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REVIEW

Treating coronary artery disease in patients with a history of cerebrovascular disease

Prise en charge des patients coronariens avec un antécédent de maladie cérébrovasculaire

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Summary Patients with coronary artery disease and a history of stroke account for as many as one in eight of all patients with coronary artery disease, and they are at higher risk of ischaemic events than patients with 'lone' coronary artery disease. It is therefore tempting to increase the potency of antithrombotic treatment in this patient subset. However, these patients are also at greater risk of intracranial haemorrhage. In recent trials of new antithrombotic agents in acute coronary syndromes, patients with a history of cerebrovascular disease derived no clinical benefit from (and were even harmed by) the potent novel antithrombotic agents, with an increased risk of intracranial haemorrhage. However, this risk did not appear to be uniform: it was higher in patients with a history of stroke than in those with a history of transient ischaemic attack, and appeared to be largely confined to the first year after stroke/transient ischaemic attack. Specific strategies to optimize the benefit/risk ratio of antithrombotic agents in this relatively common patient group should be developed and evaluated.

Abbreviations: ACS, Acute coronary syndrome; CAD, Coronary artery disease; CI, Confidence interval; HR, Hazard ratio; ICH, Intracranial haemorrhage; TIA, Transient ischaemic attack; TIMI, Thrombolysis in myocardial infarction.

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AVC

Résumé Les patients coronariens avec un antécédent d'AVC ou d'AIT représentent 1/8e des patients coronariens et ont un risque d'événement ischémique majoré. Il serait donc tentant d'augmenter l'intensité du traitement antithrombotique chez ces patients ; toutefois, ils présentent également un risque majoré d'hémorragie intracranienne. Dans plusieurs études récentes évaluant de nouveaux traitements antithrombotiques chez les patients présentant un syndrome coronaire aigu, les patients avec un antécédent de maladie cérébrovasculaire ne tiraient pas de bénéfice (ou avaient même un effet délétère) de l'utilisation de nouveaux traitement antithrombotiques plus puissants, avec un risque majoré d'hémorragie intracranienne. Ce risque n'est cependant pas uniforme. Il est plus élevé chez les patients avec un risque d'AVC que chez ceux avec un risque d'AIT et semble confiné à la 1ère année suivant l'événement cérébrovasculaire. Des stratégies spécifiques visant à optimiser la balance bénéfice/risque des traitements antithrombotiques dans ce sous-groupe de patient relativement importants doivent donc être développées et évaluées.

Background

Atherothrombosis is a generalized disease that often involves not only the coronary arteries, but also other arterial beds. For that reason, patients presenting with several atherothrombosis locations are not uncommon. Among them, patients presenting with coronary artery disease (CAD) and a history of cerebrovascular disease are of particular interest, because they occur frequently and present a therapeutic conundrum.

Patients with CAD and cerebrovascular disease: a frequent clinical problem

A history of cerebrovascular disease (including stroke or transient ischaemic attack [TIA]) is not uncommon in patients with CAD. In a cohort of more than 26,000 patients with CAD enrolled in the REACH registry of atherothrombosis, 4460 patients (approximately 17% of the CAD population) had a history of cerebrovascular disease (stroke or TIA) [1]. In the GRACE registry of acute coronary syndromes (ACSs), patients with a history of stroke constituted 8.25% of the overall population [2]. Cerebrovascular disease is therefore a common condition in patients with stable or unstable CAD.

Characteristics of patients with CAD and cerebrovascular disease

In the REACH registry, CAD patients with cerebrovascular disease were older, more frequently female and more likely to have a history of diabetes, hypertension or atrial fibrillation than patients with CAD alone. Overall, patients with a history of both CAD and cerebrovascular disease had a higher baseline risk of recurrent cardiovascular and bleeding events [1].

Risk of ischaemic events in patients with CAD and cerebrovascular disease

CAD patients with a history of cerebrovascular disease have worse clinical outcomes than patients without a history of cerebrovascular disease. In the GRACE registry, ACS patients with a history of stroke had dramatically higher hospital and 6-month mortality rates than patients without a history of stroke (8.9% vs 4.5% and 9.3% vs 3.9%, respectively); these differences persisted after adjustment for baseline characteristics [2]. In a pooled analysis of five French multicentre acute myocardial infarction registries, including nearly 10,000 patients (the Alliance project), multivariable analysis showed that a history of cerebrovascular disease was an independent factor for hospital mortality [3]. In stable patients, the same observation was made in the REACH registry: patients with a history of stroke/TIA had a higher rate of 5-year all-cause death (17.8% vs 11.2%) — mainly driven by cardiovascular death (12.2% vs 7.1%) — and cardiovascular events (24.9% vs 13.3% for cardiovascular death, myocardial infarction or stroke) — mainly driven by stroke (13.1% vs 4.1%) — compared with patients with CAD alone. These differences persisted after adjustment for differences in baseline characteristics [1].

Risk of intracranial haemorrhage in patients with CAD and cerebrovascular disease

As patients with CAD and previous stroke/TIA are at higher risk of ischaemic events, it is tempting to increase the potency of antithrombotic therapy in these patients. However, in several recent trials of new antithrombotic agents during or after ACS, patients with a history of cerebrovascular disease derived no benefit from (and in some cases were clearly harmed by) increasing the potency of antithrombotic therapy, while the rest of the patients (i.e. patients with ACS but without a history of cerebrovascular disease) derived benefit (see Table 1).