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Computed Tomographic Angiography as the First Diagnostic Tool in the Evaluation of Patients with Acute Limb Ischaemia: A Narrative Review

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Abstract

The rising number of patients with acute limb ischemia (ALI) brings the question if there is an opportunity to make a diagnosis safely and accurately. The current "gold standard" for diagnosis is digital subtraction angiography (DSA). However, current times show that computed tomography angiogram (CTA) builds popularity among doctors working in vascular surgery departments. The aim of this study is to collect evidence of the use of CTA for the assessment of patients with ALI and compare it to the "gold standard" (DSA). **Methodology**: This is a narrative synthesis, the search of 4 databases is done for relevant articles within a period from 2000 to 2021. Information extracted will be compared to leading guidelines for ALI published in 2 recent reviews by the American College of Radiology and the European Society for Vascular Surgery. **Results**: In total 48 articles were obtained: reviews (n = 13), studies (n = 4) and case reports (n = 31). Case reports were excluded from the study. CTA has multiple benefits, which can be put into 4 different groups: availability and accessibility, accuracy, affordability and additional information. Further disadvantages and similarities were discussed in 2 separate groups. **Conclusion**: The use of CTA in patients with ALI has a notable advantage in all 4 categories (availability, accuracy, affordability, and additional information). Disadvantages and similarities between CTA and DSA, do not vary and do not significantly affect the end decision. This makes CTA a valid tool as the first step in the assessment of the patient with ALI.

Keywords

Acute Limb Ischaemia, Computed Tomography

1. Introduction

Acute limb ischaemia (ALI) can be described as a sudden decrease in perfusion of the limb, it is a life-threatening condition and patients diagnosed with it have high morbidity and mortality rates [1] [2]. The incidence of admissions with ALI is steadily rising, data collected by RS von *Allmen et al.*, from 2000 to 2011 indicates that the annual increase of admission is on average 6.2% per 100,000 of the population in England [3].

Determination of the aetiology of ALI is challenging, due to the complex and extensive past medical history commonly seen in patients with such conditions. Aetiology can be categorised into embolic and thrombotic events, both categories can be separated into more detailed groups. Some conditions are less common to cause ALI, but those conditions are important to diagnose before management, as they require different treatment approaches. Examples, intracardiac masses (myxomas) or vegetations, dissection of pelvic and lower limb arteries, aneurysms [4] and partial or complete lumbar stenosis [5].

Patients often have a complex background which overcomplicates the diagnosis of ALI, many patients will be long-time smokers, with diabetes and peripheral vascular disease, and those conditions and circumstances can mask symptoms of ALI [6]. Due to such a variety of aetiological factors and complex background, management for ALI can vary from conservative treatment with heparin infusion to minimally invasive procedures and surgery or specific treatment for a given diagnosis [1] [2].

The "gold standard" of current times for diagnosis is DSA, it has been the first choice of imaging based on the opportunity for immediate treatment [1] [7]. However, as time pass ALI is more often diagnosed with non-invasive imaging, such as Doppler, computed tomography angiography (CTA) or magnetic resonance angiography (MRA). CTA is favourable among other non-invasive studies due to its multiple advantages [7]. Ultrasound Doppler is non-invasive and easily available; however, it not always can provide the necessary information to decide on management, this is usually the second choice for assessment of ALI [8]. Additionally, Doppler is sonographer-dependent, poor accessibility of the vessels and heavy calcifications can obscure the visualisation of the arterial system and in the less experienced hands of the sonographer can give inaccurate reports [7]. On other hand, MRA gives precise reports of vascular pathology, but it is rarely done in acute settings [7]. CTA is favourable among other non-invasive studies due to its multiple advantages [7]. The aim of this study is to collect evidence of the use of CTA for the assessment of patients with ALI and compare it to the gold standard (DSA).

2. Methods

This is a narrative synthesis and analysis of literature from multiple databases, published within the period from 2000 to 2021. In total, 4 databases were searched—PubMed/PubMed Central, Medline, Embase and Cochrane Library. Ad-

ditionally, the European Journal of Vascular Surgery and Endovascular Surgery was searched for relevant literature. PICO form was used to create a structured approach during data collection. This study includes all literature describing CTA as the first step of imaging in patients with clinical presentation of ALI. Articles describing ALI due to vascular deficit secondary to the injury or trauma and patients with bypass surgery, or any other vascular surgery are excluded from this study.

Collected data is compared with a current "gold standard" of imaging for a patient with a diagnosis of ALI, which is DSA. Necessary information for comparison is extracted from the article "ACR Appropriateness Criteria for Sudden Onset of Cold, Painful Leg", published in the journal of the American College of Radiology (ACR) and from the guidelines on the management of ALI, which were published by the European Society for Vascular Surgery in 2020. Extracted information from those articles is presented in comparison graphs and tables, described in the discussion part.

3. Results

In total 48 articles were extracted from all 4 databases, additionally, one more article was added from the European Journal of Vascular Surgery and Endovascular Surgery, making an overall total of 49 articles used in this study. Article types vary from reviews (n = 13), studies (n = 4) and case reports (n = 31). Further, case reports were excluded from the study.

Overall advantages of CTA can be summarised into 4 groups: availability, accuracy, affordability, and additional information; on the other hand, disadvantages can be segregated into 3 groups: complications, contraindications, reporting difficulties and delay in definitive management (Table 1). Information on DSA characteristics was summarised from 2 recent reviews by ACR and the European Society for Vascular Surgery (Table 2).

All reviews agreed that CTA is a useful tool in the diagnosis of ALI, review by *Ikuo Fukuda et al.*, stated that due to the increasing incidence of patients with atherosclerosis it is more difficult to diagnose ALI. Therefore, CTA is advisable as the first choice of imaging for assessing ALI. A review by S. Puppala and J. Patel, suggests that CTA is a preferable tool to assess the arterial system in the whole body. High-resolution 3D reconstruction was one of the benefits, reconstruction can be achieved at the level of 0.6 millimetres, giving accurate features of occlusion. Additionally, it is described that multiple anatomical pathologies, such as aneurysms, are better assessed by CTA. It is mentioned that CTA can provide high-quality imaging of vessel pathology. As mentioned by Balaji Natarajan *et al.*, the sensitivity of CTA is from 91% - 100% and specificity from 93% - 96% in the detection of aortic lesions. Overall, CTA was described as "non-invasive, rapid and precise".

In a study by Alexandra Jakubiak *et al.* availability and short examination time are mentioned as an advantage, it was described that on average it takes only 10

Table 1. Summary of advantages and disadvantages of CTA in patients presented with ALI.

Advantages	Disadvantages
Availability - Available out of hours - Available in most hospitals - Scan timing Accuracy - Three-dimensional resolution - High resolution - High sensitivity - Average sensitivity 98.5% Affordability - Cost-effective - Non-invasive - Can be reported remotely by radiologist in a timely manner - Can be done if MRA contraindicated Additional information - With clinical relevancy - Significant relevancy incidental finding - Preoperative planning - Definitive management	Delay in treatment Radiation exposure: - Repeated catheter angiography Complications: - Rare fatal reaction to iodinated contrast material - Contrast-induced nephropathy Contraindicated in patients with eGFR less than 30 mL/min Imaging limitations: - Poor evaluation of severely calcified vessels

Table 2. Summary of advantages and disadvantages in DSA for ALI diagnosis.

Advantages	Disadvantages
Availability Accuracy - Able to determine embolic or thrombotic aetiology Immediate treatment Carbon dioxide can be used if contrast is contraindicated.	Invasive Radiation exposure: - Repeated catheter angiography - Post-procedure recovery Needs Interventional radiologist present on site Prolongation of hospital stay: - Increase hospital costs - Increase morbidity and mortality Complications: - Rare fatal reaction to iodinated contrast material - Contrast-induced nephropathy - Bleeding from puncture site/pseudoaneurysm Contraindicated in patients with eGFR less than 45 mL/min Imaging limitations: - Poor evaluation of outflow vessels - Limited visualisation of pedal vessels and vessels beyond significant obstructive lesions

minutes for the patient to prepare, be positioned on the CT scan and undergo imaging. It is suggested by the authors that there is a possibility that CTA might be a new "gold standard" in diagnostic methods of ALI.

Talha Butt *et al.*, published a study showing the performance of CTA of calf

arteries in patients with ALI and known diabetes. He concluded that this patient group does not benefit from CTA, as it has poor-quality imaging due to severe calcification of the vessels. Few authors noted that heavily calcified vessels can decrease the quality of the imaging and can overestimate the level of vessel stenosis. Additionally, scan timing is an important aspect that can limit the correct evaluation of the occlusion. Imaging taken before the contrast reaches the end of the leg can potentially create the appearance of occlusion.

According to Andrew Nickinson and Matthew J Bown, nephrotoxicity is the main disadvantage, and it is advised not to perform CTA in a patient with a glomerular filtration rate of less than 60 mL/min. However, Martin Bjork *et al.*, confirmed that according to the European Society of Urogenital Radiology estimated glomerular filtration rate of more than 30 mL/min is acceptable for contrast administration. Radiation exposure and contrast allergy were other mentioned downfalls of CTA (see **Appendix 1** and **Appendix 2**).

4. Discussion

Diagnosis of ALI is challenging, due to the complex and extensive past medical history commonly seen in patients with ALI. The "gold standard" of current times is DSA, it has been the first choice of imaging based on the opportunity for immediate treatment. However, as time pass ALI is more often diagnosed with non-invasive imaging, such as Doppler, CTA or MRA. CTA is favourable among other non-invasive studies due to its multiple advantages.

Advantages:

Body tissues have different tolerance to ischemia length, muscle tissue ischemic tolerance can be up to 6 - 8 hours and skin up to 12 hours. Nerve tissues have only 2 to 4 hours before irreversible changes occur [9]. The risk of limb loss and limb amputation increases by 6% if surgical intervention is delayed by 12 hours, by 12% if delays do not excide 24 hours and by 20% if the delay is longer than 24 hours [10]. Therefore, timing is an important aspect of the successful management of ALI. Most articles agree that CTA is easily available in most hospitals and can be used out-of-hours. Additionally, short examination time is reported as another factor that positively affects overall availability and efficiency. In the study by Alexandra Jakubiak *et al.*, it was described that on average it takes only 10 minutes for the patient to be prepared and positioned on the CT scan and undergo imaging. It is suggested by the authors that CTA might be a new "gold standard" in diagnostic methods of ALI [10] some studies claim that completing CTA takes from 20 to 30 minutes only [11].

It is advised in case the vascular team out-of-hours is not available on-site, for the patient to be moved to the appropriate hospital before conducting CTA. Patients, in this case, should be assessed by a vascular surgeon and a decision for imaging should be made then [1] [12].

DSA availability is more complex; most hospitals have interventional radiology departments with available high-resolution C-arm or hybrid operating rooms,

which is a good advantage [13]. Hospitals that do not have such operating rooms, can facilitate an angio-suite in the radiology department [1]. Unfortunately, the interventional radiology team might not be quickly available out-of-hours, which potentially can delay further management of ALI. This is a possible reason why despite DSA being presented as a "gold standard" investigation technique, it is rarely used prior to other imaging [12].

Further, CTA scanning ability is significantly raised, currently, 64-row multidetector computed tomography is mainly used in most hospitals [10] [14]. Multiple detectors and spiral acquisition feature with scan reconstruction up to 0.6 millimetres, provides high-quality imaging with high-resolution three-dimensional reconstruction of the vessels and surrounding tissues. This provides an accurate assessment of the occlusion and its etiological factor [1] [2] [4] [6] [7] [12] [14] [15] [16] [17]. Reported sensitivity and specificity were as high as 100% and 96% respectively. The downfall of such high resolution is artefact formation due to severe vessel calcification; this potentially can give a false-positive impression of more significant stenosis than the patient has. Correct contrast bolus administration and scanning time is another important aspect that can give a false-positive impression of occlusion if it is not done in a timely matter. Imaging taken before the contrast reaches the end of the leg can potentially create the appearance of occlusion, to avoid a false-positive diagnosis imaging can be taken in a later arterial phase from the knees down to the bottom of the feet [7] [15] [16] [18]. Overall, CTA imaging can provide sufficient information to determine the best further management of ALI.

When CTA can assess the vascular system in the whole body, DSA is mainly focusing on the vessel lumen and area of occlusion and ischemia. DSA can differentiate between etiological factors with good sensitivity and specificity. Embolic occlusion features are crescent-shaped occlusion with a Meniscus sign and normal appearance of surrounding vessels. On other hand, in the case of thrombotic occlusion, multiple areas with atherosclerosis and the presence of collaterals will be seen. DSA is known to have a poor evaluation of distal vessels from the point of occlusion due to vasospasm, therefore vasodilators can be used in attempts to improve the visualisation of peripheral vessels [1] [7].

CTA has a significant advantage in detecting extravascular incidental findings that might be relevant to a diagnosis of ALI, such as underlying chronic vascular disease [16]. CTA includes abdominal and sometimes thoracic arteries that can show evidence of embolic origin. A. PreuB *et al.*, indicated that apart from relevant findings to ALI, a CTA scan can demonstrate incidental findings of malignancy, this will allow patients to undergo additional investigation under a 2-week pathway and possibly avoid progressive cancer disease. The checklist is advisable for radiologists to have during the CTA imaging report, as some findings can be overlooked [5] [19]. Extravascular findings are essential when the diagnosis of ALI is debatable, CTA in comparison to DSA can exclude possible differential diagnoses of ALI, for example, spinal nerve compression and partial or absolute

lumbar spine stenosis. Such an advantage helps to choose appropriate management according to those findings [1] [5].

The downfall of such an advantage is over-diagnosing the patients with benign findings which increases hospital costs due to further unnecessary investigations. Additionally, unexpected incidental findings, even if they are positively benign, bring to the patient additional psychological stress [5].

CTA being a non-invasive technique is cost-effective in comparison to DSA. DSA is a multifactorial invasive procedure; it requires more medical professionals and different equipment. Additionally, a patient who undergoes DSA imaging needs to stay in the recovery on average for 4 hours, and some hospitals advise staying over the night after imaging is done, which increases hospital costs [7].

Disadvantages:

As it was mentioned before, one of the main disadvantages is an impression of more prominent stenosis due to severe vessel calcification. Patients with ALI are commonly seen with diabetes and diabetes is associated with heavy calcified peripheral vessels [20]. Calcium-induced artefacts limit the vision of the stenosis-free lumen of the vessel. Dual-energy CTA can provide enhanced diagnostic features to differentiate between calcium deposits on the vessels and iodinated contrast. Studies showed that dual-energy CTA is more precise in imaging heavily calcified vessels [7] [20].

CTA does not have the necessary features to initiate immediate treatment if needed. In comparison, DSA can facilitate such management, for instance, thrombolysis or angioplasty etc. However, it is important to mention, that due to the complex background of patients with ALI, failed intervention during DSA is commonly seen [21].

By most authors, it was advised to use CTA only for patients with no immediate threat to the limb. CTA in ALI with Rutherford classification I - IIa is described as beneficial [16]. Patients with irreversible ALI changes (Rutherford classification III) need to have an emergency surgical intervention, such as an amputation [4] [6] [9] [15] [16] [22].

However, there is a "blind spot" with patients who have ALI Rutherford classification IIb, it's sims that the IIb type of ALI does not have a definitive/established management. Management is initiated on a case-by-case basis. In some articles, it was advised to proceed with revascularization straight away if a patient has ALI with Rutherford classification IIb [1] [6] [15] [22], in some cases considering the possibility of non-invasive imaging such as CTA, for more accurate preoperative assessment is advised [16] [22].

Similarities:

Radiation exposure is to be considered in both DSA and CTA. According to *Clifford R. Weiss et al.*, both imaging methods have a similar level of radiation exposure. Additionally, both imaging methods developed some ways how to minimise radiation exposure. CTA can be done with a single bolus contrast dose and imaging can be taken in less than 30 seconds, in addition, decreasing con-

trast tube voltage can significantly minimise radiation exposure [7]. Repeated imaging and the cumulative effect of radiation should be considered in DSA, as some patients might require repeated catheter angiography. In contrast, single use of CTA has a low radiation dose [1] [7].

Exposure to contrast can participate in two main complications: fatal systemic reaction or anaphylaxis which is extremely rare and contrast-induced nephropathy. As was mentioned before patients presenting with ALI are usually elderly with multiple comorbidities, commonly diabetes. Therefore, CTA should be requested cautiously in such patients due to the nephrotoxicity of iodinated contrast material, leading to acute kidney injury [6] [7] [18] [22]. Some reviews believe that this is a relative complication when a patient faces a life-threatening and potentially fatal prognosis. Therefore, by some authors eGFR of 30 mL/min counts as a safe level for the administration of contrast [1] [6].

Apart from allergy to iodinated contrast, patients with low eGFR should not have CTA imaging done, to avoid progressive deterioration of kidney function. Patients with eGFR of less than 30 mL/min were advised not to have CTA [1] [16] [17], some studies mentioned that eGFR should be more than 60 mL/min [4]. On other hand, DSA is not recommended if eGFR is less than 45 mL/min [7]. If a patient presented with clinical ALI with renal failure, possible DSA with carbon dioxide can be used as an alternative. Based on the responsible team, some patients with low eGFR still can undergo CTA following discussion with the renal team, as it is a relative contraindication in comparison with the life-threatening condition [1].

Being an invasive imaging DSA has additional complications, such as haemorrhage, pseudoaneurysm, arteriovenous fistula or injury to other vessels at the puncture site etc, this should be considered before this investigation [16] [21].

During analysis, CTA proved to be beneficial in patients admitted to the hospital with symptoms of ALI. It has good availability out of hours and is cost-effective. CTA accuracy is like DSA with a sensitivity of 98% - 99%. Additionally, in comparison to DSA, CTA can provide relevant information for presurgical planning, as it can assess the vascular system from the aorta down the legs. The extravascular finding can help detect possible causes of ALI and detect clinically significant findings, such as malignancy. DSA is not able to provide such detailed information and is not suitable for preoperative assessment.

Despite describing DSA with good availability, from personal experience and discussions with the senior leading consultants at Barking, Havering and Redbridge University Trust, DSA is not easily available out of hours. It takes a significant amount of time for the patient to be assessed by the interventional radiologist for suitability for the procedure and preparation of the intervention radiology theatre.

5. Conclusions

CTA can be effectively used in patients with ALI symptoms; it provides accurate

imaging of the vascular system and gives certainty in diagnosis and its origins. It is available 24 hours 7 days a week and has a quick scanning time. CTA provides information which helps with further management and procedural planning.

This study holds good clinical relevance, as the number of patients with ALI is raising and the presence of a clear pathway can ease the initial management of such patients. Despite the "gold standard"—DSA, CTA is commonly and more often used for ALI diagnosis. Several limitations of this study need to be acknowledged. Firstly, imaging techniques are broadly studied in patients with peripheral vascular disease and critical limb occlusion, unfortunately, there is a limited number of literature on the use of CTA for patients with ALI.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendices

Appendix 1. Characteristics of Included Reviews

References	Advised 1st choice investigation method	Advantages of CTA	Disadvantages of CTA
Ikuo Fukuda (2015) Japan	CTA or Doppler Ultrasound	Availability and scan timing Accurate	Radiation exposure Nephrotoxic
S Puppala (2009) UK	CTA is described as a "clinical tool" for the evaluation of the arterial system. Imaging should be used in Rutherford classification I - IIa; Revascularisation if Rutherford classification more than IIb	Availability out-of-hours and scan timing Accurate—0.6-millimetre slices and 3D reconstruction Can be used if MRA is contraindicated Additional information on structural anatomy	Radiation exposure Iodinated contrast allergy False-positive due to vessels calcification. False-positive due to unopacified vessels with the contrast (contrast timing)
Alex Wallace (2019) USA	Authors preference is CTA for ALI Rutherford classification I - IIa and in some cases IIb.	Non-invasive Available Accurate—0.6-millimetre slices and 3D reconstruction Extravascular findings Preoperative planning	Radiation exposure Nephrotoxic Contraindicated if eGFR less than 30 mL/min. False-positive results due to vessels calcification (over staging 8%, under-staging 15%) or unopacified vessels with the contrast
Anthony N. Hage (2018) USA	CTA for ALI Rutherford classification I - IIa and in some cases IIb.	Non-invasive Accurate—High resolution imaging Preoperative planning	-
Charles Gilliland (2017) USA	The authors "favoured" choice of imaging is CTA.	Preoperative planning	-
M. Duran (2016) Germany	Doppler for ALI Rutherford classification I - II DSA	Available and scan timing Helps to make definitive management	-
M. Duran (2017) Germany	Doppler and CTA	Available and scan timing Helps to make definitive management	-
T. Gregory (2009) USA	Doppler or DSA for ALI Rutherford classification I - IIa, in some cases IIb	-	Radiation exposure Use of ionizing contrast Fail to visualise target vessels
Andrew Nickinson (2018) UK	CTA	Non-invasive Availability Accurate—High resolution imaging	Nephrotoxicity
Dan-Mircea Olinic (2019) Romania	Doppler—1st imaging choice for Rutherford classification I - IIa DSA—"gold standard"	Non-invasive Accurate—High resolution imaging	Contraindicated if eGFR less than 60 mL/min. Nephrotoxicity
Balaji Natarajan (2020) USA	Doppler—1st imaging choice DSA—"gold standard".	Availability and scan timing Accurate—3D resolution Preoperative planning Sensitivity 91% - 100% Specificity 93% - 96%	Allergy to ionizing contrast Contraindications, such as chronic kidney disease Nephrotoxicity

Continued

Martin Bjorck (2020) UK	DSA—"gold standard"	Availability Accurate—High resolution imaging Extravascular findings Preoperative planning	Nephrotoxicity Contraindicated with eGFR less than 30 mL/min Delay in treatment
Clifford R. Weiss (2017) USA	DSA—"gold standard"	Noni-invasive Accurate—multidetector-row resolution Affordability—cost-effectiveness Can be used in patients with MRA contraindications Reduced radiation dosages for a single CTA examination	Radiation exposure Contraindication if eFDR less than 45 mL/min Nephrotoxicity Poor visualisation of heavily calcified vessels
Yaseen Oweis (2016) USA	-	Availability Accuracy Preoperative planning	Nephrotoxicity False-positive due to unopacified vessels with the contrast False-positive results die to vessels calcification Extravascular findings can be missed

ALI—acute limb ischemia, CTA—computed tomography angiography, MRA—magnetic resonance angiography, eGFR—estimated glomerular filtration rate.

Appendix 2. Characteristics of Included Studies

References	Intervention	Participants	Results	Conclusion	Advantages of CTA described in the study	Disadvantages of CTA described in the study
Alexandra Jakubiak (2009) Poland	CTA with 64-row detector CT in patients with ALI Duration: Nov 2007-Jan 2009	(n = 43)	Occlusion confirmed in 42 patients out of 43 Sensitivity 98%	CTA should be considered as basic diagnostic method for patient with ALI and is effective in.	Minimally invasive Short examination time (10 minutes) Availability Accuracy	Radiation exposure
Ferda J (2008) Germany	Value of CTA in: 1) Definitive diagnosis of ALI 2) Further management Duration: Jan 2006-Nov 2007	(n = 106)	Definitive diagnosis in 105 patients Sensitivity 99%	CTA in patients with suspected ALI is a valid diagnostic tool. CTA can provide information relevant for further management. Standard examination protocol should be applied to increase accuracy in reporting.	Availability Accuracy	Nephrotoxicity Radiation exposure False-positive due to vessels calcification. False-positive due to unopacified vessels with the contrast (contrast timing)
A. PreuB (2015) UK	Extravascular findings in run-off CTA inpatient with ALI Duration: 2005-2013	(n = 141)	In total 473 extravascular findings 38 patients with 52 category-I findings 67 patients with 163 category-II findings 36 patients with 258 category-III findings	Patients who had CTA for diagnostic purposes high chance of extravascular incidental findings with immediate clinical relevance.	Non-invasive Short examination time Accuracy Extravascular findings	Overdiagnosis (extra healthcare expenditure)

Continued

Talha Butt (2021) USA	CTA of calf arteries diagnostic performance in patients with and without diabetes Duration: 2001-2018	(n = 108)	23 patients had diabetes and 85 did not. Sensitivity for TASC D lesions in patients with diabetes was lower than in patients without	CTA did not show acceptable results in the assessment of patients with diabetes. Therefore, another method of imaging should be considered for patients who have diabetes.	Non-invasive Availability	Radiation exposure Nephrotoxicity False-positive due to vessels calcification

CTA—computed tomography angiography, ALI—acute limb ischemia.