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Subclinical Hyperthyroidism 'To Treat or Not to Treat?' - A Dutch Multicentre Trial

Submission date	Recruitment status	[ ] Prospectively registered
12/09/2005	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
12/09/2005	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
24/08/2009	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
NTR75

Study information

Scientific Title

Acronym
SUBstudy / SUBstudie

Study objectives
To provide evidence that restoration of euthyroidism (normal TSH) improves thyrotoxic symptoms and signs and quality of life and lowers the risk of subsequent atrial fibrillation and bone loss in subjects with endogenous subclinical hyperthyroidism.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Received from local medical ethics committee

Study design
Multicentre randomised single blind active controlled parallel group trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Not Specified

Participant information sheet

Health condition(s) or problem(s) studied
Thyrotoxic symptoms, nodular goiter, hyperthyroidism

Interventions
Randomised clinical trial comparing active treatment with 131I with no treatment in subjects with endogenous subclinical hyperthyroidism in a multicenter study.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure

1. Progression to overt hyperthyroidism: TSH, fT4, T3 every year
2. Changes in (thyrotoxic) symptoms (null-hypothesis: radioiodine does not cause improvement):
2.1. Quality of life - short form 36 Health Survey: on T=0, T=2 and T=5 years
2.2. Modified hyperthyroid symptom scale: on T=0, T=2 and T=5 years
2.3. In the treatment group on T= 1 year: duration of admission to hospital for administration of I131 (if necessary) and signs or symptoms of iodine induced thyroiditis or Graves like disease following iodine treatment making medical treatment necessary
3. Cardiac changes (null-hypothesis: radioiodine does not prevent development of atrial fibrillation):
3.1. 12-lead ECG: on T=0, T=2 and T=5 years
3.2. Holter monitoring (24 hour): mean 24-hour heart rate, number of PAC and VES: on T=0, T=2 and T=5 years
4. Changes in bone mineral density (null-hypothesis: radioiodine does not prevent deterioration of BMD): DEXA (Hologic or Lunar) L1-L4 and (right) femoral neck): on T=0, T=2 and T=5 years

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/06/2003

Completion date
01/06/2010

Eligibility

Key inclusion criteria
1. Subclinical hyperthyroidism [TSH <= 0.1 mU/L, fT4 and T3 within the normal range of the own laboratory (determined 2 times in own laboratory with an interval of at least 2 months)
2. Endogenous cause of subclinical hyperthyroidism limited to autonomous adenoma or multinodular goiter (diagnosis made by the attending physician, based on palpation and the result of a thyroid scintigram)
3. Informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
192

Key exclusion criteria

1. Medication with anti-thyroid drugs in the last 3 months (also not allowed during follow-up), thyroid hormone in the last 3 months (allowed during follow-up, but TSH levels should be kept between 0.1 mU/L and the upper limit of normal in the own laboratory) and oral glucocorticoids in the last 3 months (allowed during follow-up when absolutely necessary, but patients in whom glucocorticoids are
started cannot be evaluated with respect to changes in BMD).
2. Radioiodine therapy in the past
3. Iodine-induced subclinical hyperthyroidism
4. Pituitary or hypothalamic insufficiency
5. Pregnancy
6. Age <= 50 years and > 80 years
7. Severe non-thyroidal illness
8. Drug abuse
9. Unstable angina pectoris, (history of) atrial fibrillation, (history of) congestive heart failure.
10. (History of) osteoporotic fracture(s)
11. Patients younger than 70 years of age with a bone mineral density T-score <2.5
SD, or older than 70 years of age with a bone mineral density Z-score <-1.0 SD
12. These patients can be randomised but in case it is decided to treat them with antiosteoporotic drugs they cannot be evaluated with respect to changes in BMD.
13. Use of betablockers in the last three months. These patients can be randomised but cannot be evaluated with respect to
general and cardiac symptoms. The same applies to patients in whom betablockers are started during follow up.
14. Other symptoms or signs of hyperthyroidism or obstruction of vital structures which in the opinion of the attending physician urge to active treatment.

Date of first enrolment
01/06/2003

Date of final enrolment
01/06/2010

Locations

Countries of recruitment
Netherlands

Study participating centre
UMCN st Radboud
Nijmegen
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Sponsor information

Organisation
University Medical Centre St Radboud (Netherlands)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05wg1m734

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Medical Centre St. Radboud (Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration