Cold as a therapeutic strategy to improve cardiovascular risk factors

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON56482

Source
ToetsingOnline

Brief title
Cold exposure and cardiovascular risk factors

Condition

- Coronary artery disorders
- Glucose metabolism disorders (incl diabetes mellitus)
- Lipid metabolism disorders

Synonym
cardiovascular diseases

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: Brown adipose tissue, Cold, Lipids, South Asians

Outcome measures

Primary outcome

Part 1: Thermal comfort and practicalities upon wearing either cooling vest for 5 days

Part 2 and 3: Effects of cold exposure through wearing a cooling vest (part 1) or daily cold showers (part 2) on fat mass

Secondary outcome

Part 1: Resting energy expenditure upon wearing either cooling vest for 5 days

Part 2 and 3: Cold-induced resting energy expenditure, lipid metabolism, hepatic steatosis, skin temperature, serum markers for glucose metabolism, immune cell phenotype and response of these cells to inflammatory stimuli, markers of biological stress, experienced stress and quality of life upon wearing a cooling vest for 2 h/day for 6 weeks or after daily cold showers

Study description

Background summary

Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality in Western society. This especially accounts for the South Asian population, in which a particularly high risk to develop CVDs is present. This may be due to the presence of a disadvantageous metabolic phenotype in this population, including central obesity, dyslipidemia and low-grade inflammation. The majority of CVDs is caused by atherosclerosis (i.e. atherosclerotic (as)CVD), for which dyslipidemia and inflammation are the main risk factors. Cold exposure has been shown to acutely increase whole-body metabolism by influencing both brown adipose tissue (BAT) and skeletal muscle. Cold exposure also reshapes the immune system. Longer term highly controlled studies in

clinical research units using cold rooms or water-perfused cooling systems have shown that cold exposure leads to improvements in cardiometabolic health including lower fat mass. Importantly, these studies have also demonstrated that one can get used to daily cold exposure, with less to no (thermal) discomfort after approximately a week. However, in order to implement cold therapy in clinical practice (for example as part of a combined lifestyle intervention), cold should be applied in a feasible way, such as via cooling vests or regular cold showers. We hypothesize that 6 weeks of daily bouts of cold exposure by wearing cooling vests for 2 hours per day or by taking a cold shower for 90 seconds per day improves cardiometabolic risk factors (i.e. dyslipidemia, hyperglycemia and inflammation) by concomitantly increasing thermogenic processes in BAT and skeletal muscle resulting in improved dyslipidemia, lower (ectopic) fat accumulation and improved insulin sensitivity. Furthermore, we hypothesize that cold treatment will reduce inflammation through skewing of monocytes towards an anti-inflammatory phenotype. These may be direct effects of cold following the use of cooling vests for 2 hours per day, or more indirect effects of generating a more healthy daily routine and *resetting* the body by taking cold showers for 90 second in the early morning.

Study objective

This study will consist of three parts with three different main objectives:
- Part 1 - Pilot study;
Primary objective: To assess and compare thermal comfort upon wearing a cooling vest, based on exposed cooling packs versus shielded cooling packs, daily for 5 days in Europid and South Asian men and women
- Part 2 and 3 - Cooling vest and cold shower studies
Primary objective: To investigate and compare the effects of 6 weeks of daily bouts of cold exposure through wearing a cooling vest (part 2) or through cold showers (part 3) on fat mass in South Asian versus Europid men and women (part 2) or in Europid women only (part 3)

Study design

Part 1 - Pilot study: Cross-over intervention study, in which participants will, in random order, either wear a cooling vest with exposed cooling packs or a vest with shielded cooling packs for two hours per day for 5 consecutive days, with at least two weeks of *wash out* in between. Participants will daily answer questions on comfort and practicalities. Prior to wearing either cooling vest, a small study day will take place (e.g. two in total of approx. 1 hour each) in which acute effects on resting energy expenditure will be assessed (indirect calorimetry).

Part 2 and 3 - Cooling vest and cold shower studies: intervention study in which participants will either wear a cooling vest (Part 2; e.g. the cooling

vest that appeared most suitable in Part 1) for two hours per day for 6 weeks in total, or take daily cold showers for up to 90 seconds for 6 weeks in total (Part 3). Before and after the intervention, a study day will take place in which we will assess anthropometric measures (e.g. body weight, waist circumference), fat mass (BIA), changes in white adipose tissue metabolism (biopsy; only in Part 2), baseline blood markers for lipid and glucose metabolism (e.g. free fatty acids, total cholesterol, LDL-cholesterol, glucose, insulin) as well as inflammatory markers (e.g. immune cell phenotype and in vitro response of cells to inflammatory stimuli) and stress markers (cortisol) in blood and scalp hair. Furthermore, in part 2 we will also assess cold-induced changes in energy expenditure (indirect calorimetry) and skin temperature (infrared thermography), cold-induced changes in lipid metabolism (through regular blood sampling)

Study burden and risks

Participants in the intervention group may directly and personally benefit from participating in this research project due to the hypothesized health benefits of cold exposure. However, little burden is expected when taking part in this study. The intravenous cathether may cause bruising. The white fat biopsy (only in part 2) may cause bruising, and in rare cases sensibility of the part of the skin where the biopsy was taken may be decreased.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Part 1 - Pilot study

For the pilot study, a subject must meet the following criteria:
- Males or females with Europid ethnicity OR with South Asian ethnicity (South Asian ethnicity is defined as having 4 grandparents that originally descended from either Bangladesh, India, Nepal, Pakistan, Afghanistan, Bhudan or Sri Lanka or are from Hindu-Surinamese descent)
- Age between 20 and 50 years
- Living with overweight or obesity (Europids: BMI 25 - 35 kg/m2; South Asians: BMI 23 - 35 kg/m2, since a BMI of 23 is already regarded as *overweight* in South Asians; or a BMI < 35 kg/m² and a waist circumference of >=80 cm for females; or a BMI < 35 kg/m² and a waist circumference of >=94 cm for male Europids; or a BMI < 35 kg/m² and a waist circumference of >=90 cm for male South Asians)(BMI 25 - 35 kg/m2)
- Capable of giving written informed consent

Part 2 - Cooling vest study

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Males or females with Europid ethnicity OR with South Asian ethnicity (South Asian ethnicity is defined as having 4 grandparents that originally descended from either Bangladesh, India, Nepal, Pakistan, Afghanistan, Bhudan or Sri Lanka or are from Hindu-Surinamese descent)
- Age between 20 and 50 years
- Living with overweight or obesity (Europids: BMI 25 - 35 kg/m2; South Asians: BMI 23 - 35 kg/m2, since a BMI of 23 is already regarded as *overweight* in South Asians; or a BMI < 35 kg/m² and a waist circumference of >=80 cm for females; or a BMI < 35 kg/m² and a waist circumference of >=94 cm for male Europids; or a BMI < 35 kg/m² and a waist circumference of >=90 cm for male South Asians)
- Capable of giving written informed consent
- Able to comply with the requirements and restrictions listed in the informed

consent form

Part 3 - Cold shower study

Inclusion criteria are largely similar compared with part 2, but here only females with Europid ethnicity will be included.

Exclusion criteria

Part 1 - Pilot study

A potential subject who meets any of the following criteria will be excluded from participation in the pilot study:
- Any cardiovascular disease (i.e. ischemic heart disease, arrythmias, severe heart failure, untreated hypertension)
- A first-degree family member with sudden cardiac death
- Abuse of alcohol (regularly more than 2 glasses per day) or use of any drugs of abuse
- Smoking
- Pregnancy
- Active cold water swimmers (at least once weekly during winter)
- Taking cold showers (in the past 6 weeks at least once weekly)

In case potential participants are active cold water swimmers or take cold showers, after a wash-out period of at least 6 weeks, they can participate in Part 1.

Part 2 - Cooling vest study

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Diabetes mellitus (determined on basis of fasting glucose levels defined by ADA criteria)
- Any other active endocrine disease (thyroid disease, any signs of Cushing*s syndrome, adrenal disease and lipid-associated disorders such as familial hypercholesterolemia)
- Any cardiovascular disease (i.e. ischemic heart disease, arrythmias, severe heart failure, untreated hypertension)
- A first-degree family member with sudden cardiac death
- Any chronic renal or hepatic disease
- Abnormal laboratory values that could point towards underlying (metabolic, (auto)immune) disease and/or that could influence primary and secondary outcomes (e.g. dyslipidemia, leukopenia, abnormal liver function)
- Abuse of alcohol (regularly more than 2 glasses per day) or use of any drugs
- Smoking

- Pregnancy
- Participation in an intensive weight-loss program or vigorous exercise program during the last year before the start of the study
- Use of any medication that may influence energy metabolism (e.g. β-blockers, statins, antidepressants, antipsychotics), or may affect blood clotting (e.g. blood thinners).
- Active cold water swimmers (at least once weekly during winter in the past 3 months)
- Taking cold showers (in the past 3 months at least once weekly)
- Participation in another research project

Part 3 - Cold shower study

Equal to part 2, but exclusion criterium is also male gender

Study design

Design

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

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-12-2023
Enrollment:	138
Type:	Actual

Ethics review

Approved WMO

Date:	27-10-2023
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	11-01-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-02-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-03-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	29-11-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL84597.058.23