

What you need to know about: imaging in patients with renal failure

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Abstract

Contrast-enhanced medical imaging is commonly requested in clinical practice. Contrast media provide better differentiation of tissue enhancement, improves the soft tissue contrast resolution, and enhances the ability to study the physiology and function of the organs and/or systems. However, contrast media may cause complications, especially in patients with renal failure. This article discusses the use of contrast media in common imaging modalities and the relationship between contrast media and renal function. Administration of iodinated contrast media in computed tomography may cause contrast-associated acute kidney injury; the risk factors and preventive strategies for this are elaborated in this article. Administration of gadolinium-based contrast media in magnetic resonance imaging may lead to nephrogenic systemic fibrosis. Therefore, precautions should be taken when planning for medical imaging for patients with pre-existing acute kidney injury or end-stage chronic kidney disease, for whom contrast media administration in computed tomography or magnetic resonance imaging may be relatively contraindicated. Alternatively, ultrasound contrast agents can be safely used in patients with acute kidney injury or chronic kidney disease. Clinical teams should discuss these patients with radiologists, taking into account the risk–benefits of contrast media, to determine the optimal imaging protocol or modality to answer the clinical query.

Key words: Acute kidney injury; Contrast-associated renal injury; Contrast-enhanced computed tomography; Contrast medium; Radiology; Renal failure

Submitted: 15 December 2022; accepted following double-blind peer review: 12 April 2023

Introduction

Medical imaging uses different technologies to visualise the inner workings of the human body. It allows and aids diagnosis, screening, assessments pre- and post-surgery as well as assessment of treatment response. It has evolved to become an essential tool in modern medicine.

Medical imaging may or may not involve radiation. Imaging modalities without radiation include ultrasound and magnetic resonance imaging. Radiation is used in radiography, computed tomography, fluoroscopy, catheter angiography and radioisotope imaging. Contrast media provides better differentiation of tissue enhancement, improves the soft tissue contrast resolution and enables further study of the physiology and function of the organs and/or systems.

Computed tomography

Computed tomography is one of the most commonly used imaging modalities because of its widespread availability, speed of image acquisition and its high diagnostic accuracy for many disease processes.

Multiphasic contrast-enhanced computed tomography uses iodinated contrast media to identify and characterise lesions based on their different enhancement patterns. Some common examples include the detection of hepatocellular carcinomas (Figures 1 and 2) (Matsui et al, 2011), identification of renal lesions such as renal cell carcinomas (Figure 3) and characterisation of adrenal lesions (Figure 4) (Abou Elkassem et al, 2021).

The first computed tomography contrast media was a high-osmolar contrast agent, up to 7–8 times of the blood osmolarity. The high intrinsic osmolarity may lead to renal toxicity and other adverse effects, such as intravascular hypertension, pulmonary oedema and heart

How to cite this article:

Khaw MS, Yap CW, Lee P, Ong SJ. What you need to know about: imaging in patients with renal failure. *Br J Hosp Med.* 2023. <https://doi.org/10.12968/hmed.2022.0544>

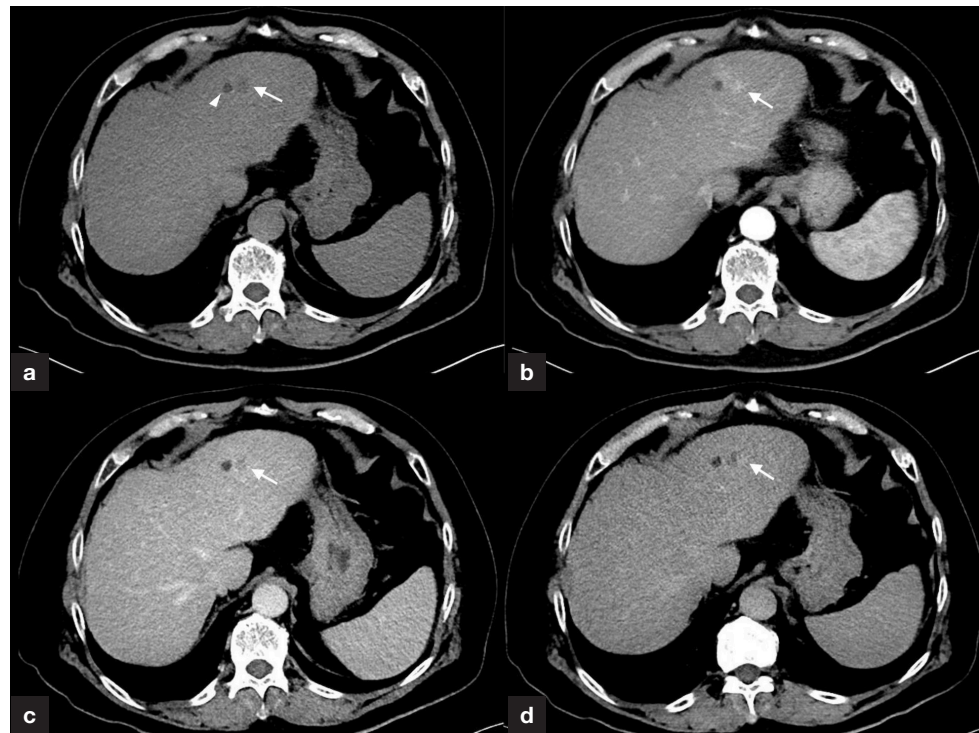


Figure 1. 64-year-old male with underlying liver cirrhosis. Axial sections multiphase computed tomography of the liver demonstrate an arterial enhancing hepatocellular carcinoma (white arrows) at segment II, which appears hypodense (a) on pre-contrast phase, (b) hyperdense and hyperenhancing compared to background liver parenchyma on late arterial phase and (c) shows contrast washed out on portal venous phase and (d) delayed phase. Left lateral segmentectomy was performed and final histology confirmed diagnosis of moderately differentiated hepatocellular carcinoma. Non-enhancing hypodense focus (arrowhead) next to the hepatocellular carcinoma, in keeping with a cyst.



Figure 2. Same patient as **Figure 1** 4 months post left lateral liver resection. Axial sections multiphase computed tomography of the liver demonstrate a new arterial enhancing lesion (white arrows) at segment V/VI which is not well seen (a) on pre-contrast phase, (b) hyperdense compared to background liver parenchyma on late arterial phase and shows (c) contrast washed out on portal venous phase and (d) delayed phase.



Figure 3. Axial sections multiphase computed tomography urography demonstrate (a) a small arterial-enhancing lesion with (b) contrast washed out in delayed phase. The lesion is not well seen on (c) pre-contrast phase, apart from mild capsular bulging (white arrows). (The lesion shows significant enhancement on (a) arterial phase relative to (c) the pre-contrast phase, although it appears hypodense to the surrounding renal parenchyma.)

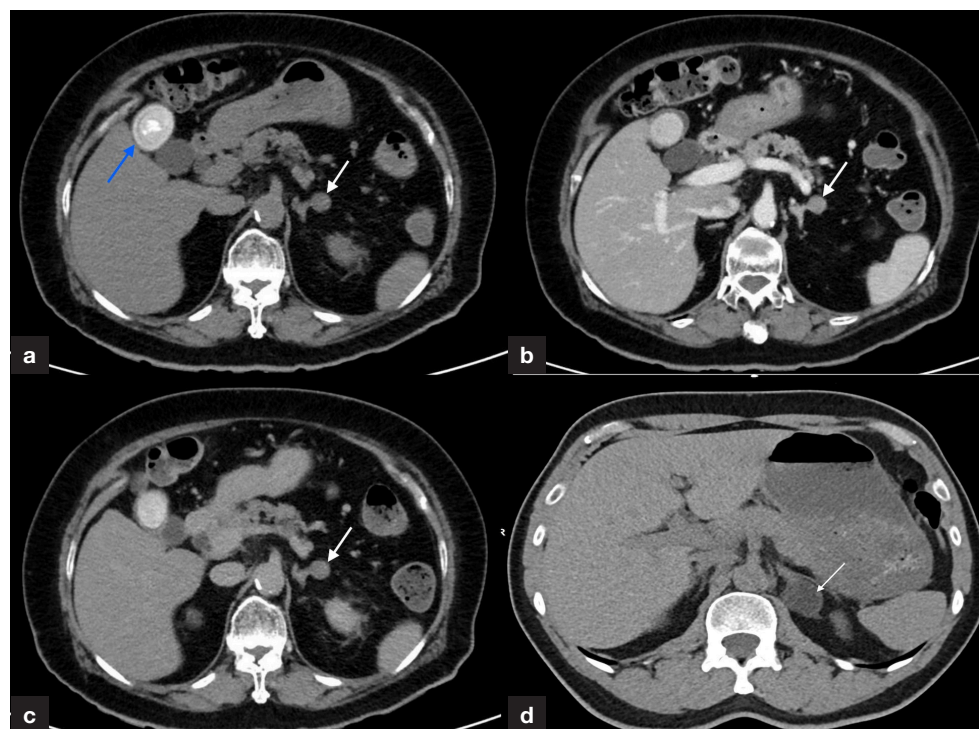


Figure 4. Axial computed tomography sections of the adrenals showing a nodule arising from the lateral limb of the left adrenal gland (white arrow). This demonstrates (a) attenuation of 33HU on pre-contrast phase, (b) 81 HU on portal venous phase and (c) 48HU on 15-minute delayed phase. The calculated absolute washout is 68.8%, in keeping with a lipid poor adenoma. d. Incidental finding of a lamellated gallbladder stone (blue arrow). A different patient with left adrenal nodule (white arrow) shows pre-contrast attenuation of 9HU, in keeping with a lipid-rich adenoma.

failure (Spampinato et al, 2017). In the late 1960s, these were replaced by second generation low osmolarity contrast media with a better safety profile, which are commonly used for contrast-enhanced computed tomography today. The newest third generation contrast media are iso-osmolar to blood, but more viscous, and are therefore frequently warmed to 37°C before intravenous administration to improve flow rate. Good injection rates are essential to optimise contrast enhancement in the correct imaging phase.

Iodinated contrast media and relationship to renal function

In 2012, the Kidney Disease Improving Global Outcomes (KDIGO) working group defined contrast-induced acute kidney injury as an increase in serum creatinine level to more than 1.5 times the baseline creatinine level within 7 days of contrast exposure, or an increase of ≥ 0.3 mg/dl (26.5 μ mol/litre) in creatinine level within 48 hours, or a decrease in urine

volume to 0.5 ml/kg/h for 6 hours after exposure to contrast media. However, multiple factors, including haemodynamic instability, low cardiac output, sepsis, anaemia and medications, can contribute to acute kidney injury. This has led to the term 'contrast-associated acute kidney injury' gaining favour. Contrast-associated acute kidney injury is also known as post-contrast acute kidney injury.

The pathophysiological mechanism of contrast-associated acute kidney injury is not fully understood. It is postulated that contrast media leads to renal toxicity via the interplay of:

1. Direct cytotoxicity to the renal endothelial and tubular cells, leading to a cycle of oxidative stress, hypoxia and further tubular damage, and
2. Viscous properties of contrast triggering vasoconstriction, reduced urinary flow rate and medullary hypoperfusion.

In view of clinical concerns about the effect of iodinated contrast media on renal function, multiple studies and meta-analyses were carried out by various speciality stakeholders from radiology to nephrology (Davenport et al, 2013; McDonald et al, 2013; Brinjikji et al, 2017; Hinson et al, 2017; Wilhelm-Leen et al, 2017; Rudnick et al, 2020). These suggest that risk of contrast-associated acute kidney injury after exposure to intravenous contrast media is minimal in adult patients with an estimated glomerular filtration rate of ≥ 60 ml/min/1.73 m² or minor renal dysfunction (estimated glomerular filtration rate 45–59 ml/min/1.73 m²).

Risk factors

Risk factors for contrast-associated acute kidney injury can be broadly divided into patient- and procedure-associated factors. Patient-associated factors include underlying chronic kidney disease, advanced age (Morcos et al, 2019), hypertension, heart failure, anaemia and periprocedural hypoperfusion. Procedure-associated factors include high osmolar iodinated contrast media, increased volume of contrast media, repeated exposure to contrast media and exposure to nephrotoxic agents, such as non-steroidal anti-inflammatory drugs and aminoglycosides (Tsai et al, 2014). Use of contrast medium at high volume (>350 ml or >4 ml/kg) or repeated administration within 72 hours after initial administration is also associated with an increased risk (Valle et al, 2017).

Preventative strategies

Intravascular volume expansion remains the mainstay of prophylaxis for contrast-associated acute kidney injury. According to the American College of Radiology (2023) guidelines, the ideal infusion rate and volume is unknown, but isotonic fluid, such as 0.9% normal saline, is preferred. The European Society of Cardiology council for cardiology practice guidelines (Mullasari and Victor, 2014) recommend intravenous isotonic saline at a rate of 1–1.5 ml/kg/h for 12 hours before and up to 24 hours after the procedure. A shorter protocol that may be more suitable for outpatient or urgent procedures involves intravenous isotonic saline 1–3 hours before and 6 hours after the procedure (Mueller et al, 2002).

Numerous studies have investigated the role of acetylcysteine in the prevention of contrast-associated acute kidney injury, with varied and inconclusive results. Despite the divergent results, acetylcysteine continues to be widely used because of its low cost, limited toxic effects, accessibility and ease of administration (ACT Investigators, 2011).

Compared to standard medical therapy, renal replacement therapy has no advantage in reducing contrast-associated acute kidney injury (Cruz et al, 2012). As such, the prophylactic application of renal replacement therapy is not currently recommended.

A consensus statement from the American College of Radiology and National Kidney Foundation (Davenport et al, 2020) suggests:

- Clinicians should consider prophylaxis for patients who have acute kidney injury or estimated glomerular filtration rate <30 ml/min/1.73 m² who are not on maintenance dialysis
- Prophylaxis is not indicated in patients who have stable estimated glomerular filtration rate (≥ 30 ml/min/1.73 m²), patients on chronic dialysis or patients at risk of heart failure

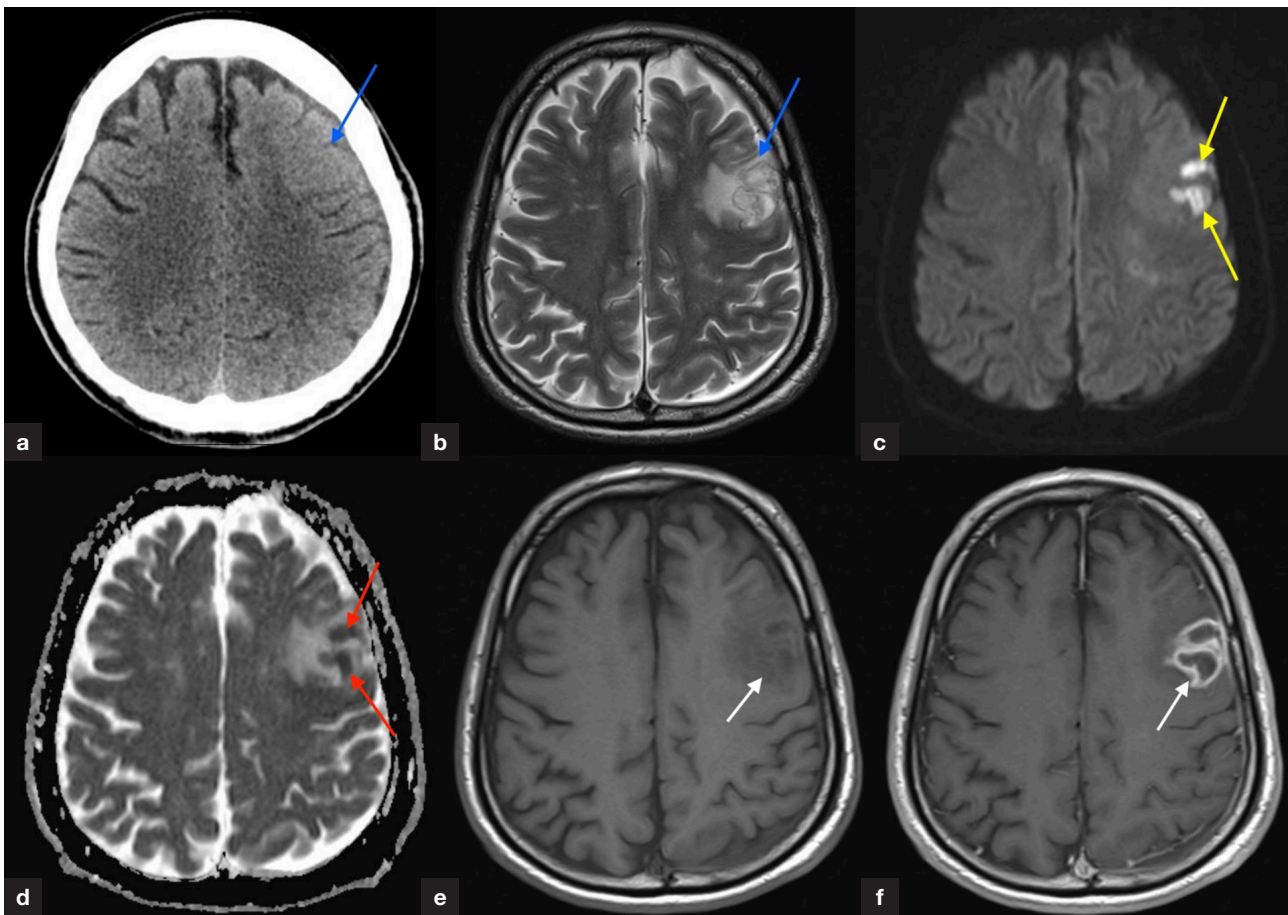


Figure 5. 56-year-old man presented with fever and acute onset of altered mental status. a. Unenhanced computed tomography (axial section through the level of basal ganglia) shows subtle cortical and subcortical thickening with effacement of the cerebral sulci at left frontal lobe (blue arrow). b. Gadolinium-based contrast enhanced magnetic resonance imaging performed on the next day confirms presence of focal increase T2 weighted hyperintense signals at the left frontal lobe. There is (c) internal high diffusion weighted imaging signal [b value=1000] with (d) corresponding low apparent diffusion coefficient signal within the centre of the lesion in keeping with diffusion restriction. e. Pre-contrast T1 weighted image. f. Post-contrast T1 weighted image shows peripheral complete rim enhancement (all images are in the axial plane). Radiological features are in keeping with a cerebral abscess.

- Prophylaxis may be considered in patients with an estimated glomerular filtration rate of 30–44 ml/min/1.73 m² in high-risk circumstances at the discretion of clinicians
- If there is insufficient time for prophylaxis, post-procedure prophylaxis may be considered
- Intravascular volume expansion is the preferred method of prophylaxis
- Timing, volume and rate of infusions can be tailored to the clinical setting and patient factors
- Oral hydration has not been well studied for patients with an estimated glomerular filtration rate <30 ml/min/1.73 m² and is not recommended
- Cessation of nephrotoxic drugs (ie non-steroidal anti-inflammatory drugs, diuretics, aminoglycosides, methotrexate) may decrease the risk of contrast-associated acute kidney injury.

Patients with chronic kidney disease CKD stage 4 or 5 (estimated glomerular filtration rate of 15–29 ml/min/1.73 m² or <15 ml/min/1.73 m²) who are not on maintenance dialysis are at risk of contrast-associated acute kidney injury, thus administration of contrast media is relatively contraindicated. The risk of developing contrast-associated acute kidney injury is proportionate to the number of episodes of contrast media exposure.

Patients on regular dialysis who are still producing urine should be treated similarly to patients with acute kidney injury or those with an estimated glomerular filtration rate <30 ml/min/1.73 m² not undergoing regular dialysis, as they may lose their residual renal function.

Gadolinium-based contrast media

Gadolinium is a heavy metal and gadolinium-based contrast media are engineered to be bound to different chelating molecules to prevent toxicity. Gadolinium-based contrast media are commonly used in magnetic resonance imaging. **Figure 5** shows an example of contrast-enhanced magnetic resonance imaging of the brain where gadolinium-based contrast media crossed the defective blood–brain barrier and resulted in abnormal intracranial enhancement (**Figure 5f**) (Rath et al, 2012).

Gadolinium-based contrast media are not considered nephrotoxic at the doses approved for magnetic resonance imaging examinations. However, they are contraindicated in patients with acute kidney injury or severe chronic kidney disease. There is a strong association between administration of gadolinium-based contrast media in patients with end-stage chronic kidney disease, particularly patients on dialysis, and the development of nephrogenic systemic fibrosis. Nephrogenic systemic fibrosis was first described in 2000. It primarily involves the skin and subcutaneous tissue, although other organs can be involved. It may lead to organ dysfunction, contracture and joint immobility. The underlying pathophysiology is not fully understood and there is no definite effective treatment (Wagner et al, 2016). The onset of nephrogenic systemic fibrosis varies from days to months after injection of gadolinium-based contrast media.

Ultrasound contrast media

Ultrasound contrast media consist of microbubbles or microspheres with an outer phospholipid or protein wall and a central inert echogenic gas. These microbubbles increase the reflection or backscatter of ultrasound waves and thus enhance the sonographic signals. Contrast-enhanced ultrasound is commonly used in the assessment of liver and renal lesions (**Figure 6**) as well as assessment of vesicoureteral reflux in children (Chung and Kim, 2014). Ultrasound contrast agents can be safely used in patients with acute kidney injury or chronic kidney disease.

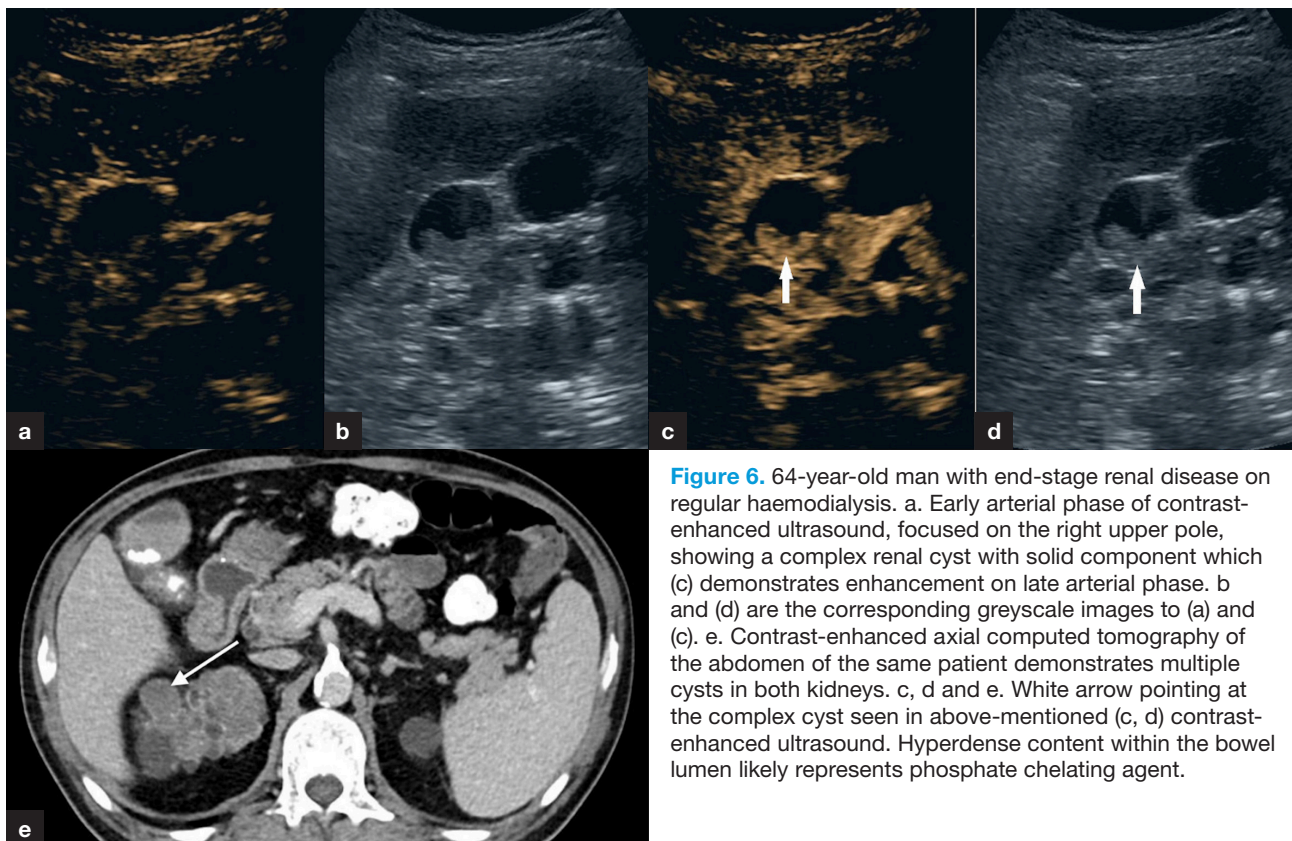


Figure 6. 64-year-old man with end-stage renal disease on regular haemodialysis. a. Early arterial phase of contrast-enhanced ultrasound, focused on the right upper pole, showing a complex renal cyst with solid component which (c) demonstrates enhancement on late arterial phase. b and (d) are the corresponding greyscale images to (a) and (c). e. Contrast-enhanced axial computed tomography of the abdomen of the same patient demonstrates multiple cysts in both kidneys. c, d and e. White arrow pointing at the complex cyst seen in above-mentioned (c, d) contrast-enhanced ultrasound. Hyperdense content within the bowel lumen likely represents phosphate chelating agent.

Conclusions

Contrast-enhanced computed tomography is an important tool in day-to-day clinical practice. Clinical teams should discuss patients with renal failure with radiology teams, taking into account the risk/benefits of iodinated contrast media, to determine the optimal imaging protocol or modality for answering the clinical query. Non-urgent contrast-enhanced computed tomography imaging can be deferred until renal function recovers. When contrast-enhanced computed tomography is unavoidable, the smallest possible volume of contrast media to produce diagnostic images is recommended. Multiple low volume contrast media protocols are being evaluated to further optimise clinical care. Prophylactic pre- and post-contrast intravenous hydration is recommended to decrease the risk of contrast-associated acute kidney injury. Prophylactic dialysis is not recommended to prevent contrast-associated acute kidney injury or renal injury. Patients at risk of contrast-associated acute kidney injury need close monitoring of renal function. Contrast-enhanced computed tomography not only carries the risk of contrast-associated acute kidney injury, but also exposes the patient to radiation and other potential complications, such as contrast reaction and contrast extravasation. These are beyond the scope of this article but are important factors to consider.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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Key points

- While most contrast media are safe to use in the majority of patients, precautions should be taken when planning contrast-enhanced medical imaging for patients with renal failure.
- The most severe complications caused by contrast media are contrast-associated acute kidney injury associated with administration of iodinated contrast media in computed tomography, and nephrogenic systemic fibrosis associated with administration of gadolinium-based contrast media in magnetic resonance imaging.
- These complications can be avoided if the risks and benefits of contrast media are considered when planning for medical imaging.
- Clinical teams should discuss patients with renal failure with radiologists, consider alternative imaging modalities or defer non-urgent contrast-enhanced computed tomography until the renal function recovers.
- When contrast-enhanced computed tomography is unavoidable, the smallest possible volume of contrast media adequate to produce diagnostic images is recommended.
- Prophylactic pre- and post-contrast intravenous hydration is recommended to decrease the risk of contrast-associated acute kidney injury. Prophylactic dialysis is not recommended to prevent contrast-associated acute kidney injury or renal injury.
- Ultrasound contrast agents can safely be used in patients with acute kidney injury or chronic kidney disease.
- Contrast-enhanced computed tomography not only carries the risk of contrast-associated acute kidney injury, but also exposes the patient to radiation and other potential complications, such as contrast reaction and contrast extravasation.

Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum:

- Is focussed on patient safety and delivers effective quality improvement in patient care
- Providing continuity of care to medical inpatients, including management of comorbidities and cognitive impairment
- Managing patients in an outpatient clinic, ambulatory or community setting, including management of long-term conditions.

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