Lack of neuregulin-1 expression is associated with CD31 shedding on cardiac microvascular endothelial cells of patients suffering from post-ischemic heart failure

Authors:
V Syvannarath¹, M Morvan¹, G Even¹, G Franck¹, C Deschildre¹, L Deschamps², P Nataf³, JB Michel¹, ANicoletti¹, G Caligiuri¹, INSERM, U1148 - Paris - France, Hospital Bichat-Claude Bernard, Patholgy - Paris - France, Hospital Bichat-Claude Bernard, Cardiac Surgery - Paris - France,

Topic(s):
Basic Science - Cardiac Diseases:Heart Failure

Citation:
Cardiovascular Research (2018) 114 (Supplement 1), S32

Funding Acknowledgements:
ANRT PhD grant Inserm-Institut de Recherche Servier

Background: Mechanic stress sensing is a major trigger of endothelial Neuregulin-1 (NRG1) re-expression in the microvessels of adult hearts in patients with heart failure (HF). CD31 is a key component of the endothelial mechanosensing receptor complex.

Purpose: To evaluate the putative link between CD31 integrity and the expression of NRG1 by CMEC in the myocardium of patients affected by post-ischemic heart failure.

Methods: the use of the hearts explanted from patients undergoing heart transplantation because of post-ischemic HF was approved by the local ethical committee and subjected to the patient’s approval. Myocardial areas remote from the site of myocardial infarction were microdissected, fixed in 4% paraformaldehyde and embedded in paraffin. Intracellular and extracellular CD31, NRG-1, collagen IV and collagen I were assessed on serial sections of 6 different donors by immunofluorescent staining and computer assisted analysis of confocal microscopy images. Microvascular endothelial cells were identified by their basal lamina (positive collagen IV staining). The presence of interstitial collagen I served to identify areas of interstitial myocardial fibrosis (pathologic remodeling). Intact CD31 in microvascular endothelial cells was documented by the co-expression of both intracellular (iCD31) and extracellular (eCD31) CD31 whereas CD31 shedding was detected by the positivity for the intracellular portion only.

Results: NRG1+ CD31+ microvessels were virtually absent in remote myocardial areas undergoing a pathologic remodeling as detected by the presence of collagen I (fibrosis) whereas they were readily detected in areas devoid of fibrosis (Figure 1). Indeed, CD31 was not absent but truncated in microvessels that not expressed NRG1. A representative image of CD31 shedding on NRG1- microvessels is shown in Figure 2.

Conclusions: CD31 shedding, which compromises the physiologic function of this mechanoreceptor, may at least in part explain the lack of NRG1 re-expression and thus lead to an inappropriate endothelial-cardiomyocyte communication in post-ischemic heart failure.
Lack of neuregulin-1 expression is associated with CD31 shedding on cardiac microvascular endothelial cells of patients suffering from post-ischemic heart failure.

Abstract:

Mechanical stress sensing is a major trigger of endothelial Neuregulin-1 (NRG1) re-expression in the microvessels of adult hearts in patients with heart failure (HF). CD31 is a key component of the endothelial mechanosensing receptor complex.

Purpose: To evaluate the putative link between CD31 integrity and the expression of NRG1 by CMEC in the myocardium of patients affected by post-ischemic heart failure.

Methods: the use of the hearts explanted from patients undergoing heart transplantation because of post-ischemic HF was approved by the local ethical committee and subjected to the patient's approval. Myocardial areas remote from the site of myocardial infarction were microdissected, fixed in 4% paraformaldehyde and embedded in paraffin. Intracellular and extracellular CD31, NRG-1, collagen IV and collagen I were assessed on serial sections of 6 different donors by immunofluorescent staining and computer assisted analysis of confocal microscopy images. Microvascular endothelial cells were identified by their basal lamina (positive collagen IV staining). The presence of interstitial collagen I served to identify areas of interstitial myocardial fibrosis (pathologic remodeling). Intact CD31 in microvascular endothelial cells was documented by the co-expression of both intracellular (iCD31) and extracellular (eCD31) CD31 whereas CD31 shedding was detected by the positivity for the intracellular portion only.

Results: NRG1+ CD31+ microvessels were virtually absent in remote myocardial areas undergoing a pathologic remodeling as detected by the presence of collagen I (fibrosis) whereas they were readily detected in areas devoid of fibrosis (Figure 1). Indeed, CD31 was not absent but truncated in microvessels that not expressed NRG1. A representative image of CD31 shedding on NRG1-microvessels is shown in Figure 2.

Conclusions: CD31 shedding, which compromises the physiologic function of this mechanoreceptor, may at least in part explain the lack of NRG1 re-expression and thus lead to an inappropriate endothelial-cardiomyocyte communication in post-ischemic heart failure.

Figure 1

Figure 2