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Preoperative contrast-enhanced computerized tomography should not delay radioiodine ablation in differentiated thyroid carcinoma patients

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ARTICLE INFO

Article history:
Received 7 May 2014
Received in revised form
18 July 2014
Accepted 30 July 2014
Available online 12 August 2014

Keywords:
Radioiodine ablation
Urinary iodine
Differentiated thyroid carcinoma
Adjuvant therapy
Total thyroidectomy

ABSTRACT

Background: There is concern about potential interference of iodinated contrast used in contrast-enhanced computerized tomography (CECT) with radioiodine therapy in differentiated thyroid carcinoma (DTC). The aim of this study was to determine the effect of iodinated contrast on urinary iodine concentration (UIC) in patients having thyroidectomy compared with control groups without CECT and without thyroidectomy.

Methods: This prospective control study consisted of 4 groups each comprising 32 patients. Group 1- DTC patients undergoing preoperative CECT, group 2- DTC patients not undergoing CECT, group 3- benign goiter patients undergoing preoperative CECT, and group 4- patients with non-thyroidal diseases undergoing preoperative CECT. Spot UIC before CECT, after surgery (5–7 d), and at follow-up (4–6 wk) were compared among the groups.

Results: The median basal UIC levels were not significantly different between the four groups (232.2 *versus* 263.9 *versus* 268.2 *versus* 178.2 μg/L, respectively, $P = 0.443$). In contrast, groups having preoperative CECT had significantly higher UIC levels at discharge (924 *versus* 329 *versus* 776 *versus* 661 μg/L, respectively, $P = 0.001$). These differences became insignificant at follow-up (225 *versus* 252 *versus* 310 *versus* 275 μg/L, respectively, $P = 0.505$). Patients having follow-up UIC values above the conventional cut-off of clinically relevant iodine excess (>200 μg/L) also had significantly higher basal values than those having lower follow-up values (283.0 *versus* 181.7 μg/L; $P = 0.037$).

Conclusions: Irrespective of the fact whether a patient is thyroidectomized or not preoperative CECT using non-lipophilic contrast does not result in long-term iodine retention.

1. Introduction

Radioiodine (RAI) therapy is the most important adjuvant therapy in differentiated thyroid carcinoma (DTC) [1,2]. Iodine excess or contamination in the perioperative period is considered to be a potential interference with RAI therapy. Therefore, some nuclear medicine centers routinely recommend low iodine diet (LID) before RAI scan. [3].

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0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2014.07.065

Contrast-enhanced computerized tomography (CECT) is an important imaging modality for planning the surgical strategy in large and locally invasive DTC. Iodinated contrasts used in CECT contain very high quantity of iodine. Previous studies have shown that after radiological contrast imaging, iodine may be retained in the body for years [4,5]. Most of the published guidelines dealing with the management of DTC caution against use of preoperative CECT but in the same vein suggest and/or recommend CECT for optimal surgical planning of invasive DTC, thus creating uncertainties in the clinicians' mind [1,2]. Furthermore, the published guidelines advise to delay RAI ablation for varying periods of time after CECT and recommendations range from 6 wk–3 mo [1,2,5–7]. In the recent past, a few studies have tried to address this contentious issue [8–10]. However, these were either retrospective or did not include control groups.

At our center, 30%–40% of DTC patients present with locally invasive disease and magnetic resonance imaging being an expensive modality we use CECT for the preoperative planning [11]. We designed the present study to clarify the existing controversy about the impact of preoperative CECT on adjuvant RAI therapy. Our hypothesis was that because more than 90% of the administered iodine is excreted via urine, and thyroid being the major reservoir of iodine the body, iodine content should fall rapidly after total thyroidectomy even in patients having preoperative CECT [12]. As a matter of fact, many studies describing long-term iodine retention after contrast administration had included patients undergoing oral cholecystography and other non-thyroidal illness who had intact thyroid. Furthermore, the recommendations against performing CECT seem to be based on studies conducted in the past when lipophilic contrast agents were in use, which tend to get stored in adipose tissues for long time whereas currently majority of centers use water-soluble ionic contrast agents [4,5]. Urinary iodine concentration (UIC) is the best indicator of iodine content of an individual. Recent literature has supported the view that spot UIC measurement provides results at par with 24 h UIC. In fact, UIC measurement is no longer interpreted as a ratio to creatinine excretion because creatinine excretion is compromised in malnutrition [8,12–14].

The aim of this study was to determine the effect of iodinated contrast on UIC in patients having thyroidectomy compared with control groups without CECT and without thyroidectomy.

2. Material and methods

This prospective study ($n = 128$) consisted of patients undergoing surgery for thyroid or non-thyroid diseases between May 2010 and January 2013. Institute Ethical Committee approved the study and informed consent was taken from the patients. Patients were divided in four groups; each consisting of 32 patients. Group 1- DTC patients undergoing preoperative CECT, group 2- DTC patients not undergoing CECT, group 3- benign goiter patients undergoing preoperative CECT, and group 4- patients with non-thyroidal diseases undergoing preoperative CECT. Group 4 consisted of patients with breast cancer ($n = 18$), adrenal tumors ($n = 9$), thoracic tumors ($n = 3$), and head and neck tumors ($n = 2$). The group size was decided based on previous information about basal UIC values in patients with DTC setting a power of 80% and significance 0.05 to detect difference in median UIC between the groups undergoing and not undergoing CECT. It was decided to enroll a minimum of 28 patients in each group and to take care of drop-outs the number was increased to 32. Patients in groups 1, 2, and 3 had total thyroidectomy performed either as primary or secondary procedure. All patients undergoing completion total thyroidectomy had at least one intact thyroid lobe. Group 4 patients had non-thyroidal operative intervention. Regarding the protocol of lymph nodal dissection in DTC, elective central compartment neck dissection is performed in all the cases of papillary thyroid carcinoma (PTC) with the exception of incidentally detected micro PTC. Decision of lateral neck dissection is based on a positive cytology report. In cases with image detected lymphadenopathy, ultrasonography guided aspiration is performed. In cases where preoperative aspirate is unsatisfactory or suspicious lymph nodes are detected during surgery, a frozen section examination is carried out and lateral neck dissection is performed if the result is positive for malignancy. Only therapeutic lymph node dissection is performed in follicular thyroid carcinoma cases.

The indication of CECT in patients with thyroid nodule and/or swelling in our practice includes suspicion or evidence of extra-thyroidal extension, large gland or bulky lymph nodes in the neck, and to rule out retrosternal extension of diseases in cases where lower extent of nodule is palpated with difficulty. None of the patients had undergone CECT imaging or any other contrast-associated procedure within last 12 mo preceding this study. Informed consent was taken from all the patients, and routine management protocol of the patients remained unchanged. CECT scans were performed wherever indicated as per routine protocol using either iohexol (Omnipaque 350 [GE Healthcare Inc. India], iodine content = 350 mg/mL) or iopromide (Ultravist 370 [Bayer Healthcare India], iodine content = 370 mg/ml) as a contrast agent. The dose of contrast was 1 mL/kg body weight. No patients had deranged renal function and none was taking any iodine containing medication at discharge or follow-up.

Three spot urine samples were collected from each patient: (1)-basal sample (before CECT), (2)-sample at the time of discharge (5–10th postoperative day), and (3)-follow-up sample (about 4–6 wk after surgery). The aforesaid timing of follow-up is governed by the fact that most of our patients undergoing total thyroidectomy report back to us at this point either for checking of adequacy of thyroxine replacement dose (benign goiters) or whole body radioiodine (WBRAI) scan (DTC). To know the magnitude of iodine contaminations, patients undergoing CECT were requested to deposit one more spot urine sample within 24 h after undergoing CECT and 21 such samples were analyzed (7 each from groups 1, 3, and 4). Urine samples were collected in sterile non-iodine contaminated containers and were later aliquoted into 5 mL cryotubes and refrigerated in -80°C deep freezer until analysis. Urinary iodine estimation was done using a kit (Bioclone Australia Pty Limited, Sydney, Australia) based on the Sandell–Koltoff reaction [15]. The sensitivity and range of the test in our laboratory were 10 μg/L and 10–400 μg/L, respectively. The intra- and inter-assay CV were 6.5% and 10.5%,