

World Journal of *Radiology*

World J Radiol 2019 January 28; 11(1): 1-18



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World Journal of Radiology is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Ying-Na Bian* Proofing Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL

World Journal of Radiology

ISSN

ISSN 1949-8470 (online)

LAUNCH DATE

January 31, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Venkatesh Mani

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1949-8470/editorialboard.htm>

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

January 28, 2019

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<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

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Retrospective Study

Extravascular findings during upper limb computed tomographic angiography focusing on undiagnosed malignancy

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Author contributions: Nourzaie R performed the data collection and data analysis; Nourzaie R and Das J wrote the paper; Das J, Diamantopoulos A, Moser S and Abbas H revised and corrected the paper; Diamantopoulos A and Abbas H revised the data analysis; Thulasidasan N, Gkoutzios P, Ilyas S and Sabharwal T critically revised the manuscript for important intellectual content; Moser S and Diamantopoulos A designed the research and revised the final paper.

Institutional review board statement: Exempted due to retrospective nature of study.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: No conflict of interest.

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Abstract

BACKGROUND

Computer tomography angiography (CTA) has been an established method for diagnostic vascular disease of lower limbs. Recently, the method is widely used for diagnosis of vascular pathologies in the upper limbs too. It also has increased the possibilities of this scans being reviewed by no specially trained radiologists. This increases the risk of incidental non vascular findings to be missed or misinterpreted. The study is focusing in the frequency of extravascular incidental finding (EVIF) and highlights the importance for both the reporting radiologist and the referring physician recognizing the frequency of EVIFs.

AIM

To analyse the frequency of EVIF identified on computed angiography (CT) of the upper limb.

METHODS

A total of 1383 CT angiographic studies of the peripheral arterial system were performed between August 2015 and August 2017. All upper limb CTAs ($n = 79$) were retrospectively reviewed for the presence of non-vascular incidental findings within the chest, abdomen/pelvis, musculoskeletal system or head and neck. These EVIFs were subsequently grouped into 3 categories based on clinical significance. EVIFs of immediate clinical relevance were included in category A, findings considered indeterminate but most likely benign were placed in category B, while incidental findings of no clinical significance were included in category C.

RESULTS

Complete imaging datasets were available in 74/79 (93.7%). Patient

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Manuscript source: Invited manuscript

Received: October 24, 2018

Peer-review started: October 24, 2018

First decision: December 10, 2018

Revised: January 1, 2019

Accepted: January 10, 2019

Article in press: January 10, 2019

Published online: January 28, 2019

demographics included 39 (52.7%) females and 35 (47.2%) males with a mean age of 59 ± 19.5 years (range 19-93 years). A total of 153 EVIFs were reported in 52 patients (70.3%). Of these, 44 EVIFs (28.7%) were found in the chest, 83 (54.2%) in the abdomen, 14 (9.2%) in the musculoskeletal system and 9 (5.8%) in the head and neck. Thirteen EVIFs (8.4%) identified in 11 patients were noted to be of immediate clinical significance (Category A), 50 EVIFs (32.3%) were identified in 20 patients and were considered indeterminate but most likely benign, while the remaining 91 EVIFs (59.5%) identified in 21 patients were determined to be of no clinical significance (Category C). One index case of malignancy (1.3%) and four cases of new disseminated metastatic disease (5.4%) were identified.

CONCLUSION

Our study of upper limb CTA examinations demonstrated a frequency of 8.4% for extravascular incidental findings of immediate clinical significance. We highlight the importance for both the reporting radiologist and the referring physician of the need to recognize the frequency with which EVIFs are identified in the upper limb peripheral arterial system and of the necessity for further clinical and imaging work-up.

Key words: Extravascular incidental findings; Computed angiography; Upper limbs; Arterial; Extravascular findings

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Core tip: We retrospectively analysed 79 upper limb computer tomography angiographies for extravascular incidental findings (EVIFs). These were grouped into 3 categories based on clinical significance, category A (immediate), category B (indeterminate) and category C (no clinical significance). A total of 153 EVIFs were reported in 52 patients. Of these 13 EVIFs (8.4%) were Category A, 50 EVIFs (32.3%) were Category B, while 91 EVIFs (59.5%) were Category C. One index case of malignancy (1.3%) and four cases of new disseminated metastatic disease (5.4%) were identified. This highlights the importance for both the reporting radiologist and the referring physician to recognize the frequency of EVIFs.

Citation: Nourzaie R, Das J, Abbas H, Thulasidasan N, Gkoutzios P, Ilyas S, Monzon L, Sabharwal T, Moser S, Diamantopoulos A. Extravascular findings during upper limb computed tomographic angiography focusing on undiagnosed malignancy. *World J Radiol* 2019; 11(1): 10-18

URL: <https://www.wjgnet.com/1949-8470/full/v11/i1/10.htm>

DOI: <https://dx.doi.org/10.4329/wjr.v11.i1.10>

INTRODUCTION

Invasive and cross-sectional arterial phase imaging of the upper extremities are performed less frequently in comparison with lower limb or "run-off" computer tomography angiography (CTA)^[1]. Indications for CTA of the upper limb include trauma, suspected upper limb ischaemia, preoperative planning prior to reconstructive surgery or haemodialysis access, or as follow-up post open surgical or endovascular arterial procedure^[2].

Digital subtraction angiography (DSA) has conventionally been used as the preferred imaging modality for the upper limb arterial vasculature. However, recent developments and improvements in image acquisition and spatial resolution with multi-detector computed tomography (MDCT), combined with its inherently less-invasive nature, has resulted in CTA becoming the first-line investigation for upper limb arterial pathology^[2-4].

For investigation of arterial steno-occlusive disease, CTA has been demonstrated similar diagnostic capabilities compared to DSA, as well as reduced cost, better patient tolerance and the ability to image the extravascular anatomy^[2].

The discovery of extravascular incidental findings (EVIFs) can be considered an added advantage of cross-sectional arterial phase imaging. Incidental findings

discovered on CT are defined as an unforeseen pathology encountered in a patient being scanned for another indication. In the case of CT angiography, EVIFs are becoming ever more frequently encountered in daily clinical practice, especially with the exponential proliferation of CT imaging and the gradual phasing out of DSA as a first-line modality for peripheral arterial disease and acute emergent arterial imaging.

CTA offers the possibility of identifying potentially life-threatening or life-shortening pathologies and providing improved health outcomes for patients^[6]. EVIFs and their clinical relevance have been well described in CT imaging of the aorta and lower-limb arterial system^[5-7], CTA for EVAR planning^[8], aortic dissection^[9] and CTA of the head and neck^[10]. The frequency and significance of EVIF on CTA of the upper limb, however, has yet to be described.

The purpose of this study was to report the frequency and more importantly the clinical relevance of extravascular lesions in patients undergoing upper limb CTA, including the frequency of index cases and progression of known cancer cases.

MATERIALS AND METHODS

Patient selection and demographics

Institutional review board review was obtained for this retrospective study (approval number: 7669, 21/09/2017). Radiology reports, digital medical records and 1383 CTA datasets of the peripheral arterial system performed between August 2015 and August 2017 at Guys and St Thomas hospitals were identified.

Peripheral CTAs imaging the upper limbs were included in the study. Patients with incomplete imaging datasets were excluded. Data on patient demographics, study indication and EVIF were reviewed. Those with significant EVIFs were reviewed to determine their clinical outcome

CT image acquisition and technique

Patients were placed supine with the extremity of interest placed above the head, palm ventral and fingers extended and straightened. CT imaging was performed with a 128 slice MDCT scanner (Siemens Somatom Definition), using bolus tracking software used to trigger intravenous contrast injection (Omnipaque 350, GE Healthcare) at a rate of 4-5 mL per second, followed by saline flush. Images were obtained using a kV between 100-120 with a delay of 20-40 s.

Standard of reference

Radiology reports, digital records, radiological information systems (RIS) records, laboratory and procedure reports were reviewed where available to confirm the presence of pre-existing malignancy and all prior imaging studies were used as the standard of reference (SOR).

Data analysis

One consultant interventional radiologists (15 years of clinical experience) and one radiology IR fellow (6 years of clinical experience) examined all upper limb CTAs and reviewed digital reports for EVIFs. All incidental findings were compared to the SOR and subsequently grouped into three categories, based on clinical significance, category A (Immediate clinical relevance), category B (findings considered indeterminate but most likely benign) and category C (incidental findings of no clinical significance).

Statistical analysis

Statistical analysis was done using the SPSS statistical software (SPSS, version 18.0 for Windows; SPSS Inc., Chicago, IL, United States). Discrete and continuous variables are presented as counts and percentages, and as mean \pm SD respectively. Non-normal variables were expressed as medians and interquartile ranges (25th and 75th percentiles).

RESULTS

A total of seventy nine cases (79/1343, 5.8%) of peripheral CTAs imaged the upper limbs and were subsequently analyzed. From these studies, four patients were excluded as a result of incomplete imaging datasets. Of the 74 patients (52.7% females, 47.3% males) with complete upper limb CTA imaging, the mean age was 59 \pm 19.5 years (range 19-93 years).

One hundred fifty-three EVIFs were identified in 52 patients (70.3%). 44 EVIFs

(28.7%) were noted in the chest, 83 (54.2%) were found in the abdomen, 14 (9.2%) in the musculoskeletal system and 9 (5.8%) in the head and neck.

Thirteen (8.4%) EVIFs were identified in 11 patients and were considered of immediate clinical significance (category A), demonstrated in Table 1. The majority of category A findings were noted in the chest ($n = 8$), with additional highly significant findings (all cases were of ascites) noted in the abdomen/pelvis ($n = 3$) with sclerotic bone lesions ($n = 1$) and osteomyelitis ($n = 1$) identified on examination of the musculoskeletal system.

Six category A EVIFs were concerning for a new malignancy diagnosis ($n = 1$) or disease progression ($n = 4$) or recurrence ($n = 1$). Details regarding further investigation and follow-up are outlined in Table 2. One male patient, symptomatic with acute upper limb ischaemia was found to have an irregular 16mm nodule in the right upper lobe with ipsilateral hilar lymphadenopathy on CT. Subsequent CT-guided biopsy confirmed histopathological diagnosis of lung adenocarcinoma.

Three patients demonstrated new progression of existing malignancy on upper limb CTA, one case of cholangiocarcinoma with new pulmonary and osseous metastases and two patients with prostate cancer and new pulmonary metastasis. Breast cancer recurrence, confirmed on CT-guided mediastinal lymph node biopsy in a patient with new chest lymphadenopathy, was also diagnosed on upper limb CTA.

A single patient with a history of prior breast cancer was found to have a new spiculated breast nodule identified on upper limb CTA but did not have follow-up imaging available at our institution.

Fifty EVIFs (32.3%) were identified in 20 patients and were considered indeterminate but most likely benign (category B) and are demonstrated in Table 3.

The majority of EVIFs were of no clinical significance ($n = 21$, 59.5%) and placed in category C (Table 4). The most common category C finding was simple renal cysts ($n = 12$).

DISCUSSION

CTA has become the principal investigation when assessing vascular patients and with the added capability of imaging extravascular structures, it offers the opportunity to discover incidental findings unrelated to the study indication. Such incidental findings can subsequently lead to the diagnosis of a life-threatening condition and can be of paramount importance in these groups of patients.

In 13 (8.4%) patients, the EVIF were identified as requiring immediate follow-up with further diagnostic tests. This is of particular importance in cases of new cancer diagnosis or progression of malignancy as survival rates may decrease significantly the earlier the cancer is identified and treated.

The results of our study compare similarly with prior studies looking at EVIF with regards to the frequency of detecting new (1.3%) or progression of pre-existing malignancy (5%). Naidu *et al*^[6] described 40 highly significant EVIFs of which nine (3%) were confirmed malignancies. Iezzi *et al*^[5] noted 15 index cancer cases (3.5%) in their series while Preuß *et al*^[7] identified 4 malignancies (2.8%). The most common solid malignancies identified in all studies were pulmonary neoplasms. Belgrano *et al.* identified 36 solid masses of possible malignant nature (4.5%) but did not provide follow-up or correlation with histopathology^[11]. Of note, and similarly to the studies by Naidu *et al*^[6] and Preuß *et al*^[7], we correlated the EVIFs identified in our patient cohort with the patient's clinical background, including any past history of malignancy.

Our sample size was smaller ($n = 79$) in comparison with prior reports regarding the frequency and clinical relevance of EVIFs on CTA studies, with patient cohorts ranging from 141^[7] to 821^[12], despite the fact that our retrospective study was performed over a similar time-period (24 mo) to previous articles pertaining to this topic. We can potentially account for this by recognizing that CTA of the upper limb is a relatively infrequently performed examination in comparison with arterial CT imaging of the lower limbs, the latter performed far more consistently and for a wider variety of indications.

Furthermore, the mean age of patients in our study was 59 years old, a much younger demographic in comparison to prior studies examining for EVIF on CTA exams^[5-7,12]. For example, the mean age of patients in the study by Preuß *et al*^[7] was 80 years old. The younger mean age in our report can be accounted for by the fact that our study demonstrated a much broader range of patient ages (18-90 years old), the median age was 67 years old, which was similar to the median age of previous studies.

To the best of our knowledge, this study is the first to evaluate for the presence of

Table 1 A total of 13 category A extravascular incidental findings (immediate clinical significance) were identified

Region	EVIF	Number of cases
Chest	Lung nodule > 1 cm	4
	Breast nodule	1
	Mediastinal lymphadenopathy	1
	Oesophageal wall thickening	1
	Pleural effusion	1
Abdomen/pelvis	Ascites	3

EVIF: Extravascular incidental finding.

head and neck extravascular incidental findings on CTA of the upper limb. Nine EVIF were present in the head and neck, however, no Category A EVIFs were identified.

Our work shows the importance of detecting EVIFs. The early detection of cancer can be significant for patient outcomes and can ultimately reduce health costs by offering a curative surgical option. This may therefore, justify reporting and following up on incidental findings. However, a cost-effective analysis of pursuing incidental findings in addition to long term studies comparing CTAs in vascular patients who did not have their extravascular findings reported needs to be conducted to adequately understand the true value of EVIFs. Attempts to provide guidance on the management of incidental findings have been made^[43] however data on cost-effectiveness is sparse.

Limitations

As a retrospective study, the correlation of clinical symptoms with radiological findings was not performed for all EVIFs. In our study, follow-up data was available in 5/13 (38.5%) of Category A EVIFs, all of which pertained to suspected primary malignancy or progression of disease. This was a limitation noted in past studies^[5-9] of a similar nature where there was a lack of follow up imaging. For example, in the study by Naidu *et al*^[6], 42% of patients did not have follow-up imaging. Secondly, the use of arterial phase imaging in the examination of the abdominal and pelvic viscera can limit evaluation of hypovascular lesions and pathology more reliably detected on portal venous or delayed phase studies. Thirdly, unilateral imaging was performed in all 79 patients, of either the left or right arm, or hemithorax, therefore potentially reducing the number of EVIFs identified in each patient.

We propose a new emailing alert system in which the radiologist reporting the scan flags up any significant EVIF which would send an automated email to both the referrer and the consultant the patient is under. In addition, a clinical nurse specialist has been allocated the responsibility of ensuring these are correctly followed up. This minimises the risk of losing patients to follow-up and we recommend a similar system is put into place across all hospitals.

Conclusion

In conclusion, our work signifies the importance of reporting both vascular and extravascular findings in CTAs, especially in this patient group of higher risk. Incidental findings are very common, and although most are of a benign nature, they do lead to the detection of serious life-threatening pathology which would otherwise be missed or diagnosed late. Although arterial phase CT imaging of the upper limb is a less commonly requested and performed peripheral arterial examination, both referring physicians and interpreting radiologists must recognize the frequency and relevance of incidental findings in this patient cohort allowing timely and appropriate clinical and imaging follow up.

Table 2 Details of the follow-up for the six patients with suspicious incidental findings

Incidental finding	Follow-up imaging study	Diagnosis
Multiple pulmonary nodules and sclerotic bone lesions	Plain film radiography of hip, femur, knee, CT TAP (staging)	Metastatic cholangiocarcinoma (new lung and bone lesions)
Pulmonary nodule (> 1 cm) with hilar lymph node enlargement	CT TAP (staging)	Lung adenocarcinoma (index diagnosis)
Mediastinal lymphadenopathy (prior breast cancer)	CT TAP (staging), CT-guided lymph node biopsy	Metastatic breast cancer (recurrence of primary cancer)
Breast nodule (prior breast cancer)	Breast ultrasound (recommended)	Follow up imaging unavailable
Multiple lung nodules	CT TAP (staging)	Metastatic prostate cancer (new lung lesions)
Lung nodule	CT TAP (staging)	Metastatic prostate cancer (new lung lesions)

CT: Computer tomography.

Table 3 Category B lesions (indeterminate but most likely benign) accounted for 50 extravascular incidental findings

Region	EVIF	Number of cases
Chest	Lung nodule (> 4, < 10 mm)	2
	Lung lobar atelectasis	1
	Pleural thickening	1
Abdomen/pelvis	Prominent lymph nodes (≤ 1 cm)	13
	Hiatal hernia	5
	Enlarged prostate gland	3
	Adrenal hyperplasia	2
	Renal infarct	1
	Urinary bladder wall thickening	1
	CBD dilatation	1
	Gallbladder distension	1
	Intrahepatic biliary duct dilatation	1
	Prostatic calcification	1
Musculoskeletal	Inguinal hernia	1
	Sclerotic bone lesions	5
	Pectoralis major atrophy	1
	Spinal stenosis	1
	Spondylolisthesis	1
	Spinal scoliosis	1
Head/neck	Thyroid nodule	1
	Prominent lymph nodes (≤ 1 cm)	6

EVIF: Extravascular incidental findings.

Table 4 Category C abnormalities (lesions of no clinical significance) accounted for 91 extravascular incidental findings

Region	EVIF	Number of cases
Chest	Interstitial lung disease	11
	Emphysema	8
	Pulmonary consolidation	5
	Pleural calcification	3
	Pneumatocele	3
	Bronchiectasis	1
	Pulmonary nodule < 4 mm	1
	Renal cyst	12
Abdomen/pelvis	Diverticular disease	10
	Cholecystolithiasis	6

	Atrophic kidney	5
	Focal liver fat sparing	4
	Hepatic cyst	4
	Fatty infiltration of the liver	3
	Adrenal lipoma	2
	Atrophic pancreas	1
	Calcified uterine fibroid	1
	Omental fat stranding	1
	Renal scar	1
	Splenic cyst	1
	Scrotal hydrocele	1
	Groin sinus tract	1
Musculoskeletal	Clavicle fracture (old)	1
	Pelvic fracture (old)	1
	Humeral head fracture (old)	1
	Generalised osteopenia (humeral head)	1
Head/neck	Thyroid goitre	1
	Paranasal sinus mucocele	1

EVIF: Extravascular incidental finding.

ARTICLE HIGHLIGHTS

Research background

Recent developments and improvements in image acquisition and spatial resolution with multi-detector computed tomography has resulted in computed tomographic angiography (CTA) to become the first line-line investigation for upper limb pathology, replacing the more invasive digital subtraction angiography. It has the added capability of imaging the surrounding extravascular anatomy leading to the detection of incidental mass/lesions. The significance of these “incidental” findings has mixed opinions. Whilst evidence has shown them to identify potentially life-threatening pathologies, they can also lead to an unnecessary diagnostic cascade of investigations only for the end result to be benign. We set out to report the frequency and more importantly the clinical relevance of these incidental findings to better understand their significance.

Research motivation

We set out to establish the frequency of incidental findings and to follow-up to determine their end significance in upper limb CTA. This has yet to be described in the literature. Incidental findings can lead to an unnecessary investigation cascade and therefore we wanted to determine the proportion of incidental findings which do lead to the diagnosis of a life-threatening pathology. This will raise awareness in the medical field of the importance for both the reporting radiologist and the referring physician of the need to recognise these findings and arrange appropriate follow-up. Evidence has shown cancer pathology is picked up through their detection and therefore highlights the importance of the reporting radiologist spending extra time to report structures outside of the scan indication.

Research objectives

Our objective was to report the frequency of incidental findings in CTA of the upper limb over a 2 year period. Those with findings of significance were followed up to determine their clinical outcome. We found incidental findings in over two thirds of patients, with 8.4% of them being of immediate clinical significance and detecting one index case of malignancy and four cases of new disseminated metastatic disease. Spending extra time reporting masses/lesions outside of the intended anatomy can significantly improve patient outcomes.

Research methods

Consecutive upper limb CTAs performed at Guys and St Thomas hospitals between August 2015 to August 2017 were retrospectively reviewed for inclusion. Patient demographics, incidental findings and their follow-up were entered into an excel spreadsheet and statistical analysis was done using SPSS statistical software (SPSS, version 18.0 for Windows; SPSS Inc., Chicago, IL, United States). Incidental findings were grouped into category A (immediate), category B (indeterminate) or category C (no clinical significance). Conversely to other work in the literature, we retrospectively reviewed CTA reports rather than re-reviewing CTA images for incidental findings. This was to better reflect the current clinical practice as re-evaluation of images for incidental findings would theoretically increase their detection. Prior imaging studies were used as the standard of reference. Those with suspicious findings were followed to determine their significance.

Research results

A total of 153 extravascular incidental findings (EVIFs) were reported in 52 patients. Of these 13 EVIFs (8.4%) were Category A, 50 EVIFs (32.3%) were Category B, while 91 EVIFs (59.5%) were Category C. One index case of malignancy (1.3%) and four cases of new disseminated metastatic disease (5.4%) were identified. This is the first study to describe incidental findings in CTAs of the upper limbs. Detecting incidental findings can be of paramount importance however a large proportion also end of being benign. More work is needed in the recommendation of their follow-up and on cost-effective.

Research conclusion

The purpose of this study was to report the frequency and more importantly the clinical relevance of extravascular lesions in patients undergoing upper limb CTA, including the frequency of index cases and progression of known cancer cases. We identified one index case of malignancy, and four cases of new disseminated metastatic disease. Our work shows the importance of detecting EVIFs. The early detection of cancer can be significant for patient outcomes and can ultimately reduce health costs by offering a curative surgical option. This may therefore, justify reporting and following up on incidental findings. To the best of our knowledge, this study is the first to evaluate for the presence of head and neck extravascular incidental findings on CTA of the upper limb. Nine EVIF were present in the head and neck, however, no category A EVIFs was identified. Although arterial phase CT imaging of the upper limb is a less commonly requested and performed peripheral arterial examination, both referring physicians and interpreting radiologists must recognize the frequency and relevance of incidental findings in this patient cohort allowing timely and appropriate clinical and imaging follow up. However, a cost-effective analysis of pursuing incidental findings in addition to long term studies comparing CTAs in vascular patients who did not have their extravascular findings reported needs to be conducted to adequately understand the true value of EVIFs. Attempts to provide guidance on the management of incidental findings have been made however data on cost-effectiveness is sparse.

Research perspectives

Incidental findings are very common, and although most are of a benign nature, they do lead to the detection of serious life-threatening pathology which would otherwise be missed or diagnosed late. It is important for the reporting radiologist to be aware of their frequency to lead to their detection. More work is needed on guidelines for their management to aid in appropriate follow-up and to avoid an unnecessary cascade of investigations. Future work on their cost-effectiveness is needed and clinical outcomes to quantitatively measure their importance. This can be completed in a long-term CTA study to assess if earlier detection of malignancy improves patient survival rates.

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