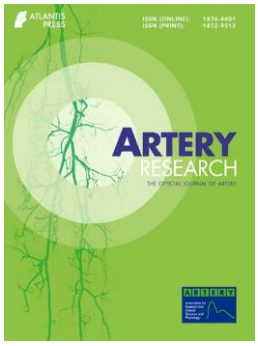

**Artery Research**

**ISSN (Online): 1876-4401 ISSN (Print): 1872-9312**
**Journal Home Page: https://www.atlantis-press.com/journals/artres**

# 6.4: CARDIOTROPHIN-1 INDUCES STRUCTURAL AND MECHANICAL CHANGES IN AORTA

R. Akhtar, N. López-Andrés, C. Labat, J. Díez, F. Zannad, X. Zhao, B. Derby, J.K. Cruickshank, P. Lacolley, P. Rossignol

**To cite this article**: R. Akhtar, N. López-Andrés, C. Labat, J. Díez, F. Zannad, X. Zhao, B. Derby, J.K. Cruickshank, P. Lacolley, P. Rossignol (2011) 6.4: CARDIOTROPHIN-1 INDUCES STRUCTURAL AND MECHANICAL CHANGES IN AORTA, Artery Research 5:4, 145–145, DOI: https://doi.org/10.1016/j.artres.2011.10.228

**To link to this article**: https://doi.org/10.1016/j.artres.2011.10.228

Published online: 14 December 2019

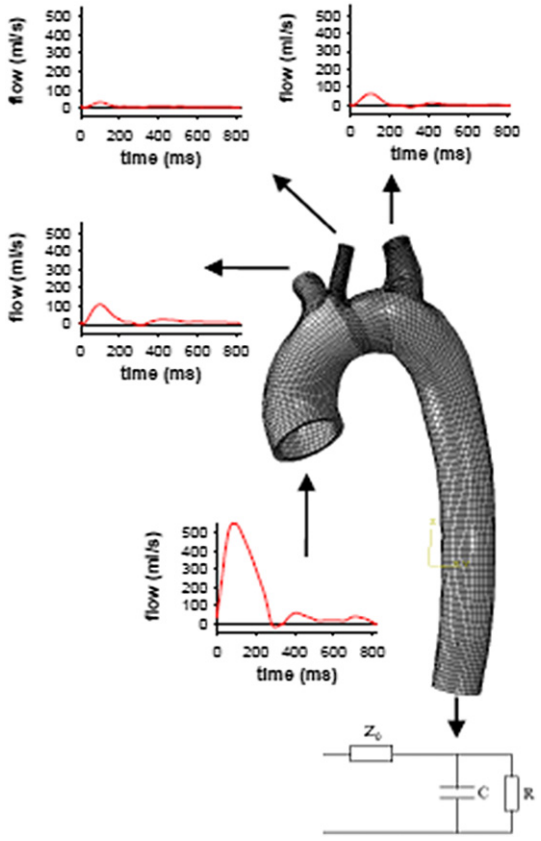


**Figure 1** Patient-specific geometry and boundary conditions.

### 6.3
### OXIDATIVE STRESS AND INFLAMMATION: IMPLICATION IN ENDOTHELIAL DYSFUNCTION AND CARDIOVASCULAR AGING ON MURINE MODELS

S. Baron [1,*], T. Bedarida [1,*], M. M. Strelcyn [1], C. H. Cottart [1,2], F. Vibert [1], G. Renault [3], B. Saubamea [4], E. Veissieres [5], D. Henrion [5], J. L. Beaudeux [1,2], V. Nivet-Antoine [1,6]
[1]*Groupe VIVA , EA4466, Université Paris Descartes, Paris, France*
[2]*APHP, Hôpital Pitié Salpêtrière-Charles Foix, Service de biochimie-hématologie Charles Foix, Ivry sur seine, France*
[3]*PIPA, Institut Cochin, Université Paris Descartes, Paris, France*
[4]*SCICM, Université Paris Descartes, Paris, France*
[5]*Laboratoire CNRS- INSERM 771 Faculté de médecine, Angers, France*
[6]*APHP, Laboratoire de Biochimie, Hôpital Européen Georges Pompidou, Paris, France*

The aim of the study was to characterize cardiovascular aging with functional (Doppler) and molecular (RT-qPCR and immunohistochemistry quantifications) approaches using three murine models. Molecular studies on aorta (AO) and mesenteric arteries (MA) were used to explore the role of oxidative stress and inflammation. Time-induced aging model corresponded to 25 months-old C57Bl/6J mice feed with standard diet. Doppler exhibited a concentric left ventricle hypertrophy with a decreased aortic distensibility, and an increased aortic thickening. This model presented both a decreased Thioredoxin1 expression (AO and MA) and an increased NADPH oxidase (MA) expression. Inflammation markers were increased in MA (IL-1beta in MA and in AO (IL-6, TNF-alpha). Three months with High Fat and Protein Diet (HFPD) at 9 months induce a major hyperlipidemia. This model exhibited a dilated cardiopathy with both a decreased aortic distensibility and an increased aortic thickening. HFPD increased NADPH oxidase, IL1-beta and TNF-alpha expressions and decreased Thioredoxin1 expression (AO and MA). The mixed model corresponded to 25-months old C57Bl/6J mice feed for 3 months with HFPD. They presented a major cardiopathy with a decreased aortic distensibility, and exhibited both a major oxidative stress (increased NADPH oxidase and decreased Thioredoxin1 in AO and MA) and a major endothelial inflammation (increased IL-1beta, IL-6 and TNF-alpha in AO and MA). eNOS gene was not modify in any model. We conclude that NADPH oxidase and Thioredoxin1 seem to play a key role in the arterial aging process and might be interesting potential targets for therapeutics assays.

### 6.4
### CARDIOTROPHIN-1 INDUCES STRUCTURAL AND MECHANICAL CHANGES IN AORTA

R. Akhtar [1], N. López-Andrés [2], C. Labat [2], J. Díez [3,5], F. Zannad [2,4], X. Zhao [1], B. Derby [1], J. K. Cruickshank [6], P. Lacolley [2], P. Rossignol [2,4]
[1]*The University of Manchester, Manchester, United Kingdom*
[2]*Inserm, Vandoeuvre-lès-Nancy, France*
[3]*Division of Cardiovascular Sciences, Centre for Applied Medical Research, Pamplona, Spain*
[4]*CIC-INSERM CHU de Nancy, Vandoeuvre-lès-Nancy, France*
[5]*Department of Cardiology, University Clinic, Pamplona, Spain*
[6]*King's College, London, United Kingdom*

**Aims**: Cardiotrophin-1 (CT-1), a cytokine belonging to the interleukin-6 family, exerts proliferative and secretory effects in vascular smooth muscle cells. We investigated the morphological, micromechanical and molecular vascular changes induced by chronic CT-1 administration in rats.
**Methods**: Recombinant rat CT-1 (20 μg/Kg, IP) or vehicle (n=10/group) was administrated to Wistar rats for six weeks. Vascular structure and function were determined with an echo-tracking device. Aortic extracellular matrix (ECM) protein production and attachments were quantified by immunohistochemistry, RT-PCR and Western blot. Acoustic wavespeed within the aorta was determined using a novel scanning acoustic microscopy (SAM) method at 1 GHz which enables tissues stiffness to be determined with a ~1 μm spatial resolution.
**Results**: In normotensive CT-1-treated rats, the incremental elastic modulus-circumferential wall stress curve was shifted leftward compared to vehicle, indicating increased arterial stiffness. Aortic media thickness was higher (40%) in CT-1-treated rats. Aortic collagen type I (80%), fibronectin (80%), metalloproteinases activities (40%), integrins (70%) and focal adhesion proteins (60%) were also increased in whereas elastin levels were similar to controls. Further, increased acoustic wavespeed in CT-1 rats ($1694 \pm 2$ $ms^{-1}$ compared to $1673 \pm 2$ $ms^{-1}$, $p<0.001$) was found in parallel with increases in collagen volume fraction (21 % as compared to 9 % in controls).
**Conclusions**: We demonstrate that CT-1 is a key player in arterial remodelling and stiffness by modulating aortic mechanical properties, media thickness, ECM production and attachments. Thus, CT-1 could be a new biotarget to reduce arterial stiffness and decrease ECM deposition in vascular diseases.

### 6.5
### ACUTE β-ADRENERGIC BLOCKADE INCREASES AORTIC WAVE REFLECTION IN YOUNG MEN AND WOMEN: DIFFERING MECHANISMS BETWEEN SEXES

D. P. Casey, T. B. Curry, M. J. Joyner, N. Charkoudian, J. N. Barnes, E. C. Hart
*Mayo Clinic, Rochester, MN, United States of America*

Acute β-adrenergic blockade increases aortic wave reflection, however, the mechanisms remain unclear. Evidence suggests that β-adrenergic receptor sensitivity in the peripheral vasculature differs between sexes. Therefore, the goal of this study was to examine whether β-adrenergic blockade alters aortic wave reflection and forearm vasoconstrictor responsiveness to a similar extent in young men and women. In thirty-one subjects (16M/15F; 26±1 years) non-invasive aortic pressure waveforms were synthesized from high-fidelity radial pressure waveforms via applanation tonometry before and during systemic β-blockade (0.25 mg/kg bolus, followed by 0.004 mg/kg/min continuous infusion of propranolol). Forearm vasoconstrictor responses to exogenous intra-arterial norepinephrine (NE) were also assessed in a subset of subjects (13M/9F). Wave reflection characteristics are summarized in Table 1. β-blockade increased aortic augmentation index (AIx) and wave reflection amplitude (aortic augmented pressure (AG)) in both sexes. However, the increase in wave reflection tended to be greater ($P<0.05$ and $P=0.07$ for AG and AIx, respectively) in women following β-blockade. AIx adjusted for HR (AIx@75bpm) increased in women following β-blockade, whereas it was unchanged in men. Moreover, the change (Δ) in AIx was inversely associated to ΔHR only in men ($r=-0.54$, $P<0.05$). Finally, β-blockade caused an enhanced forearm vasoconstrictor response to exogenous NE in women (Figure 2). Our data suggest that: 1) aortic wave reflection is increased to a greater extent in women following systemic β-blockade; and 2) the mechanism for enhanced aortic wave reflection