Letters to the Editor

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High Plasma Brain Natriuretic Peptide Level in Thromboembolism Patients Associated With Nonvalvular Atrial Fibrillation: Cause or Effect?

To the Editor:

We read with great interest the recent article by Shimizu et al entitle “High Plasma Brain Natriuretic Polypeptide Level as a Marker of Risk for Thromboembolism in Patients With Nonvalvular Atrial Fibrillation.” Although in this article the authors concluded that plasma brain natriuretic peptide (BNP) may be a useful marker to predict vulnerability to thromboembolism in patients with nonvalvular atrial fibrillation (AF), we have some reservations about the word predict or predictor used in this report.

The authors mentioned that there was a significant difference in plasma BNP levels between the group with an embolic event and the group with no embolic event (126±53 versus 84±45 ng/L) and that overall analysis of the continuous variables with multiple logistic regression analysis revealed that the plasma BNP level was an independent predictor of thromboembolic complication. However, it seems doubtful whether plasma BNP level may be a useful predictor of thromboembolic complication for reasons mentioned below; we believe there is some statistical relationship between the plasma BNP levels and the occurrence of the thromboembolic events in this study. If the blood sampling for BNP measurements had been performed before thromboembolic events in all the patients of the embolic event group, we would agree with the authors that plasma BNP level might be a useful predictor of thromboembolic complication. In this study, unfortunately, the blood sampling was performed before the events in only 3 of 11 patients who had a history of thromboembolic events and after the events in the other 8 patients.

BNP has been considered to be secreted mainly from the heart, especially the left ventricle2 or the left atrium.3 Recent evidence,4 however, showed that there was some immunoreactivity of BNP also through the brain, including the cerebral cortex, thalamus, cerebellum,pons, and hypothalamus, thus indicating that BNP secretion may be induced by pathological processes involving these regions. Actually, there has recently been increasing evidence that plasma BNP levels increase after subarachnoid hemorrhage,5 especially in patients with symptomatic cerebral vasospasm.6 In addition, Saper et al7 demonstrated that the internal carotid artery and the proximal portions of the middle and anterior cerebral and posterior communicating arteries were the most intensely innervated by BNP-immunoreactive fibers in the rat. These findings suggest that an ischemic insult to brains may also induce BNP secretion. In this study 7 of 11 patients who had a history of systemic thromboembolic events had a history of cerebral infarction, thus possibly leading to an increase of plasma BNP level. We therefore think that further prospective studies are required to assess the usefulness of measuring plasma BNP levels in detecting patients at high risk for thromboembolic complications in nonvalvular AF.


Response

We appreciate the interesting comments of Dr Fukui and his colleagues regarding our recent article.1 Previous investigations have shown that patients demonstrate an elevation of brain natriuretic polypeptide (BNP) several days after subarachnoid hemorrhage.2,3 We performed sampling using catheters in patients with nonvalvular atrial fibrillation (AF) and reported that the left atrium mainly secretes BNP in AF.4 On the other hand, the mechanism and source of BNP are not yet clarified in patients with subarachnoid hemorrhage. Patients with subarachnoid hemorrhage sometimes demonstrate cardiac damage, including serial changes in ECGs and wall motion abnormality.4,6 Some of these conditions could stimulate cardiac BNP secretion. In our study blood sampling for BNP assay was performed in an outpatient clinic at least 6 months after the onset of cerebral embolism (range, 6 months to 5 years). Moreover, plasma BNP levels in the patient group with cerebral infarction (n=7) were 121±53 ng/L. This is not statistically different, however, from that in the group with other arterial embolism (120±45 ng/L; n=6). Taken together, we think it is unlikely that BNP is secreted from the brain in these patients with chronic healed cerebral infarction.

We used a logistic regression model for data analysis. This method is usable in a clinical investigation designed to retrospectively detect factor(s) predicting a certain dichotomous variable.7 We therefore can state that “BNP predicts thromboembolism.” We hope that the clinical usefulness of BNP in predicting the risk of arterial embolism is verified by a prospectively designed study in a larger patient population with nonvalvular AF.

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Cardiac Enzyme Elevations After Stroke: The Importance of Specificity

To the Editor:

We read with great interest the recent article by Ay et al.1 examining cardiac enzyme levels after stroke. The authors are to be commended for drawing attention to the seldom-recognized cardiac complications of stroke. In this study, levels of troponin T, a very specific marker of myocardial damage, were measured in 32 acute hemispheric stroke patients. As there were no significant elevations in troponin T, even in patients with increased serum creatine kinase–MB (CK-MB) levels, it was concluded that the latter was not cardiac in origin.

Cardiac sequelae including myocytolysis, serum enzyme elevations, and arrhythmias are known to develop in a portion of stroke patients. There is a great deal of clinical and experimental evidence that cardiac changes in stroke result from excessive sympathetic nervous activity secondary to insular cortical damage.2–6 It is unclear whether the insula was included, and if so to what extent, in the infarcts of the present cohort. As has been previously reported, the current study demonstrated elevated CK-MB levels in a number of patients.7 Unlike previous investigations, however, this study did not correlate increases in CK-MB with measures of sympathetic nervous activity.8 Although CK-MB rises in the current report appear to have a noncardiac source, this may not be the case in all patients with enzyme elevations. Those patients in whom sympathetic tone is perturbed may in fact develop specific cardiac enzyme changes.

The ultimate clinical goal is the identification of those patients at risk for autonomic and cardiac disturbances after stroke. Future studies may be aided by stratification of patients according to other factors thought to be important in the pathogenesis of poststroke autonomic changes, including age, right hemispheric involvement, and premorbid blood pressure.5,6,9 In addition, correlation of cardiac enzyme increases with other indices of altered autonomic activity including changes in diurnal blood pressure variation, heart rate variability, or QTc interval may also assist in the identification of those patients at risk for neurogenic cardiac damage.10,11

This study assessed the heart with a more specific serological marker than has previously been reported. Importantly, it has revealed that CK-MB elevations are not always related to the heart. The same degree of specificity may need to be applied to the neurological condition of the patients to definitively conclude that enzyme elevations are never cardiac in origin. Thus, in the future, troponin T levels should be correlated with both insular cortical lesions and serum catecholamine levels.

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Response

We thank Drs Butcher and Parsons for their interest in our article. In the referred study,1 we serially determined cardiac enzyme levels including troponin T and CK-MB from day 1 to day 5 of stroke in 32 consecutive patients, 24 of whom had large middle cerebral artery territory infarctions, also including the insula. The study outlined a specific signature of cardiac enzyme changes, “normal troponin T along with elevated CK-MB.” Given that troponin T is a more sensitive and specific marker for minor myocardial injury, our results led us to two clinically important conclusions. First, CK-MB elevations after stroke are not cardiac in origin, and second, CK-MB falsely increases after stroke. The latter might be especially important for the diagnosis of acute coronary syndromes occurring within the acute phase of stroke. This is not a rare event and can occur in up to 9% of all stroke patients.2

Neurogenic influence on the heart is a well-known phenomenon with pathological proof of myocytolysis and electrophysiological proof of cardiac conduction abnormalities. The third proof, however, specific enzyme changes (subtle and gradual CK-MB elevations), is now in question. Indeed, the evidence linking human cerebral lesions to CK-MB elevations from a cardiac source is not concrete. Previous novel studies introducing CK-MB elevations after human cerebral injury fail to provide any direct proof of the heart as the cause of CK-MB elevations3–5; autonomic perturbations and elevated systemic catecholamine levels might have used sources other than the heart to cause the CK-MB elevations observed in these studies. The authors raise the issue that cardiac contribution to the CK-MB elevations observed in our patients (34% of all stroke patients) might still have occurred, especially in those with infarctions in the high-risk brain regions for myocardial injury. This assumption requires that underlying myocardial mechanisms that mediate troponin T release differ from those that mediate CK-MB release. Thus, neurogenic influences could increase CK-MB levels without altering troponin T. To our knowledge, there are no data compatible with this. In contrast, troponin T has been
shown to be superior to CK-MB in both ischemic and nonischemic modes of myocardial injury.\(^6,7\) It seems more likely that if ever a cardiac contribution to the CK-MB elevations occurs, then troponin-T should also increase.

It is often problematic to identify the cause of cardiac perturbations and sudden deaths observed in patients with stroke. A concomitant coronary artery disease complicated by a coincidental plaque rupture triggered by stroke-related factors might be a cause. An accurate differentiation between the neurogenic and cardiogenic influences through the use of a serologic marker is the ultimate goal. Our study solves a piece of the puzzle by showing that CK-MB is not appropriate for this role. Drs Butcher and Parsons have delicately outlined the direction of future research in this field. While concurring with all, we should like to add that studies examining other cardiac-specific enzymes such as troponin I are also needed. Furthermore, these studies should be tailored with the capability to correlate cardiac enzyme levels with a more properly defined gold standard for neurogenic cardiac injury. Finally, they should not only enroll patients with isolated insular lesions, but also investigate unselected patients with various infarction patterns because the clinical importance of their results should have an impact in more general stroke populations.

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"Spontaneous" Cervical Arterial Dissection

To the Editor:
The editorial on “spontaneous” cervical arterial dissection (CAD) by Brandt and Grond-Ginsbach\(^1\) was an interesting and informed review of a subject that in the past has received inappropriately little attention, considering that CAD represents possibly the most common cause of ischemic stroke in persons below 45 years of age. However, the heavy emphasis on constitutional and genetic factors could prove misleading, and there is no conclusive evidence that such factors play a major role in CAD.

The diagnosis of “spontaneous” dissection is entirely dependent on history, and retrospectively reviewing patient’s medical charts is unlikely to accurately reflect the events occurring at the time of dissection. In a current study of this topic by the Canadian Stroke Consortium, dissections were initially diagnosed as spontaneous in patients doing push-ups or lifting heavy weights and engaged in other activities where violent or trivial neck movements were involved. The moment of arterial dissection is easily determined because neck pain occurs in most cases (82% in our series) at the moment of dissection, but unless patients are carefully questioned this factor is easily overlooked.

True, as the authors state, chiropractic maneuvers produce CAD only in a minority of cases,\(^2\) but they were responsible for 42 of 178 (24%) in our series, so this cause cannot be dismissed as a rare occurrence.

The jury is still out regarding the role of homocysteine in stroke, the usual relationship being an acceleration of atherosclerosis, so its role in CAD must still remain tentative and uncertain.\(^3\) Only a minority of the patients in our series had demonstrated abnormalities such as fibromuscular dysplasia on angiogram (15%), although histopathology may prove more sensitive.\(^4\) However, only a tiny minority of patients have a family history of dissection. There is clearly a spectrum of trauma versus a genetic factor as the causal agent for dissection, but in most cases trauma, severe in a minority of cases and trivial in many, seems to play a major role.

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Response
We thank Dr Norris and colleagues for their comments on our editorial on spontaneous cervical arterial dissections (sCAD). Our finding of electron microscopic connective tissue aberrations in the majority of skin biopsies from patients with sCAD, but not in skin biopsies from healthy control subjects,\(^1\) suggests that the majority of patients have a predisposition for dissection. Moreover, we recently demonstrated in some families from patients with sCAD that the connective tissue aberrations are inherited and follow an autosomal dominant pattern.\(^2\) These findings show that genetic factors do play a role in the development of sCAD at least in a subgroup of patients.

We agree with Dr Norris and colleagues that constitutional and genetic factors alone do not sufficiently explain why sCAD occurs at a certain moment and in typical locations.\(^3\) Furthermore, only very few patients have a family history of dissection. It is an important finding of the Canadian Stroke Consortium that many dissections that were initially diagnosed as “spontaneous” were in fact triggered by minor or severe injury that was overlooked in earlier records. This underlines that mechanical stress can indeed be an important (co-) factor in the etiology of sCAD. In our first prospective series, however, with inclusion of sCAD patients only within 4 weeks after the event and the
history very carefully taken, in 12 of 25 (48%) of the patients no possible trigger movement at all could be found. 4

We do not believe in an opposition between genetic factors on one side and trauma or injury on the other. Dissection is probably in most cases the outcome of a complex interplay of genetic and environmental factors. 5 Severe trauma alone can lead to cerebral artery occlusions 6 and mechanical trauma might even be a triggering factor for the development of most dissections. However, the finding of preceding trivial trauma in the majority of patients does not rule out the possible importance of constitutional and genetic factors. In fact, trivial trauma is a common event, but dissections are rare; and similarly most of a patient’s relatives with a connective tissue phenotype do not develop dissections. 3

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Multimodal CT Imaging in Acute Stroke

To the Editor:

Kilpatrick et al 1 retrospectively studied the prospective value of unenhanced CT, CT angiography (CTA), and xenon-enhanced perfusion CT (pCT) in acute stroke on the incidence of infarction on follow-up CT and on discharge disposition. To my knowledge, this is the first observation supporting the view that the assessment of arterial obstruction with CTA could be used as a surrogate for the measurement of cerebral blood flow (CBF). Of 10 patients with occlusions of the internal carotid artery or middle cerebral artery (MCA) and no infarctions on baseline CT could not be discharged home (positive predictive value [PPV] = 90% [95% confidence interval = 60% to 98%]; specificity = 92% [65% to 99%]) compared with 9 of 11 patients with compromised CBF < 30 mL/100 g per minute (PPV = 82% [52% to 95%]; specificity = 83% [55% to 95%]). The authors concluded from their observations that the combination of pCT and CTA in conjunction with CT is more capable of predicting new infarction and discharge disposition than is the admission National Institutes of Health Stroke Scale (NIHSS) score plus CT. Of 19 patients were studied between 6 and 24 hours. The remarkable finding of this relatively small study was that statistically significant improvements in the ability to predict both discharge diagnosis and the occurrence of cortical infarction was provided by the addition of CT angiography or the CBF assessment. Unfortunately, too few patients were available to assess the possible additive insights gained by integrating vascular anatomy and quantitative CBF.

Dr von Kummer was correct in identifying 2 typographical errors in Table 2, but it should be noted that the statistical assessments reported in the article utilized the correct data set and are therefore valid. Dr von Kummer’s decision to perform an assessment of the positive predictive value on this relatively small data set, first with the erroneous tabular data and then with his assessment of the corrected data, is interesting. He rightfully points out that strong statements about the predictive value of the type of data we have assessed will require larger prospective trials.

Dr von Kummer was appropriately concerned because our analysis discussed only cortical infarction without distinguishing the role of infarctions of the basal ganglia. From a reexamination of the films it is apparent that basal ganglion infarction was not a late occurrence but, when present, was there from the time of the initial CT study. Thus, the cortical mantle appears to have been appropriately defined as the territory that may continue to be at increased ischemic risk. Clearly the viability of the cortical MCA territory has an impact on clinical outcome.

The significant occurrence of “no cortical MCA occlusion, no cortical infarction and reversible levels of flow” well beyond 3 hours after occlusion we believe remains the major contribution of this article. Combining three CT-based data sets, not least of which is the absence of CT evidence of cortical infarction, provides a useful basis for focusing efforts to expand the therapeutic window to a far larger group than we are able to treat with current treatment guidelines.

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Response

We would like to thank Dr von Kummer for his very thoughtful and meticulous review of our article, which examined the potential clinical insights gained by an initial ischemic stroke assessment consisting of a traditional clinical and CT assessment to which was added a CT angiogram and a xenon/CT CBF study. Thirty-one patients were studied between 0 and 6 hours from onset and 19 patients were studied between 6 and 24 hours. The remarkable finding of this relatively small study was that statistically significant improvements in the ability to predict both discharge diagnosis and the occurrence of cortical infarction was provided by the addition of CT angiography or the CBF assessment. Unfortunately, too few patients were available to assess the possible additive insights gained by integrating vascular anatomy and quantitative CBF.

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Aspirin Versus Low-Molecular-Weight Heparin for Ischemic Stroke in Children: An Unanswered Question

To the Editor:

We read with interest the article entitled “Aspirin Versus Low-Dose Low-Molecular-Weight Heparin: Antithrombotic Therapy in Pediatric Ischemic Stroke Patients: A Prospective Follow-Up Study.” As addressed by the authors, there is scant evidence to guide the treatment of children with stroke. Thus, the authors have contributed important and significant knowledge regarding the treatment of pediatric stroke. This includes valuable information on the safety and feasibility of administering aspirin or low-molecular-weight heparin (LMWH) in a large number of children with stroke. However, the design and results of the present study cannot substantiate the following conclusion: “This prospective multicenter follow-up study has provided evidence that low-dose LMWH is not superior to aspirin and vice versa in preventing recurrent stroke . . .” Because the treatment was assigned by multiple treating physicians and was not prospectively standardized, it is possible that patients deemed to have an increased risk of recurrence were treated with LMWH and low-risk patients were treated with aspirin (or vice versa). Although these shortcomings are addressed in the article, they are not reflected in the conclusions.

Readers should be aware of the fact that low-dose LMWH (at “prophylactic” doses) was used in the study, as has been clearly stated by the authors. Therapeutic doses of LMWH may prevent stroke recurrence in children, as has been shown in adults with stroke, but without the risks of hemorrhagic complications seen in adults. This is because in children there is a lack of hypertension, atherosclerosis, and other age-related factors known to increase the risk of hemorrhagic complications. In our institutional consecutive cohort studies, 81 infants and children with arterial strokes have received therapeutic LMWH for initial treatment of arterial stroke, and there were no major bleeding complications (Dix et al2 and W. Ng, MHSc, et al, unpublished data, 2002).

A randomized, controlled trial is the appropriate trial design for assessing efficacy in prevention of stroke. Given the risk of recurrent arterial stroke or transient ischemic attacks in children of up to 45%, a trial assessing aspirin and other alternative treatments is both timely and necessary in children with stroke. Multicenter studies, such as Strater and colleagues have conducted, are critical to the feasibility of such trials.

In summary, we suggest that the conclusion in the article remains a speculation and that insufficient evidence has been provided to conclude that aspirin and low-dose LMWH are equivalent in the prevention of pediatric stroke.

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Response

We wish to thank our colleagues deVeber and Chan for their letter, discussing our data on secondary prevention of recurrence after childhood stroke. In their comments on our article, deVeber and Chan raised important issues.

The first issue relates to our conclusion, “This prospective multicenter follow-up study has provided evidence that low-dose LMWH is not superior to low-dose aspirin and vice versa in preventing recurrent stroke in white pediatric stroke patients.” The treatment options used in our study are only 2 chosen from a wide spectrum of possibilities. Only prophylactic dosage regimens were used in this survey, and aspirin and low-molecular-weight heparin (LMWH) seemed to be similarly effective without major side effects. We therefore completely agree with deVeber and Chan that because treatment modalities were assigned by multiple physicians and therapy was not prospectively standardized, the possibility that children deemed to have an increased risk were treated with LMWH and children with a lower risk for a second stroke were treated with aspirin or vice versa must be discussed. Despite the nonrandomization, discussed as a limitation in the present article, for the white German stroke patients treated in our study, we have shown that there was no statistical difference with respect to age, vascular territory involved, or presence of inherited thrombophilia in the 2 treatment arms. We have additionally discussed that our findings that no significant difference was observed between low-dose aspirin and low-dose LMWH with respect to stroke recurrence were based on a nonrandomized intervention or decision or choice of treatment modalities and therefore have the potential for considerable bias. The latter fact was clearly pointed out in the Discussion as a further limitation of the study. In addition, the conclusions drawn from the present cohort study, with all the limitations mentioned in the article, apply only to the German children treated here and are not transferable to stroke children of other countries or other ethnic populations. Thus, we kindly acknowledge that deVeber and Chan clarified this important issue.

The second issue relates to the dosage used for LMWH. The patients treated by us did not receive high doses of LMWH even in the acute phase of stroke onset, mainly because no safety data are available. Thus, the only possibility for us was to use a low-dose LMWH regimen as one drug for secondary long-term stroke prophylaxis. In addition, in contrast to the Canadian pediatric population, the majority of German children suffering from ischemic stroke or venous thromboembolic events received LMWH as a secondary prophylactic treatment beyond the acute thromboembolic onset in a low-dose regimen administered once daily only. This regimen beyond the acute phase in the cohort presented here was safe, without any bleeding complications within the entire study period. This may not be true for high-dose LMWH, however.2 In this prospective follow-up study including 29 children with ischemic stroke and an additional cohort with venous thrombosis, the event-free survival was no different between high- and low-dose LMWH.3 On the other hand, major bleeding complications were observed in 5% of patients in the high-dose LMWH group, including 1 intracerebral hemorrhage into an old ischemic stroke area in a child suffering from congenital heart disease. No such complication was mentioned for children treated with low-dose
It is therefore possible that major bleeding complications are more common in children treated with higher doses of LMWH, eg, 1.5 mg/kg every 12 hours. In the unpublished data cited by the authors, which was kindly offered to us by deVeber before publication (W. Ng, MD, et al, unpublished data, 2002), the Canadian group reports on 51 children who received high-dose LMWH therapeutically for a median of 11 days after acute stroke onset; no major bleeding complication was observed. In our German study, children with a 2-phase initial stroke onset were not included as “second stroke patients,” and recurrent stroke events were diagnosed at a median (range) of 5 (2 to 13) months after first stroke onset with antithrombotic medication still being administered. Interestingly, however, the recurrence rate reported in the Canadian cohort, eg, 1 second stroke event in 51 children (2%) treated with high-dose LMWH, is within the rates (with estimated 95% CIs) reported for recurrent stroke in our cohort (spontaneous stroke, 4.8% [3.7 to 20.2]; cardiac stroke, 10% [0.2 to 44.5]; vascular stroke, 16.7% [20 to 48.4]; infectious stroke, 0% [0 to 45.9]).

Additionally, there are concerns that LMWH is possibly associated with dose-dependent adverse effects, eg, a reduction of bone mineral density, which has been reported in children using long-term warfarin therapy. Thus, additional safety data on the short- and long-term use of high- and low-dose LMWH are urgently needed to make a final decision regarding whether LMWH is a candidate for trials of secondary stroke prevention in children.

Stroke types in children differ essentially from those in the elderly, and therefore therapeutic guidelines from adult stroke patients are not simply transferable to children. Thus, since there is still scant evidence of stroke treatment in children, we agree with deVeber and Chan that randomized controlled trials in stroke children with an appropriate design, including comparable stroke classification, clearly defined study endpoints based on suitable and comparable imaging methods, and the analysis of underlying thrombotic risk factors, are urgently required on the basis of an International Pediatric Stroke Consensus. Which drugs besides aspirin should be used, however, in the specific pediatric stroke subtypes, eg, high-dose LMWH, low-dose LMWH, or vitamin K antagonists, remains an unanswered question, with the need for more basic pharmacological data obtained in children.

Finally, we again gratefully acknowledge the comments made by deVeber and Chan; they are indeed critical for further stroke studies in children, which we hope will be conducted as multicenter international studies in the near future.

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MRI imaging of the cerebrum is 20 to 30 minutes, which is more than acceptable. Thus, MRA has already signposted the way out of the DUS-versus-CA dilemma in prevalent and preinterventional diagnostics of carotid stenoses. The combination of DUS and MRA makes possible optimal, noninvasive carotid diagnosis. CA can then be restricted to a few selected cases, eg, when DUS and MRA yield different results. However, these cases will most likely confirm the opinion of those authors who claim that the excellent DUS results provided under study conditions cannot be reproduced in general practice.

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Response
We read the letter from Drs Fellner and Lang with great interest. We certainly agree that medical professionals involved in the management of patients with carotid stenosis are faced with a dilemma. Physicians want a high degree of certainty regarding the diagnosis and severity of carotid stenosis. However, they want to avoid invasive testing such as contrast angiography that carries inherent risks. Unfortunately, an ideal situation does not exist at present. The noninvasive nature and low cost of carotid Doppler ultrasound would make it an ideal diagnostic modality for patients with carotid stenosis. However, in general practice, the inaccuracy of Doppler ultrasound makes it relatively unreliable for making decisions regarding the appropriateness of carotid endarterectomy.1,2 Drs Fellner and Lang have provided a valuable concept of using magnetic resonance angiography (MRA) to confirm the severity of stenosis in patients with carotid stenosis demonstrated by Doppler ultrasound. With recent developments in image acquisition and reconstruction,1 MRA definitely has the potential to replace contrast angiography for the assessment of patients with carotid stenosis before decisions are made regarding carotid endarterectomy. Johnston and Goldstein3 reported the misclassification rates of carotid Doppler ultrasound and MRA in 569 consecutive patients undergoing conventional angiography. Patients were classified as to whether carotid endarterectomy was indicated on the basis of the findings of each study. Overall, the misclassification rate was higher for Doppler ultrasound (28%) than for MRA (18%). Both imaging studies were performed in 11% of the 569 patients. The results of the two tests were concordant for assessment of the degree of carotid stenosis in 40 cases. When the results were discordant, the misclassification rate for the combination of Doppler ultrasound and MRA was lower than that for either test used independently (8% misclassification rate).

Using a combination of Doppler ultrasound and MRA, patients can be classified into 2 groups, as follows: (1) patients with moderate to severe stenosis demonstrated on both modalities and (2) patients with moderate to severe stenosis visualized on one modality but not confirmed by the other modality. It needs to be determined whether the accuracy of MRA justifies denying the second group of patients any further diagnostic tests or revascularization therapy or these patients should undergo contrast angiography for further characterization of lesion. Nonetheless, a certain proportion of patients in whom there is good agreement between Doppler ultrasound and MRA may not require contrast angiography. The exact proportion of these patients may be variable in different settings depending on the performance of carotid Doppler ultrasound and MRA. The methodology proposed by Drs Fellner and Lang appears to have merit and deserves evaluation in future studies.

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Response
We read the letter from Drs Fellner and Lang with great interest. We certainly agree that medical professionals involved...
Multimodal CT Imaging in Acute Stroke
Rüdiger von Kummer

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