De-escalation of treatment for Papillary Thyroid Cancer followed by Active Surveillance - a pilot study

Published: 15-09-2020
Last updated: 14-03-2025

Primary Objective: The aim of this pilot study is to determine the willingness of patients to participate in a RCT regarding de-escalation of treatment of PTC and to observe adherence to this less aggressive approach. This will be accomplished by...

Ethical review	Approved WMO
Status	Completed
Health condition type	Thyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON55252

Source
ToetsingOnline

Brief title
Dutch De-escalation Pilot Study (DDPS)

Condition

- Thyroid gland disorders
- Endocrine neoplasms malignant and unspecified
- Endocrine gland therapeutic procedures

Synonym
Papillary thyroid carcinoma, Thyroid cancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Active Surveillance, De-escalation of treatment, Papillary thyroid carcinoma

Outcome measures

Primary outcome

Primary study outcome

Primary endpoint consists of the participation of patients eligible for the

study

Secondary outcome

Secondary outcomes

1. Time needed to include 12 patients

2. Reasons for patients to deny participation

3. Total number of patients and percentage of patients in the active

surveillance group who wish to be treated according to the current guidelines

4. Quality of life outcomes as assessed by EQ5D5L, SF-36, ThyPro39 and the Fear

of Cancer Recurrence questionnaires.

5. Logistical hurdles

Study description

Background summary

The worldwide incidence of papillary thyroid cancer (PTC) is increasing and thyroid cancer is the most common endocrine malignancy worldwide. The incidence rises due to increased use of imaging modalities such as ultrasonography, MRI and PET/CT scan, which mainly leads to the identification of thyroid incidentalomas, small well-differentiated papillary thyroid carcinomas. Despite a shift towards a less aggressive treatment in the USA, described in the latest

American Thyroid Association guideline, the Dutch guidelines are more aggressive in treating PTC. They recommend a total thyroidectomy (TTx) followed by radioactive iodine (RAI) in all patients with a PTC >1 cm. This treatment strategy comes with significant costs and morbidity rates caused by hypothyroidism, iatrogenic hypo-parathyroidism, recurrent laryngeal nerve damage, dysgeusia and xerostomia, resulting in a poor quality of life. The stable overall survival rate suggests widespread overtreatment following current treatment strategy. Therefore, changing treatment strategies for low-risk PTC patients is of great importance. This is reflected by the 2015 ATA guidelines stating that hemi thyroidectomy is sufficient for patients with low-risk PTC based on large national USA registration database studies. These studies show neither survival benefit nor difference in recurrence rate between TTx versus hemi thyroidectomy (HTx) in this group of patients. Unfortunately, the lack of strong evidence, such as randomized trials demonstrating equivalent oncological outcomes is currently withholding widespread worldwide de-escalation and is urgently required to update guidelines in non-American countries. Prior to performing such a large-scale randomized controlled trial, a pilot study is necessary to assess willingness to participate and adherence to the active surveillance strategy. This pilot study will function as a stepping stone to the aforementioned national RCT.

Study objective

Primary Objective:
The aim of this pilot study is to determine the willingness of patients to participate in a RCT regarding de-escalation of treatment of PTC and to observe adherence to this less aggressive approach. This will be accomplished by measuring the participation rate of patients eligible and informed about the study.

Study design

This is a single-center randomized controlled pilot study.

Intervention

Patients diagnosed with PTC on FNA prior to surgery are randomized between the interventional treatment (HTx+AS) and regular care (TTx+RAI).
The investigational treatment is thus a hemi-thyroidectomy followed by active surveillance.

Patients included after the diagnostic hemi thyroidectomy will be randomized between the interventional treatment (AS) or regular care (completionTx+RAI).

Study burden and risks

There is a chance that a higher recurrence rate of PTC will be found in the intervention group, which creates a greater burden due to re-operations. However, this does not affect survival.
Potential reduced per/post-operative complications will benefit the intervention group.

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 this study, a subject must meet all of the following criteria:
- Able to undergo surgery
- Age of 18 years and older
- Diagnosed with unilateral papillary thyroid cancer with a diameter of 1-4 cm,

as defined by:
o Histologically proven well differentiated (classic or follicular variant) PTC after diagnostic hemithyroidectomy 1-4cm
or
o Cytologically proven Bethesda 6
or
o Cytologically proven Bethesda 5 nodule with confirmed BRAF mutation
- Size of index nodule / tumor must be between 1 and 4cm, measured by ultrasound or on histopathology. Histopathology may overrule ultrasound measurements.
- Ultrasound of the neck excluding lymph node involvement
- Signed informed consent by patient

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Positive resection margins or extensive extrathyroidal extension as defined for in the 8th edition of the AJCC/TNM classification of thyroid cancer for extension of a T3 tumor upon histology or ultrasound.
- Lymph node involvement confirmed by ultrasound and FNA prior to randomization
- Multifocality
- Vascular invasion
- Aggressive histology (e.g. poorly differentiated, tall cell, columnar cell, hobnail variant, diffuse sclerosing variant PTC)
- Certain classification of NIFTP on histology
- A contralateral nodule requiring intervention (if applicable)
- Pregnant women
- Insufficient understanding of the Dutch language to understand the study documents
- Minors (age < 18 years) and incapacitated subjects do not meet the eligibility criteria and will therefore not be enrolled

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-11-2020
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	15-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-03-2021
Application type:	Amendment
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	NL73675.078.20