

SIGNIFICANCE STATEMENT

The development of antibodies recognizing antigens expressed on transplanted organs is a known risk factor for transplant rejection and graft loss. The pathogenic potential of less-studied antibodies, such as natural antibodies (Nabs), is increasingly recognized. Nabs are IgG binding to self-antigens, including the oxidation-related epitope malondialdehyde (MDA). In this study, the development of Nabs in the year after transplant, defined by an increase in serum reactivity to MDA, was measured in a kidney transplant cohort. The development of Nabs correlated with worse graft injury at 1 year post-transplant and poorer long-term outcomes. This association between Nabs, kidney graft injury, and graft loss suggests a detrimental role for Nabs in antibody-mediated rejection. Further study on the mechanisms of injury is warranted.