Characterization of blood coagulation in cancer patients for the development of an algorithm to predict the risk of thrombosis.

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Primary Objective: The primary objective of this study is to measure a broad panel of coagulation tests in a cohort of cancer patients to determine whether one or a combination of these tests is able to predict the risk of thrombotic events in the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON45551

Source
ToetsingOnline

Brief title
Blood Coagulation in Cancer Patients

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Embolism and thrombosis

Synonym
blood clot, thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Gelre Ziekenhuizen
Source(s) of monetary or material Support: Ministerie van OC&W,Synapse Research Institute;Maastricht

Intervention

Keyword: Algorithm, Coagulation, Thrombin generation, Thrombosis

Outcome measures

Primary outcome

The main clinical outcome of the current study is the occurrence of a thrombotic event in the cancer patient cohort. Blood will be collected at baseline patient inclusion and several coagulation tests described below will be performed. The results of these tests will be compared between the group of patients that did and did not suffer from thrombosis, with the aim of discovering potential biomarkers that allow for prediction of thrombosis risk in a cancer patient.

Secondary outcome

Secondary Objectives

The secondary objective of this study is to determine the effect of the cancer type and stage and the effect of treatment on the probability to develop thrombosis. Another secondary objective is to assess the effectiveness of anticoagulant therapy in the patients who have suffered from a thrombotic event. In addition, we aim to study the changes in coagulation parameters in a cancer patient at baseline and after a thrombotic event.

Study description

Background summary

Cancer associated thrombosis (CAT) is the second leading cause of death in cancer patients (1). Patient and cancer or cancer-therapy specific risk factors are associated with a 4-7 fold increased risk of venous thromboembolism (VTE) in cancer patients. VTE is reported to occur in 4-20% of cancers patients, and an additional 2-5% of cancer patients develop arterial thrombosis. From epidemiological studies it is known that brain cancer, haematological malignancies and adenocarcinomas of the pancreas, stomach, ovary, uterus, lungs, and kidneys are associated with the highest risk of VTE development.

Three classes of risk factors for VTE are distinguished in the cancer population (Table 1): patient related, treatment related and cancer related risk factors (1). Patients with advanced-stage cancer tend to be less mobile, which can lead to venous stasis and VTE, and are more prone to infection because of immunosuppression (2). In addition, there are several mechanisms through which chemotherapy can induce a hypercoagulable state: direct tissue toxicity, increase in coagulation factor levels, induction of tumor and endothelial cell apoptosis causing increased tissue factor expression, induction of platelet activation, and induction of monocyte tissue factor expression (2). Hormonal agents such as Tamoxifen and Raloxifen increase the risk of VTE (3), and antiangiogenic agents such as thalidomide and Lenalidomide are associated with a VTE rate of 12-28%, when given in combination with dexamethasone or chemotherapy (4-6).

Cancer cells themselves can cause intravascular coagulation via multiple mechanisms, such as tissue factor expression, inflammatory cytokine release and cancer procoagulant expression (1), but also by compression of large blood vessels by the tumor.

Treatment of VTE in the cancer population
Effective treatment of VTE reduces morbidity and mortality. Low molecular weight heparin (LMWH) is the first line treatment for VTE (1). Vitamin K antagonists (VKA) are given if LMWH treatment is not available, but its use is associated with higher VTE recurrence rates. Direct oral anticoagulants (DOACs) that directly inhibit thrombin (FIIa) or Factor Xa (FXa) are promising for the prophylaxis and long-term treatment of VTE in cancer. However, there is insufficient evidence to support the use of DOACs in cancer patients with thrombosis until the results of ongoing clinical trials comparing LMWH to DOACs become available (10, 11).

Study objective

Primary Objective:

The primary objective of this study is to measure a broad panel of coagulation tests in a cohort of cancer patients to determine whether one or a combination of these tests is able to predict the risk of thrombotic events in the cancer population. To study this objective, we will compare the outcome of each coagulation assay in the group of patients that did not suffer from a thrombotic event in the 2-year follow-up and patients that did suffer from thrombosis. In addition, we will determine the predictive power of each coagulation test for the risk of thrombosis in cancer.

Secondary Objectives
The secondary objective of this study is to determine the effect of the cancer type and stage and the effect of treatment on the probability to develop thrombosis. Another secondary objective is to assess the effectiveness of anticoagulant therapy in the patients who have suffered from a thrombotic event. In addition, we aim to study the changes in coagulation parameters in a cancer patient at baseline and after a thrombotic event.

Study design

Brief description of the study design:
* Prospective observational cohort study.
* Patients will be enrolled in the inpatient hospital setting of the Gelre Hospitals.
* We aim to include patients with cancer without prior venous thrombosis and patients with cancer with prior venous thrombosis, to obtain a blood sample from each patient at inclusion and perform baseline coagulation tests. We will follow the patients up to 2 years to document whether they experience a thrombotic event. If a patient is admitted to the hospital because of thrombosis, a second blood sample will be taken. Treatment of a thrombotic event usually requires anticoagulation. We will take another blood sample two weeks after the start of anticoagulation to determine the effectiveness of the anticoagulant.

* Rationale for design features: In this study we aim to study the differences in the coagulation parameters between the patients who develop a thrombotic event and those who do not. Ideally, we would like to be able to predict the risk of thrombosis in a patient as soon as possible, in order to treat patients at risk with prophylactic anticoagulation. In this study our goal is to identify (a panel of) coagulation tests that can discriminate between patients that will or will not develop thrombosis in the future. Therefore, we want to study coagulation tests in a cohort of cancer patients prospectively to see which patients develop a thrombosis in the future and whether or not coagulation tests could have predicted this risk.

* We expect the study to last for 2.5 years in total, from the inclusion of the first patient in August 2017 until the last day of the 2-year follow-up of patient in February 2020.

* In this study we perform 4 main types of coagulation assays: thrombin generation assays, platelet function tests, coagulation factor determinations, and assessment of clot lysis. In addition, we aim to characterize the disease state of the patients through the use of a cancer biomarker panel, and by having access to patient information including age, sex, type of cancer, tumor histology results, PET/MRI/CT scan results, and autopsy if conducted.

* The purpose of the study is to cover the whole spectrum of the coagulation system and identify abnormalities in cancer patients that could explain their increased incidence of thrombotic events

Study burden and risks

Potential risks: Blood samples will be obtained by venepuncture, which is a standard procedure with minimal risks. During the process of obtaining a blood sample from the patient*s vein, it is possible to develop a bruise. Application of pressure on the site of blood drawing for several minutes minimizes the risk of bruising. The patient might feel minor pain or be light-headed from this or may experience some temporary discomfort and short-term swelling at the site of a needle stick. Importantly, the patient would also experience this minor burden from the blood drawal without this study; blood will be drawn for routine patient care, for this study only extra tubes will be drawn.

Potential Benefits: As this is an observational study, the participating patients will not benefit directly from the results. However, the obtained knowledge may help predict what cancer patients may benefit from thromboprophylaxis in the future.

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

- Cancer (of any type, any stage) diagnosis
- Prior history of VTE (regarding population of 100 patients) or no history of VTE (population of 278 patients)

Exclusion criteria

- Previously documented coagulation defects
- Prior history of venous thromboembolism (regarding the population of 278 patients)
- Age < 18 years
- Localized squamous or basal cell carcinoma of the skin
- Patient unable to provide informed consent
- Life expectancy < 6 months.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2017
Enrollment:	662
Type:	Anticipated

Ethics review

Approved WMO

Date:	24-07-2017
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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	NL60514.075.17