

Stroke Prevention

What Are the Options?

Stroke is a leading cause of physical disability, functional impairment and mortality. Prevention—through risk factor modification, antiplatelet therapy, immediate management of transient ischemic attack and carotid endarterectomy—remains the best approach to reducing the stroke burden.

A.D. Bell, MD

Tom's case

Tom, 59, is a construction worker. He complains of a 10-minute episode of speech disturbance and clumsiness of his right hand, which occurred three days ago.

Tom has no history of similar events.



Past history

- Tom has had hypertension for the last 10 years.
- He has been smoking 15 cigarettes/day for the past 40 years.

Family history

- Tom's brother and father suffered premature coronary artery disease.

Current medications

- He is currently prescribed atenolol, 50 mg, once daily.

Physical exam

- Height: 170 cm
- Weight: 95 kg
- Blood pressure: 148/86 mmHg
- Pulse: 86 beats per minute

Neurologic

- Normal speech, gait, strength

Cardiovascular

- Normal heart sounds, no signs of heart failure, no carotid bruits
- Electrocardiogram: Normal sinus rhythm, voltage left ventricular hypertrophy, no ischemic changes.

For more on Tom, go to page 40.

Stroke is a leading cause of morbidity and mortality, accounting for 7% of all deaths in Canada or 2,400 events for every million Canadians per year.¹

Patients recovering from even a mild stroke or a recent transient ischemic attack (TIA) are at high risk of stroke recurrence, physical and intellectual disability, long-term institutionalization and death.

Primary and secondary stroke prevention strategies remain critical for reducing the overall burden of atherothrombotic disease.

What are the major risk factors to consider?

All patients who have suffered a stroke or TIA should receive the best possible management of any risk factors present.

1. Hypertension

Treating any degree of blood pressure (BP) elevation, including mild hypertension, has been shown to significantly reduce stroke risk.

Recent evidence suggests blockade of the renin-angiotensin system with either angiotensin receptor blockers (ARBs) or angiotensin-converting enzyme (ACE) inhibitors may provide benefits in stroke prevention beyond BP control.

The Losartan Intervention For End point reduction in hypertension (LIFE) study, for

Table 1

Antithrombotic therapy in patients with atrial fibrillation

Patient features	Antithrombotic therapy
<ul style="list-style-type: none"> • Patients with any of the following: <ul style="list-style-type: none"> - Prior stroke, TIA or systemic embolism - Age over 75 years - Impaired LV function/CHF - Hypertension - Diabetes - Mitral stenosis 	<ul style="list-style-type: none"> • Oral anticoagulation INR: 2.0-3.0
<ul style="list-style-type: none"> • Age 65-75 years with no other risk factors 	<ul style="list-style-type: none"> • Oral anticoagulation INR: 2.0-3.0 or ASA, 325 mg/day
<ul style="list-style-type: none"> • Age under 65 years with no other risk factors 	<ul style="list-style-type: none"> • ASA, 325 mg/day
<ul style="list-style-type: none"> • With prosthetic heart valve 	<ul style="list-style-type: none"> • Oral anticoagulation (INR: 2.0-3.0) plus ASA, depending on type and position of valve

TIA: Transient ischemic stroke
 LV: Left ventricular
 CHF: Chronic heart failure
 INR: International normalized ratio
 ASA: Acetylsalicylic acid

Adapted from Singer DE, Albers GW, Dalen JE, et al: Antithrombotic therapy in atrial fibrillation: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004; 126(3):429S-56S.

example, found a significant 25% reduction in stroke in patients treated with losartan (an ARB) compared to those treated with atenolol (a beta blocker).² A LIFE substudy demonstrated an even more impressive 40% stroke reduction in patients with isolated systolic hypertension who were treated with losartan compared to atenolol.³

Current guidelines recommend ARBs, ACE inhibitors and thiazide diuretics as first-line antihypertensive therapies following the acute phase of stroke or TIA. Treatment should be targeted to achieve BP of < 140/90 mmHg.

2. Hyperlipidemia

Lowering elevated lipid levels with statins is associated with a reduction in stroke occurrence.

Recent evidence suggests all patients with prior TIA, ischemic stroke or high risk for

vascular disease should be treated with a statin irrespective of their serum cholesterol level. The Heart Protection Study (HPS) demonstrated marked reductions in all vascular events, including stroke, in such patients with baseline low-density lipoprotein levels as low as 2.5 mmol/L.⁴

3. Diabetes

Current guidelines emphasize aggressively aiming for glycemic targets as close to normal as early as possible to reduce the risk of microvascular and macrovascular events in patients with diabetes. The United Kingdom Prospective Diabetes Study (UKPDS) found a significant 12% decrease in fatal and nonfatal stroke for every 1% reduction in hemoglobin A1c.⁵

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4. Smoking

Evidence suggests smoking cessation is highly beneficial for stroke prevention. After cessation, the risk of stroke decreases within two to five years.⁶

5. Atrial fibrillation

Atrial fibrillation (AF) is the single greatest independent risk factor for ischemic stroke, with one in every six strokes occurring in patients with AF.⁷

Recommendations have been developed for the use of either warfarin or acetylsalicylic acid (ASA) to reduce stroke risk in patients with AF (Table 1).

Table 2

Recommendations for the management of symptomatic carotid stenosis

Degree of stenosis	Recommendations
≥ 70% stenosis	<ul style="list-style-type: none"> • Carotid endarterectomy of definite benefit if done with acceptable morbidity and mortality • Antiplatelet agents
50-69% stenosis	<ul style="list-style-type: none"> • Carotid endarterectomy of potential benefit depending on risk factors • Antiplatelet agents
< 50% stenosis	<ul style="list-style-type: none"> • Carotid endarterectomy of no benefit • Antiplatelet agents

Adapted from Wolf P, Clagett GP, Easton JD, et al: Preventing ischemic stroke in patients with prior stroke and transient ischemic attack. AHA Scientific Statement. Stroke 1999; 30(9):1991-4.

Is there a role for carotid endarterectomy in stroke prevention?

Carotid endarterectomy for symptomatic, severe carotid stenosis remains one of the most effective methods of preventing recurrent stroke (Table 2).

Although prior studies have shown minimal benefit of endarterectomy for asymptomatic carotid stenosis, recent data from the international Asymptomatic Carotid Surgery Trial (ACST) suggest the surgery may be appropriate in select asymptomatic patients when it can be performed in low-risk centres.⁸

What's the role of antiplatelet therapy?

Stroke is often a manifestation of atherothrombosis; therefore, many patients presenting with evidence of cerebrovascular disease also have cardiovascular and peripheral arterial disease. In fact, evidence suggests 20% to 40% of stroke patients have asymptomatic cardiac ischemia.⁹

Antiplatelet therapy is the standard of care for the secondary prevention of atherothrombotic events after TIA or stroke. Treatment options include ASA, clopidogrel or combination ASA/dipyridamole (Table 3).

Table 3

Estimated benefit of antiplatelet agents vs. placebo

Treatment	Number of trials	Number of patients	% odds reduction (MI, stroke or vascular death)
All trials with any antiplatelet agent	195	144,051	25% ¹
Any acetylsalicylic acid	65	59,395	23% ¹
Dipyridamole	15	5,430	16% ¹
Ticlopidine**	42	6,910	32% ¹
Clopidogrel	1	19,185	30% ^{2*}

* The % odds reduction for clopidogrel is the result of a statistical analysis that uses data from the Antithrombotic Trialists' Collaboration and the CAPRIE trial to estimate the effect of clopidogrel vs placebo.

** Due to the risk of thrombotic thrombocytopenic purpura, the use of ticlopidine should be avoided.

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2. Fisher LD, Gent M, Buller HR: Active-control trials: How would a new agent compare with placebo? A method illustrated with clopidogrel, aspirin, and placebo. *Am Heart J* 2001; 141(1):26-32.

The optimal dose of ASA for stroke prevention is 81 mg/day. Higher doses are more gastrotoxic and have not shown greater efficacy in reducing the risk of vascular events.


The European Stroke Prevention Study-2 (ESPS-2) found the combination of dipyridamole and ASA to be more effective in reducing the risk of cerebrovascular events than ASA alone.¹⁰ It should be noted, however, that the dose of ASA in combination therapy may not provide adequate prophylaxis for coronary events. Furthermore, dipyridamole may worsen cardiac ischemia in patients with coronary artery disease due to coronary steal.

Results from the Clopidogrel vs. Aspirin in Patients at Risk of Ischemic Events (CAPRIE) study suggest clopidogrel is significantly more effective than ASA in reducing the risk of ischemic stroke, myocardial infarction or vascular death in patients at high risk.¹¹

The addition of ASA should be avoided in cerebrovascular patients using clopidogrel, as it is associated with an increased risk of bleeding and provides no additional benefits.

TIA: A golden opportunity for stroke prevention

Patients experiencing a TIA face an estimated 8% to 10% risk of stroke in the first 30 days following TIA.¹² Furthermore, the risk is time-dependent, with 50% of strokes occurring within the first two days of the index TIA.¹²

The standard of care for TIA patients is a rapid investigation, ideally within 24 hours. Cranial imaging by computed tomography (CT) or magnetic resonance imaging (MRI) is an essential part of the workup of suspected TIA to provide evidence of silent prior ischemic events, rule out a hemorrhagic mechanism and assist in the differential diagnosis. Carotid vascular imaging should be performed to rule out critical stenosis. 

References

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More on Tom

Tom's history is consistent with right hemispheric transient ischemic attack and requires rapid workup and treatment.

Antiplatelet therapy with acetylsalicylic acid (ASA), 81 mg, clopidogrel, 75 mg, or ASA/extended-release dipyridamole, 50/200 mg, should be started immediately.

His blood pressure should be further reduced, preferably with the use of an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker.

A statin should be started, regardless of Tom's cholesterol level and he must quit smoking. Nicotine replacement or bupropion may be helpful.

Cerebral and carotid vascular imaging are required as soon as possible. If Tom has evidence of advanced left carotid stenosis, he should be referred for surgical intervention.

Take-home message

- All stroke patients should receive the best possible management of modifiable risk factors, such as hypertension, hyperlipidemia, diabetes, smoking and atrial fibrillation.
- Carotid endarterectomy of symptomatic, severe stenosis remains one of the most effective strategies for stroke prevention.
- Antiplatelet therapy is the standard of care for the secondary prevention of atherothrombotic events after TIA or stroke.
- TIA requires urgent evaluation (that includes cranial imaging by CT or MRI) and treatment with antiplatelet agents to prevent disabling stroke and death.