Adrenal vein sampling as a tool to identify biomarkers that aid the diagnosis of adrenocortical carcinoma

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To detect differences between ACC patients and controls without ACC, and between the diseased and healthy adrenal gland of ACC patients, in microRNA (miRNA), circulating cell-free tumor DNA (ctDNA), circulating tumor cells (CTCs), and steroid...

Ethical review	Approved WMO
Status	Completed
Health condition type	Adrenal gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON51376

Source
ToetsingOnline

Brief title
AVS for ACC

Condition

- Adrenal gland disorders
- Endocrine neoplasms malignant and unspecified

Synonym
adrenal cancer, Adrenocortical cancer

Research involving
Human

Sponsors and support

Primary sponsor: Interne Geneeskunde, Endocrinologie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Adrenal vein sampling, Adrenocortical carcinoma, Biomarkers

Outcome measures

Primary outcome

The main study parameters will be the differences in miRNA, ctDNA, circulating tumor cells and steroid profiles between ACC patients and controls without ACC, and between the diseased adrenal gland and the healthy adrenal gland of ACC patients.

Secondary outcome

Secondary endpoints include the differences in the amount of detection of miRNAs, ctDNA, circulating tumor cells and steroid profiles between adrenal venous and peripheral or central venous blood of ACC patients.

Study description

Background summary

Many patients currently undergo an adrenalectomy for an eventually benign adenoma, because the current preoperative diagnostic workup of adrenal incidentalomas cannot always rule out the diagnosis of adrenocortical carcinoma (ACC). Many biomarkers have been implied in previous research to possibly be associated with ACC. However, these markers cannot be measured reliably in peripheral blood samples. We hypothesize that assessment of undiluted biomarkers in adrenal veins is a promising strategy to diagnose or exclude ACC without the need for surgery. Rationale is that the adrenal vein harbors a 100-fold higher measurable concentration of adrenal hormones compared to peripheral blood samples from the inferior caval vein. It is likely that not only hormones, but also molecules produced by an adrenal tumor, can be detected more reliably and robustly in adrenal venous samples. We aim to preoperatively identify biomarkers for either diagnosing or ruling out ACC, in blood obtained directly from the adrenal vein instead of in peripheral blood.

Study objective

To detect differences between ACC patients and controls without ACC, and between the diseased and healthy adrenal gland of ACC patients, in microRNA (miRNA), circulating cell-free tumor DNA (ctDNA), circulating tumor cells (CTCs), and steroid profiles in adrenal venous blood, in order to optimize preoperative possibilities for diagnosing ACC.

Study design

Prospective case-control study.

Study burden and risks

This study has no specific benefits for the participating patients, but the results are likely to have beneficial effects for future patients. The technique to selectively sample the adrenal vein is frequently applied at the Erasmus MC in the workup of patients with primary hyperaldosteronism, and it can be safely performed with a success rate of >90% and with low risks. Possible complications include rupture of the adrenal vein with a reported incidency of 0.61%, inguinal bleeding or pain, dissection, thrombosis and adrenal insufficiency, all with an incidency of <1% with current techniques. Management of complications can be done conservatively in almost all cases. Patients could possibly experience pain due to the blood sampling procedures. Besides, the burden of patients included in this study consists of being admitted to the hospital for one day, and therefore the time they invest in this study. Furthermore, patients are exposed to Synacthen administration, contrast fluid and approximately 3.6mSv of X-radiation. Patients in the control group will not be subjected to any extra interventions for research purposes, so these patients are not subjected to any additional risks associated with 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

In order to be eligible to participate in the study group, a subject must meet all of the following criteria:
- Patient age >=18 years
- High clinical suspicion of adrenocortical carcinoma (ACC), based on clinical signs (due to hormonal overproduction) steroid hormone profile and radiological features (e.g. tumor size >=4cm, inhomogenous aspect and tumor attenuation of HU >=10)
- Able to provide signed informed consent

In order to be eligible to participate in the control group, a subject must meet all of the following criteria:
- Patient age >=18 years
- Routine diagnostic process includes adrenal vein sampling (AVS)
- No suspicion of malignancy
- Able to provide signed informed consent

In case pathological diagnosis from a subject who was initially assessed as eligible for the study group does not confirm ACC, this subject will be included in the control group and the samples will be analyzed as such.

Exclusion criteria

Patients are not able to participate if:
- They have a known allergy to (iodinated) contrast fluid
- They use vitamin K antagonizing anticoagulants or DOAC*s, except for when on the day of the AVS the anticoagulants are already stopped for the following adrenal surgery, and in case of using vitamin K antagonizing anticoagulants the

INR is <3
- The platelet count is below 20
- Anatomy of the adrenal vein is not suitable for performing the AVS procedure, based on the judgement of an experienced interventional radiologist
- Contraindications for use of Synacthen
- They have a known hypersensitivity to any of the substances of Synacthen
- They are pregnant

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:	Completed
Start date (anticipated):	23-10-2022
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO

Date:	04-08-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL81124.078.22