The Role of Platelets in Chronic Kidney Disease and Renal Fibrosis

Published: 17-02-2025
Last updated: 19-04-2025

The objective of this study is to investigate the role of platelets in fibrosis and inflammation by examining their effects on key cellular processes. Specifically, we aim to:1. Determine whether activated platelet stimulation induces fibrosis...

Ethical review	Approved WMO
Status	Pending
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational invasive

Summary

ID

NL-OMON57408

Source
ToetsingOnline

Brief title
PICKS (Platelets in Chronic Kidney Disease Study)

Condition

- Renal disorders (excl nephropathies)

Synonym
Renal Fibrosis, tubulointerstitial fibrosis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: BPPLN Dikti Indonesian Scholarship

Intervention

Keyword: Chronic Kidney Disease (CKD), Platelets, Renal Fibrosis

Outcome measures

Primary outcome

We will conduct an in vitro study by isolating platelets and monocytes from volunteer blood to observe their effects on cells. Since participants are not direct subjects of our research, the data we will obtain are in vitro data related to changes in epithelial-to-mesenchymal transition (EMT) in epithelial cells, molecular changes in endothelial cells, monocyte adhesion, and migration after platelet stimulation. Therefore, there are no data related to primary outcomes that can be observed directly in participants.

The primary outcomes of this study focus on investigating the influence and mechanisms of platelets in fibrosis and inflammation. Specifically, we aim to determine whether activated platelet stimulation induces fibrosis through epithelial-to-mesenchymal transition (EMT) and whether inhibiting platelet activation can mitigate fibrosis and EMT. Additionally, we intend to explore the molecular pathways potentially involved in these processes.

Another key focus is the impact of activated platelet stimulation on endothelial integrity and its effects on monocyte/macrophage adhesion and transendothelial migration. We will also examine the mechanisms of platelet-macrophage interactions that contribute to inflammation, such as

extracellular trap formation.

Secondary outcome

Not applicable

Study description

Background summary

Chronic Kidney Disease (CKD), is characterized by a deterioration of kidney function as a result of progressive loss of functional kidney parenchyma and tissue fibrosis and its treatment remains inadequate. Innovative therapeutic targets can only be identified through better understanding of primary pathogenetic mechanisms. Recent studies emphasize the links between CKD as a result of persistent renal damage caused by underlying medical conditions such diabetes, high blood pressure, glomerular diseases, urinary tract issues like prolonged obstruction, and other renal illnesses which result in inflammation and renal injury.
There is growing evidence that platelet activation contributes to progression of CKD due to factors such as inflammation, oxidative stress, and endothelial dysfunction. Although platelets are best known for their pivotal role in hemostasis, mounting evidence shows that platelets are active players in inflammation and many other biological processes as well, wound healing and fibrosis. Besides their ability to directly interact with endothelial cells and leukocytes, platelets are known to produce many inflammatory and immune-modulating factors.
We and others have previously shown that activated platelets contribute to renal inflammation, oxidative stress, immunoreactivity, and fibrosis processes. Our prior research has revealed the involvement of platelets in experimental acute kidney injury (AKI) and diabetic kidney disease (DKD). We observed that activated platelets promote renal injury, platelet-granulocyte interaction and formation of neutrophil extracellular traps (NETs) and fibrosis.
The concept that platelets can actively promote ETosis in neutrophils and macrophages (NETs/METs) is a novel concept of which we are only beginning to understand the implications. The involvement of platelets in the mechanism of Epithelial-to-Mesenchymal Transition (EMT), which is a pivotal step in the pathogenesis of fibrosis, also still largely limited to studies on malignancies. While the potential contribution of systemic endothelial dysfunction to CKD pathology has been explored, the precise role of platelet interaction with renal endothelium in initiating and perpetuating kidney inflammation remains uncertain.
Understanding the molecular mechanisms involved in renal injury and renal fibrosis in CKD is an active area of research. Targeting these processes may

offer potential therapeutic avenues for slowing down or preventing the progression of CKD and associated renal fibrosis. This study aims to explore the potential contribution of platelets to renal EMT, their interactions with endothelial cells and monocytes, the roles of platelets and NETs/METs in renal disease and uncovering its underlying mechanism. Thus, understanding platelets' functions and mechanisms in CKD, especially, holds promise for reducing morbidity and mortality in CKD patients.

Study objective

The objective of this study is to investigate the role of platelets in fibrosis and inflammation by examining their effects on key cellular processes. Specifically, we aim to:

1. Determine whether activated platelet stimulation induces fibrosis through epithelial-to-mesenchymal transition (EMT) in epithelial cells, and whether inhibiting platelet activation can mitigate these effects.
2. Explore the molecular pathways potentially involved in these processes, particularly those influencing EMT and fibrosis.
3. Examine the impact of activated platelet stimulation on endothelial integrity, as well as its effects on monocyte/macrophage adhesion and transendothelial migration.
4. Investigate the mechanisms of platelet-macrophage interactions that contribute to inflammation, including extracellular trap formation.

By studying these mechanisms, the research aims to gain insights into how platelets contribute to the progression of fibrosis and inflammation, with potential implications for understanding conditions like chronic kidney disease and other inflammatory disorders.

Study design

In vitro experimental study

Study burden and risks

We will draw blood from each donor up to three times within a year, should they agree to donate more than once. However, if a donor prefers to donate only once, that is also acceptable. Each collection will require 10-30 ml of blood. Since blood collection is a routine procedure in medical settings and will be performed by a doctor, the risk of injury is minimal. The potential risks for volunteers include pain during the blood draw, minor bleeding, or hematoma at the blood draw site.

As this is an in vitro experimental study, there are no direct benefits for the volunteers participating. We will, however, provide compensation for travel

expenses to the participants.

Although there are no direct benefits for the volunteers, this study will help researchers gain a better understanding of the effect of platelet hyper-reactivity in the progression of chronic kidney disease and renal fibrosis. This research may contribute to advancing medical knowledge and potential treatments in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Male and female
- Age 18-55 years old
- In healthy condition

Exclusion criteria

- Refusal to become volunteer in this study.
- Using antiplatelets drugs

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	24-02-2025
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	17-02-2025
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL87140.018.24