SIGNIFICANCE STATEMENT

IL-33 has been described as a potent inflammatory mediator with deleterious effects in nephrotoxic and obstructive AKI models. However, direct proof of the involvement of IL-33 in experimental kidney ischemia-reperfusion injury (IRI) has not been available. This study shows an early alarmin-like release of IL-33 mainly by renal microvascular endothelial cells during IRI preceding the phase of neutrophil cell infiltration. Mice lacking IL-33 were protected against IRI, a phenomenon that was associated with decrease of IL-33–specific receptor-expressing innate cells. The findings suggest IL-33 as a potentially a useful diagnostic marker for AKI. Neutralizing IL-33 could be beneficial for long-term graft survival after kidney transplantation.