SIGNIFICANCE STATEMENT

Renal fibrosis, characterized by the accumulation of extracellular matrix around the tubules, is a hallmark of chronic renal failure independent of the underlying disease. Although various cell types, including hematopoietic cells, can express collagen, it is unclear to what extent these cells contribute to deposition of collagen and how fibrosis affects renal function. Using newly generated cell type–specific collagen I knockout mice, we show that collagen-producing hematopoietic cells contribute to 38%–50% of the deposition of collagen I. Functionally, collagen deposition is essential for renal survival after unilateral ureteral obstruction, whereas it is deleterious in the chronic model of adenine-induced nephropathy. Our work leads to a better understanding of the cellular origin and functional relevance of renal fibrosis.