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Dependent contrast layering sign on CT in patients irrespective of cardiac dysfunction and its clinical implications: A preliminary retrospective study

Ji Yang Kim *, Youssef Mohsen, Yashant Aswani and Archana Laroia

University of Iowa Hospitals and Clinics, 200 Hawkins Dr. Iowa City, IA, 52242.

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Abstract

Purpose: CT findings of contrast layering in dependent areas of the central venous system and solid organs have been reported in the literature to be associated with imminent cardiac arrest. However, no systematic research has explored the association of this distinctive CT finding with cardiac arrest and mortality. Therefore, we investigated the radiological manifestations of dependent layering of contrast in various vascular structures and organs and its clinical implications.

Methods: A computerized search of radiological database was conducted using keywords "layering contrast" between January 2008 and January 2022. After reviewing CT scans of 226 patients that met the keyword criteria, 21 patients who exhibited the dependent contrast layering sign (DCLS) in vascular structures and organs were included in the final study population. Clinical data such as cardiac arrest within 2 hours, in-hospital mortality, and shock index ≥ 0.9 were collected. Number of involved structures in each patient is also investigated. Statistical significance and frequency regarding the association between radiologic findings and clinical data were analyzed.

Results: The distribution of DCLS across anatomical structures reveals IVC is involved in 90.5% of patients and followed by hepatic vein (80.9%), liver parenchyma and right atrium. Cardiac arrest within 2 hours is significantly more common in patients with DCLS in right atrium ($p=0.02$, odds ratio = 21.6) and liver parenchyma ($p=0.01$, odds ratio = 24.8). DCLS in liver parenchyma is associated with the highest rate of in-hospital mortality (4 of 7, 57.1%). The total number of involved structures ($p=0.01$) and the number of common structures ($p=0.001$) are significantly higher in patients with cardiac arrest within 2 hours.

Conclusions: The presence of DCLS in the right atrium and liver, as well as the larger number of involved structures, are significantly associated with impending cardiac arrest. Thus, it may offer additional insights for both radiologists and clinicians and aid in prompt initiation of resuscitative interventions before the onset of cardiac arrest. Nevertheless, larger prospective studies are warranted to validate the clinical relevance of DCLS across various vascular structures and organs.

Keywords: Venous layering of contrast; Dependent contrast layering sign; Computed tomography; Cardiac arrest; In-hospital mortality

1. Introduction

The findings of contrast layering or pooling in the dependent portion of the venous system and solid abdominal organs on contrast enhanced computed tomography (CT) is considered a significant indicator of critically low cardiac output and impending cardiac arrest. Tsai et al. reported this CT sign for the first time in five patients who experienced cardiac arrest during CT examinations (1). Commonly implicated structures include inferior vena cava (IVC), hepatic vein, liver,

* Corresponding author: Ji Yang Kim

and right atrium. Other structures, such as renal vein, iliac veins, superior vena cava (SVC), and right kidney, have also been reported to be involved. (1-11). These patients presented with a variety of underlying conditions, including septic shock (1), aortic dissection (1, 8, 10, 11), pulmonary embolism (2, 6, 8), brain hemorrhage (4), pericardial effusion (5), myocardial infarction (9, 11), constrictive pericarditis (9), hypovolemic shock due to trauma (1, 7, 8, 11), and exacerbation of chronic obstructive pulmonary disease (10).

Most of the existing studies on this CT findings consist of case reports or case series (1-10). Lee et al. assessed the accuracy of this finding in predicting imminent cardiac arrest and its association with survival involving 128 patients who presented at the emergency department, underwent contrast-enhanced CT (CECT), and subsequently experienced cardiac arrest. Among these patients, 11 demonstrated dependent contrast layering in the venous system on CT scans, and they displayed a higher likelihood of experiencing imminent cardiac arrest and a lower likelihood of survival (11). It is important to note that all previous studies have described CT findings of contrast layering in venous structures exclusively in the patients who had suffered cardiac arrest (1-11).

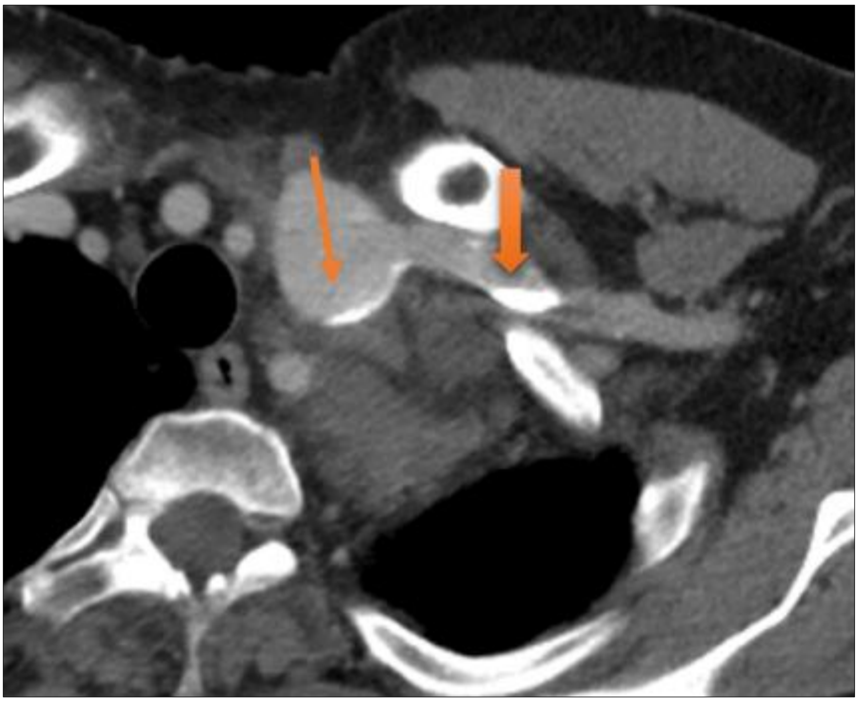
To the best of our knowledge, there has been no comprehensive investigation about the clinical relevance of contrast layering within venous structures in a diverse patient cohort, encompassing individuals both with and without cardiac dysfunction. Therefore, our study aims to investigate the radiological manifestations of contrast layering across various vascular structures and abdominal solid organs, as well as their potential clinical implications regarding patients irrespective of cardiac dysfunction who have undergone CECT of chest and/or abdomen.

2. Material and Methods

2.1. Patients and Image Interpretation

This retrospective, single-institution study was approved by the Institutional Review Board of our institution. A computerized search of our institution's radiological database was conducted by one of our authors to identify patients who underwent CECT of the chest and/or abdomen between January 2008 and January 2022. The search focused on CT interpretations containing keywords such as "layering of contrast," "dependent layering of contrast," and "pooling of contrast". Out of 141,012 patients who underwent CECT of chest and/or abdomen, a list of 226 patients matching the keyword criteria was compiled. Two fellowship-trained body radiologists inspected the radiologic reports and reviewed CT images of these 226 patients. The image evaluation took place on a Picture Archiving and Communication System (PACS) workstation monitor with consensus reached regarding the presence of CT findings indicating dependent layering or pooling of contrast. In our study, this specific CT finding was termed the "dependent contrast layering sign" (DCLS). Among the 226 patients, most of the patients (n=192) were excluded from the study population because layering of contrast was demonstrated in the organs other than vascular structures as follows: 1) vicarious secretion of gallbladder (n=142), 2) urinary tract (n= 41), 3) oral contrast in gastrointestinal tract (9). 34 were confirmed to exhibit DCLS in at least one vascular structure. However, 13 patients were excluded from the final analysis for the following reasons: 1) DCLS in both subclavian veins due to contrast injection through the upper extremity veins was considered as residual contrast (n=12) (Figure 1A), 2) DCLS in the superior mesenteric vein during portal venous phase images was interpreted as a mixing artifact (n=1) (Figure 1B-D). Consequently, a total of 21 patients were included in the final study population (15 men and 6 women, age range: 34-85 years, mean age: 67.4±12.4 years). The count of vascular structures and solid organs demonstrating DCLS was determined. For consistency, if two or more vessels of the same name were involved, they were counted as one vessel. For instance, the involvement of both common iliac veins was counted as one, and the involvement of multiple hepatic veins was also calculated as one. IVC, hepatic vein, liver, and right atrium were categorized as "common" structures due to their frequent involvement, while other vessels and organs less frequently implicated were classified as "uncommon." The total number of affected structures was calculated, and distinct counts were also computed for both "common" and "uncommon" structures.

Clinical data were extracted from electronic medical records, encompassing patient's underlying conditions, instances of cardiac arrest and the corresponding timing, occurrences of death during the same hospitalization as the CT examination (in-hospital mortality), blood pressure, and pulse rate at the time of the CT scan. Blood pressure and pulse rates were not documented for certain patients as they are not routinely assessed during CT examinations. The shock index, calculated as the pulse rate divided by systolic blood pressure, was also recorded. Shock index of 0.9 or higher predicts the increased risk of mortality (11).



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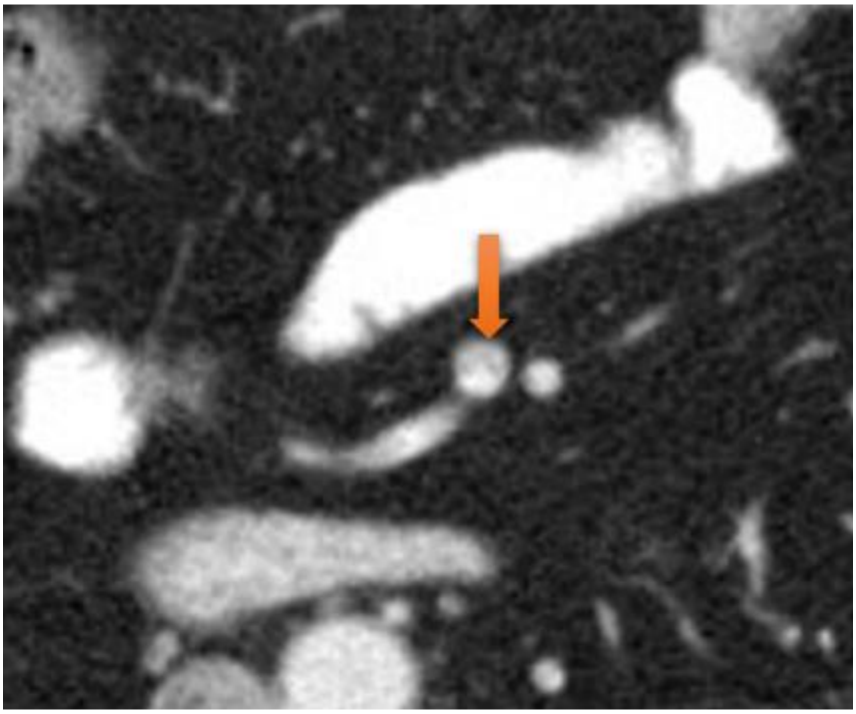

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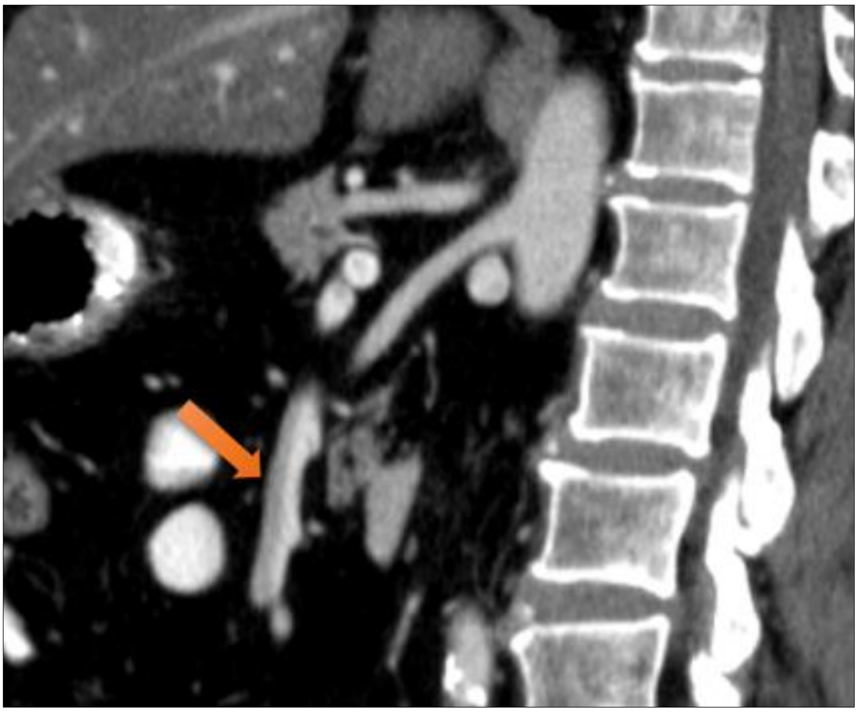

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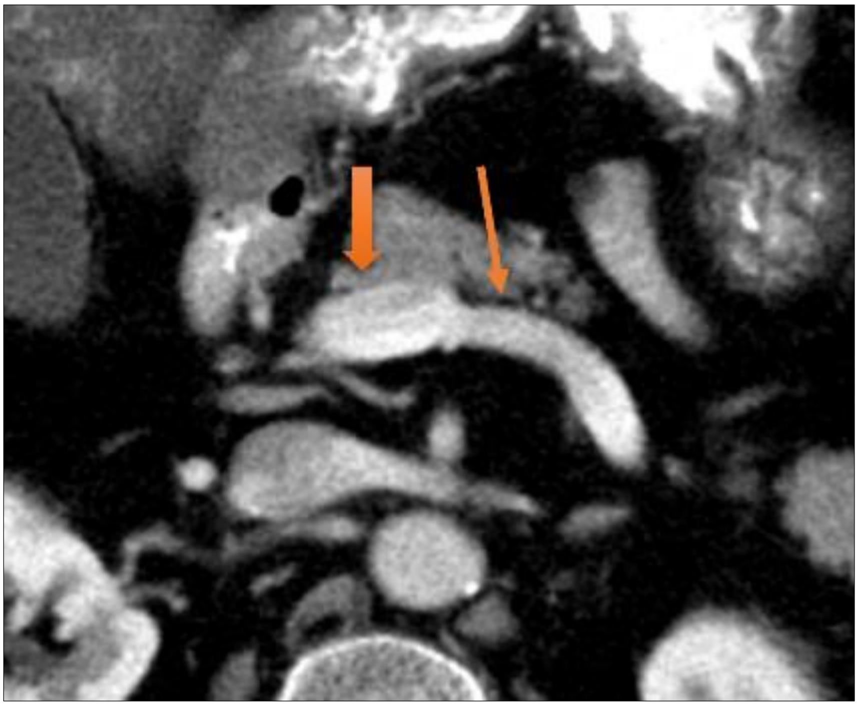


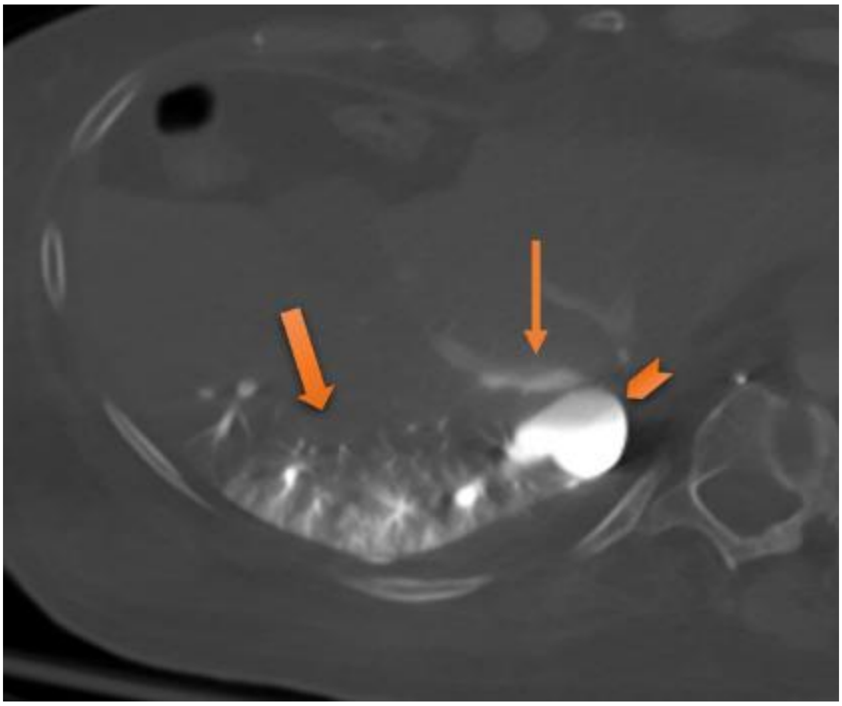
1(D)

Figure 1 (A) 56-year-old man with a mediastinal mass and no underlying cardiac dysfunction. CECT chest through left arm vein demonstrates dependent contrast layering in left subclavian vein (arrow) and distal internal jugular vein (thin arrow), which is regarded as residual contrast agent incompletely pushed by the injected saline. (B-D) 72-year-old man with diabetes underwent CECT abdomen and pelvis by indication of abdominal bloating. Portal venous phase shows contrast layering in superior mesenteric artery (arrow) on (B) axial and (C) sagittal scans, which is regarded as mixing artifact, given incomplete contrast opacification of portal vein (arrow) and splenic vein (thin arrow) (D).

2(A)

2(B)

Figure 2 77-year-old man with no underlying cardiac dysfunction. CECT abdomen and pelvis was performed for a follow-up of liver abscess and pancreatic cancer. The patient's systolic blood pressure was 115 mmHg at the time of CT and the patient have not experienced cardiac arrest. Arterial phase images demonstrate DCLS in (A) IVC and, (B) hepatic vein (arrows) without involvement of liver, right atrium, or other structures



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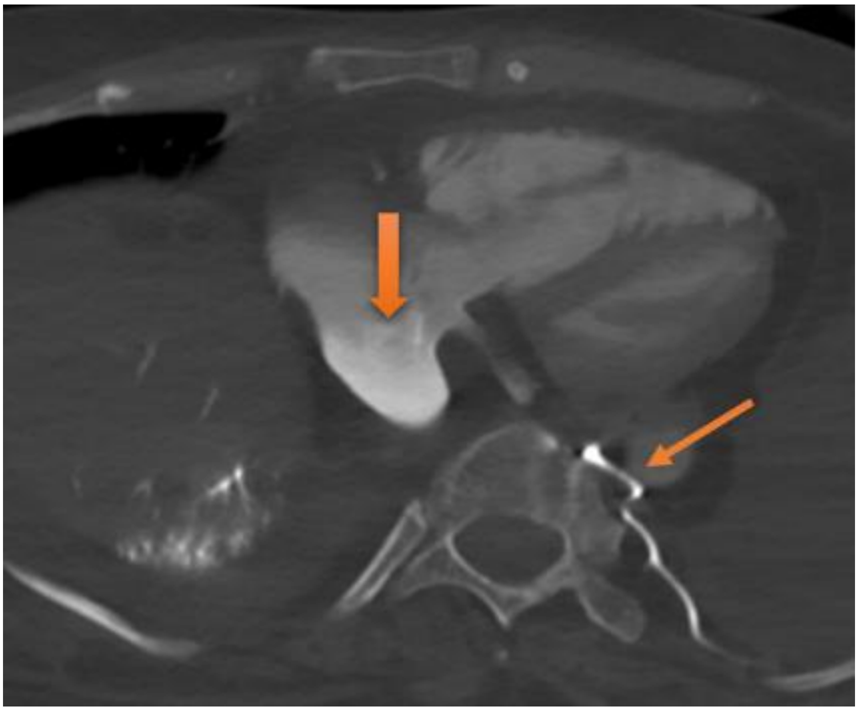

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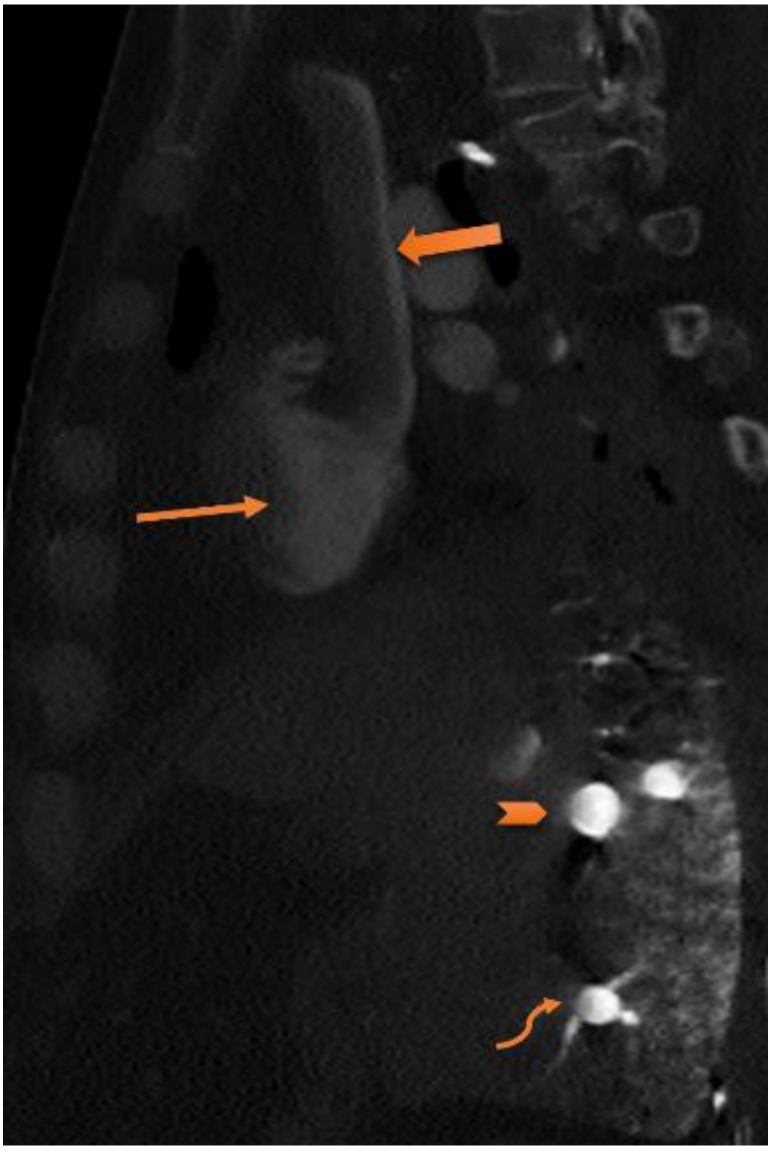
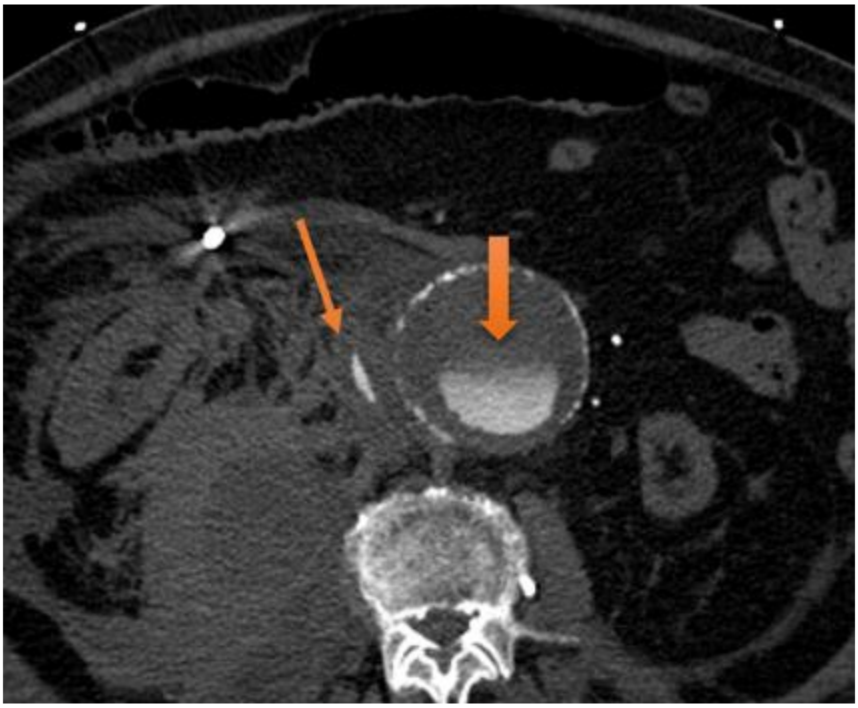


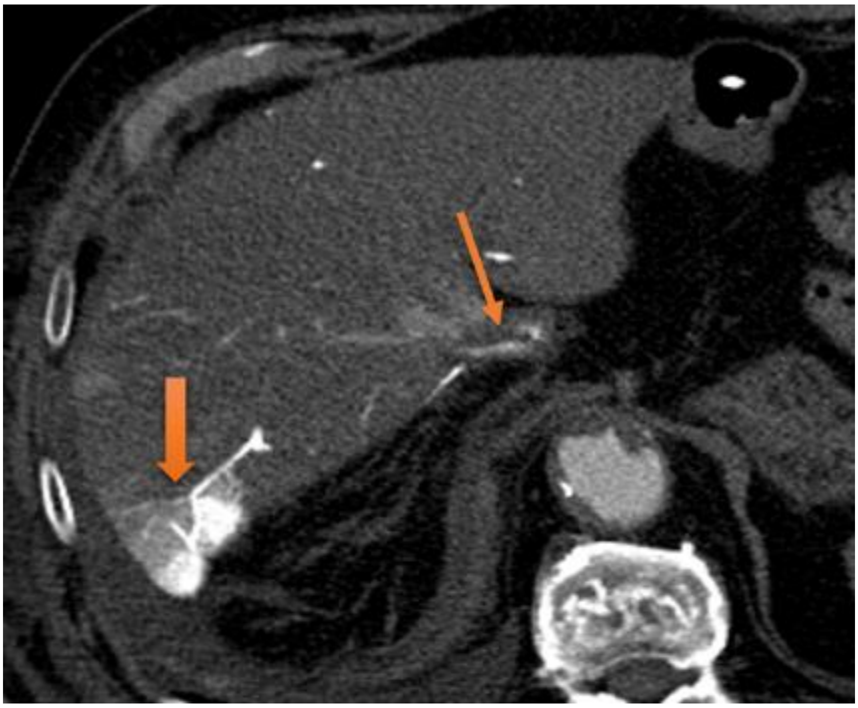
3(C)

Figure 3 66-year-old female with restrictive lung disease and respiratory failure. The pulse rate was 98 at the time of CT. The patient had cardiac arrest after 15 minutes of CT and expired. Arterial phase of chest CT demonstrates DCLS in (A) right lobe of liver (arrow), middle hepatic vein (thin arrow), IVC (arrowhead), (B) right atrium (arrow), and posterior intercostal vein (thin arrow). (C) Reconstructed sagittal scan demonstrates DCLS in SVC (arrow), right atrium (thin arrow), right hepatic vein (arrowhead) and accessory right hepatic veins (curved arrow).



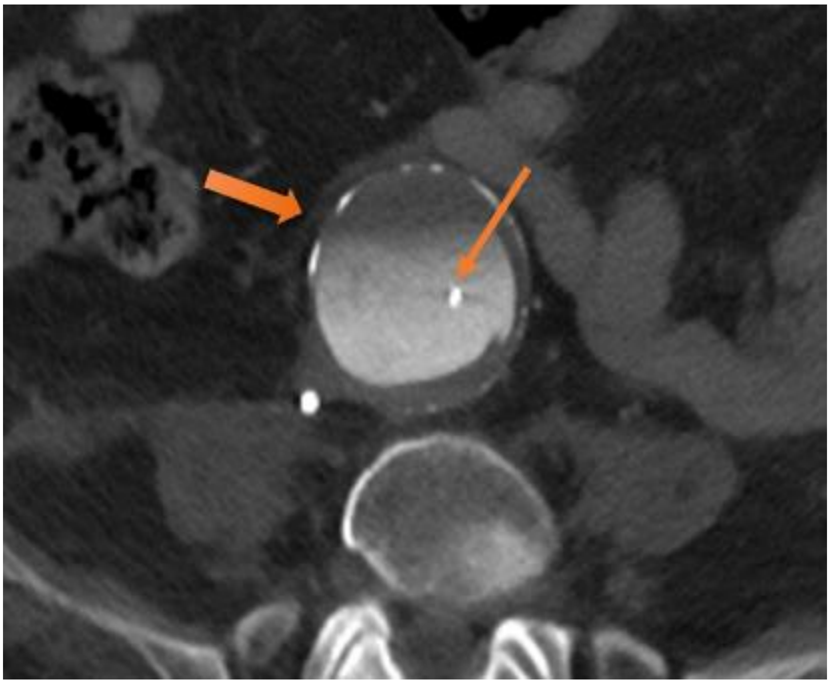
4(A)

4(B)



4(C)

Figure 4 82-year-old man with hypertension and COPD underwent CT angiogram chest abdomen pelvis for the evaluation of aortic aneurysm. The patient experienced cardiac arrest 30 minutes after CT and subsequently expired. Arterial phase axial scan demonstrates (A) aneurysm of abdominal aorta with periaortic hematoma, consistent with aortic aneurysm rupture. DCLS is observed in aorta (arrow). Refluxed contrast in IVC (thin arrow) is noted with compression of lumen by hematoma. (B) DCLS is also demonstrated in left common iliac vein (arrow) and right external iliac vein (thin arrow). Both iliac arteries are not well opacified with contrast agent (arrowheads). (C) DCLS is also observed in VII segment of liver (arrow) and IVC (thin arrow).



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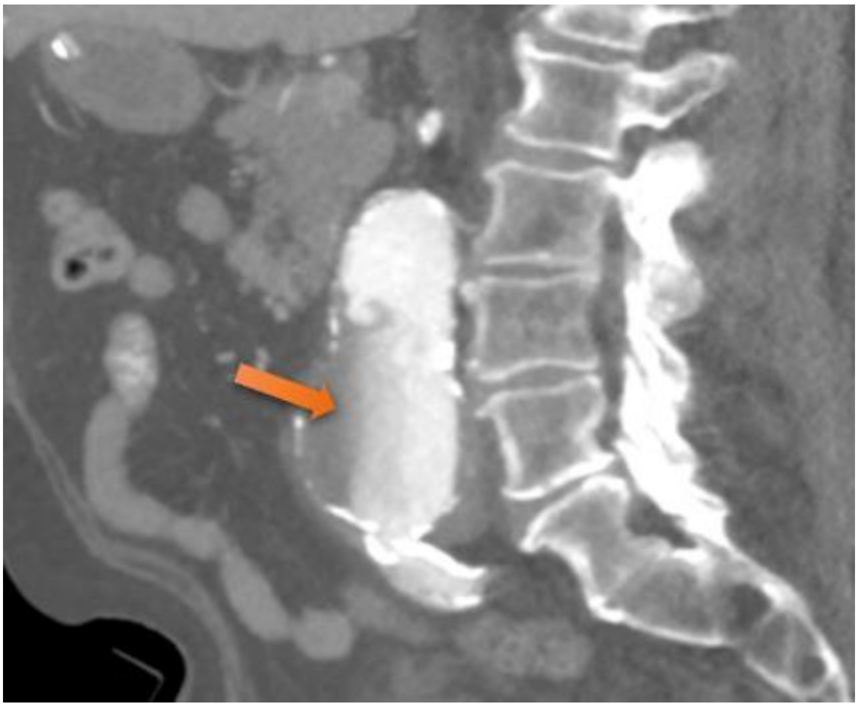
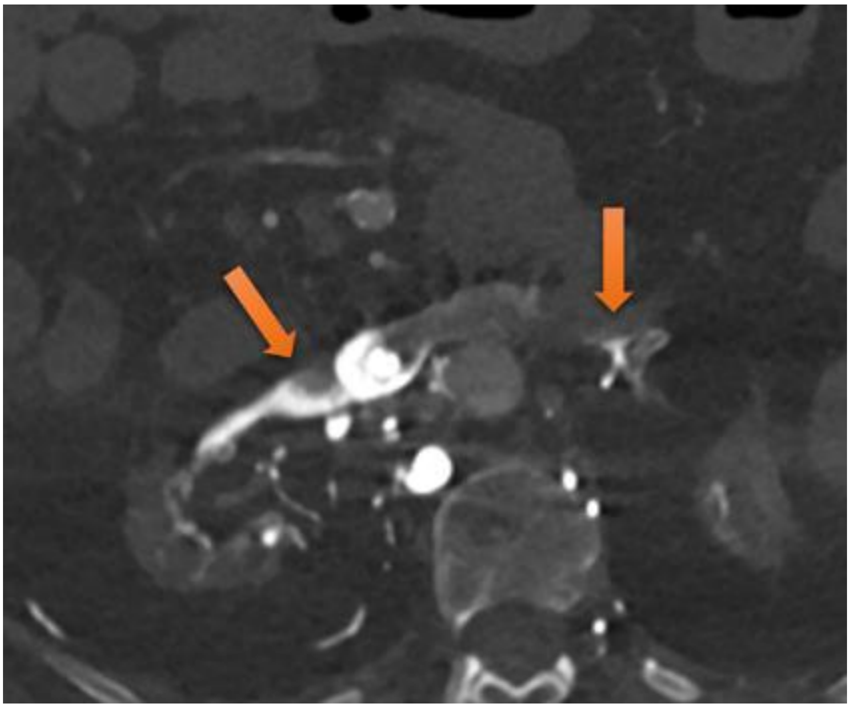


5(B)

Figure 5 68-year-old man with acute myocardial infarction and abdominal aortic aneurysm. The patient's systolic blood pressure was 80 mmHg, pulse rate was 112 bpm, and shock index was exceeded 0.9 (1.4) at the time of CT. The patient had experienced cardiac arrest, not within 2 hours, but after 30 hours of CT and expired. Axial (A) and sagittal (B) scan of CT angiogram of abdomen and pelvis demonstrates layering of contrast only within the aneurysmal segment of infrarenal aorta (arrows). Arterial line (thin arrow) is noted. Notably, no other DCLS in venous structures or solid organs was observed.



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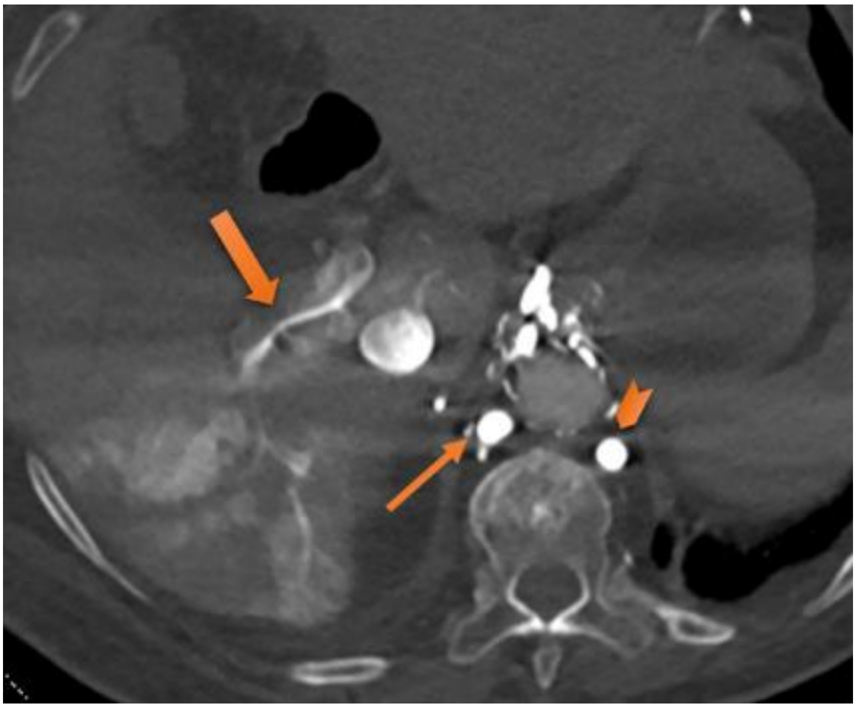

6(B)

Figure 6 70-year-old female with coronary artery disease and hypertension. Shock index was normal (0.8) at the time of CT. CT angiogram chest was performed with indication of pulmonary embolism. The patient has not experienced cardiac arrest and discharged survived. Axial images show DLCS in both renal veins (arrows) (A), portal vein (arrow) and right lobe of liver (B). Pooling of contrast is also noted in dilated azygous (thin arrow) and hemiazygos veins (arrowhead) (B).

2.2. CT Technique

Dual-source CT scanners (Somatom Definition Flash or Somatom Force, Siemens Healthcare, Erlangen, Germany) were utilized for the CT examinations. Intravenous contrast agents (Iopamidol - Isovue 370, Bracco; Iodixanol - Visipaque™ - 320, GE Healthcare) were administered as bolus injections, with injection rates of 3 cc/sec (n=5, 23.8%), 4 cc/sec (n=13, 61.9%), or 5 cc/sec (n=3, 14.3%). The volume of contrast agent ranged from 75 cc to 150 cc, adjusted based on the patient's body mass index and CT protocol. A scan time delay was 20-60 seconds following contrast injection as per protocol. Bolus tracking was employed for CT angiograms in cases with indications of pulmonary embolism.

2.3. Statistical Analysis

The presence of the DCLS in different vascular structures and organs was correlated with clinical data, such as cardiac arrest within 2 hours, in-hospital mortality, and a shock index of ≥ 0.9. Mean and standard deviation were calculated for age and the number of involved vascular structures and organs. The normality of variables was assessed using Shapiro-Wilk tests. P-values were derived from Mann-Whitney U tests for continuous variables and Fisher's exact tests for categorical variables. Significance was set at 0.05 level. Odds ratios and their corresponding 95% confidence intervals were calculated. Spearman's correlation coefficient (ρ) was employed to determine the correlation between the total number of affected vessels and the shock index. The statistical analysis was conducted using R Statistical Software v. 4.2.2.

3. Results

Among the 141,012 patients who underwent CECT of chest and/or abdomen, a total of 21 patients demonstrated the findings of the DCLS, representing a prevalence of 0.015%. The average age of these 21 patients was 67 years, with the majority being male (n=15, 71.4%). The major underlying diseases among the patients included coronary artery disease (n=10), myocardial infarction (n=2), atrial fibrillation (n=5), aortic valve stenosis (n=3), aortic dissection (n=2), pulmonary embolism (n=2), nonischemic cardiomyopathy (n=1), hypertrophic cardiomyopathy (n=1), chronic obstructive pulmonary disease (COPD) (n=1), restrictive lung disease (n=1), abdominal aneurysm rupture (n=1), trauma (n=1), pancreatic cancer (n=1), and cerebrovascular disease (n=1). Hypertension (n=12) and diabetes (n=2) were also noted. Many patients had multiple coexisting conditions.

The CT protocols includes both CT angiograms (CTA) (n=16, 76.2%) and non-CTA (n=5, 23.8%) of chest and/or abdomen. Indications for CT scans encompass aortic disease (n=10, 47.6%), pulmonary embolism (n=3, 14.3%), heart disease (n=3, 14.3%), and other reasons (n=5, 23.8%), including retroperitoneal mass, trauma, infection, pancreatic cancer, and respiratory failure. DCLS was commonly observed in CTA protocols (n=16, 76.2%), primarily indicated for cardiovascular disease evaluation (n=16, 76.2%), and involving high injection rates of contrast agents, exceeding 4cc/s (n=16, 76.2%). The distribution of DCLS across anatomical structures reveals IVC is involved in 90.5% of patients and followed by hepatic vein (80.9%) (Figure 2), liver parenchyma and right atrium (Figure 3). All the patient showed DCLS in at least one of the four "common" structures. DCLS is noted in "uncommon" structures in 10 patients (Table 1). "Uncommon" structures encompass iliac vein (n=5) (Figure 4), femoral vein (n=1), SVC (n=2) (Figure 3), aorta (n=2) (Figure 4,5), renal vein (n=2) (Figure 6), adrenal vein (n=1), portal vein (n=1) (Figure 6), azygous (n=1) (Figure 6), and hemiazygos vein (n=1) (Figure 6), posterior intercostal vein (n=1) (Figure 3), and renal parenchyma (n=1). One patient with acute myocardial infarction and abdominal aortic aneurysm demonstrated DCLS exclusively within the aneurysmal segment of abdominal aorta without involving venous structures or solid organs (Figure 5).

Among the 21 patients, 6 (28.5%) had cardiac arrest within 24 hours, all of which occurred within 2 hours of their CT examinations. Among these 6 patients, 3 had cardiac arrest within 1 hour. Patients with DCLS in right atrium had highest rate of cardiac arrest within 2 hours (80%, 4 of 5), followed by those with liver parenchyma involvement (71.4%, 5 of 7). On the other hand, patients with DCLS in hepatic vein and IVC had a cardiac arrest within 2 hours in less than 40% of cases (Table 1). Statistical analysis reveals that the occurrence of cardiac arrest within 2 hours is significantly higher in patients with DCLS in right atrium (p=0.02, odds ratio = 21.6) and liver parenchyma (p=0.01, odds ratio = 24.8) (Table 2). Among the 21 patients, 8 (38.1%) experienced in-hospital mortality which was higher in patients with DCLS in liver (57.1%, 4 of 7), followed by other vessels (50%). DCLS in IVC was least frequently associated with in-hospital mortality, observed in 36.8% of patients (Table 1). However, these differences did not establish statistical significance ($p > 0.05$) (Table 2).

The mean number of involved vessels or organs per patient was 3.3±2.4 (range 1-13). Patients who experienced cardiac arrest within 2 hours exhibit a higher mean (5.7±2.7) compared to those who did not experience cardiac arrest (2.7±2.0). The total number of involved structures (p=0.01) and the number of "common" structures (p=0.001) are significantly higher in patients with cardiac arrest within 2 hours, while the number of "uncommon" structures demonstrate no statistical significance. The total number of involved structures is higher in patients who died during the same hospital stay (4.3±2.7) compared to those who survived (3.1±2.2), although this difference is statistically insignificant (Table 3).

Table 1 Frequencies of implicated structures, cardiac arrest within 2 hours and In-hospital mortality.

DCLS (Total n=21)	**Cardiac arrest within 2 hours (n=6, 28.5%)**		**In-hospital mortality (n=8, 38.1%)**	
	Number	**Percentage (%)**	**Number**	**Percentage (%)**
IVC (n=19, 90.5%)	6	31.5	7	36.8
Hepatic vein (n=17, 81.0%)	6	35.5	7	41.2
Liver (n=7, 33.3%)	5	71.4	4	57.1
Right atrium (n=5, 23.8%)	4	80	2	40
"Uncommon" structures (n= 10, 47.6%)	4	40	5	50

Table 2 Statistical significance of the association between presence of DCLS in "common" structures and clinical data

DCLS in "common" structures	Cardiac arrest within 2 hours (n=6)		In-hospital mortality (n=8)	
	p-value	Odds Ratio (Confidence interval)	p-value	Odds Ratio (Confidence interval)
IVC	0.91	*	0.99	0.60 (0.01, 52.3)
Hepatic vein	0.43	*	0.98	2.03 (0.13,125.7)
Liver	0.01	24.8 (1.73, 1624.9)	0.43	3.13 (0.35, 33.0)
Right atrium	0.02	21.6 (1.38,1452.5)	0.99	1.11 (0.07, 12.9)

* Odds ratios cannot be calculated for some variables that had cell counts of 0

Table 3 Numbers of implicated vessels and organs and their statistical significance in association with clinical data.

Number of involved vessels and organs	Mean (SD)	Cardiac arrest within 2 hours (n=6)			In-hospital mortality (n=8)		
		Yes Mean(SD)	No Mean(SD)	p-value	Yes Mean(SD)	No Mean(SD)	p-value
Total	3.3 (2.4)	5.7 (2.0)	2.7 (2.0)	0.01	4.3 (2.7)	3.7 (2.2)	0.95
Common	2.3 (1.2)	3.5 (0.9)	1.8 (0.9)	0.001	2.5 (1.3)	2.2(1.1)	0.58
Uncommon	1.3 (2.0)	2.3 (2.6)	0.9 (1.6)	0.13	1.9 (2.4)	0.9 (1.7)	0.88

Mean (SD): mean value (Standard deviation)

The mean shock index was 1.08±0.50 (range 0.5-2.6), with shock index of 0.9 or higher observed in 66.6% (12 of 18) of patients. However, no statistically significant differences were observed in association with CT findings. The correlation coefficient between the total number of involved structures and shock index did not attain statistical significance ($p = 0.47$).

4. Discussion

DCLS is a rarely reported sign but significant CT finding associated with severely compromised cardiac function and cardiac arrest, conditions that are seldom evaluated using imaging studies (8,9). Hemodynamic changes resulting from heart failure leads to blood stasis in dependent organs, which is visually manifested by pooling and layering of contrast agent on imaging studies (5). Our investigation also reveals that DCLS is rarely observed, considering the substantial number of CECT of chest and abdomen conducted over a 14-year period at our institution. Among patients exhibiting DCLS on CT, a notable proportion had cardiac arrest within 2 hours, yet it is noteworthy that a larger number did not; this data was previously undisclosed as prior investigations encompassed only the patients who had cardiac arrest as their study population (1-11). Lee et al. termed this CT sign "contrast agent pooling sign" and reported an 85.94% accuracy in predicting cardiac arrest within 1 hour (11). The heightened incidence of impending cardiac arrest in the study may have stemmed from its inclusion of patients from emergency department and had cardiac arrest. Importantly, our study represents the first instance of investigating radiologic findings of DCLS in patients who underwent CECT, irrespective of cardiac arrest or dysfunction, with systematic analysis of their statistical significance concerning clinical outcomes.

The frequent involvement of structures such as IVC and hepatic vein is remarkable; however, it does not exhibit statistical significance in relation to cardiac arrest or in-hospital mortality. Yeh et al. proposed that reflux of contrast agent into IVC or hepatic veins on CT serves as a specific yet insensitive sign of right heart disease, especially when contrast injection rates are lower. This relevance decreases when higher injection rates are used, which is important to recognize because many institutions increasingly apply high-injection-rate CT (12). A patient with underlying pancreatic cancer of our study was hemodynamically stable, still DCLS of IVC and hepatic vein is demonstrated on CT.

Given that a significant portion of CT in this study employed high injection rates, the clinical significance of DCLS within IVC and hepatic vein is doubtful and warrants further investigation.

Our study outcome indicates that DCLS involving the liver and right atrium is significantly related to impending cardiac arrest. Moreover, both the total number of involved vascular structures and organs, as well as the number of "common" structures affected, exhibited statistical significance in association with impending cardiac arrest. These results have not been reported previously.

DCLS encompasses various vascular structures and abdominal solid organs, predominantly involving venous structures and right-sided abdominal organs such as liver and right kidney. The precise hemodynamic mechanism of this unique CT sign in patients with impending cardiac arrest remains incompletely understood. However, it is theorized that due to the loss of the normal pressure gradient between arteriovenous and venovenous structures, the distribution of contrast agent is influenced partly by manually applied pressure and partly by the hydrostatic pressure exerted by the contrast agent. This phenomenon leads to the accumulation of contrast material in the superior and inferior vena cava, along with the dependent parts of the body including organs and vessels (1). The absence of blood flow in the vascular structures causes the contrast agent to accumulate in the dependent areas due to its greater density compared to blood (3).

Among our study population, two patients demonstrated DCLS in the aorta. A weakly pumping heart was suggested as the underlying hemodynamic cause of contrast layering in the aorta (1). One of the patients exhibited DCLS solely within the aneurysmal segment of the abdominal aorta, without involving venous structures or solid organs. This patient showed high shock index at the time of CT, and experienced cardiac arrest 30 hours later which was followed by death. This unique case that demonstrated DCLS only in the aorta is the first to be reported. Underlying mechanism is presumed to be related to either patient's low blood pressure which made blood flow slow down or partial filling of contrast agent on arterial phase within the large area of aneurysmal segment of aorta, although it requires further investigation. We also observed DCLS in the portal vein in a patient with coronary artery disease. The contrast agent within portal vein is likely originated from right lobe of liver in which contrast was pooled, by reverse flow through sinusoid communication. Still, the reason for the regurgitation of contrast material into portal vein which is located more anteriorly than IVC and right lobe of liver, remains unknown (1).

We intended to explore the correlation between DCLS and left ventricular ejection fraction (LVEF) as assessed by echocardiography. However, due to inconsistent timing between LVEF assessment and CT examination, the collected data lacked relevance. Conducting a prospective study that synchronizes LVEF assessment with CT would elucidate the clinical significance of DCLS more effectively.

This study has certain limitations. First, this is retrospective study in which the study population was identified through specific keyword searches within CT interpretation reports. Consequently, cases with layering contrast findings not described with the specific keywords may have been overlooked, as this distinctive CT finding is not yet widely recognized. Second, the sample size is relatively small, which may result in limited statistical power for the analysis. Third, a control group without presence of DCLS was not included in this study. Had the enormous number of the patients without DCLS been included in control group, statistical significance may not be achieved. Fourth, the method of calculating the number of involved vessels was determined based on consensus rather than reflecting the actual count of involved vessels. Fifth, the true clinical benefit of DCSL cannot be conclusively demonstrated due to the limitations of this retrospective study, including its small cohort size.

5. Conclusion

The presence of DCLS in the right atrium and liver, as well as the larger number of involved structures, are significantly associated with impending cardiac arrest. Thus, it may offer additional insights for both radiologists and clinicians and aid in prompt initiation of resuscitative interventions before the onset of cardiac arrest. Nevertheless, larger prospective studies are warranted to validate the clinical relevance of DCLS across various vascular structures and organs.

Abbreviations

DCLS: Dependent Contrast Layering Sign

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work is retrospective study and does not contain any studies performed on animals/humans subjects by any of the authors for the purpose of this research.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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