Evaluation of Prostate-Specific Antigen Glycomics Assay for the Early Detection of Prostate Cancer

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON49657

Source
ToetsingOnline

Brief title
PSA Glyomics Assay (PGA)

Condition

- Reproductive neoplasms male malignant and unspecified
- Prostatic disorders (excl infections and inflammations)

Synonym
Prostate Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: PCa, Prostate Cancer, Prostate-specific antigen, PSA

Outcome measures

Primary outcome

The following parameters/outcomes are expected:

Regarding patient information:

- Study number
- ID-code
- Birth date
- Ethnicity
- Date of sample collection
- Volume of prostate (echo)
- PSA-concentration
- Gleason score
- Number of biopsies taken
- Number of positive biopsies
- cT-stage
- Positive lymph nodes
- Metastasis in the bone
- Other diseases
- Medication
- BRCA mutation

• Treatment

• Prostate MRI

• Cribriform growth

• Family anamneses

The research will provide the following outcomes:

• Relative ratio of different glycoforms in urine and plasma

• Normalization of glycoforms per glycosylation trait (derived trait)

• The difference (delta) between urine and plasma for the found derived traits

Secondary outcome

Not applicable

Study description

Background summary

In the Netherlands, approximately 12,000 men are yearly diagnosed with prostate cancer (PCa), making PCa the most frequent type of cancer in men. Elevated prostate-specific antigen (PSA) levels (>3 ng/mL) are a first indicator of PCa. Namely, a small amount of this protein can *leak* into the circulation, because with PCa, the cells are misaligned causing elevated PSA concentrations (PSA gets better access to the circulation). When an elevated level of PSA is found, further examination is needed to determine the diagnosis (e.g. digital rectal examination (DRE), prostate MRI) and prostate biopsies). Unfortunately, other prostate related diseases (e.g. benign prostate hyperplasia or an inflammation) can also result in elevated PSA levels. Furthermore, the PSA-test is unable to differentiate aggressive from non-aggressive PCa. In the case of non-aggressive PCa, the cancer is slowly growing and the chance that the patient will encounter progression or any symptoms due to the cancer are rather small. Taking this into account it is recommend to not immediately treat the patient, but rather to start active surveillance (patient comes back on a regularly basis and treatment will only be started when the cancer seems to progress). With the abovementioned examples it is clear that there is a need for a better test that is able to distinguish PCa from other prostate related diseases, to

avoid overdiagnosis and overtreatment of the patient.

Study objective

The current research is focused on finding a method that is able to better stratify the patients. A possible method could be to study PSA in more detail, specifically the modifications which are present on the protein. One of these modifications is glycosylation (sugars attached to the protein). These sugar groups can be very diverse and recent studies have shown that changes in the glycosylation can be related to various cancers and autoimmune diseases. The purpose of this study is to examine whether changes in the glycosylation of PSA can also be related to PCa. As certain changes might be able to distinguish whether the patient has PCa and its aggressiveness. This knowledge would be a huge benefit compared to the conventional PSA-test.
Recently, we have developed an in-depth PSA Glycomics Assay (PGA) that can determine all these glycosylation features of PSA derived from urine. Unfortunately, no direct correlations could be made between the clinical diagnosis and the PSA-glycosylation features in urine. Our hypothesis is that PSA from the circulation, but not from urine carries the cancer glycosylation signature that can stratify PCa from other prostate related diseases and can differentiate between aggressive and non-aggressive PCa. PSA that leaks into the blood is expected to be largely tumour-derived, since only the tumour region will show increased leakage of PSA into the circulation. We will compare the glycosylation of the possibly tumour-derived plasma PSA (pPSA) with uPSA that is derived from the entire prostate gland and presumably exhibits a healthy-type glycosylation profile. We expect that this personalized diagnostic approach that takes the individual glycosylation of a patient into account, will result in improved diagnostic performance of the PGA.

Study design

In total, 225 patients are needed for this research, who will donate a blood (15 mL) and urine (20 mL) sample.
It is estimated that 15% of the included patients samples will be incomplete (either a blood or urine sample is missing), due to this 25 patients will not be included in the research. Additionally, 50 patients are estimated to belong to Group 2 (patients with elevated PSA concentrations but no indication for biopts based upon DRE and MRI) and will also not be taken along in the research question. From the remaining samples (Group 1) the protein PSA will be immunocaptured and analyzed with capillary electrophoresis coupled to a mass spectrometer at the LUMC. The samples will be anonymized and only the participating urology departments will have access to the clinical details of the patient (eg. Gleason score, cT stage, pT stage, prostate MRI results, etc). This to avoid any bias that could be introduced while analyzing the samples.After the analysis (100 samples per biofluid), the participants will be divided into three groups after the analysis of the samples has been performed.

Group a will consist of the patients with elevated PSA concentration, but where prostate cancer was excluded due to a negative biopsy. Group b will consist of the patients with elevated PSA concentration where prostate cancer was found. Group 2 will consist of patients with elevated PSA concentration (>3 ng/mL) but no indication for prostate cancer based on MRI and DRE.
By making use of the abovementioned groups, it can be investigated whether the PSA Glycomics Assay has an added value next to the current PSA-test. For each sample a PSA glycosylation profile will be obtained and per patient their urine profile will be first compared to their plasma profile. The difference in the glycosylation profile will result in a delta per glycoform for each patient.
This will be used to eventually compare the observed delta*s per glycosylation form between the different groups. Potential biomarkers will be compared to current diagnostic tools such as histology, digital rectal examination and prostate MRI to evaluate whether the found biomarkers are a true added value. Validation will be performed in the case one or several biomarkers are found with a new cohort consisting of 50 participants. During this phase the specificity, sensitivity and positive predictive value will be determined. Next to the evaluation whether the PSA Glycomics Assay can predict the presence of prostate cancer it will also be evaluated if the assay can predict the level of aggressiveness of the prostate cancer. For this purpose the Gleason scores (obtained from histology after biopsy), TNM score and the PSA concentration will be used. Patients with prostate cancer will be subdivided into three risk groups: low-, medium- and high-risk.

Study burden and risks

The patient will be asked to donate urine (20 mL) and a blood sample (15 mL) next to the regular examination (digital rectal examination, prostate MRI and biopsy). This procedure will cost the patient some extra time. Every time when blood is drawn a local bruising can occur. Where possible, the blood will be drawn with a routine blood draw to minimize the risk. The patient will be asked to collect his own urine sample, it is not expected there will be any burden/risk due to this procedure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients with a PSA concentration >3 ng/mL that visit the urologist for further examination.

Exclusion criteria

Patients with a PSA concentration <3 ng/mL, patients that have a cystitis (bladder infection), are in the process of undergoing chemo therapy or using 5-alpha reductase inhibitors will be excluded from the study. Patients with a history or presence of cancers, or non-prostate urological disorders.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2020
Enrollment:	225
Type:	Actual

Ethics review

Approved WMO Date:	03-07-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	30-10-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO Date:	06-02-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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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	NL73261.018.20