MÉCANISMES PHYSIOPATHOLOGIQUES ET CONSÉQUENCES DES CALCIFICATIONS CARDIOVASCULAIRES

Cardiovascular Research

JOURNAL ARTICLE

Aortic valve calcification is promoted by interleukin-8 and restricted through antagonizing CXC motif chemokine receptor 2

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Kawthar Dhayni, Yuthiline Chabry, Lucie Hénaut, Carine Avondo, Cedric Boudot, Hakim Ouled-Haddou, Edith Bigot-Corbel, Gilles Touati, Thierry Caus, Hind Messaoudi ...
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https://doi.org/10.1093/cvr/cvad117
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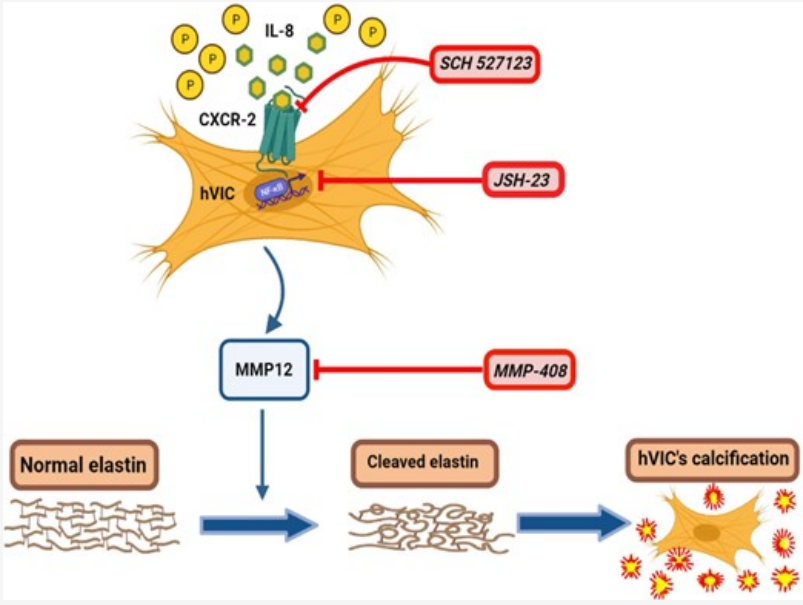
Abstract

Aims

Inflammatory cytokines play a critical role in the progression of calcific aortic valve disease (CAVD), for which there is currently no pharmacological treatment. The aim of this study was to test the hypothesis that interleukin-8 (IL-8), known to be involved in arterial calcification, also promotes aortic valve calcification (AVC) and to evaluate whether pharmacologically blocking the IL-8 receptor, CXC motif chemokine receptor 2 (CXCR2), could be effective in preventing AVC progression.



Journal of Cellular Physiology

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RESEARCH ARTICLE | Open Access

Vasorin plays a critical role in vascular smooth muscle cells and arterial functions

Loïc Louvet, Gaëlle Lenglet, A. Michaela Krautzberger, Romuald Mentaverri, Frédéric Hague, Clara Kowalewski, Nassim Mahtal, Julie Lesieur, Anne-Laure Bonnet ... See all authors

First published: 26 July 2022 | https://doi.org/10.1002/jcp.30838

Acces au texte integral

Loïc Louvet and Gaëlle Lenglet contributed equally to this study.

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Abstract

Within the cardiovascular system, the protein vasorin (Vasn) is predominantly expressed by vascular smooth muscle cells (VSMCs) in the coronary arteries and the aorta. *Vasn* knockout (*Vasn*$^{-/-}$) mice die within 3 weeks of birth. In the present study, we investigated the role of vascular Vasn expression on vascular function. We used inducible *Vasn* knockout mice (*Vasn*$^{\text{CRE-ERT KO}}$ and *Vasn*$^{\text{SMMHC-CRE-ERT2 KO}}$, in which respectively all cells or SMCs only are targeted) to analyze the consequences of total or selective Vasn loss on vascular function. Furthermore, in vivo effects were investigated in vitro using human VSMCs. The death of *Vasn*$^{\text{CRE-ERT KO}}$ mice 21 days after tamoxifen injection was concomitant with decreases in blood pressure, angiotensin II levels, and vessel contractibility to phenylephrine. The *Vasn*$^{\text{SMMHC-CRE-ERT2 KO}}$ mice displayed concomitant changes in vessel contractibility in response to phenylephrine and angiotensin II levels. In vitro, *VASN* deficiency was associated with a shift toward the SMC contractile phenotype, an increase in basal intracellular Ca^{2+} levels, and a decrease in the SMCs' ability to generate a calcium signal in response to carbachol or phenylephrine. Additionally, impaired endothelium-dependent relaxation (due to changes in nitric oxide signaling) was observed in all *Vasn* knockout mice models. Our present findings highlight the role played by Vasn SMC expression in the maintenance of vascular functions. The mechanistic experiments suggested that these effects are mediated by SMC phenotype switching and changes in intracellular calcium homeostasis, angiotensin II levels, and NO signaling.

Kidney International

Kidney International
Volume 99, Issue 6, June 2021, Pages 1382-1391

Basic Research

Decreased monocyte calcium sensing receptor expression in patients with chronic kidney disease is associated with impaired monocyte ability to reduce vascular calcification

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Kidney International, Volume 99, Issue 6, June 2021, Pages 1251

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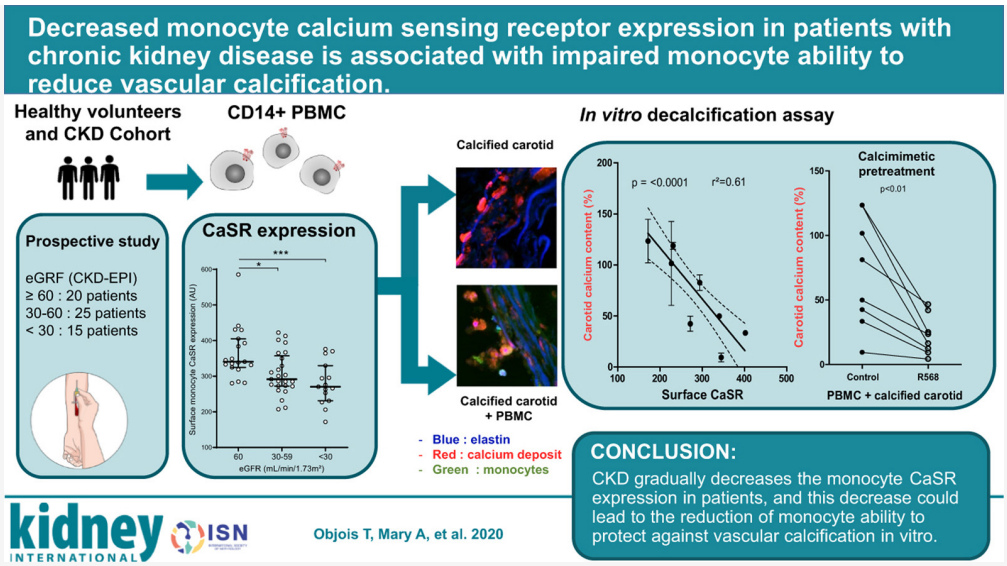
In chronic kidney disease (CKD), calcium-sensing receptor (CaSR) expression and function have been extensively studied in parathyroid tissue and vascular tissues. To examine whether similar changes occurred in other tissues, we measured total and surface CaSR expression in monocytes of patients with various stages of CKD and healthy volunteers respectively in cross-sectional studies. We further explored *in vitro* the impact of uremic serum on CaSR expression in monocytes (U937 and THP-1 cell lines), and whether human peripheral blood mononuclear cells or U937 and THP-1 monocytes might modify vascular calcium deposition in rat carotid arteries *in vitro*. CKD was associated with a decrease in peripheral blood mononuclear cell CaSR expression both in total and at the monocyte surface alone (43% and 34%, respectively in CKD stages 4-5). This decrease was associated with a reduction in the ability of monocytes to inhibit vascular calcification *in vitro*. Pretreatment with the calcimimetic NPSR568 of peripheral blood mononuclear cells isolated from patients with CKD significantly improved monocyte capacity to reduce carotid calcification *in vitro*. The fewer peripheral blood mononuclear cells expressing cell surface CaSR, the more calcimimetic treatment enhanced the decrease of carotid calcium content. Thus, we demonstrate that monocyte CaSR expression is decreased in patients with CKD and provide *in vitro* evidence for a potential role of this decrease in the promotion of vascular calcification. Hence, targeting this alteration or following monocyte CaSR expression as an accessible marker might represent a promising therapeutic strategy in CKD-associated arterial calcification.



American Journal of Kidney Diseases

American Journal of Kidney Diseases
Available online 10 November 2023
In Press, Journal Pre-proof What's this?

Original Investigations

Kidney Function Decline and Serious Adverse Drug Reactions in Patients With CKD

Solène M. Laville PharmD, PhD [1 2], Valérie Gras-Champel PharmD, PhD [2 3], Aghilès Hamroun MD, PhD [4 5], Julien Moragny PharmD [3], Oriane Lambert MSB [5], Marie Metzger PhD [5], Christian Jacquelinet MD, PhD [5 6], Christian Combe MD, PhD [7 8], Denis Fouque MD, PhD [9 10], Maurice Laville MD, PhD [10], Luc Frimat MD, PhD [11 12], Bruce M. Robinson MD [13], Brian Bieber MPH [14], Bénédicte Stengel MD, PhD [5], Natalia Alencar De Pinho PhD [5], Ziad A. Massy MD, PhD [5 15], Sophie Liabeuf PharmD, PhD [1 2]
CKD-REIN Study Group

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Abstract

Rationale & Objective

Adverse drug reactions (ADRs) are common in patients with chronic kidney disease (CKD). The impact of kidney function decline on serious ADR risk has been poorly investigated. We sought to comprehensively describe ADRs and assess the relationship between eGFR and serious ADR risk.

Journal of American College of Cardiology : cardiovascular Imaging

JACC: Cardiovascular Imaging
Available online 8 November 2023
In Press, Corrected Proof What's this?

Original Research

Additive Prognostic Value of Left Ventricular Dispersion and Deformation in Patients With Severe Aortic Stenosis

Nicolas Thellier MD [a], Alexandre Altes MD [a], Michael Rietz MD [a], Aymeric Menet MD, PhD [a], Jeremy Layec MD [a], François Outteryck MD [a], Ludovic Appert MD [a], Christophe Tribouilloy MD, PhD [b c], Sylvestre Maréchaux MD, PhD [a]

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Referred to by Multiparametric Approach to Asymptomatic Aortic Stenosis
JACC: Cardiovascular Imaging, Available online 29 November 2023, Pages
Bernard Cosyns, Kristina H. Haugaa

View PDF

Abstract

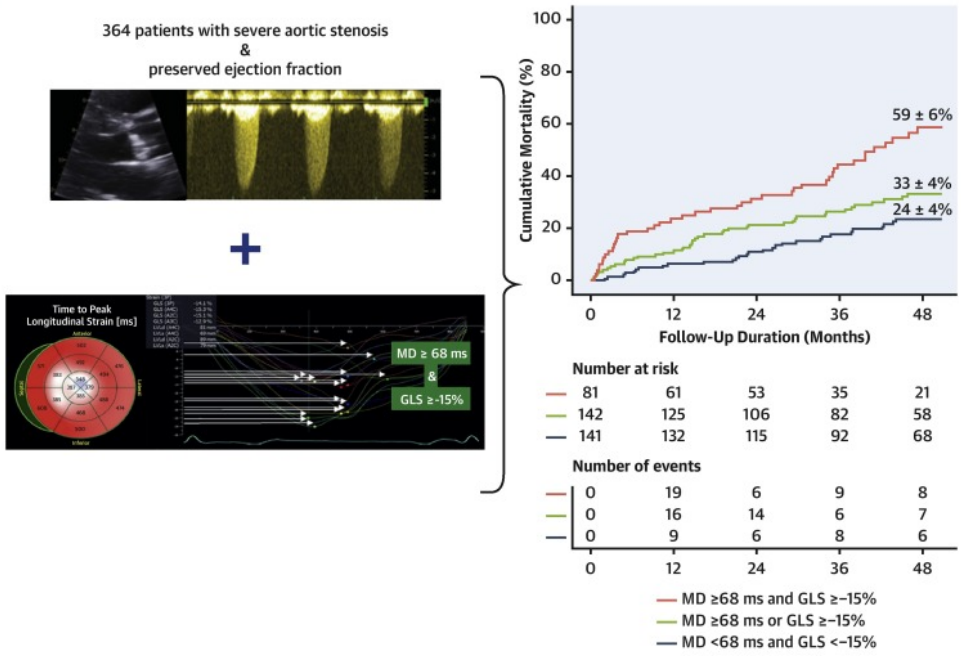
Background

Speckle tracking strain echocardiography allows one to visualize the timing of maximum regional strain and quantifies left ventricular-mechanical dispersion (LV-MD). Whether LV-MD and LV-global longitudinal strain (LV-GLS) provide similar or complementary information in mortality risk stratification in patients with severe aortic stenosis (SAS) remains unknown.

Objectives

We hypothesized that LV mechanical dyssynchrony assessed by LV-MD is associated with an increased risk of mortality and provides additional prognostic information on top of LV-GLS in patients with SAS.

CENTRAL ILLUSTRATION: Prognostic Implications of Left Ventricular Mechanical Dispersion in Severe Aortic Stenosis, Preserved Left Ventricular Ejection and Without Severe Symptoms



Thellier N, et al. J Am Coll Cardiol Img. 2023;■(■):■-■.

Journal of Molecular an Cellular Cardiology

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Journal of Molecular and Cellular Cardiology

journal homepage: www.elsevier.com/locate/yjmcc

Indoxyl-sulfate activation of the AhR- NF-κB pathway promotes interleukin-6 secretion and the subsequent osteogenic differentiation of human valvular interstitial cells from the aortic valve

Alexandre Candellier [a,b,1], Nervana Issa [a,1], Maria Grissi [a], Théo Brouette [a], Carine Avondo [a], Cathy Gomila [a], Gérémy Blot [a], Brigitte Gubler [c,d,e], Gilles Touati [f], Youssef Bennis [a], Thierry Caus [a,f], Michel Brazier [a,g], Gabriel Choukroun [a,b], Christophe Tribouilloy [a,h], Saïd Kamel [a,g], Cédric Boudot [a,2], Lucie Hénaut [a,*,2], On Behalf Of The Stop-As Investigators

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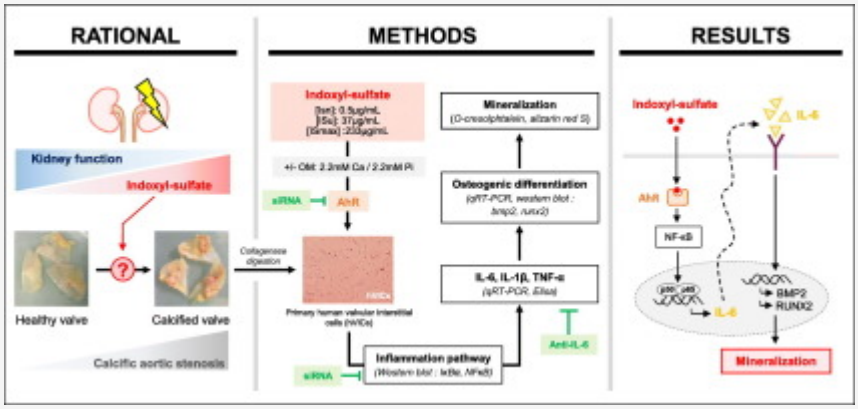

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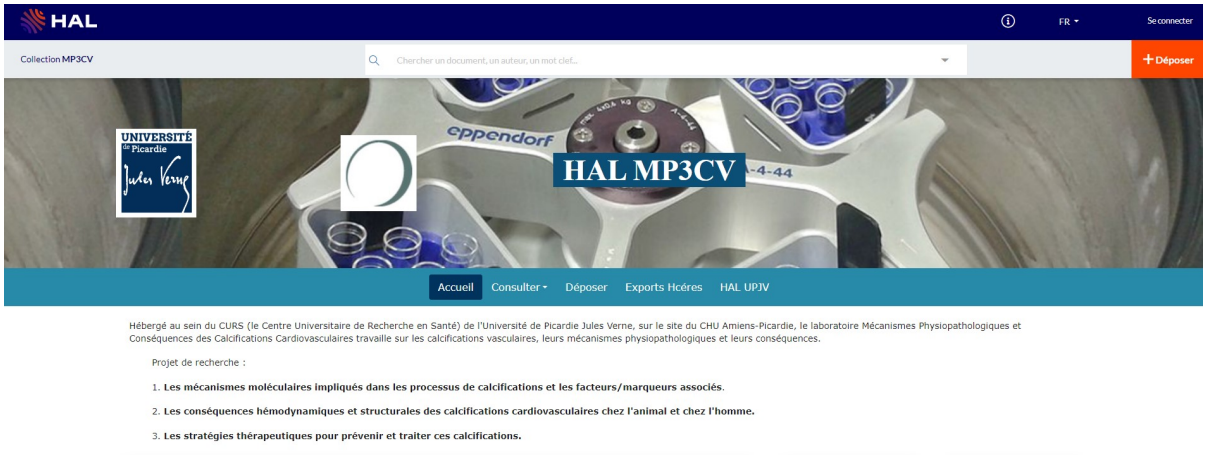

Hébergé au sein du CURS (le Centre Universitaire de Recherche en Santé) de l'Université de Picardie Jules Verne, sur le site du CHU Amiens-Picardie, le laboratoire Mécanismes Physiopathologiques et Conséquences des Calcifications Cardiovasculaires travaille sur les calcifications vasculaires, leurs mécanismes physiopathologiques et leurs conséquences.

Projet de recherche :

1. **Les mécanismes moléculaires impliqués dans les processus de calcifications et les facteurs/marqueurs associés.**
2. **Les conséquences hémodynamiques et structurales des calcifications cardiovasculaires chez l'animal et chez l'homme.**
3. **Les stratégies thérapeutiques pour prévenir et traiter ces calcifications.**

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