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## Changes in taste and smell function, dietary intake, food preference, and body composition in testicular cancer patients treated with cisplatin-based chemotherapy

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#### SUMMARY

*Background & aims:* Taste and smell changes due to chemotherapy may contribute to the high prevalence of overweight in testicular cancer patients (TCPs). This study investigates the taste and smell function, dietary intake, food preference, and body composition in TCPs before, during, and up to 1 year after cisplatin-based chemotherapy.

*Methods:* Twenty-one consecutive TCPs participated. At baseline TCPs were compared to healthy controls (N = 48). Taste strips and 'Sniffin' Sticks' were used to determine psychophysical taste and smell function. Subjective taste, smell, appetite, and hunger were assessed using a questionnaire. Dietary intake was analyzed using a food frequency questionnaire. Food preference was assessed using food pictures varying in taste (sweet/savoury) and fat or protein content. A Dual-Energy X-ray Absorptiometry (DEXA) scan was performed to measure whole body composition.

*Results*: Compared to controls, TCPs had a lower smell threshold (P = 0.045) and lower preference for high fat sweet foods at baseline (P = 0.024). Over time, intra-individual psychophysical taste and smell function was highly variable. The salty taste threshold increased at completion of chemotherapy compared to baseline (P = 0.006). A transient decrease of subjective taste, appetite, and hunger feelings was observed per chemotherapy cycle. The percentage of fat mass increased during chemotherapy compared to baseline, while the lean mass and bone density decreased (P < 0.05).

*Conclusions:* Coping strategies regarding subjective taste impairment should especially be provided during the first week of each chemotherapy cycle. Since the body composition of TCPs already had changed at completion of chemotherapy, intervention strategies to limit the impact of cardiovascular risk factors should probably start during treatment.

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#### 1. Introduction

Taste and smell perception play a significant role in appetite, dietary intake, and food choice [1]. Cancer patients often

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experience changes in taste and smell perception during chemotherapy. These chemosensory changes can result in change of dietary intake, malnutrition, weight loss, and a decreased quality of life [2–4].

The nature of taste and smell changes is variable among cancer patients during chemotherapy [5]. Data regarding the affected taste quality (sweet, sour, salty or bitter) are inconsistent and both increased and decreased sensations have been found. This can be

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due to the fact that most studies regarding taste and smell changes are performed in heterogeneous cancer populations with various malignancies, treatments, and different disease phases. A recent longitudinal study investigated the taste function, food liking, and appetite in 52 breast cancer patients treated with anthracycline and/or taxane based chemotherapy [2]. In that study, a decreased taste function was found, particularly during the first days (day 4-6) of a chemotherapy cycle. The changes in taste, appetite, and food liking were temporary per chemotherapy cycle. Another longitudinal study investigated the taste and smell function in 87 patients with breast cancer or a gynaecologic malignancy, heterogeneous regarding chemotherapy regimen and disease stage [6]. A decreased taste and smell function was found during chemotherapy, which recovered almost completely within 3 months after chemotherapy. In addition, a decrease in taste and smell function was found in a subset of that study, consisting of 12 ovarian cancer patients treated with carboplatin based therapy [7].

Testicular cancer patients (TCPs) are an interesting study population to investigate the effect of taste and smell changes due to chemotherapy, given the homogeneity regarding treatment with cisplatin-based chemotherapy and the curative intent. The downside of this treatment is the possible development of long-term complications, such as the high prevalence of overweight and metabolic syndrome, and the increased risk of cardiovascular disease (CVD) [8–10]. Moreover, hypogonadism is a common side effect of an orchidectomy, influencing body composition. Given these possible complications of a curative treatment in this young population, attention to dietary intake, food preference, and body composition is warranted, both during and after chemotherapy.

The aim of this study was to investigate whether a systematic pattern of changes in taste and smell function, food preference, dietary intake, and body composition can be found and persists over time in TCPs treated with cisplatin-based chemotherapy.

#### 2. Materials and methods

#### 2.1. Study population

TCPs scheduled to receive first line chemotherapy consisting of bleomycin, etoposide and cisplatin (BEP) or etoposide and cisplatin (EP) were eligible to participate. Patients received three or four 3weekly cycles of chemotherapy. Patients received a standard regime with intravenous antiemetics during each cycle of chemotherapy on day 1 before start (150 mg fosaprepitant, 1 mg granisetron, and 10 mg dexamethasone), 8 mg dexamethasone at day 1, 2 and 3 after chemotherapy, and metoclopramide if necessary  $(3 \times 10 \text{ mg})$ . Patients eligible to participate were 18–50 years of age at start of treatment and were able to comprehend Dutch. Patients were excluded when they had a mental disability and/or comorbidities affecting taste and/or smell function. Forty patients were planned to recruit. Patients were compared to a healthy control group just before start of chemotherapy to explore possible differences in taste and smell function, food preference, dietary intake, and body composition due to the presence of disseminated disease. The controls were recruited as part of a cross-sectional study. In that study, controls were matched to a group of testicular cancer survivors regarding age, gender, and nationality. Inclusion criteria of the controls were: 18–50 years old and ability to comprehend Dutch (both reading and writing). Exclusion criteria were: medication use, mental disability, a history of cancer, and taste and/or smell abnormalities. All participants gave written informed consent. The longitudinal as well as the cross-sectional study were approved by the ethical committee at the University Medical Center Groningen (NCT01641172).

#### 2.2. Methods

Figure 1 displays the collected data at each time point. For the healthy controls, all measurements were performed only once. The questionnaire regarding subjective taste, smell, appetite, and hunger was only completed by the patients. Data on height, smoking status, level of education, and sports level were collected during a structured interview at baseline. Data concerning disease and treatment were derived from medical records.

#### 2.2.1. Psychophysical taste function

Filter-paper taste strips (Burghart, Wedel, Germany) were used to determine sweet, sour, salty, and bitter taste thresholds [11]. The following standard concentrations of each taste were used: sweet: 0.05, 0.1, 0.2, and 0.4 g/ml sucrose; sour: 0.05, 0.09, 0.165, and 0.3 g/ ml citric acid; salty: 0.016, 0.04, 0.1, and 0.25 g/ml sodium chloride; bitter: 0.0004, 0.0009, 0.0024, and 0.006 g/ml quinine hydrochloride. Participants had to choose one of five possible answers: sweet, sour, salty, bitter or no taste. Scores for each taste range from 0 to 4. A total taste score was derived by summing the scores of each taste and ranged from 0 to 16.

#### 2.2.2. Psychophysical smell function

To assess the psychophysical smell function, 'Sniffin' Sticks' (Burghart, Wedel, Germany) were used [12,13]. This test consists of pen-like odour dispensing devices. The measurement includes three parts: a threshold (THR) test, a discrimination (DIS) test, and an identification (ID) test. A standard series of pens with 16 dilutions of *n*-butanol was used to measure the THR. Three pens were presented in a randomized order, of which one contained the odorant and two solvent. Participants had to identify the pen containing the odorant. To measure the DIS, 16 triplets (two equal odorants and one different odorant) were presented. Participants had to discriminate which of the three pens smelled differently. To measure the ID, 16 common odours were presented and the participants had to identify the odour using a multiple choice task. The THR score ranges from 1 to 16. The DIS and ID scores range from 0 to 16. A total smell score was derived by summing the THR, DIS and ID, resulting in a threshold, discrimination, identification (TDI) score (range 1–48). The extended version of the 'Sniffin' sticks' was used, which contains 32 odour combinations for the DIS test and 32 odours for the ID test [14]. The combinations of pens were randomized across participants and test sessions.

#### 2.2.3. Dietary intake

Dietary intake was assessed using a food frequency questionnaire (FFQ), which has been validated to estimate the intake of energy, macronutrients, fatty acids, cholesterol, fiber, folate, vitamin B6, and B12 for the Dutch population [15–17]. It is an 183item questionnaire, in which participants report the consumption frequency of a defined list of foods over the past month. The FFQs were checked for missing or unusual reports, and if necessary, additional information was obtained from participants by telephone. Unusual reports were defined as a difference between the amount of bread and sandwich fillings of more than two and/or reports with less than 16 or more than 40 dinners per month. The Dutch food composition database 2011 was used to convert the data into nutrients [18].

#### 2.2.4. Food preference

Food preference was assessed using a computer task consisting of food pictures varying in taste (sweet/savoury) and in fat or protein content [19,20]. Relative food preference was investigated by showing paired food pictures on a tablet device (Apple, iPad2).

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