Lifelong Learning

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Stroke in the Elderly:
Predictable, Preventable and Treatable

Stroke is the second most common cause of death worldwide, with most of the disease burden falling to the elderly and the very elderly. Effective treatments are available for acute management and for primary and secondary prevention of stroke. GPs are particularly well placed for identifying at-risk patients and for initiating 'triple therapy' of aspirin, a high-dose statin and blood pressure lowering therapy.

Stroke is a common cause of death and disability, especially in elderly patients.[1] The definition of elderly varies widely but most publications refer to the elderly as those older than 65 with 'very elderly' defined as those over 80. Stroke is both predictable and preventable, and treatments exist that can significantly alter the natural history of the disease.[2] Although major strides have been made in our understanding of the diseases responsible for stroke, and development of treatments to prevent and treat acute stroke, most information comes from studies in a younger population. With an ageing population, stroke is predicted to increase in incidence, emphasising the need to optimise acute and preventive interventions.

Epidemiology

Stroke is the second most common cause of death worldwide. Of those affected by stroke, some 80% are older than 65 and 25% are over 85. The incidence of stroke doubles every decade after the age of 55, and with increasing life expectancy the incidence of stroke in the population will also increase. Indeed, stroke is a significant cost to society and is predicted to be the leading cause of death in developed countries by 2030.[1]

Hypertension, diabetes, smoking and atrial fibrillation have all been identified as modifiable risk factors for stroke. These account for about 60% of stroke cases. The remaining 40% are due to as yet unidentifiable causes, but may involve possible genetic mechanisms.[2] Age is the main unmodifiable risk factor for stroke and has a profound effect on both incidence and outcome. Age-associated risk factors, such as atrial fibrillation, congestive cardiac disease and carotid artery atherosclerosis, explain a large part of the increased incidence of stroke among the elderly and comorbidities may explain the poorer outcome. However, even adjusting for these factors, mortality, length of hospital admission and final discharge destination are all poorer in the older patient who has had a stroke.

Aetiology and subtypes

Over 80% of strokes are ischaemic in nature; the remaining causes are secondary to haemorrhage.[2] Three main stroke subtypes cause 75% of ischaemic strokes, with a roughly equal distribution. These subtypes affect prognosis and treatment.

- **Large vessel atherosclerosis strokes.** These classically affect the origin of the internal carotid but may occur at any point both intra- and extra-cranially. This subtype may result in thrombosis at the site of disease or artery-to-artery distal embolisation. Antiplatelet and antithrombotic therapies are the best treatment options.

Key points

- Stroke is the second most common cause of death worldwide and predominantly affects the elderly.
- Aspirin therapy, referral to a stroke unit and thrombolysis within 4.5 hours of onset are interventions that are of proven benefit for acute ischaemic stroke.
- A transient ischaemic attack (TIA) is a medical emergency and presents an urgent window of opportunity to prevent a completed stroke.
- Stroke prevention can be achieved by urgent diagnostic evaluation of a TIA and by starting 'triple therapy' with aspirin, a high-dose statin and blood pressure lowering therapy.
- Treatment with an anti-platelet agent should be started immediately in patients who have experienced a transient focal neurological event.
- Anticoagulation therapy is vastly superior to treatment with antiplatelet agents for patients with atrial fibrillation.
- Carotid imaging is one of the most critical investigations in preventing stroke and should be performed urgently, followed by referral for surgery if a significant symptomatic stenosis is identified.

About the authors

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- **Cardioembolic strokes.** These are mainly due to atrial fibrillation but are also caused by mural wall thrombosis following myocardial infarction, left ventricular failure or mitral valve disease. This subtype is an increasingly common cause of stroke in the elderly and anticoagulation is the treatment of choice.
- **Lacunar ischaemic strokes.** These are caused by small vessel disease. This subtype, in general, is associated with a significantly better outcome and much lower recurrence rate compared with other subtypes of ischaemic stroke. Treatment should include an antiplatelet agent.

Most strokes resulting from haemorrhage are caused by hypertensive small vessel lipohyalinotic disease, cerebral amyloid or aneurysm rupture. A minority of cases are secondary to vascular malformations. Prognosis is poor in patients who have had a haemorrhagic stroke, with 50% mortality at one month.

Acute management

Patients with acute stroke should be referred to hospital immediately as treatments are critically time sensitive. There are three proven interventions for acute ischaemic stroke:

- Aspirin given within 48 hours of symptom onset reduces both death rate and further stroke at one month.
- Stroke units have a large effect on reducing mortality and morbidity, are applicable to the vast majority of patients, and are effective across all age groups.[2]
- Thrombolysis with alteplase is beneficial when given appropriately to those presenting within 4.5 hours of ischaemic stroke symptom onset.[3,4]

Most evidence for the benefit of these interventions comes from studies in younger patients. There is less evidence, to date, of benefit in those over 80 because of their exclusion from the major trials. The Third International Stroke Trial (IST-3) has investigated thrombolysis for acute ischaemic stroke in those over 80.[5] Current practice for the acute management of stroke is that age alone is not an exclusion criterion. If pre-morbid physical and cognitive functions are good then thrombolysis should be considered. The outcome is poor in elderly patients with a significant deficit at presentation, particularly when a vessel occlusion can be identified on imaging. However, if the elderly patient is not independent before the event then alteplase is not generally offered because the aim of treatment is to return the patient to independent living.

Transient ischaemic attacks

A transient ischaemic attack (TIA) presents an urgent window of opportunity to prevent a completed stroke. Early, intensive assessment and treatment of herald events such as a TIA is essential for stroke prevention. This can be achieved by urgent diagnostic evaluation of patients suspected of having a TIA and by starting 'triple therapy' with aspirin, a high-dose statin and blood pressure lowering therapy.[6]

In a patient with a transient focal neurological event that has fully resolved and who is back to normal, immediate loading with aspirin is appropriate – waiting for a CT scan before initiation only raises risk while rarely changing management acutely. This is not the case if neurological signs persist or red flags are present, such as prior malignancy that may have metastasised or if the patient is currently on anticoagulation. A history of paroxysmal atrial fibrillation or identifying atrial fibrillation on an electrocardiogram should prompt immediate anticoagulation rather than antiplatelet therapy.

Urgent assessment of the extracranial carotid arteries is the other key step in the management algorithm of TIA because carotid stenosis is a particularly sinister and time-critical cause of transient symptoms. Indeed, a significant proportion of patients will have a completed stroke within days of a herald event if there is a significant carotid stenosis.

A recent focus of research has been identifying 'high-' and 'low-'risk TIAs based on clinical features. The role of these scoring systems is as yet unproven and does little in directing treatment to alter the natural history of individual events. Rapid assessment in specialised clinics, where available, is of proven benefit.

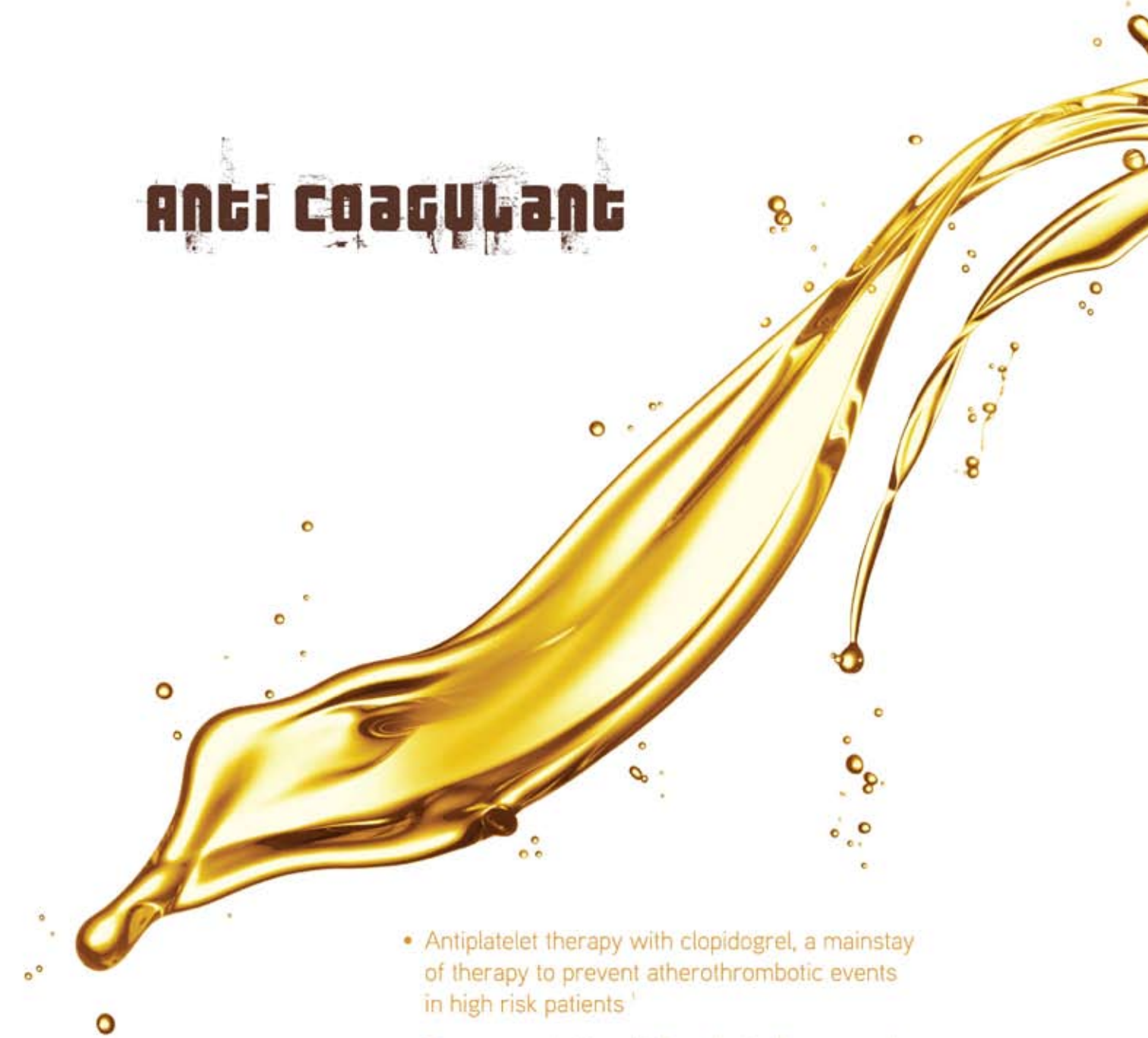
Secondary prevention

Appropriate antithrombotic therapy is the first step of secondary prevention. The choice lies between antiplatelet treatment and anticoagulation. In the setting of a cardioembolic source such as atrial fibrillation, anticoagulation with warfarin is the treatment of choice. Strong evidence now exists that warfarin is superior to aspirin for atrial fibrillation, even in the very elderly, and while the risk of haemorrhage increases with age and comorbidities, so does the risk of ischaemic stroke, with the risk–benefit balance in favour of anticoagulation.[7] The newer anticoagulant agents (eg, dabigatran, apixaban and rivaroxaban) appear to offer many advantages for secondary prevention of stroke. Caveats exist regarding the use of these newer agents in the elderly, with studies suggesting that adverse events are increased in the older age group. If a cardiac source of stroke cannot be identified, therapy with either aspirin plus slow-release dipyridamole or clopidogrel alone are the optimum treatments, and are equivalent.[8] The combination of clopidogrel and aspirin offers no additional benefit due to the increased haemorrhagic risk of this combination for those patients with prior stroke.[9]

Hypertension is a main risk factor for stroke and while early intensive treatment in the first week following a stroke may be harmful, controlling blood pressure in the long term is of major importance in preventing further cardiovascular events.[10] Furthermore, blood pressure lowering treatment is appropriate for both ischaemic and haemorrhagic stroke. There are concerns regarding optimum blood pressure targets in the very elderly, for whom a balance is needed between treatment and over-treatment, but benefit has been demonstrated in primary prevention for those over 80, and for all ages in secondary prevention.[11]

Statin therapy reduces risk of cardiovascular events and is of proven effect in the secondary prevention of stroke, including in the very elderly, in whom atorvastatin has the most robust evidence.[12]

Carotid endarterectomy is one of the most powerful interventions in preventing stroke. In patients with symptomatic



- Antiplatelet therapy with clopidogrel, a mainstay of therapy to prevent atherothrombotic events in high risk patients [1]
- Recommended in anti-thrombotic therapy and prevention of thrombosis, 9th edition: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [2]

S3 MISTRO
clopidogrel 75 mg
PREVENTION PROTECTION

References: 1. Nayak K, Cavendish J. Risk reduction with clopidogrel in the management of peripheral arterial disease. *Vascular Health and Risk Management* 2007; (3):289-97. 2. Guyatt G, Akl E, Crowther M, Gutterman D, Schuunemann J, for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive Summary – Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *CHEST* 2012; 141(2)(Suppl):7S-47S.

moderate (50% to 70%) or severe (greater than 70%) stenosis, early intervention (within two weeks of symptom onset) results in a major absolute risk reduction of further stroke.

The benefit of carotid endarterectomy is even more substantial in the elderly; therefore, age alone should not be an exclusion criterion for this intervention if the patient is otherwise well.[13] Carotid stenting is inferior to surgery and thus should be performed only if the patient is unsuitable for endarterectomy or because of patient preference.

The presence of other vascular risk factors should also be addressed, including smoking (stopping smoking can reduce future vascular risk by half), diabetes and lifestyle changes such as diet modification and increasing physical activity levels.

Life after a stroke

The sequelae of a stroke are variable and depend, to a large degree, on the extent and location of the infarction or haemorrhage. Recovery is most dramatic in the weeks and months following the event but significant functional gains can be seen up to a year or more after the initial event, particularly with intensive rehabilitation and input from allied healthcare professionals.

Non-focal symptoms such as fatigue and mood disturbance are very common. These can be particularly troublesome, especially when on a superficial level all other signs have resolved. Typically, patients who have such symptoms launch back into their previous routine only to find that their physical and intellectual reserves are not what they were. Emphasising a graded return to duties and giving reassurance that these symptoms are to be expected and will gradually improve with time is helpful. As these issues can persist for months and even years, a low threshold for initiating an anti-depressant is worthwhile (the best evidence is for SSRIs), especially when mood and irritability are a problem.

Driving can generally be resumed one month after the stroke event, provided deficits do not interfere with ability. Motor function and visual field assessment are important factors in determining this, but issues with judgement also have a significant impact on safety and can best be assessed on family reports of behaviour. If there are any doubts, an on-road driving test can be helpful.

Conclusion

Stroke is a common cause of death and disability in the elderly, but good treatments now exist for both acute stroke and primary and secondary prevention. Primary care physicians are particularly well placed in identifying at-risk patients, such as those with a TIA and atrial fibrillation, and for commencing therapy. Treatment includes 'triple therapy' (aspirin, a high-dose statin and blood pressure lowering therapy), warfarin for atrial fibrillation and urgent imaging of carotids, with referral for surgery if a significant symptomatic stenosis is identified. In addition, rapid TIA assessment clinics, where available, are an excellent resource.

References are available on request.

Migraine Triggers Fail to Match Patient Reports

The migraine triggers cited most frequently by patients are physical exertion and bright or flickering light, yet in a small prospective study few participants with a history of migraine with aura developed headaches when exposed to those triggers.

Only three of 27 patients (11%) reported attacks of migraine with aura following provocation, and three others reported migraine without aura.

All of the attacks occurred in response to exercise; provocation with light elicited no headaches, Jes Olesen, MD, DMsc, of the University of Copenhagen, and co-authors reported in the journal Neurology.

"Experimental provocation using self-reported natural trigger factors causes migraine with aura only in a small subgroup of patients with migraine with aura," the authors wrote in conclusion.

Exertion and light most often blamed

"Naturally, when having an attack, patients will think back to identify possible causes but, just as naturally, patients rarely seek confirmation by exposing themselves to suspected trigger factors," the authors noted in their introduction.

Olesen and colleagues previously reported that more than half of patients with a history of migraine with aura could describe a stimulus that always or often provoked attacks (Cephalalgia 2010; 30: 346-353). Most often, those were exertion and light.

In the 27 patient study, exercise alone triggered migraine attacks in four of 12 patients (one preceded by aura). Two of seven patients developed migraine with aura after exercise and exposure to light. None of 11 patients had migraine attacks with photostimulation only.

The results were "less than spectacular" as compared with nitroglycerin infusion, which reliably provokes symptoms in about 75% of patients, an accompanying editorial pointed out.

Are patients simply wrong?

"There can be several reasons for this," wrote Dr Peter Goadsby and Dr Stephen Silberstein of the University of California San Francisco. "Perhaps patients are wrong. This is the least attractive option. The reporting is so consistent across the world and so many patients have so many attacks, it is hard to think they are all just incorrect."

A second possibility relates to possible differential effects of triggers on aura and migraine headache.

A third possibility revolves around the classic clinical advice to identify and avoid triggers, advice that could be wrong, as suggested in migraine literature.

"Many questions are unresolved and require continued careful, bedside approaches to studying this common, disabling brain disorder," Goadsby and Silberstein concluded.