COVID-19 in the Radiology Literature: A Look Back

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The unexpected and sudden appearance of the novel SARS-Cov-2 respiratory virus led to a rush to understand the pathogen and develop appropriate methods of diagnosis and treatment for the COVID-19 disease. The rapid acquisition and dissemination of medical research has been enabled by electronic medical record systems and the internet, leading to the new phenomenon of near real-time production of scientific knowledge. This rapidity of scientific work has also led to important challenges and caveats. In this article, we select two features of COVID-19 in the radiology literature, use of diagnostic CT and pulmonary embolism frequency, that led to frequently cited publications and examine the consistency of those results over time.

Use of CT for COVID-19 Diagnosis

Soon after the emergence of SARS-CoV-2, early reports described the pulmonary CT imaging features of COVID-19 (1,2). The most common CT imaging appearance was that of peripheral and basilar predominant ground-glass opacities (3). More importantly, these reports demonstrated an exceedingly high sensitivity of chest CT for the diagnosis of COVID-19, some even higher than reverse transcriptase polymerase chain reaction (RT-PCR) (4,5). Therefore, it was argued that chest CT should be used for diagnosis of COVID-19 in conjunction with RT-PCR or as screening for asymptomatic individuals prior to surgery (6–8). Indeed, this strategy was endorsed by the World Health Organization and Fleischner Society and has been used, particularly early in the pandemic, in areas across the world with limited access to RT-PCR testing (9,10).

Notably, these early reports used CT in a method not previously used in any other clinical scenario, where diagnosis of pneumonia was based on essentially any pulmonary opacity, even a solitary nodule (5). Indeed, these reports did not include any control groups and did not report specificity (4,5). It is difficult to imagine translating this type of research-style image interpretation into clinical practice. Moreover, the patient population of these studies was unclear and likely suffered from spectrum bias (ie, containing a high fraction of patients with clinically severe COVID-19). (Note that spectrum bias is different from including a patient cohort with high disease prevalence, although the latter often causes the former.)

Following those early reports, other studies demonstrated that CT sensitivity was more limited, especially early in the infection or in patients who are asymptomatic or mildly symptomatic (11,12). Meta-analyses of CT versus RT-PCR showed relatively high sensitivity (87%–97%) for CT but low specificity (<50%) (13,14). These meta-analyses generally included studies performed on very high-prevalence populations (mean prevalence of 48% in one meta-analysis) (13); therefore, these studies also likely suffered from spectrum bias.

In parallel to assertions that CT was highly sensitive for COVID-19, several groups suggested using CT to distinguish COVID-19 from other respiratory pathogens, because the imaging manifestations of COVID-19 pneumonia were thought to be different from other pneumonias. One such group reported a range of high specificities (93%–100%, though with one outlier at 7%) for the diagnosis of COVID-19 versus other viral pneumonias using CT (3). This would serve as a unique role for chest CT given that previous studies have shown substantial overlap between the imaging features of bacterial and viral pneumonias (15).

Due to the increasing use of CT as at least an adjunct for diagnosis of COVID-19, several societies developed reporting guidelines, including the Radiological Society of North America (RSNA) (16). Using these guidelines led to a substantially lower sensitivity but higher specificity than the early reports, with 65% sensitivity for "typical" findings and 95% specificity (17). A real-world study using the RSNA guidelines found similar sensitivity and specificity; however, given the low prevalence of COVID-19 in the real-world setting, the positive predictive value of CT was only 52% (18), amounting to a near-coin flip when using CT as the sole diagnostic tool. Later work also showed substantial overlap in CT appearance among COVID-19 pneumonia, influenza pneumonia, and noninfectious organizing pneumonia (19).

Frequency of Pulmonary Embolism

A number of reports early in the pandemic highlighted an unexpectedly high rate of pulmonary embolism in patients with COVID-19 (23%–37%) (20–23). While not clearly indicated, many of these studies included mostly or exclusively patients with clinically severe illness admitted to an intensive care unit. Notably, most of these studies did not include control groups and did not report standard criteria for patients to undergo testing for pulmonary embolism. Following these reports, the use of CT pulmonary angiography (CTPA) dramatically increased in patients with COVID-19 (24), and some institutions even adopted CTPA as a standard practice in all patients with COVID-19 (25).

A subsequent meta-analysis was reported in *Radiology* showing a lower overall rate of pulmonary embolism in patients with COVID-19 of 16% (26), with substantial heterogeneity (I^2 = 93%). A heterogeneity value near 100% calls into question the relevance of reporting an average of the included studies because the underlying patient populations must have been considerably different. Likely, some studies were performed in institutions that used CTPA more widely in patients with COVID-19, leading to a lower prevalence of pulmonary embolism, whereas other studies may have included patients with more clinically severe disease, leading to a higher prevalence. Recent studies conducted on less biased samples have shown lower prevalence of pulmonary embolism (6%–12%), and studies that compared COVID-19–positive to COVID-19–negative control patients found no evidence of differences in rates of pulmonary embolism (25,27). Similarly, at least one study looking at venous thromboembolism rates found no difference in patients with COVID-19 versus other hospitalizations (28).

Conclusion

The appearance of a new respiratory disease understandably led to a need for rapid acquisition and dissemination of medical knowledge. However, many early reports were plagued by selection or spectrum (severity) bias and lack of control groups, leading to exaggerated conclusions. Some studies used research-style CT interpretation (eg, any pulmonary opacity is considered positive) that is not directly applicable to clinical practice. Additionally, many studies were performed in patient populations that are substantially different from those observed in the real world. While ostensibly an improvement from single-center studies, some meta-analyses suffered from the same potential biases and heterogeneous patient populations.

Those of us undertaking scientific inquiry in the modern era, particularly in the face of an emerging threat, need to consider what lessons can be learned from the COVID-19 experience. Clearly, a balance must be struck between the need to provide information as soon as possible and the danger of biased and uncontrolled studies. Journals can help serve this purpose by encouraging follow-on studies that add control groups and requiring authors to clearly display patient selection criteria. Journals should also publish commentary alongside articles that contain substantial limitations to contextualize the results. Finally, journals should give equal weight in considering the publication of studies on important topics with negative results as those with positive or dramatic results. Thus, while COVID-19 has undoubtedly been a tragedy for many, the lessons learned by the scientific community will likely help further medical knowledge and address future medical crises.

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