Adrenoreceptor Polymorphisms and Subarachnoid Hemorrhage

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See related article, pages 1680–1685.

Neurogenic stunned myocardium (NSM) is reversible cardiac dysfunction, typically after subarachnoid hemorrhage (SAH). The most likely pathophysiology of NSM is a catecholamine surge that leads to transient ventricular dysfunction. The pathophysiology is probably similar to Tako-Tsubo cardiomyopathy and cardiac dysfunction caused by fright. SAH presents a different and acute clinical scenario, however, because these patients often require hyperdynamic therapy for symptomatic or radiographic vasospasm. Both increasing cardiac output and blood pressure increase cerebral perfusion, but hyperdynamic therapy with a failing left ventricle can quickly lead to pulmonary edema, hypoxia, hypotension and cerebral infarction.

Methods to predict which patients will develop NSM would be very helpful. Serum catecholamine levels might reasonably be expected to coincide with the catecholamine surge and NSM; however, the available data have not borne this out. Cardiac troponin I (cTII) has emerged as a fast, cheap and prognostic test for predicting NSM, as well as poor outcome and death. Although cTII is helpful, it does not answer several important questions: Why do some patients have an elevation in cTII and others do not? What are the underlying mechanisms that lead to NSM? Do they offer further insights into diagnosis than measuring cTII?

An article in this issue of Stroke offers some insights. Genotyping was done for catecholamine receptor subtypes. Several genetic receptor subtypes were associated with both cTII release and depressed ejection fraction on echocardiography. This implicates the genetic code of receptor subtypes, and probably receptor function, in cTII release and NSM.

These data increase our understanding of NSM, and may indicate that the relationship between catecholamine release and NSM is not linear. Rather, the effect of serum catecholamine levels depends on adrenoreceptor subtype. Some patients, by virtue of their adrenoreceptor genetic subtype, will be at higher risk for cTII release, myocardial damage and NSM with an equivalent catecholamine surge and serum catecholamine level. It is unfortunate that many poor grade patients (only 5 Hunt & Hess grade 5 patients had genetic analysis) could not provide consent for genetic analysis, and that these patients could not be studied. Poor-grade patients tend to have higher cTII levels and a higher likelihood of NSM, so we have the most to learn from them. Concerns about the privacy of medical information and research are likely to be a recurring theme in clinical research, and we must find ways to ensure every patient’s privacy is protected while we continue to search for refinements in diagnosis and treatment of neurologically devastating diseases. These findings should be confirmed in a second set of patients. The frequencies of these alleles among SAH patients in general are not known because the patients under study are a subset of SAH patients, but such information is needed to estimate the importance of screening for these variations.

Perhaps genetic adrenoreceptor subtyping will one day provide rapid prognostic information for risk-stratification, but it is unlikely to be a clinically useful test in the near future. This sort of research provides unique insights into pathophysiology and further develops the fields of neurocardiology, neurocritical care, and cerebrovascular science.

References


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