Radiology's Role in the Detection and Management of Long-Term Complications Associated with COVID-19: A Comprehensive Review

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Abstract

The ongoing COVID-19 pandemic, caused by the SARS-CoV-2 virus, has led to significant challenges in healthcare systems worldwide. Beyond acute respiratory symptoms, many patients experience long-term complications, often termed "long COVID." Radiology plays a crucial role in identifying and managing these complications, allowing for timely interventions and improved patient outcomes. This review examines the current literature on the use of various radiological modalities, including chest X-rays (CXR), computed tomography (CT), and lung ultrasonography (LUS), in detecting and assessing COVID-19-related pulmonary complications. A comprehensive analysis of imaging findings and their correlation with clinical outcomes was performed, drawing from multiple studies that highlight the efficacy and limitations of these imaging techniques. The findings indicate that while CT is highly sensitive in diagnosing COVID-19 pneumonia, CXR remains a valuable initial imaging tool, especially in emergency settings. LUS has emerged as a useful bedside alternative, particularly in critically ill patients. Each modality presents unique advantages and limitations, with varying efficacy in different clinical contexts. Scoring systems for assessing the severity of pulmonary involvement were also reviewed, emphasizing the importance of standardized reporting in clinical practice. Radiological imaging is integral to the detection and management of long COVID-19 complications. Combining multiple imaging modalities can enhance diagnostic accuracy and facilitate better patient care. Future research should focus on refining imaging protocols and establishing guidelines for the effective use of radiology in managing long COVID-19.

Keywords: COVID-19, Radiology, Long COVID, Chest Imaging, Pulmonary Complications.

Introduction

The COVID-19 pandemic, instigated by the new coronavirus SARS-CoV-2, persists in exerting pressure on global healthcare systems and adversely affecting the economies of several nations [1,2]. Despite COVID-19 was officially identified in Wuhan, Hubei Province, China, in December 2019, the pandemic may have begun far earlier. COVID-19 is a multi-organ illness characterized by diverse manifestations, ranging from asymptomatic cases to pneumonia, gastrointestinal and neurological symptoms, and acute respiratory distress syndrome (ARDS) [3-7]. Early anxiety and dysphagia may occur [3,6]. SARS-CoV-2 is often spread by airborne droplets and contaminated surfaces. Nonetheless, there is additionally proof of fecal–oral transfer [5,7]. While COVID-19 may be present as a multi-organ illness, the lungs are regarded as the virus's primary target.

Currently, reverse-transcription polymerase chain reaction (RT-PCR) screening is regarded as the definitive method for diagnosing or screening COVID-19. Although RT-PCR exhibits excellent specificity, its sensitivity varies between 37% and 71%, with false negative findings occurring in 50% of instances [8,9]. The restricted testing capability may result from inadequate viral burden in the specimen or the timing of sample collection. Thoracic imaging using chest radiography (CXR) and computed tomography (CT) is often regarded as an essential instrument for aiding in the diagnosis and treatment of lung diseases [10]. Chest imaging is now warranted for COVID-19 patients exhibiting an acute respiratory condition and for

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suspected cases to facilitate prompt medical triage when there is a high pretest likelihood in patients at moderate to high risk of progression [11,12]. While chest X-ray (CXR) is typically recommended as the initial imaging modality for suspected respiratory cases in the emergency department (ED) [13-18], the selection between CXR and computed tomography (CT) is generally determined by the clinical team's discretion, local resource availability, and radiologists' expertise [11,12,18].

CT is most beneficial in suspected COVID-19 pneumonia patients with complications when there is a significant risk of complications [19,20]. Nonetheless, CT may facilitate care by isolating probable patients exhibiting typical imaging characteristics while awaiting swab RT-PCR findings [21]. The function of lung ultrasonography (LUS) is still debated. Consequently, the principal radiology associations do not yet endorse the application of imaging for testing or as a sole diagnostic instrument for COVID-19. RT-PCR confirmation is usually necessary, even when typical imaging results are present [21,22]. Chest imaging plays a crucial role in diagnostic assistance when characteristic imaging features for COVID-19 are present with numerous negative RT-PCR results and a high pretest likelihood [23]. In these specific instances, confirmation should be performed using serology in conjunction with laboratory tests [24].

Thoracic Radiography

Chest computed tomography (CT) as well as chest radiography (CXR) are the imaging techniques often used to identify lung abnormalities in the early stages of infection, as well as to evaluate the severity and track the evolution of COVID-19 pneumonia [25,26]. CT has mostly been used for the diagnosis of COVID-19 pneumonia [27-29]. This is attributable to China's experience, where access to CT was comparatively straightforward at the onset of the global epidemic, and the limited sensitivity of CXR in detecting pulmonary involvement, especially in the first phase of the illness [25,27,28]. Utilizing RT-PCR as the benchmark, the sensitivity of CRX, influenced by disease stage, severity, regional COVID-19 prevalence, and radiologist proficiency, potentially augmented by artificial intelligence (AI), varies significantly from 41.7% to 90%, remaining inferior to CT, which ranges from 60% to 98% [30-32]. The specificity ranges from 33% to 60.6% [33,34]. Currently, there is a paucity of research on the diagnostic value of CXR, and their relevance is constrained by restricted sample numbers, often excluding healthy people or non-COVID-19 patients [33,35].

In emergency treatment, particularly inside biocontainment units (BUs) as well as intensive care units (ICUs), the significance of chest X-rays (CXR) is pertinent for critically sick patients [15,27,35]. The European Society of Radiology (ESR) as well as the European Society of Thoracic Imaging (ESTI) recommended chest X-ray (CXR) for the follow-up of patients in the ICU who are too delicate to undergo CT scans [19]. Conversely, most radiology associations recommend chest X-ray as the primary diagnostic modality for evaluating COVID-19 patients [13-18]. Nonetheless, it is important to recognize that the choice of imaging modality often relies on the clinical team's discretion, the accessibility of local assets, and the radiologists' experience. Chest CT use was predominant in Italy and China at the onset of the global epidemic [21,36].

Recent literature indicates that chest X-rays (CXR) exhibit radiographic characteristics in the majority of COVID-19 patients, including reticular changes, ground-glass opacities (GGO), reorganizations, bilateral participation, peripheral dispersion, lower zone predominance, pleural effusion, and diminished lung volume, along with adverse effects including pneumothorax (PNX), pneumomediastinum (PM), as well as subcutaneous emphysema, corroborating earlier findings on computed tomography (CT) [8,35,37]. The effective dosage (mSv) decreases for chest X-rays (CXR) compared to computed tomography (CT) [38]. Consequently, several limitations, such as increased ionizing radiation exposure from CT compared to CXR, limited access to specialized CT scanners, challenges in expediting CT room disinfection, the potential for SARS-CoV2 transmission during patient transport to the CT over CXR [11,23,25,35]. Furthermore, the escalation of radiological assessments accompanying the surge in hospitalized patients renders the ongoing use of chest CT along the illness trajectory challenging [26]. The American College of Radiology (ACR) indicated that decontaminating CT rooms after scanning COVID-19 patients might hinder the provision of radiological services and proposed that portable CXR could be the most effective instrument to reduce

the risk of cross-infection [23]. Consequently, European hospitals, especially in Italy as well as Great Britain, are increasingly utilizing chest X-rays (CXR), whether bedside or standard, as the initial radiological approach for patients exhibiting respiratory distress and potential COVID-19, as well as for monitoring the progression of pulmonary anomalies especially in critically ill patients in the ICU, where CXR can also assess chest tube placement (Figure 1) [12,23,27,39].



Figure 1. The Bedside Chest X-Ray (CXR) Of A COVID-19 Patient, Seen in the Anterior-Posterior Projection, Reveals Diffuse Linear Opacities Accompanied With Ground-Glass Opacity (GGO).

Chest X-ray (CXR) is an economical and readily accessible diagnostic instrument. Various procedures have been suggested for the utilization of CXR in imaging departments, bedside settings in hospital wards and BUs, as well as in emergency departments. All chest X-rays are obtained as computational or digital images [27,40]. In the present pandemic environment, CXR practices in isolation rooms inside emergency departments are very critical. To mitigate the risk of SARS-CoV2 transmission, similar to Ebola virus disease (EBD), descriptions for temperatures and transitional areas in BUs have been established; adherence to dressing and undressing protocols for operators is mandated; and disinfection of both the surroundings and the machinery is required [39,41]. The operations need two specialized operators, often two radiographers. Personal protective equipment (PPE) must be used, with the degree of protection varying based on the specific duties to be executed [39,41]. The third degree of protection is designated for operators present in the same location as a patient presumed or proven to be infected with SARS-CoV-2 [39,41,42]. The third degree of protection necessitates the implementation of a comprehensive barrier, including airborne and contact safety measures, along with eye protection, in conjunction with normal precautions [39,41,42]. Chest X-rays (CXRs) conducted at the bedside, even for critically ill individuals in isolation rooms, are performed in the supine position, often with an antero-posterior (AP) projection with a portable CXR equipment [35,39]. The advised source-detector spacing is 100 cm, with exposure parameters of 75-85 KV when using an X-ray grid and 65-70 KV in the absence of an X-ray grid [35]. Radiographic cassettes must be enclosed in a double- or triple-sealed fluid-proof plastic container or a plastic cover along with a clean pillowcase, and they must be adequately cleaned after the operation [35]. The photos are preserved in a picture archives and communications system (PACS) [30,37].

Various CXR scoring methods and structured reports have been established to evaluate COVID pneumonia and track its course [27,35,43-47]. In 2015, Taylor et al. [27,43] introduced a scoring method intended for non-radiologist physicians, applicable to COVID pneumonia, to enhance clinical grading into five intensity groups of CXR data for hospitalized people with acute respiratory infections [27,43]. Maroldi et al. [27] introduced a novel experimental CXR scoring method, termed the Brixia score, for the semi-quantitative evaluation of COVID-19 pneumonia in hospitalized patients with RT-PCR confirmed infection. The first phase involves segmenting the lungs into six zones based on a postero-anterior (PA) or antero-posterior (AP) perspective. In the second stage, a score ranging from 0 to 3 is allocated to each zone according to lung conditions (0 = no lung anomalies; 1 = interstitial penetrates; 2 = intermittent as well as alveolar enters with interstitial dominance; 3 = interstitial as well as alveolar penetrates with alveolar dominance). The results from the six lung zones are aggregated to get a cumulative CXR score, which ranges from 0 to 18 (Figure 2) [27].



Figure 2. CXR Scores Derived from the Criteria Established by Maroldi Et Al. [27] In Relation to COVID-19 Pneumonia.

Cozzi et al. [47] used the radiographic measurement of lung edema (RALE) rating, introduced by Warren et al. [44], in the evaluation of COVID-19 pneumonia; values range from 0 (no pathology) to 48 (complete pathological involvement of the lungs) [47]. Wong et al. [35] refined and modified the RALE score, assigning a value from 0 to 4 to each lung based on the degree of participation with consolidation or ground-glass opacities (GGO), where 0 indicates no involvement, 1 signifies less than 25%, 2 represents 25–50%, 3 denotes 50–75%, and 4 reflects more than 75% involvement) [35]. The ratings for each lung are aggregated to get the ultimate severity score, which ranges from 0 to 8 [35]. Toussie et al. [45] examined the correlation between clinical and first chest X-ray results and the end result factors of hospitalization and/or admission in COVID-19 patients aged 21 to 50 years. The lungs were segmented into three zones, with each zone assigned a binary value based on the presence (1) or absence (0) of opacity; total scores vary from 0 to 6 [45]. An elevated illness score at baseline correlates with the need for mechanical ventilation, heightened likelihood of ICU admission, and increased in-hospital mortality. Recent evidence indicates that AI systems may enhance performance in the assessment of chest X-rays, including the triggering of parametric globes, and may potentially assist radiologists in assessing COVID-19 pneumonia in the future [30,48].

Pulmonary Ultrasound

Although chest computed tomography (CT) is regarded as the definitive imaging modality for COVID-19 pneumonia [27,28,29], challenges such as the transportation of critically ill patients, the potential for crossinfection during transfers to imaging facilities, the necessity for decontamination post-scanning, and significant exposure to ionizing radiation constrain its application [11,35]. Conversely, LUS offers benefits as a portable as well as radiation-free instrument. LUS is an economical imaging modality that may be rapidly executed and repeated at the bedside by emergency doctors, intensivists, or cardiologists (point-ofcare (POC) LUS). This technology enables a dynamic examination of the lung without exposure to ionizing radiation and minimizes the total risk of nosocomial transmission, making it advantageous for sensitive populations including kids and pregnant women [49-55]. LUS can identify bilateral, subpleural, predominantly posterobasal interstitial–alveolar injury in COVID-19 pneumonia, characterized by thickening or irregularity of the pleural line, varying degrees of increased B lines with concentrated pleural B lines in the initial disease stage, and numerous coalescent B points (white lung) in patients who are critically ill [53-56]. LUS may identify tiny multifocal consolidations attached to the subpleural surface, in addition to pleural effusions [53-55]. Nonetheless, LUS is unable to reliably identify the existence of air bronchograms or pneumothorax [57,58]. Certain authors have observed that LUS may provide a possible function in emergency departments for the triage of symptomatic patients, ventilation management, weaning of ICU patients, and monitoring the progression of COVID-19 pneumonia towards ARDS in critically sick individuals [49-65]. A bedsidefocused cardiac ultrasound examination (FoCUS) may be beneficial for COVID-19 individuals experiencing cardiac episodes [64]. Consequently, LUS may be regarded as a primary substitute to chest X-ray as well as CT scan in critically sick patients [54,59-66]. Nonetheless, despite the increased sensitivity and diagnostic precision attributed to LUS, the specificity remains poor, fluctuating between 59 and 76.2 percent [49,65]. Despite the potential of LUS, a worldwide agreement about its use in COVID-19 management remains unachieved. This might be attributed to its many restrictions. LUS is perpetually constrained by artifacts associated with air in the lungs, relying mostly on the interpretation of these imaging artifacts [67-72]. The chemical reaction of the ultrasonic radiation with the tissue-air contact produces two primary artifacts: the horizontal A line and the vertical B line [67,68]. B lines are often seen in pleuropulmonary physiology or in different pathological states that affect the air-liquid interface. Consequently, line B does not serve as definitive indicators of interstitial edema. Multiple B lines may also be seen in many pulmonary disorders, including pulmonary edema resulting from cardiovascular illness, aspiration, ARDS, interstitial pulmonary or different forms of pneumonia [66-80].

Sperandeo et al. [71] indicates that the specificity of lung ultrasound (LUS) in COVID-19 patients is often poor due to the presence of concurrent illnesses including chronic obstructive pulmonary disease, cystic fibrosis, or heart failure. In comparison to volumetric chest CT, lung ultrasound (LUS) examines, at most, 70% of the pleural surface with the patient seated, and fails to adequately visualize the central regions, in addition to the perihilar or subpleural areas that do not contact the pleural surface, due to the presence of a thin layer (micron or mm) of air separating the pleural surface from the aerated lung. LUS is efficiently used for investigating lesions or conditions localized to the pleural or subpleural areas, including the assessment of pleural edema, subpleural infections, the chest wall, as well as the upper anterior mediastinum. Conversely, LUS is significantly reliant on the operator [71,72,77]. The potential ineffectiveness of LUS in inexperienced hands may pose more damage than benefit. LUS depends primarily on subjective observations. Pleural line abnormalities may differ depending on the probe type, the angle of incidence, the ultrasound scan orientation (long-term, diagonal, or oblique), and the operator's expertise [77,80]. Quarato et al. [76,80] and Sperandeo et al. [75] emphasized the technical limitations of LUS. The intra- and inter-operator variation in B line number is contingent upon the kind and frequency of the probe used, as well as the settings of the ultrasonic scanning machine [71,75-79]. The application of medium to low rate or excess total gain, together with the absence of tissue harmonic imaging, might produce a greater quantity of artifacts [77,79].

Tinti et al. [74] emphasized that to get accurate and reliable measurement of B lines, the doctor must freeze the ultrasound picture and count the lines each time the probe location changes. Carrer et al. [59] proposed an automated technique for identifying pleural lines. Ultimately, even with the use of complete personal protective equipment and strict adherence to decontamination protocols, operators doing LUS may face heightened risk of developing COVID-19 [39].

CT Staging of COVID-19 Pneumonia

The disease's dynamic alterations have been primarily established via Chinese longitudinal research conducted over a brief follow-up time. Zhou et al. [81] delineated three phases: early rapid progressive phase; advanced phase, marked by the simultaneous presence of development and absorption indicators; and late phase, wherein augmented signs of repair manifest as subpleural paths, bronchial errors, and fibrotic stripes. Barenhaim et al. [28] categorized the interval between the onset of first symptoms and subsequent chest alterations on CT as early, middle, or late. In the first stage, ground-glass opacity (GGO) alone or in conjunction with a reticular pattern or aggregation is often seen. This phase is characterized by the first invasion of parenchyma close to the bronchioles, subsequently affecting the secondary pulmonary lobule with widespread alveolar destruction [81]. Enlargement of small vessels may be associated with localized lung vasculitis resulting from inflammatory cytokines triggered by the virus, which enhance vascular permeability [82-84]. This trait may also be associated with the existence of microthrombi seen in histological analyses of post-mortem investigations [82]. The progressive stage is often marked by the

expansion of ground-glass opacities (GGO) or crazy paving, along with first consolidation. In the later stages, dense condensation gets more prevalent. During the progressive stage, if the patient's immunity is compromised or there is a lack of therapeutic response, COVID-19 pneumonia may advance to ARDS [83]. During the absorption phase, pulmonary changes begin to diminish, and manifestations of fibrosis, including fibrotic lines, tension bronchiectasis, bronchial deformation, and subpleural fibrotic lines, may become prominent [81,83].

Histopathological and Imaging Correlations

Limited research has linked imaging results in severe instances of COVID-19 pneumonia with histological findings [85-87]. This matter was examined mostly via case reports and a case series focused on CT characteristics identified in ante-mortem or post-mortem assessments [86]. CT imaging results, including ground-glass opacities (GGO) and consolidations, often align with histological assessments revealing diffuse alveolar damage (DAD) at various stages [85]. DAD is often a generic pulmonary reaction to several injurious substances, marked by edema, endothelium and alveolar damage with hyaline membrane development during the acute stage, and fibroblast growth and fibrosis of the interstitial space in the organizing stage [87].

Henkel et al. [85] compared the histological results of 14 patients who succumbed to COVID-19, validated by RT-PCR, with ante-mortem CT examinations. The presence of GGO was associated with capillary dilatation and congestion, interstitial swelling, bleeding, and acute DAD. The dilation of pulmonary arteries as well as CT vascular indicators, including small vessel enlargement, were attributed to severe microangiopathy, underscoring the significance of vascular changes. The acute DAD lasted around 7 days. CT findings of bronchial wall enlargement and mergers indicated the presence of superimposed acute bronchopneumonia. These characteristics intensified during the proliferative phase of diffuse alveolar damage (DAD), which was also marked by fibroblast proliferation in the interstitium as well as alveoli. The investigation revealed no histological characteristics indicative of organized pneumonia. The case series by Recalde-Zamacona et al. [86] substantiated these associations.

Post-mortem CT could be helpful in determining the cause of death in individuals suspected of having COVID-19. Suess et al. [87] delineated the CT characteristics of a 59-year-old patient with COVID-19 confirmed by RT-PCR, who initially exhibited stable clinical circumstances; nevertheless, after a few days, he had a rapid decline in respiratory symptoms and subsequently succumbed to home a few days later. The post-mortem CT showed bilateral ground-glass opacities with consolidations, and gross lung specimens exhibited pulmonary edema with bleeding on the pleural surface, absent symptoms of pleurisy. Immunohistochemical labeling revealed pronounced type two pneumocyte hyperplasia characterized by enlarged nuclei with viral cytopathic-like alterations. Elevated quantities of vascular megakaryocytes as well as interstitial lymphocytic cells had been additionally reported. Moreover, the authors found no indication of organized pneumonia in this instance.

Ducloyer et al. [88] reported an instance of a 75-year-old male who arrived at a French institution with a 4day history of fever, and whose oropharyngeal as well as nasopharyngeal swabs tested positive for COVID-19. Due to his clinical stability, he was sent home; nevertheless, just a few days afterwards, he was discovered dead in his bed. The post-mortem examination revealed bilateral pneumonia characterized by a crazy paving pattern, affecting 85% of the lung tissue. Histopathological examination revealed diffuse alveolar damage at various stages, including an acute stage marked by diffuse hyaline membranes accompanied by alveolar edema, and an organized stage characterized by expansion of alveolar septa, alveolar fibrin contributions, as well as hyperplasia of type 2 pneumocytes. Almeida Mointer et al. [89] established a correlation between post-mortem CT scans and histology results in fatal COVID-19 patients. The histological features seen in fatal instances of COVID-19 pneumonia closely resemble those associated with severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1), Middle East respiratory syndrome coronavirus (MERS-CoV), and Ebola virus [90].

Conclusions

This review succinctly summarizes the current findings and applications of imaging modalities, including CXR, LUS, and CT, in the identification and treatment of COVID-19 respiratory infections, along with the proposed scoring systems for each modality to evaluate the severity and complications of the disease. Chest imaging is crucial in the context of the epidemic. The selection of the appropriate imaging modality, whether CXR or CT, is often determined by the clinical team's discretion, the accessibility of nearby assets, and the radiologists' competence. Recent studies indicate that CT may serve as a prognostic as well as predictive marker for COVID-19 patient outcomes. COVID-19 pneumonia may result in several pulmonary consequences, including PMS, PMX, ruptures, as well as atypical ARDS. Cytokine storm-induced vascular injury may result in the unusual characteristics of CARDS. The histological findings associated with COVID-19 mostly resemble those seen in severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1), Middle East respiratory syndrome coronavirus (MERS-CoV), as well as Ebola virus. Nonetheless, a toxin-like mechanism warrants investigation.

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الملخص

الخلفية :تسببت جائحة COVID-19، الناجمة عن فيروس SARS-CoV-2، في تحديات كبيرة لأنظمة الرعاية الصحية في جميع أنحاء العالم. إلى جانب الأعراض التنفسية الحادة، يعاني العديد من المرضى من مضاعفات طويلة الأمد تُعرف باسم ."COVID-19" يلعب علم الأشعة دورًا حيويًا في تحديد هذه المضاعفات وإدارتها، مما يتيح التدخل العلاجي في الوقت المناسب وتحسين نتائج المرضى.

المنهجية :تستعرض هذه المراجعة الأدبيات الحالية حول استخدام تقنيات التصوير الشعاعي المختلفة، بما في ذلك الأشعة السينية للصدر (CXR)، والتصوير المقطعي المحوسب(CT)، وتصوير الرئة بالموجات فوق الصوتية(LUS)، في الكشف عن المضاعفات الرئوية المرتبطة بـ COVID-19وتقييمها. تم إجراء تحليل شامل لنتائج التصوير وعلاقتها بالمخرجات السريرية، وذلك بالاعتماد على العديد من الدراسات التي تبرز فعالية هذه التقنيات وحدود استخدامها.

النتائج :أشارت النتائج إلى أن التصوير المقطعي المحوسب (CT) يتمتع بحساسية عالية في تشخيص الالتهاب الرئوي الناتج عن COVID-19، بينما لا تزال الأشعة السينية للصدر (CXR) أداة قيمة للفحص الأولي، خاصة في بيئات الطوارئ. كما ظهر التصوير بالموجات فوق الصوتية للرئة (LUS) كبديل فعال بجانب سرير المريض، خاصةً للمرضى ذوي الحالات الحرجة. تتمتع كل وسيلة تصوير بمزاياها وتحدياتها الفريدة، وتختلف فعاليتها حسب السياق السريري. كما تم استعراض أنظمة التقييم المستخدمة لتحديد شدة تأثر الرئة، مع التأكيد على أهمية توحيد تقارير التصوير في الممارسة السريرية.

الاستنتاج بيُعتبر التصوير الشعاعي جزءًا لا يتجزأ من الكشف عن مضاعفات COVID-19طويلة الأمد وإدارتها. يمكن أن يؤدي الجمع بين تقنيات التصوير المختلفة إلى تحسين دقة التشخيص وتعزيز رعاية المرضى. ينبغي أن تركز الأبحاث المستقبلية على تحسين بروتوكولات التصوير ووضع إرشادات واضحة لاستخدام علم الأشعة في التعامل مع .19-COVID

الكلمات المفتاحية COVID-19 :، علم الأشعة، كوفيد الطويل، تصوير الصدر، المضاعفات الرئوية.