The chronic occlusion of the left anterior descending coronary artery (LAD) has been used extensively to induce myocardial ischemia and postinfarction disturbance in different animal species. Functional parameters, such as left ventricular end-diastolic pressure (LVEDP), cardiac output, or the first derivative of pressure of time (dp/dt max), are assessed in this model. The non-infarcted myocardium maintained normal blood flow, while the blood flow in the infarcted myocardium was significantly reduced to normal (Pfeffer and Braunwald 1990). This is an essential model for a subset of patients in whom postinfarction dilated cardiomyopathy developed after a single, moderate-sized infarct. Since there are no confounding variables (arteriosclerosis, several infarcts, hypertension, diabetes, etc.), this model provides an opportunity to understand the progression of a normally perfused and contractile myocardium to a hypocontractile status after transmural infarction.

The Pfeffer group was the first who used this model and observed that the angiotensin-converting enzyme inhibitor "captopril" therapy reduced LV chamber dilation, improved LV systolic function, and increased survival in rats with moderate or large MIs (Pfeffer and Braunwald 1990). This groundbreaking work in the rat MI model led to clinical trials testing the utility of the angiotensin-converting enzyme inhibitor, captopril, in post-MI patients with reduced LV function. A multicenter Survival and Ventricular Enlargement (SAVE) trial was conducted in which captopril or placebo was administered 3–16 days following MI in patients with reduced LV function. Captopril decreased all-cause mortality by 19% with a 22% reduction in heart failure hospitalizations after a mean follow-up period of 42 months; the reductions in mortality and morbidity were associated with less LV dilation or remodeling during the first year of therapy (Pfeffer et al. 1985). This study demonstrated very elegantly the utility of small animal models to explore new and potentially important therapies for heart failure. The rat MI model was also essential in establishing the beneficial effects of angiotensin II type 1 receptor antagonists (ARAs) on LV structure and function following MI (Pfeffer et al. 1985).

2.3 HF Induced by DOCA

The treatment with deoxycorticosterone acetate (DOCA)-salt, a synthetic mineralocorticoid derivative, is widely used to induce HF mediated by volume overload in several species and conditions and reviewed in detail by Iyer et al. (2010). The DOCA-salt model results in hypertension via salt retention and an increase in circulating blood volumes (Gavras et al. 1975). These changes are also accompanied with the development of cardiac hypertrophy, fibrosis, conduction abnormalities, and endothelial dysfunction, followed by cardiovascular remodeling. Furthermore, the DOCA-salt hypertensive rat is a model for human primary aldosteronism and is associated with a markedly depressed renin-angiotensin system and thus has been regarded as an angiotensin-independent model with significantly decreased circulating plasma renin activity. Similar characteristics have been made in patients with hypertension and heart failure.