Management of age-induced cardiomyopathy and its associated cardiovascular diseases remains a major clinical challenge. This is mainly because cardiac aging is regulated by a combination of cell autonomous quality control systems (such as autophagy), and cell non-autonomous factors (such as inflammatory cytokines). Among all known longevity-regulating hormonal systems, TGF-beta/activin signaling holds promises as a therapeutic target for treatment of age-related diseases because of its important roles in inflammation, fibrosis and tissue regeneration. However, how activin signaling contributes to tissue aging, especially cardiac aging, is largely unknown. Using the fruit fly Drosophila as a model system, we found that activin acts as a pro-aging factor that inhibits autophagy and tissue homeostasis in fly hearts. Besides its cell-autonomous role in cardiac autophagy and arrhythmicity, activin is highly expressed in fly liver and controls cardiac function by activating the liver production of unpaired 3 (upd3), the fly homology of mammalian interleukin 6 (IL6). Our findings suggest that there are autonomous and non-autonomous factors that coordinately regulate tissue homeostasis during cardiac aging.