Dietary supplementation with polyunsaturated fatty acids (PUFAs) alters the course of experimental kidney disease in dogs. In particular, supplementation with omega-6 PUFAs hastens the decline of kidney function, and omega-3 PUFAs are renoprotective. We investigated the early stages of renal insufficiency to determine whether PUFA supplementation altered the magnitude of hypercholesterolemia or glomerular hemodynamics. Two months after 11/12 nephrectomy, dogs were randomly divided into three groups of 6 animals each. Each group of dogs was then fed a low-fat basal diet supplemented with one of three sources of lipid to achieve a final concentration of 15% added fat. Fat sources were rich in omega-3 PUFAs (menhaden fish oil, group FO), omega-6 PUFAs (safflower oil, group SO), or saturated fatty acids (beef tallow, group C). Early in renal insufficiency, before significant kidney damage, group FO had a lower (P<.05) serum cholesterol concentration and tended to have a lower urinary prostaglandin E2 (PGE2) and thromboxane A2 (TxA2) excretion than group C. In contrast, group SO had a higher mean glomerular capillary pressure (P<.05) and more glomerular enlargement (P<.05) and tended to have higher eicosanoid excretion rates than group C. These differences in lipid metabolism, glomerular hypertension and hypertrophy, and urinary eicosanoid metabolism could explain, in part, the beneficial effects of omega-3 PUFAs and the detrimental effects of omega-6 PUFAs when administered on a long-term basis in this model of renal insufficiency.