurg* 2009 Jul;**111**:141–6.
23 Heider P, Poppert H, Wolf O, Liebig T, Pelisek J, Schuster T, et al. Fibrinogen and high-sensitive C-reactive protein as serologic predictors for perioperative cerebral microembolic lesions after carotid endarterectomy. *J Vasc Surg* 2007 Sep;**46**:449–54.
24 Rerkasem K, Shearman CP, Williams JA, Morris GE, Phillips MJ, Calder PC, et al. C-reactive protein is elevated in symptomatic compared with asymptomatic patients with carotid artery disease. *Eur J Vasc Endovasc Surg* 2002;**23**:505–9.
25 Voeks JH, Howard G, Roubin GS, Malas MB, Cohen DJ, Sternbergh WC, et al. Age and outcomes after carotid stenting and endarterectomy: the carotid revascularization endarterectomy versus stenting trial. *Stroke* 2011;**42**:3484–90.
26 Howard G, Roubin GS, Jansen O, Hendrikse J, Halliday A, Fraedrich G, et al. Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. *Lancet* 2016;**387**:1305–11.
27 Van Lammeren GW, Reichmann BL, Moll FL, Bots ML, De Kleijn DPV, De Vries JPPM, et al. Atherosclerotic plaque vulnerability as an explanation for the increased risk of stroke in elderly undergoing carotid artery stenting. *Stroke* 2011;**42**:2550–5.
28 Gupta A, Baradaran H, Schweitzer AD, Kamel H, Pandya A, Delgado D, et al. Carotid plaque MRI and stroke risk: a systematic review and meta-analysis. *Stroke* 2013;**44**:3071–7.
29 Sakamoto S, Kiura Y, Okazaki T, Shinagawa K, Ishii D, Ichinose N, et al. Carotid artery stenting for vulnerable plaques on MR angiography and ultrasonography: utility of dual protection and blood aspiration method. *J Neurointerv Surg* 2016 Oct;**8**:1011–5.
30 Naggara O, Touzé E, Beyssen B, Trinquart L, Chatellier G, Meder JF, et al. Anatomical and technical factors associated with stroke or death during carotid angioplasty and stenting: results from the endarterectomy versus angioplasty in patients with symptomatic severe carotid stenosis (EVA-3S) trial and systematic review. *Stroke* 2011;**42**:380–8.
31 Müller M, Von Hessling Van Der Lugt A, Doig D, Nederkoorn PJ, Macdonald S, Lyrer PA, et al. The risk of cerebral ischaemia in carotid artery stenting is associated with vascular anatomy - results from the ICSS-MRI substudy. *Cerebrovasc Dis* 2014;**37**:349.
32 Kuliha M, Roubec M, Procházka V, Jonszta T, Hrbáč T, Havelka J, et al. Randomized clinical trial comparing neurological outcomes after carotid endarterectomy or stenting. *Br J Surg* 2015;**102**:194–201.
33 Yamada R, Guimaraes M, Adams J, Schonholz C. New technologies for CAS that might overcome the burden of microembolization. *J Cardiovasc Surg (Torino)* 2015;**56**:859–65.
34 Vos JA. Evidence overview: benefit of cerebral protection devices during carotid artery stenting. *J Cardiovasc Surg (Torino)* 2017;**58**:170–7.
35 Patti G, Tomai F, Melfi R, Ricottini E, Macri M, Sedati P, et al. Strategies of clopidogrel load and atorvastatin reload to prevent

ischemic cerebral events in patients undergoing protected carotid stenting. Results of the randomized ARMYDA-9 CAROTID (Clopidogrel and Atorvastatin Treatment during Carotid Artery Stenting) study. *J Am Coll Cardiol* 2013;**61**:1379–87.
36 Mizobe T, Nakamura M, Motooka Y, Ashida N, Sugihara M. Impact of additional lipid-lowering therapy on new ischemic lesions of diffusion-weighted imaging in carotid artery stenting. *J Stroke Cerebrovasc Dis* 2018;**27**:764–70.
37 Meershoek AJA, de Borst GJ. Timing of carotid intervention. *Br J Surg* 2018;**105**:1231–3.
38 Strömberg S, Gelin J, Österberg T, Bergström GML, Karlström L, Österberg K. Very urgent carotid endarterectomy confers increased procedural risk. *Stroke* 2012;**43**:1331–5.
39 De Borst GJ, Naylor AR. In the end, it all comes down to the beginning! *Eur J Vasc Endovasc Surg* 2015;**50**:271–2.
40 de Vries EE, Meershoek AJA, Vonken EJ, den Ruijter HM, van den Berg JC, de Borst GJ, et al. Effect of stent design on clinical and radiological outcomes of carotid artery stenting: a meta-analysis. *J Vasc Surg.* 2019;**69**(6):1952–61.
41 Nakagawa I, Park HS, Wada T, Yokoyama S, Yamada S, Motoyama Y, et al. Efficacy of cilostazol-based dual antiplatelet treatment in patients undergoing carotid artery stenting. *Neurol Res* 2017;**39**:695–701.
42 Abiko M, Sakamoto S, Ochiai J, Yamada N, Kuroki K, Kurisu K. Applicability of carotid artery stenting for patients 80 years or older: a single-center experience. *World Neurosurg* 2018 Nov:e323–7.
43 Akpinar MB, Sahin V, Sahin N, Abacilar AF, Kiris I, Uyar IS, et al. Previous chronic cerebral infarction is predictive for new cerebral ischemia after carotid endarterectomy. *J Cardiothorac Surg* 2015 Nov:141.
44 Aso K, Ogasawara K, Sasaki M, Kobayashi M, Suga Y, Chida K, et al. Preoperative cerebrovascular reactivity to acetazolamide measured by brain perfusion SPECT predicts development of cerebral ischemic lesions caused by microemboli during carotid endarterectomy. *Eur J Nucl Med Mol Imaging* 2009 Feb:294–301.
45 Burow A, Lyrer PA, Nederkoorn PJ, Brown MM, Sztajzel R, Engelter ST, et al. Echographic risk index and cerebral ischemic brain lesions in patients randomized to stenting versus endarterectomy for symptomatic carotid artery stenosis. *Ultraschall Med* 2014 Jun:267–72.
46 Chung GH, Jeong JY, Kwak HS, Hwang SB. Associations between Cerebral Embolism and Carotid Intraplaque Hemorrhage during Protected Carotid Artery Stenting. *AJNR Am J Neuroradiol* 2016 Apr:686–91.
47 Groschel K, Ernemann U, Schnaudigel S, Wasser K, Nagele T, Kastrup A. A risk score to predict ischemic lesions after protected carotid artery stenting. *J Neurol Sci* 2008 Oct:112–5.
48 Gunduz Y, Akdemir R, Ayhan LT, Keser N. Can Doppler flow parameters of carotid stenosis predict the occurrence of new ischemic brain lesions detected by diffusion-weighted MR imaging after filter-protected internal carotid artery stenting? *AJNR Am J Neuroradiol* 2014 Apr:760–5.
49 Huang K-L, Chang Y-J, Chang C-H, Chang T-Y, Liu C-H, Hsieh I-C, et al. Impact of coexisting coronary artery disease on the occurrence of cerebral ischemic lesions after carotid stenting. *PLoS One* 2014. e94280.
50 Jongen LM, Hendrikse J, Moll FL, Mali WPTM, van der Worp HB. Cerebral perfusion affects the risk of ischemia during carotid artery stenting. *Cerebrovasc Dis* 2010:538–45.
51 Kashiwazaki D, Kuwayama N, Akioka N, Noguchi K, Kuroda S, D. K., et al. Carotid plaque with expansive arterial remodeling is a risk factor for ischemic complication following carotid artery stenting. *Acta Neurochir (Wien)* 2017 Jul:1299–304.
52 Kastrup A, Groschel K, Schnaudigel S, Nagele T, Schmidt F, Ernemann U. Target lesion ulceration and arch calcification are associated with increased incidence of carotid stenting-associated ischemic lesions in octogenarians. *J Vasc Surg* 2008 Jan:88–95.
53 Koyanagi M, Yoshida K, Kurosaki Y, Sadamasa N, Narumi O, Sato T, et al. Reduced cerebrovascular reserve is associated with an increased risk of postoperative ischemic lesions during carotid artery stenting. *J Neurointerv Surg* 2016 Jun:576–80.
54 Krapf H, Nagele T, Kastrup A, Buhring U, Gronewaller E, Skalej M, et al. Risk factors for periprocedural complications in carotid artery stenting without filter protection: A serial diffusion-weighted MRI study. *J Neurol* 2006 Mar:364–71.
55 Lee JH, Suh BY. Risk factor analysis of new brain lesions associated with carotid endarterectmy. *Ann Surg Treat Res* 2014 Jan:39–44.
56 Lin C, Tang X, Shi Z, Zhang L, Yan D, Niu C, et al. Serum tumor necrosis factor α levels are associated with new ischemic brain lesions after carotid artery stenting. *J Vasc Surg* 2018:771–8.
57 Maggio P, Altamura C, Lupoi D, Paolucci M, Altavilla R, Tibuzzi F, et al. The Role of White Matter Damage in the Risk of Periprocedural Diffusion-Weighted Lesions after Carotid Artery Stenting. *Cerebrovasc Dis Extra* 2017 Jan:1–8.
58 Maruyama D, Fukuda K, Kataoka H, Morita Y, Nishimura K, Kawamura Y, et al. Evaluation of carotid artery outward remodeling by T1-weighted magnetic resonance imaging in carotid endarterectomy and stenting. *J Vasc Surg* 2015 Jun:1464–71. e1.
59 Matsukawa H, Fujii M, Uemura A, Suzuki K, Yamamoto D, Takahashi O, et al. Pathology of embolic debris in carotid artery stenting. *Acta Neurol Scand* 2015 Apr:197–202.
60 Muller MD, Ahlhelm FJ, von Hessling A, Doig D, Nederkoorn PJ, Macdonald S, et al. Vascular Anatomy Predicts the Risk of Cerebral Ischemia in Patients Randomized to Carotid Stenting Versus Endarterectomy. *Stroke* 2017 May:1285–92.
61 Pini R, Faggioli G, Fittipaldi S, Pasquinelli G, Tonon C, Beltrandi E, et al. Inflammatory mediators and cerebral embolism in carotid stenting: new markers of risk. *J Endovasc Ther* 2013 Oct:684–94.
62 Rosenkranz M, Thomalla G, Havemeister S, Wittkugel O, Cheng B, Krutzelmann A, et al. Older age and greater carotid intima-media thickness predict ischemic events associated with carotid-artery stenting. *Cerebrovasc Dis* 2010:567–72.
63 Russjan A, Goebell E, Havemeister S, Thomalla G, Cheng B, Beck C, et al. Length of stenosis predicts treatment related ischemic lesions after carotid artery stenting. *Cerebrovasc Dis* 2011:14.
64 Sfyroeras GS, Bessias N, Moulakakis KG, Lyra S, Kotsikoris I, Andrikopoulos V, et al. New cerebral ischemic lesions after carotid endarterectomy. *Ann Vasc Surg* 2013 Oct:883–7.
65 Song TJ, Suh SH, Min PK, Kim DJ, Kim BM, Heo JH, et al. The influence of anti-platelet resistance on the development of cerebral ischemic lesion after carotid artery stenting. *Yonsei Med J* 2013:288–94.
66 Stojanov D, Ilic M, Bosnjakovic P, Zivkovic M, Jolic S, Vukasinovic N, et al. New ischemic brain lesions on diffusion-weighted MRI after carotid artery stenting with filter protection: frequency and relationship with plaque morphology. *AJNR Am J Neuroradiol* 2012 Apr:708–14.
67 Takemoto K, Ueba T, Takano K, Abe H, Hirata Y, Higashi T, et al. Quantitative evaluation using the plaque/muscle ratio index panels predicts plaque type and risk of embolism in patients undergoing carotid artery stenting. *Clin Neurol Neurosurg* 2013 Aug:1298–303.
68 Tanabe J, Tanaka M, Kadooka K, Hadeishi H. Efficacy of high-resolution cone-beam CT in the evaluation of carotid atheromatous plaque. *J Neurointerv Surg* 2016 Mar:305–8.
69 Timaran CH, Rosero EB, Martinez AE, Ilarraza A, Modrall JG, Clagett GP. Atherosclerotic plaque composition assessed by virtual histology intravascular ultrasound and cerebral embolization after carotid stenting. *J Vasc Surg* 2010 Nov:1188–94.
70 Tulip HH, Rosero EB, Higuera AJ, Ilarraza A, Valentine RJ, Timaran CH. Cerebral embolization in asymptomatic versus symptomatic patients after carotid stenting. *J Vasc Surg* 2012 Dec:1579–84. discussion 1584.
71 Uchiyama N, Misaki K, Mohri M, Watanabe T, Hirota Y, Nakada M, et al. Association between carotid plaque composition assessed by multidetector computed tomography and cerebral embolism after carotid stenting. *Neuroradiology* 2012 May:487–93.

72 Varetto G, Gibello L, Faletti R, Gattuso A, Garneri P, Castagno C, et al. Contrast-enhanced ultrasound to predict the risk of microembolization during carotid artery stenting. *Radiol Med* 2015 Nov:1050–5.
73 Yamada K, Yoshimura S, Kawasaki M, Enomoto Y, Takano K, Asano T, et al. Prediction of silent ischemic lesions after carotid artery stenting using virtual histology intravascular ultrasound. *Cerebrovasc Dis* 2011:106–13.
74 Yamada K, Kawasaki M, Yoshimura S, Enomoto Y, Asano T, Minatoguchi S, et al. Prediction of silent ischemic lesions after carotid artery stenting using integrated backscatter ultrasound and magnetic resonance imaging. *Atherosclerosis* 2010 Jan:161–6.
75 Yoshimura S, Yamada K, Kawasaki M, Asano T, Kanematsu M, Takamatsu M, et al. High-intensity signal on time-of-flight magnetic resonance angiography indicates carotid plaques at high risk for cerebral embolism during stenting. *Stroke* 2011 Nov:3132–7.
76 Zhou W, Zareie R, Tedesco M, Gholibeikian S, Lane B, Hernandez-Boussard T, et al. Risk factors predictive of carotid artery stenting associated subclinical microemboli. *Int J Angiol* 2011:25–31.

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COUP D'OEIL

Pyoderma Gangrenosum After Common Femoral Artery Endarterectomy and Patch Plasty

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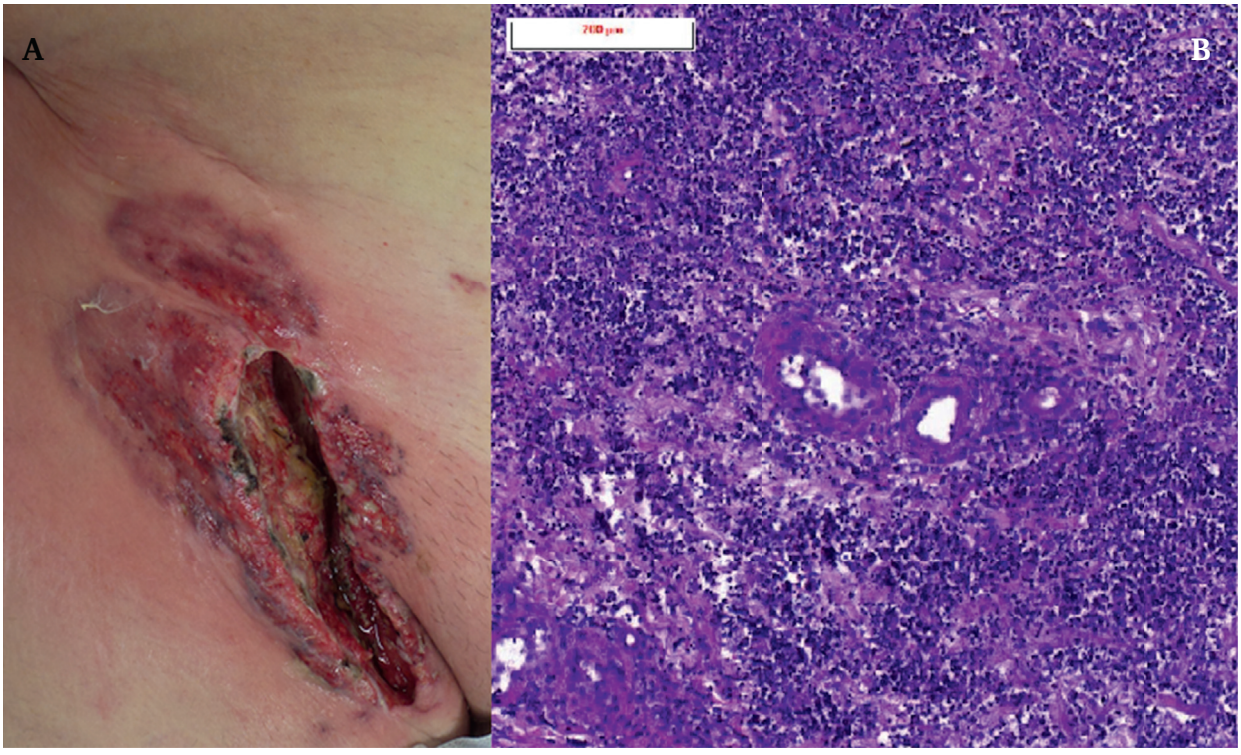

Right common femoral artery endarterectomy with bovine patch plasty was performed in an 81 year old man. Post-operatively the patient developed a fever and erythema around the wound; antibiotics were administered. Subsequently, the wound started to produce turbid exudate. Debridement was performed and negative-pressure wound therapy applied. This led to a dramatic deterioration of the wound edges (panel A). Biopsy of the edge of the lesion showed necrosis and a dense neutrophilic infiltrate also involving the blood vessels, compatible with pyoderma gangrenosum (panel B). Intra-operative cultures remained negative. Corticosteroids were initiated, which led to an important improvement of the wound. The wound healed by secondary intention.

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