Table 4. GRADE evidence profile Table for PICO 5.

Question: Permissive or induced hypertension compared to conventional blood pressure (BP) management (target normotension) for outcome

Setting: patients with an acute ischemic stroke or transient ischemic attack related to a high-grade intracranial atherostenosis causing severe hemodynamic compromise.

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Permissive or induced hypertension	conventional blood pressure (BP) management (target normotension)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
1	Randomized trials	Not serious	Not serious	Not serious	Serious[a]	None	0/59 (0.0%)	0/52 (0.0%)	Not estimable		⊕⊕⊕◯ Moderate	CRITICAL

CI: confidence interval.
[a]RCT not adequately powered compared to required sample size calculation.

Analysis of current evidence. Blood pressure management in patients during the acute phase of ischemic stroke still remains a matter of debate. Treatment with specific blood pressure lowering agents like glyceryl trinitrate patches and candesartan showed their significant effect on blood pressure lowering, but failed to prove any beneficial effect on clinical outcome.[46,47] A recent post-hoc analysis of the Efficacy of Nitric Oxide in Stroke (ENOS) trial indicated a shift toward a worse outcome measured by the modified Rankin Scale by day 90 (OR 1.46, 95% CI 1.01–2.11).[48] In a more recent trial of patients treated with intravenous thrombolysis comparing intensive versus standard blood pressure lowering treatment did not show a significant difference in the effect on death or disability at 90 days, but did show increased mortality caused by intensive blood pressure lowering treatment (OR 1.52, 95% CI 1.09–2.13).[49] All of the trials included patients regardless of the atherosclerosis status of the intracranial arteries. The European Stroke Organisation (ESO) and American Heart Association/American Stroke Association (AHA/ASA) guidelines specify evidence-based upper limits of blood pressure in all ischemic stroke patients and also in patients treated with intravenous thrombolysis and mechanical thrombectomy.[50,51] Neither of the guidelines refer specifically to blood pressure management in patients with acute ischemic stroke and ICAD. The AHA/ASA guideline states that induced hypertension in acute ischemic stroke is not well established.[51] Regarding the ESO general guidelines on acute BP management, induced hypertension in cases of clinical deterioration due to hemodynamic compromise is suggested only as a rescue therapy after other conservative measures to improve brain hemodynamics have been tried.[50]

It is a matter of deep concern whether blood pressure should be lowered intensely in patients with acute ischemic stroke and intracranial arterial stenosis as it may cause cerebral perfusion compromise. Mechanism preventing hypoperfusion in such patients has been established.[52,53]

Our systematic review has not identified any RCT answering which BP regimen is the most favorable during the acute phase of stroke in patients with ICAD. We have although identified one RCT (see Table 4 for GRADEpro ratings) comparing intensive (target SBP $<$ 120 mmHg) and modest (target SBP $<$ 140 mmHg) blood pressure lowering in patients with $>$50% or occlusion of the distal internal carotid artery (ICA) or the M1 segment of the MCA in patents with a recent ipsilateral ischemic stroke.[54] It has included mainly patients between 7 and 42 days following the index ischemic stroke. Therefore, the trial should be rather considered as an early secondary prevention trial. It has a randomized-controlled, single-blinded design. Patients with blood pressure exceeding 140 mmHg were eligible. Patients with intractable hypertension (systolic BP $\geqslant$ 150 mmHg with more than 3 antihypertensives) were excluded. The allocated blood pressure target was