Osteoglycin prevents the development of age-related diastolic dysfunction during pressure overload by reducing cardiac fibrosis and inflammation

Sophie Deckx\textsuperscript{a,b}, Ward Heggermont\textsuperscript{b}, Paolo Cara\textsuperscript{a,b}, Marieke Rienks\textsuperscript{a}, Tom Dresselaers\textsuperscript{c}, Uwe Himmelreich\textsuperscript{c}, Rick van Leeuwen\textsuperscript{a}, Wies Lommen\textsuperscript{c}, Jolanda van der Velden\textsuperscript{d,e}, Arantxa Gonzalez\textsuperscript{f,g}, Javier Diez\textsuperscript{f,g,†}, Anna-Pia Papageorgiou\textsuperscript{a,b,†} and Stephane Heymans\textsuperscript{a,b,e}

\textsuperscript{a} - Center for Heart Failure Research, Cardiovascular Research Institute Maastricht, The Netherlands
\textsuperscript{b} - Molecular and Vascular Biology, Department of Cardiovascular Sciences, KU Leuven, Belgium
\textsuperscript{c} - Biomedical MRI Unit, Department of Imaging and Pathology, KU Leuven, Belgium
\textsuperscript{d} - Department of Physiology, Institute for Cardiovascular Research, VU University Medical Center, Amsterdam, The Netherlands
\textsuperscript{e} - ICIN—Netherlands Heart Institute, Utrecht, The Netherlands
\textsuperscript{f} - Program of Cardiovascular Diseases, Centre for Applied Medical Research, University of Navarra, Spain
\textsuperscript{g} - CIBERCV, National Health Institute Carlos III, Ministry of Economy and Competitiveness, Spain

Correspondence to Anna-Pia Papageorgiou: Department of Cardiology, University Hospital Maastricht, Universiteitsingel 50, 6202 AZ Maastricht, The Netherlands. anna.papageorgiou@maastrichtuniversity.nl


Abstract

The small leucine-rich proteoglycan osteoglycin has been implicated in matrix homeostasis in different organs, including the ischemic heart. However, whether osteoglycin modulates cardiac hypertrophy, fibrosis or inflammation in hypertensive heart disease and during aging remains unknown. Angiotensin-II-induced pressure overload increases cardiac osteoglycin expression, concomitant with the onset of inflammation and extracellular matrix deposition. Interestingly aging led to decreased cardiac levels of osteoglycin, yet absence of osteoglycin did not affect organ structure or cardiac function up to the age of 18 months. However, Angiotensin-II infusion in combination with aging resulted in exaggerated cardiac fibrosis and inflammation in the osteoglycin null mice as compared to wild-type mice, resulting in increased diastolic dysfunction as determined by magnetic resonance imaging. In vitro, stimulation of bone marrow derived macrophages from osteoglycin null mice with Angiotensin-II resulted in significantly higher levels of ICAM-1 as well as pro-inflammatory cytokines and chemokines IL-1\textbeta and MCP-1 as compared to WT cells. Further, stimulation of human cardiac fibroblasts with osteoglycin reduced cell proliferation and inhibited TGF-\beta induced collagen gene expression. In mouse cardiac tissue, osteoglycin expression inversely correlated with TGF-\beta expression and in cardiac biopsies of aortic stenosis patients, osteoglycin expression is significantly higher than in control biopsies. Interestingly, osteoglycin levels were higher in patients with less severe myocardial fibrosis and overall in the aortic stenosis patients osteoglycin levels negatively correlated with collagen content in the myocardium. In conclusion, osteoglycin expression is increased in the heart in response to pressure overload and its absence results in increased cardiac inflammation and fibrosis resulting in increased diastolic dysfunction.

Introduction

Despite continuous improvements in the treatment of hypertension, the prevalence of hypertension and hypertension-related morbidity and mortality remains high. Amongst adults over twenty, the prevalence of hypertension is estimated to be around 30% in the USA\textsuperscript{[1]} and around 45% in Europe\textsuperscript{[2]}, with a dramatic increase with advanced age in both regions\textsuperscript{[1,2]}. This resulted in an estimated 72,000 deaths in the USA alone in 2013\textsuperscript{[1]}. Importantly, up to 20% of hypertensive people are not aware of their condition\textsuperscript{[1]}. © 2017 Elsevier B.V. All rights reserved.
Fig. 1. (legend on next page)
دریافت فوری متن کامل مقاله

امکان دانلود نسخه تمام متن مقالات انگلیسی
امکان دانلود نسخه ترجمه شده مقالات
پذیرش سفارش ترجمه تخصصی
امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
امکان دانلود رایگان ۲ صفحه اول هر مقاله
امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
دانلود فوری مقاله پس از پرداخت آنلاین
پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات