

## **COVID-19 and chest CT: do not put the sensitivity value in the isolation room and look beyond the numbers**

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With interest we read the systematic review and meta-analysis by Kim et al. (1) on the value of chest CT in diagnosing COVID-19 infection. Kim et al. reported chest CT to have a high pooled sensitivity of 94% (95% confidence interval: 91%-96%), but a low specificity of 37%

(95% confidence interval 26%-50%). However, we believe that there is no convincing evidence yet that chest CT achieves such a high sensitivity in diagnosing COVID-19 in clinical practice. Note that the far majority of studies that were included in the meta-analysis by Kim et al. (1) (58 of 63 studies) only enrolled patients with proven COVID-19 infection while cases without the disease were lacking. Strikingly, this is not in line with their exclusion criterion number 3: “lack of extractable data for a two-by-two contingency table”. As a result, these 58 studies only allowed for the calculation of sensitivity, and not specificity. However, the diagnostic value of a test depends on its ability to discriminate between diseased and non-diseased cases (2). Sensitivity and specificity are intertwined entities and are both dependent on the threshold value which is applied to discriminate between positive and negative cases (2). Generally, creating a high sensitivity by applying a low threshold is at the expense of specificity (2). Multiple studies in Kim et al.’s meta-analysis did not report which criteria were used as threshold value (1). The possibility that a low threshold was used, remains a realistic scenario. Applying a low threshold in cohorts of patients suspected of the disease (both with and without an actual COVID-19 infection) may result in virtually all cases being classified as having the disease. As a result, sensitivity values in these individual studies and the pooled estimate that was calculated by Kim et al. (1) may have been overestimated. It should also be noted that the 5 studies that did provide a 2×2 diagnostic contingency table, suffered from numerous methodological flaws. The lack of high-quality evidence, rather than the mathematical numbers, should have been the main conclusion in the otherwise excellent work by Kim et al. (1).

## **References**

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## Response

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We thank the authors for their interest in our study (1). We admit that the third exclusion criterion was described limitedly. To be exact, studies with a lack of extractable data for true positives and disease positives to calculate the sensitivity, or true negatives and disease negatives to calculate the specificity, were excluded.

We understand their concern about the potential of overestimation of the sensitivity for chest CT. The sensitivity and specificity are inter-dependent measures, and thus higher sensitivity may result in lower specificity of a diagnostic test. Given the circumstance that the majority of studies we analyzed reported only the sensitivity, the threshold effect could not be identified. Nevertheless, we performed a subgroup analysis for the five articles which reported both sensitivity and specificity of chest CT (2-6). In these studies, the pooled sensitivity was 96% (95% confidence interval [CI]: 94%, 97%;  $I^2=0\%$ ), which was similar to that of the primary analysis (94%; 95% CI: 91%, 96%;  $I^2=95\%$ ). For the five

studies, the reported sensitivity ranged from 94% to 100%, and the specificity ranged from 25% to 56%. Based on the visual evaluation of the coupled forest plot, there was no decrease in sensitivities according to increase in specificities.

Furthermore, we conducted an additional subgroup analysis for the studies with a low risk of bias for the CT interpretation, which clarified that the image readers were blinded to the clinical information or used radiology reports obtained from the routine clinical practice (2, 7-29). Again, the pooled sensitivity (93%; 95% CI: 86%, 96%;  $I^2=96%$ ) was comparable to that of the primary analysis. Although there was a huge heterogeneity in the included studies, we believe our findings would help guide the radiology practice during the outbreak of coronavirus disease 2019.

### **Conflicts of interest**

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