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Review

Delayed Enhancement in Cardiac CT: A Potential Alternative to Cardiac MRI? Technical Updates and Clinical Considerations

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Abstract: Despite cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) being the current gold standard for non-invasive myocardial characterization and fibrosis quantification, its accessibility is limited, particularly in acute settings and in certain patient populations with contraindications to magnetic resonance imaging. Late iodine enhancement (LIE) in computed tomography (CT) imaging has emerged as a potential alternative, capitalizing on the similarities in the contrast kinetics between gadolinium and iodinated contrast agents. Studies have investigated LIE-CT's effectiveness in myocardial infarction (MI) detection, revealing promising outcomes alongside some disparities compared to LGE-CMR. LIE-CT also proves beneficial in diagnosing non-ischemic heart diseases such as myocarditis, hypertrophic cardiomyopathy, and sarcoidosis. While LIE-CT demonstrates good accuracy in detecting certain myocardial pathologies, including acute MI and chronic fibrotic changes, it has limitations, such as the inability to detect diffuse myocardial enhancement. Nonetheless, thanks to the availability of optimized protocols with minimal radiation doses and contrast medium administration, integrating LIE-CT into cardiac CT protocols could enhance its clinical utility, particularly in acute settings, providing valuable prognostic and management insights across a spectrum of cardiac ischemic and non-ischemic conditions.

Keywords: cardiac imaging techniques; cardiac computed tomography; delayed enhancement; late enhancement; myocardial scar; cardiac magnetic resonance imaging; late iodine enhancement; heart diseases; diagnostic imaging; contrast media

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1. Introduction

In current clinical practice, cardiac magnetic resonance (CMR) utilizing late gadolinium enhancement (LGE) is considered the gold standard for the non-invasive characterization of the myocardial structure and assessment of myocardial infarction (MI). This technique helps to identify characteristic patterns of both ischemic and non-ischemic scars, providing insights into the underlying causes of myocardial damage [1,2]. Beyond structural characterization, LGE holds significant value in risk stratification, acting as an indicator of unfavorable cardiovascular consequences. The magnitude of LGE reflects the deposition of contrast media in the interstitial space, which increases in cases of myocardial fibrosis and is associated with adverse ventricular remodeling, ventricular arrhythmias, a heightened heart failure risk, and an increased likelihood of sudden cardiac death. Despite its unquestionable clinical significance, CMR is not universally accessible, particularly in acute medical settings. Moreover, its application faces limitations in certain patient populations, such as those who experience claustrophobia or have a low tolerance for extended scanning

times, or patients with implanted cardiac devices. While newer devices are considered MR-conditional, the presence of cardioverter defibrillators or pacemakers can still impede the assessment of LGE images, primarily due to artifacts associated with the generators [3].

It has already been highlighted in the literature that iodinated contrast media exhibit similar kinetics to gadolinium chelates, resulting in delayed wash-out in the myocardial scar compared to the normal myocardium. The disparity in the iodine concentrations between scarred and non-scarred regions could be seen through late iodine enhancement (LIE) areas identified with a 10–15 min delayed computed tomography (CT) scan [4]. Numerous studies have thus explored the potential of cardiac CT (CCT) in detecting MI by examining LIE to identify myocardial scar tissue. These studies have yielded some promising results, while others have been less conclusive or have shown discordant findings [5–7].

The purpose of this review is to examine the existing literature to extend and analyze the main work conducted thus far about the potential diagnostic and prognostic value of LIE-CT in ischemic and non-ischemic heart diseases.

2. Protocol

The acquisition protocol of LIE-CT can vary depending on the specific clinical practice or study conducted, as well as the availability of dual-energy technology. Generally, whether involving stress CT perfusion or coronary CT angiography, the acquisition of the LIE image typically occurs 10 min after intravenous contrast medium administration, with or without minimal additional contrast medium injection [8].

Due to concerns related to radiation exposure, practitioners generally conduct the LIE-CT scan using a reduced tube voltage or tube current, or a combination of both. Although a lower tube voltage helps in enhancing the image contrast, it simultaneously leads to increased image noise, consequently impacting both the contrast-to-noise ratio (CNR) and the signal-to-noise ratio (SNR) [9,10]. This constraint has been a crucial consideration in the utilization of LIE-CT. Conventional single-energy CT imaging is prone to technical challenges arising from the polychromatic nature of X-rays, including artifacts like blooming and beam hardening. The introduction of dual-energy CT (DECT) has alleviated some of these technical limitations [11]. Hence, studies employing dual-energy technology have yielded the most favorable outcomes. For instance, among the protocols proposed, in a study by Palmisano et al., CT scans were performed using a second-generation dual-source scanner with a triphasic bolus injection of iodinated contrast medium. The injection protocol included 75 mL of contrast medium, followed by 40 mL of a mixed solution (25% contrast medium and 75% saline) and an additional 40 mL of pure saline. The choice between prospective electrocardiogram-triggering or retrospective gating depended on the patient's pulse rate. Following the CT angiography acquisition, an additional dose of contrast medium was administered promptly, with the goal of reaching a total iodine dose of 0.6 g per kilogram of body weight. The LIE scan was acquired 10 min later, using a low-voltage axial prospective scan synchronized to 75% of the cardiac cycle phase. The scan parameters included kV adjusted based on the patient's body mass index (body mass index $< 30 = 80$ kV, body mass index $\geq 30 = 100$ kV), a rotation time of 0.28 s, detector collimation of 128 mm $\times$ 0.6 mm, a matrix size of 512 $\times$ 512, and a display field of view limited to the heart [6]. Another example of protocol implementation comes from Yasutoshi Ohta et al., who conducted a study aimed at evaluating the diagnostic performance of DECT-LIE in identifying and categorizing myocardial scars in heart failure patients, using CMR-LGE as the gold-standard reference. They employed a rapid kilovolt peak-switching 64-detector row DECT scanner. Following coronary CT angiography, an additional infusion of 0.5 mL/kg contrast media was administered for 60 s. Subsequently, a CT scan was conducted after 7–8 min with the following parameters: a tube voltage ranging from 80 to 140 kVp; rapid kilovolt peak switching; a tube current set at 600 mA; a rotation time of 0.35 ms; collimation of 0.625 mm; prospective electrocardiographically gated axial scanning at the mid-diastolic phase; a display field of view measuring 180 mm $\times$ 180 mm; and a matrix of 512 $\times$ 512. For the quantification of the iodine density in a voxel, a two-material

decomposition technique was employed, utilizing water as the foundational material, with the iodine density expressed as 100 μg/cm^3 on iodine density images [12]. Additionally, to enhance the image quality in iodine density imaging, they applied an adaptive statistical iterative reconstruction intensity of 80%, based on prior research findings. Indeed, a study by Kishimoto J et al. demonstrated that employing an adaptive statistical iterative reconstruction intensity between 80% and 100% in LIE images could improve the image quality without compromising the signal integrity, thus maximizing the accuracy in determining the transmural extent in the infarcted myocardium [13].

In this regard, a study evaluated the image quality and diagnostic effectiveness of LIE-CT with knowledge-based iterative model reconstruction (IMR) for MI detection, comparing it with LGE-CMR. It confirmed that the use of IMR significantly improves the image quality and diagnostic accuracy of LIE-CT. However, despite this, they also emphasized that LIE-CT cannot completely replace LGE-CMR, as it lacked precision in accurately assessing the extent of MI compared to the latter [14]. Nonetheless, further technological advancements could overcome these limitations in the future and achieve additional incremental improvements in LIE-CT.

3. Ischemic Heart Disease

3.1. Pathogenesis and General Principles of LIE

Acute MI is primarily caused by the sudden disruption of an unstable coronary atherosclerotic plaque and acute intracoronary thrombosis [15]. Cellular changes begin within minutes of ischemia onset, with temporary effects lasting up to 20 min, depending on the collateral circulation robustness. The gross pathological effects of MI, including edema, inflammation, necrosis, and hemorrhage, appear after approximately 4 h, followed by the infiltration of neutrophils and myocyte changes after 12 h. Muscle fiber disintegration and debris removal occur within 3 days, leading to scarring characterized by fibrous tissue deposition lasting up to 2 months. MI affects the left ventricle, impacting heart contraction and eventually resulting in a reduced ejection fraction, with initial myocardial "stunning", followed by a hibernated myocardium in prolonged ischemia. If myocardial reperfusion does not occur within 6 h, MI with cellular necrosis develops. At a macroscopic level, the left ventricle can exhibit a more rounded and enlarged shape, known as ventricular remodeling. The ischemic process progresses in a wave-like manner from the endocardium to the epicardium and may extend throughout the entire thickness of the myocardial wall, becoming transmural [16]. Ventricular remodeling may occur, leading to a rounder, dilated left ventricle shape, and transmural MI can involve the entire myocardial wall, potentially leading to rupture, hemopericardium, tamponade, or aneurysm development.

The mechanism of myocardial hyper- and hypo-enhancement in injured myocardial areas after iodinated contrast medium administration is similar to that of LGE-CMR, since both gadolinium and iodinated contrast agents exhibit similar kinetics, enabling comparable myocardial characterization through CMR and CCT at delayed enhanced imaging [17]. In normal conditions, sarcolemmal membranes serve to exclude iodine from the intracellular space. After the injury and myocyte necrosis, due to membrane dysfunction, iodine molecules are able to penetrate the cell. Since about 75% of myocardial volume is intracellular, this leads to significant increases in the distribution volume, resulting in a pronounced hyper-enhancement compared to non-injured myocytes. Furthermore, in cases of acute MI, imaging performed immediately after contrast medium injection often reveals distinct areas of hypo-enhancement within the infarct core (attributed to the diminished delivery of the contrast medium to the infarcted regions, primarily due to microvascular obstruction [4]), while later acquisition (approximately 10 to 15 min after contrast medium administration) typically reveals the presence of hyper-enhanced zones, which accurately correspond to the extent of the necrotic core. Conversely, hyper-enhancement in healed MI or collagenous scar is attributed to contrast media accumulation in the interstitial space between collagen fibers, leading to an increased volume of distribution relative to tightly packed myocytes [18,19].

3.2. LIE-CT versus LGE-CMR

Numerous studies support the growing prognostic significance of delayed enhancement as a surrogate marker of fibrosis across various etiologies. In comparison to LIE-CT, LGE-CMR exhibits a superior contrast resolution, attributed in part to the use of specific pulse sequences that facilitate the differentiation between the normal and infarcted myocardium. Scarred areas assessed with single-energy CT in stable patients are often vaguely defined, portraying regions with unclear discrimination between the myocardium and the left ventricular cavity [17]. Studies in the literature have revealed discrepant results when comparing LIE-CT and LGE-CMR. For example, a study by Palmisano et al., aimed at assessing the diagnostic performance of LIE-CT compared to LGE-CMR, yielded promising results. The study showed a stronger correlation between the scar tissue burdens measured by LIE-CT and LGE-CMR for readers with more experience (correlation coefficients of 0.95 and 0.80, respectively; p-value < 0.001). In cases of ischemic cardiomyopathy, there was perfect agreement (100%) between both imaging techniques in identifying the presence or absence of scar tissue and its pattern, regardless of the reader's experience level. This strong agreement between imaging techniques fell to 90% and 75% for non-ischemic cardiomyopathy scars, highlighting the importance of reader experience in interpreting scans for non-ischemic heart diseases [6]. In another study by Tanabe et al., the researchers assessed the image quality and diagnostic performance of LIE-CT using knowledge-based IMR in detecting MI, comparing LIE-CT with LGE-CMR. The study evaluated the SNR, CNR, sensitivity, specificity, image quality scores, and diagnostic performance of the imaging techniques. Among 35 patients, LIE-CT with IMR demonstrated the highest image quality and sensitivity, significantly improving the diagnostic performance ($p < 0.05$) [14]. In reperfused acute MI, Jacquier et al. demonstrated a strong correlation of delayed enhancement between LIE-CT and LGE-CMR, with better image quality at 5 min compared to 10 min imaging [20].

3.3. LIE in Acute MI versus Chronic MI

In cases of acute MI, in which membrane disruption leads to extracellular volume expansion and a subsequent increase in the distribution of iodinated contrast medium in a way similar to gadolinium, LIE-CT has demonstrated its efficacy in assessing the infarct size and myocardial viability, as evidenced by various studies [17]. In individuals who received a primary percutaneous coronary intervention for ST segment elevation acute MI, Rodriguez-Granillo et al. found an association between the LIE-CT, thrombolysis in MI, the myocardial perfusion grade following stent placement, and the electrocardiogram ST segment resolution [21]. In another study conducted by Watabe et al., 92 patients with acute MI underwent CCT immediately after a percutaneous coronary intervention. In this cohort, the heterogeneous enhancement detected by CCT after the percutaneous coronary intervention showed promise in predicting microvascular obstruction and left ventricular remodeling [22]. Furthermore, LIE-CT may decrease from the acute to chronic phases of MI due to the reduction in the surrounding edema [23]. Despite the initially promising results in the acute setting, among the major limitations, most clinical LIE-CT studies have used small sample sizes.

In case of chronic MI, the literature results are discordant. In the study conducted by Bettencourt et al. using LGE-CMR as the reference standard, LIE-CT identified only 9 out of 17 ischemic scars, demonstrating high specificity (98%) but poor sensitivity (53%) among chronic MI patients [24]. This weakness in LIE-CT's performance in chronic MI cases may be attributed to various factors, including the relatively poor contrast resolution compared to LGE-CMR and the involvement of different physio-pathological mechanisms in the extracellular expansion of acute and chronic MI. On the other hand, in a study conducted by Wichmann et al., the effectiveness of dual-energy LIE-CT, selective myocardial iodine mapping, and 3-tesla CMR in detecting chronic MI was compared. Dual-energy LIE-CT showed high sensitivity, specificity, and accuracy in identifying chronic MI, with the best image quality score and infarct size correlation found at certain settings. However, the

iodine distribution maps were less accurate, with sensitivity of 52%, specificity of 88%, and accuracy of 81%, overestimating transmural scars [25].

4. Non-Ischemic Heart Diseases

4.1. Myocarditis

Myocarditis, or inflammation of the myocardium, is primarily associated with various viral infections [26]. For the diagnosis of acute myocarditis, according to the Lake Louis criteria, LGE with a non-ischemic distribution pattern is often required. The most frequent LGE distribution consists of patchy, non-contiguous lesions localized in the subepicardial or intramural layers of the lateral or septal walls [27]. The use of CCT is generally restricted in the assessment of suspected myocarditis, primarily serving to identify alternative etiologies of acute chest pain, such as coronary artery disease and acute pericarditis [28–30]. However, CCT was helpful in diagnosing myocardial inflammation [31] and in the assessment of global and regional wall motion abnormalities throughout the cardiac cycle [32]. In fact, LIE-CT has demonstrated high sensitivity and specificity in diagnosing acute myocarditis compared to LGE-CMR [32]. Specifically, dual-source CT has demonstrated encouraging outcomes utilizing the spectral mode, which facilitates the differentiation of tissue components according to their distinct attenuation curves [31,33]. Bouleti et al. aimed to compare LIE on spectral CT with the reference LGE-CMR in acute myocarditis, finding the overall accuracy of spectral CT to be 95% [34]. Baudry et. al. reported that spectral imaging could reveal LIE in the subepicardial layer of the myocardial wall, indicating edema, hyperemia, and capillary leaks consistent with myopericarditis. The accumulation of iodine-based contrast medium in inflamed tissue reflects increased uptake associated with cellular membrane permeability, suggesting tissue injury in active myocarditis [35]. Furthermore, Hernández-Martos et al. reported a case of myocarditis associated with immune checkpoint inhibitor therapy diagnosed using spectral CT technology, reaffirming the utility of DECT in identifying myocardial inflammation, particularly in cases where CMR may not be feasible due to patient instability or contraindications [36]. The concept of quadruple-rule-out CT angiography has been recently introduced, combining the triple-rule-out CT angiography approach (based on the simultaneous evaluation of the coronary arteries, aorta, and pulmonary arteries with a single CT acquisition) with DECT in cases of acute chest pain. Studies have shown that quadruple-rule-out CT angiography offers promising results for myocarditis evaluation, with sensitivity, specificity, and positive and negative predictive values of 69%, 100%, 100%, and 94%, respectively. This performance suggests its potential to effectively assess myocardial perfusion deficits. Consequently, quadruple-rule-out CT angiography expands the diagnostic capabilities of the standard triple-rule-out method for myocarditis assessment [37]. In a recent study by Palmisano et al., the diagnostic value of a comprehensive CT protocol combining angiographic and LIE-CT scans was investigated in troponin-positive acute chest pain patients. Among the 84 participants, triple-rule-out CT and LIE-CT were performed. Among 42 participants without obstructive coronary disease, LIE-CT identified myocarditis in 52%, takotsubo cardiomyopathy in 10%, and other specific diagnoses in 19% of cases. LIE-CT demonstrated the mild underestimation of the scar extension compared to LGE-CMR. However, it showed a good correlation (rho = 0.902) with extracellular volume fraction measured by CMR [38]. These findings highlight the potential of a comprehensive CT protocol, including LIE scans, to accurately diagnose myocarditis and other cardiac conditions in troponin-positive acute chest pain patients, demonstrating promising results in providing valuable information for clinical management.

4.2. Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a prevalent genetic heart condition distinguished by left ventricular hypertrophy without any other systemic or cardiac ailment capable of inducing a similar level of hypertrophy. The evaluation of myocardial fibrosis in HCM is crucial for risk stratification and prognosis prediction. The guidelines from the

American Heart Association and the American College of Cardiology for the diagnosis and treatment of patients with HCM emphasized the incorporation of extensive LGE as a risk factor in stratifying the risk of sudden cardiac death. They also suggested using LGE as a criterion to assist in selecting patients for implantable cardioverter–defibrillator placement [39]. The basal to mid-interventricular septum (especially at the right ventricular insertion site) and anterior wall emerged as the most frequent sites for LGE [40]. The effectiveness and reliability of LIE-CT in assessing coronary artery disease and myocardial fibrosis in patients with HCM have been explored by Lei Zhao et al. They compared LIE-CT's performance with that of CMR imaging and coronary angiography. Their findings unveiled a robust correlation between wall thickness measurements obtained from LIE-CT and those from CMR (r = 0.91). Furthermore, LIE-CT and LGE-CMR exhibited significant concordance in identifying myocardial fibrosis, with the typical pattern (patchy intramyocardial fibrosis at the right ventricular insertion site) [41]. This study showed the potential of LIE-CT as a robust alternative to LGE-CMR in evaluating myocardial fibrosis in HCM patients, especially those with contraindications to CMR imaging. The main limitations concerned diffuse myocardial LIE, which was not detected by CT due to poor contrast between the enhanced myocardium and normal myocardium.

4.3. Mitral Valve Prolapse and Mitral–Annulus Disjunction

Malignant arrhythmias can arise from myocardial fibrosis secondary to various conditions, including valvular anomalies. Among these, mitral–annulus disjunction (MAD) stands out, characterized by the atrial displacement of the posterior mitral valve leaflet hinge point [42]. This anomaly may present independently or, more commonly, in conjunction with mitral valve prolapse. There is speculation that MAD might precede mitral valve prolapse, yet the precise relationship between the two remains poorly understood. MAD, therefore, may be linked to ventricular arrhythmias, ranging from frequent premature ventricular contractions to cardiac arrest. One plausible physiological mechanism hypothesized is that the anatomical anomaly induces mechanical stress and myocardial stretching on the infero-basal wall and papillary muscle fibers, potentially leading to myocardial hypertrophy and scarring, ultimately serving as an arrhythmogenic focus [43]. In a study by Boccalini et al., myocardial fibrosis of the lateral wall, identified through DECT, was reported in a patient with mitral valve prolapse and MAD [44]. In this case report, the patient presented to the emergency department, where magnetic resonance imaging was not available. Therefore, a CCT scan was performed, consisting of two acquisitions with retrospective electrocardiogram gating. The first acquisition was performed in the arterial phase (with no evidence of coronary stenosis and plaques), and the second, for LIE assessment, was conducted 10 min after contrast medium administration. The myocardium of the left ventricle displayed a uniform thickness, except for the mid-ventricular lateral wall, which exhibited increased LIE compared to the rest of the myocardium. Additionally, the prolapsed appearance of the mitral valve was observed, along with a significant space between the mitral valve annulus and the myocardium of the left ventricle. In this case, LIE proved to be crucial in assessing the presence of fibrosis in the papillary muscles and lateral wall.

Although CT could be considered a potentially valuable imaging modality for the assessment of the mitral valve and valvular apparatus in any plane and in three dimensions, careful consideration of the risks and benefits is necessary for each patient. This is because obtaining such imaging requires a retrospectively electrocardiogram-gated acquisition (with its associated radiation dose) and contrast media administration.

4.4. Sarcoidosis

Some studies have investigated the potential role of LIE-CT in sarcoidosis, a systemic granulomatous disease of unknown etiology with cardiac involvement, encountered in only 2–5% of patients [45]. In these patients, the existence and extension of LGE have been documented to forecast unfavorable cardiac outcomes [46]. Typically, it exhibits a diverse

range of patterns, commonly involving the mid-wall and/or epicardium while sparing the sub-endocardium at the base of the heart, particularly affecting the septum and lateral wall [47]. A study conducted by Aikawa et al. aimed to assess the diagnostic value of LIE-CT for cardiac sarcoidosis in patients with and without implantable devices compared to LGE-CMR. A cohort of 24 patients underwent analysis, demonstrating high interobserver agreement in visually identifying segments with increased signal intensity on LIE-CT. This agreement was consistent regardless of the presence or absence of implantable devices. Additionally, comparisons between LIE-CT and LGE-CMR revealed good correlations in quantifying the extent of the hyper-enhanced myocardium, with correlation coefficients of 0.96 for the per-patient analysis and 0.83 for the per-segment analysis (both statistically significant, $p < 0.001$). LIE-CT demonstrated sensitivity of 94% and specificity of 33% in diagnosing cardiac sarcoidosis [48]. However, despite these promising results, it is important to consider the limited sample size of the study. Additionally, in a case report by Gregor Muth, a patient with suspected cardiac sarcoidosis and an implanted cardioverter–defibrillator underwent a DECT examination to assess LIE, as CMR was contraindicated. DECT images were acquired immediately after contrast media injection and repeated after 10 min. First-pass images revealed myocardial thinning in the apical and basal septum, while LIE images showed hyper-enhancement in corresponding regions, as well as patchy, subepicardial areas in the apical and lateral walls, characteristic of cardiac sarcoidosis [49]. This case underscores the utility of CCT as a viable alternative in patients with metallic implants that are not magnetic resonance imaging-conditional.

See Figure 1 as an example of LIE-CT in a patient with both ischemic and non-ischemic enhancement due to a stenotic right coronary artery and cardiac sarcoidosis.

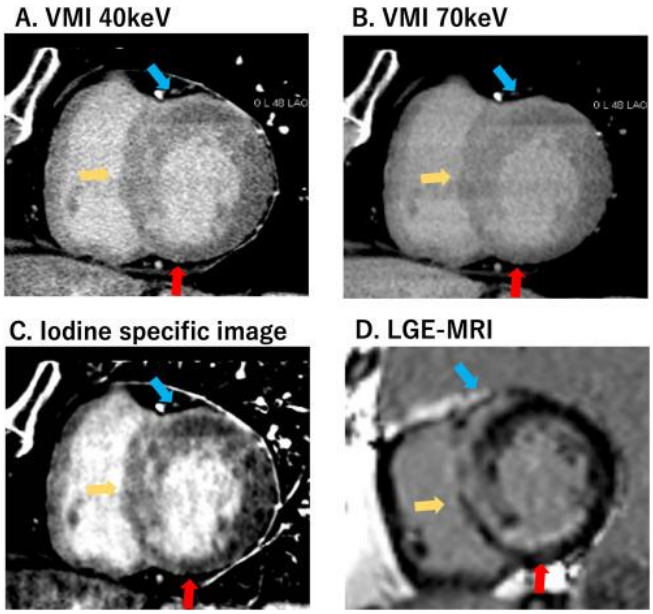

Figure 1. LIE-CT imaging using DECT in a patient presenting with a blocked right coronary artery and cardiac sarcoidosis. The myocardial LIE-CT image indicates subendocardial infarction in the inferior wall (red arrow), striated non-ischemic enhancement (yellow arrow) in the mid-wall of the interventricular septum, and non-ischemic enhancement (blue arrow) in the epicardium of the anterior wall. The lesion contrast appears higher in the virtual monoenergetic images of 40 keV (**A**) and the iodine-specific images (**C**) compared to the 70 keV image (**B**). These findings are consistent with those observed in LGE-CMR (**D**). Modified from Oyama-Manabe et al. [50].

4.5. Amyloidosis

Amyloidosis encompasses a spectrum of rare systemic disorders characterized by the deposition of insoluble fibrillar amyloid proteins in extracellular spaces. The cardiac involvement is observed in approximately half of patients with the light-chain amyloidosis

subtype, serving as an adverse prognostic indicator [51,52]. CMR represents a potent noninvasive tool for the detection of cardiac amyloidosis (CA): amyloid infiltration leads to the expansion of extracellular spaces and alters the gadolinium distribution kinetics, resulting in contrast medium accumulation within the myocardium. Consequently, numerous studies have described a distinctive global subendocardial or diffuse transmural pattern on the LGE-CMR sequence [53,54]. In a pilot study led by Jean-François Deux et al., LIE-CCT was utilized to assess CA, involving thirteen patients and 11 controls. The "first-pass" contrast-enhanced acquisition was performed after the injection of 1.5 mL/kg of contrast medium, and the LIE acquisition was conducted 5 min after injection using the same parameters. They performed a qualitative analysis of the images (anonymously reviewed by two authors, who evaluated the left ventricle, right ventricle, and atria, assessing enhancement abnormalities in the first-pass and LIE images and resulting in a final global score) and a quantitative analysis (calculating the myocardial attenuation, SNR, CNR between the blood pool and myocardium, and relative attenuation index, defined as the variation in myocardial attenuation between delayed and first-pass acquisitions). The study revealed two false negatives (15%) and three false positives (27%) on qualitative analysis. The SNR of the myocardium was significantly lower in CA patients during the first-pass and higher during the LIE acquisition compared to the controls. Myocardial attenuation was also higher in CA patients during LIE acquisition [55]. Despite the small sample size, the study suggests the potential of LIE-CT even in amyloidosis, particularly for quantitative parameters, as the qualitative analysis emerged as less accurate in detecting CA. However, larger and more robust studies are needed to validate these initial findings, considering the small sample size of patients included in this study.

4.6. Ventricular Aneurysm

Aneurysms and pseudoaneurysms of the left ventricle typically arise as complications of transmural MI and often present with similar clinical features. It is crucial to distinguish between these two entities, as pseudoaneurysms carry a 30–45% risk of rupture compared to true aneurysms [56]. If echocardiography cannot definitively rule out a pseudoaneurysm, according to the guidelines of the European Society of Cardiology, LGE-CMR is recommended, allowing the assessment of the morphology and kinetics of the left ventricular wall bulging and, most importantly, facilitating the identification of post-ischemic fibrotic changes in LGE images [57]. These changes can demonstrate continuity with the left ventricular wall in the case of true aneurysms or discontinuity in the case of pseudoaneurysms. In this context, a case report conducted by Samarjit Bisoyi et al. investigated the potential value of LIE-CT with DECT for the differential diagnosis of true versus false left ventricular aneurysms. LIE-CT iodine mapping and virtual monoenergetic imaging reconstructions at 70 kV revealed transmural iodine accumulation within the wall of an asymmetric apical bulge extending to the apex and the adjacent subendocardial portion of the interventricular septum, indicating myocardial scar tissue. This asymmetrical bulging likely resulted from apical remodeling due to midventricular hypertrophy and post-ischemic fibrotic changes, effectively excluding the diagnosis of pseudoaneurysm [56]. This case highlights the potential of CCT, when complemented by LIE imaging, as a comprehensive tool to assess coronary arteries and morphological changes in the myocardium. Particularly in complex cases with diagnostic uncertainties regarding a left ventricular aneurysm versus a pseudoaneurysm, it offers a convenient "one-stop-shop" solution.

Table 1 summarizes the main typical patterns of LIE in both ischemic and non-ischemic heart diseases and some of the key authors investigating the role of LIE-CT in these conditions, as reviewed in this study.

Table 1. The most typical distribution patterns of delayed enhancement in both ischemic and non-ischemic heart diseases and some of the key authors investigating the role of LIE-CT in these pathologies.

Pathology	Authors Investigating LIE-CT's Role	Typical Pattern
Myocardial infarction	Palmisano et al. [6] Rodriguez-Granillo et al. [17,21] Tanabe et al. [14] Jacquier et al. [20] Watabe et al. [22] Bettencourt et al. [24] Wichmann et al. [25]	Subendocardial, potentially progressing to transmural involvement, within coronary artery distribution.
Myocarditis	Meinel et al. [33] Terzian et al. [31] Bouleti et al. [34] Baudry et al. [35] Hernández-Martos et al. [36] Cetin et al. [37] Palmisano et al. [38]	Patchy, non-contiguous lesions localized in the subepicardial or intramural layers of the lateral or septal walls.
Hypertrophic cardiomyopathy	Zhao et al. [48]	Basal interventricular septum, particularly at the anterior and posterior right ventricular insertion points.
Sarcoidosis	Aikawa et al. [48] Muth et al. [49]	Variable, usually observed in the mid-wall and/or epicardium, with sparing of the sub-endocardium. At the base of the heart, specifically involving the septum and lateral wall.
Amyloidosis	Deux et al. [55]	Global subendocardial or diffuse transmural pattern.
Mitral valve prolapse and mitral–annulus disjunction	Boccalini et al. [44]	Papillary muscles and lateral wall.

5. Potential Indications, Advantages, and Disadvantages of LIE-CT in Clinical Practice

Given the promising results observed in the literature, we aim to provide readers with a concise overview of the main clinical applications, advantages, and disadvantages of LIE-CT. In the acute setting, LIE-CT scanning could be integrated into the protocol for patients presenting with chest pain at low to intermediate risk for acute coronary syndrome requiring coronary CT angiography. An LIE-CT scan, indeed, aims to identify potential cases of acute myocarditis, Takotsubo cardiomyopathy, and myocardial infarction with non-obstructed coronary arteries, as proposed by Palmisano et al. [38]. However, their study demonstrated the slight underestimation of the scar extension compared to LGE-CMR. Nonetheless, LIE-CT remains a valuable tool in acute scenarios. In non-acute settings, LIE-CT may assist in identifying myocardial scars in patients with contraindications to magnetic resonance imaging or those unable to undergo prolonged scans. This aids in diagnosis based on the location and distribution patterns of the myocardial enhancement in both ischemic and non-ischemic conditions, albeit with lower sensitivity compared to LGE-CMR.

Among the main advantages of LIE-CT are its wide availability (especially in the acute setting), short scan times with optimized protocols allowing for minimal contrast agent and ionizing radiation exposure, and the ability to perform the exam in patients with contraindications to CMR. Among the major disadvantages are the use of ionizing radiation, the unsuitability for patients with contraindications to iodinated contrast media,

the difficulty in detecting diffuse myocardial LIE due to poor contrast between the enhanced and normal myocardium, and the unavailability of dual-energy technology, which has shown the best results in the literature. The major advantages and disadvantages of LIE-CT are summarized in Table 2.

Table 2. The primary advantages and disadvantages of LIE-CT.

Advantages	Disadvantages
Wide availability	Use of ionizing radiation
Short scan times	Availability of dual-energy CT
Possibility of being utilized in acute settings, integrating it into triple-rule-out protocols	Difficulty in detecting diffuse myocardial LIE
Useful in patients with contraindications to magnetic resonance imaging or patients who cannot tolerate long scan times	Patients with contraindications to iodinated contrast media

6. Conclusions

Over the past decade, LGE-CMR has played a crucial role in various heart diseases due to its advantages, including the absence of ionizing radiation, a high contrast resolution, and robust clinical evidence supporting the prognostic value of myocardial late enhancement. Despite its appeal, LGE-CMR faces safety concerns, higher costs, and longer scanning times, which has prompted the exploration of alternatives, particularly LIE-CT. The potential for LIE-CT as an alternative is driven not only by the costs but also by the growing population with implantable cardiac devices, impacting the CMR image quality, and other CMR limitations, such as claustrophobia. Nowadays, several studies have demonstrated the high accuracy of LIE, in most cases overlapping with those shown by CMR, in the diagnosis and differentiation of myocardial pathologic entities, from acute MI to chronic fibrotic modifications, as well as in non-ischemic heart diseases. Thus, despite some evident limitations, such as its inability to detect diffuse myocardial delayed enhancement, LIE-CT should be included in CCT protocols. This is particularly useful in acute clinical settings where magnetic resonance imaging availability is not always guaranteed, providing valuable prognostic and management information with optimized protocols characterized by low radiation doses and minimal contrast medium administration. However, it is important to consider that, despite the overall promising results, only a few studies support these findings, and many of them have limitations. Indeed, several studies have a very limited number of patients or are presented as case reports, particularly in non-ischemic pathologies. Due to these reasons, we cannot yet assert that LIE-CT can fully replace LGE-MRI when the latter is available and feasible. Future studies with larger sample sizes are needed to validate these findings.

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Abbreviations

CA	cardiac amyloidosis
CCT	cardiac computed tomography
CMR	cardiac magnetic resonance
CNR	contrast-to-noise ratio
DECT	dual-energy computed tomography
HCM	hypertrophic cardiomyopathy
IMR	iterative model reconstruction
LGE	late gadolinium enhancement
LIE	late iodine enhancement
MI	myocardial infarction
SNR	signal-to-noise ratio

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