#### **REVIEW ARTICLE**



# Know your way around acute unenhanced CT during global iodinated contrast crisis: a refresher to ED radiologists

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## Abstract

Due to a contrast shortage crisis resulting from the decreased supply of iodinated contrast agents, the American College of Radiology (ACR) has issued a guidance statement followed by memoranda from various hospitals to preserve and prioritize the limited supply of contrast. The vast majority of iodinated contrast is used by CT, with a minority used by vascular and intervention radiology, fluoroscopy, and other services. A direct consequence is a paradigm shift to large volume unenhanced CT scans being utilized for acute and post traumatic patients in EDs, an uncharted territory for most radiologists and trainees. This article provides radiological diagnostic guidance and a pictorial example through systematic review of common unenhanced CT findings in the acute setting.

Keywords Contrast crisis · Emergency radiology · Emergency department · Fat stranding · Unenhanced CT

#### Abbreviations

AAST ACR	American Association for the Surgery of Trauma American College of Radiology	
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COVID-19	Corona virus disease 2019 (acronym by the
	World Health Organization to describe the
	SARS-CoV-2 illness)
CT	Computed tomography
DECT	Dual-energy computed tomography
ED	Emergency department
EHR	Electronic health record
EMR	Electronic medical record
GB	Gallbladder
MVC	Motor vehicle collision
MRI	Magnetic resonance imaging
VME	Virtual mono-energetic

# Introduction

The number of emergency department (ED) visits and computed tomography (CT) utilization in the ED has been increasing since the turn of the century, with utilization increased about 150% from 2006 to 2016 [1]. Furthermore, in a 2021 study, Bunn et al. reported increased utilization of whole-body CT in the evaluation of motor vehicle collision (MVC), particularly in those with lower injury severity scores [2]. With CT considered the power horse of ED imaging, radiologists' on-call workload more than doubled the growth rate of ED visits over an 8-year period [3]. However, the upward trend was abruptly reversed in 2020 following declaration of COVID-19 pandemic and related measures [4].

As the USA is adjusting to the COVID-19 pandemic, an unanticipated consequence has occurred in the USA and worldwide which threatens quality patient healthcare: a break in the supply chain of iodinated contrast media [5]. This is brought about by the strict measures of zero-COVID policy in Shanghai, China, which led to both a decrease in production of iodinated contrast agents and an inability to ship outbound from China [5]. The extent and duration of the iodinated contrast shortage is uncertain but projected to last for several months with potential to significantly impact the diagnosis and treatment of patients presenting to EDs nationwide with acute and emergent undiagnosed health conditions or traumatic injuries. In response, the American College of Radiology (ACR) committee on drugs and contrast media issued a statement May 6th and updated May 13, 2022, acknowledging the rapidly evolving critical supply shortage and outlining a few considerations for mitigation [6]. These include performing as many ED CT scans without contrast as possible — after active discussion with ED physicians and other referring clinicians, and optimizing utilization of other imaging modalities whenever possible, thus essentially transforming unenhanced CT into a screening modality and reserving contrast only for critically ill patients following moderate-to-major traumas or as a problem-solving tool after a positive screening unenhanced CT.

Radiologists and radiologists-in-training have most commonly been presented with IV contrast-enhanced CTs for interpretation of patients in the acute care and trauma setting. The optimized interpretation of unenhanced CT is not a skill set to which radiologists and radiology training programs haves aspired to achieve. Hence, this article's aim is to provide a guide with pictorial examples for systematic review of important imaging findings in unenhanced CT scans in the acute setting.

The latest update from the iodinated contrast media manufacturer in July 15, 2022, mentions that albeit Shanghai facility is now operating at 100% production, some ongoing reduced availability of iodinated contrast media is expected [7].

For sake of brevity, there is purposeful omission of discussion on tissues, organs and findings that have been routinely assessed without contrast before the current crisis. This includes the brain, lungs, and bones. The article's focus is on the uncharted territory of acute findings of vessels, musculature, solid, and hollow viscera as seen in NCCT presenting to EDs inclusive of level 1 or 2 trauma. This article aims to be a refresher not only whenever contrast is unavailable or in low supply but also whenever contrast is contraindicated such as in allergy.

### Discussion

# Utilizing a standardized systematic interpretative approach

Systematic use of brief, focused checklists or search patterns and matching structured or semi-structured reporting are a recognized tool to limit errors in radiology [8, 9]. Checklists have been shown to reduce perceptual errors in critical care medicine and aviation [10] with promising results in radiology [11]. The use of systematic approach has been shown to also reduce some types of cognitive and perceptual biases [12, 13]. Figure 1 shows three examples of perceptual errors from our practice. Of note, the effectiveness of checklists in reducing errors and improving reporting accuracy is still debatable. Powell et al. showed no automatic value of checklists for improving radiology resident reporting accuracy [14]. Standardizing radiological diagnosis (for example, through checklists or otherwise defined search patterns) and reporting (through structured or semi-structured reporting and using of a common lexicon) are error and risk mitigation strategies in systembased quality improvement and patient safety [15]. Hence, the authors of this article are advocating for adhering to a standardized interpretative approach combined with structured or semi-structured reporting templates.

#### Use the electronic health/medical record more frequently

Comparison to prior radiologic examinations, particularly for cancer follow-up and screening as well as in cases of positive or equivocal findings, has been common practice among radiologists globally, with cross-sectional radiology reports nowadays have a distinct comparison section in every report [9, 16, 17]. Interestingly, there are no available accuracy studies to measure the added value of such comparison apart from mammography. Roelofs et al. found that comparison with prior mammograms significantly improved overall performance, decreased image annotations, and reduced referrals [18].

During the iodinated contrast crisis, a prior exam can be contrast-enhanced and hence may provide incremental information and context for any new or otherwise potentially equivocal finding, particularly if the prior scan is recent. Given the lack of specificity associated with many findings in non-contrast CT, it is crucial to fully understand the clinical context of the patient. Thus, not only must radiologists leverage clinical data obtained from order requests, but also diligently explore the electronic health/medical record for pertinent clinical findings. We recommend comparison with prior studies available to the ED radiologist whenever feasible.

# Emphasis on adjusting window width and level settings and utilizing dual-energy CT

The main clinical utilization of iodinated contrast is to increase perceptual contrast between healthy and diseased tissues, rendering lesions detectable to the human eye [19]. Without iodinated contrast, CT becomes significantly limited because of low inherent contrast between different types of soft tissues [19]. Adjusting the window width and level settings, aka "windowing," is a process used to adjust the grey tones in CT images during their visualization, with the aim to adjust window width and level for optimum tissue contrast for lesion detection [20]. Different areas of anatomy or organ systems are interpreted using different window level and width settings, and generally accepted default settings are available for examination [21]. Additionally, some evidence-based modifications have been proposed, such as utilizing liver window settings to improve conspicuity of small renal cell carcinomas [22], stroke window settings to detect subtle abnormalities that were not readily detected on the default brain window settings [23], and even specific de novo window parameters for particular mediastinal-invasive adenocarcinomas [24]. Today, as our main contrast-boosting agent is critically absent, we strongly recommend to strictly utilize dedicated preset window settings for each body part examined to maximize inherent tissue contrast (e.g., mediastinal, liver and abdominal windows for respective body regions) and additionally to manually adjust window settings as needed to optimize contrast between adjacent structures of interest (Fig. 2).

Dual-energy CT (DECT) offers postprocessing possibilities that are valuable during this contrast shortage crisis. Postprocessing, automated or user-initiated on commercially available software, can be utilized to obtain a superior image quality, particularly virtual monoenergetic imaging (VME) [25]. At low voltages, more tissue contrast is achieved, albeit at the expense of higher noise [26, 27]. This is obviously more advantageous in contrast-enhanced studies such as pulmonary angiography, but still useful in ED NCCT studies. For instance, VME is useful to show non-calcified impacted gallbladder (GB) neck stones in suspected cholecystitis or biliary colic and to accentuate bowel wall density difference from surrounding tissues in suspected bowel ischemia [28, 29]. It's important to stress that clinically suspected bowel ischemia is an all-time priority and should still be performed with IV contrast even in times of contrast shortages [25, 30]. With a gradual adoption of more conservative approach

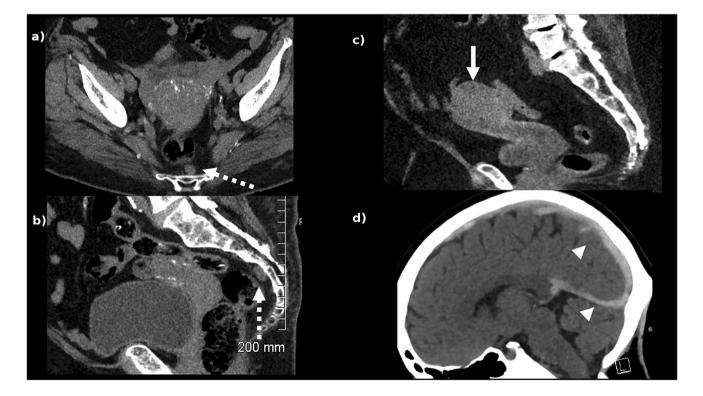


Fig. 1 Examples of perceptual errors that can be minimized by utilizing a systematic interpretive approach with a checklist. **a**, **b** Axial and sagittal unenhanced CT of the pelvis shows pre-sacral oval nodule (interrupted white arrows). Review of prior contrast-enhanced CT from 2012 showed same lesion (previously missed as well), as con-

tinuous with anterior sacral plexus nerves, likely representing neurofibroma/schwannoma. c Sagittal unenhanced CT pelvis shows a missed adnexal mass, abutting posterior uterus (arrow) in a patient presenting with acute abdomen. d Sagittal unenhanced head CT shows missed cerebral venous sinus thrombosis in postpartum patient

to preserve contrast (such as performing CT pulmonary angiography scans with 70 cc instead of 90 cc of iodinated contrast), VME at 40 keV can be useful to improve image quality, vessel attenuation and overall contrast-to-noise ratio [31–33]. At high voltages, VME is proven to significantly reduce beam-hardening and metallic artifacts [32]. Moreover, DECT non-contrast applications have been shown to be powerful, accurate problem solving tools in the acute setting, such as bone marrow edema [34], gout [35], and renal stone [36] applications. If no logistical constraints, we strongly recommend performing more ED unenhanced CTs in dualenergy mode whenever applicable.

#### Imaging signs relevant to ED scans

**Vessels** Arteries and veins are subject to a wide variety of traumatic events [37]. We recommend the examination of the entire length of the vessel in an outside-to-inward approach with emphasis on periadventitial tissue, wall, and lumen. Perivascular fat stranding can be a sign of dissection or vascular injury [38]. Additionally, perivascular edema/fluid is always abnormal and might be due to active bleed-ing, vessel perforation, or transection [28]. A more localized fluid collection may be due to perivascular abscess or evolving hematoma [25]. Next is to examine vessel caliber and

vessel wall. A vessel caliber is increased in case of aneurysm (traumatic or non-traumatic) and may be increased in dissections (Fig. 3). Acute thrombosis (particularly of veins) can lead to vessel enlargement [39, 40] and perivenous fat stranding (Fig. 4). Arterial mural thickening with or without hyperdensity can be a sign of intramural hematoma and dissection [28]. Calcification within the arterial lumen can be a sign of aortic dissection. Lastly, vessel lumen density can be a useful clue if hyperdense, as it points out to possible acute thrombosis (among other signs), such as in central pulmonary embolism [37, 40] (Fig. 5). On the other hand, intraluminal gas is an ominous sign of necrosis, such as in portal venous gas in cases of bowel ischemia [41] (Fig. 6).

**Solid organs** Application of AAST trauma scale will be very difficult without contrast, but detection of traumatic solid organ injuries is still possible on unenhanced CT [42]. A similar outside to inward approach is recommended, with the surrounding fat, edema, and fluid the first to assess. The common saying of "fat is the radiologist friend" is particular meaningful when interpreting non-contrast studies [43]. In the absence of iodinated contrast, fat stranding is a significant — and sometimes the only — clue for the presence of pathology. Focal and localized disproportionate fat stranding and/or edema at the edge of an organ following trauma might

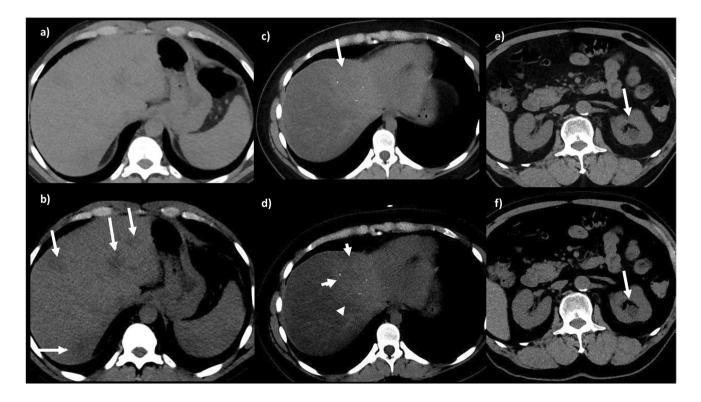


Fig. 2 Value of utilization of preset liver window in detecting subtle hepatic and renal lesions. All are axial unenhanced CT abdominal scans, with routine abdominal window (a, c, e) versus liver window

(b, d, f) showing multiple hepatic hypodense metastases (a, b), large hepatic mass (c, d) and left renal hypodense lesion (e, f)



**Fig. 3** Acute aortic dissection, type B. **a**, **c** Pre-contrast phase shows crescentic-shaped hyperattenuation at the posterolateral aspect of the descending thoracic aorta (white arrows), suspicious for acute dissection. **b**, **d** Post-contrast images confirm the presence of an intimal

be a clue to underlying contusion, laceration, or hematoma [44]. More extensive fat stranding and/or edema around most or the entire organ can still be traumatic or due to infective or inflammatory causes such as pancreatitis, prostatitis, enteritis, or pyelonephritis [28] (Fig. 7). Fluid — particularly if high attenuation — can be an indirect sign of bleeding, such as sentinel clot surrounding a solid organ bleeding site, or more generalized in the form of hemoperitoneum [45] (Fig. 8). Mesenteric fat stranding and/or edema can be the only sign of mesenteric and intestinal contusion, perforation,

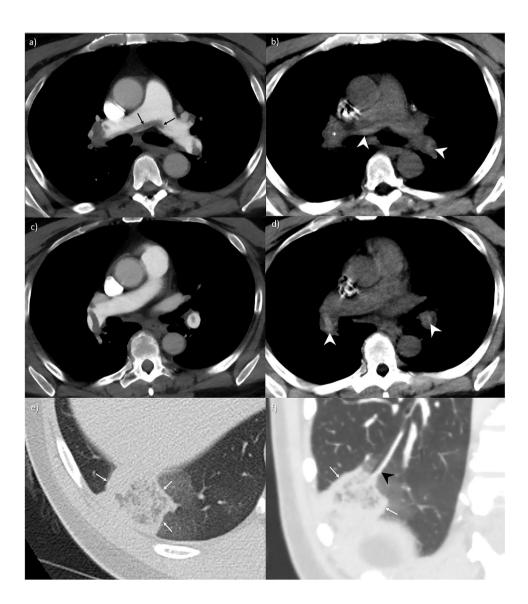
flap at the proximal descending aorta (black arrowhead in **b**) with a false lumen (black asterisk in **b**) and an distal intramural hematoma (white asterisk in **d**). Also note the presence of periaortic fat stranding (white arrowhead in **a**) and small pleural effusions

transection, or degloving [30] (Fig. 9). Of note, fat stranding is non-specific and can be seen with infiltrative tumors or obstructive uropathy and might be a completely insignificant finding, such as the frequently encountered perirenal fat stranding [42, 46].

The next feature to examine is the contour. Focal enlargement is more commonly encountered in solid organ trauma and is usually due to focal hematoma, contusion, or pseudoaneurysm [42, 47]. Surface irregularity might also be related to laceration [42]. Diffuse enlargement may be secondary to **Fig. 4** Acute common femoral vein thrombosis. Unenhanced CT scan image of upper thighs shows left common femoral vein distension in comparison to the right (white arrow). Also note the fat stranding and edema within left upper thigh in comparison to the right. This was proved by same day Doppler ultrasound



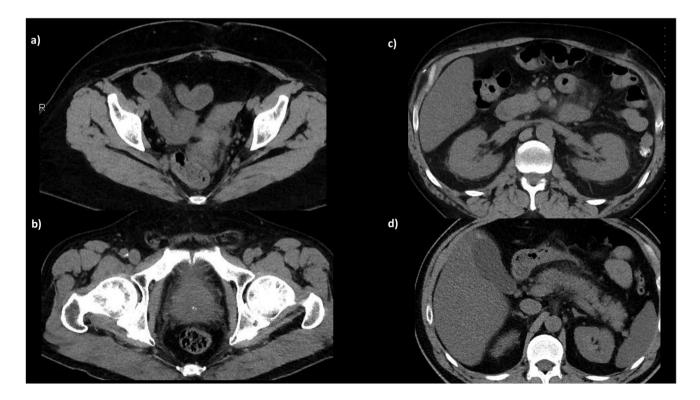
Fig. 5 Two cases of pulmonary embolism, findings on unenhanced chest CT (for purpose of illustration as these cases were performed as contrast-enhanced pulmonary angiograms). Original (a, c) and corresponding virtual non-contrast images (**b**, **d**) obtained around the level of the main pulmonary artery bifurcation in a patient with chest pain and shortness of breath. Central pulmonary embolism was diagnosed on the contrast-enhanced images, including a saddle embolus (black arrows in a). Note the expanded appearance at the bifurcation of the right pulmonary artery (asterisk in **b**), which corresponds to a large embolus as seen in a. Acute emboli are hyperattenuating on virtual non-contrast images (white arrowheads in **b** and **d**). e, f Pulmonary findings consistent with pulmonary infarct in another patient referred for pulmonary CT angiography. Lung window settings show a polygonal-shaped opacity in the right lower lobe abutting the parietal and diaphragmatic with a "reverse halo" sign (white arrows in e and f. Note the presence of a feeding vessel at the apex of the opacity (black arrowhead in f), consistent with a lung infarct





**Fig.6** Bowel ischemia. Axial (**a**, **b**) and coronal (**c**) unenhanced abdomen and pelvis CT images show bowel wall pneumatosis in proximally dilated small bowel loops (arrow in **a**), antidependent gas

within inferior mesenteric vein (arrow in **b**), and portal venous gas (arrows in **c**). Note markedly distended stomach. Patient was taken to surgery which revealed SBO secondary to partial mesenteric volvulus



**Fig.7** Value of fat stranding in four different ED cases of unenhanced abdomen and pelvis CT: **a** terminal ileitis, **b** prostatitis, **c** jejunitis, and **d** pancreatitis (with elevated lipase)

**Fig. 8** Hemoperitoneum with ruptured ovarian cyst. Axial (**a**) and coronal (**b**) unenhanced abdomen and pelvis CT images in 29-year-old woman presented to ED with acute lower abdominal pain. Note high attenuation moderate pelvic free fluid (solid arrow) and hypodense right ovarian cyst (interrupted arrows). She underwent diagnostic laparoscopy with cauterization of a bleeding focus at the location of ruptured ovarian cyst



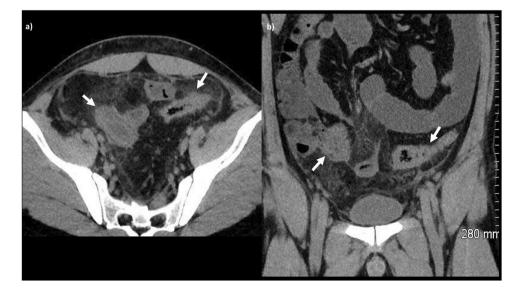
large hematomas (especially in smaller solid organs, such as the kidney). However, long-standing conditions can also cause diffuse enlargement (e.g., hepatomegaly due to steatosis, sarcoidosis, or other infiltrative process including primary and secondary neoplasms) [28].

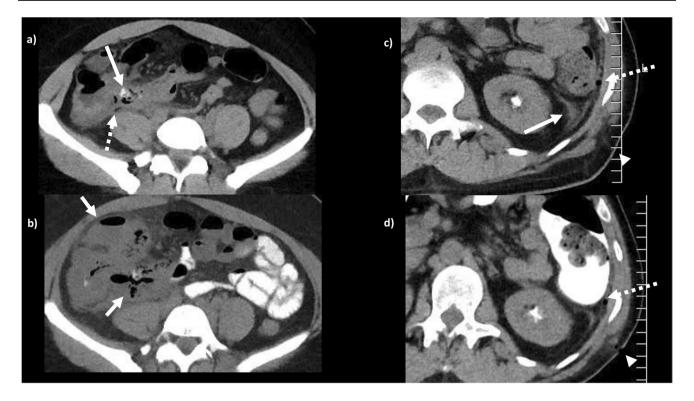
Checking abnormal organ density can be a significant clue to underlying acute abnormalities [40]. The presence of abnormal linear or branching low-density structures should raise suspicion of lacerations [44]. Focal high, low, or mixed attenuation lesions may be seen in hematomas at various stages of development, particularly if irregular or new in comparison to prior studies [47].

Hollow viscus (gastrointestinal, gallbladder, ureters, and urinary bladder) Fat stranding, edema, extraluminal gas, and free fluid surrounding any hollow viscus are usually related to acute abnormalities, such as traumatic mesenteric or intestinal contusion, perforation, transection, degloving or infectious/ inflammatory etiologies (colitis, cholecystitis, or medicationinduced angioedema) [30]. Small, irregular fluid collections surrounding the GB or urinary bladder can be secondary to traumatic rupture (with resultant bile leak into peritoneal cavity or intra or extraperitoneal urine leak) [28, 48].

Peri-intestinal (extra-luminal gas) is always abnormal and points to hollow viscus perforation in context of trauma, infection, or inflammation, such as diverticulitis, appendicitis, and peptic ulcer disease [30] (Figs. 10 and 11). Increased hollow viscus caliber is a sign seen in acute etiologies, including mechanical obstruction or ileus (may demonstrate additional signs such as air-fluid levels), or in GB (a sign of cholecystitis), or urinary bladder, where it may be associated with an penile or urethral trauma [30, 40, 49].

Fig. 9 Post-traumatic bowel injury and necrosis. Axial (a) and coronal  $(\mathbf{b})$  unenhanced abdomen and pelvis CT images show segmental wall thickening of terminal and distal ileum as well as sigmoid colon (arrows) with surrounding extensive fat stranding and edema. The patient was taken to surgery where right hemicolectomy was performed due to bowel necrosis (sigmoid was reported viable). Unfortunately, this patient was CT scanned 3 days earlier following high speed MVC and discharged home albeit CT report of small focus of mesenteric fat stranding suspicious of mesenteric contusion





**Fig. 10** Two cases of extraluminal gas due to perforated appendicitis  $(\mathbf{a}, \mathbf{b})$  and penetrating stab wound  $(\mathbf{c}, \mathbf{d})$ . **a**, **b** Sequential unenhanced abdomen and pelvis CT images in 39-year-old female presents with abdominal pain and fever. The initial CT image  $(\mathbf{a})$  shows localized perforated appendix with extraluminal gas (interrupted arrows) and appendicolith (solid arrow). A follow-up unenhanced CT (with oral contrast) 4 days later  $(\mathbf{b})$  shows interval development of a fluid and gas collection (arrows in b). **c**, **d** Sequential unenhanced abdomen and pelvis CT images following left flank stab wound. The first CT image

(a) shows stab trajectory (arrowhead), extraluminal gas adjacent to descending colon (interrupted arrow), and left pararenal hematoma (solid arrow). The contrast within renal pelvis is from previous IV-contrast enhanced CT done a day earlier. The following image (d) shows descending colon distension with rectal contrast without leak. Note the location of extraluminal gas (interrupted arrow) outside lateral conal fascia denoting its outside origin rather than colonic perforation. No surgery was performed, and the patient was discharged



**Fig. 11** Perforated diverticulitis. Axial (**a**, **b**) and coronal (**c**) unenhanced pelvic CT images of a 33-year-old male presented to ED with left lower quadrant pain and fever. Note sigmoid wall thickening and

fat stranding on background of diverticulosis (long arrow in **a**), pericolonic air-and-fluid collection (short arrow in **a**), colo-colic fistula (arrow in **b**) and colo-vesical fistula (arrow in **c**) Wall thickening with and without high or low attenuation, although not exclusively acute, may be seen in bowel contusion in context of trauma [46] (Fig. 9). A hyperdense or hypodense thickened intestinal wall with or without pneumatosis may be seen in bowel ischemia, a life-threatening diagnosis [41] (Fig. 6). A hyperdense wall is also seen with intramural traumatic contusion and hematoma (bowel, GB) while a hypodense wall might be seen in case of edema secondary to trauma, infection, or inflammation [39, 46]. Wall discontinuity or irregularity may result from traumatic laceration, perforation, or transection [30].

Rarely, intraluminal high attenuation bleeding might be seen in the bowel, GB (hemobilia), or urinary bladder (a sign of perforation) [30, 49]. Foreign bodies such as ingested BBQ metallic brush fragment [28, 40] or cocaine drug packs can be detected with careful screening of bowel segment by segment utilizing the appropriate window settings, e.g., lung window for body stuffers [50].

**Abnormal gas and fluid** Abnormal collections of high attenuation fluid (e.g., hemothorax, hemoperitoneum) and gas (pneumothorax, pneumomediastinum, and pneumoperitoneum) are known post-traumatic complications that need careful screening in the correct window level and width settings. Special attention should be paid to frequently missed locations, such as apical and para mediastinal locations for small pneumothoraces, and perihepatic and subdiaphragmatic small air locules in pneumoperitoneum [51]. A well-defined

fluid collection is frequently seen in chronic conditions, although may also be seen in acute conditions such as evolving hematoma, abscess, peripancreatic pseudocyst, urinoma, or biloma [40, 49]. Post-infectious/inflammatory or post-traumatic fistulas can be also readily seen on unenhanced CT, especially if containing air [41] (Figs. 10 and 11).

*Musculature of the neck, chest, abdominal, and pelvic walls* Any asymmetric muscular enlargement is abnormal and may be a clue to intramuscular hematoma, particularly if adjacent fractures are detected (Fig. 12). This is non-specific and can be seen also in tumors such as sarcomas and in inflammatory conditions such as myositis [52, 53]. Diffuse neck, chest, and abdominal wall stranding and edema is seen in cases of third spacing or anasarca due to generalized causes of edema or volume overload [44].

Knowledge dissemination and education Most radiologists and trainees have never been in a situation where NCCT is widely utilized in ED and acute inpatient studies. Faced with ubiquitous, unprecedented crisis at short notice, radiologists can be stressed, particularly residents and fellows. We recommend immediate department-wide initiatives to inform and keep trainees in the loop of communications about the contrast crisis with daily or weekly updates regarding mitigation strategies. This should be combined with review lectures focusing on the radiologic signs in ED unenhanced CT scans (Table 1).

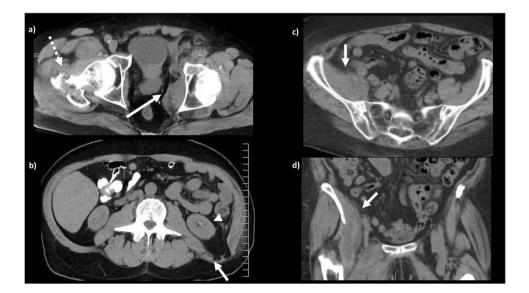


Fig. 12 Acute muscular abnormalities in unenhanced CT in 3 different patients. **a** LT pelvic wall and retroperitoneal hematoma, involving obturator internus muscle (arrow) with adjacent left pubic rami fractures (not sown). Note associated right intercondylar femoral fracture (interrupted arrow). **b** Left flank stab wound with lacerated

left latissimus dorsi muscle (arrow). Note subtle pararenal hematoma (arrowhead). c, d axial and coronal unenhanced CT images show spontaneous right iliopsoas hematoma (arrow in c) with loss of architecture, increased density fluid around the muscle, and surrounding iliopsoas bursitis (arrow in d)

#### Table 1 Step-by-step checklist

Number	Steps
1	Utilizing a standardized systematic interpretative approach
2	Use the electronic health/medical record (EHR/EMR) more frequently. Compare with previous examinations
3	Adjust window width and level settings. Utilize dual-energy CT (DECT) whenever applicable
4	<ul> <li>Imaging signs relevant to ED scans:</li> <li>a-Vessels:</li> <li>Perivascular fat stranding, edema, free or localized fluid</li> <li>Caliber</li> <li>Mural thickening (with or without abnormal density)</li> <li>Vessel lumen density</li> <li>Intraluminal gas</li> <li>b-Solid organs</li> <li>Surrounding fat stranding, edema, free or localized fluid, including sentinel blood clot</li> <li>Contour and surface irregularity</li> <li>Organ density</li> <li>c-Hollow viscus (Gastrointestinal, GB, ureters and UB)</li> <li>Surrounding fat stranding, edema, free or localized fluid or extraluminal gas</li> <li>Caliber</li> <li>Mural thickening (with or without abnormal density)</li> <li>Intramural gas</li> <li>d-Abnormal gas and fluid</li> <li>e-Musculature of neck, chest, abdominal and pelvic walls:</li> <li>Asymmetric focal muscular enlargement</li> <li>Diffuse edema/anasarca</li> </ul>
5	Knowledge dissemination and education

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# Limitations

Many of the aforementioned findings are non-specific and hence can be used as indirect signs of trauma or acute abnormality that may warrant further workup, which may include laboratory and other non-imaging tests, additional imaging studies, and contrast enhanced studies. For example, peripancreatic fat stranding warrants lipase correlation [54] while post-traumatic mesenteric fat stranding warrants close observation and low threshold for repeat CT imaging after surgical consultation [55].

# Conclusion

The practice of triage in time of scarcity of resource has long been a staple pin in the practice of medicine, especially in the emergency or urgent care setting. This crisis of iodinated contrast shortage is of similar vein in how radiologists, referring physicians, and US health care systems will adjust to provide ongoing patient care. Whereas health care systems can mitigate the loss of contrast-enhanced CT availability, radiologist can and will facilitate ongoing quality diagnostic assessment by sharpening a tool that was only dulled by lack of necessity usage. The skill and expertise in interpretation of non-contrast enhanced CT scans can be refreshed through continuing medical education and review of articles such as this on unenhanced CT along with the some of the aforementioned best practice recommendations.

Author contribution All authors meet the full requirements to be considered as co-authors. All authors gave final approval to the submitted paper and agree to be accountable for all aspects of the work. The study fully complies with ethical standards.

#### **Declarations**

Informed consent and ethical approval Not applicable.

**Conflict of interest** The authors declare that they have no conflict of interest.

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