Myocardial fatty acid (FA) oxidation is regulated acutely by the FA supply and chronically by changes at the gene transcriptional level via the PPAR family. The aim of the present study was to examine the effects of tetradecylthioacetic acid (TTA, a pan PPAR agonist) on myocardial metabolism and ventricular function. Balb/c mice were treated for 8 days with TTA (0.5%, added to the diet). Using the isolated working heart we examined myocardial FA and glucose oxidation, cardiac efficiency (the relationship between myocardial work (pressure-volume area, PVA) and myocardial oxygen consumption (MVO₂)) as well as functional recovery following 40 min low-flow ischemia.

In contrast to previous reports showing no changes in cardiac metabolism following PPAR treatment of normal mice, TTA treatment caused a 2.4 fold increase in myocardial FA oxidation with a concomitant reduction in glucose oxidation. Hearts from TTA-treated mice showed a marked reduction in cardiac efficiency, due to a near two-fold increase in the oxygen used for non-contractile processes (i.e. unloaded MVO₂). These hearts also showed decreased recovery of ventricular function following low-flow ischemia. We conclude that TTA have a direct and strong stimulatory effect on FA oxidation in the normal mouse heart. This elevation of myocardial FA oxidation leads to a marked increase in MVO₂ which could contribute to the reduced ischemic tolerance.