ABSTRACT
The tumor suppressor BRCA1 or BRCA2 gene is mutated in familial breast and ovarian cancer, however its role in protecting other tissues from DNA damage has not been explored. For the first time, we have shown new roles for BRCA1 and BRCA2 (BRCA) as a gatekeeper of cardiac and vascular function, as well as survival. In mice, tissue-specific loss of BRCA1 or BRCA2 results in adverse cardiac remodeling, poor ventricular function, endothelial dysfunction and higher mortality in response to various stress. Our data reveal BRCA as novel and essential adaptive response molecules shielding cardiac and vascular system under stress. We also demonstrate that BRCA mutation carriers, in addition to risk of breast and ovarian cancer, may be at a previously unrecognized risk of cardiovascular diseases.