Emboli detection to evaluate risk of stroke

Background:

Improved methods are required to identify patients with asymptomatic carotid stenosis at high risk for stroke. Whether surgery is beneficial for patients with asymptomatic carotid stenosis is controversial. Carotid endarterectomy clearly benefits patients with symptomatic severe stenosis (SCS), but the risk of stroke is so low for asymptomatic patients (ACS) that the number needed to treat is very high. Better methods of identifying patients who are likely to develop stroke would improve the risk-benefit ratio for carotid endarterectomy.

Literature:

Micro embolic signals (MES) detection in acute stroke by transcranial doppler (TCD)

Author	*M. Pradeep, M. Mazharudin, C. Ramakrishnan* KG Hospital & Post graduate Medical Institute, Coimbatore, India
Content/Summary	Micro emboli signal detection is one of the main applications of Transcranial Doppler (TCD) in stroke. MES are reported to be an independent risk factor for stroke. MES al- so helps in identifying the underlying pathophysiology of stroke. MES also helps in assessing the response to treatment **Aim of study:** To evaluate the yield of TCD in detecting MES, predictors for positive MES & recurrence of stroke. **Method:** 260 patients with stroke were evaluated with TCD over a period of 3 years from January 2012 to january 2015. TCD monitoring of MCA, ACA & PCA were done bilaterally for one hour. Positive MES TCD monitoring was defined by the presence of more than or equal to 1 MES on either hemisphere.
Comment	Study showed that that the presence of valvular heart disease and presence of multiple infarcts on neuro imaging are associated with positive MES on TCD emboli monitoring.
Doppler-device	Not known
Quantification	Patients with positive MES on TCD monitoring are twice at risk of stroke recurrence than patients with negative MES.

A novel method for transcranial Doppler microembolic signal monitoring at the vertebrobasilar junction in vertebral artery dissection patients.

Author	Yamaoka Y[1], Ichikawa Y, Kimura T, Sameshima T, Ochiai C, Morita A.
Content/Summary Abstract	**BACKGROUND:** Vertebral artery dissection (VAD) is one of the most important etiologies in young stroke patients. VAD causes ischemic stroke by embolism and transcranial Doppler (TCD) monitoring can detect microemboli originating from the dissection point as high intensity transient signals (HITS). We developed a simple but novel method of TCD monitoring at the vertebrobasilar junction in VAD patients. **METHODS:** We placed a Welder TCD headband upside down on the patient's head and rotated it by 90°. Then we fixed a pulsed-wave 2-MHz TCD probe to the headband and put it on the suboccipital paramedian area of the patient. With a patient in the lateral decubitus position, the vertebrobasilar junction was identified at a depth of approximately 80 mm. **RESULTS:** We examined 11 patients with VAD and detected HITS in 2 patients (18%). In 1 patient HITS disappeared after heparinization, and in the other patient HITS disappeared after treatment with aspirin. All of 9 HITS-negative patients and 1 of 2 HITS-positive patients experienced no ischemic recurrence during hospitalization.
Comment	**Authors** successfully detected HITS at the vertebrobasilar junction in VAD patients, which may lead not only to an appropriate choice of antithrombotic drugs but also to individual evaluation of early risk of ischemic recurrence.
Doppler-device	Viasys Healthcare, Madison, WI, USA
Quantification	This is a small study but it shows how a simple rotation of the probe holder enlarges the area for TCD monitoring. It confirms again that HITS can be used as a measure of effectiveness of different antithrombotic therapies.

Dual antiplatelets reduce microembolic signals in patients with transient ischemic attack and minor stroke: subgroup analysis of CLAIR study.

Author	Lau AY1, Zhao Y, Chen C, Leung TW, Fu J, Huang Y, Suwanwela NC, Han Z, Tan KS, Ratanakorn D, Markus HS, Wong KS; CLAIR Study Investigators.
Content/Summary Abstract	**BACKGROUND:** Short course of dual antiplatelet therapy for early secondary prevention is a promising treatment for patients with minor stroke or transient ischemic attack at high risk of recurrence. **METHODS:** We examined the efficacy and safety of dual antiplatelets in patients with transient ischemic attack or minor stroke, defined as National Institute of Health Stroke Scale scores 0-3, in a subgroup analysis of Clopidogrel plus aspirin versus Aspirin alone for Reducing embolization in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR) study. Microembolic signals on transcranial Doppler monitoring was used as surrogate marker for recurrent stroke risk. Patients with ≥1 microembolic signals at baseline were randomized to receive dual therapy (aspirin 75-160 mg daily and clopidogrel 300 mg day 1 then 75 mg daily) or monotherapy (aspirin 75-160 mg daily) for seven-days. **RESULT:** 30 received dual therapy and 35 received monotherapy. Mean onset-to-randomization was 2·3 days in dual therapy group and 3·2 days in monotherapy group (P = 0·03). At day 7, the proportion of patients with ≥1 microembolic signals was 9 of 29 patients in dual therapy group and 18 of 34 patients in monotherapy group (adjusted relative risk reduction 41·4%, 95% CI 29·8-51·1, P < 0·001). The median number of microembolic signals on day 7 was 0 in dual therapy group and 1·0 in monotherapy group (P = 0·046). No patients had intracranial or severe systemic hemorrhage.
Comment	Sixty-five of 100 patients recruited had transient ischemic attack or minor stroke
Doppler-device	Not known
Quantification	Early dual therapy with clopidogrel and aspirin reduces microembolic signals in patients with minor ischemic stroke or transient ischemic attack, without causing significant bleeding complications.

Literature:

Spontaneous preoperative microembolic signals detected with transcranial Doppler are associated with vulnerable carotid plaque characteristics.

Author	Van Lammeren GW[1], Van De Mortel RH, Visscher M, Pasterkamp G, De Borst GJ, Moll FL, Vink A, Tromp SC, De Vries JP.
Content/Summary Abstract	**AIM:** Carotid plaque composition is associated with ipsilateral cerebrovascular events. Among patients with carotid artery stenosis, presence of microembolic signals (MES) detected with transcranial Doppler (TCD) is associated with increased stroke risk. We aimed to investigate whether MES detected with TCD in the outpatient clinic among patients scheduled for carotid endarterectomy, was associated with underlying carotid plaque composition. **METHODS:** TCD was used to detect MES among 38 symptomatic patients scheduled for carotid endarterectomy. Measurements were performed for 30 minutes. Carotid plaques harvested during CEA were subjected to histopathological examination. Plaques from patients without spontaneous MES were compared with plaques from patients with ≥1 MES. **RESULT:** At least 1 MES was detected in 10/38 (26%) patients. Five of ten (50%) patients with spontaneous MES had lipid-rich plaques, compared with 5/28 (17.2%) plaques from patients without MES (P=0.048). Luminal thrombus was observed in 6/10 (60.0%) of plaques from patients with MES compared with 7/28 (25.0%) of plaques from patients without MES (P=0.045).
Comment	Median time between TCD and surgery was 4 days.
Doppler-device	Not known
Quantification	Spontaneous MES were detected in 26% of symptomatic patients scheduled for CEA and were associated with unstable carotid plaque characteristics. TCD might be a useful tool to help identify patients with vulnerable plaques.

The changes of the size of carotid arterial plaque during 10 years in acute stroke patients

Author	J.-H. Lee[1], S.-H. Hwang[2], E.-G. Kim[3], I.-S. Koh[4], S.-H. Suk[5], J.-H. Park[6] [1] Department of Neurology, National Health Insurance Service Ilsan Hospital, Goyang-si, South Korea [2] Department of Neurology, Kangnam Sungsim Hospital, Seoul, South Korea [3] Department of Neurology, Inje University Paik Hospital, Busan, South Korea [4] Department of Neurology, National Medical Center, Seoul, South Korea [5] Department of Neurology, Wonkwang University Sanbon Medical Center, Sanbon, South Korea [6] Department of Neurology, Sanggye Paik Hospital, Seoul, South
Content/Summary	**Background:** Carotid arterial stenosis becomes more common and important risk factor for stroke patients in Asian area.
Comment	Acute stroke patients with available carotid ultrasound, transcranial Doppler (TCD) ex- amination and ankle-brachial indexes (ABI) formed the analysis cohorts.
Doppler-device	Not known
Quantification	Among the acute stroke patients, the prevalence of carotid arterial stenosis tend to be increased during 10 years and more than a half of them have carotid arterial stenosis above moderate degree, and these patients tend to have higher burden of advanced atherosclerosis as evidenced by a higher prevalence of peripheral arterial occlusive disease.

Difficult differential diagnosis of intracranial occlusive disease: Clinical case

Author	*D. Jatužis, J. Valaikiene, L. Beliak* Vilnius University Hospital Santariskiu Clinics, Department of Neurology, Vilinus, Lithuania
Content/Summary	Authors present a clinical case of young women with TCD/TCCS findings of intracranial high-velocity flow signals compatible with intracranial severe stenotic disease. She presented on 2011 with sudden left hemiparesis and hemihypoesthesia, intention tremor and ataxia of left extremities which resolved spontaneously. Multiple TIA-like episodes of stereotypic neurological deficit recurred several times a day, with duration up to 1 hour, during the first week. TCD findings included high velocities and marked turbuence in right MCA, compatible with severe M1 stenosis, as well as microembolic signals 1-2 per minute. Cranial MRI showed acute cortical ischemic abnormalities in right F-P region. 4 years of follow up showed gradual progression of high-graded MCA M1 stenosis to complete occlusion. Patient did not have vascular risk factors, and only few transient episodes of left arm numbness recurred in 2012. Major efforts have been made to determine the etiopathogenesis of intracranial occlusive disease, including repeated TCD with HITS monitoring (no more HITS were detected in 2012-2014), TCCS, CTA, DSA, MRI, cardiac echo, blood tests for hypercoagulation conditions. Differential diagnosis included fibromuscular dysplasia, intracranial vasculitis, dissection, moya- moya syndrome.
Comment	TCD was used to detect HITS
Doppler-device	Not known
Quantification	

Optimizing protocols for risk prediction in asymptomatic carotid stenosis using embolic signal detection: the Asymptomatic Carotid Emboli Study.

Author	(Alice King, Martin Shipley, u. a., 2011)
Content/Summary	ES status on the 2 recordings was significantly associated (P<0.0001), but there was poor agreement between ES positivity on the 2 recordings (κ=0.266). For the primary outcome of ipsilateral stroke or transient ischemic attack, the use of 2 baseline recordings lasting 1 hour had greater predictive accuracy than either the first baseline recording alone (P=0.0005), a single 30-minute (P<0.0001) recording, or 2 recordings lasting 30 minutes (P<0.0001). For the outcome of ipsilateral stroke alone, two recordings lasting 1 hour had greater predictive accuracy when compared to all other recording protocols (all P<0.0001).
Comment	Of 477 patients, 467 had baseline recordings adequate for analysis; 77 of these had ES on 1 or both of the 2 recordings.
Doppler-device	various
Quantification	Two baseline recordings lasting 1 hour as used in Asymptomatic Carotid Emboli Study gave the best risk prediction.

Ultrasonic plaque echolucency and emboli signals predict stroke in asymptomatic carotid stenosis.

Author	(R Topakian u. a., 2011)
Content/Summary	The combination of ES detection and plaque morphology allows a greater prediction than either measure alone and identifies a high-risk group with an annual stroke risk of 8%, and a low-risk group with a risk of <1% per annum.
Comment	A total of 435 recruited subjects with ACS ≥70% had baseline ultrasound images and TCD data available. Subjects were prospectively followed up for 2 years.
Doppler-device	various
Quantification	TCD Emboli detection and TCCD of of carotid plaques allows risk stratification of stroke.

Silent cerebral events in asymptomatic carotid stenosis.

Author	(Jayasooriya u. a., 2011)
Content/Summary	A median of 28% of microemboli positive patients experienced a stroke or transient ischemic attack during follow-up compared with 2% of microemboli negative patients (P = .001). The same was true for the end point of stroke alone with a median of 10% of microemboli positive patients experiencing a stroke vs 1% of microemboli negative patients (P = .004)
Comment	Review. Fifty-eight full text articles met the inclusion criteria.
Doppler-device	none
Quantification	There is level 1 evidence for the use of TCD to detect microembolization as a risk stratification tool. However, this technique requires further investigation as a stroke prevention tool and would be complemented by improvements in carotid plaque imaging.

The role of transcranial Doppler embolic monitoring in the management of intracranial arterial stenosis.

Author	(Sebastian u. a., 2011)
Content/Summary	We report a case of IAS where TCD emboli monitoring proved useful in establishing the mechanism of stroke by being artery-to-artery emboli and guiding therapy based on the frequent symptoms and number of MES.
Comment	Case report
Doppler-device	Spencer
Quantification	Case reports a TCD guided therapy in a patient suffering intracerebral stenosis.

Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study.

Author	(Hugh S Markus u. a., 2010)
Content/Summary	The absolute annual risk of ipsilateral stroke or transient ischaemic attack between baseline and 2 years was 7.13% in patients with embolic signals and 3.04% in those without, and for ipsilateral stroke was 3.62% in patients with embolic signals and 0.70% in those without. The hazard ratio for the risk of ipsilateral stroke and transient ischaemic attack for patients who had embolic signals on the recording preceding the next 6-month follow-up compared with those who did not was 2.63 (95% CI 1.01-6.88; p=0.049), and for ipsilateral stroke alone the hazard ratio was 6.37 (1.59-25.57; p=0.009).
Comment	482 patients were recruited, of whom 467 had evaluable recordings.
Doppler-device	various
Quantification	Detection of asymptomatic embolisation on TCD can be used to identify patients with asymptomatic carotid stenosis who are at a higher risk of stroke and transient ischaemic attack, and also those with a low absolute stroke risk. Assessment of the presence of embolic signals on TCD might be useful in the selection of patients with asymptomatic carotid stenosis who are likely to benefit from endarterectomy.

Doppler embolic signals in cerebrovascular disease and prediction of stroke risk: a systematic review and meta-analysis.

Author	(Alice King und Hugh S Markus, 2009)
Content/Summary	For symptomatic carotid stenosis, ES predicted stroke alone (OR, 9.57; 95%CI, 1.54 to 59.38; P=0.02) and stroke/TIA (OR, 6.36; 95% CI, 2.90-13.96; P<0.00001). For asymptomatic carotid stenosis, ES predicted stroke alone (OR, 7.46; 95% CI, 2.24-24.89; P=0.001) and stroke/TIA (OR, 12.00; 95% CI, 2.43-59.34; P=0.002) but with heterogeneity (P=0.004). In acute stroke ES predicted stroke alone (OR, 2.44; 95% CI, 1.17-5.08; P=0.02) and stroke/TIA (OR, 3.71; 95% CI, 1.64-8.38; P=0.002). A high frequency of ES immediately after carotid endarterectomy predicted stroke alone (OR, 24.54; 95% CI, 7.88-76.43; P<0.00001) and stroke/TIA (OR, 32.04; 95% CI, 11.36-90.39; P<0.00001).
Comment	A systematic review and meta-analysis
Doppler-device	none
Quantification	ES predict stroke risk in acute stroke, symptomatic carotid stenosis, and postoperatively after carotid endarterectomy; in asymptomatic carotid stenosis, data are less robust. In these conditions ES may be useful in risk stratification and in assessing therapeutic efficacy. For other embolic sources, further prospective data are required.

Determinants of micro-embolic signals in patients with atherosclerotic plaques of the internal carotid artery.

Author	(Telman u. a., 2009)
Content/Summary	The degree of stenosis, ultrasonic characteristics of texture and the density of plaques were not found to be associated with the presence or quantity of MES. MESs are present significantly more often in stenosed, stroke-related carotid arteries as compared with TIA-related or asymptomatic arteries. Neither the ultrasonic characteristics nor the degree of stenosis were found to influence the presence or rate of MES.
Comment	
Doppler-device	Not known
Quantification	Emboli detection (ED) by TCD is independently necessary despite of carotid ultrasound to evaluate stroke risk because neither plaque characteristics nor grade of stenosis without ED can stratify stroke risk.

Microembolic signals and carotid plaque characteristics in patients with asymptomatic carotid stenosis.

Author	(Zhang u. a., 2009)
Content/Summary	MES were more frequently found in patients with irregular and/or heterogeneous plaques than in those with regular ($p = 0.028$) and/or homogeneous plaques ($p = 0.021$). The incidence of TIA/stroke occurred more frequently in patients with MES than those without MES ($p = 0.009$). Asymptomatic patients (with 50-99% carotid stenosis) with MES presented a significantly increased frequency of severe stenosis, with irregular and heterogeneous plaques.
Comment	Sixty-two asymptomatic patients with 50-99% carotid stenosis. The patients were followed for 1 year, and the incidence of transient ischemic attack (TIA)/stroke was studied.
Doppler-device	Not known
Quantification	Asymptomatic patients (with 50-99% carotid stenosis) with MES presented a significantly increased frequency of severe stenosis, with irregular and heterogeneous plaques.

Occurrence and clinical impact of microembolic signals (MES) in patients with chronic cardiac diseases and atheroaortic plaques--a systematic review.

Author	(Dittrich und Ringelstein, 2008)
Content/Summary	In all cardiac diseases there is a lack of large prospective studies allowing to reliably correlating MES with clinical events.
Comment	Reviewed the currently available literature about chronic cardiac diseases and atheroaortic plaques leading to MES apart from cardiosurgical procedures.
Doppler-device	none
Quantification	Compared to carotid artery disease, the current knowledge about the impact of cardiogenic MES on the patient's risk is sparse. This should encourage the clinical research in this promising field.

Prevalence and prognostic impact of microembolic signals in arterial sources of embolism. A systematic review of the literature.

Author	(Ritter u. a., 2008)
Content/Summary	MES were reported in 43% of 586 patients with symptomatic and in 10% of 1066 patients with asymptomatic carotid stenosis. Presence of one MES indicated an increased risk of future events [odds ratio (OR): **7.5,** 95% confidence interval (CI): 3.6-15.4, p<0.0001 for symptomatic, and OR: **13.4**, 95% CI: 6.5-27.4, p<0.0001 for asymptomatic disease). Data were insufficient to reliably predict future events in patients with intracranial stenosis, cervical artery dissection, and aortic embolism.
Comment	Review
Doppler-device	None
Quantification	MES are a frequent finding in varying sources of arterial brain embolism, MES detection is useful for risk stratification in patients with carotid stenosis.

Absence of microemboli on transcranial Doppler identifies low-risk patients with asymptomatic carotid stenosis.

Author	(Spence u. a., 2005)
Content/Summary	Our findings indicate that TCD- ACS (asymptomatic carotid stenosis) will not benefit from endarterectomy or stenting unless it can be done with a risk <1%; TCD+ may benefit as much as SCS (symptomatic severe stenosis) if their surgical risk is not higher. These findings suggest that ACS should be managed medically with delay of surgery or stenting until the occurrence of symptoms or emboli.
Comment	319 patients were studied, age (standard deviation) 69.68 (9.12) years; 32 (10%) had microemboli at baseline (TCD+)
Doppler-device	Nicolet TC 4040 Pioneer for the first 150 patients, and for the remainder, a PMD 100.
Quantification	TCD is an important tool in risk management of SCS.

Summary:

The Asymptomatic Carotid Emboli Study recently showed embolic signals (ES) detected by transcranial Doppler on 2 recordings that lasted 1-hour independently predict 2-year stroke risk. In this context the authors recommend two baseline recordings lasting 1 hour as the best method of stroke risk prediction.
Plaque morphology or grade of stenosis alone did not show any significance of stroke prediction. Due to this it is necessary to perform ED by TCD to evaluate if risk of stroke or risk of carotid surgery is more precarious.

Experts:

King
Markus

Literature

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