Journal of Medical Radiation Sciences

Open Access

ORIGINAL ARTICLE

Iodinated contrast media and their effect on thyroid function – Routines and practices among diagnostic imaging departments in Norway

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Keywords
Computerised tomography, contraindications, contrast media, quality assurance

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Received: 11 September 2019; Revised: 2 March 2020; Accepted: 2 March 2020

J Med Radiat Sci **00** (2020) 1–8

doi: 10.1002/jmrs.390

Abstract

Introduction: In order to minimise adverse effects or patient injuries related to the effect of iodinated contrast media (ICM) on the thyroid, international guidelines and research recommend developing routines for identification and management of patients at risk of developing a thyroid dysfunction. This study aimed to investigate thyroid-related ICM administration practices among diagnostic imaging departments in Norway. **Methods:** The cross-sectional survey included 24 hospitals and 75 respondents with a 69% response rate. The survey covered practices for assessment and management of at-risk patients and the participants' perceived rationale for the routines. **Results:** The use of written checklists as recommended by international guidelines was quite modest (15%) and the respondents preferred various methods to identify risk and contraindications. Only 20% reported checking for any scheduled thyroid-scintigraphy and/or radioactive-iodine therapy. 42% indicated that they did not have thyroid-related ICM routines, and the main perceived reason was lack of knowledge on the topic. Radiographers and radiologists expressed uncertainty about each other's roles and routines. **Conclusion:** This study revealed the need of optimisation of routines regarding ICM administration to patients at risk for thyroid dysfunction.

Introduction

In diagnostic imaging, optimisation is usually associated with radiation doses and diagnostic performance. However, optimising involves more than radiation doses and image quality, and one aspect is minimisation of adverse effects or patient injuries during an examination. Some adverse effects that can occur are related to the effect of iodinated contrast media (ICM) on the thyroid. International guidelines and previous research recommend developing of routines for identification and management of patients at risk of developing ICM-induced thyroid dysfunctions.[1-6] The first step in an optimising process is to assess the actual practice regarding the issue in scope. Hence, this study aimed to investigate routines on administration of ICM among diagnostic imaging departments in Norway.

Iodine is essential in the synthesis of thyroid hormones triiodothyronine (T3) and thyroxine (T4). Hyperthyroidism is defined as excessive secretion of thyroid hormones while excessive T3 and T4 blood levels are termed thyrotoxicosis.[7] Thyrotoxicosis caused by high iodine intake is described as Jod-Basedow effect.[7] The increasing use of computerised tomography (CT) makes ICM an important source of iodine intake. Both empirical studies and reviews show a correlation between ICM administration and thyrotoxicosis, sometimes even in patients with no history of thyroid pathology and ICM caused hypothyroidism has also been reported.[8-14] ICM caused thyroid dysfunctions can be transient or permanent, and the risk is higher in elderly patients, patients with autoimmune thyroid disease, multinodular goitre and cardiac disease.[8-14] While it is acknowledged that high-osmolar ionic ICM have more side effects than the low- and iso-osmolar non-ionic ICM, no difference between their effect on thyroid function has been reported.[8] Another issue of relevance is the ICM's influence on the thyroid iodine uptake, which may be

impeded for 2 months or longer after administration of ICM. This exposure may therefore disturb planned later examinations of diagnostic thyroid-scintigraphy and radio-iodine treatment.[3,11]

Administration of ICM to children requires special caution. Some studies show increased risk of iodine-induced thyroid dysfunction in children compared to adults and recommend monitoring of thyroid function particularly during the first year after exposure[9] while others claim that alteration of thyroid function after ICM administration is transient in most children.[15,16]

Both the European Society of Urogenital Radiology (ESUR) and the American College of Radiology (ACR) have developed evidence-based guidelines for ICM administration.[1,2] Their thyroid-related recommendations are quite similar and include the following: manifest hyperthyroidism as contraindication, monitoring at-risk patients and a washout period of up to two months prior to radioactive-iodine therapy and thyroid-scintigraphy. In addition, ESUR define patients with Graves' disease, multinodular goitre and thyroid autonomy as risk patients, especially if they are elderly and/or live in dietary iodine deficiency areas. Further, ESUR also recommends monitoring infants' thyroid function if ICM is administrated to the mother during pregnancy.[1]

Some countries have national guidelines while others use either ESUR or ACR guidelines. Sweden for example has guidelines that are very similar to ESUR's[17] while Germany has stricter guidelines that require routine assessment of thyroid function with laboratory tests (TSH) prior to administration of ICM.[11] Norway does not have national guidelines, and the present study therefore uses ESUR's guidelines as reference for quality assessment of local routines in Norwegian hospitals.

To our knowledge, no literature exists on how guidelines regarding management of patients at risk due to thyroid conditions are implemented in Norway or elsewhere. Previous studies on implementing and compliance of guidelines for safe administration of ICM[18,19] do not focus on thyroid-related aspects. There is a significant gap between the amount of studies analysing the effect of ICM on thyroid function and those that investigate how this knowledge is reflected in practices at radiology departments.

The aim of the present survey was to investigate the actual practices in Norway related to administration of ICM to patients at risk for thyroid dysfunction and to patients who will shortly later undergo radioactive thyroid treatment or scintigraphy examinations. The study also aimed to explore radiographers' and radiologists' knowledge of ESUR's guidelines and their perception of the rationale for the hospitals' local routines.

Methods

Procedure and participants

The cross-sectional survey was conducted across Norwegian hospitals serving a population above 25000 inhabitants. Invitation e-mails were sent to the head of the radiological departments in 24 hospitals (six from each regional health authority). The e-mail contained information about the study's purpose, ethical considerations and a requirement to recruit minimum six participants, preferably equal distribution between radiographers and radiologists. Inclusion criteria were broad experience with ICM and CT.

Thirteen hospitals participated, representing three of the four regional health authorities in Norway. The survey was sent to the 75 participants chosen by the department leaders via an e-mail with information about the study and a link to the digital questionnaire hosted on 'no.surveymonkey.com' (SurveyMonkey Inc., San Mateo, CA, USA). The survey was available for a period of 8 weeks; reminders were sent fortnightly.

Questionnaire

The questionnaire was developed based on international guidelines for the use of ICM and current evidence on the risk of ICM related thyroid dysfunctions.[1,2] Pilot testing was performed on eight university employees with radiographer professional background.

The final questionnaire included 26 questions from the following categories: demographic, at-risk patient identification method, routines for assessment and management of at-risk patients and rationale for the routines followed by an open-ended question with any comments related to the subject in scope. Non-exhaustive response options were followed by 'other' where respondents could freely write an open answer.

Data analysis

Data were exported from SurveyMonkey to an Excel file (Microsoft) and then exported to SPSS (version 24, IBM Corp. Amonk, NY, USA). The responses were analysed using descriptive statistics. Differences in responses between different regions and between professions were analysed by using Cramer's V correlation test as a strength test for the significant differences provided by the chi-square test. A difference with P-value <0.05 was considered statistically significant. Free text answers were analysed to identify potential patterns.

Ethical statement

The Regional Committee for Medical and Health Research Ethics waived the need of approval as the project was considered a quality assurance project and it did not involve any health-related information. An ethical revision of the questionnaire was performed in collaboration with a consultant from the Norwegian Centre for Research Data. The anonymity function of the SurveyMonkey software turned off IP-address tracking. Participants were informed about the purpose of the study, preservation of anonymity, and that participation was voluntary and submitting the survey was regarded as implied consent. Small hospitals were not included due to low number of potential participants (radiologists in particular), which presented a risk for identification of participants.

Results

Participants

Of the recruited 75 participants, 52 (from 13 hospitals) responded, which provides a response rate of 69%. The majority of participants were radiographers. Most respondents were experienced in working with ICM and had been working at the department for more than six years (Table 1).

Table 1. Participant demographics.

	Number	Percent
Profession		
Radiographer	37	71%
Radiologist	15	29%
Profession		
South-Eastern Norway	11	21%
Central Norway	22	42%
Western Norway	19	37%
Service at the department		
<3 years	8	15%
3-6 years	12	23%
>6 years	32	62%
Experience with ICM*		
<3 years	5	10%
3-6 years	12	23%
<6 years	35	67%

*Iodinated contrast media.

At-risk patient identification methods

There was considerable variability in assessing risk related to the effect of ICM on thyroid function across the hospitals, with statistically significant regional differences (Table 2). Almost all radiologists reported reading the patient's medical record in special cases while only few read it regularly; in contrast, most radiographers did not have access to the medical record (Table 3).

The most common procedure/routine used to identify contraindications to ICM was asking questions to the patient directly (Table 4) either following a written

Table 3. Practices regarding management of at-risk patients.

	Radiographers	Radiologists	All respondents
Medical record reading patterns			
Regularly	24%	7%	20%
Only in special cases	19%	93%	39%
Never	5%	0%	4%
No access to patient journals	52%	0%	37%
Profession responsible for follow-up of at-risk patients			
Endocrinologist	11%	100%	33%
General practitioner	22%	0%	17%
Other	67%	0%	50%

P-value < 0.005 (calculated with Cramer's V).

Table 4. The method used to identify contraindications to iodinated contrast media.

Method	%
Questions based on written procedure	72
Questions based on tradition	14
Referral approved by the radiologist is considered sufficient	8
Other	6

Table 2. Regional differences in compliance with European Society of Urogenital Radiology (ESUR)'s recommendations related to risk of iodinated contrast media (ICM)-induced thyroid dysfunction.

	South-Eastern Norway	Central Norway	Western Norway
The department follows ESUR's recommendation* regularly or irregularly	72%	38%	84%
Screening for manifest hyperthyroidism prior to ICM administration	18%	9%	65%
No screening for any thyroid condition	63%	77%	26%
Follow-up of patients with thyroid-related risk	18%	15%	37%

P-value < 0.01 (calculated with Cramer's V).

*Recommendation to not administer ICM to patients with manifest hyperthyroidism.

procedure (72%) or an informal procedure (14%). Other reported routines were searching for thyroid-related information in the radiology information system (RIS), or in the referral. One respondent indicated that it is the referring physician's responsibility to mention any contraindications.

Written checklists were seldom used (15%), and the form was filled in either by the radiologist (31%), the radiographer (25%) or the patient (19%). 25% of the respondents reported that they did not know who should fill in the form. The checklist was subsequently checked by the radiographer (70%), radiologist (7%) or the radiographer in consultation with the radiologist (23%).

The majority reported that they did not check for any of the specified thyroid diseases prior to ICM administration. The type of diseases they checked for varied among the respondents (Figure 1). The number of diseases the patient was checked for prior to ICM administration varied from 1 to 7 or more (Figure 2).

Routines for management of at-risk patients

Most respondents reported that their department follows the ESUR's recommendation to not administrate ICM to patients with manifest hyperthyroidism either regularly (39%) or irregularly (24%) while one third (37%) stated that the recommendation was not followed. When asked what patients are checked for thyroid disease before administrating ICM the majority (61%) reported that no patient is checked, while 16% stated that they check all patients. Among the 33% of the respondents who chose 'other' 42% of them reported that they check the patient for thyroid disease only if they have information about any clinical suspicion regarding that, and 18% considered that it is the referring physician's responsibility to check that. Some radiographers mentioned that they are not aware of whether the radiologists check if the patient has any thyroid disease (12%).

Most of the respondents (77%) checked if the patient had recently been administrated ICM. It was quite common to check that before intravenous ICM administration (86%) and less common when using other administration ways (oral and rectal with 8% each). The radiographers who chose 'other' expressed uncertainty about the radiologists' routines related to that. Scheduled thyroid-scintigraphy and radioactive-iodine therapy were checked to varying degrees (20% and 18%, respectively), while half of the respondents were not aware of whether these aspects are checked or not.

According to the respondents, only 20% of the departments had routines for prophylaxis in relation to ICM administration to patients at risk of thyrotoxicosis. Follow-up of patients at risk of ICM-induced thyrotoxicosis was not very common (24%) and radiographer and radiologists gave statistically significant different answers when asked who does the follow-up of these patients (Table 3). Half of the respondents who chose 'other' mentioned that they do not know who follows up the patients, and the other half wrote that the patient is followed up by the referring physician.

Perception of the rationales for the department's routines regarding ICM administration to patients with high risk of thyrotoxicosis or lack of such routines

Most of the respondents who had such routines at their department indicated ESUR's guidelines or other research

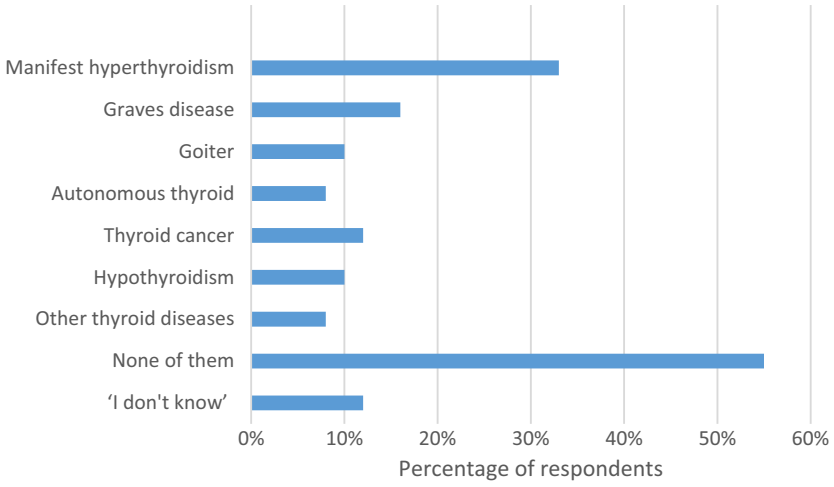

Figure 1. Thyroid diseases the patient is checked for prior to iodinated contrast media administration.

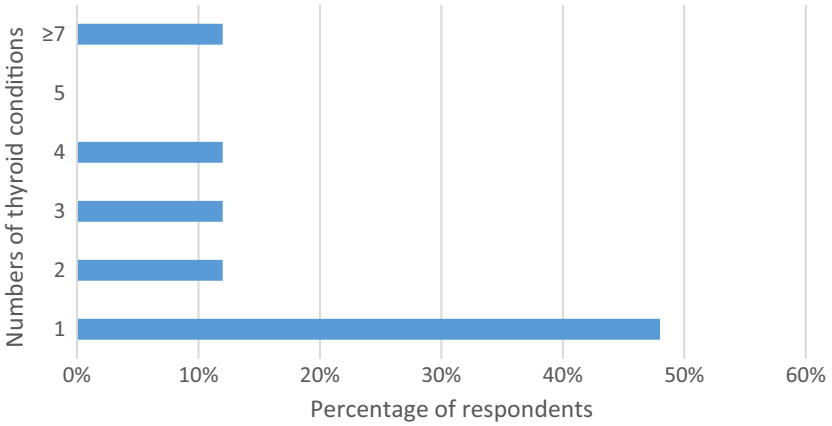

Figure 2. The number of diseases the patient is checked for prior to iodinated contrast media administration.

results (47%) followed by initiative from the department's employees (27%) when asked about the rationale for the routines regarding ICM administration to patients with high risk of thyrotoxicosis.

Almost half of the respondents (42%) reported lack of routines and indicated different rationales for that (Table 5), and the leading reason was lack of knowledge on the topic (46%). The most common answer among the respondents who chose 'other' was 'I don't know' (44%).

Table 5. The profession's perceived rationale for the lack of routines regarding iodinated contrast media administration to patients at risk of thyrotoxicosis.

Rationale	Radiographers	Radiologists	All respondents
Not recommended by research	11%	0%	9%
Lack of knowledge on this topic	44%	50%	46%
Lack of national guidelines	6%	0%	4%
Other	39%	50%	41%

P-value = 0.006 (calculated with Cramer's V).

Radiographers were significantly less familiar with the relation between ICM exposure and thyrotoxicosis and ESUR's recommendation to not administer ICM to patients with manifest hypothyroidism than radiologists (Table 6).

Discussion

This study was the first to analyse the current clinical practices related to identification and management of patients at risk of developing ICM-induced thyroid conditions who undergo ICM-enhanced CT in Norwegian hospitals. Assessing the current status in order to identify any improvement potential is always the first phase in an optimising process with focus on patient safety. Both radiographers and radiologists have a central role in administration of ICM and respondents from both professional groups were therefore invited to participate in order to get better insight into the local practices. The findings from this study show variation in routines both among hospitals and regional health authorities.

The results show that the most common method used to identify contraindications to ICM was asking questions to the patient (86%) followed by screening the referral or the RIS for thyroid-related information. Medical records

Table 6. The (two) professions' knowledge about the relationship between iodinated contrast media (ICM) exposure and thyrotoxicosis and European Society of Urogenital Radiology (ESUR)'s recommendation to not administer ICM to patients with manifest hypothyroidism.

	Radiographers	Radiologists	All respondents
Know about the relation between ICM exposure and thyrotoxicosis	61%	86%	68%
Familiar with ESUR's recommendation	41%	66%	48%
Heard about this recommendation but not familiar with it	27%	21%	26%
Did not know that ESUR's has such recommendations	16%	13%	16%
Not familiar with ESUR	14%	0%	10%

P-value = 0.2 (calculated with Cramer's V).

in Norway are electronic and while radiologists have direct access to them, radiographers can request access by completing a form and justifying their request. That might explain why reading the medical record prior to the examination was practiced differently by the two professions (Table 3). Radiographers had to rely on information from the patient, the referral or RIS to detect patients at risk of ICM-induced thyroid impairment or simply rely on the fact that a referral approved by a radiologist guarantees that no contraindication is present.

Although written checklists for screening for risk factors related to ICM administration are recommended by multiple instances[1-2,20] as a measure to increase patient safety, the findings of this study show quite moderate use of such checklists (15%) and that radiologists and radiographers prefer other methods to identify risk and contraindications related to the use of ICM. Similar practice was reported in an Iranian cross-sectional study which showed that only 2.3% of the respondents used checklists to identify patients at risk for adverse reactions from contrast agents, while 88.6% of them reported assessing risk but without having any local guidelines for that.[21] In contrast, a Korean study showed that 50% of the hospitals had routines for screening patients for hyperthyroidism prior to administration of ICM[22] while other countries had national guidelines that included assessing thyroid-related risk factors by using checklists[17] or even routine TSH blood tests prior to ICM administration.[11]

Nordic prevalence studies indicate Graves' disease as the most relevant thyroid-related risk factor for the Norwegian population, particularly among female patients.[23-25] However, checking the patients for Graves' disease prior to ICM administration is not common according to the findings of the current study (Figure 1). Multinodular goitre is also mentioned as a risk factor for developing ICM-induced thyrotoxicosis, especially in elderly patients; nevertheless, few respondents (10%) indicated that patients are checked for this condition.[3,5] Screening for other thyroid-related risk factors as autonomous thyroid and thyroid cancer follows the same pattern and half of the respondents reported that patients are not being checked for any of the mentioned thyroid conditions, while some of the respondents have no knowledge of whether the patients are screened for any thyroid condition (Figure 1). There is no consensus regarding the effect of ICM on children[9,15,16] and international guidelines[1,2] only recommend adjusting ICM doses to age and weight without mentioning thyroid effect. None of the respondents mentioned children among the patient groups they screen for thyroid conditions either.

The results are somehow ambiguous when it comes to the consistency between the formal routines and the actual practice at the hospitals. Both ESUR and ACR clearly state that manifest hyperthyroidism is a contraindication to administration of ICM.[1,2] Two thirds of the participants reported that their departments follow the ESUR's recommendation to not administer ICM to this patient group (39% regularly and 24% irregularly), and one third indicated that the recommendation is not followed.

The findings indicate that there is no guarantee that patients are checked for thyroid-related risk factors prior to ICM administration. Even among the respondents who claimed that their department follow ESUR's recommendation only half of those who stated that they follow the mentioned recommendation actually screen patients for manifest hyperthyroidism.

Despite documented disturbance of diagnostic thyroid-scintigraphy and radio-iodine treatment due to altered iodine uptake in the thyroid after administration of ICM[3,11] only one of five respondents report checking for any scheduled thyroid-scintigraphy and/or radioactive-iodine therapy.

The free text answers to several questions revealed that the two professional groups are not always aware of each other's roles regarding screening for thyroid-related risk and contraindications. One fourth of all respondents reported that they do not know who fills in the written checklists. Some radiographers reported that they are not aware of whether the radiologists check if the patient has any thyroid disease or any scheduled thyroid-scintigraphy and/or radioactive-iodine therapy, and others expressed uncertainty about the radiologists' routines in general. The radiographers were also much more uncertain about who should follow-up the at-risk patients after ICM examinations than radiologists with 67% 'I don't know' answers among the radiographers. The two professions' uncertainty about each other's roles and routines might explain the inconsistency between the formal routines and the actual practice.

The findings of the current study indicate the need for optimising the practice related to ICM administration in risk patients. Previous results show that implementation of guidelines for ICM use is essential and feasible despite the challenges, such as increased workload and logistical difficulties in rescheduling the examinations to a date compatible with the patient's condition and other planned examinations.[18] The reported workload directly related to the use of a written checklist is 2 min and 40 sec per patient (which includes explaining the questions to the patient).[19] One unwanted consequence of implementing guidelines regarding thyroid-related risk was a transient increase of requests for T3, T4 and TSH determinations not justified by the patients' clinical situations.[18] Previous studies have found that implementing of guidelines included a concise checklist covering all risk factors can get

positive reactions from both radiographers and radiologists.[19]

Evidence shows that training courses for personnel are imperative to ensure proper implementation of guidelines and might be more effective than sending out formal and informal reminders about using various checklists.[18] Interprofessional collaboration and awareness of each other's routines and responsibilities might be improved by activities that increase interprofessional interaction. A literature review shows that such measures can have a positive effect on adherence to recommended practices.[26] Different levels of knowledge about ICM-induced thyrotoxicosis and different levels of familiarity with the ESUR's recommendations related to patients with hyperthyroidism between radiographers and radiologists (Table 6) and the lack of knowledge on the topic reported by the majority of respondents as the reason for the lack of local routines, reinforce the need for increased interprofessional knowledge sharing.

The study has some limitations. There was no investigation into actual hospital guidelines, and the study relied solely on individual staff perception of the guidelines. In addition, the low number of radiologists might reduce the precision of estimate and mask potential significant differences between the occupational groups. Further, the questionnaire was developed for the purpose of this study and pilot tested in a small group but has not yet gone through a validation procedure (content and convergent validity). However, the questions and response options were quite straight forward, as such, possibilities for misinterpretation should be minimised. The strength of this study is the relatively high total response rate and that the survey covered the highest population density areas in Norway.

Conclusion

The findings of this study revealed the Norwegian hospitals' need of optimisation of practices regarding ICM administration to patients with thyroid-related risk and contraindications. Future investigation of the hospitals' written procedures would give a better overview of the extent of compliance with international guidelines.

Training courses and activities that improve the interprofessional network might facilitate an effective implementing of guidelines. The regional differences related to routines and actual practices indicate the need for national guidelines.

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