Periodontitis Risk In Venous Acute Trombotic Events

Published: 14-09-2010
Last updated: 04-05-2024

Primary Objective: To assess the relative risk of deep vein thrombosis associated with periodontal disease.Secondary Objective(s): To detect the prevalence of periodontal disease in subjects with and without deep vein thrombosis thrombosis.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON34495

Source
ToetsingOnline

Brief title
Private-study

Condition

- Other condition
- Embolism and thrombosis

Synonym
deep vein thrombosis, venous thrombosis

Health condition

Tandvleesontsteking

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: deep vein thrombosis, Epidemiology, Periodontitis, risk factors

Outcome measures

Primary outcome

The proportion of patients with periodontitis in both groups will be the main

study endpoint.

Secondary outcome

not applicable

Study description

Background summary

Venous thrombosis is a disease with an incidence of about 0.1% in Europe and carrying substantial morbidity and increased mortality (1). Venous thrombosis is multi factorial etiology (2). However, in about 50% percent of the cases no cause can be identified (3). Recently, focus has been shifted towards known cardiovascular risk factors as potential risk factors for venous thrombosis, including body mass index, diabetes mellitus and microalbumiuria (4, 5).
Periodontal disease is a common infectious disease of the oral cavity including gingivitis and periodontitis. Pathogenic oral bacteria in the biofilm or dental plaque play a major role in the development of periodontal disease. Gingivitis, the mildest form of periodontal disease, is highly prevalent and readily reversible by simple, effective oral hygiene promoting measures. Inflammation that extends deep into the tissues and causes loss of supporting connective tissue and alveolar bone is known as periodontitis. Periodontitis results in the formation of soft tissue pockets or deepened crevices between the gum and tooth root. Severe periodontitis can result in loosening of teeth, occasional pain and discomfort, impaired mastication, and eventual tooth loss (6). A large study estimated that about 22% of US adults had mild disease and 13% had moderate or severe disease (7).
Both inflammation and infection have been associated with an increased risk of

cardiovascular disease and venous thrombosis (8-11). Furthermore, it is known that inflammation and coagulation share common pathways (12). Recently, periodontitis has been identified as a risk factor for cardiovascular disease (13). The relative risk of cardiovascular disease associated with periodontitis has been estimated between 1.6 and 2.2. The biologic model of the plausibility of periodontitis as a risk factor for cardiovascular disease holds that periodontitis poses an inflammatory burden through the production of local inflammatory mediators entering the circulation. This inflammatory burden is amongst others evidenced by increased serum C-reactive protein (CRP) levels associated with periodontitis (14, 15). Periodontitis may also pose an infectious burden, through bacteria and their products, which enter the systemic circulation. Circulating oral bacteria and lipopolysacharides are also able to stimulate hepatocytes to secrete CRP (16-18), adding again to an increased inflammatory state. This increased inflammatory state caused by periodontitis has been associated with increased risk of atherosclerosis and cardiovascular diseases (19-22).
Thus, periodontitis appears to be a risk factor for cardiovascular disease. Since many of the risk factors for cardiovascular disease have recently been implicated as potential risk factors for venous thrombosis (4, 5), periodontitis may also be a risk factor for venous thrombosis.
Currently, there are no data on the relationship between periodontitis and venous thrombosis. Therefore, the aim of this study was to assess the prevalence of periodontitis in both patients with and without deep vein thrombosis, and calculate the relative risk of deep vein thrombosis associated with periodontitis.

Study objective

Primary Objective: To assess the relative risk of deep vein thrombosis associated with periodontal disease.
Secondary Objective(s): To detect the prevalence of periodontal disease in subjects with and without deep vein thrombosis thrombosis.

Study design

Out-patients presenting with complaints of the leg suspected of deep vein thrombosis at the emergency department, will be evaluated by the primary investigator, or another physician of the division of Haemostasis and Thrombosis, according to routine clinical practice. This includes a peripheral vena puncture for taking blood to determine standard laboratory measures, including hemoglobine, thrombocytes, leucocytes, liver and kidney function tests, D-dimers, fibrinogen and C-reactive protein.
After taking history and performing a physical examination, the physician will inform patients about the study. Patients have 30 minutes to think about participating in the study. Patients* periodontal status has to be evaluated before diagnosis is made or laboratory tests become available, to decrease the

possibility of observer bias and the possibility of healthy-user bias (patients with DVT could be getting more motivation to behave in a more healthy style compared to controls, and therefore measurement of the periodontal status could be influenced by this when measuring after more time). Furthermore, anticoagulant medication prescribed to treat DVT likely increases the tendency of bleeding on probing of the gingiva when measuring the depths of crevices between the gum and tooth root. Since bleeding on probing is a parameter used to indicate periodontitis presence and severity, this could obscure our results. Thus, we want to perform the assessment when patients are present at the emergency department, before laboratory tests become available, compression ultra sound (CUS) will be made and before any therapy is initiated. An additional advantage of this approach is that no additional visit to the outpatient clinic is needed, reducing the burden of participating in this study.
Next, after 30 minutes, patients who have agreed to participate are asked to sign informed consent. They then will be asked a few questions, according to a standardized questionnaire assessing their DVT symptoms, previous venous thrombotic events, known cardiovascular and pro-thrombotic risk factors, education level, length, weight, concomitant disease, and their dental status (edentulous). This will take about 5 minutes of time. After that, they will get the periodontal assessment while waiting for the results of the laboratory tests and further work-up. One of two trained dental students will examine patients, to assess the presence of periodontitis. This will also take place at the emergency department, and will take about 30 minutes.
Consequently, laboratory tests will be available and D-dimer levels are used together with the clinical decision rule according to Wells (23) by the physician to calculate the probability of the presence of deep vein thrombosis (DVT). When DVT can not safely be ruled out by this, CUS will be made, according to normal clinical routine. Patients, in whom the presence of DVT safely can be ruled out, are assigned to the control (no DVT) group. In patients with a high probability of DVT, DVT will be proven or ruled out by CUS. This allocates patients to the case (DVT) or control (no DVT) group, and they will receive the appropriate treatment for their disease, according to routine clinical practice. All can be viewed in the flowchart at the end of this document (Figure 1.).
Patients will be informed about their periodontal status and are asked whether they want their own dentist to get informed by means of a letter containing the results of the periodontal examination. The latter requires patients to explicitly indicate this on the informed consent letter. Hereafter, the study participation will end for the patient.
Estimated duration of inclusion is about 6 months.

Study burden and risks

Participants are asked a few additional questions about their medical history, periodontal disease and risk factors, venous thrombotic risk factors and cardiovascular risk factors. Thereafter, they will undergo a oral cavity

examination to assess the presence and extent of periodontitis, which is an extended version of a part of the normal clinical routine performed by dentists at (half) yearly check-up. This will be performed by one of two trained dental students, and will take about 30 minutes. The examination will be performed before definite diagnosis of the complaints of the leg has been made, during the time needed to wait for the results of laboratory tests. In this way, we achieve a blinded condition for both patients and examiners and reduce the burden of participation because no additional visits at the outpatient clinic are needed. Patients will benefit of participation by receiving an update of their periodontal status. Their treating dentist can receive this information by letter if the patient explicitly approves of this. Finally, they will receive a token for participating; there are no risks or adverse outcomes expected by participating in this study.

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

- Out-patients with suspicion of deep vein thrombosis of the leg
- Presenting at the emergency department of the UMCG

Exclusion criteria

- Under 18 years of age
- Not able to understand written Dutch language
- Not able to sign informed consent

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2011
Enrollment:	260
Type:	Actual

Ethics review

Approved WMO

Date:	14-09-2010
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Not approved Date:	14-03-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL33279.042.10