# NETosis in burn wound patients

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In this clinical pilot study we want to gather data in order to calculate a power for correct subject group to answer the following research question: to explore the relation between NETs/cfDNA in the blood and NETosis in burn wounds and their...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON54153

**Source**
ToetsingOnline

**Brief title**
NETosis in burns/NIB

### Condition

- Other condition
- Embolism and thrombosis

**Synonym**
NETosis and thrombosis formation

**Health condition**

Brandwonden

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** Nederlandse brandwonden stichting;Health

Holland en stichting Proefdiervrij

## Intervention

**Keyword:** Burn wounds, NETosis, Thrombosis, Wound expansion.

## Outcome measures

### Primary outcome

Burn wound severity will be determined at day of admission (day 0/1), day 2-5 post-burn and at day of surgery (if applicable) or day 10 - 20 post-burn by clinical evaluation, Laser Doppler Imaging (LDI) (not day 10 - 20), and (immuno)histochemical analyses in burn skin biopsies. In biopsies taken at the same time points the occurrence of intra-microvascular thrombi and NETosis will be quantified. In addition, in blood samples collected simultaneously with clinical routine lab up to day 30 post-burn, the levels of cfDNA/NETs, DNase1 and endogenous pdC1inh will be quantified. MBL serum levels will be examined in relation to bacterial presence and wound healing.

From healthy volunteers only blood samples will be collected for the quantification of cfDNA/NETs, DNase1 and endogenous pdC1inh levels.

### Secondary outcome

Correlations/associations between wound deepening, thrombosis/NETosis, levels of cfDNA/NETs, DNase1 and endogenous pdC1inh will be investigated. In addition, associations of thrombosis/NETosis with burn wound parameters and characteristics of the patients collected from the medical file e.g. wound size (% burned of TBSA), wound closure time, co-morbidities, inhalation trauma, graft take, length of stay, number of surgical procedures will also be

investigated.

# Study description

### Background summary

Upon burn injury a massive inflammatory reaction is induced, which is initially essential to combat invading microorganisms, debride the wound from damaged tissue and regulate the wound healing. However, in burn wound patients this massive inflammatory response seems to be *uncontrolled* and persist for up to months after the initial trauma, which not only negatively affects the local healing process of the burn wound, but additionally exerts systemic effects may result in e.g. secondary (organ) injury and burn wound extension. In addition, prevention of microbial contamination and infection is vital for burn wound care. Bacterial presence can namely result in further wound healing problems.
Part 1. Inflammation and burn wound extension: Neutrophil extracellular traps in expansion of necrosis of the burn wound In burn wound patients, the expansion of partial thickness burn wounds to deeper or full thickness burn wounds in the first 48 hours is a common phenomenon. This post-burn wound deepening leads to increased tissue loss, delayed healing, more hypertrophic scarring and contractures, an increased need for surgical excisions and grafting and an increased chance of burn wound infections and death. Despite the use of e.g. cerium nitrate and anticoagulants in order to prevent thrombosis, so far no effective treatment exists to prevent post-burn wound deepening. We recently found extensive microvascular thrombosis in and around burn wounds, in both animals and human tissue, which persisted for up to weeks after the initial burn injury. This coincided with neutrophil extracellular traps (NETs) formation (i.e. NETosis), the process whereby neutrophils eject net-like structures of their DNA. NETosis has been shown in general to be a major initiator of blood coagulation and microvascular damage and may therefore be a promising therapeutic target in order to prevent microvascular thrombosis and wound deepening in burn wound patients.
Part 2. Immunological factors of infection
In burn wounds, Staphylococcus aureus and Pseudomonas aeruginosa are the most frequently isolated microbial species. Deficiency for mannose-binding lectin (MBL) may predispose patients to colonization and infection. MBL is a broad-spectrum pattern recognition molecule that plays a role in innate immunity and in the inflammatory response after skin injury. A low serum level of MBL together with other comorbid factors may predispose the host to increased susceptibility to colonization and infection.

### Study objective

In this clinical pilot study we want to gather data in order to calculate a

power for correct subject group to answer the following research question: to explore the relation between NETs/cfDNA in the blood and NETosis in burn wounds and their prognostic potential with regards to clinical outcome. In addition, we will investigate whether there are links between the concentration of MBL in blood, the presence of P. aeruginosa and/or S. aureus in burns and wound healing problems.

### Study design

Prospective observational cohort pilot study.

### Study burden and risks

The burden of this study is burned skin biopsy collection, LDI and clinical assessments, daily/weekly blood withdrawals (combined with clinical routine sampling as much as possible).
The collection of skin biopsies will take place at day of admission (day 0/1), at day 2 - 5 post-burn and at day of surgery (if applicable) or at day 10 - 20 post-burn.
Clinical parameters e.g. pain and wound healing parameters will be assessed during routine clinical assessments.
The burden of the study for healthy volunteers is limited to two blood withdrawals via venepunctures.

## Contacts

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## Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Patients:
- >= 18 years
- Acute burns
- Competent and temporarily incompetent patients
- Informed Consent by patient or the legal representative
- Admitted to the Burn Center of the Red Cross Hospital in Beverwijk, who are expected to be admitted at least until the second measurement moment
- No acute psychiatric disorders
- Sufficient Dutch proficiency

Healthy volunteers:
- >= 18 years
- Competent
- Informed Consent
- Sufficient Dutch proficiency

## Exclusion criteria

Patients:
- Known underlying diseases: cancer, immune deficiency, hypertension, complement, thrombosis disorder.

Healthy volunteers:
- Pregnancy or lactating
- Any medication except contraceptives
- Known underlying diseases: cancer, immune deficiency, hypertension, complement, thrombosis disorder.

# Study design

## Design

| | |
|---|---|
| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 13-11-2023 |
| Enrollment: | 20 |
| Type: | Actual |

# Ethics review

Approved WMO

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|---|---|
| Date: | 14-04-2023 |
| 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 | NL77890.029.21 |