Multi-centre analysis of incidental findings on low-resolution CT attenuation correction images

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Multi-Centre Analysis of Incidental Findings on Low-Resolution CT Attenuation Correction Images

Abstract

Objectives: To review new incidental findings detected on low-resolution CT attenuation correction (CTAC) images acquired during SPECT-CT myocardial perfusion imaging (MPI). To determine whether the CTAC images had diagnostic value and warrant reporting.

Methods: A multi-centre study was performed in four UK Nuclear Medicine departments. CTAC images acquired as part of MPI performed using SPECT were evaluated to identify incidental findings. New findings considered to be clinically significant were evaluated further. Positive predictive value (PPV) was determined at the time of definitive diagnosis.

Results: Of 1819 patients studied, 497 (27%) had a positive CTAC finding. Fifty-one (2.8%) patients had findings that were clinically significant at the time of CTAC report and had not been previously diagnosed. Only 4 (0.2%) of these were potentially detrimental to patient outcome.

Conclusion: One centre had a PPV of 0% and the study suggests that these CTAC images should not be reported. Two centres with more modern equipment had low PPVs of 0% and 6%, respectively, and further research is suggested prior to drawing

a conclusion. The centre with best quality CT had a PPV of 67% and the study suggests that CTAC images from this equipment should be reported.

Advances in knowledge: This study is unique compared with previous studies which have reported only the potential to identify incidental findings on low-resolution CT images. This study both identifies and evaluates new clinically significant incidental findings and it demonstrates that the benefit of reporting the CTAC images depends on the type of equipment used.

Introduction

Myocardial perfusion imaging (MPI) performed using single-photon emission computed tomography (SPECT) is often subject to artifact due to the scatter and absorption of photons prior to detection. These artifacts can mimic myocardial perfusion defects leading to false-positive findings. It has been demonstrated that CT attenuation correction (CTAC) can compensate for these errors in SPECT MPI, resulting in image quality improvement and more accurate diagnosis. [1,2] The low-resolution/low-dose CT scan is performed through the area of the chest which is aligned with the SPECT scan of the heart, so only a limited CT scan of the thorax is acquired. CT images are essentially a by-product of the attenuation correction (AC) process, the CT acquisition being primarily for AC purposes.

Acquisition using a low tube current (mA) and large slice thickness results in images that have low signal-to-noise ratio, poor spatial resolution and an increased potential for partial volume artifacts compared to those of diagnostic CT studies. Motion

artifacts may also be evident, as patients are not required to hold their breath during the CT acquisition. The resulting images are adequate for the purpose for which they have been acquired, but are often not considered to be of diagnostic quality. The latest guidelines from the British Nuclear Cardiology Society suggest that if the CTAC images are of diagnostic quality then it is good practice to review them according to a local policy [3], but the guidelines do not specify what constitutes 'diagnostic quality'. However, the CTAC images often reveal incidental findings. [4,5] This would suggest that whilst the images are of lower quality than a diagnostic CT scan they could potentially have some diagnostic value.

In the UK, the Ionising Radiation (Medical Exposure) Regulations 2000 (IR(ME)R 2000) [6] stipulate that each medical radiation exposure should be evaluated and a record kept of any findings. Although this implies that CTAC images should be reported this is ambiguous because of the non-diagnostic nature of the images and lack of professional body guidance. [3,7]

The objectives of this study were:

1. To review the new incidental findings that were detected on low-resolution CTAC images acquired during SPECT-CT MPI that were thought to be clinically significant at the time of reporting.
2. To determine whether the CTAC images had diagnostic value and warranted reporting.

In this study we considered ‘clinically significant’ to mean that there was a high suspicion that the pathology, if any, underlying the incidental radiologic finding could impact negatively on patient well-being and that further investigation was required.

Method

A multi-centre study of four UK nuclear medicine departments was carried out. Low-resolution CTAC images from all SPECT MPI studies acquired between 1 July 2010 and 30 June 2011 were included in the study and evaluated in order to determine the number of incidental findings. All patients referred for MPI with CTAC whose examination resulted in a written report by a consultant radiologist were included. . Their demographics are indicated in Table 1. The mean ages of patients were similar and typical of patients undergoing CTAC for MPI.

To reduce inter-interpreter reporting bias, studies were reported by a consultant radiologist. A proforma informed by the Royal College of Radiologists guidance [8] was used to determine the content and structure of the written consultant report. Each report stated that the images formed part of a low-resolution/low quality CT that was produced as part of a nuclear medicine myocardial perfusion study. This ensured that it was clear to any clinician reading the report that the CT scan had not been performed for diagnostic purposes. Both non-significant and potentially significant abnormalities were noted in the report and if there was no abnormality detected, this was also noted. Identification of previously unknown significant findings was communicated [9] and managed in accordance with the policy of each individual hospital.

The four consultant radiologists held regular case discussion meetings where they were able to share interesting cases and discuss discrepancies. This, in addition to the use of the standard proforma, helped to ensure reporting concurrence and so provide a method of quality assurance. [8]

As incidental findings were possible in any of the tissues within the thorax, the images were reviewed on a variety of CT window settings in order to adequately visualise lung, bone and soft tissue.

After taking advice from the Health Research Authority (HRE), approval for this study was sought locally from each participating hospital and was granted as medical audit from one centre and as service evaluation from the other three centres. Ethical approval was obtained from the University of Salford.

Technical Scanning Parameters

The SPECT-CT equipment installed in the four centres utilised CT scanners with varying capabilities. Scan parameters for each CT system are shown in Table 2. Centre 1 used a GE Infinia Hawkeye 1-slice incremental CT scanner. The parameters available with this scanner were the most limited. The CT images from centres 2 and 3 were acquired using a GE Infinia Hawkeye 4 system which had a 4-slice multi-detector CT (MDCT) scanner. The scan parameters available were still limited and the available tube currents were 1, 1.5, 2.0 and 2.5 mA. Centre 4 utilised a Philips Precedence 16-slice MDCT with the availability for diagnostic parameters to be selected.

The GE Infinia Hawkeye 1 used a low tube current of 2.5 mA in axial mode (effective pitch of 1), with a tube rotation time of 30 seconds. Half-scan mode was utilized, meaning that the x-ray tube was only “on” for 18 seconds per slice, corresponding to an effective 45 mAs. The GE Infinia Hawkeye 4 scanner used 1.5 mA in helical mode with a pitch of 1.9, which equates to an effective 24 mAs. The Philips Precedence 16-slice scanner used approximately 33 mA with a rotation time of 1.5 seconds and a pitch of 0.98 to produce 50 mAs. The acquired slice thickness and pitch used with the Philips Precedence was similar to diagnostic MDCT although the reconstructed slice thickness was close to the reconstructed slice thickness of the Infinia Hawkeye 4. The Infinia Hawkeye 4 used a larger acquired slice thickness and pitch and the Infinia Hawkeye 1 had the largest acquired slice thickness of 10mm.

Acquisition using a large slice thickness and the use of a large pitch both contribute to reduced spatial resolution and the potential for increased partial volume averaging. Also, the Hawkeye acquisitions were performed with the patient free-breathing whereas the Philips Precedence images were acquired with a breath-hold. It was therefore expected that the CTAC images produced by the Infinia Hawkeye systems would have reduced quality relative to the CTAC images produced by the Philips Precedence CT. This would be consistent with findings from a lesion detection study performed by Thompson et al, 2014 using an anthropomorphic phantom to acquire images on different SPECT-CT systems. [10] The SPECT-CT systems were operated with site-specific acquisition parameters and observer performance of lesion detection was found to correlate with variation in CTAC protocols.

Image Evaluation

From the four centres a total of 1819 patients were reported and included in this study. If patients had both stress and rest studies performed these were considered as one examination for the purpose of this study. The radiologists' written reports were reviewed retrospectively. Reports which identified only previously known pathology were not included in the final evaluation because, if necessary, this pathology would be followed up with diagnostic CT as part of the patient's routine management. Review of the CTAC images would not influence management for these patients. In addition, CTAC images are not suited to longitudinal assessment of pathology and so could not substitute for diagnostic CT as a follow-up tool. Therefore, only findings of previously unknown conditions were considered; we have called these new positive findings.

Patients who had positive findings were noted and their case history records were then reviewed. New positive findings were classified according to the clinical significance at the time of report. The classification system was adapted from the one used by Goetze et al (2006) [11] and is shown in table 3.

Only findings that were classified as major were considered to be clinically significant and warranted follow-up. Potentially, these findings could affect the clinical management of the patient. For the purposes of this analysis only major findings of pathology that were not previously known have been considered as significant new incidental findings. All other findings were considered to be insignificant.

The primary outcome was to determine the positive predictive value (PPV) of the CTAC images for patients who had clinically significant new positive findings. These patients all received follow-up procedures (e.g. diagnostic CT, plain radiographs or interventional procedures) over a period of up to two years. This enabled assessment of the final diagnostic outcome in these patients, which in turn informed the value of interpreting the CTAC images. It was not possible, either practically or ethically, to follow-up patients who had no positive findings on the CTAC images and so this study could not determine the number of true- and false-negative results.

In order to indicate the performance of detecting pathology on the CTAC images that would be detrimental to the patient if undetected, the PPV has been calculated at the time the definitive diagnosis was made, rather than at the time of the CTAC report. Therefore, PPV was calculated as the percentage of new significant findings which ultimately affected patient outcome.

Results

Table 4 summarises the results. Out of 1819 patients studied 497 (27%) had a positive finding of any type, of which 423 (23%) were new findings. Fifty-one (2.8%) patients had findings that were considered clinically significant at the time of CTAC report and which had not been previously diagnosed. However, only 4 (0.2%) of these findings had the potential to be detrimental to patient outcome.

Although there was a much higher number of findings that were considered to be significant new incidental findings at the time of the CTAC scan, many of these pathologies resolved, remained stable (no change in size or appearance which might otherwise suggest malignancy) or proved to be insignificant when the patient was followed-up.

Location and Characterisation of New Significant Incidental Findings

Only 51 out of 497 (10%) of positive findings were both new and clinically significant. The location of these findings fell into three categories; pulmonary (8%), cardiovascular (1.8%) and para-spinal (0.4%) (see table 5). The most common lesions detected on CTAC were pulmonary in nature and included pulmonary nodules (2.2%), effusion (2.0%), consolidation (1.6%), pulmonary mass (0.6%), lung metastases (0.4%), ground glass opacities (GGO) (0.2%), atelectasis (0.2%), pneumonia (0.2%) and lobar collapse (0.2%). Findings within the cardiovascular system were predominantly coronary artery calcifications (1.6%) but there was also one aortic aneurysm detected (0.2%). The two para-spinal lesions were masses located adjacent to thoracic vertebrae (0.4%).

Discussion

Out of 1819 patients undergoing SPECT-CT MPI studies, 423 patients (23%) had some abnormality found on the CT image that was not previously known. Of these, 51 (2.8%) were serious enough to require further investigation. However, after follow-up the significance of the diagnosis for 47 of these patients was downgraded, leaving only 4 (0.2%) with confirmed clinically significant pathology. Three patients (0.16%) had life-threatening pathologies that were treated as a result of their

detection on CTAC images. One patient (0.05%) was diagnosed with a condition that had advanced beyond curative treatment.

Centre 1 used an Infinia Hawkeye 1-slice CT system. Out of 322 patients they found 12 who were considered to have new significant incidental findings at the time of the report. However, on follow-up none of these findings were considered to be significant. Six patients had consolidation that resolved over time and one had a pleural effusion which also resolved. Three patients were reported to have pulmonary nodules, but on follow-up two cases were found to be due to fibrotic changes or atelectasis and in the third case the lesion was benign rheumatoid in nature (Fig. 1). This was confirmed on diagnostic MDCT (Fig. 2) along with a further lesion in the left upper lobe (Fig. 3) which was not within the area of the CTAC acquisition. The lesions were surgically resected before a diagnosis of a benign condition was made. There was also a para-spinal mass which was considered insignificant when followed up and an aortic aneurysm that did not warrant follow-up.

Centre 2 used an Infinia Hawkeye 4-slice CT system. Out of 1011 patients they found 31 who were considered to have new significant incidental findings at the time of report. However, only 2 had clinically significant pathology. One patient was reported to have a pulmonary mass on the initial CTAC images (Fig.4). This was confirmed with diagnostic MDCT (Fig.5) and MR, which demonstrated invasion of the right atrium with involvement of the atrial septum. The mass was resected and confirmed as a 5-cm carcinoid lesion.

The second case at centre 2 with clinically significant pathology was confirmed as lung metastases from pancreatic cancer. There was a further case of suspected pulmonary metastases which was later found to be Wegner's granulomatosis. Three lung nodules at the time of report were considered to be insignificant at follow-up. As with centre 1, pulmonary effusions and consolidations considered to be significant at the time of the report had often resolved on follow-up imaging. One case of lobar collapse was thought to be long-standing. There were 8 cardiovascular cases which were considered significant in the CTAC report but this was not thought to be the case subsequently.

Centre 3 used an Infinia Hawkeye 4-slice CT system. Out of 275 patients they found 5 who had new significant incidental findings at the time of report, but none of these had clinically significant pathology. One patient was reported to have a pleural effusion but when followed up this was due to left ventricular failure. Another patient was reported to have ground glass opacities but appearance 12 weeks later on the follow-up diagnostic MDCT thorax was normal. A further patient was found to have atelectasis. Two pulmonary nodules were identified; one was reclassified as emphysema with fissural thickening on follow-up imaging and the other (Fig. 6) was confirmed as a 6-mm pulmonary nodule by diagnostic MDCT (Fig. 7). This was found to be stable over a 24-month follow-up period.

Centre 4 used a Precedence 16-slice CT system. Out of 211 patients they found 3 who had previously undiagnosed single pulmonary lung nodules (SPN) identified at the time of report. All 3 SPNs were confirmed with follow-up CT. One nodule

remained stable but the other two were confirmed carcinomas with staging of T3 (two lesions within lobe) (Fig. 8) and the other T2a N0 M0 (Fig. 9).

Implications of the findings

The distinctive feature of this study is that it not only demonstrates the possibility of detecting incidental findings on CTAC, as already reported in current literature, but also goes on to evaluate the significance and value of those findings in relation to the quality of the images on which they have been detected.

There is a common conception that detection of incidental findings will ultimately benefit the patient.[12] Detection of pre-clinical disease on CTAC images could potentially lead to early and more effective treatment of the disease with a consequent improvement in patient outcome. This would be consistent with the aim of a screening programme. However, the overall detection rate (4 cancers detected out of 1819 patients) and the low PPV (8%) across all centres means that its value as an investigative procedure appears to be limited.

Incidental findings that are considered to be significant or indeterminate at the time of reporting will warrant further diagnostic follow-up, which often carries with it a further risk to the patient.[13] Diagnostic imaging usually has an associated radiation burden. Similarly, intervention from biopsy or surgery will also involve associated risk to the patient.

Consideration of clinically relevant findings is important when patient outcome can be improved. [14] However, thought needs to be given to the proportion of false-positives detected on the low-resolution CT images and over-diagnosis (where a cancer is detected that would not otherwise have become apparent in that patient's lifetime). These will undoubtedly result in patients having follow-up diagnostic tests which affect the balance of harms versus benefit to the patient. [12,15,16] Benefit exceeding harm is an important aspect of any diagnostic procedure. [12,15]

The case illustrated in Figs 1, 2 & 3 shows a good example of this. Here, a pulmonary nodule was detected on CTAC and confirmed with diagnostic MDCT with identification of a further lesion. Both lesions were surgically removed and subsequently found to be benign. Ultimately, the resection of these asymptomatic lesions was found to be unnecessary, so there was no actual benefit to the patient.

A large proportion of incidental findings are pulmonary in nature[14] with pulmonary nodules being a frequent finding.[13,17] There is considerable controversy surrounding whether CT screening for lung cancer is effective.[13,18,19] A suitable screening test with a high enough sensitivity and specificity to reduce mortality from the detection of lung cancer has not yet been established and currently a lung cancer screening programme does not exist in the UK.[13,14,18] Given that diagnostic quality images do not reduce mortality in this situation, it has to be questioned whether low-resolution CTAC images are likely to have any net patient benefit.

As well as an increase in morbidity and mortality from follow-up and intervention, there is also the increase in healthcare costs to consider and an inevitable increase

in patient anxiety.[13,17,20] There is an obvious psychological effect of diagnosing a healthy patient with disease, the effects of which can be long-term even after normal follow-up results. [21] Radiological imaging cannot always offer definitive reassurance. [20,22] Patient tolerance of further imaging could be affected as a result, which could result in non-compliance with necessary imaging procedures. [14]

The CTAC images produced during SPECT-CT MPI are low-resolution and taken through a limited area of the thorax. As such, not only will some cancers not be detected on the images but inevitably pathology outside the scan range will remain undetected. Whilst pathology might be detected on the images, absence of pathology on the images does not mean that the patient is disease free.

The varied CT performance among the centres in this study is an important consideration. Centre 4 (utilising the Philips Precedence 16-slice) performed considerably better than centres 2 and 3 (utilising the GE Infinia Hawkeye 4) and centre 1 (utilising GE Infinia Hawkeye 1). This is consistent with the findings of the lesion detection phantom study performed by Thompson et al, 2014. [10] In our study the PPV at centre 4 was 67% compared with 6% for centre 2 and 0% from centres 1 and 3. The PPV for centre 4 was significantly better than for the other three centres combined ($p=0.01$ using Fisher's exact test). In previous studies PPV for detection of pulmonary nodules with contrast enhanced diagnostic CT was found to be 80%. [23]

To give this some perspective, from 211 patients imaged with CTAC at centre 4, 3 (1.4%) had significant new findings of which 2 (0.95%) lives were likely to be saved from lung cancer. This is higher than the detection rate of the breast screening

programme (0.8%). Both patients were referred for surgical resection and have survived so far. Of the 1011 patients imaged with CTAC at centre 2, 31 (3%) had new significant findings of which 1 (0.1%) had their life saved. The 5 (1.8%) patients from centre 3 and 12 (3.7%) patients from centre 1 with new significant findings resulted in no improvement in patient outcome in relation to survival rate.

With the equipment used at centre 4, image quality of the CTAC images would be expected to be closer to diagnostic quality than CTAC images acquired at the other three centres. In particular, the short rotation time and overall scan time would greatly reduce the chance of motion artifact on the resultant images from patient respiration. This would be inevitable on the images acquired with the much longer rotation times of the Infinia Hawkeye scanners, which are not designed for diagnostic quality imaging. CTAC images from centre 4 had also been acquired with a smaller slice thickness and a low pitch factor leading to improved spatial resolution and reduced partial volume effect compared with CTAC images acquired at the other centres.

It is likely that improved image quality will lead to improved confidence in reporting. For example, the radiologist from centre 1 who was used to viewing the CTAC images from the Infinia Hawkeye 1-slice system commented on the difficulty of expressing radiopacity in Hounsfield units because a larger slice thickness lead to greater partial volume averaging (Fig 10).

Conclusion

The primary question addressed by this multi-centre study was to determine whether low-resolution CTAC images have diagnostic value and would warrant reporting.

Poor quality CT images were produced by the centre which used the older GE Hawkeye 1 single slice system. This centre had a PPV of 0% and this study suggests these images do not warrant reporting. Good quality CT images were produced by the centre using the Philips Precedence system. This centre had a PPV of 67% and this study suggests that there is merit in reporting these images.

The two centres using the GE Hawkeye 4 system produced medium quality CT images. These centres had PPVs of 0% and 6%, respectively. The PPVs are extremely low because most of the correctly identified new findings which were thought to be significant at the time of reporting turned out to be clinically insignificant after further investigation. Further research is clearly needed to establish the actual diagnostic value of CT used for attenuation correction in MPI, especially in the case of medium-resolution CT sub-systems in SPECT-CT scanners.

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Tables

Table 1 – Patient demographics

Centre	1	2	3	4	All
Male:Female	1:0.8	1:0.9	1:0.9	1:0.5	1:0.8
Mean Age (years)	62.6	69.6	64.9	66.5	65.9
Age Range (years)	36-85	40-91	25-89	42-83	25-91

Table 2 - Scan Parameters of the SPECT-CT Systems

Centre	1	2 and 3	4
Scanner	GE Infinia Hawkeye 1 1-slice	GE Infinia Hawkeye 4 4-slice	Philips Precedence 16-slice
kV	120	120	120
mA	2.5	1.5	~33
Rotation Time (s)	18	30	1.5
Effective mAs	45	24	50
Acquired slice thickness (mm)	10	5	1.5
Reconstructed slice (mm)	10	6.1	5
Pitch	1.0	1.9	0.98
Contrast to noise ratio	2.4	2.2	0.74
Low contrast resolution	3-mm	4-mm	4-mm
High contrast resolution	≥ 4 lp/cm	≥ 3 lp/cm	≥ 24 lp/cm

Table 3 - Classification of Findings

Classification	Description
Major (clinically significant)	Requires further investigation in view of clinical information and history. This includes findings such as pleural effusions or lung nodules
Minor	Less significant than major findings; however they do have clinical significance. For example, cardiomegaly, liver lesions or hiatus hernia
Minimal	Less significant than minor findings, minimal or no clinical significance given patient history. These include degenerative changes.
Equivocal	Findings unclear. These include abnormalities in the liver that cannot be characterized.

Table 4 – Number of Incidental CTAC Findings

Centre	1	2	3	4	Total
Total number of patients in study	322	1011	275	211	1819
Number with positive finding	212	190	71	24	497
Number with new positive findings	202	158	43	20	423
Clinically significant findings	12	31	5	3	51
Minor findings	62	66	31	2	161
Minimal findings	126	48	7	14	195
Equivocal findings	2	13	0	1	16
Confirmed clinically significant	0	2	0	2	4
Positive Predictive Value	0%	6%	0%	67%	8%

Table 5 - Characterisation of significant new CTAC findings. Numbers in parentheses represent the number of patients whose outcome was affected by the significant new finding.

	Centre	1	2	3	4	Total
Pulmonary	Nodules	3	3	2	3 (2)	11
	Mass		3 (1)			3
	Lung Metastases		2 (1)			2
	GGO			1		1
	Atelectasis			1		1
	Effusion	1	8	1		10
	Consolidation	6	2			8
	Ill-defined		2			2
	Pneumonia		1			1
	Lobar Collapse		1			1
	Total	10 (0)	22 (2)	5 (0)	3 (2)	40 (4)
Cardiovascular	Aortic Aneurysm	1				1
	CAC		8			8
	Total	1 (0)	8 (0)			9 (0)

Para-spinal	Mass	1	1		2
	Total	1 (0)	1 (0)		2 (0)

GGO = Ground glass opacities

CAC = Coronary artery calcification

Figure captions

Fig. 1 Patient from centre 1. CTAC image acquired using GE Infinia Hawkeye 1-slice SPECT-CT system which reveals a single pulmonary nodule in the left lower lobe. This was confirmed by diagnostic CT (Fig 2)

Fig. 2 Same patient as in Fig. 1 Diagnostic MDCT confirming diagnosis of pulmonary lesion detected on the CTAC acquisition

Fig. 3 Same patient as in Figs. 1 and 2 Diagnostic MDCT demonstrating a further lesion in the left upper lobe

Fig. 4 Patient from centre 2. CTAC image (lung windows) from cardiac SPECT-CT study using GE Infinia Hawkeye 4-slice demonstrating mass in right lower lobe abutting heart.

Fig. 5 Same patient as in Fig. 4 Contrast enhanced diagnostic MDCT image demonstrating lung mass with serpiginous vessels

Fig. 6 Patient from centre 3. CTAC images using GE Infinia Hawkeye 4-slice. Red cross-hairs identifying an approximately 6 mm nodule.

Fig. 7 Same patient as Fig 6. Diagnostic MDCT confirming presence of nodule (N3). This was considered stable on subsequent CT images over a period of 24 months.

Fig. 8 Patient from centre 4. CTAC image from Philips Precedence 16-slice MDCT demonstrating a right lower lobe nodule in a 77 year old male patient which was confirmed as T3 carcinoma at resection

Fig. 9 Another patient from centre 4. CTAC image from Philips Precedence 16-slice MDCT demonstrating single pulmonary nodule in a 77 year old male patient which was confirmed as T2a N0 M0

Fig. 10 illustrating a suspected pulmonary nodule on GE Infinia Hawkeye 1-slice CTAC image which was confirmed as pulmonary fibrosis on diagnostic MDCT.