First impressions are good, but appearances can be deceptive!

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This editorial refers to 'Carotid artery stenting in octogenarians: results from the ALKK Carotid Artery Stent (CAS) Registry'† by Zahn et al., on page 370.

We want the facts to fit the preconceptions. When they do not, it is easier to ignore the facts than change the preconceptions.

Jessamyn West (1902–84)

Zahn et al. publish the latest analyses from the Carotid Artery Stent (CAS) Registry of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausarzte (ALKK) of Germany.1 This reports outcomes following CAS in octogenarians (n = 321) compared with younger patients (n = 2557). As indicated in the introduction, this analysis was prompted by conflicting published data regarding the safety of CAS in elderly patients. Having reviewed their experience, the authors conclude that 'the in-hospital stroke or death rate does increase significantly with older age; however, there was no excess complication rate in octogenarians'. Is this conclusion valid and how should the ALKK findings influence practice?

Notwithstanding the marked disparity in numbers between the two groups, the ALKK Registry make a number of important observations in patients aged >80 years undergoing CAS. (i) The case volume (proportional to the total annual workload) is increasing rapidly (6% in 1996 vs. 14% in 2005). (ii) CAS took longer to perform (45 vs. 40 min, P = 0.008). (iii) CAS was associated with a higher incidence of residual stenosis at the end of the procedure (10 vs. 5%, P = 0.006). (iv) CAS was more frequently aborted in patients aged >80 years (7 vs. 2%, P < 0.001). (v) Elderly patients were less likely to undergo CAS while receiving statin therapy (71 vs. 84%, P < 0.001). (vi) Elderly CAS patients faced no excess risk of access complications (2.5 vs. 1.3%, P = 0.13). (vii) Octogenarian CAS patients did face a significantly higher in-hospital death/stroke rate (5.5 vs. 3.2%, P = 0.032). (viii) Not surprisingly, octogenarian CAS patients encountered a significantly higher in-hospital rate of death/stroke and TIA (11 vs. 6%, P = 0.003).

These findings will, of course, be open to individual interpretation. However, to this reader, observations (ii)–(iv) are interesting but probably unimportant; (v) is worrying, because it suggests sub-optimal medical therapy (a criticism common to many cardiovascular studies), whereas (vi) is reassuring. Observation (i) is only clinically important if the indications for intervening on patients aged >80 years are inappropriate, while everyone accepts that the inclusion of TIA within a 'hard' peri-operative endpoint is unnecessary. Like its counterpart carotid endarterectomy (CEA), the rationale underlying CAS is that it is performed to prevent stroke. If randomized trials showed that the only difference in peri-operative risk was a higher incidence of TIA with CAS, then CEA would (almost certainly) become the 'silver' standard overnight. Accordingly, the 'real meat' of the debate is observations (i) and (vii).

Fundamental to interpretation of observations (i) and (vii) is that the reader not only considers what the ALKK Registry has said, but more importantly what it has not said! Let us start with a simple question; 'why do we treat octogenarian patients with severe carotid disease?' The answer should be that these patients are (i) at higher risk of suffering a stroke if CAS/CEA is withheld and (ii) the procedural risks of CEA/CAS are not so high that long-term stroke prevention is compromised. The answer cannot simply be that, 'intervention is justified in symptomatic and asymptomatic patients over 80, the only debate being whether CAS is preferable to CEA!'

First, consider the symptomatic patient. Since the landmark trials published, we now have more evidence to guide practice than ever before. Symptomatic patients face a significantly higher risk of stroke than their asymptomatic counterparts. However, within this ‘recently symptomatic’ cohort, we know that several clinical and imaging features mark out those who gain greatly increased benefit from intervention provided the procedural risks are <8%. These include male gender, hemispheric symptoms, recurring symptoms for >6 months, very recent symptoms (within one month), CEA performed within 4 weeks of the most recent event, contralateral occlusion, increasingly severe stenosis (but not near occlusion), plaque irregularity, tandem intracranial disease, failure to recruit intracranial collaterals, and patients aged >75 years.2

Previously, many clinicians thought that elderly, symptomatic patients gained little long-term benefit from CEA because it was assumed that the procedural risks would be
too high. In fact, the complete opposite was observed. In a reanalysis of NASCET data, 74 strokes would be prevented at 5 years by performing 1000 CEAs in patients aged <65 years with 70–99% stenoses. This increases to 173 strokes prevented in patients aged 65–74 years and a very creditable 289 strokes prevented per 1000 CEAs at 5 years in recently symptomatic patients who were aged >75 years. To put this into context: operating on 1000 asymptomatic patients with 60–99% stenoses with a 2.3% procedural risk will only prevent 59 strokes at 5 years.

Accordingly, the ALKK observation that the procedural death/stroke rate was '5.5% in patients aged >80' is meaningless unless we know the symptom status. This is provided (of sorts) when the reader is told that the in-hospital death/stroke rate was 7.1% in symptomatic octogenarians. This figure fits the risk guidelines highlighted above and supports the Registry's conclusion that 'there was no excess complication rate in octogenarians'. However, although the 7% risk cited by ALKK is commendable, its impact is diminished by the Registry's incomprehensible failure to report 30-day outcomes. This is so disappointing. CAS could be of immense clinical value in the very elderly symptomatic patient if it really could be shown that the 30-day risk of death/stroke was <8%. The authors add the caveat that they believe few strokes/deaths occur after hospital discharge (very much open to debate), but the 30-day risk of death/stroke after intervention (whether it be CEA or CAS) is a fundamental reporting standard throughout the world and is one of the cornerstones of risk-modelling.

A second and equally important issue regarding interpretation of the ALKK data is a failure to inform the reader about the delay from symptom to CAS. One of the criteria for entry into every randomized trial is that the patient had to report recent onset symptoms. In the much maligned EVA-3S study, the threshold for inclusion was 120 days. EVA-3S has been subject to virulent criticism (because of the excessively high risk following CAS) amid accusations that the interventionists were inexperienced and did not perform the procedure properly. However, what was completely overlooked was the vital fact that 45% of EVA-3S patients were treated within 4 weeks of their most recent symptom. This is a time frame when 66% of carotid plaques will have overlying thrombus present, almost certainly making CAS more risky. Critics who argue that delay to treatment is justifiable so as to reduce the procedural risk are clearly unaware of the literature. It is an incontestable fact that CEA (and thus by inference CAS) confers the maximum benefit provided it is undertaken as soon as possible after the onset of symptoms. Put more starkly, if you perform CEA or CAS in symptomatic patients within 2 weeks of the index event with a 10% procedural risk, you will still prevent more strokes in the long term than if you deferred surgery for 4–12 weeks and then performed CEA or CAS with zero morbidity and mortality. Perhaps, the ALKK will consider providing this data in future publications. It may considerably enhance their hypothesis if they can show that their good results were still maintained in patients treated very early after the symptom onset.

Finally, let us consider the asymptomatic octogenarian. The ALKK Registry has been accumulating data since 1996 and the authors can be forgiven for recruiting elderly asymptomatic individuals for most of that time. What is extremely puzzling, however, is how the current paper casually dismisses the 2004 level I (grade A) evidence from ACST, which showed that CEA conferred no significant benefit in asymptomatic patients aged >75 years. Supporters of intervention (CAS or CEA) may argue that because the 3.4% complication rate in the ALKK cohort was very low, it is still reasonable to treat these patients. The data, I am afraid, does not support this. ACST observed that patients aged >75 who were randomized to immediate CEA had a 5-year stroke risk of 5.5%. This compares with only 8.8% in patients randomized to medical therapy. This equates to a non-significant 3.3% absolute reduction in stroke risk at 5 years (P = 0.21). However, ACST did not include the operative risk in this analysis. Accordingly, when the 3.4% ALKK risk is factored into the equation, it is clear that their performance of CAS was probably causing slightly more strokes than could have been prevented.

In conclusion, the ALKK Registry has highlighted some very important points; some good and some bad. On the 'good' side, I am now more encouraged about the potential role of CAS in elderly symptomatic patients than previously. If CAS can be shown to work safely in the elderly symptomatic patient, this has to be where it will offer considerable advantages over surgery. On the 'down' side, I remain disappointed that the ALKK Registry still does not report 30-day outcomes. How this was missed by the various Ethics Committees when authorization was being sought to establish a national registry of what was (in 1996) an experimental procedure is quite baffling. Finally, given that level I evidence has shown that elderly, asymptomatic patients do not gain significant benefit from prophylactic intervention; it is now hard to conclude that a policy of offering CAS to asymptomatic octogenarians can be sustained outside the protection of randomized trials. Just like the surgeon, you cannot pick and choose which bits of trial data best suit your preconceptions!

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References