

The Impact of Iodinated Contrast Media Used in Epidural Steroid Injections on Thyroid Function Tests

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Abstract

Objective: The use of iodinated contrast media (ICM) inevitably increases in conjunction with the growing number of epidural steroid injection (ESI) administrations. The purpose of this study was to investigate the relationship between thyroid functions and ICM exposure through ESI procedures.

Design: This is a prospective observational study.

Setting: The study was conducted at a university hospital pain management center.

Methods: This study was conducted between June 2022 and February 2023. Participants between the ages of 18 and 65 who had received an ESI at our outpatient pain clinic comprised the study's population. Thyroid function tests (free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH)) were measured before and three weeks after the procedure.

Results: A total of 124 participants (80 women and 44 men) were analyzed. The average amount of contrast media administered was 1.34 ml. A significant increase was observed only in the FT4 value compared to pre-procedure ($p = 0.017$), and no patient developed thyroid disorders.

Conclusion: The current study presents an analysis of the relationship between ICM and thyroid functions in the ESI population.

Categories: Radiology, Endocrinology/Diabetes/Metabolism, Pain Management

Keywords: contrast media, epidural injection, iodine, thyroid functions, thyroid pathology

Introduction

Spinal pain management has become a major health issue as a result of longer life expectancies and an increase in the frequency of age-related spinal disorders. The current clinical treatment of spinal conditions is composed of nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, therapeutic injections, and surgery.

Epidural steroid injections (ESIs) are one of the most often used procedures for managing spinal pain among the various treatment modalities that are available [1]. There have been reports of substantial increases in ESI utilization among the US Medicare population, reflecting a 24% annual growth rate [2]. ESI can be implemented precisely and securely with the use of computed tomography (CT) or fluoroscopy. Even so, in order to confirm the exact needle tip position and avoid inadvertent non-epidural injections (intravascular, subdural, subarachnoid, etc.), the use of iodinated contrast media (ICM) is crucial and imperative [3].

The amount of contrast used in ESIs varies depending on factors such as procedure type, number of procedures, practitioner experience, and anatomical structures. Since many factors are involved in the procedures, even though a small dosage of contrast media is generally adequate, these doses may be raised, which might also elevate the risk of the contrast media's adverse effects.

The amount of iodine in ICM is considerable. The amount of iodine that the patient may receive during a single CT scan might range from 100 to thousands of times the normal limit [4,5]. Free iodine in the serum is utilized by the thyroid gland to synthesize thyroid hormone for metabolic processes. The normal thyroid gland is capable of adapting to an increase in iodine. When rapid overload iodine doses are administered suddenly, the regulation of thyroid hormone is disrupted, which can lead to either hyperthyroidism (the Wolff-Chaikoff effect) or hypothyroidism (the Jod-Basedow effect) [6-8].

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The impact of ICM on nephrotoxicity has been widely explored; however, several studies have addressed ICM's effects on the normal thyroid gland in clinical practice, and most of those studies were related to the use of CT scans [9,10]. To the best of our knowledge, there have been no reports examining the association between ICM exposure and ESI procedures applied with fluoroscopy guidance and subsequent thyroid functionality. We hypothesize that ICM used in ESIs may compromise thyroid gland functions and the dysfunction of thyroid hormones may be correlated with ICM's dose.

Hence, the aim of this prospective research is to determine whether exposure to ICM is linked to thyroid dysfunction in the ESI population.

The manuscript is presented as a preprint at <https://www.researchsquare.com/article/rs-3401473/v1> on October 16, 2023.

Materials And Methods

This prospective observational study was carried out at Marmara University Pendik Training and Research Hospital outpatient pain clinic from June 2022 to February 2023. The study was approved by the Marmara University School of Medicine Ethics Committee (approval number: 07.01.2022.82) and conducted in accordance with the principles of the Declaration of Helsinki. The study was registered at ClinicalTrials.gov (NCT05404412). The population of the study consisted of patients between the ages of 18 and 65, who had undergone any type of ESI, including lumbar, cervical, and caudal ESIs, for any reason in our outpatient clinic (Figure 1, Figure 2, and Figure 3).

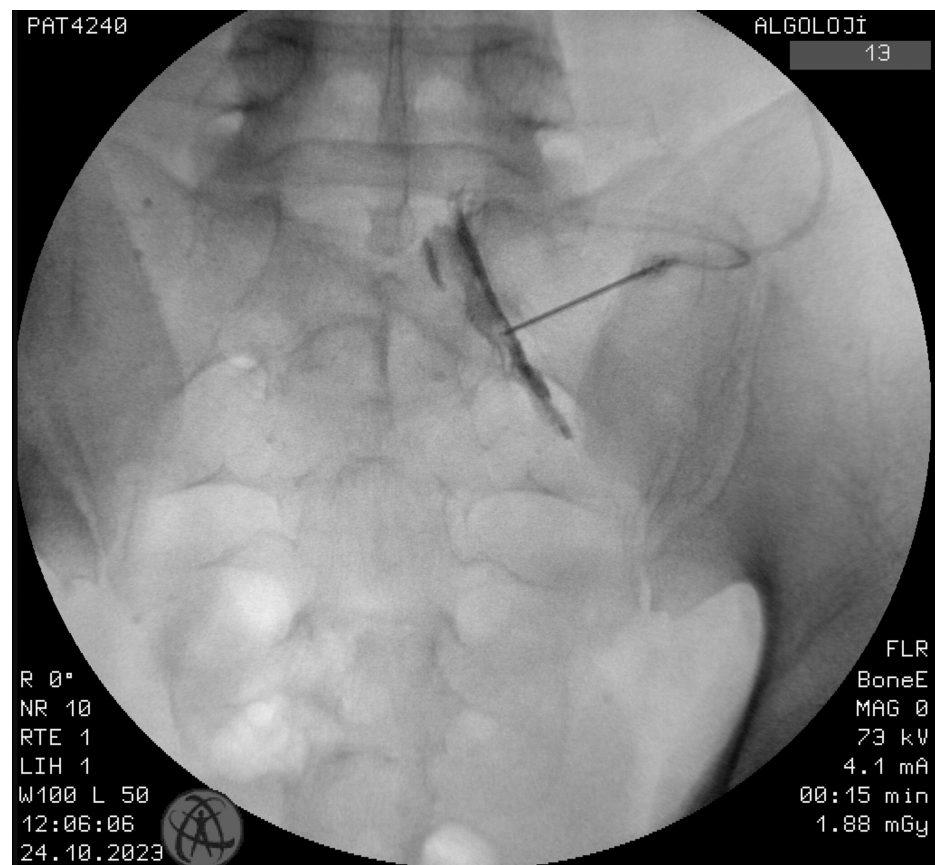


FIGURE 1: Contrast media spreading during lumbar transforaminal epidural injection



FIGURE 2: Contrast media spreading during lumbar interlaminar epidural injection

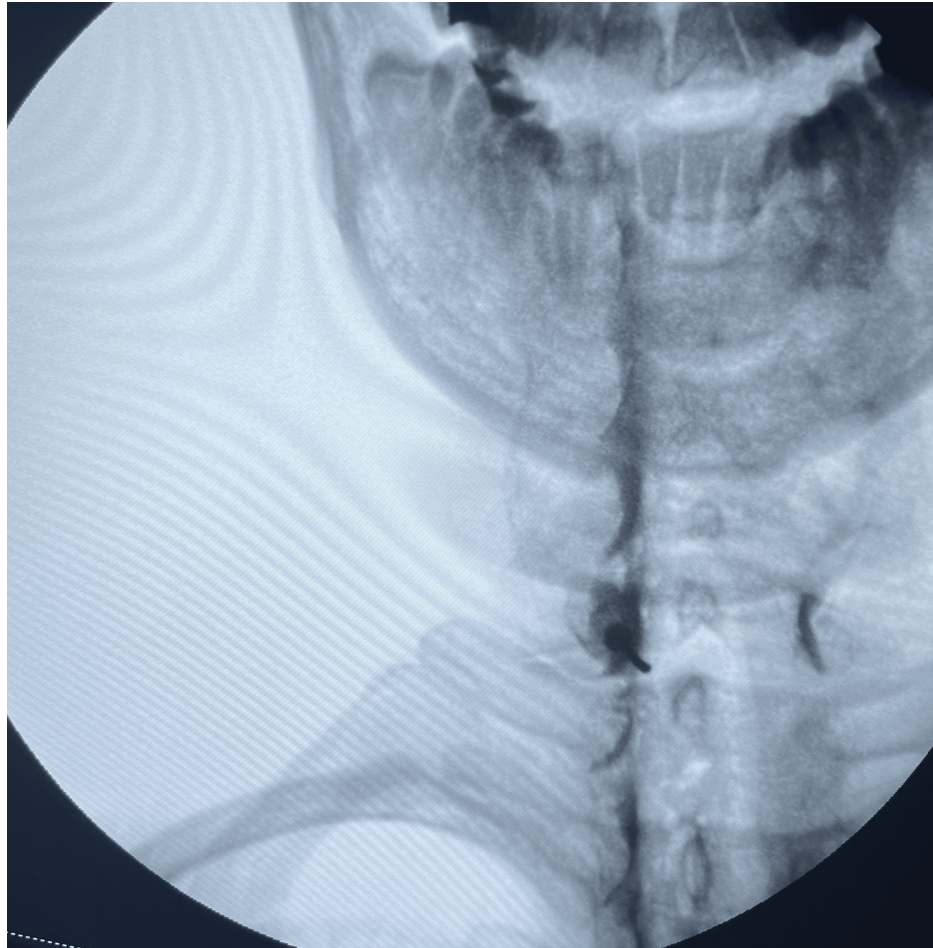


FIGURE 3: Contrast media spreading during cervical interlaminar epidural injection

Exclusion criteria were as follows: (A) suffering or had suffered thyroid or metabolic diseases, thyroid dysfunction, or thyroid surgery; (B) suffering or had suffered hypothalamic or pituitary diseases; (C) a current prescription for levothyroxine, antithyroid drugs, amiodarone, or lithium; (D) systemic and/or local infections, malignancy, or bleeding diathesis; (E) a known allergy to contrast material and/or local anesthetic substances; (F) a known history of any psychiatric disorder; and (G) a history of pregnancy and pregnant women. Verbal and written informed consent was obtained from all patients participating in the study.

The flowchart for determining the study population is displayed in Figure 4.

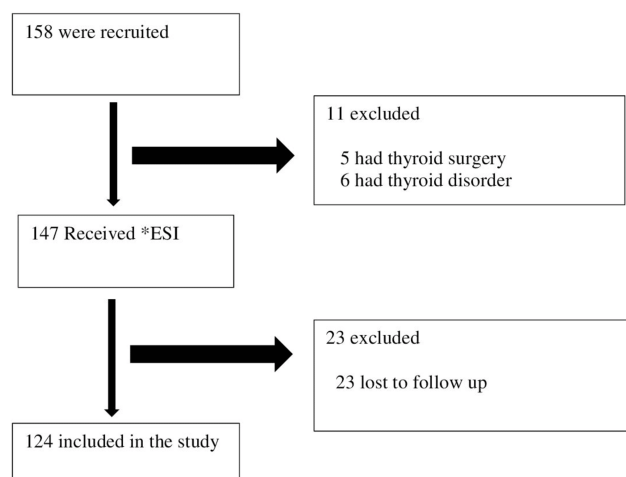


FIGURE 4: Flowchart of the study

*ESI: epidural steroid injection

In conjunction with the recording of the demographic data of the patients participating in this study (age, sex, body mass index (BMI), contrast medium doses, etc.), the values of thyroid function tests (TFTs) including free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) were analyzed before the procedure and the third week after the procedure. The Immuno-Serology Laboratory measured serum TSH, FT3, and FT4. Blood samples were collected from the participants at the same hours of the day before and after the procedure while fasting.

TSH, FT4, and FT3 were measured using electrochemiluminescence immunoassay (Cobas Integra 8000, Roche Diagnostics, Germany). The reference ranges for TSH, FT3, and FT4 were 0.48-4.81 mIU/L, 2.02-4.42 ng/L, and 0.78-1.51 ng/dL, respectively.

The laboratory analyses have been authorized for use in clinical settings. ESIs were performed by a 10-year experienced interventional pain specialist (SS) under sterile conditions with the C-arm fluoroscopy guidance. Throughout the process, details on the procedure that can affect the outcomes were recorded, including the type of ESI, the number of interventions, the frequency of inadvertent injections, the volume of the contrast, and the route of the contrast administration.

The total contrast volume was measured manually after the procedure. The same injector type was used throughout all procedures. All patients were given the low-osmolar, nonionic contrast medium iohexol (Omnipaque, 300 mg iodine/mL, GE HealthCare, Chicago, IL, USA) for ESIs.

Results

A total of 124 participants who had received an ESI were analyzed. Forty-four (35.5%) of the patients were male, and 80 (64.5%) were female. While the mean age of the patients was 49.32 ± 9.70 , the BMI was 28.38 ± 4.46 . Of the 124 procedures performed, 99 (79.8%) were lumbar, 21 (16.9%) were cervical, and four (3.2%) were caudal ESIs. After contrast agent administration, thyroid functions have not deteriorated, and all patients were euthyroid (Table 1).

Variable values	Mean ± SD
Age (years)	49.32 ± 9.70
BMI (kg/m ²)	28.38 ± 4.46
The amount of contrast media (ml)	1.34 ± 0.63
Gender	n (%)
Male	44 (35.5)
Female	80 (64.5)
Procedure	n (%)
Lumbar ESI	99 (79.8)
Cervical ESI	21 (16.9)
Caudal ESI	4 (3.2)
Post-procedure thyroid function	n (%)
Euthyroidism	124 (100)

TABLE 1: Demographic data, procedure types, and post-procedure thyroid function

The descriptive data was provided as n (%), mean ± SD (min-max), and median (min-max) values.

ESI: epidural steroid injection; BMI: body mass index

There was a significant increase in FT4 post-contrast injection related to the FT4 measurement before injection (p = 0.017). In contrast, no significant changes were detected in serum TSH (p = 0.810) and serum FT3 (p = 0.972) (Table 2). No major adverse events were observed during the procedures. As a result of the correlation analysis performed between the contrast agent doses and TFTs, no strong correlation was found (Table 3 and Table 4).

TFTs	Pre-procedure	Post-procedure	P-value
T3	2.98 ± 0.44	2.98 ± 0.53	0.972
T4	1.21 ± 0.24	1.25 ± 0.24	0.017
TSH	1.59 (0.13-4.72)	1.54 (0.10-9.83)	0.810

TABLE 2: Comparison of TFT values before and after contrast administration

Statistical analyses were conducted using the paired t-test for T3 and T4 and the Wilcoxon test for TSH.

TSH: thyroid-stimulating hormone; TFT: thyroid function test; T3: triiodothyronine; T4: thyroxine

-	Contrast media		preT3	preT4	postT3	postT4
Contrast media	r	1	0.194*	0.002	0.025	-0.149
	p	-	0.038	0.982	0.785	0.099
preT3	r	-	1	-0.090	0.441*	-0.109
	p	-	-	0.341	<0.001	0.247
preT4	r	-	-	1	-0.066	0.724*
	p	-	-	-	0.481	<0.001
postT3	r	-	-	-	1	0.090
	p	-	-	-	-	0.331
postT4	r	-	-	-	-	1

TABLE 3: Correlation between contrast media and T3-T4 values

*Correlation is significant at the 0.05 level.

T3: triiodothyronine; T4: thyroxine

-		Contrast media	preTSH	postTSH	
Contrast media	rho	1	0.135	0.059	
	p	-	0.136	0.518	
preTSH	rho	-	1	0.667*	
	p	-	-	<0.001	
preTSH	rho	-	-	1	

TABLE 4: Correlation between contrast media and TSH values

*Correlation is significant at the 0.05 level.

TSH: thyroid-stimulating hormone

Discussion

This prospective observational study was carried out to evaluate the impact of contrast media on thyroid function in patients who received ESI. First, we revealed that the serum level of FT4 was significantly elevated but still remained in normal ranges following ESI. Second, none of our patients developed thyroid dysfunction. Third, we discovered that these conditions were unrelated to the ICM dosage.

ICM is routinely and necessarily employed in ESI procedures. An average 1.5-2 ml dosage of ICM with a 35 µg/ml concentration is used in the procedure, providing 70 µg of free iodide, which is much lower than CT or angiography ranges [11,12]. Some research indicates that repeated ICM exposure and large ICM volumes are more likely to elevate the risk of thyroid disorders [13,14]. Contrary to these studies, we found no correlation between contrast volume and thyroid hormone dysregulation. This might be due to the low amount of contrast media and the short follow-up period.

The iodine or iodide load provided by ICM likely explains the observed connection between ICM exposure and hyperthyroidism. Once the iodine has entered the thyroid follicles, it is used to produce the thyroid hormones T4 and T3 [15]. After an iodine dose, defective autoregulation is the mechanism behind ICM-induced hyperthyroidism, and a high consumption of iodine will lead to either temporary or permanent hyperthyroidism [16-18]. This mechanism may shed light on the link between ICM exposure and thyroid function changes in the studies. Similar to the findings of Chen et al., we discovered a slight difference in T3

and TSH levels but a significant change in T4 levels compared to pre-treatment. However, when compared, the amount of contrast material used differs [10]. We postulated that this may be due to non-dose-dependent personal and other variables, including living in an iodine-deficient region and having an underlying autoimmune disease or thyroid issues (euthyroid goiter, euthyroid sick syndrome, etc.).

None of the participants in our research experienced any thyroid function deterioration after ICM exposure. A prospective observational cohort research examined the long-term consequences on thyroid function in euthyroid individuals employing ICM for coronary angiography. After eight weeks, they discovered that ICM may give rise to subclinical hyperthyroidism [19]. It has been proposed that the association between ICM exposure and developing thyroid dysfunction may be more widespread than previously anticipated [20]. A nested case-control study between 1990 and 2010 consisting of 3678 individuals was conducted in the euthyroid population by Rhee et al. [6]. They showed that overt hypothyroidism and hyperthyroidism were significantly associated with ICM exposure. Over the course of a year, one million patients in the general population of Taiwan showed a considerably greater incidence of ICM-induced thyroid dysfunction after six years of observation [5]. Using Taiwan's National Health Insurance Research Database, a later investigation discovered that individuals with euthyroid nodular goiter had a nearly fivefold greater incidence of ICM-induced thyroid dysfunction than those without thyroid nodules [21]. Yet, in certain studies, ICM exposure caused thyroid dysfunction, particularly in patients with a history of thyroid illness or renal insufficiency [14,21,22]. However, since we were unable to recruit adequate patients with thyroid dysfunction, our investigation focused on participants with normal thyroid function. In our subsequent investigation, we intend to include individuals with thyroid disorders.

Despite convincing retrospective research, the outcomes of prospective observational studies in various regions assessing changes in thyroid hormone levels after a single exposure to ICM are highly diverse [23–25]. In accordance with a recent systematic review and meta-analysis, during radiographic processes, the frequency of thyroid dysfunction following ICM injection is remarkably low [23]. These differences may be caused by the selection of participants (based on thyroid functions), the amount and type of contrast agent used, and the follow-up period, which cause substantial heterogeneity among studies [26].

Our study has several limitations. First, our study has a short follow-up period. On the other hand, the relationship between ICM volume and the long-term risk of thyroid illness, as well as the requirement of thyroid function monitoring, remains obscure. Second, due to the nature of the technique, we carried out ESI utilizing low-dose contrast volumes. Third, participants in our study were not strictly selected from an iodine-sufficient region. Fourth, contrast media absorption may vary in different epidural regions; therefore, subgroup analysis may be required. Finally, due to the difficulties in diagnosing asymptomatic autoimmune diseases and goiter, this population may be mistakenly included. It might affect our clinical results.

We also have strengths in our study. It is the first study to address the change in TFTs due to ICM exposure in ESIs.

We demonstrated that even though there is a substantial elevation of T4 level, yet within the normal limit, those procedures could not deteriorate thyroid function values and lead to a thyroid disorder in euthyroid individuals. Nevertheless, interventional pain specialists should keep in mind that the contrast medium used during procedures may worsen this condition in patients with thyroid hormone disorders. Given the growing prevalence of ESI implementations in clinical practice, the results obtained are of importance in the daily routine practice of ESI.

Conclusions

The current study provides an overview of the association between ICM and thyroid functions in the ESI population. In this study, there was no meaningful difference in TSH and T3 values before and after injection, whereas a significant increase in T4 value was observed in post-injection individuals, but still remained within normal limits. Given the widespread use of contrast media in interventional pain management such as ESI, routine thyroid examinations prior to and after ESI are required, particularly for patients who are inclined to thyroid dysfunction. Consequently, physicians and patients should be acquainted with the possible thyroid issues related to ICM, and in order to clarify this issue, further studies with various contrast media volumes and longer follow-up periods are needed.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Ridvan Isik, Yucel Olgun, Savas Sencan

Drafting of the manuscript: Ridvan Isik, Yucel Olgun, Hakan Gunduz

Acquisition, analysis, or interpretation of data: Serdar Kokar, Yucel Olgun, Hakan Gunduz

Critical review of the manuscript for important intellectual content: Serdar Kokar, Savas Sencan

Supervision: Hakan Gunduz

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Marmara University School of Medicine Ethics Committee issued approval 07.01.2022.82. The study was registered at ClinicalTrials.gov (NCT05404412). **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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References

1. Manchikanti L, Knezevic NN, Navani A, et al.: Epidural interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) Comprehensive Evidence-Based Guidelines. *Pain Physician*. 2021, 24:S27-S208.
2. Manchikanti L, Sanapati MR, Soin A, Manchikanti MV, Pampati V, Singh V, Hirsch JA: An updated analysis of utilization of epidural procedures in managing chronic pain in the medicare population from 2000 to 2018. *Pain Physician*. 2020, 23:111-26.
3. Furman MB, Cuneo AA: Image and contrast flow pattern interpretation for attempted epidural steroid injections. *Phys Med Rehabil Clin N Am*. 2018, 29:19-33. [10.1016/j.pmr.2017.08.003](https://doi.org/10.1016/j.pmr.2017.08.003)
4. van der Molen AJ, Thomsen HS, Morcos SK: Effect of iodinated contrast media on thyroid function in adults. *Eur Radiol*. 2004, 14:902-7. [10.1007/s00330-004-2238-z](https://doi.org/10.1007/s00330-004-2238-z)
5. Kornelius E, Chiou JY, Yang YS, Peng CH, Lai YR, Huang CN: Iodinated contrast media increased the risk of thyroid dysfunction: a 6-year retrospective cohort study. *J Clin Endocrinol Metab*. 2015, 100:3372-9. [10.1210/jc.2015-2329](https://doi.org/10.1210/jc.2015-2329)
6. Rhee CM, Bhan I, Alexander EK, Brunelli SM: Association between iodinated contrast media exposure and incident hyperthyroidism and hypothyroidism. *Arch Intern Med*. 2012, 23:153-9. [10.1001/archinternmed.2011.677](https://doi.org/10.1001/archinternmed.2011.677)
7. Markou K, Georgopoulos N, Kyriazopoulou V, Vagenakis AG: Iodine-induced hypothyroidism. *Thyroid*. 2001, 11:501-10. [10.1089/105072501300176462](https://doi.org/10.1089/105072501300176462)
8. Wolff J, Chaikoff IL: Plasma inorganic iodide as a homeostatic regulator of thyroid function. *J Biol Chem*. 1948, 174:555-64. [10.1210/endo-42-6-468](https://doi.org/10.1210/endo-42-6-468)
9. Lee SY, Rhee CM, Leung AM, Braverman LE, Brent GA, Pearce EN: A review: radiographic iodinated contrast media-induced thyroid dysfunction. *J Clin Endocrinol Metab*. 2015, 100:376-83. [10.1210/jc.2014-3292](https://doi.org/10.1210/jc.2014-3292)
10. Chen Y, Zheng X, Li N, et al.: Impact of iodinated contrast media in patients received percutaneous coronary intervention: focus on thyroid disease. *Front Endocrinol (Lausanne)*. 2022, 23:917498. [10.3389/fendo.2022.917498](https://doi.org/10.3389/fendo.2022.917498)
11. Jensen CT, Wagner-Bartak NA, Vu LN, et al.: Detection of colorectal hepatic metastases is superior at standard radiation dose CT versus reduced dose CT. *Radiology*. 2019, 290:400-9. [10.1148/radiol.2018181657](https://doi.org/10.1148/radiol.2018181657)
12. Martens B, Hendriks BM, Eijvoogel NG, Wildberger JE, Muhl C: Individually body weight-adapted contrast media application in computed tomography imaging of the liver at 90 kVp. *Invest Radiol*. 2019, 54:177-82. [10.1097/RLI.0000000000000525](https://doi.org/10.1097/RLI.0000000000000525)
13. Hsieh MS, Chiu CS, Chen WC, et al.: Iodinated contrast medium exposure during computed tomography increase the risk of subsequent development of thyroid disorders in patients without known thyroid disease: a nationwide population-based, propensity score-matched, longitudinal follow-up study. *Medicine (Baltimore)*. 2015, 94:2279. [10.1097/MD.0000000000002279](https://doi.org/10.1097/MD.0000000000002279)
14. Bonelli N, Rossetto R, Castagno D, et al.: Hyperthyroidism in patients with ischaemic heart disease after iodine load induced by coronary angiography: long-term follow-up and influence of baseline thyroid functional status. *Clin Endocrinol (Oxf)*. 2018, 88:272-8. [10.1111/cen.13494](https://doi.org/10.1111/cen.13494)
15. Bizhanova A, Kopp P: Minireview: the sodium-iodide symporter NIS and pendrin in iodide homeostasis of the thyroid. *Endocrinology*. 2009, 150:1084-90. [10.1210/en.2008-1437](https://doi.org/10.1210/en.2008-1437)
16. Apsan J, Antal Z: Possible iodine-induced thyrotoxicosis in a previously healthy adolescent following administration of iodinated contrast media. *Case Rep Endocrinol*. 2021, 2021:5930515. [10.1155/2021/5930515](https://doi.org/10.1155/2021/5930515)
17. Leung AM, Braverman LE: Consequences of excess iodine. *Nat Rev Endocrinol*. 2014, 10:136-42. [10.1038/nrendo.2013.251](https://doi.org/10.1038/nrendo.2013.251)
18. Thomsen HS, Faber J: Iodine-based contrast media cause hyperthyroidism - another important adverse reaction to contrast media?. *Acta Radiol*. 2012, 1:1079-80. [10.1258/ar.2012.12A013](https://doi.org/10.1258/ar.2012.12A013)

19. Özkan S, Oysu AS, Kayataş K, Demirtunç R, Eren M, Uslu H, Altuntaş Y: Thyroid functions after contrast agent administration for coronary angiography: a prospective observational study in euthyroid patients. *Anadolu Kardiyol Derg.* 2013, 13:363-9. [10.5152/akd.2013.134](#)
20. Hudzik B, Zubelewicz-Szkodzińska B: Radioccontrast-induced thyroid dysfunction: is it common and what should we do about it?. *Clin Endocrinol (Oxf).* 2014, 80:322-7. [10.1111/cen.12376](#)
21. Kornelius E, Chiou JY, Yang YS, Lo SC, Peng CH, Lai YR, Huang CN: Iodinated contrast media-induced thyroid dysfunction in euthyroid nodular goiter patients. *Thyroid.* 2016, 26:1030-8. [10.1089/thy.2016.0051](#)
22. Leung AM, Braverman LE: Iodine-induced thyroid dysfunction. *Curr Opin Endocrinol Diabetes Obes.* 2012, 19:414-9. [10.1097/MED.0b013e3283565bb2](#)
23. Bervini S, Trelle S, Kopp P, Stettler C, Trepp R: Prevalence of iodine-induced hyperthyroidism after administration of iodinated contrast during radiographic procedures: a systematic review and meta-analysis of the literature. *Thyroid.* 2021, 31:1020-9. [10.1089/thy.2020.0459](#)
24. Jarvis C, Simcox K, Tamatea JA, McAnulty K, Meyer-Rochow GY, Conaglen JV, Elston MS: A low incidence of iodine-induced hyperthyroidism following administration of iodinated contrast in an iodine-deficient region. *Clin Endocrinol (Oxf).* 2016, 84:558-63. [10.1111/cen.12818](#)
25. Skórkowska-Telichowska K, Kosińska J, Szymczak R, et al.: Comparison and assessment of thyroid morphology and function in inhabitants of Lower Silesia before and after administration of a single dose of iodine-containing contrast agent during cardiac intervention procedure. *Endokrynol Pol.* 2012, 63:294-9.
26. Bednarczuk T, Brix TH, Schima W, Zetting G, Kahaly GJ: 2021 European thyroid association guidelines for the management of iodine-based contrast media-induced thyroid dysfunction. *Eur Thyroid J.* 2021, 10:269-84. [10.1159/000517175](#)