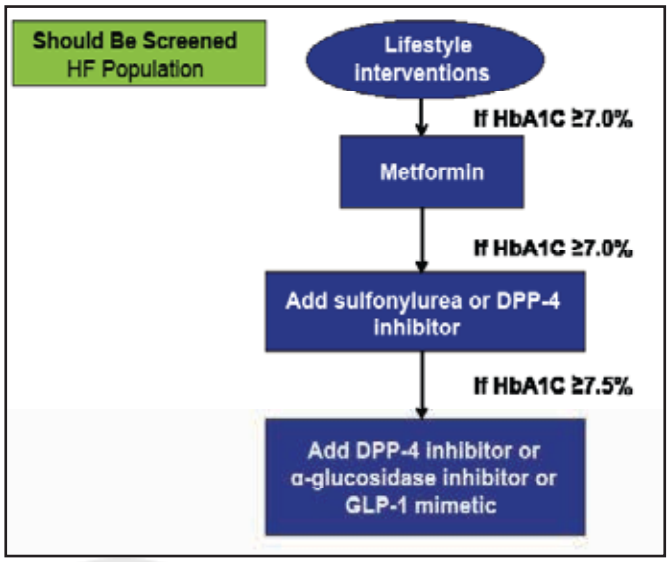
Figure 1. Glycemic Control Strategy.



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Patients with diabetes often develop HF, which places a substantial burden on healthcare resources. Diabetes appears to directly affect the myocardium, but pathophysiologic data for humans are not available. HF patients should be screened for diabetes. Prospective studies examining therapeutic strategies in patients with diabetes and acute or chronic HF are warranted.

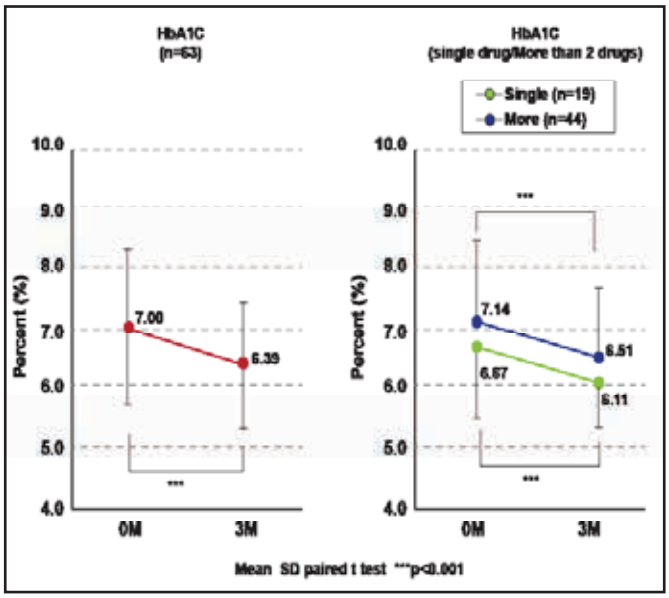
Incretins in Cardiovascular Disease

Junichi Oyama, MD, PhD, Saga University, Saga, Japan, discussed the potential benefits of incretin therapies in patients with cardiovascular disease (CVD). The 2 main incretin hormones are glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide. Glucose in the small intestine triggers release of incretins, which stimulate insulin secretion by pancreatic beta-cells; glucagon and glucose concentrations decline as insulin increases. GLP-1 also exerts beneficial effects on myocardial and endothelial function by inhibiting upregulation of reactive oxygen species and vascular cell adhesion molecule-1 mRNA in endothelial cells.

Current incretin therapies available in Japan include the GLP-1 analogues, exenatide and liraglutide, and the DPP-4 inhibitors sitagliptin, vildagliptin, alogliptin, and linagliptin. Liraglutide reduces TNF-α-induced oxidative stress and inflammation in endothelial cells and decreases mortality and infarct size in murine myocardial ischemia/reperfusion injury. In diabetes patients with stable coronary artery disease, GLP-1 infusion improved endothelial function. GLP-1 improved ejection fraction, 6-minute walk distance, maximal oxygen consumption (VO_2 max), and quality of life in heart failure patients.

The Saga-challenge Antidiabetes Observation Study for Sitagliptin [S-DOG], a nonrandomized, single-arm study, evaluated the efficacy and safety of sitagliptin in diabetes patients. The interim analysis showed that sitagliptin significantly reduced HbA1C ($p<0.001$; Figure 1), triglycerides ($p<0.01$), and blood pressure ($p<0.001$).

Figure 1. HbA1C Reductions.



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The Program of Vascular Evaluation Under Glucose Control by DPP-4 Inhibitor [PROLOGUE; UMIN000004490] study is a prospective, randomized, multicenter trial to evaluate the effects of sitagliptin versus conventional therapy on carotid artery atherosclerosis in diabetes patients. The primary endpoint is the annual change in carotid artery intima-media thickness, evaluated by ultrasonography. As of March 2012, 326 patients had been enrolled.

There is increasing evidence of the potential beneficial effects of incretin therapies on CVD beyond glycemic control. However, clinical data are insufficient, and future studies of incretin therapy for CVD are needed.

DPP-4 in Diabetic Cardiomyopathy

Dipeptidyl peptidase-4 (DPP-4) is a serine exoprotease that is expressed on the surface of many cells. DPP-4 truncates bioactive molecules, including incretin and nonincretin substrates. Among the substrates degraded by DPP-4 are stromal cell-derived factor-1 alpha (SDF-1α)