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## Level of Evidence during the COVID-19 Pandemic: Making the Case for Case Series and Case Reports

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I recently peer-reviewed case report and case series manuscripts of Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19). Case reports and case series can lack the power to distinguish a statistically significant difference, which could hide a potential risk or benefit to diagnostic testing or treatment. The hierarchy of research evidence has worked its way into medical education and clinical practice. The research applied to clinical practice is often considered more trustworthy when using higher levels of research evidence (such as high-powered, prospective, randomized controlled trials or a meta-analysis of high-quality studies). Several national organizations, scientific panels, and clinical academies give case reports and case series some of their lowest rankings with regard to level of research evidence.<sup>1</sup> Some journals have gone a step further and discontinued case reports, accepting only higher-level research study designs for publication. Academic promotions also consider the rigor of research, giving little credit for case reports and case series.

However, we still need case reports and case series. They provide us with data for rare diseases, as well as early news and potential clinical insights for evolving illnesses. Initial cases may provide the impetus for more organized, higher-level research. Higher-powered, prospective, randomized controlled trials provide a high quality of research evidence but may require funding, organization, and time to collect and analyze data, and a delay in information publication during a rapidly evolving global pandemic may not be optimal. A meta-analysis requires other research to be completed and published before one can even consider taking the time to do the meta-analysis. Applying higher levels of research evidence is absolutely vital to the practice of medicine, but lower levels of research evidence should not be dismissed.

During this COVID-19 pandemic, I have seen neuroimaging findings differ between separate case series. The astute radiologists and ordering clinicians may assimilate case series into their practice, realizing that the limitations will necessitate adaptation when additional information and better research become available. For example, the article “Leukoencephalopathy Associated with Severe COVID-19 Infection: Sequela of Hypoxemia?”<sup>2</sup> found a lack of hemorrhage in their entire case series, but we have seen case

reports and case series with petechial hemorrhage in patients with COVID-19.<sup>3,4</sup> There were also no changes in enhancement or cerebral perfusion for this case series, but we have observed these changes in other reported cases.<sup>5</sup> Publication of this case series<sup>2</sup> without any hemorrhages, enhancement, or cerebral perfusion abnormality is not necessarily to contradict the literature, but instead adds data to the scientific community when we have a new illness in evolution. Combined with other publication findings, this case series<sup>2</sup> will perhaps, in the future, help distinguish patient variables protective from hemorrhage (or clarify risk factors for hemorrhage) in COVID-19. Hopefully, these data motivate the clinical and scientific communities to do further research for better information so that one day we might have good knowledge for evidence-based medical practice and eventual medical wisdom.

In a busy clinical practice, it can be difficult to piece together the vast array of case series with inconsistent variables being reported. Maybe an ambitious researcher will tie it all together, perhaps with a meta-analysis. I remain hopeful that good evidence-based medical knowledge will eventually be available from high-level research evidence, but until then, careful incorporation of case reports and case series may have to suffice.

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