Measuring carotid stenosis

Comparing a new test with a standard involves measuring disagreement. In the case of measuring carotid artery stenosis, some of the disagreement between different tests is because of inherent differences in how the stenosis is demonstrated (test characteristics). This is what we are most interested in when assessing a new technique. However, some of the disagreement simply reflects variability in how we physically make the measurement with the standard technique. Choosing the point of maximum stenosis, choosing the point in the common carotid artery for use as a denominator, measuring from an eyepiece, or measuring from calipers all introduce variation when measuring carotid stenosis. The resulting observer variability in reporting contributes to disagreement between methods but to some extent is independent of the method used to generate the angiogram in the first place.

In the medical literature, disagreement between methods is often attributed entirely to test characteristics, with little appreciation of the role of observer variability in reporting. When one method is compared with another and agreements emerge, it is not readily apparent how much of the disagreement is caused by the method used and how much by the process of measurement, unless observer variability is also presented. The recent paper from Patel et al, interobserver variability data are presented but their significance in relation to overall agreement does not appear to have been appreciated.

Using the data from Patel et al (tables 2 and 4) for symptomatic carotid arteries, it is noted that when 34 carotid digital subtraction angiograms (DSA) are measured by one radiologist, there was disagreement in seven cases when the same films were reported by a second radiologist. Therefore if only DSA was used, seven patients would have had “inappropriate” surgery according to which radiologist read the angiogram. This is not surprising, and such disagreement is a consistent finding in observer variability studies.1 Observer variability in reporting DSA therefore accounted for approximately 20% of disagreement in this particular series of angiograms. This sets a limit on the maximum agreement that any alternative method can demonstrate when compared with DSA. It is clearly not reasonable to expect better agreement from another method than can be obtained by re-reporting the DSA’s themselves. In Patel’s table 2, when the same arteries are assessed by computed tomographic angiography (CTA) and ultrasound there was disagreement with DSA in seven cases, while with magnetic resonance angiography (MRA) and ultrasound there was disagreement in six and seven cases, respectively. The three alternative methods may improve on patient management, we used non-invasive tests were used rather than alone) would eventually replace angiography. Our “snap shot” of CTA, MRA, and ultrasound is already out of date because contrast MRA is now increasingly used. While we would hope that non-invasive tests (probably in combination rather than alone) would eventually replace intra-arterial angiography in the majority of patients being considered for carotid intervention, we feel it likely that there will always be a need for some intra-arterial angiography in specific cases, or depending on local resources. In any case DSA did not become less popular than MRA among the patients in our study. There is certainly room for much more in depth examination of existing data but we shouldn’t close the door on the need for further studies.

Author’s reply

Doctors Young and Humphrey highlight that differences between tests arise from several factors, some of which are inherent to the test and some of which arise from aspects attributable to observer variation. Some of the aspects to do with observer variation apply to interpretation of all tests and some are specific to certain tests. In our study we were endeavouring to quantify the effect on patient management if non-invasive tests were used instead of intra-arterial angiography to assess carotid stenosis. Our study has several limitations, including a relatively small sample size and the fact that we were not able to get all scans read by all observers but rather had to get pairs of observers to concentrate on reading only CTA, or MRA, or DSA. A better design would have been to keep the same workers together in pairs but randomly assign the CTA, MRA, or DSA films to each pair. As it is, it is possible that some of the apparent difference between imaging modalities is specific to the pair of observers, not to the modality. However, imaging studies are difficult to fund and expensive to do, and the result and design of our study was a compromise involving all these factors.

We identified that the observer reliability of CT angiography or MR angiography was worse than that for digital subtraction angiography, as highlighted by Drs Young and Humphrey. Also in general there was more disagreement between the observers for the reading of asymptomatic stenoses than for symptomatic stenoses (emphasising the importance of considering patient characteristics, not just the imaging technique). In the determination of the effect of this disagreement might have on patient management, we used non-invasive tests in the European carotid surgery trial which were based on intra-arterial angiographic measurement of stenosis. We therefore had to use the comparison of non-invasive test reading with DSA rather than being able to use the individual observers readings of non-invasive tests. Thus as Drs Young and Humphrey point out, the actual effect of using non-invasive tests maybe worse than we have estimated.

Finally, Drs Young and Humphrey suggest that more studies are not required but we are not entirely sure that this is completely true. Non-invasive imaging tests are continually undergoing modifications, and there may be improvements in accuracy or practicality, but this cannot be assumed to be the case. Much of this tinkering with technology is driven by the manufacturer’s desire to encourage purchase of new machines. Improvements have also occurred in intra-arterial angiography with smaller and more manoeuvrable catheters and greater awareness of the risks, which may have helped to reduce the risk of angiography. Our “snap shot” of CTA, MRA, and ultrasound is already out of date because contrast MRA is now increasingly used. While we would hope that non-invasive tests (probably in combination rather than alone) would eventually replace intra-arterial angiography in the majority of patients being considered for carotid intervention, we feel it likely that there will always be a need for some intra-arterial angiography in specific cases, or depending on local resources. In any case DSA did not become less popular than MRA among the patients in our study. There is certainly room for much more in depth examination of existing data but we shouldn’t close the door on the need for further studies.
Cerebral metastasis after primary renal cell carcinoma

The article by Roser et al., in which it was shown that the treatment of intracranial metastases originating from renal cell carcinoma can on occasion be successful, was most interesting.

We have followed the clinical course of a patient with a renal cell carcinoma with a low mitotic index since 1989. In this patient the course was distinctly more malignant but the disease has also been successfully treated to date. In the last 13 years, this patient has had four metastases surgically removed and a further nine treated with stereotactically guided percutaneous single dose convergent beam irradiation therapy (stereotactic modified linear accelerator, 6–15 MV photons, 18–20 Gy prescribed to the 80% isodose). Apart from slight mnemonic deficits, the patient is in good health.

The following factors which affect the prognosis were all met by our patient:

- The interval between the diagnosis of renal cell carcinoma and the first detected brain metastasis exceeds 17 months (our patient, 18 months; the patient described by Roser et al., 36 months);
- Age below 60 years at the time of initial diagnosis;
- Primary tumour of the left kidney, initial nephrectomy;
- Diameter of primary metastasis < 2 cm;
- Not more than one brain metastasis at the time of initial treatment;
- Solely intracranial metastases;
- Karnofsky > 70%;
- No systemic symptoms such as fever or weight loss at the time of diagnosis;
- Blood sedimentation rate under 50 mm/h at diagnosis of renal cell carcinoma.

Patients in whom prognostic factors predict a good outcome should be treated with intent to cure.

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References

BOOK REVIEWS

Seizures, medical causes and management

This book is unusual among books about seizures because it focuses on acute symptomatic seizures, rather than “epilepsy” (although there is inevitably some overlap between the two). It provides definitions and describes the epidemiology and pathophysiology of acute symptomatic seizures in the initial section, which is followed by chapters detailing the specific circumstances in which such seizures are likely to occur, often (although not invariably) including points of management specific to the situation. Subjects covered include seizures occurring in the context of multisystem disease, infection, hypoxic-ischaemic cardiopulmonary conditions, endocrine disorders, cancer, and other conditions. Situation-related seizures occurring as a result of drugs or alcohol misuse are also addressed, as are those occurring in the intensive care situation, and the difficult, but important, differentiation of seizures from syncope. The book ends with a very practical chapter entitled “Antiepileptics in acute medical illness”, in which the considerations affecting the choice of antiepileptic drug in the acute situation are reviewed. Although situation-related seizures are usually discussed in books about epilepsy, they do appear to constitute a distinct group in a number of respects including prognosis. To a certain extent the topics discussed in the book form a rather disparate group linked only by their detailing the specific circumstances in which such seizures occur, as a reflection of central nervous system disturbance. Nevertheless, they are all conditions likely to be encountered at various times by general physicians, neurologists, and those working in the accident and emergency department, and this book, which is both readable and comprehensively referenced, will be of interest to all these groups.

Yvonne Hart

Subcortical stroke, 2nd edition

This is a very useful, reasonably comprehensive yet succinct multiauthor small book on medical risks associated with epilepsy. Areas covered include methodological aspects; accidents and risks in everyday life; traffic accidents; driving regulations; mortality, including SUDEP; psychiatric comorbidity and suicide; fatal adverse drug reactions reporting data (which are rather difficult to interpret); seizure-warning systems and risk prevention; as well as insurance related issues. In addition, this book highlights many areas where further research is required. The book generally provides an overview of the more recent research and publications in this area and includes some regulatory issues. Inevitably it has a Nordic emphasis; it includes very useful advice on precautionary measures to minimise risk of injury for people with uncontrolled epilepsy, including clothing and safety. Several chapters, by necessity, serve purely as a compilation of available incomplete data. Others are written by key researchers directly involved in the area addressed and provide a very balanced review of current knowledge. On psychiatric comorbidity, while agreeing that “the positive
effects of drug therapy on cognitive and affective functioning because of the reduction in seizure activity are usually far greater than the negative effects”, more information would have been welcome in an otherwise very well balanced chapter. The book would well serve those who wish for a range of topics, in addition to the recent advances in genetics, neuropathology, neurology, and psychiatry, and to those who are interested in a more comprehensive approach to the understanding and treatment of neurological disorders.

Lina Nashef

**Greenfield’s neuropathology, 7th edition**


What can one say. The latest (7th) edition of Greenfield’s Neuropathology has hit the bookshops, and indeed what is a resounding thud it makes! The present edition is bigger than ever, again running into two volumes, but now totalling 2330 pages and ending an equally staggering £395. It comes equipped with a handy CD version of the illustrations, a mere snip at £145.

The 7th edition has undergone considerable changes in content, since the last edition five years ago, reflecting the ever expanding increase in knowledge of diseases of the nervous system and muscle that has come from the exponential growth in neuroscience research over the past decade. Areas of cellular and molecular neurobiology, and the contributions that genetics and neuroimaging have made towards improving our understanding of the causes of disease and our clinical investigative and diagnostic skills, are more strongly featured. Hence, while greater emphasis has been placed on the basic science of disease, the classic descriptive morphology for which Greenfield is renowned is well maintained. There are new chapters on “Metabolic and neurodegenerative diseases of childhood” and “Peroxinomial and mitochondrial diseases”. The chapter on “Pathology of schizophrenia” has been shrewdly expanded to cover “The pathology of psychiatric disorders”. Other chapters have been retained as such, but many have been rewritten with new authors reflecting the pre-eminence of each within their particular subspecialty. There is increased reliance on colour illustrations, line diagrams and tables to illuminate the text, and these are of excellent quality throughout. As to be expected, all chapters are written authoritatively with clarity and style, comprehensively illustrated, and lavishly referenced. Judging by the content of the chapters on ageing and dementia, prion disease, and movement disorders, it is my guess that if anything is not included in each chapter, it’s probably not worth including anyway. The accompanying CD rom is user friendly, and the images are downloadable—a boon to those wishing to produce a ready made lecture or presentation of distinction. The book is a must for practicing and trainee pathologists, but is equally compelling for workers in other clinical neuroscience disciplines and basic researchers interested in the roots of the dysfunctional nervous system.

Possession of the 7th edition is guaranteed lasting quality and full value, but before lashing out make sure both your arms and shelves are strong enough to accommodate its presence.

David MA Mann

**Smell and taste complaints**


Despite the fact that problems with tasting and smelling are common in the general population, few physicians have the knowledge and training to authoritatively deal with them. Christopher Hawke’s Smell and Taste Complaints provides a straightforward guide to the understanding and management of chemosensory disturbances, reflecting the first clinically oriented book of its kind since Ellis Douek’s The Sense of Smell and its Abnormalities (Edinburgh: Churchill Livingstone, 1974). This 180 page pocket sized book provides a cogent overview of the anatomy and physiology of the olfactory and gustatory systems, practical approaches towards their assessment, and suggestions for therapy and management. Importantly, it provides the practitioner with the names and addresses of specialised taste and smell clinics throughout the world, aiding the referral process. Although there is little new in this guide, and much of the material seems to have been derived from second hand sources, it presents the available information in a well organised and easy to read manner. Moreover, it addresses basic clinical issues rarely addressed in a single publication. Its major drawback is the lack of reference backing for many of its statements, some of which are questionable. I found, for example, some of the “facts” unfamiliar, and would have welcomed knowledge of their source. Bits of the material are dated (for example, the role of IP, receptors in olfactory function, the nature of olfactory receptor cell regeneration) and several sections of the book seem lengthy, uncritical, and of little practical value. Thus, nearly seven pages are devoted to the topic of odour memory, a topic with inherent theoretical issues and problems that are not addressed by the author. However, the book is not intended to be a research book and, despite such shortcomings, it accomplishes its goal of educating the practitioner and providing him or her with a practical roadmap for clinical assessment and treatment. Indeed, the clinical information provided is comprehensive and well illustrated. This inexpensive book is a must for any physician who has the occasion to see patients with chemosensory disturbances or has even a casual interest in chemosensation, and should serve to elevate the level of appreciation of these senses within the medical community at large.

Richard L Doty

**CORRECTIONS**

The following errors occurred in the short report by Merlini L, Carbone I, Capanni C, et al. Familial isolated hyperCKaemia associated with a new mutation in the caveolin-3 (CAV-3) gene. J Neurol Neurosurg Psychiatry 2002;73:65–7. On page 66, left column, line 9, proline should replace leucine, line 12, protein should replace enzyme; and in table 1, line 8 Del-TFT (63–65) should replace ?TFT (63–65).

We regret that an editing error occurred in the correspondence from Jaster JH, Dohan FC, and O’Brien TF. Demyelination in the brain as a paraneoplastic disorder: candidates include some cases of seminoma and central nervous system lymphoma. J Neurol Neurosurg Psychiatry 2002;73:332. The description of a patient was altered, in the first line of the fourth paragraph the text should read “ . . . patient who had a non-neurological malignancy, seminoma, and subsequently developed a paraneoplastic syndrome . . . “. 

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