EDITORIAL
The visible radiologist: balancing clinical expertise and technological advances

IN-DEPTH REVIEW
Advanced cardiac imaging in preventing cardiac death in athletes

FULL RESEARCH ARTICLES
Computed tomography-quantitative evaluation (CT-QE) score of patients with COVID-19 pneumonia: a simple and practical approach
TVUS soft markers in clinically significant superficial endometriosis: an ultrasonographic, clinical, and laparoscopic correlation
Ultrasonographic findings of papillary breast lesions with clinical and pathological correlation
Missing the PECARN rule is related to head CT overuse in Mexican children with mild head trauma

BRIEF RESEARCH ARTICLE
Hippocampal MRI volumetry is associated with mild cognitive impairment in patients with HIV infection

CASE REPORT
CT and transthoracic echocardiographic findings of cardiac rhabdomyosarcoma in an adult: a case report

IMAGES IN RADIOLOGY
MRI findings of spinal intramedullary tuberculoma

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Advances in radiology and diagnostic imaging have revolutionized medicine1-4, especially technological advances that generate diagnostic images and reveal diagnoses in seconds to minutes, a process that previously took hours. In many cases, imaging has transformed medical practice, replacing clinical judgment.

The speed with which diagnostic images are obtained has contributed to the increased reliance on services provided by radiologists as imaging is often performed before patients are fully clinically evaluated. Often, the work of a radiologist is measured by the number of cases interpreted rather than the accuracy of the diagnoses that directly impact patient outcomes. However, this speedy turnover in imaging results has increased the reason that radiologists are seen as “interpreters” or “reporters” increasingly tethered to their workstations3 and the blue room. Despite their indispensable role in modern healthcare, radiologists face a dilemma regarding visibility3. Radiologists are often isolated in imaging areas, which has resulted in a loss of visibility on three critical fronts: the patient, the referring clinician, and the hospital or radiology unit authorities.

The radiologist visible to the patient: Radiologists play a pivotal role in patient care. They require technical prowess and a high level of clinical expertise4. In the clinical setting, referring clinicians frequently request examinations without providing a preliminary diagnosis or pertinent clinical data to guide the search or confirm a specific ailment. Consequently, it falls upon the radiologist to directly glean clinical information from patients. Additionally, radiologists should dedicate time to explain the imaging results to patients addressing their inquiries and concerns1-5. It is crucial to provide pertinent, easily understandable information devoid of ambiguity7,3,5. Radiologists should exercise caution, recognizing that they may not have access to the results of laboratory tests, pathological examinations, or other imaging studies; thus, they should provide information judiciously.

One of the pivotal roles of the radiologist is to safeguard the patient from excessive radiation exposure, guided by the ALARA principle, which stands for “As Low As Reasonably Achievable.” This principle dictates that radiologists recommend the most appropriate imaging study for the patient’s condition while considering the referring clinician’s input. Furthermore, it is imperative to ensure that patients are well-informed about the potential risks of radiation and contrast agents so that they can provide informed consent for any necessary procedures3.

The radiologist visible to the referring clinician: Radiology is an indispensable cornerstone of modern medicine. In contemporary medical practice, diagnoses are inconceivable without the integration of at least one imaging modality. Radiologists can actively engage with referring clinicians in several ways:1,3

- Provide a more accurate interpretation of images to understand the clinical case.
- Assist in the planning of diagnostic or interventional procedures.
- Offer a second opinion in complex cases.
These actions are facilitated by direct communication between radiologists and clinicians, organizing multidisciplinary meetings to discuss complex cases, attending academic meetings to update clinicians on the latest imaging advancements, and ensuring radiologists remain abreast of developments in medicine and surgery. It is worth noting that radiologists and clinicians may have distinct approaches or perspectives. Therefore, continuing medical education and fostering effective communication are vital to bridge these differences. Implementing systems that facilitate patient referral and information exchange related to clinical presentations, results from paraclinical studies, and suspected diagnoses is equally crucial.

The radiologist visible to hospital authorities: Radiologists are frequently perceived by hospital authorities as image interpreters. This narrow perspective can hinder collaboration and the exploration of opportunities for interdisciplinary growth, limiting the full potential of radiology departments in both educational and clinical contexts. A visible radiologist is not only a mere luxury but also an absolute necessity. Hospital authorities should tap into the capacities of radiologists not only to enhance patient care but also to ensure efficient and effective hospital management. Achieving this requires a focus on education, research, collaboration, and technological integration aimed at optimizing the use of hospital resources. There is an imperative need to promote their integration and recognition to ensure that the visibility of radiologists is meaningful and impactful. This change will empower them to play a more effective role in hospital operations and contribute to the broader mission of healthcare institutions.

The visible radiologist and artificial intelligence: Given the increasing impact of artificial intelligence, the future of radiology should not be framed as a human-versus-machine scenario. Nevertheless, historical instances of machines replacing humans in various domains are hard to forget. Today, it is paramount for radiologists to adapt and evolve, positioning themselves as central figures in patient care. Fostering the aspiration to become visible radiologists enhances their professional growth and holds promise in transforming patient care within clinical settings.

In conclusion, the visible radiologist must be a physician who actively engages in direct patient care and garners trust, respect, and recognition through the performance and interpretation of imaging studies. It is crucial to recognize that artificial intelligence can never fully supplant the human connection, reasoning, and empathy that radiologists offer. Understanding this dynamic is crucial in preparing for a future where visibility and collaboration are essential.

The visible radiologist and teleradiology: It is increasingly common for radiology practices and services to engage teleradiology services for interpreting imaging studies, primarily to reduce costs. Unfortunately, this practice has resulted in job losses for many radiologists. Regrettably, there are currently no established guidelines or regulations governing this practice. It is probable that these teleradiology services do not adhere to the fundamental standards required by certified hospitals, such as monitors meeting specified resolution and light intensity criteria. Furthermore, teleradiology may contribute to the diminishing visibility of radiologists.

The visible radiologist in training: Another significant challenge lies in developing the profile of the visible radiologist, starting with basic medical training and extending through radiology residency programs. Radiology residents represent the future of the specialty. Fostering the aspiration to become visible radiologists enhances their professional growth and holds promise in transforming patient care within clinical settings.

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Use of artificial intelligence for generating text. The author states that he did not use generative artificial intelligence in the preparation of this manuscript.
REFERENCES


Advanced cardiac imaging in preventing sudden cardiac death in athletes

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ABSTRACT

Competitive athletes are known to undergo physiological adaptations to meet the demands of rigorous training which can mimic pathological conditions, leading to an overlap between normal physiological changes and potentially life-threatening cardiac abnormalities. Sudden cardiac death (SCD) in athletes is a rare but devastating event, underscoring the need for early detection of cardiac abnormalities to prevent such tragedies. This review highlights the pivotal role of advanced cardiac imaging techniques, specifically cardiac magnetic resonance imaging (CMR) and coronary computed tomography angiography (CCTA), in the prevention of SCD in competitive athletes. CMR and CCTA offer non-invasive, comprehensive assessments of cardiac morphology and function, providing valuable insights into the athlete's heart. Various physiological adaptations observed in athletes' hearts will be presented, including left ventricular hypertrophy and right ventricular dilation, which can be mistaken for pathological conditions. The “grey zone” concept underscores the importance of advanced imaging in distinguishing between normal and potentially abnormal cardiac changes. For specific pathological conditions linked to SCD in athletes, CMR aids in accurate diagnosis by differentiating tissue characteristics and assessing late gadolinium enhancement (LGE) patterns. Additionally, CMR plays a critical role in identifying coronary artery anomalies, myocarditis, and coronary artery disease in athletes over 35 years old, enabling early intervention and treatment. The new Padua criteria will also be discussed, which incorporate tissue characterization and novel ECG criteria to diagnose arrhythmogenic cardiomyopathy more accurately. Collaborative efforts between sports medicine specialists, cardiologists, and radiologists are essential in establishing standardized protocols for responsible imaging use, ultimately enhancing the safety and well-being of competitive athletes.

Keywords: Athletes. Cardiac Imaging. Sudden cardiac death. Cardiac abnormalities. Imaging and athlete safety.

INTRODUCTION

According to the 2015 European Society of Cardiology (ESC) Guidelines, sudden cardiac death (SCD) is defined as an unforeseen and non-traumatic death occurring within one hour of the onset of symptoms in a patient with a known cardiac condition that carries a potential risk of fatality. Alternatively, SCD can be determined when a post-mortem examination reveals a cardiac or vascular anomaly as the likely cause, or when no extracardiac factors are found, pointing towards arrhythmia as the probable cause of death1,2.

The incidence of SCD varies based on age, gender, ethnicity and the specific type of physical effort the athlete’s heart is exposed to. Its actual occurrence athletes remain a subject of significant controversy due to the diverse nature of the existing data on the topic, however it has been estimated that from March 2021
In contrast, static exercise involves force development at a rise in blood pressure, primarily volume-related. Dynamic exercise emphasizes motion, necessitating a distinction between dynamic and static exercise. Different types of exercise result in distinct cardiac adaptations, often combining both dynamic and static elements, highlighting the non-rigid nature of Mitchell’s classification.

The primary objective of this review article is to examine the prospective clinical implications of advanced cardiac imaging techniques, specifically CCTA and CMR imaging, in the prevention of SCD and improved risk stratification of individuals at high risk.

**Left ventricular changes**

Athletic cardiac adaptation significantly influences left ventricular systolic function, including fractional shortening and ejection fraction. A meta-analysis by Fagard et al., comparing long-distance runners, cyclists, and strength athletes with control subjects found similar systolic function measures at rest. Additionally, indicators like peak posterior wall velocity, peak velocity of internal diameter change, peak ejection rate, and right ventricular ejection fraction showed no significant differences. Pelliccia et al. conducted echocardiographic assessments on 947 amateur competitive athletes, identifying 16 individuals with left ventricular wall thickness exceeding 12 mm, indicating an enlarged left ventricular cavity. Athletes with wall thickness exceeding 16 mm but without dilation may have underlying pathological hypertrophy. Pelliccia et al. also studied 1309 elite athletes, finding normal global systolic function and no abnormalities in regional wall motion despite variations in left ventricular cavity dimensions. Rigorous training did not show indications of elevated cardiovascular events or impaired global left ventricular systolic function among athletes.
Right ventricular changes

Another significant adaptation of the athlete’s heart occurs at the level of the right ventricle. There are several reasons for this, the main one being the fact that during vigorous exercise, there is a considerable increase in left atrial filling and pressure during systole, due to the high flow state developed. This increased left auricle (LA) pressure eventually backs up through the pulmonary circulation, posing an increased afterload on the right ventricle, resulting in its dilation. Due to the RV’s pericardial constraint, an increase in its volume leads to a shift of the interventricular septum towards the left ventricle (LV), further attenuating its early diastolic filling and increasing LA pressure10,20.

Concerning the right chambers, another factor that must be considered is the increased venous return due to the augmented left ventricular stroke volume. This once again poses the right heart in a condition of progressive enlargement, increasing wall thickness and altering the diastolic filling. All these factors lead to physiologic adaptations of the heart to exercise, which in the acute setting can be potentially reversed following detraining, but in the long run could lead to chronic structural changes and a decreased right ventricular function10,20.

The grey zone

In such scenarios, the concept of a “grey zone” becomes pertinent. Considering the earlier discussions regarding the physiological adaptations in the athlete’s heart, there exists a substantial overlap between normal myocardial changes, such as RV dilation and LV hypertrophy. In the absence of specific findings indicating a completely benign condition, these physiological changes can be easily mistaken for pathological alterations. In this context, the significance of advanced cardiac imaging techniques, such as CMR and CCTA, becomes evident. These imaging modalities play a crucial role in gaining a deeper understanding of the athlete’s heart and enable improved screening and diagnosis in this specific patient population. By utilizing CMR and CCTA, healthcare professionals can obtain comprehensive and detailed information to distinguish between physiological adaptations and potential pathological conditions in athletes.

Imaging study domains in athletes’ hearts

The ongoing debate on pre-participation screening for athletes involves existing guidelines5. The American Heart Association proposes a screening approach with a 12-element checklist, considering medical history, cardiovascular symptoms, family history of SCD, and a thorough physical examination7. European guidelines, on the other hand, emphasize a screening method centered around the use of 12-lead ECG8.

While ECG-inclusive screening enhances sensitivity in identifying cardiovascular disorders and the risk of SCD21,22, interpreting exercise-related ECG findings in athletes is challenging due to the “grey zone” between normal physiological adaptations and potentially abnormal cardiac adaptations5. Athlete’s heart exhibits

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<tr>
<th>SPORTS CLASSIFICATION</th>
<th>DYNAMIC</th>
<th>STATIC</th>
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<tr>
<td>LOW</td>
<td>Baseball</td>
<td>Archery</td>
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<tr>
<td>MODERATE</td>
<td>Table tennis</td>
<td>Surfing</td>
</tr>
<tr>
<td>HIGH</td>
<td>Volleyball</td>
<td>Rugby</td>
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Table 1. Sports classification based on static and dynamic component intensity levels.
various electrical changes, influenced by factors such as lower resting heart rate, increased vagus nerve activity, decreased sympathetic tone, structural adaptations, and uneven ventricular repolarization\(^\text{11}\). Notably, these electrophysiological changes are more commonly observed in high-intensity and dynamic sports\(^\text{11}\). ECG findings in athlete’s heart include rhythm disturbances like bradycardia and sinus arrhythmia, second-degree atrioventricular blocks (mainly Mobitz type 1), and repolarization abnormalities\(^\text{11}\). To address ECG’s limitations as a screening tool, transthoracic echocardiography (TTE) is commonly employed, providing valuable morpho-functional information\(^\text{23}\). However, TTE may still show normal results in certain conditions like catecholaminergic ventricular tachycardia, anomalous coronary arteries, Brugada syndrome, and long QT syndrome (LQTS)\(^\text{2}\).

As per current guidelines, if echocardiography yields inconclusive results or there are suspicions of coronary abnormalities or cardiomyopathies, further diagnostic tests such as CCTA and CMR are recommended. These advanced imaging techniques can provide additional insights and aid in accurate diagnosis\(^\text{10,24,25}\). CMR has gained significant prominence as a valuable noninvasive imaging modality, offering three-dimensional imaging, excellent spatial and temporal resolution, and precise measurement of wall thickness in any segment of the left ventricle\(^\text{26}\). CMR has gained significant prominence as a valuable noninvasive imaging modality, offering detailed cardiac tissue characterization with three-dimensional imaging, excellent spatial and temporal resolution, and precise measurement of wall thickness in any segment of the left ventricle\(^\text{26}\). In a recent study, CMR identified structural heart disease in 25.5% of patients with normal echocardiography results\(^\text{2,27}\). Finally, CCTA plays a vital role in diagnosing different conditions related to the coronary arteries. CCTA imaging allows for detailed assessment and detection of congenital anomalies of the coronary arteries, providing valuable information about their anatomical variations. In addition, it is an essential tool for diagnosing atherosclerotic coronary disease\(^\text{2}\).

### Main pathological conditions associated with SCD in athletes

When examining the underlying pathophysiological alterations leading to SCD, it is important to consider the age of the athletes involved (Table 2)\(^\text{2}\). In younger athletes (under 35 years old), the primary causes of SCD are hypertrophic cardiomyopathy, which accounts for approximately one-third of competitive athlete deaths in the United States\(^\text{3}\), and arrhythmogenic right ventricular cardiomyopathy (ARVC), which is the main cause of SCD among athletes in the Veneto region of northeastern Italy\(^\text{4}\).

Other possible etiologies include congenital coronary artery anomalies (the second most common cause of SCD), congenital heart defects, myocarditis, and other inflammatory diseases\(^\text{10}\) (Table 2). In contrast, among athletes aged 35 years and older, the majority of deaths (80%) are attributed to atherosclerotic coronary heart disease, with the rest being less common causes\(^\text{24}\). This emphasizes the importance of employing advanced imaging modalities to mitigate the risk of SCD in both age groups.

### Hypertrophic cardiomyopathy

Cardiac hypertrophic remodeling in athletes is influenced by various factors, including age, sex, ethnicity, genetics, and physical activity. TTE initially detects significant observations, like increased ventricular dimensions and biventricular wall thickness, while CMR confirms and provides comprehensive characterization\(^\text{10}\). The “grey zone” athletes with LV wall thickness ranging from 13 mm to 15 mm present a diagnostic challenge to differentiate physiological hypertrophy from hypertrophic cardiomyopathy (HCM)\(^\text{10,28}\).

HCM, an inherited cardiomyopathy caused by sarcomere protein gene mutations, specifically affects the LV with wall thickness of 15 mm or more without over-load conditions\(^\text{29,30}\). CMR plays a critical role in distinguishing HCM from an athlete’s heart, where late gadolinium enhancement (LGE) is generally absent, but its presence in athletes indicates the need for

<table>
<thead>
<tr>
<th>Table 2: Main pathological conditions associated with SCD in athletes in its relationship with age</th>
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<tr>
<td>Young athletes (&lt; 35 years)</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
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<tr>
<td>Arrhythmogenic right ventricular cardiomyopathy</td>
</tr>
<tr>
<td>Coronary arteries anomalies</td>
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<tr>
<td>Long QT syndrome</td>
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<tr>
<td>Myocarditis</td>
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<tr>
<td>Catecholaminergic right ventricular tachycardia</td>
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SCD: sudden cardiac death.
follow-up and further evaluation\textsuperscript{31}, LGE is often present in HCM (approximately 65\% of cases) and associated with a twofold increase in the risk of SCD\textsuperscript{31}. LGE reflects the amount of interstitial fibrosis associated with fibers disarray, which are typical hallmarks of the disease (Figure 1).

Assessment of extracellular volume and T1 mapping have more recently implemented CMR methods to differentiate between HCM and physiological hypertrophy\textsuperscript{32}. Fibers disarray and extracellular volume expansion can be detected as peculiar features of HCM and reported non-invasively with CMR. Additional features, such as the pattern of hypertrophy, apical thickness, and quantity of myocardial crypts, contribute to a comprehensive characterization and differentiation of pathological HCM from physiological hypertrophy in athletes. Expert evaluation and comprehensive assessments are crucial\textsuperscript{33,34}. Advanced CMR imaging is essential, particularly in the “grey zone,” providing invaluable insights for accurate diagnosis and management of athletes’ heart and HCM.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{A 28-year-old soccer player fully asymptomatic with ECG changes suggestive of HCM. A: CMR shows apical HCM with a maximum thickness of 28 mm of the apical septum (yellow line). B: consensus T2 increased (54 msec), and C: huge fibrosis in the apical segment with LGE at the same level (circle). D: increased T1 time (1072 msec). CMR: cardiac magnetic resonance; ECG: electrocardiogram; HCM: hypertrophic cardiomyopathy; LGE: late gadolinium enhancement.}
\end{figure}
Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically inherited heart condition characterized by the replacement of the right ventricular myocardium with fibrofatty tissue, leading to ventricular arrhythmias and an elevated risk of SCD. ARVC accounts for approximately 20% of SCD cases in individuals under 35 years of age and is even more prevalent among athletes experiencing SCD (4-22%)35-38.

Physiological remodeling in athletes can resemble ARVC, but advanced cardiac imaging, such as CMR, plays a crucial role in more accurate differentiation. The diagnosis of ARVC was primarily established in 2010 by the International Task Force criteria (ITF), focusing on structural, functional, electrophysiological, and histological abnormalities10. The Padua criteria, introduced in 2020, recognized biventricular and left-dominant variants in ARVC 38,39. The condition was renamed arrhythmogenic cardiomyopathy (ACM) to highlight its biventricular nature 40,41. The Padua criteria include tissue characterization and novel ECG criteria for LV involvement40.

Right ventricular dilation was defined in the ITF 2010 criteria as an end-diastolic volume (EDV) greater than 110 ml/m² in men and greater than 100 ml/m² in women10. Advanced CMR cine techniques have improved diagnostic accuracy. Specific reference values have been established for athlete's heart to differentiate between pathological and physiological conditions39,41,42. To discriminate between ARVC and physiological ventricular enlargement in athletes, certain factors can be considered. Athletes show RV enlargement primarily confined to the inflow tract, whereas ACM involves both inflow and outflow tracts43,44. ARVC often exhibits bulging or aneurysmal formations in the lateral wall10,45. Tissue characterization using CMR has gained importance with the Padua criteria. LGE in the right ventricle has been observed in 88% of ACM patients, enhancing diagnostic accuracy35,46,47. Endurance athletes commonly show LGE in the interventricular septum48.

CMR and tissue characterization are central in diagnosing left-dominant ACM, where LGE is observed in the sub-pericardial layers of the left free wall, even in mild dilation49,50,51. The significance of CMR, especially tissue characterization, is emphasized by the Padua criteria, serving as a crucial tool to identify functional and morphological abnormalities, distinguishing pathological and physiological characteristics of RV and LV (Figure 2).

Coronary artery anomalies

Coronary artery anomalies (CAA) exhibit a prevalence of 0.17% to 1.3% in the general population2. They can be classified as normal variants if found in over 1.0% of an unselected population, and as anomalies if occurring in less than 1.0% of the population52. In athletes, they represent the second cause of SCD in the USA and the third cause in Italy2,10. Anomalous origin of the left or right coronary artery from the opposite Valsalva sinus is a significant risk factor for SCD, particularly when it involves an inter-arterial course, which is considered malignant. Interestingly, when the anomaly originates from the contralateral cusp but does not involve an inter-arterial course, it may have a benign presentation10. The mechanism involves ventricular arrhythmia triggered by ischemia, induced when exercise leads to the expansion of the aortic root and pulmonary trunk, compressing the coronary artery passing through them53.

Symptoms occur in approximately 50% of cases, including angina, shortness of breath, palpitations, and syncope (Figure 3). SCD can also be the initial presentation without prior symptoms52,53. Activity restrictions based on specific CAA types are dictated by the 2015 AHA guidelines52. Therapeutic approaches involve surgical and medical interventions, with athletes possibly resuming competitions three months after cardiac corrective surgery and a negative stress test10. Non-invasive cardiac imaging techniques, including CCTA and CMR, play a crucial role in identifying CAA and guiding management52,54-56.

CCTA is the gold standard for studying CAA due to its advantages52,54-56. It allows for the identification of the origin, course, and malignant variants of coronary arteries, particularly when an inter-arterial course is present. In contrast, CMR, while emerging as an alternative, may serve as a viable option for detecting benign anomalies in the origin and proximal course of coronary arteries in young athletes. It provides valuable information on myocardial tissue characterization through LGE57,58. Importantly, CMR does not involve ionizing radiation, making it a safer option59. However, CCTA remains the preferred first-line examination due to its superior spatial resolution and ability to identify malignant CAA related to inter-arterial courses52.
Myocarditis

Myocarditis is characterized as an inflammation of the myocardium induced by a diverse range of external antigens, such as viruses, bacteria, parasites, toxins, drugs, or stemming from autoimmune disorders. It is mainly of viral origin, with coxsackie and parvovirus being the primary causative agents. It accounts for 2–20% of sudden deaths in athletes, and post-mortem studies have identified it as the cause in up to 8% of SCDs among athletes. The diagnosis relies on a comprehensive assessment, including clinical evaluation, laboratory studies, ECG, echocardiography, and CMR. The Lake Louise criteria (LLC), employed for cardiac MRI-based diagnosis since 2009, focused on edema, hyperemia, and necrosis/fibrosis as indicators.
of myocardial inflammation. However, the original LLC had limitations in detecting subtle or diffuse inflammation, impacting diagnostic accuracy\(^7\)-\(^10\).

To overcome these limitations, the 2018 LLC was revised with the incorporation of robust cardiac MRI techniques such as myocardial T1 and T2 mapping\(^63\). These mapping techniques provide pixelwise quantitative characterization of myocardial tissue and have shown distinct advantages over the original LLC in detecting and characterizing myocardial inflammation\(^7\)-\(^10\). The updated criteria now require at least one T1-based criterion (increased myocardial T1 relaxation times, extracellular volume fraction, or LGE) and at least one T2-based criterion (increased myocardial T2 relaxation times, visible myocardial edema, or increased T2 signal intensity ratio) for CMR-based myocarditis diagnosis\(^11\).

Both the current position statement from the European Society of Cardiology (ESC) and the scientific statement on the management of myocarditis by the American Heart Association (AHA) acknowledge the value of CMR in assessing suspected myocarditis\(^63\). CMR imaging sequences are highly responsive to tissue alterations that occur during myocardial inflammation\(^61\). These changes include dilatation of the myocardial vascular bed with hyperemia, presence of intracellular and interstitial edema, myocyte necrosis, accumulation of debris in the extracellular space, and collagen deposition resulting in fibrosis and scar formation\(^61\). CMR plays a pivotal role in assessing edema through T2 mapping and hyperemia through early gadolinium enhancement, which helps in the evaluation of hyperemia during myocardial inflammation\(^61,64\). Another significant CMR finding with diagnostic relevance in myocarditis is the presence of LGE, indicating severe inflammation, myocyte injury, necrosis, fibrosis, and ultimately scarring\(^61\) (Figure 4).

For athletes with diagnosed myocarditis, refraining from sporting activities for at least 6 months is recommended. Subsequently, a 24-hour Holter monitoring and a stress ECG should be performed before considering a return to competitive sports. Several criteria must be met for reentry into sports competition, including restoration of systolic function to a normal range, normalization of inflammation and heart failure serum markers, and the absence of clinically relevant arrhythmias during stress ECG or Holter monitoring. Both the American Heart Association (AHA) and the European Society of Cardiology (ESC) advise against sports competition if myocarditis is diagnosed and active inflammation is present, until inflammation resolves as indicated by CMR\(^10,20,65\).
Coronary artery disease in athletes

In athletes over 35 years old, atherosclerotic disease is the primary reason for SCD, accounting for up to 80-90% of cases during post-mortem examinations. Within the sports context, SCD can be triggered by the rupture of arterial plaques, which leads to the blockage of coronary arteries, resulting in ischemia, ventricular arrhythmias, or vasospasm. More specifically, the mechanisms responsible for SCD induced by coronary artery disease (CAD) in athletes involve several factors including: elevated stress on the coronary artery walls, vasospasm in the diseased segment of the vessel, increased flexing of the coronary artery, and enhanced platelet aggregation. Over time, these factors can lead to the disruption of arterial plaques and subsequent thrombotic occlusion, creating an environment conducive to the development of malignant arrhythmias triggered by ischemia.

The diagnosis of CAD in athletes primarily relies on assessing risk factors and conducting exercise stress...
tests. If CAD is suspected, advanced cardiac imaging, such as CCTA, is recommended, following the guidelines outlined in the 2019 ESC Guidelines for the management of coronary disease\textsuperscript{10,68}. Additionally, in the case of master athletes with an exercise test result that is borderline or difficult to interpret, and when a more precise imaging stress test is advised, stress CMR should be taken into consideration for the identification of myocardial ischemia\textsuperscript{10,69,70}.

**CONCLUSION**

In conclusion, the review strongly supports the crucial roles of advanced cardiac imaging techniques, namely CMR and CCTA in the prevention of SCD in competitive athletes and in the differentiation between pathological changes and normal physiological variations in athletes’ hearts. Early identification of cardiac abnormalities allows for timely preventive measures, reducing SCD risk in athletes. The non-invasive nature of CMR and CCTA ensures safe and comprehensive evaluations and are set to become increasingly vital in promoting long-term cardiovascular health in competitive athletes.

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**Conflicts of interest**

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**Protection of individuals:** This study was conducted in compliance with the Declaration of Helsinki (1964) and its subsequent amendments.

**Confidentiality of data.** The authors declare they followed their center’s protocol for sharing patient data.

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**REFERENCES**


Computed tomography-quantitative evaluation (CT-QE) score of patients with COVID-19 pneumonia: a simple and practical approach

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ABSTRACT

Introduction: A simple visual score based on chest computed tomography (CT) findings is desirable for defining prognosis in patients with COVID-19 pneumonia. This study evaluated the diagnostic performance of chest CT using a visual quantification score of lung involvement that predicts the clinical outcome and management area of patients with COVID-19 pneumonia. We also compared the accuracy of this score with clinical severity scores and inflammatory markers. Materials and methods: A chest CT quantitative evaluation (CT-QE) ranging from 0 to 15 points was created. Scores were found to be correlated with the patient management areas such as home, hospital ward, and intensive care unit (ICU). Receiver operating characteristic (ROC) curves were compared with the diagnostic performance of the CT-QE score with clinical severity scales and inflammatory markers to predict clinical outcomes. Results: A total of 178 patients with COVID-19 pneumonia were included. The CT-QE score (AUC, 0.78) had a higher accuracy for adverse clinical outcomes than the CURB-65 score (AUC, 0.65) and the P/F ratio (AUC, 0.69) (p < 0.001). Furthermore, the CT-QE score (AUC, 0.86) outperformed CRP (AUC, 0.77), D-dimer (AUC, 0.73), and ferritin (AUC, 0.76) (p < 0.001) in predicting the clinical outcomes. The CT-QE score was 6-9 points for hospital ward management (p < 0.001) and ≥ 10 points for admission to the ICU or death (p < 0.001). Conclusion: The CT-QE score is a simple and practical visual quantification tool based on chest CT findings for prognosis, which predicts the clinical outcome and management area in patients with COVID-19 pneumonia.


INTRODUCTION

Since the coronavirus disease 2019 (COVID-19) pandemic, fear of a patient with a fatal outcome has prevailed among healthcare workers. Therefore, it is crucial to determine the factors that predict a poor outcome in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to provide timely medical care and effective therapeutic decision-making. Chest computed tomography (CT) has proven useful not only for detecting early disease and identifying patients with false-negative results for SARS-CoV-2 but also for assessing the progression of infection to predict the clinical outcome.
Several tools have been evaluated for appropriate clinical categorization of patients with COVID-19, such as clinical severity scores like the CURB-65 score, the PaO₂/FiO₂ (P/F) ratio and the Quick Sequential Organ Failure Assessment (qSOFA). Laboratory inflammatory markers, such as C-reactive protein (CRP), D-dimer, and ferritin, also provide useful information for reliable clinical prognosis throughout the disease. The use of predictive scores to facilitate medical decision-making leads to improvement in clinical decisions that determine whether the patient with COVID-19 can be cared for at home or requires hospitalization.

Various methods have been developed to quantify pulmonary involvement in chest CT and provide an accurate prognosis. Quantitative assessment of the extent of pulmonary involvement in patients with severe acute respiratory syndrome (SARS) sequelae showed a good correlation with clinical and laboratory parameters and was adopted in patients with COVID-19 with variations. Most methods assign scores to each lobe or segment. These scores are time-consuming and require training. To date, there is no consensus on which to use. It would be desirable to have a simple visual score based on chest CT findings for prognosis, allowing prediction of clinical outcomes and appropriate management in the hospital setting according to the patient’s needs to prevent complications and correctly use resources.

This study evaluated the diagnostic performance of chest CT using a visual quantification score of pulmonary involvement to predict the clinical outcome and management area of patients with COVID-19 pneumonia through a retrospective observational analysis. We also compared the score’s accuracy with clinical severity scores (CURB-65 and P/F ratio) and inflammatory markers (CRP, D-dimer, and ferritin).

**MATERIALS AND METHODS**

A retrospective cohort study was conducted from March 15 to July 31, 2020, at the Radiology Department of the Hospital General “Isidro Ayora” in Loja, Ecuador. Patients who tested positive for reverse transcription polymerase chain reaction (RT-PCR) of a nasopharyngeal swab and diagnosed with COVID-19 pneumonia were included. Exclusion criteria were patients without available imaging studies and with decompensated comorbidities requiring complex clinical management, regardless of pulmonary and clinical involvement related to COVID-19 pneumonia. Informed consent was not required for this retrospective study of information collected during routine clinical care. The institutional ethics and research committees approved the study.

**Clinical and laboratory variables**

The variables recorded were sex, age, chronic diseases such as type 2 diabetes mellitus (T2DM), chronic heart disease (CHD), high blood pressure (HBP), chronic obstructive pulmonary disease (COPD), preexisting lung disease, and chronic kidney disease (CKD).

The laboratory tests were neutrophil ($\times 10^3/\mu l$), lymphocyte ($\times 10^3/\mu l$), and platelet ($\times 10^3/\mu l$) counts, prothrombin time (PT, s), partial prothrombin time (PTT, s), INR (international normalized ratio), neutrophilia (> 65.0%), leukocytosis (> 10.8 $\times 10^3/\mu l$), thrombocytopenia (< 130.0 $\times 10^3/\mu l$), lymphopenia (< 30.5%), leukopenia (< 4.8 $\times 10^3/\mu l$), urea (mg/dl), creatinine (mg/dl), glucose (mg/dl), lactate dehydrogenase (LDH), U/L, and inflammatory markers such as C-reactive protein (CRP), D-dimer, and ferritin.

We assessed two clinical severity scores within 24 hours of examination in the respiratory triage room. The CURB-65 score (confusion, uremia, respiratory rate, blood pressure, and age ≥ 65 years) and the P/F ratio; this was calculated based on the partial pressure of arterial oxygen (PaO₂) and the fraction of inspired oxygen (FiO₂).

**Patient management area and clinical outcomes**

Clinical records were reviewed, and data were recorded from the patient’s arrival at the respiratory triage room. Patients were classified based on the clinical criteria according to the severity of symptoms, pneumonia, respiratory insufficiency, and lung involvement on chest CT for initial treatment. The cases were divided into three categories depending on where the patient was treated: at home, in the hospital ward, or in the intensive care unit (ICU). The treatment area was defined as the place with the highest complexity where the patient was treated for the longest time.

Patients with a CURB-65 score of 0-1 point, a P/F ratio > 300 mmHg, or mild lung involvement on chest CT were treated at home. Patients with a CURB-65 score of 2 points, a P/F ratio of 200-300 mmHg, or moderate lung involvement were treated in the hospital ward, and patients with a CURB-65 score of ≥ 3 points, a P/F ratio < 200 mmHg, or severe lung involvement were treated in the ICU.

Patients were subclassified into two groups: favorable or adverse clinical outcomes. The latter included...
patients who required invasive ventilation or died in the ICU, while those treated at home, in a hospital ward, or in an intermediate care unit without invasive ventilation were classified as having a favorable clinical outcome.

**Image acquisition and analysis**

All chest CT examinations were performed while the patients were in a supine position with inspiratory apnea and without intravenous contrast medium using the helical technique on a SOMATOM Emotion 16-Slice CT scanner (Siemens Healthineers, Erlangen, Germany). The scanning range was from the base of the neck to the upper third of the abdomen. All images were acquired in full inspiration with a standard-dose protocol (120 kVp, 150 mA) and a detector width of 1.5 mm and reconstructed with a slice thickness of 0.75 mm × 0.75 mm and the kernel U91s ultrasharp. The acquisition direction was from the lung base to the apices. The chest CT was recorded in the picture archiving and communication system (PACS) (Actualpacs, Actualtec Innovacion Tecnologica SL, Castellón de la Plana, Castellón, Spain).

Chest CT images on a workstation with OsiriX MD v.11.0.2 (Pixmeo, Geneva, Switzerland) were read independently by two cardiothoracic radiologists with 8 (MAEB) and 10 (ALS) years of experience. All images were analyzed with orthogonal multiplanar reconstruction (MPR) in the lung window (range WW: 1000-2000 and WL: -700 to -500 HU). Chest CT findings were described based on the term glossary of the Fleischner Society for Thoracic Imaging.

**Development of the CT-QE score**

A visual quantification score of pulmonary involvement was adapted by simplifying the method described by Kazerooni, which was also previously used in patients with SARS to describe ground-glass opacity, interstitial opacity, and air trapping.

The CT-QE score was created based on visual quantification of the percentage of pulmonary involvement in each of the five lobes and classified as follows: no involvement (0%), 0 points; involvement of 1-29%, 1 point for each affected lobe; involvement of 30-70% scored with 2 points for each affected lobe; and involvement of > 70% scored with 3 points for each affected lobe (Figure 1). The overall extent of pulmonary involvement was determined by the sum of points for each lobe, which ranged from 0 to 15. The CT-QE score was found to be correlated with the patient management area (home, hospital ward, or ICU) and clinical outcome.

Interobserver agreement between the two cardiothoracic radiologists was assessed using the CT-QE score to evaluate pulmonary involvement. The two readers were blinded to the patient’s clinical and laboratory data. In cases where the readers disagreed, the score was determined by consensus.

**Statistical analysis**

Data are presented as frequencies, percentages, or mean ± SD and ranges. The association between the CT-QE score and the patient management area and clinical outcome was determined using the Fisher’s exact and chi-square tests. Differences with a p-value < 0.05 were considered significant. The cutoff values of the CT-QE score that accurately determined the patient management area and clinical outcome were defined using the Youden index. The diagnostic performance of the CT-QE score with a 95% confidence interval (CI) was compared with clinical severity scores (CURB-65 and P/F ratio) and inflammatory markers (CRP, D-dimer, and ferritin) to determine the clinical prognosis of patients by constructing receiver operating characteristic (ROC) curves. The intraclass correlation coefficient tested the reproducibility of the CT-QE score between the two readers. The statistical analysis was performed using the IBM SPSS software, version 25.0 (IBM Corp., Armonk, NY, USA).

**RESULTS**

A total of 184 patients with COVID-19 pneumonia who tested positive for RT-PCR were analyzed. Four patients were excluded because the decision of their treatment in the hospital was based on their comorbidities, and two were excluded because their chest CT was not available. A total of 178 patients were included: 109 (61.2%) men and 69 (38.8%) women aged between 17 and 90 years, with a mean age of 51.11 ± 16.64 years.

**Patient management area and clinical outcome**

Out of 178 patients, 76 (42.7%) were treated at home, 57 (32.0%) required admission to a hospital ward, and 45 (25.3%) required ICU management (Table 1). The length of stay on the ward until discharge from the
hospital was 7.14 ± 4.93 days. The average length of stay in the ICU was 18.80 ± 14.52 days. A significant risk factor for the need for a more complex medical management area was age > 60 years (n = 55 patients, 30.9%), T2DM (n = 32, 17.9%), and CHD or HBP (n = 47, 26.4%). A total of 126 (70.8%) patients had a favorable clinical outcome, while 52 (29.2%) had an adverse clinical outcome. Notably, 38 (21.3%) patients died, 7 (18.4%) were in a hospital ward, and 31 (81.6%) were in the ICU. The mean time from onset of symptoms to death was 24.87 ± 13.15 days.

**Clinical severity scores according to the patient management area and clinical outcome**

The CURB-65 score and the P/F ratio were assessed in a sub-analysis of 118 and 96 patients,
Table 1. Characteristics of patients with COVID-19 pneumonia according to the management area and clinical outcome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Home (n = 76)</th>
<th>Hospital ward (n = 57)</th>
<th>ICU (n = 45)</th>
<th>p-value</th>
<th>Favorable outcome (n = 126)</th>
<th>Adverse outcome (n = 52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n (%)</td>
<td>38 (50.0)</td>
<td>36 (63.2)</td>
<td>35 (77.8)</td>
<td>&lt; 0.001</td>
<td>67 (53.2)</td>
<td>41 (78.8)</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>38 (50.0)</td>
<td>21 (36.8)</td>
<td>10 (22.2)</td>
<td></td>
<td>59 (46.8)</td>
<td>11 (21.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age, mean ± SD (range)</td>
<td>41.5 ± 14</td>
<td>54.74 ± 16.06</td>
<td>62.71 ± 11.80</td>
<td>&lt; 0.001</td>
<td>45.74 ± 15.29</td>
<td>64.13 ± 11.98</td>
<td>0.002</td>
</tr>
<tr>
<td>Age &gt; 60 years, n (%)</td>
<td>4 (5.4)</td>
<td>22 (38.9)</td>
<td>29 (64.4)</td>
<td>&lt; 0.001</td>
<td>19 (15.1)</td>
<td>36 (69.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>T2DM, n (%)</td>
<td>5 (6.6)</td>
<td>15 (26.3)</td>
<td>12 (26.7)</td>
<td>0.003</td>
<td>19 (15.1)</td>
<td>13 (25.0)</td>
<td>0.117</td>
</tr>
<tr>
<td>Pre-existing lung disease a</td>
<td>0</td>
<td>3 (5.3)</td>
<td>2 (4.4)</td>
<td>0.143</td>
<td>2 (1.6)</td>
<td>3 (5.8)</td>
<td>0.125</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>0</td>
<td>0</td>
<td>3 (6.7)</td>
<td>0.011</td>
<td>0</td>
<td>3 (5.8)</td>
<td>0.007</td>
</tr>
<tr>
<td>CHD or HBP, n (%)</td>
<td>7 (9.2)</td>
<td>19 (33.3)</td>
<td>21 (46.7)</td>
<td>&lt; 0.001</td>
<td>22 (17.5)</td>
<td>25 (48.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>0</td>
<td>6 (10.5)</td>
<td>6 (13.3)</td>
<td>0.007</td>
<td>4 (3.2)</td>
<td>8 (15.4)</td>
<td>0.003</td>
</tr>
</tbody>
</table>


respectively (Table 2). A higher CURB-65 score was found in patients who required ICU management (2.02 ± 0.82) and had adverse clinical outcomes (2.04 ± 0.82) (p < 0.004 and p < 0.001, respectively). The P/F ratio values were also lower in patients who required ICU management (149.25 ± 84.93; p < 0.001) and had adverse clinical outcomes (153.50 ± 82.46; p < 0.001).

Laboratory values associated with patient management area and clinical outcome

Patients with an adverse clinical course had higher absolute neutrophil counts and urea, glucose, and LDH levels compared with patients with a favorable clinical outcome (p < 0.001) (Table 3). In addition, patients with an adverse clinical course were more likely to have neutrophilia (94.1%) and thrombocytopenia (15.6%) (p < 0.001).

CRP and ferritin levels were higher in patients with an adverse clinical course than in patients with a favorable prognosis (p < 0.001). However, there were no significant differences in leukopenia, creatinine, and D-dimer. The mean interval between the onset of symptoms and sampling for inflammatory markers was 7.92 ± 6.77 days for CRP, 7.63 ± 6.23 days for D-dimer, and 8.09 ± 6.84 days for ferritin.

Chest CT findings according to the patient management area and clinical outcome

Tomographic findings in patients with COVID-19 pneumonia are shown in Table 4. The predominant pattern was ground-glass opacities with a primarily subpleural distribution (n = 167, 93.8%). Airspace consolidation (n = 69, 38.7%) and crazy paving (n = 30, 16.8%) were less common. Only 11 (6.1%), 8 (4.4%), and 5 (2.8%) patients had pleural effusion, unilateral involvement, and subpleural sparing, respectively. Notably, 9 (5.0%) of 178 patients with confirmed COVID-19 pneumonia had no abnormal CT findings. The mean interval between the first visit and the chest CT scan was 1.43 ± 4.16 days, with a CT evaluation within 24 hours. The mean interval between the onset of symptoms and the performance of RT-PCR and chest CT was 7.29 ± 6.03 and 7.88 ± 6.41 days, respectively. The interval between the evaluation of the chest CT and the RT-PCR results was 3.29 ± 4.21 days.

In the initial phase, patients were more frequently treated at home (n = 37, 48.7%). In contrast, patients in the progression phase were more frequently treated in the hospital ward (n = 26, 45.6%) and in the ICU (n = 28, 62.2%), with significant differences between the groups (p < 0.001).

CT-QE score for predicting the patient management area and clinical outcome

The interobserver agreement of the CT-QE score was almost perfect, with a mean of 0.86 (p < 0.001). Figure 2 shows the CT-QE score according to a visual quantification of pulmonary involvement in three patients with COVID-19 pneumonia. The CT-QE score was obtained by adding the points of each lobe according to the percentage of pulmonary involvement. In the first
Table 2. Clinical severity scores related to patient management area and clinical outcome in patients with COVID-19 pneumonia

<table>
<thead>
<tr>
<th>Description</th>
<th>Home</th>
<th>Hospital ward</th>
<th>ICU</th>
<th>p-value</th>
<th>Favorable outcome</th>
<th>Adverse outcome</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURB-65 score, mean ± SD</td>
<td>20</td>
<td>1.25 ± 0.85</td>
<td>54</td>
<td>1.43 ± 0.82</td>
<td>44</td>
<td>2.02 ± 0.82</td>
<td>0.004</td>
</tr>
<tr>
<td>P/F ratio, mean ± SD</td>
<td>5</td>
<td>390.40 ± 98.37</td>
<td>50</td>
<td>221.92 ± 79.76</td>
<td>41</td>
<td>149.25 ± 84.93</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

COVID-19: coronavirus disease 2019; ICU: Intensive Care Unit; CURB-65: confusion, uremia, respiratory rate, blood pressure, and age ≥ 65 years; P/F ratio: partial pressure of arterial oxygen in blood (PaO₂) divided by the fraction of inspired oxygen (FiO₂).

Table 3. Laboratory values and inflammatory markers according to patient management area and clinical outcome in patients with COVID-19 pneumonia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Home</th>
<th>Hospital ward</th>
<th>ICU</th>
<th>p-value</th>
<th>Favorable outcome</th>
<th>Adverse outcome</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils, x10³/μl</td>
<td>62</td>
<td>4.61 ± 3.05</td>
<td>57</td>
<td>7.98 ± 4.0</td>
<td>44</td>
<td>9.79 ± 5.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lymphocytes, x10³/μl</td>
<td>62</td>
<td>1.61 ± 0.72</td>
<td>57</td>
<td>1.19 ± 0.54</td>
<td>44</td>
<td>1.18 ± 0.73</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Platelets, x10³/μl</td>
<td>62</td>
<td>238.19 ± 67.14</td>
<td>57</td>
<td>267.42 ± 103.80</td>
<td>44</td>
<td>223.00 ± 94.41</td>
<td>0.545</td>
</tr>
<tr>
<td>PT, sec</td>
<td>46</td>
<td>12.45 ± 1.10</td>
<td>49</td>
<td>13.91 ± 6.44</td>
<td>44</td>
<td>13.89 ± 2.26</td>
<td>0.240</td>
</tr>
<tr>
<td>PTT, sec</td>
<td>46</td>
<td>35.37 ± 8.24</td>
<td>48</td>
<td>39.10 ± 12.61</td>
<td>44</td>
<td>40.34 ± 12.45</td>
<td>0.038</td>
</tr>
<tr>
<td>INR</td>
<td>46</td>
<td>11.15 ± 0.42</td>
<td>49</td>
<td>13.00 ± 0.64</td>
<td>44</td>
<td>1.30 ± 0.22</td>
<td>0.078</td>
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</tbody>
</table>

COVID-19: coronavirus disease 2019; ICU: Intensive Care Unit; PT: prothrombin time; PTT: partial prothrombin time; INR: international normalized ratio; LDH: lactate dehydrogenase; CRP: C-reactive protein. Values refer to mean ± SD unless otherwise stated.

Table 4. Tomographic findings in patients with COVID-19 pneumonia in relation to patient management area and clinical outcome

<table>
<thead>
<tr>
<th>Description</th>
<th>Home</th>
<th>Hospital ward</th>
<th>ICU</th>
<th>p-value</th>
<th>Favorable outcome</th>
<th>Adverse outcome</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical pattern, n (%)</td>
<td>61 (80.3)</td>
<td>52 (91.2)</td>
<td>42 (93.3)</td>
<td>0.020</td>
<td>108 (85.7)</td>
<td>48 (92.3)</td>
<td>0.221</td>
</tr>
<tr>
<td>Ground-glass opacity, n (%)</td>
<td>65 (85.5)</td>
<td>57 (100)</td>
<td>45 (100)</td>
<td>&lt; 0.001</td>
<td>115 (91.3)</td>
<td>52 (100)</td>
<td>0.046</td>
</tr>
<tr>
<td>Crazzy paving, n (%)</td>
<td>5 (6.6)</td>
<td>7 (12.3)</td>
<td>16 (35.6)</td>
<td>&lt; 0.001</td>
<td>10 (7.9)</td>
<td>18 (34.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Airspace consolidation, n (%)</td>
<td>19 (25)</td>
<td>24 (42.1)</td>
<td>26 (57.8)</td>
<td>0.002</td>
<td>42 (33.3)</td>
<td>27 (51.9)</td>
<td>0.025</td>
</tr>
<tr>
<td>Peribronchovascular thickening, n (%)</td>
<td>28 (36.8)</td>
<td>47 (61.8)</td>
<td>44 (97.8)</td>
<td>&lt; 0.001</td>
<td>70 (55.6)</td>
<td>49 (94.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nonspecific pattern, n (%)</td>
<td>5 (6.6)</td>
<td>5 (8.8)</td>
<td>2 (4.4)</td>
<td>0.020</td>
<td>8 (6.4)</td>
<td>4 (7.7)</td>
<td>0.221</td>
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<tr>
<td>Subpleural sparing, n (%)</td>
<td>0</td>
<td>2 (3.5)</td>
<td>3 (6.7)</td>
<td>0.098</td>
<td>2 (1.6)</td>
<td>3 (5.8)</td>
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<td>Pleural effusion, n (%)</td>
<td>3 (3.9)</td>
<td>5 (8.7)</td>
<td>3 (6.7)</td>
<td>0.538</td>
<td>7 (5.6)</td>
<td>4 (7.7)</td>
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<td>Unilateral involvement, n (%)</td>
<td>7 (9.2)</td>
<td>1 (1.8)</td>
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<td>0.026</td>
<td>8 (6.4)</td>
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<td>No lung involvement, n (%)</td>
<td>9 (11.8)</td>
<td>0</td>
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<td>0.020</td>
<td>9 (7.1)</td>
<td>0</td>
<td>0.221</td>
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</table>

Figure 2. CT-QE score to define pulmonary involvement in three clinical cases. A: chest CT of a 37-year-old woman diagnosed with COVID-19 pneumonia. In the upper panel, the presence of ground glass opacity (blue arrows) was scored 0-29% in all lobes (one point each), except the LLL (0 points). In the lower panel, the areas with ground-glass opacity are shown in blue, and the lung fissures are shown in yellow. The CT-QE was scored with a total of 4 points. B: chest CT of a 49-year-old man diagnosed with COVID-19 pneumonia. The upper panel shows ground-glass opacity and airspace consolidation (blue arrows) with 30-70% impairment, scored as 2 points per lung lobe. In the lower panel, the areas with ground-glass opacity are shown in blue, and the lung fissures are shown in yellow. The CT-QE score was a total of 10 points. C: chest CT of a 57-year-old woman diagnosed with COVID-19 pneumonia. The upper panel shows areas of ground glass opacity, airspace consolidation, and crazy paving (blue arrows) > 70% involvement, scored with 3 points per lung lobe. In the lower panel, the areas with ground glass opacity are shown in blue, and the lung fissures are shown in yellow. The CT-QE score was a total of 15 points.

A.S. Lozano-Samaniego et al. CT-QE score of COVID-19 pneumonia

In the second case, pulmonary involvement in each lobe was between 50% and 70% of the total volume per lobe and was assigned 2 points, giving a cumulative total of 10 points. In the third case, the pulmonary involvement in each lobe was > 70% and scored 3 points per lobe, giving a CT-QE score of 15.

The Youden index showed that the best cutoff of the CT-QE score was 6-9 points for management in the hospital ward (p < 0.001) and ≥ 10 points for ICU admission with adverse clinical outcomes or death (p < 0.001). In a ROC curve, the CT-QE score (AUC, 0.78) showed higher accuracy for predicting an adverse clinical outcome than CURB-65 (AUC, 0.65) and the P/F ratio (AUC, 0.69). B: the CT-QE score (AUC, 0.86) outperformed CRP (AUC: 0.77), D-dimer (AUC, 0.73), and ferritin (AUC, 0.76) in determining the prognosis of adverse clinical outcome in patients with COVID-19 pneumonia.

**DISCUSSION**

This study proposed a simplified and easy-to-use CT-QE score based on visual quantification of tomographic pulmonary involvement in Ecuadorian patients with COVID-19 pneumonia. The proposed CT-QE score based on tomographic findings had a higher diagnostic performance than two clinical severity scores (CURB-65 and P/F ratio) and inflammatory markers for predicting clinical outcomes. This CT-QE score can guide optimized management and resource use in the care of patients with COVID-19 pneumonia.

Chest CT is a widely used tool for assessing pulmonary infections. In an environment of limited resources and high pre-test probability, its use has been established for diagnosing COVID-19 pneumonia in patients with moderate or severe infection. These advantages are complemented by the simultaneous use of clinical severity scores and inflammatory markers that allow clinicians to select the optimal management area.

Some scores use a complex system that assigns 0-5 points to each lobe or scores of 0-5 in each of the 20 lung segments. Based on the results of our study in the proposed CT-QE score, only 0-3 points are assigned to the visual quantification of each lung lobe, making the evaluation of tomographic pulmonary involvement simple and practical. The CT-QE score showed high diagnostic performance with an AUC of 0.78 for predicting the clinical outcome and classifying the management area of patients with COVID-19 pneumonia.
It was superior to the CURB-65 score (AUC, 0.65) and the P/F ratio (AUC, 0.68). The CT-QE score has a higher diagnostic performance based on visual quantification of tomographic pulmonary involvement.

The CURB-65 score is routinely used in patients with respiratory symptoms for clinical prognosis and to guide treatment. We found a significant difference in the CURB-65 score between patients with favorable and adverse clinical prognoses (1.30 ± 0.78 vs. 2.04 ± 0.82, respectively; \( p < 0.001 \)). The cutoff points for predicting mortality (> 2.04) were comparable with the Guo's study. On the other hand, the CURB-65 score in our study allowed patients to be adequately classified according to the area of management at home (1.25 ± 0.85), in the hospital ward (1.43 ± 0.82), and in the ICU (2.02 ± 0.82) (\( p = 0.004 \)). In contrast, in the study by Nguyen, the accuracy of the CURB-65 score in guiding the decision for inpatient or outpatient care was low.

The CT-QE score was found to be correlated with the CURB-65 score in predicting a favorable or adverse clinical outcome. Laboratory inflammatory markers, such as CRP, D-dimer, and ferritin, provide useful information for reliable clinical prognosis in patients with COVID-19. In this study, patients with an adverse clinical course had elevated levels of inflammatory markers, which is consistent with previous findings. The CT-QE score (AUC, 0.86) outperformed CRP (AUC, 0.77), D-dimer (AUC, 0.73), and ferritin (AUC, 0.76) in determining the prognosis of adverse clinical outcomes in patients with COVID-19 pneumonia.

The strengths of this study were the population, which included patients with COVID-19 pneumonia with favorable and adverse outcomes, and the fact that the CT-QE score is a simple and practical visual quantification of chest CT findings. The interobserver agreement between readers was almost perfect. The limitations of the study include its retrospective design performed at a single center. In addition, visual quantification of tomographic pulmonary involvement is subjective and may need validation to achieve reproducible and comparable results for radiologists with initial and intermediate experience in chest CT assessment. The CT-QE score must be validated before it can be widely used in clinical practice.

**CONCLUSION**

This study showed that the proposed CT-QE score is simple and easy to use, with high diagnostic performance for patients with COVID-19 pneumonia, and provides an even more accurate prognosis than some clinical severity scores and inflammatory markers in predicting adverse clinical outcomes and classification for outpatient and inpatient management. There is a need to validate the clinical application of the CT-QE score in prospective cohort studies and larger populations.

**Acknowledgments**

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**Conflicts of interest**

The authors declare no conflicts of interest.

**Ethical disclosures**

Protection of individuals. This study complied with the Declaration of Helsinki (1964) and its amendments. Confidentiality of data. The authors declare that they followed their center’s protocol for sharing patient data. Right to privacy and informed consent. Informed consent was not required for this observational study of information collected during routine clinical care. Use of artificial intelligence. The authors state that they did not use generative artificial intelligence to prepare this manuscript and/or create tables, figures, or figure legends.

**REFERENCES**


TVUS soft markers in clinically significant superficial endometriosis: an ultrasonographic, clinical, and laparoscopic correlation

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FULL RESEARCH ARTICLE

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ABSTRACT

Introduction: Ultrasonographic soft markers can be useful diagnostic findings in endometriosis. We evaluated women with superficial endometriosis with only soft markers on basal transvaginal ultrasound (TVUS) with bowel preparation and their relationship with chronic pelvic pain and laparoscopy findings. Materials and methods: This retrospective cohort study included patients with clinical suspicion of endometriosis. They had soft markers on basal TVUS with bowel preparation and underwent laparoscopy for the first time. Symptoms, such as dysmenorrhea, dyschezia, deep dyspareunia, and dysuria, were quantified with a visual analog scale. The ultrasonographic soft markers were ovarian tenderness, adhesions, obliteration of the cul-de-sac (CDS), and obliteration of the vesico-uterine pouch (VUP). Laparoscopic findings were adhesions and superficial endometriotic lesions. Results: A total of 25 women with superficial endometriosis with only soft markers on basal TVUS with bowel preparation and who underwent therapeutic laparoscopy were included. The mean age was 32.28 ± 5.67 years. The type and intensity (mean ± SD) of chronic pelvic pain were severe dysmenorrhea (7.60 ± 3.08), moderate dyspareunia (4.84 ± 3.51), and mild dyschezia and dysuria (3.44 ± 3.89 and 2.12 ± 2.92, respectively). All had at least one positive ultrasonographic soft marker. Most patients had moderate-to-severe dysmenorrhea and only soft markers on ultrasound examinations. Patients with superficial endometriotic lesions, regardless of size or extension, found at laparoscopy reported severe dysmenorrhea. Conclusion: TVUS soft markers were associated with clinically significant superficial endometriosis. TVUS soft markers are not usually reported during routine examination. They may improve the diagnostic yield of superficial endometriosis.


INTRODUCTION

Endometriosis is endometrial-like tissue found outside the uterine cavity. It is a gynecologic disease that represents one of the greatest gynecologic challenges in diagnosis and treatment today. There are three types of endometriosis: peritoneal, ovarian, and deep infiltrative endometriosis (DIE). Peritoneal endometriosis, also called superficial endometriosis, is the most common type. It occurs in up to 80% of women with a confirmed diagnosis and is associated with infertility and chronic pelvic pain, such as severe dysmenorrhea and dyspareunia. Early diagnosis of endometriosis can lead to more effective treatment.
and an improved quality of life for affected women. Transvaginal ultrasound (TVUS) is a first-line imaging tool for assessing women with endometriosis. A systematic review by the Cochrane group states that TVUS with bowel preparation has high sensitivity and specificity for diagnosing endometriomas and DIE, compared to laparoscopic results. However, no recommendations were made regarding superficial endometriosis or its correlation with ultrasound, clinical, or laparoscopic findings.

The literature on the role of TVUS with bowel preparation for detecting superficial endometriosis is sparse. Okaro et al. first described the concept of soft markers based on the degree of ovarian and uterine mobility and tenderness on ultrasound examination in contrast with a hard marker defined as a structural abnormality (an endometrioma or hydrosalpinx). Soft markers as indirect ultrasound findings have been associated with superficial endometriosis, but their diagnostic usefulness is unknown. This study focused on soft markers in basal TVUS with bowel preparation and their relationship to chronic pelvic pain and surgical findings visualized by laparoscopy in women with superficial endometriosis.

MATERIALS AND METHODS

This retrospective cohort study was conducted from January 2018 to December 2019 at the Clinica of Excelencia in Endometriosis in Zapopan, Jalisco, Mexico. Women referred with a clinical suspicion and with only soft markers on basal TVUS with bowel preparation for endometriosis and who underwent therapeutic laparoscopy for the first time were included. Women with ultrasound findings suggestive of DIE or endometriomas, missing clinical and/or laparoscopic data, or conversion to open surgery were excluded. Informed consent was not required for this study of information collected during routine clinical care. The Institutional Ethics and Research Committees approved the protocol.

Developmental study and clinical variables

A search for ultrasound reports and images of women with chronic pelvic pain referred with a clinical suspicion of endometriosis and presenting only soft markers on basal TVUS with bowel preparation with failure of drug treatment, defined as persistence of pain on a visual analog scale over 6, with at least 6 months of progestin use, and who underwent therapeutic laparoscopy for the first time.

The variables were age and chronic pelvic pain lasting at least 6 months, assessed by clinical interview as dysmenorrhea, dyschezia, dyspareunia, and/or dysuria. A visual analog scale was used to classify pain, with 0 being absent, 1-3 mild, 4-7 moderate, and 8-10 severe.

Definition of ultrasonographic soft markers

Ovarian tenderness was categorized by severity as absent, mild, moderate, or severe, according to the patient. A tenderness-guided ultrasound examination was performed with or without an acoustic window between the transvaginal probe and the surrounding vaginal structures, coupled with an ‘active’ role of the patient, who indicated the site and intensity of any tenderness during the examination.

Ovarian adhesions were considered absent, mild (+), or strong (+++) by applying pressure with the transducer and external pressure with the other hand and visualizing in real time if the ovary was fixed to the uterus or the pelvic wall. Direct visualization of adhesions is possible when there is pelvic fluid.

Obliteration of the cul-de-sac (CDS) if there is no sliding between the uterus and the anterior rectal wall when pressure is applied with the transducer and the left hand of the operator.

Obliteration of the vesico-uterine pouch (VUP) if there is no sliding between the bladder dome and the anterior wall of the uterus when pressure is applied to the abdomen with the transducer and the operator’s left hand.

Image acquisition protocol

Grayscale TVUS and power Doppler examinations were performed using a Samsung Accuvix XG system (Samsung Group, Suwon, South Korea) with a 4-9 MHz endocavitary transducer. The patient was in the lithotomy position, and the TVUS bowel preparation protocol for endometriosis was performed according to the International Deep Endometriosis Analysis (IDEA) group. The TVUS technique for detecting superficial endometriosis was performed with detailed scanning of the peritoneum in the right anterior compartment (RAC), the left anterior compartment (LAC), the right posterior compartment (RPC), and the left posterior compartment (LPC) of the pelvis. The surface of the ovaries and the serosa of the rectosigmoid were also evaluated.
in detail. All ultrasound examinations were performed by a single radiologist (VGG), who is an expert in endometriosis with 15 years of experience.

**Surgical laparoscopic findings**

After the ultrasound examination, all women underwent laparoscopic surgery performed by a team of endometriosis experts (MLT and MLZ) who were informed of the ultrasound findings. The presence of adhesions on laparoscopic examination of both ovaries, CDS, VUP, RAC, LAC, RPC, LPC, and RPC was determined as absent, mild (+), moderate (++), or severe (+++), referred to as a qualitative finding by the surgeon\(^{10}\). The presence and length of superficial endometriotic lesions directly visualized during laparoscopic examination in the RAC, LAC, RPC, LPC, and RPC were considered absent, \(< 1 \text{ cm}\), 1-3 cm, or \(> 3 \text{ cm}\)\(^{10}\).

**Statistical analysis**

The variables are described as means and standard deviations for numerical data and frequencies and percentages for categorical data. An analysis of variance (ANOVA) was performed between each variable. Pearson’s chi-square test was then performed to determine \(p\)-values. A significance level of \(p < 0.05\) was used. The statistical analysis was performed using SPSS version 26 (IBM Corp., Armonk, NY, USA).

**RESULTS**

A total of 33 women were assessed. Eight patients were excluded: seven due to a lack of clinical and/or laparoscopic data and one who converted to open surgery. We included 25 women with clinically suspected endometriosis and only ultrasonographic soft markers on basal TVUS with bowel preparation who underwent therapeutic laparoscopy for the first time (Table 1). In all patients, the type and intensity (mean \(\pm SD\)) of chronic pelvic pain found were severe dysmenorrhea (7.60 \(\pm 3.08\)), moderate dyspareunia (4.84 \(\pm 3.51\)), and mild dyschezia and dysuria (3.44 \(\pm 3.89\) and 2.12 \(\pm 2.92\), respectively). Dysmenorrhea was the predominant pain reported by all patients. Patients with dyschezia and dysuria tended to have stronger adhesions, represented by a severity of ++++. These results suggest that patients with suspected endometriosis should be thoroughly examined for dyschezia and dysuria, as these symptoms may indicate severe adhesions.

Figure 1, a power Doppler TVUS, shows the presence of adhesions after external mobilization maneuvers without a separation plane between the right ovary (RO) and the abdominal wall. Figure 2, a grayscale TVUS, shows the findings of a patient with severe dysmenorrhea, moderate dyschezia, and dyspareunia. No movement was detected when performing external mobilization maneuvers on the RO and anterior rectal wall, and the patient reported severe pain, concluding adhesions as a soft marker for superficial endometriosis. Figure 3 shows a static laparoscopic image of a patient with CDS obliteration and focal tenderness on TVUS (data not shown), and superficial endometriotic lesions and adhesions on the CDS and pelvic peritoneal defects are seen at the retrocervical level. The laparoscopic findings confirmed the severity and extent of the endometriotic lesions, with many patients having lesions larger than 3 cm. Case 24 presents a woman with moderate dysmenorrhea, dyspareunia, and significant adhesions in multiple compartments (RAC 1-3 cm, LAC 1-3 cm, RPC 1-3 cm, and LPC 1-3 cm).

**Association of ultrasonographic soft markers with type and intensity of chronic pelvic pain**

The frequency of ultrasonographic soft markers and chronic pelvic pain is shown in Table 2. Patients with moderate tenderness in the RO reported moderate dysmenorrhea (6.62 \(\pm 2.44\)) and dyspareunia (5.00 \(\pm 3.29\)). Those with severe tenderness in the RO reported severe dysmenorrhea (8.50 \(\pm 1.73\)). Moderate tenderness was found in patients with moderate pain (4.81 \(\pm 3.37\)). In contrast, patients with mild tenderness in the left ovary (LO) had severe dysmenorrhea (9.00 \(\pm 1.67\)). Those with moderate tenderness reported severe dysmenorrhea (8.27 \(\pm 1.42\)), and those with severe tenderness had moderate dysmenorrhea (5.00 \(\pm 4.54\)). Figure 4 shows a grayscale TVUS of a patient with severe dysmenorrhea and dyspareunia, in which the LO is shown without a separation plane of the uterus and abdominal wall. No movement was seen, and the patient reported severe pain with external mobilization maneuvers, concluding adhesions as a soft marker of superficial endometriosis. Figure 5 shows a grayscale TVUS of a patient with severe dysmenorrhea, moderate dyschezia, and dyspareunia, in which CDS obliteration and focal tenderness were found. There is no separation plane, and adhesions were seen during dynamic maneuvers.
### Table 1. Pain characteristics, ultrasonographic soft markers, and laparoscopic findings in 25 patients with clinically significant superficial endometriosis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, years</th>
<th>Chronic pelvic pain*</th>
<th>Ultrasonographic soft markers</th>
<th>Laparoscopic findings</th>
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<td></td>
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*Visual analogue scale; aAdhesion severity represented by +, ++ or +++ as mild, moderate, and strong; RO: right ovary; LO: left ovary; CDS: Cul-De-Sac; VUP: vesico-uterine pouch; RAC: right anterior compartment; LAC: left anterior compartment; RPC: right posterior compartment; LPC: left posterior compartment.
Figure 1. Power Doppler TVUS, of a woman with severe dysmenorrhea. The image shows the RO without any separation plane from the abdominal wall (arrowheads). When performing external mobilization maneuvers, no movement was seen, and the patient reported moderate pain, suggesting adhesions as a soft marker for superficial endometriosis.

TVUS: transvaginal ultrasound; RO: right ovary.

An association was found between patients with mild and strong right-side adhesions and severe dysmenorrhea (7.16 ± 3.76 and 7.66 ± 1.86, respectively). Women with mild adhesions reported severe dyspareunia (7.33 ± 2.25). Figure 6 shows a laparoscopic static image of a woman with severe dysmenorrhea and moderate dyspareunia with superficial endometriotic lesions at the RAC. Grayscale TVUS demonstrated RO adhesions and focal tenderness (data not shown). Patients with mild adhesions on the left side reported severe dysmenorrhea (8.75 ± 1.38) and moderate dyschezia and dyspareunia (5.37 ± 3.54 and 6.00 ± 3.20, respectively). Those with severe adhesions reported moderate dysmenorrhea (6.50 ± 3.77). Figure 7 shows a laparoscopic static image of superficial endometriotic lesions and adhesions in the LAC in a patient with severe dysmenorrhea and focal LO tenderness on TVUS (data not shown).

The CDS was obliterated in women with severe dysmenorrhea (8.83 ± 1.47) and moderate dyschezia and dyspareunia (4.33 ± 4.80 and 5.50 ± 3.39, respectively).

**Association between the severity of adhesions visualized during laparoscopy and the type and intensity of chronic pelvic pain**

Laparoscopic findings are shown in Table 3, and there were no complications. Patients with moderate or severe right-sided adhesions reported severe dysmenorrhea (9.50 ± 9.57 and 8.16 ± 2.04, respectively). Patients with moderate right-sided adhesions had moderate dyschezia and dyspareunia (4.00 ± 3.28 and 6.50 ± 4.50, respectively). Patients with severe right-sided adhesions reported moderate dyspareunia (4.00 ± 3.28). Severe dysmenorrhea (9.50 ± 0.70) was found in women with moderate left-sided and severe adhesions (7.55 ± 3.32). Patients with moderate left-sided adhesions reported moderate dyschezia, dyspareunia, and dysuria (4.50 ± 6.36). Patients with severe left-sided adhesions reported moderate dyspareunia (5.66 ± 3.64).
Figure 2. Grayscale TVUS of a woman with severe dysmenorrhea, moderate dyschezia, and dyspareunia. The image shows the RO without any separation plane from the uterus or anterior rectal wall. When performing external mobilization maneuvers, no movement was seen, and the patient reported severe pain, concluding adhesions as a soft marker for superficial endometriosis (arrowheads).

RO: right ovary; TVUS: transvaginal ultrasound; U: uterus; R: rectum.

Figure 3. Static laparoscopic image of a woman with severe dysmenorrhea and dyspareunia, with CDS obliteration on TVUS (data not shown). The image shows superficial endometriotic lesions (dotted circles) and pelvic peritoneal defects (arrowheads) causally related to endometriosis, as this patient had neither pregnancy nor previous surgical procedures.

CDS: Cul de Sac; TVUS: transvaginal ultrasound.

Patients with mild adhesions in the CDS had severe dysmenorrhea. Women with moderate adhesions at this level had moderate dysmenorrhea and dysuria (6.33 ± 5.50 and 6.00 ± 2.64, respectively) and severe dyschezia and dyspareunia (7.66 ± 3.21 and 9.33 ± 0.57, respectively). Patients with severe adhesions reported severe dysmenorrhea (8.00 ± 1.89) and moderate dyspareunia (4.50 ± 3.67). Patients with moderate adhesions of the VUP reported severe dysmenorrhea and dyschezia (9.50 ± 0.70 and 8.00 ± 2.82, respectively). Patients with severe adhesions at this level reported severe dysmenorrhea, dyschezia, and dyspareunia (9.00 ± 0, 8.00 ± 0, and 8.00 ± 0, respectively). Ultrasonographic RO and LO adhesions were associated with surgical RO adhesions (p = 0.02) and LO adhesions (p = 0.04), respectively. There were no significant differences compared with other parameters.
Table 2. Association between ultrasonographic soft markers and type and intensity of chronic pelvic pain* in 25 patients with clinically significant superficial endometriosis

<table>
<thead>
<tr>
<th>Description</th>
<th>n (%)</th>
<th>Dysmenorrhea Mean ± SD</th>
<th>Dyschezia Mean ± SD</th>
<th>Dyspareunia Mean ± SD</th>
<th>Dysuria Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RO tenderness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>6 (24.0)</td>
<td>6.33 ± 4.96</td>
<td>3.66 ± 3.14</td>
<td>4.83 ± 4.07</td>
<td>2.16 ± 2.56</td>
</tr>
<tr>
<td>Mild</td>
<td>7 (28.0)</td>
<td>9.28 ± 1.49</td>
<td>4.57 ± 4.42</td>
<td>4.85 ± 4.01</td>
<td>1.71 ± 2.98</td>
</tr>
<tr>
<td>Moderate</td>
<td>8 (32.0)</td>
<td>6.62 ± 2.44</td>
<td>1.62 ± 3.02</td>
<td>5.00 ± 3.29</td>
<td>1.75 ± 2.71</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (16.0)</td>
<td>8.50 ± 1.73</td>
<td>4.75 ± 5.50</td>
<td>4.50 ± 3.69</td>
<td>3.50 ± 4.35</td>
</tr>
<tr>
<td><strong>LO tenderness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1 (4.0)</td>
<td>10.00 ± 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mild</td>
<td>6 (24.0)</td>
<td>9.00 ± 1.67</td>
<td>4.50 ± 3.67</td>
<td>3.33 ± 2.80</td>
<td>2.66 ± 3.20</td>
</tr>
<tr>
<td>Moderate</td>
<td>11 (44.0)</td>
<td>8.27 ± 1.42</td>
<td>1.81 ± 3.18</td>
<td>4.81 ± 3.37</td>
<td>1.27 ± 2.41</td>
</tr>
<tr>
<td>Severe</td>
<td>7 (28.0)</td>
<td>5.00 ± 4.54</td>
<td>5.57 ± 4.39</td>
<td>6.85 ± 3.62</td>
<td>3.28 ± 3.45</td>
</tr>
<tr>
<td><strong>RO adhesions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>13 (52.0)</td>
<td>7.76 ± 3.39</td>
<td>4.53 ± 4.03</td>
<td>4.30 ± 3.90</td>
<td>2.92 ± 2.95</td>
</tr>
<tr>
<td>Mild</td>
<td>6 (24.0)</td>
<td>7.16 ± 3.76</td>
<td>4.50 ± 3.88</td>
<td>7.33 ± 2.25</td>
<td>1.16 ± 3.71</td>
</tr>
<tr>
<td>Strong</td>
<td>6 (24.0)</td>
<td>7.66 ± 1.86</td>
<td>-</td>
<td>3.50 ± 2.73</td>
<td>0.33 ± 0.61</td>
</tr>
<tr>
<td><strong>LO adhesions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>7 (28.0)</td>
<td>7.85 ± 3.23</td>
<td>2.00 ± 3.46</td>
<td>3.57 ± 3.40</td>
<td>1.85 ± 3.18</td>
</tr>
<tr>
<td>Mild</td>
<td>8 (32.0)</td>
<td>8.75 ± 1.38</td>
<td>5.37 ± 3.54</td>
<td>6.00 ± 3.20</td>
<td>2.62 ± 3.73</td>
</tr>
<tr>
<td>Strong</td>
<td>10 (40.0)</td>
<td>6.50 ± 3.77</td>
<td>2.90 ± 4.17</td>
<td>4.80 ± 3.85</td>
<td>1.90 ± 3.73</td>
</tr>
<tr>
<td><strong>CDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6 (24.0)</td>
<td>7.21 ± 3.37</td>
<td>3.15 ± 3.67</td>
<td>4.63 ± 3.62</td>
<td>2.10 ± 3.05</td>
</tr>
<tr>
<td>Obliterated</td>
<td>19 (76.0)</td>
<td>8.83 ± 1.47</td>
<td>4.33 ± 4.80</td>
<td>5.50 ± 3.39</td>
<td>2.16 ± 2.71</td>
</tr>
<tr>
<td><strong>VUP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>25 (100)</td>
<td>7.60 ± 3.08</td>
<td>3.44 ± 3.89</td>
<td>4.84 ± 3.51</td>
<td>2.12 ± 2.92</td>
</tr>
</tbody>
</table>

*Visual analogue scale; †Adhesion severity represented by †, ++ or +++ as mild, moderate, or severe/strong. ‡No case with obliterated VUP; RO: right ovary; LO: left ovary; CDS: Cul-De-Sac; VUP: vesico-uterine pouch.

Figure 4. Grayscale TVUS of a woman with severe dysmenorrhea and dyspareunia. The image shows the LO without any separation plane between the uterus and AW. When performing external mobilization maneuvers, no movement was seen, and the patient reported severe pain, concluding adhesions as a soft marker for superficial endometriosis (arrowheads).

AW: abdomino-pelvic; LO: left ovary; TVUS: transvaginal ultrasound; U: uterus.

Figure 5. Grayscale TVUS of a woman with severe dysmenorrhea, moderate dyschezia, and dyspareunia. CDS obliteration and focal tenderness. There is no separation plane (arrowheads) and adhesions were seen during dynamic maneuvers.

AW: abdomino-pelvic wall; CDS: Cul de Sac; LO: left ovary; TVUS: transvaginal ultrasound; U: uterus.
Figure 6. Laparoscopic static image showing superficial endometriotic lesions at the RAC (dotted circle) of a woman with severe dysmenorrhea and moderate dyspareunia. In grayscale TVUS, RO had adhesion and focal tenderness (data not shown).
RAC: right anterior compartment; RO: right ovary; TVUS: transvaginal ultrasound.

Association between the severity of endometriotic lesions and the type and intensity of chronic pelvic pain

Patients with moderate and severe pelvic pain had endometriotic lesions. There was no association between lesion length and pain severity (Table 4). Patients with lesions less than 1 cm in length in the RAC reported severe dysmenorrhea ($8.66 \pm 2.30$), moderate dyschezia ($4.33 \pm 4.04$), mild dyspareunia ($1.66 \pm 2.88$), and dysuria ($3.00 \pm 3.00$). Patients with lesions 1-3 cm in length at this level reported severe dyspareunia ($7.50 \pm 2.12$).

Patients with lesions less than 1 cm in length in the LAC reported severe dysmenorrhea ($8.00 \pm 2.00$). Those with lesions 1-3 cm in length reported moderate dysmenorrhea ($5.00 \pm 4.58$) and severe dyspareunia ($8.00 \pm 1.73$). Patients with lesions larger than 3 cm reported severe dysmenorrhea ($9.00 \pm 1.41$) and moderate dyschezia ($5.50 \pm 0.70$).

Patients reported severe dysmenorrhea with endometriotic lesions in the RPC smaller than 1 cm ($7.50 \pm 0.70$), 1-3 cm ($8.12 \pm 1.64$), and larger than 3 cm
Table 3. Association between adhesion severity visualized at laparoscopy and the type and intensity of chronic pelvic pain\(^a\) in 25 patients with clinically significant superficial endometriosis

<table>
<thead>
<tr>
<th>Description</th>
<th>n (%)</th>
<th>Dysmenorrhea Mean ± SD</th>
<th>Dyschezia Mean ± SD</th>
<th>Dyspareunia Mean ± SD</th>
<th>Dysuria Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>RO adhesions(^b,c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>15 (60.0)</td>
<td>6.86 ± 3.60</td>
<td>4.46 ± 3.58</td>
<td>4.73 ± 3.45</td>
<td>2.16 ± 2.56</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 (16.0)</td>
<td>9.50 ± 9.57</td>
<td>04.75 ± 5.50</td>
<td>6.50 ± 4.50</td>
<td>3.50 ± 4.35</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (24.0)</td>
<td>8.16 ± 2.04</td>
<td>-</td>
<td>4.00 ± 3.28</td>
<td>0.33 ± 0.81</td>
</tr>
<tr>
<td>LO adhesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>12 (48.8)</td>
<td>7.91 ± 2.57</td>
<td>3.91 ± 3.70</td>
<td>3.83 ± 3.21</td>
<td>2.25 ± 2.92</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (8.0)</td>
<td>4.00 ± 5.65</td>
<td>2.00 ± 2.82</td>
<td>7.50 ± 2.12</td>
<td>2.00 ± 2.82</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (8.0)</td>
<td>9.50 ± 0.70</td>
<td>4.50 ± 6.36</td>
<td>4.50 ± 6.36</td>
<td>4.50 ± 6.36</td>
</tr>
<tr>
<td>Severe</td>
<td>9 (36.0)</td>
<td>7.55 ± 3.32</td>
<td>2.88 ± 4.37</td>
<td>5.66 ± 3.64</td>
<td>1.44 ± 2.40</td>
</tr>
<tr>
<td>CDS adhesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>15 (60.0)</td>
<td>7.53 ± 3.13</td>
<td>3.13 ± 3.66</td>
<td>4.40 ± 3.18</td>
<td>1.80 ± 2.75</td>
</tr>
<tr>
<td>Mild</td>
<td>1 (4.0)</td>
<td>10 ± 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (12.0)</td>
<td>6.33 ± 5.50</td>
<td>7.66 ± 3.21</td>
<td>9.33 ± 0.57</td>
<td>6.00 ± 2.64</td>
</tr>
<tr>
<td>Severe</td>
<td>6 (24.0)</td>
<td>8.00 ± 1.89</td>
<td>2.66 ± 4.13</td>
<td>4.50 ± 3.67</td>
<td>1.33 ± 2.42</td>
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<tr>
<td>VUP adhesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>21 (84.0)</td>
<td>7.71 ± 2.83</td>
<td>2.95 ± 3.72</td>
<td>4.61 ± 3.63</td>
<td>2.28 ± 3.01</td>
</tr>
<tr>
<td>Mild</td>
<td>1 (4.0)</td>
<td>4.00 ± 5.65</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (8.0)</td>
<td>9.50 ± 0.70</td>
<td>8.00 ± 2.82</td>
<td>3.50 ± 0.70</td>
<td>2.50 ± 3.53</td>
</tr>
<tr>
<td>Severe</td>
<td>1 (4.0)</td>
<td>9.00 ± 0</td>
<td>8.00 ± 0</td>
<td>8.00 ± 0</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\)Visual analogue scale; \(^b\)Adhesion severity represented by +, ++ or +++ as mild, moderate, or severe. \(^c\)None case with mild adhesions in RO; RO: right ovary; LO: left ovary; CDS: Cul-De-Sac; VUP: vesico-uterine pouch.

Table 4. Association between endometriotic lesion length found at laparoscopy and type and intensity of chronic pelvic pain\(^a\) in 25 patients with clinically significant superficial endometriosis

<table>
<thead>
<tr>
<th>Description</th>
<th>n (%)</th>
<th>Dysmenorrhea Mean ± SD</th>
<th>Dyschezia Mean ± SD</th>
<th>Dyspareunia Mean ± SD</th>
<th>Dysuria Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriotic lesion length in the RAC(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>20 (80.0)</td>
<td>7.90 ± 2.82</td>
<td>3.65 ± 4.00</td>
<td>5.05 ± 3.48</td>
<td>2.20 ± 3.03</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>3 (12.0)</td>
<td>8.66 ± 2.30</td>
<td>4.33 ± 4.04</td>
<td>1.66 ± 2.88</td>
<td>3.00 ± 3.00</td>
</tr>
<tr>
<td>1-3 cm</td>
<td>2 (8.0)</td>
<td>3.00 ± 4.24</td>
<td>-</td>
<td>7.5 ± 2.12</td>
<td>-</td>
</tr>
<tr>
<td>Endometriotic lesion length in the LAC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>17 (68.0)</td>
<td>7.82 ± 3.06</td>
<td>3.41 ± 4.00</td>
<td>4.52 ± 3.79</td>
<td>2.23 ± 2.68</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>3 (12.0)</td>
<td>8.00 ± 2.00</td>
<td>2.66 ± 4.61</td>
<td>3.66 ± 3.21</td>
<td>2.00 ± 3.46</td>
</tr>
<tr>
<td>1-3 cm</td>
<td>3 (12.0)</td>
<td>5.00 ± 4.58</td>
<td>3.00 ± 5.19</td>
<td>8.00 ± 1.73</td>
<td>3.00 ± 5.19</td>
</tr>
<tr>
<td>&gt; 3 cm</td>
<td>2 (8.0)</td>
<td>9.00 ± 1.41</td>
<td>5.50 ± 0.70</td>
<td>4.50 ± 2.12</td>
<td>-</td>
</tr>
<tr>
<td>Endometriotic lesion length in the RPC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>6 (24.4)</td>
<td>6.00 ± 4.51</td>
<td>6.00 ± 3.57</td>
<td>5.50 ± 3.27</td>
<td>3.66 ± 3.01</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>2 (8.8)</td>
<td>7.50 ± 0.70</td>
<td>-</td>
<td>5.50 ± 0.70</td>
<td>-</td>
</tr>
<tr>
<td>1-3 cm</td>
<td>8 (32.0)</td>
<td>8.12 ± 1.64</td>
<td>3.37 ± 3.77</td>
<td>4.25 ± 3.99</td>
<td>3.00 ± 3.5</td>
</tr>
<tr>
<td>&gt; 3 cm</td>
<td>9 (36.0)</td>
<td>8.22 ± 3.27</td>
<td>2.55 ± 4.03</td>
<td>4.77 ± 3.96</td>
<td>0.77 ± 1.71</td>
</tr>
<tr>
<td>Endometriotic lesion length in the LPC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>6 (24.0)</td>
<td>8.83 ± 1.60</td>
<td>6.00 ± 3.52</td>
<td>3.83 ± 3.25</td>
<td>3.50 ± 3.01</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>4 (16.0)</td>
<td>7.75 ± 1.70</td>
<td>1.50 ± 3.00</td>
<td>3.50 ± 2.64</td>
<td>-</td>
</tr>
<tr>
<td>1-3 cm</td>
<td>7 (7.0)</td>
<td>5.71 ± 3.72</td>
<td>2.71 ± 3.77</td>
<td>6.71 ± 3.19</td>
<td>3.57 ± 3.64</td>
</tr>
<tr>
<td>&gt; 3 cm</td>
<td>8 (32.0)</td>
<td>8.25 ± 3.49</td>
<td>2.25 ± 4.20</td>
<td>4.62 ± 4.20</td>
<td>0.87 ± 1.80</td>
</tr>
</tbody>
</table>

\(^a\)Visual analogue scale; \(^b\)No case with length of endometriotic lesions > 3 cm in the RAC; RAC: right anterior compartment; LAC: left anterior compartment; RPC: right posterior compartment; LPC: left posterior compartment.
Patients with lesions at this level reported moderate dyspareunia (5.50 ± 0.70) for lesions smaller than 1 cm, lesions 1-3 cm (4.25 ± 3.99), and lesions larger than 3 cm (4.77 ± 3.96). Patients with lesions smaller than 1 cm in this area reported severe dysmenorrhea (7.75 ± 1.70). Those with lesions between 1 and 3 cm reported moderate dysmenorrhea (5.71 ± 3.72) and severe dyspareunia (6.71 ± 3.19). Patients with lesions larger than 3 cm in this area reported severe dysmenorrhea (8.25 ± 3.49). A one-way ANOVA showed a significant association between dyspareunia intensity and VUP adhesions (p = 0.010).

Ultrasonographic CDS obliteration was significantly associated with LO adhesions and CDS adhesions found at laparoscopy (p = 0.01 and p < 0.02, respectively). No significant differences were found compared with other parameters.

**DISCUSSION**

This study demonstrates the association between soft markers on basal TVUS with bowel preparation in patients with clinically significant superficial endometriosis and laparoscopy findings. Our study sheds light on the complexity of endometriosis. It emphasizes the need for comprehensive assessment, including an evaluation of the ultrasound-based soft markers.

Superficial endometriosis has been diagnosed with a median delay of 5 years. The detection of ultrasound-based soft markers may be helpful for an early diagnosis. Okaro et al. in a study of 120 women, demonstrated only ultrasonographic soft markers in 51 (53.1%) of 96 patients. Pelvic adhesions and peritoneal endometriotic lesions were found in 37 (72.5%) of 51 patients. On the other hand, Reid et al. studied the accuracy of ultrasound in predicting the site of endometriotic involvement during laparoscopy. They found that ovarian immobility on TVUS was significantly associated with ipsilateral pelvic pain, uterosacral ligamentous lesions, pelvic wall adhesions, endometriomas, and CDS obliteration. The authors suggested that a patient with mobile ovaries is unlikely to have superficial endometriosis without endometriomas, which is consistent with our findings. In summary, ultrasonographic soft markers are defined as focalized tenderness, adhesions, absence of uterine and ovarian mobility, and obliteration of VUP or CDS. Site-specific tenderness and ovarian mobility as indirect ultrasound-based markers of pelvic pathology improved the ability to predict or rule out diagnosis in women with chronic pelvic pain. Soft markers on TVUS with bowel preparation may be sufficient to indicate clinically significant superficial endometriosis.

The severity of symptoms is not directly related to the severity of the disease and should be considered along with the soft markers in the TVUS to determine the presence and extent of clinically significant superficial endometriosis. Menakaya et al. showed an overall accuracy of 84.9% in predicting the exact level of laparoscopic findings with an excellent correlation (0.82). However, the authors did not consider symptom severity, which was addressed in our study. Most of the patients in our study suffered moderate to severe dysmenorrhea and had only soft markers on their ultrasound examination, all of whom had at least one positive ultrasonographic soft marker. Dyspareunia, dyschezia, and dysuria can also be present without DIE. This finding is consistent with a previous study that found a significant association between ovarian tenderness on ultrasound and CDS adhesions and a strong association between right-sided adhesions on ultrasound and laparoscopy findings. Patients with severe dyspareunia also had right-sided adhesions on ultrasound and at surgery, adhesions in the LO, CDS, and VUP, and endometriotic lesions in the RAC and LAC. The relevance of the diagnosis of clinically significant superficial endometriosis lies in its significant impact on the health of women, especially those suffering from chronic pelvic pain. Soft markers found in TVUS are often classified as mild disease but may indicate clinically significant superficial endometriosis, so laparoscopic examination and timely treatment are recommended.

This study has several strengths. All patients were referred with a clinical suspicion of endometriosis and underwent surgery performed by experienced laparoscopic gynecologists. One of the main limitations is the sample size, which was reduced for various reasons. A very specific patient selection was conducted, excluding those who had DIE, ovarian involvement, or other surgical procedures. Patients who previously underwent surgery may have adhesions due to their surgical history, making assessment more difficult. An analysis of the excluded patients revealed that most patients undergo multiple surgeries at a young age to relieve chronic pelvic pain, leaving us with only younger patients (mean age, 32.28 years) with a shorter duration of disease. Ovarian mobility assessment and site-specific tenderness are subjective and require experience in the use of TVUS in assessing pelvic pain.
CONCLUSION

Our study showed that soft markers on a well-performed ultrasound examination were the only findings that indicated clinically significant superficial endometriosis. These subjective ultrasound findings are not usually reported during routine examinations. TVUS-based soft markers can triage appropriate patients for further investigation. Our results must be confirmed in prospective studies with a larger and more diverse patient population.

Acknowledgments

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of individuals. This study complied with the Declaration of Helsinki (1964) and its amendments.

Confidentiality of data. The authors declare they followed their center’s protocol for sharing patient data.

Right to privacy and informed consent. Informed consent was not required for this observational study of information collected during routine clinical care.

Use of artificial intelligence. The authors state that they did not use generative artificial intelligence to prepare this manuscript and/or create tables, figures, or figure legends.

REFERENCES

Ultrasonographic findings of papillary breast lesions with clinical and pathological correlation

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ABSTRACT

Introduction: The spectrum of ultrasonographic findings of benign, atypical, and malignant papillary lesions is broad. This study describes the ultrasonographic findings, clinical manifestations, and histopathological correlation of papillary breast lesions in Mexican patients. Material and Methods: We reviewed the pathology database of ultrasound (US)-guided core needle biopsies (CNB) to identify all papillary breast lesions diagnosed between January 2012 and December 2016. US findings were described using the BI-RADS lexicon. Clinical data and histopathologic diagnosis were recorded. Results: Thirty-four papillary breast lesions from 34 women were included. There were 22 (64.7%) benign, 10 (29.4%) atypical, and 2 (5.9%) malignant papillary lesions. The most common clinical presentation was a palpable mass (n = 24, 70.6%); two (5.9%) patients had nipple discharge, while 8 (23.5%) were asymptomatic. The most common ultrasonographic features were an oval shape (n = 18, 53.0%), a not-circumscribed margin (n = 20, 58.8%), parallel orientation (n = 33, 97.0%), a hypoechoic pattern (n = 27, 79.4%), and no posterior features (n = 31, 91.2%). Vascularity (n = 24, 70.6%) and ductal ectasia (n = 4, 11.8%) were associated findings. Calcifications were not observed. The pathological diagnoses of the benign papillary lesions were intraductal papilloma (n = 21, 61.8%) and intraductal papillomatosis (n = 1, 2.9%). Ten (29.5%) atypical papilloma cases were intraductal papilloma with atypical hyperplasia. Intracystic papillary carcinoma (n = 1, 2.9%) and invasive micropapillary carcinoma (n = 1, 2.9%) were the malignant lesions. Conclusion: This study is the first in Mexico that presents the ultrasonographic findings, clinical characteristics, and histopathological correlations of benign, atypical, and malignant papillary breast lesions.

Keywords: Ultrasound. BI-RADS. Papillary breast lesion. Breast carcinoma. Benign breast lesion.
but it is not uncommon for papillary breast lesions to be detected in asymptomatic women during cancer screening. Ultrasound (US) findings of papillary breast lesions typically show an oval, hypoechoic, intraductal mass often associated with ductal dilation. A cystic-solid component is also common, and lesions may appear hypervascular on color Doppler US. They are usually central (retroareolar) but may also be in the periphery. Multiple papillary lesions are more likely to be peripheral and located in multiple separate ducts.

Papillary breast lesion US findings are not characteristic to define if the lesion is benign, atypical, or malignant. The diagnosis and management are challenging due to heterogeneous imaging features. In Mexico, no studies describe the imaging features of papillary breast lesions. In this study, we describe the spectrum of US findings, clinical manifestations, and histopathological correlation of papillary breast lesions in Mexican patients.

**MATERIAL AND METHODS**

This cross-sectional study was conducted from January 2012 to December 2016 in the Department of Breast Imaging of the “Dr. Jose Eleuterio Gonzalez” University Hospital in Monterrey, Nuevo Leon, Mexico. We included all papillary breast lesion cases diagnosed by percutaneous US-guided core needle biopsy (CNB) during the study period. Patients with another histopathologic diagnosis were excluded. Informed consent was not required for this retrospective analysis of data obtained in routine medical care. The Institutional Research Ethics Committee and the Research Committee approved the study.

**Study development and variables**

We reviewed the pathology database of ultrasound-guided CNB to identify all cases of papillary breast lesions. We then identified cases that underwent excisional biopsy after a histopathologic diagnosis of a papillary breast lesion by CNB.

The variables were the age of the patient, the reason for the US examination (screening or diagnostic), and clinical signs such as a palpable mass or nipple discharge. The color of the discharge (white, yellow-greenish, hyaline, or bloody) and its occurrence spontaneously or with compression were recorded. The lesions were classified as central or peripheral, single or multiple.

**US acquisition and analysis protocol**

Avius™ (Hitachi Co. Tokyo, Japan) and MyLab Seven™ (Esaote Co. Genoa, Italy) equipment were used with a linear 14 MHz multifrequency transducer. Images were stored in a Picture Archiving and Communication System (PACS) (Carestream™, Health Inc. Version 12.1.5. Rochester, NY. USA).

Image analysis was performed by a radiologist (YRG) specializing in breast imaging with five years of experience. Ultrasonographic features were described using BI-RADS lexicon, and benign, atypical, and malignant papillary lesions were confirmed by histopathologic examination.

**Breast biopsy**

All patients underwent CNB using a MAGNUM® core biopsy instrument (BARD, Covington, GA. USA) with a 14 G × 10 cm needle (Becton, Dickinson and Co. Franklin Lakes, NJ. USA). Breast biopsies were assessed by a gynecology and breast pathology specialist with 12 years of experience (GGM) and a clinical pathology specialist with 5 years of experience (HHZ). Some patients underwent excisional biopsy after a histopathologic diagnosis of a papillary breast lesion by CNB. The excisional biopsy was performed before placement of an ultrasound breast localization wire Dualok 20G × 7.7 cm or 20G × 10.7 cm (Becton, Dickinson and Co. Franklin Lakes, NJ. USA). In the operating room under general anesthesia, a periareolar incision was made, followed by excision of the papillary breast lesion. Complete removal of the mass was confirmed by US.

**Statistical analysis**

Data are presented with frequencies, percentages, mean, and standard deviation. Excel version 18.0 (Microsoft Co. Seattle, WA. USA) was used.

**RESULTS**

Thirty-four papillary breast lesions from 34 women were included. The mean age was 57.7 ± 13.9 years (range, 29 to 82). There were 22 (64.7%) benign papillary lesions, 10 (29.5%) atypical papillary lesions, and 2 (5.9%) malignant papillary lesions (Table 1). The pathological diagnoses of the benign papillary lesions were intraductal papilloma (n = 21, 61.8%) and intraductal papillomatosis (n = 1, 2.9%). Ten (29.5%)
Table 1. Histopathologic diagnostic spectrum of papillary breast lesions according to the CNB

<table>
<thead>
<tr>
<th>Description</th>
<th>Histopathologic diagnosis</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign papillary lesion</td>
<td>Intraductal papilloma</td>
<td>21 (61.8)</td>
</tr>
<tr>
<td></td>
<td>Intraductal papillomatosis</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Atypical papillary lesion</td>
<td>Intraductal papilloma with atypical hyperplasia</td>
<td>10 (29.5)</td>
</tr>
<tr>
<td>Malignant papillary lesion</td>
<td>Intracystic papillary carcinoma</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td></td>
<td>Invasive micropapillary carcinoma</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>34 (100)</td>
</tr>
</tbody>
</table>

CNB: core needle biopsy.

Table 2. Histopathological diagnosis by CNB compared with surgical excision diagnosis in 5 papillary breast lesion cases

<table>
<thead>
<tr>
<th>Diagnosis by CNB</th>
<th>Diagnosis by surgical excision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1: Intraductal papilloma</td>
<td>Intraductal papilloma</td>
</tr>
<tr>
<td>Case 2: Intracystic papillary carcinoma</td>
<td>Intracystic papillary carcinoma</td>
</tr>
<tr>
<td>Case 3: Intraductal papilloma with atypical hyperplasia</td>
<td>Intraductal papilloma with atypical hyperplasia</td>
</tr>
<tr>
<td>Case 4: Intraductal papilloma with atypical hyperplasia</td>
<td>Intraductal papilloma with atypical hyperplasia</td>
</tr>
<tr>
<td>Case 5: Intraductal papilloma with atypical hyperplasia</td>
<td>Invasive micropapillary carcinoma</td>
</tr>
</tbody>
</table>

CNB: core needle biopsy.

Lesions were atypical papillomas with a histopathologic diagnosis of intraductal papilloma with atypical hyperplasia. Malignant papillary lesions were intracystic papillary carcinoma (n = 1, 2.9%) and invasive micropapillary carcinoma (n = 1, 2.9%).

An excisional biopsy was performed in 5 (14.7%) of 34 patients. A comparison of the histologic findings by CNB and the histopathologic diagnosis after surgical excision is shown in Table 2. In four cases, the diagnoses were concordant between CNB and surgical excision, but in one case, there was a discordance because an intraductal papilloma with atypical hyperplasia was defined by CNB while invasive micropapillary carcinoma was diagnosed after surgical excision.

Eight (23.5%) of 34 patients were asymptomatic and underwent US breast screening (Table 3). A diagnostic US was performed in 26 (76.5%) of 34 symptomatic patients. The most common clinical sign was a palpable mass in 24 (92.3%) of 26 symptomatic patients. A benign lesion was confirmed in 13 patients with a palpable mass.

All the cases (n = 10) with atypical papillar lesions, and one malignant papillary lesion had a palpable mass. Nipple discharge was noted in only two of 26 symptomatic patients. It appeared with compression in one case and spontaneously in another. In both cases, the papillary lesions were benign.

All papillary lesions appeared as breast masses on the ultrasonographic examination. In 30 (88.2%) of the 34 patients, a single mass was observed, while four (5.8%) presented with multiple masses. In the latter cases, the described ultrasonographic features corresponded to the largest mass. Sixteen (53.3%) of 30 single papillary lesions were found in the central region and 14 (46.7%) in the periphery. In contrast, the four multiple papillary lesions were in the central region. Central localization was more common in benign lesions, observed in 14 patients, while peripheral localization was more common in atypical papillary lesions (n = 6, 60%). Both malignant papillary lesions were centrally located.
Table 4 compares the US findings with the histopathologic diagnosis of benign, atypical, and malignant papillary lesions. Oval masses were the most common (n = 18, 53.0 %), followed by an irregular shape (n = 15, 44.1 %). An oval shape was most common in the 22 benign papillary lesions (n = 14, 63.6%), while an irregular shape was most common in the 10 atypical lesions (n = 6, 60.0%). Malignant papillary lesions were oval (n = 1) and irregular (n = 1).

A not circumscribed margin was more common (n = 20, 58.8%) than a circumscribed margin (n = 14, 41.2%). Figure 1 shows a grayscale US image of an oval mass with a circumscribed margin in a 65-year-old woman. The histopathologic diagnosis was an intraductal papilloma with atypical hyperplasia. One malignant lesion had a circumscribed margin, and another a non-circumscribed margin. Thirty-three (97.0%) of 34 papillary lesions showed parallel orientation, regardless of histopathologic diagnosis. Only one benign papillary lesion showed no parallel orientation. Figure 2 shows a grayscale US breast examination of a 48-year-old woman with a mass with a not parallel orientation and microlobulated margins. The histopathologic diagnosis was intraductal papilloma.

A hypoechogenic pattern was the most common (n = 27, 79.4%) of the 34 papillary lesions. It was found in 19 (86.4%) of 22 benign lesions, 7 (70.0%) of 10 atypical

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total (n = 34)</th>
<th>Benign papillary lesions n = 22 (64.7%)</th>
<th>Atypical papillary lesions n = 10 (29.4%)</th>
<th>Malignant papillary lesions n = 2 (5.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oval, n (%)</td>
<td>18 (53.0)</td>
<td>14 (63.6)</td>
<td>3 (30.0)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Round, n (%)</td>
<td>1 (2.9)</td>
<td>0</td>
<td>1 (10.0)</td>
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<tr>
<td>Irregular, n (%)</td>
<td>15 (44.1)</td>
<td>8 (36.4)</td>
<td>6 (60.0)</td>
<td>1 (50.0)</td>
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<tr>
<td>Margin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circumscribed, n (%)</td>
<td>14 (41.2)</td>
<td>10 (45.4)</td>
<td>3 (30.0)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Not-circumscribed</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Indistinct, n (%)</td>
<td>6 (17.6)</td>
<td>2 (9.1)</td>
<td>4 (40.0)</td>
<td>0</td>
</tr>
<tr>
<td>Angular, n (%)</td>
<td>7 (20.6)</td>
<td>6 (27.3)</td>
<td>1 (10.0)</td>
<td>0</td>
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<tr>
<td>Microlobulated, n (%)</td>
<td>6 (17.7)</td>
<td>4 (18.2)</td>
<td>1 (10.0)</td>
<td>1 (50.0)</td>
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<tr>
<td>Spiculated, n (%)</td>
<td>1 (2.9)</td>
<td>0</td>
<td>1 (10.0)</td>
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<tr>
<td>Orientation</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Parallel, n (%)</td>
<td>33 (97.0)</td>
<td>21 (95.4)</td>
<td>10 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Not parallel, n (%)</td>
<td>1 (3.0)</td>
<td>1 (4.6)</td>
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<td>0</td>
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<tr>
<td>Echo pattern</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hypoechoic, n (%)</td>
<td>27 (79.4)</td>
<td>19 (86.4)</td>
<td>7 (70.0)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Complex cystic and solid, n (%)</td>
<td>7 (20.6)</td>
<td>3 (13.6)</td>
<td>3 (30.0)</td>
<td>1 (50.0)</td>
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<tr>
<td>Posterior features</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Enhancement, n (%)</td>
<td>3 (8.8)</td>
<td>0</td>
<td>2 (20.0)</td>
<td>1 (50.0)</td>
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<tr>
<td>No features, n (%)</td>
<td>31 (91.2)</td>
<td>22 (100)</td>
<td>8 (80.0)</td>
<td>1 (50.0)</td>
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<tr>
<td>Associated features</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Vascularity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent, (%)</td>
<td>10 (29.4)</td>
<td>9 (40.9)</td>
<td>0</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Present, n (%)</td>
<td>24 (70.6)</td>
<td>13 (59.1)</td>
<td>10 (100)</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>Duct changes (Duct dilation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent, n (%)</td>
<td>30 (88.2)</td>
<td>18 (81.8)</td>
<td>10 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Present, n (%)</td>
<td>4 (11.8)</td>
<td>4 (18.2)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

BI-RADS: Breast Imaging Reporting and Data System. *In posterior features no mass with a shadow or combined pattern were found. No mass was found associated with calcifications.
papilloma lesions, and one of the two malignant papillary lesions. A complex cystic and solid echo pattern was observed in 7 (20.6%) of the 34 papillary lesions: three benign lesions, three atypical papilloma lesions, and one malignant lesion. Figure 3 shows a grayscale US of a complex cystic and solid mass with posterior enhancement. The histopathologic diagnosis was an intracystic papillary carcinoma.

Posterior findings were observed in 3 (8.8%) of 34 papillary lesions: two atypical papillary lesions and one malignant lesion. Vascularity was detected in 24 (70.6%) of 34 papillary lesions: 13 (59.1%) of 22 benign lesions, all atypical lesions (n = 10), and one of the two malignant lesions. Ductal ectasia was observed in 4 (11.8%) of the 34 papillary lesions. These cases were all benign papillary lesions. Figure 4 shows a grayscale US examination with a dilated duct with an intraductal mass and posterior enhancement. Color Doppler US showed vascularization. A CNB was recommended. The patient decided not to proceed with the procedure. She returned 10 months later with a significant increase in the size of the mass. The histopathologic diagnosis was an intraductal papilloma with atypical hyperplasia.

**DISCUSSION**

This study is the first in Mexico that shows ultrasonographic findings, clinical manifestations, and the histopathological correlation of benign, atypical, and malignant papillary breast lesions. The spectrum of ultrasonographic findings of the papillary breast lesions was heterogeneous.
There are no specific features that distinguish benign, atypical and malignant papillary lesions. In our study, benign papillary breast lesions were the most frequently confirmed histopathologic diagnosis ($n = 22, 64.7\%$). The most common ultrasonographic findings were oval shape, parallel orientation, non-circumscribed margin, hypoechoic pattern, and no posterior features. These results are comparable to Kuzmiack et al.$^8$, who included 51 papillary lesions, and the most frequent ultrasound findings in 23 benign lesions were a hypoechoic pattern ($n = 20, 86.9\%$) and the absence of posterior features ($n = 17, 3.9\%$). The presence of a Doppler signal in papillary breast lesions has been reported to be frequently due to the vascularity of a feeding pedicle; therefore, this increased vascularity is also seen in benign lesions.$^6,^8,^9,^{10}$ Vascularity does not define the lesion as benign or malignant. In our study, most lesions were vascular ($n = 24, 70.6\%$), and neither the morphologic characteristics nor the presence of vascularity or ductal status allowed us to distinguish benign, atypical, and malignant papillary lesions.

Atypical papillary lesions demonstrate ultrasonographic characteristics similar to those of benign papillary lesions in our study. The most common findings include an irregular shape, non-circumscribed margins, parallel orientation, a hypoechoic pattern, absence of posterior features, and the presence of vascularity. Kuzmiack et al.$^8$, who included 51 papillary lesions, found 14 cases with atypical ductal hyperplasia. The most frequent ultrasonographic findings were oval shape ($n = 10, 71.4\%$), circumscribed margin ($n = 10, 71.4\%$), parallel orientation ($n = 12, 85.7\%$), complex echogenic pattern ($n = 10, 71.4\%$), posterior acoustic enhancement ($n = 8, 57.1\%$), and absence of vascularity.
These findings are not comparable to our results. It is likely that the differences in ultrasonographic characteristics between the two studies are related to the small number of patients. Our study found that atypical papillary lesions were comparable to benign papillary lesions.

A palpable mass is the most common clinical sign of a papillary breast lesion. In our study, a palpable mass was found in 24 (70.6%) of 34 women. The diagnosis of a benign lesion was confirmed in 13 (59.1%) patients with a palpable mass, while all the cases (n = 10) with atypical papillary lesions, and one malignant papillary lesion had a palpable mass. In contrast, in a retrospective study that included 70 breast papillary lesions, 37 (52.8%) were symptomatic, and 33 (47.2%) were asymptomatic. The most common manifestation was nipple discharge (n = 27, 73.0%). A palpable mass was less frequent (n = 10, 27.0%)\textsuperscript{11}. In one retrospective study, 4450 papillary lesions were examined from November 1999 to July 2017. A palpable mass was found in 2290 (51.5%) patients, of which 1542 (67.33%) were benign, and 748 (32.67%) were malignant\textsuperscript{12}. The clinical presentation of breast papillary lesions varies, with a palpable mass and nipple discharge being the most common clinical manifestations.

The indication for a surgical excisional biopsy is controversial, especially for benign papillary lesions detected by CNB. Identifying a benign papillary lesion by CNB does not completely exclude the presence of atypia or malignancy elsewhere in the lesion. Therefore, excision is recommended, although the need for surgical treatment of benign papillary lesions remains controversial\textsuperscript{13}. Mac Coll et al.\textsuperscript{14}, in a retrospective, multicenter study in Canada, reported the frequency of upgrading the diagnosis to malignancy in benign papillary breast lesions previously diagnosed by CNB; 182 (68.4%) of 266

![Figure 3. A 30-year-old woman with a palpable breast mass. A-B: grayscale breast US shows a mass at 6 o’clock, periareolar, oval with microlobulated margins, parallel, complex cystic/solid (arrowheads), with posterior enhancement, BI-RADS 4B. C: color Doppler US showing a vascularized mass (arrow). D-E: CNB demonstrates a malignant epithelial neoplasm infiltrating the mammary stroma, with a predominantly papillary architecture and lacking a fibrous capsule, consisting of fibrovascular pedicles lined by epithelial cells with significant nuchal atypia, H&E. The histopathologic diagnosis was intracystic papillary carcinoma. US: ultrasound; BIRADS: Breast Imaging Reporting and Data System; CNB: core needle biopsy; H&E: hematoxylin and eosin]
patients diagnosed with a benign papillary lesion underwent excision. In 159 (87.36%) of the 182, a benign diagnosis was confirmed, while 21 cases were malignant papillary lesions, representing an incidence of diagnostic upgrading of 11.5%. In our study, the histopathologic diagnosis after surgical excision was consistent with CNB in 4 (80.0%) of 5 patients. Only one patient (20.0%) had discordance; CNB indicated atypical papilloma; however, intracystic papillary carcinoma was diagnosed after excision. This discordance between the CNB result and the excision biopsy indicates that the entire lesion must be investigated. However, surgical excision is not routinely recommended14. Removal of a papillary lesion by US-guided vacuum-assisted biopsy (VAB) is currently recommended as an alternative to surgical excision with comparable results12.

The strength of this study is the imaging method. The usefulness of US examination in diagnosing papillary lesions has been demonstrated, and when an expert performs US examination, an accurate diagnosis is made in most cases. Moreover, in all papillary lesions, the diagnosis was confirmed by histopathological examination.

There are several limitations of this study. The sample size is small and from a single center. It was not possible to characterize the findings of malignant papillary lesions because there were only two cases. In addition, because of the cross-sectional design of the study, the clinical follow-up and imaging evolution of the papillary lesions that did not undergo surgery were not recorded.

CONCLUSION

In our study, ultrasonographic findings of papillary breast lesions in Mexican patients were not specific to distinguish benign papillary lesions, atypical papillary lesions, or malignant lesions. If a breast papillary lesion is detected with US, a histopathologic diagnosis must be made.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

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Use of artificial intelligence. The authors state that they did not use generative artificial intelligence to prepare this manuscript and/or create tables, figures, or figure legends.

REFERENCES


Missing the PECARN rule is related to head CT overuse in Mexican children with mild head trauma

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ABSTRACT

Introduction: Computed tomography (CT) overuse in children with mild head trauma can be avoided by applying the Pediatric Emergency Care Applied Research Network (PECARN) rule. The aims of this study were (1) to apply the PECARN rule to predict traumatic brain injury on head CT in Mexican pediatric patients with mild head trauma and (2) to evaluate the extent of head CT overuse in cases that did not meet the criteria of the PECARN rule. Materials and methods: We conducted a cross-sectional study of children aged 0-10 years with mild head trauma (Glasgow Coma Scale 14-15 points) in which a head CT was ordered by referring clinicians in the emergency department. The PECARN rule was applied retrospectively. Results: A total of 145 children with mild head trauma were included: 64 (44.8%) girls and 80 (55.2%) boys. The mean ages were 3.7 ± 2.5 and 2.7 ± 2.2 years, respectively. The PECARN rule was not fulfilled in 29 (20.0%) of 145 children; therefore, a head CT should have been omitted. The PECARN rule had a sensitivity of 97.5% (95% confidence interval [CI] 92.6-100) and a negative predictive value of 96.5% (95% CI 60.7-100) for predicting clinically important traumatic brain injury on CT in pediatric patients with mild head trauma. Conclusion: This is the first study in Mexico which shows that there is head CT overuse in pediatric patients with mild head trauma. This finding may be due to emergency department clinicians overlooking the PECARN rule.

Keywords: Brain injury. Head injury. Pediatric trauma. Children. Clinical decision rules. PECARN.

INTRODUCTION

Head trauma in the pediatric population is an important cause of death and disability worldwide1. In Mexico, unintentional injuries or accidents are a public health concern. In 2021, head trauma was the leading cause of death in children between 5 and 14 years, the second cause in children between 1 and 4 years, and the third cause in children under 1 year2. Head trauma assessment is key to providing appropriate treatment and is a challenge for emergency room clinicians. Children with mild head trauma, according to the Glasgow Coma Scale (GCS), have a clinically important traumatic brain injury in less than 5% of cases3. Head computed tomography (CT) is performed in up to one-third of mild head trauma cases. This finding represents the overuse of this imaging examination3. Moreover, radiation exposure in children is estimated to result in lethal malignancy in 2-10 out of every 10,000 head CT scans3.
Decision rules such as the Pediatric Emergency Care Applied Research Network (PECARN)\(^4\), the Children’s Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE)\(^5\), and the Canadian Assessment of Tomography for Childhood Head injury (CATCH)\(^6\) have been proposed to identify clinically important traumatic brain injuries that should be evaluated with CT. The PECARN rule was validated in large pediatric cohorts at multiple centers and had higher sensitivity and specificity for identifying clinically important traumatic brain injury in children with mild head trauma compared to other decision rules\(^1,7,8\).

The PECARN rule is specifically aimed at avoiding head CT overuse in children with mild head trauma evaluated by clinicians in the emergency department\(^1\). The application of the PECARN rule has not been reported in Mexico. Thus, this study aimed (1) to apply the PECARN rule to predict traumatic brain injury on CT in Mexican pediatric patients with mild head trauma and (2) to evaluate the extent of head CT overuse in cases that did not meet the criteria of the PECARN rule.

**MATERIALS AND METHODS**

A retrospective cross-sectional study was conducted from January 2021 to May 2023 in the Departamento of Radiología and Imagen, Hospital of Alta Especialidad of Ixtapaluca, Secretaria of Salud, Ixtapaluca, Estado of Mexico, Mexico. Pediatric patients aged 0-10 years admitted to the emergency department with a diagnosis of mild head trauma and who underwent head CT were included. Patients were assessed by emergency room clinicians who ordered a head CT based on a clinical diagnosis of head trauma. Patients from other hospitals with other pathologies and insufficient data in their medical history were excluded. Informed consent was not required as the source of information was secondary. The study was approved by the institutional ethics and research committees.

**Study development and variables**

Clinical records were reviewed, and patients with mild head trauma with a GCS of 14-15 were selected. Sex, age, head trauma mechanism and classification, and the GCS were recorded. Clinical data included headache, vomiting, altered consciousness manifested by drowsiness or agitation, frontal subgaleal hematoma, post-traumatic seizure, palpable fracture, and signs of a basilar skull fracture.

**Definitions**

**Trauma mechanism:** this finding was classified as a traffic accident, a vehicle collision, a fall from own height, a fall from more than 0.9 m (3 feet) in children under 2 years of age, a fall from more than 1.5 m in children over 2 years of age, and other trauma mechanisms.

**Classification of trauma mechanisms:** traffic accidents, a vehicle collision, a fall from more than 0.9 m (3 feet) in children under 2 years of age, and a fall from more than 1.5 m in children over 2 years of age were classified as severe trauma; a fall from own height or a collision with stationary objects were considered mild trauma, and all other mechanisms were considered as moderate trauma.

**Traumatic brain injury on head CT:** a clinically important injury was defined as the presence of any of the following tomographic findings: intracranial hemorrhage or contusion, cerebral edema, traumatic infarction, diffuse axonal injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of cerebral herniation, skull diastasis, pneumocephalus, and a depressed skull fracture.

**The PECARN rule**

Compliance with the PECARN rule was determined retrospectively using the decision tree described by Kupperman et al.\(^4\) in two age groups. In children younger than 2 years, the criteria were altered mental status, scalp hematoma, loss of consciousness, mechanism of injury, palpable or nuclear skull fracture, and not acting normally as reported by parents; criteria in children older than 2 years included altered mental status, loss of consciousness, history of vomiting, mechanism of injury, clinical signs of basilar skull fracture, and severe headache.

Based on the presence of a risk predictor, the case was defined as PECARN+ with a recommendation to perform a head CT. PECARN− was the absence of any risk predictor, and a head CT was considered not warranted. A radiology resident (JDMC), using information from the medical record, evaluated the PECARN rule. The evaluator was aware of the head CT findings.

**Image acquisition and analysis protocol**

A Revolution Evo 128-slice tomograph (General Electric Co., Boston, MA, USA) was used. A head CT without contrast agent and axial slices was performed with the following parameters: 90-110 kVp, 190-210 mA,
and 2 mm thickness for reconstructions. The images were evaluated in the RIS PACS system (General Electric Co., Boston, MA, USA) and analyzed by a radiologist (LMS) with 12 years of experience who knew the clinical diagnosis of head trauma.

**Statistical analysis**

Data are presented as frequencies and percentages. Sensitivity, specificity, positive predictive value, negative predictive value, and 95% confidence intervals (CIs) of the PECARN rule for predicting traumatic brain injury on head CT were calculated. Microsoft Excel for Mac version 16.78 (Impressa Systems, Santa Rosa, CA, USA) and RStudio version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) were used.

**RESULTS**

A total of 145 pediatric patients aged 0-10 years with mild head trauma (GSC 14-15) were assessed. There were 65 (44.8%) girls and 80 (55.2%) boys. The mean ages were 3.7 ± 2.5 and 2.7 ± 2.2 years, respectively. The trauma mechanisms are described in Table 1. The most common mechanism was a fall of more than 0.9 m in children younger than 2 years or >1.5 m in children older than 2 years, which occurred in 48 (33.1%) of the 145 cases. Table 2 describes the classification of trauma mechanisms. The most common was severe trauma (n = 69, 47.6%).

The emergency department clinicians did not use the PECARN rule to decide which children with head trauma underwent head CT. Table 3 describes the head CT findings. A traumatic brain injury was found in 40 (27.6%) of 145 children. Intracranial hemorrhages or contusions were the most common findings (n = 36, 24.0%). In 11 (27.5%) of 40 children, two or more traumatic brain injuries were detected on CT. Head CT was normal in 92 (87.6%) of 105 children, with no evidence of a clinically important traumatic brain injury. In contrast, 13 children had a nondisplaced linear fracture that was not considered a clinically significant traumatic brain injury. Figures 1-3 show head CT findings of cases with and without traumatic brain injury.

Table 4 shows the clinical manifestations associated with the presence or absence of traumatic brain injury on CT. Regarding asymptomatic children, there were 12 (30.0%) of 40 with traumatic brain injury and 39 (37.0%) of 105 without traumatic brain injury on CT. Vomiting was the most common manifestation in both groups of symptomatic patients.

Table 5 shows the compliance with the PECARN rule. In 39 (97.5%) of 40 children with traumatic brain injury on CT, the rule was fulfilled (PECARN+); in contrast, 28 (26.7%) of 105 children did not meet the criteria of the rule (PECARN−), and the head CT showed no signs of traumatic brain injury (PECARN−). In these cases, a head CT should have been omitted. Only one child (2.5%) who did not meet the PECARN rule criteria had a traumatic brain injury on CT. The tomographic finding in this case was an epidural hematoma, and the clinical course was favorable.
Figure 1. A 1-year-old child was admitted to the emergency room with vomiting and altered consciousness after suffering head trauma from a fall from his height. The clinical diagnosis was mild head trauma (GCS 14, PECARN+). A and B: non-contrast head CT shows traumatic brain injury due to right subdural hematoma (asterisk) with frontal, temporal, and parietal extension leading to subfalcine herniation and collapse of the right lateral ventricle (arrow).


Figure 2. A 3-month-old infant with head trauma due to a fall from a height of 2 m. In the emergency room, a palpable skull fracture without accompanying neurological symptoms was found. The clinical diagnosis was mild head trauma (GSC 15, PECARN+). A: non-contrast head CT with 3D reconstruction shows a nondisplaced linear fracture (arrow) extending from the anterior region of the sagittal suture to the left parietal bone. B: non-contrast head CT with a bone window showing the fracture trace.

CT: computed tomography; GCS: Glasgow coma scale; PECARN: Pediatric Emergency Care Applied Research Network.
A 4-year-old girl with nausea and projectile vomiting following head trauma from a motor vehicle. The clinical diagnosis was mild head trauma (GCS 14, PECARN+).

**A:** non-contrast head CT shows a traumatic brain lesion due to an acute epidural hematoma (87 HU) in the right parietal region.

**B:** non-contrast head CT shows a multifragmentary fracture of the right parietal bone with a collapse of the fragments (asterisk).

CT: computed tomography; GCS: Glasgow coma scale; HU: Hounsfield Units; PECARN: Pediatric Emergency Care Applied Research Network.

### Table 4. Clinical manifestations associated with traumatic brain injury on head CT in pediatric patients with mild head trauma aged 0 to 10 years

<table>
<thead>
<tr>
<th>Description</th>
<th>Traumatic brain injury on CT, (n = 40)</th>
<th>No traumatic brain injury(^a) on CT, (n = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms, n (%)</td>
<td>12 (30.0)</td>
<td>39 (37.0)</td>
</tr>
<tr>
<td>With symptoms, n (%)</td>
<td>28 (70.0)</td>
<td>66 (63.0)</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
<td>8 (20.0)</td>
<td>25 (23.8)</td>
</tr>
<tr>
<td>Altered state of consciousness, n (%)</td>
<td>4 (10.0)</td>
<td>18 (17.1)</td>
</tr>
<tr>
<td>Parietal subgaleal hematoma, n (%)</td>
<td>5 (12.5)</td>
<td>5 (4.8)</td>
</tr>
<tr>
<td>Loss of consciousness, n (%)</td>
<td>1 (2.5)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Abnormal behavior reported by parents, n (%)</td>
<td>2 (5.0)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Posttraumatic seizure, n (%)</td>
<td>4 (10.0)</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Frontal subgaleal hematoma, n (%)</td>
<td>1 (2.5)</td>
<td>4 (3.8)</td>
</tr>
<tr>
<td>Signs of skull basilar fracture, n (%)</td>
<td>3 (7.5)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Headache, n (%)</td>
<td>-</td>
<td>3 (2.9)</td>
</tr>
</tbody>
</table>

\(^a\)Glasgow coma scale 14-15; CT: computed tomography.

The diagnostic performance of the PECARN rule for predicting traumatic brain injury on CT in children with mild head CT is shown in Table 6. The sensitivity was 75.0% (95% CI 92.6-100) and the NPV was 96.5% (95% CI 60.7-100), while the specificity was low at 26.6% (95% CI 0-100) and the accuracy was 46.2% (95% CI 30.7-61.6).

**DISCUSSION**

This is the first study in Mexico which shows that there is head CT overuse in pediatric patients with mild head trauma, which may be associated with missing the PECARN rule by emergency room clinicians. The head CT should be omitted in 1 in 4 children with minor head trauma.
Table 6. Diagnostic performance of the PECARN+ rule for predicting traumatic brain injury on head CT in pediatric patients aged 0 to 10 years with mild head trauma

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPP</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (95% CI)</td>
<td>97.5 (92.6-100)</td>
<td>26.6 (0-100)</td>
<td>33.6 (18.7-48.4)</td>
<td>96.5 (60.7-100)</td>
<td>46.2 (30.7-61.6)</td>
</tr>
</tbody>
</table>


The PECARN rule is an important tool for predicting clinically important traumatic brain injury in the pediatric population. Kupperman et al. included 42,412 children under 18 years of age with mild head trauma to evaluate the diagnostic performance of the PECARN rule for detecting clinically important traumatic injuries. They found a sensitivity of 100% (95% CI 86.3-100) and an NPV of 100% (95% CI 99.7-100) in children under 2 years of age. In children over 2 years of age, sensitivity was 96.8% (95% CI 89.0-99.6), and the NPV was 99.5% (95% CI 98.0-99.9). Due to its retrospective nature, our study examined only the association between PECARN rule compliance and tomographic findings of traumatic brain injury in children with mild head trauma. Our results show that PECARN rule compliance was associated with the detection of a traumatic brain injury on head CT. The sensitivity of the PECARN rule was 97.5% (95% CI 92.6-100), and the NPV was 96.5% (95% CI 90.0-99.6). The PECARN rule allows the identification of children with mild head trauma who require CT and avoids CT misuse when it is not indicated.

The most common symptoms of head trauma are vomiting and headache. Dunning et al. analyzed predictors of mild traumatic brain injury in a meta-analysis that included 22,420 patients. They concluded that headache, vomiting, loss of consciousness, and seizures represent a low relative risk for traumatic brain injury in head CT. In our pediatric patients with mild head trauma, the most common manifestation was vomiting, which was found in 8 (20.0%) of 40 children with traumatic brain injury on CT. On the other hand, the absence of symptoms was observed in 12 (30.0%) of these cases. The absence of symptoms should not influence the decision to perform a head CT; therefore, it is recommended to apply the PECARN rule.

The strengths of our study are related to the characteristics of the population studied, which include the different trauma mechanisms. Limitations are related to its retrospective design with possible data collection.
bias and that the study included only one institution. In addition, patients were not followed until hospital discharge, and readmissions were not recorded.

CONCLUSION

Our study shows head CT overuse in pediatric patients with mild head trauma, which may be due to missing the PECARN rule by emergency department clinicians. The use of the PECARN rule in pediatric patients with mild head trauma allows the reduction of radiation exposure without missing a traumatic brain injury on CT. Strategies need to be developed to promote the use of the PECARN rule by emergency room physicians to reduce CT misuse in mild head trauma. The increasing availability and speed of CT contribute to its increased use. Therefore, parents who would otherwise push for CT in a child in whom a CT is not indicated should be educated about the risks and benefits of CT³.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of individuals. This study complied with the Declaration of Helsinki (1964) and its amendments.

Confidentiality of data. The authors declare they followed their center’s protocol for sharing patient data.

Right to privacy and informed consent. Informed consent was not required for this observational study of information collected during routine clinical care.

Use of artificial intelligence. The authors state that they did not use generative artificial intelligence in the preparation of this manuscript and/or in the creation of tables, figures, or figure legends.

REFERENCES

Hippocampal MRI volumetry is associated with mild cognitive impairment in patients with HIV infection

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ABSTRACT

The relationship between hippocampal volume and neurocognitive impairment in patients with human immunodeficiency virus (HIV) infection has not been studied in the Mexican population. This study compared the hippocampal volume in Mexican patients with HIV infection and normal cognition or mild cognitive impairment (MCI). Hippocampal volume was determined manually with structural magnetic resonance imaging (MRI). A Montreal Cognitive Assessment (MoCA) score ≥ 26 defined patients with normal cognition and 19 to < 26 points defined patients with MCI. A total of 76 patients living with HIV were included: 56 men and 20 women with a mean age of 34.1 ± 10.11 years. Out of 76 patients, 50 (65.8%) were diagnosed with MCI with a MoCA test < 26. The mean MoCA score was lower in patients with MCI (22.9 ± 1.8) than in patients with normal cognition (26.6 ± 0.8) (p < 0.001). Hippocampal volume was lower in patients with MCI, with a mean of 2.81 ± 1.47 cm³ (right hippocampus) and 2.70 ± 1.35 cm³ (left hippocampus). In contrast, in patients with normal cognition, the mean was 3.34 ± 1.91 cm³ (right hippocampus) and 3.21 ± 1.70 cm³ (left hippocampus) (p < 0.001). This is the first study in Mexican patients with HIV infection, showing that a decrease in hippocampal MRI volume is associated with MCI.

Keywords: Magnetic resonance imaging. Hippocampal volumetry. Montreal cognitive assessment. Mild cognitive impairment. Human immunodeficiency virus.

INTRODUCTION

Cognitive impairment is a complication of human immunodeficiency virus (HIV) infection that can have a profound impact on an individual’s function and quality of life1,2. Approximately 50% of people living with HIV have some degree of cognitive dysfunction. This dysfunction has been described as HIV-associated neurocognitive disorders (HAND) that include asymptomatic cognitive impairment, mild cognitive impairment (MCI), and HIV-associated dementia with a prevalence of 23.5%, 13.3%, and 5.0%, respectively3. Cognitive impairment risk factors are related to prolonged evolution of the HIV infection, poor adherence to antiretroviral drugs or suboptimal treatment regimens, repeated treatment failures, co-infection with hepatitis C virus, low CD4+ T-cell count, and age over 50 years4.

Cognitive impairment assessment can be broadly divided into three areas: clinical history, performance on cognitive testing, and MRI examination1. MRI evidence of brain damage is the most objective measure2. Volumetric structural MRI examination of
the brain has shown that patients with HAND have poorer neurocognitive performance and smaller brain volumes\(^5\). The hippocampus has a critical role in memory and cognitive function. The HIV viral load in the brain is particularly high in the hippocampus, which damages its functional and structural integrity\(^5\). Decreased hippocampal volume has been associated with MCI in patients with HIV infection\(^1\)\(^-\)\(^3\). This study compared the hippocampal volume on structural MRI in Mexican patients with HIV infection and normal cognition or MCI.

**MATERIALS AND METHODS**

This cross-sectional study was conducted from February to August 2020 in the Imaging Department of the Centro Médico Nacional “La Raza” in Mexico City, Mexico. Adult patients from the HIV clinic with confirmed infection were included. Patients with conditions associated with decreased brain volume, such as ischemic brain disease, vasculitis, dementia of any etiology, or related to HIV, drug use, and patients with incomplete MRIs were excluded. Informed consent was obtained from the patients. The institutional ethics and research committees approved the study.

**Study development and variables**

Data were obtained from the clinical records of patients with a confirmed HIV infection. The variables recorded were age, sex, viral load, CD4 count, years of evolution with HIV, years of treatment, body mass index (BMI), marital status, education, and physical activity.

**Montreal Cognitive Assessment (MoCA)**

The MoCA evaluates eight cognitive domains (i.e., attention and concentration, executive functions, memory, language, visuconstruction skills, conceptual thinking, calculations, and orientation). The assessment is scored 0-30 points (higher scores indicate better cognitive function). Normal scores are ≥ 26 points, and MCI is 19 to < 26 points. This screening tool takes about 10 min to complete. The Mexican version 8.1\(^5\)\(^,\)\(^7\) was used.

**Image acquisition and analysis protocol**

A Philips Ingenia 1.5T resonator (Koninklijke Philips, Cambridge, MA, USA) with a skull antenna was used. The structural MRI protocol of the hippocampus used the following sequences: T1 3D isotropic: axial and oblique plane perpendicular to the longitudinal axis of the hippocampus. CUBE T2FLAIR FS: TE 110 ms and TR 4125 ms.

Hippocampal delineation, manual segmentation, and volumetry using the Volume Rendering software of the Intellispace-Philips post-processing package (Koninklijke Philips, Cambridge, MA, USA) was performed by a neuroradiologist with 6 years of experience (REM). Figure 1 shows the manual delineation of the two hippocampi in the structural MRI of the brain.

**Statistical analysis**

Variables are described as means, standard deviation, and range for numerical data and frequency and percentages for categorical data. Analysis of variance (ANOVA) was used to analyze the hippocampal volume in patients with normal cognition and MCI. Bivariate analysis using Pearson’s \(X^2\) test or Fisher’s exact test identified factors associated with MCI (\(p < 0.05\)). The IBM® SPSS® 25 software (IBM Co. Armonk, NY, USA) was used for data analysis.

**RESULTS**

We included 76 HIV-infected patients. Their mean age was 34.1 ± 10.11 years (range 26-41 years). Of them, 56 (73.7%) were males and 20 (26.3%) were females. Table 1 shows the characteristics of HIV-infected patients with normal cognition or MCI determined by the MoCA. MCI was detected in 50 (65.8%) patients. The mean MoCA score was significantly lower in patients with MCI (22.9 ± 1.8) than in patients with normal cognition (26.6 ± 0.8) (\(p < 0.001\)).

The hippocampal volume was significantly lower in 50 HIV-infected patients with MCI. It was 2.81 ± 1.47 cm\(^3\) in the right hippocampus and 2.70 ± 1.35 cm\(^3\) in the left hippocampus compared with 26 patients with normal cognition who had a mean right hippocampal volume of 3.34 ± 1.91 cm\(^3\) and a left hippocampal volume of 3.21 ± 1.70 cm\(^3\). The volume of both hippocampi was lower in patients with HIV who had MCI (\(p < 0.001\)). Figure 2 shows MRI 3D volume reconstructions of both hippocampi in an HIV-infected patient with MCI (MoCA score, 20 points).

A significant difference in the years of evolution of HIV infection was found between patients with normal cognition and MCI (5.42 ± 2.90 and 4.29 ± 2.82 years, respectively) (\(p < 0.027\)). Viral load, CD4 cells, years
of treatment, BMI, marital status, scholarship, exercising, and not exercising were comparable between HIV-infected patients with normal cognition or MCI.

DISCUSSION

This is the first study in Mexico that demonstrates the association between decreased hippocampal MRI volume and MCI in HIV-infected patients. MRI hippocampus volume could be a biomarker for detection of cognitive impairment in HIV-infected patients.

An effort to standardize hippocampal volumes is underway. A hippocampal volume > 3 cm³ is normal, while a volume < 2 cm³ is abnormal. Interestingly, in a study of 76 Mexican patients not infected with HIV, Mondragon et al. evaluated hippocampal volume in Alzheimer’s disease (n = 26), MCI (n = 20), and normal aging (n = 30). They used a 3.0T MRI scanner and performed manual hippocampal volumetry. The mean normalized hippocampal volume in patients with Alzheimer’s disease was 2.38 ± 0.51 cm³ (p < 0.001), while in the subgroup of patients with MCI, it was 2.91 ± 0.78 cm³ (p = 0.019). These results are comparable with our study in HIV-infected patients with MCI who had a mean hippocampal volume of 2.81 ± 1.47 cm³ (right hippocampus) and 2.70 ± 1.35 cm³ (left hippocampus), suggesting that the decrease in hippocampal volume in HIV-infected patients with MCI could be a biomarker for detection of cognitive impairment.
Table 1. Comparison of characteristics of HIV-infected patients with normal cognition or MCI assessed by the MoCA test and their relationship to hippocampal volumetry

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 76)</th>
<th>Normal cognition (n = 26)</th>
<th>MCI (n = 50)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>34.1 ± 10.11</td>
<td>32.3 ± 7.25</td>
<td>37.0 ± 12.66</td>
<td>0.587</td>
</tr>
<tr>
<td></td>
<td>(26, 41)</td>
<td>(26, 43)</td>
<td>(26, 37)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>20 (26.3)</td>
<td>7 (26.9)</td>
<td>13 (26.0)</td>
<td>0.887</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>56 (73.7)</td>
<td>19 (73.1)</td>
<td>37 (74.0)</td>
<td>0.931</td>
</tr>
<tr>
<td>MoCA test</td>
<td>76</td>
<td>26.6 ± 0.8</td>
<td>22.9 ± 1.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(26, 29)</td>
<td>(19, 25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume of the right hippocampus, cm³</td>
<td>76ᵃ</td>
<td>3.34 ± 1.91</td>
<td>2.81 ± 1.47</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(1.43, 5.25)</td>
<td>(1.34, 4.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume of the left hippocampus, cm³</td>
<td>76ᵃ</td>
<td>3.21 ± 1.70</td>
<td>2.70 ± 1.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>(1.41, 4.91)</td>
<td>(1.35, 4.05)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral load, copies/mL</td>
<td>45.13 ± 12.64</td>
<td>51.27 ± 13.56</td>
<td>49.88 ± 10.3</td>
<td>0.417</td>
</tr>
<tr>
<td></td>
<td>(36, 53)</td>
<td>(34, 53)</td>
<td>(39, 56)</td>
<td></td>
</tr>
<tr>
<td>CD4, cells per mm³</td>
<td>605 ± 59.57</td>
<td>589 ± 47.08</td>
<td>578 ± 45.89</td>
<td>0.285</td>
</tr>
<tr>
<td></td>
<td>(567, 640)</td>
<td>(560, 678)</td>
<td>(569, 509)</td>
<td></td>
</tr>
<tr>
<td>Evolution, years</td>
<td>5.01 ± 2.30</td>
<td>5.42 ± 2.90</td>
<td>4.29 ± 2.82</td>
<td>0.027</td>
</tr>
<tr>
<td></td>
<td>(4, 6)</td>
<td>(4, 6)</td>
<td>(4, 5)</td>
<td></td>
</tr>
<tr>
<td>Years of treatment</td>
<td>4.09 ± 2.30</td>
<td>5.41 ± 2.92</td>
<td>4.30 ± 2.79</td>
<td>0.103</td>
</tr>
<tr>
<td></td>
<td>(3, 6)</td>
<td>(3, 6)</td>
<td>(4, 5)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal weight, n (%)</td>
<td>15 (19.7)</td>
<td>7 (26.9)</td>
<td>8 (16.0)</td>
<td>0.509</td>
</tr>
<tr>
<td>Overweight, n (%)</td>
<td>20 (26.3)</td>
<td>5 (19.2)</td>
<td>15 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Class 1 obesity, n (%)</td>
<td>40 (52.6)</td>
<td>14 (53.9)</td>
<td>26 (52.0)</td>
<td></td>
</tr>
<tr>
<td>Class 2 obesity, n (%)</td>
<td>1 (1.4)</td>
<td>0</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Marital statusᵃ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>38 (50.0)</td>
<td>12 (46.2)</td>
<td>26 (52.0)</td>
<td>0.981</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>19 (25.0)</td>
<td>7 (26.9)</td>
<td>12 (24.0)</td>
<td></td>
</tr>
<tr>
<td>Divorced, n (%)</td>
<td>6 (7.9)</td>
<td>2 (7.7)</td>
<td>4 (8.0)</td>
<td></td>
</tr>
<tr>
<td>Common law, n (%)</td>
<td>2 (2.6)</td>
<td>1 (3.8)</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school, n (%)</td>
<td>15 (19.7)</td>
<td>7 (26.9)</td>
<td>8 (16.0)</td>
<td>0.670</td>
</tr>
<tr>
<td>Technician, n (%)</td>
<td>16 (21.0)</td>
<td>10 (38.5)</td>
<td>6 (12.0)</td>
<td></td>
</tr>
<tr>
<td>Bachelor, n (%)</td>
<td>10 (13.1)</td>
<td>7 (26.9)</td>
<td>3 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Exercises, n (%)</td>
<td>14 (18.4)</td>
<td>3 (11.5)</td>
<td>11 (22.0)</td>
<td>0.264</td>
</tr>
<tr>
<td>Does not exercise, n (%)</td>
<td>62 (81.6)</td>
<td>23 (88.5)</td>
<td>39 (78.0)</td>
<td></td>
</tr>
</tbody>
</table>

mL: milliliter; mm³: cubic millimeter; BMI: body mass index; CD4: cumulus of differentiation 4 or cluster of fourfold differentiation expressed in T lymphocytes; *Total number of observations was 152, corresponding to the sum of the two hippocampi in 76 patients; †Two patients with unspecified marital status; cm³: cubic centimeters; MoCA: Montreal Cognitive Assessment; HIV: human immunodeficiency virus; MCI: mild cognitive impairment. Values refer to mean ± SD (min, max) unless otherwise stated.

patients is similar to that in MCI patients not infected with HIV. In a study by Wang et al., which included 30 HIV-infected patients and a control group of 15 healthy people, the hippocampal volume was lower in the HIV-infected group than in the control group. In addition, the hippocampal volume was smaller in the group with severe cognitive deficits than in the MCI group; these differences were not statistically significant. On the other hand, Archibald et al. reported postmortem MRI findings of 21 HIV-positive cases with increased cerebrospinal fluid and significantly decreased volumes of cerebral white matter, hippocampus, and cerebral cortex. Brain MRI can detect abnormalities or specific MRI features with accuracy to detect neurocognitive impairment in HIV-infected patients. This findings could be included in HAND classification criteria in the future.
Screening tests are crucial for diagnosing neurocognitive disorders and must be very sensitive for MCI assessment\(^{13}\). In a systematic review, Ciesielska et al.\(^{13}\) compared the MoCA with the Mini-Mental Status Examination (MMSE) in detecting MCI in patients over 60 years of age not infected with HIV. A total of 20 studies of the MoCA test and 13 of the MMSE were included. Analysis of the ROC curve for the MoCA test showed that the best detection of MCI was achieved with a cutoff of 24/25 (\(n = 9350\), 80.5% sensitivity, and 81.2% specificity). The AUC was 0.846 (95% CI 0.823-0.868). The cutoff was 27/28 (\(n = 882\), 66.3% sensitivity, and 72.9% specificity) for the MMSE. The AUC was 0.736 (95% CI 0.718-0.767).

The authors concluded that MoCA screened MCI better than the MMSE. In a study with 100 HIV-infected patients, Hasbun et al.\(^{14}\) found neurocognitive impairment in 75%. The median age was 43 years (22-64 years), and the majority were males (75%). The MoCA with a score < 26 was associated with neurocognitive impairment (OR 4.83, 95% CI 1.70-12.74) (\(p = 0.003\)) and had good screening accuracy with a sensitivity of 85%, a specificity of 40%, a negative predictive value of 48%, and a positive predictive value of 81%. In our study, we found a significant difference in the MoCA score in HIV-infected patients with MCI compared with patients with normal cognition (22.9 ± 1.8 vs. 26.6 ± 0.8) (\(p < 0.001\)). The MoCA is a quick, quantitative, sensitive tool that can be used for screening neurocognitive impairment in HIV-infected patients\(^{13}\).

The study strengths were using MoCA to identify MCI and using freely available software to perform reproducible hippocampal volumetry MRI. Study limitations include the small sample size and the cross-sectional design. In addition, comorbidities that could influence cognitive performance were not assessed. Another disadvantage of this study was the use of a 1.5T MRI scanner, as the tissue contrast and the definition of the hippocampal edges in the images are inferior to the contrast and definition provided by a 3.0T MRI scanner.

**CONCLUSION**

Our study demonstrated a significant reduction in hippocampal MRI volumetry in HIV-infected patients with MCI compared with patients with normal cognition. Hippocampal MRI volumetry is a valuable diagnostic quantitative tool for detecting decreased hippocampal volume. However, its clinical use is not yet recommended due to the lack of evidence and standardization of the cutoff points of the diagnostic threshold. There is still much to learn about its use and clinical relevance in HIV-infected patients. Further research with prospective studies in a larger and more diverse
patient population is needed to determine the impact of HIV infection on hippocampal volume and explore therapeutic interventions.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Right to privacy and informed consent. Informed consent was obtained from the patients included in this study.

Use of artificial intelligence. The authors did not use generative artificial intelligence to prepare this manuscript or create tables, figures, or figure legends.

REFERENCES

CT and transthoracic echocardiographic findings of cardiac rhabdomyosarcoma in an adult: a case report

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CASE REPORT

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ABSTRACT

Cardiac rhabdomyosarcomas are rare in adults and are symptomatic when they become large or invade adjacent structures. We present the case of a 30-year-old woman with a left atrial tumor detected with contrast-enhanced computed tomography (CECT) and transthoracic echocardiogram (TTE). The patient presented severe mitral stenosis with heart and respiratory failure, requiring advanced airway management and emergency cardiac surgery. CECT showed a filling defect in the left atrium caused by a 66 x 37 x 33 mm, oval, hypodense, and homogeneous solid mass with a well-defined margin occupying the left atrium. The mass originated from the atrial septum and invaded the right atrium. Mild enhancement was noted in the contrast phase. TTE showed a mobile hyperechogenic, homogeneous, non-vascularized mass with a well-defined margin adhering to the interatrial septum and prolapsing into the left ventricle during atrial systole, causing severe mitral stenosis. The tumor was excised, and a diagnosis of embryonal rhabdomyosarcoma was confirmed. This case is the first reported in Mexico of a cardiac embryonal rhabdomyosarcoma detected in the left atrium in an adult. CECT and TTE imaging findings are reported for educational purposes.

Keywords: Cardiac tumors. Embryonal rhabdomyosarcoma. Rhabdomyosarcoma. Primary cardiac tumors. Case report.

INTRODUCTION

Primary cardiac tumors are rare in adults, and embryonal rhabdomyosarcoma is rarer. This condition mainly affects children with an average age of 5 years. It is usually asymptomatic until it reaches a large size and affects adjacent structures, causing heart failure, although symptoms vary according to location and size. The diagnostic modalities include transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), contrast-enhanced computed tomography (CECT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT). TTE shows a hyperechogenic homogeneous mass, sometimes with hypoechoic areas suggesting necrosis. Computed tomography (CT) shows a hypodense tumor with smooth, well-defined margins. On MRI, the tumor is isointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Additionally, enhancement on CECT and MRI with contrast is usually homogeneous, but it may be heterogeneous due to necrosis. We present a 30-year-old woman with severe mitral stenosis and heart and respiratory failure with a left atrium tumor detected by CECT and TTE.
Figure 1. CECT of a 30-year-old woman with severe mitral stenosis, heart and respiratory failure, and a left atrium tumor. **A**: two-chamber view. **B**: four-chamber view. **C**: coronal view showing a filling defect in the left atrium at the expense of an oval, hypodense, homogeneous, solid mass measuring $66 \times 37 \times 33$ mm, with a well-defined margin occupying the entire left atrium (yellow star). The mass originated in the interatrial septum and invaded the left atrium. Mild enhancement was seen in the contrast phase. **D**: coronal view showing peribronchovascular airspace opacification suggestive of acute pulmonary edema (yellow dashed circles).

Ao: aorta; MPa: main pulmonary artery; CECT: contrast-enhanced computed tomography; IAS: interatrial septum; IVS: interventricular septum; LA: left atrium; LMB: left main bronchus; LPv: left pulmonary vein; LV: left ventricle; RV: right ventricle; RA: right atrium; RMB: right main bronchus; RPa: right pulmonary artery; TRA: trachea.
CASE DESCRIPTION

A 30-year-old woman with no underlying pathology came to the emergency department with a one-month history of progressive dyspnea (NYHA II), orthopnea, and paroxysmal nocturnal dyspnea accompanied by activity-related syncope. Her symptoms had worsened. On admission, she presented hemodynamic instability and respiratory failure requiring advanced airway management, a central venous catheter, and an endopleural tube due to pneumothorax.

Imaging findings

A pulmonary embolism was initially suspected, and she underwent CECT (LightSpeed VCT 64 Slice CT Scanner, General Electric Inc., Norwalk, CT, USA), which showed a filling defect in the left atrium consistent with a hypodense mass $66 \times 37 \times 33$ mm with a well-defined margin with contrast phase enhancement. Pulmonary embolism was excluded (Figure 1). A myxoma was suspected, and a TTE (Vivid E95 Cardiac, General Electric Inc. Norwalk, CT, USA) was performed with a 2-12 MHz sector transducer. TTE showed a hyperechogenic homogeneous, non-vascularized, mobile mass $67 \times 36$ mm in diameter, with a well-defined margin suggestive of a thrombus adhered to the interatrial septum (Supplementary Video 1) prolapsing into the left ventricle during atrial systole with severe mitral stenosis (Figure 2).

Clinical outcome

An oval, smooth, light brown, congestive, semisolid tumor measuring $65 \times 40 \times 40$ mm was excised (Figure 3). Histopathologic examination showed a cardiac embryonal rhabdomyosarcoma. The surgical margin was free of malignancy. Immunohistochemical markers were MYOD1 positive, DESMINA positive, TLE1 positive, FLI-1 positive, KI67 positive, HHH3 positive, CD34 negative, CD31 negative, ERG negative, and MYOGENIN negative.

The clinical outcome was good, with no complications. A postoperative follow-up echocardiogram showed normal systolic ventricular function with mild tricuspid regurgitation. No primary valve damage, residual tumor, or intra-atrial thrombus was found. Chest CECT showed no residual tumor or metastatic lesions.
at immediate postoperative follow-up (Figures 4 A, B, and C). The patient did not require chemotherapy or radiotherapy and was discharged in good clinical condition. At her 8-month clinical follow-up, she was asymptomatic, and CECT examinations of the head, chest, abdomen, and pelvis did not show evidence of tumor recurrence or metastasis (Figures 4 D, E, and F).

**DISCUSSION**

This report is the first in Mexico of a cardiac embryonal rhabdomyosarcoma in the left atrium of a 30-year-old symptomatic adult who developed severe mitral stenosis and heart and respiratory failure requiring emergency cardiac surgery due to the large size. The CECT and TTE imaging findings are reported for educational purposes.

Intracardiac embryonal rhabdomyosarcoma imaging findings vary. There are a few case reports of cardiac embryonal cardiac rhabdomyosarcoma in the left atrium in adults. Heart and respiratory failure symptoms as an initial presentation have been reported, making its initial approach and diagnosis difficult. Jing et al. reported a large tumor occupying almost the entire left atrium, causing flow obstruction by protruding into the left ventricle. Our patient had heart and respiratory failure at baseline, prompting us to perform CECT with a suspected diagnosis of pulmonary thromboembolism. It is important to distinguish embryonal rhabdomyosarcoma from myxomas and intracardiac thrombi. Myxomas are usually pedunculated and more mobile, unlike malignant tumors, which tend to have a wide base and greater vascularity. Thrombi rarely show contrast enhancement. In our case, TTE with Doppler showed no vascularity, probably due to motion artifacts caused by the patient’s agitation and hemodynamic instability. These situations and the urgent need for tumor removal did not allow adequate characterization of vascularity. CECT and TTE findings such as a wide base, vascularity on Doppler, and contrast enhancement on CECT are key in this diagnosis.

The treatment and prognosis of cardiac embryonal rhabdomyosarcoma vary according to the stage of the disease and patient characteristics, with 5-year survival rates ranging from 35.0-100%. There are no standardized or globally accepted management guidelines due to the lack of information and publications being mostly case reports. Treatment always involves complete tumor resection, which may be impossible in cases of extensive infiltration into the interatrial septum as in the case reported by Rodrigues et al. In this case, surgical resection was not possible because of extensive infiltration of the lateral wall of the left ventricle and mitral valve. In our case, complete surgical resection with a tumor-free margin was possible despite originating from the interatrial septum’s wall. The prognosis and treatment of embryonal rhabdomyosarcoma can vary widely depending on factors such as stage at diagnosis, success of surgical resection, and treatment response. Early diagnosis and prompt treatment are critical to improving the patient’s prognosis.

Embryonal rhabdomyosarcoma is a characteristically aggressive malignant tumor with up to 46.0% of metastases found at diagnosis. The brain, lung, liver, and bone are the most common sites of dissemination. In our case report, no invasion of adjacent structures or metastases was found despite its large size. In the clinical and imaging follow-up after 8 months, no metastases were documented. PET-CT allows a better search and staging for metastatic lesions but was unavailable at our institution.

The strengths of this case report are the clinical, imaging, and histopathologic correlations. The limitations were that, given the severity, sudden onset of symptoms, and urgent need for cardiac surgery, it was not possible to perform complementary studies such as TEE or cardiac MRI. Another limitation was that tomography was not synchronized with cardiotomography, which made it more susceptible to motion artifacts.
CONCLUSION

This case report presents a 30-year-old woman with a mass in the left atrium. A cardiac embryonal rhabdomyosarcoma was confirmed by histopathology. CT and TTE imaging findings were decisive for surgical treatment. Our case report shows that TTE and CECT are sufficient for diagnosis and surgical management in urgent situations. The radiologist should be aware of the possible differential diagnoses of cardiac tumors in adults beyond myxoma and thrombi and their imaging findings, keeping in mind the subtle but crucial differences.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare they followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. Informed consent was not required for this case report of routinely acquired clinical data.

Use of artificial intelligence. The authors state that they did not use generative artificial intelligence to prepare this manuscript and/or create figures, or figure legends.

Supplementary data

Supplementary data are available at DOI: 10.24875/JMEXFRI.23000007. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

REFERENCES

A 74-year-old man was admitted for evaluation of lower limb paraplegia and anesthesia. He also suffered constipation and urinary retention. Neurologic examination revealed subacute transverse myelopathy at the anatomic level of thoracic (T) vertebra 8 and a functional level at T10. Magnetic resonance imaging (MRI) (1.5T, Phillips Healthcare, Best, The Netherlands) of the thoracolumbar region showed increased volume of the spinal cord between T2-T6 on T1-and T2-weighted images and short tau inversion recovery (STIR) sequence.
(Figure 1A). On the T1-weighted image, the lesion was hyperintense in the center, probably due to bleeding (Figure 1B). Annular enhancement was seen at T11/T12 after administration of a gadolinium-based contrast agent (Figure 2A). Necrosis and cystic degeneration were observed on fat-saturation (FATSAT) imaging (Figure 2B). CSF culture and the GeneXpert MTB/RIF assay were positive for Mycobacterium tuberculosis. The diagnosis was spinal intramedullary tuberculoma (IMT).

IMT is an atypical initial manifestation of tuberculous meningitis. Most spinal tuberculomas are located in the thoracic region. MRI has high sensitivity (100%) and specificity (88.2%) for IMT and typically shows hypointense rings on T1-weighted images that are enhanced with contrast on T2-weighted images. A ring-enhanced lesion with peripheral edema is characteristic. The main advantage of MRI is that the entire spine can be visualized to diagnose noncontiguous lesions.

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