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Coronary Allograft Vasculopathy: Importance of Microvascular Dysfunction

Junho Hyun
Asan Medical Center, University of Ulsan, Republic of Korea

Cardiac allograft vasculopathy (CAV) is a major cause of graft loss, death in heart transplant recipients with long-term survival. Prevalence of CAV is reportedly about 30% at 5 years, over 50% at 10 years after transplantation. Presence of CAV significantly affects long-term outcomes. Patterns in development and progression of CAV could be different with individuals. Although CAV can be diagnosed accurately with pathologic examination, coronary angiography (CAG) is currently accepted as a standard method to detect presence and severity of CAV. Current consensus from the International Society for Heart and Lung Transplantation recommends diagnosis of CAV with any detectable lesion by CAG. However, because CAG is basically luminography and CAV typically involves concentric, diffuse lesions, Sensitivity of CAG is quite low. For this reason, intravascular ultrasound (IVUS) during CAG examination is accepted as a gold standard method to detect CAV even at early stage. Increase in maximal intimal thickness more than 0.5 mm during the first year of heart transplant was reported to be associated with higher risk for adverse cardiac events. There are still clinical unmet needs to resolve. There are no convincing therapeutic modalities to prevent and regress CAV. mTOR inhibitors were reported to prevent development and progression of CAV especially used during the early period after transplantation. Nevertheless, initiation of mTOR inhibitors should preferentially be used in the early stage of CAV, and efficacy of mTOR inhibitors is reportedly low after progression to remarkable disease burden. However, there are no screening methods to reliably predict development of CAV. Previous studies suggested that microvasculopathy of transplanted heart was prevalent and significantly affected post-transplant outcomes, and microvasculopathy could precede before stenotic lesion in epicardial coronary vessel. Therefore, detection of microvasculopathy may be important clue for development of CAV. Because previous studies detected microvasculopathy only with tissue biopsy, coronary physiologic study is one of the promising methods to detect microvascular dysfunction. Recent studies suggested that measurement of FFR, IMR could predict post-transplant outcomes including rejection, adverse cardiac events. Detection of microvascular dysfunction in the first year of transplantation can give us important prognostic value and may possibly implicate tailored

immunosuppressive therapy such as conversion of mTOR inhibitors before development of prominent CAV.