Cardioembolic Stroke and Postmyocardial Infarction Stroke

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KEYWORDS

• Stroke • Myocardial infarction • Thrombus • Atrial fibrillation • Inflammation

KEY POINTS

- The stroke risk is highest in the acute phase after myocardial infarction, but persists even thereafter.
- The pathophysiology leading to ischemic stroke following acute coronary syndrome is multifactorial: the leading subtype is the cardioembolic stroke, second is stroke of undetermined pathogenesis.
- The risk of cardiac thromboembolism originating from the left ventricle is mainly caused by akinetic segments of the left ventricle predisposing to mural thrombus formation.
- New onset of atrial fibrillation following acute myocardial infarction not only increases the risk of ischemic stroke but is also accompanied by a significant increase in overall mortality.

INTRODUCTION

Epidemiologic studies have proven that patients who have recently suffered an acute myocardial infarction (AMI), in consequence have an increased risk for the occurrence of ischemic stroke. These patients not only have a higher incidence for strokes when compared with the general population,[1,2] ischemic strokes after AMI remain associated with a worse mortality rate when compared with patients without cerebrovascular complications.[3,4] The odds ratio of in-hospital death is 4.3 in case of a stroke. The in-hospital mortality after ischemic stroke can be up to 10% to 20%, and even higher in patients with hemorrhagic stroke.[2,5] The mortality rates after 30 days and in long-term follow-up have been estimated to be 45% and up to 28%, respectively.[1,6–8]

The stroke risk is highest in the acute phase after myocardial infarction but persists even thereafter. The stroke risk is increased up to 44-fold within the first month but is also increased 3 years after the acute event.[9] The incidence of stroke during a hospital stay after acute coronary syndrome ranges from 0.7% to 2.2%.[10–15] Hachet and colleagues[16] reported the results of 8485 patients admitted to their intensive care unit for AMI between 2001 and 2010. Of those, 168 patients (1.9%) had a stroke within 1 year after AMI. Two-thirds (n = 123) were in-hospital strokes, of which the most occurred within the first 5 days after admission with a 30-day mortality of 34%. One year after the AMI, mortality was significantly increased: 57 patients with an in-hospital stroke died (46%) compared with 1056 patients (12%) without a stroke complicating the AMI ($P<.001$). Although the stroke risk progressively decreases in the months after AMI, the annual stroke rate (in-hospital and postdischarge) remained stable over the period 2001 to 2010.[16]

These rates could be confirmed by observational studies of American and Swedish patient registries showing the results of representative patient populations.[3,17,18] The evaluation of the

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American Nationwide Inpatient Sample revealed 1,924,413 patients admitted for AMI between 2006 and 2008. The overall rate of in-hospital neurologic complications was 2%: ischemic stroke 1.5%, transient ischemic attack (TIA) 0.3%, and hemorrhagic stroke 0.2%.[17] Female gender, age older than 65 years, and black race were found to be predictive of an increased risk for in-hospital neurologic complications. Independent risk factors were congestive heart failure, peripheral vascular disease, and the presence of atrial fibrillation.[17] Data collected from 173,233 patients from the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admission registry for 1998 to 2008 showed an ischemic stroke rate within 1 year of 4.1% (7185 patients). The 1-year mortality rate of these patients was 36.5%, compared with 18.3% for AMI patients without cerebral event.[3] But the mortality decreased over time (1998–2000 vs 2007–2008) in patients with and without a complicating stroke. There is an absolute decrease of 9.4% and 7.5%, and a relative decrease of 24% and 35%, respectively ($P<.001$).[3,18] This is mainly caused by the implementation of early reperfusion strategies in the therapy for myocardial infarction and secondary preventive therapies. A Cox regression of the registry results reveals age, female gender, transmural myocardial infarction, history of previous stroke, diabetes, reduced ejection fraction at admission, and atrial fibrillation as independent predictors of stroke complicating AMI, whereas reperfusion strategies using fibrinolysis or percutaneous coronary intervention (PCI) and medical treatment with aspirin, adenosine diphosphate (ADP)-receptor blockers, and statins reduce the stroke risk.[18]

Van de Graaff and colleagues[19] evaluated the beneficial effect of early reperfusion strategies for diminishing the risk of ischemic stroke following AMI. They used the National Registry of Myocardial Infarction to identify a total of 93,873 patients with an AMI. Of these, 45,997 patients were treated with thrombolytic therapy and 47,876 patients underwent primary PCI. The in-hospital stroke rates were 0.5% and 0.3%. Univariate analysis showed a statistically significant linear correlation between time to revascularization and the in-hospital stroke risk. A multivariate analysis revealed a significantly lower ischemic stroke risk in case of thrombolytic therapy, beginning within 15 minutes (odds ratio 0.58), and a nonsignificant trend toward a lower stroke risk in PCI started within 90 minutes of hospital arrival. However, the mechanism of decreasing the ischemic stroke risk did not seem to be related to an improved left ventricular ejection fraction (LV-EF).[19]

NONCARDIOEMBOLIC STROKES FOLLOWING ACUTE MYOCARDIAL INFARCTION

The pathophysiology leading to ischemic stroke following acute coronary syndrome is multifactorial. An evaluation of in-hospital strokes according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification showed 2 dominant stroke types: the leading subtype was the cardioembolic stroke (60%), the second was stroke of undetermined pathogenesis (36%).[16]

Regarding the group of noncardioembolic strokes, the underlying pathophysiological processes are multifactorial. Ischemia itself induces a systemic procoagulant effect, facilitating thrombus formation and embolization in the cerebral circulation. Although in patients with AMI a hypercoagulable state can be detected by increased prothrombin fragment 1 and 2, and fibrinopeptide A levels, which remain increased for up to 6 months after the index event, the appropriate blood levels in patients with stable coronary artery disease do not increase.[20] Furthermore, ischemia results in the release of inflammatory cytokines, causing the activation of neutrophils and the synthesis of acute phase reactants.[21,22] These might trigger the destabilization and rupture of plaques in the cerebral circulation.[23] The acute mediators of inflammation serve as both propagators and markers of plaque instability. The C-reactive protein (CRP) has a proinflammatory and a procoagulant effect.[20,24] CRP levels are increased in response to myocardial injury.[25,26] The inflammatory effect of the released cytokines is not limited to the coronary vasculature. Therefore, complex and unstable carotid plaques are common in patients with AMI (42% vs 8% in patients with stable angina).[27] This may cause plaque rupture and subsequent thrombus formation in supra-aortic vessels and cerebral circulation. These ischemia and cytokine-mediated processes also explain the beneficial effect of a fast restoration of coronary flow with respect to the risk of ischemic strokes following AMI.

CARDIOEMBOLIC STROKES FOLLOWING MYOCARDIAL INFARCTION

The previously listed cytokine mediated reactions also play a role in the development of cardiac thrombi. However, cardioembolic strokes following an AMI are mainly caused by (1) the formation of left ventricular thrombi and (2) atrial fibrillation.

Left Ventricular Thrombus Formation

The risk of cardiac thromboembolism originating from the left ventricle is mainly caused by an