INTERNET NEWS

Reviews and Commentary

Editorial

A Simplified Approach to Adnexal Lesions May Be Enough

presentation, immediate MRI or surgical consultation may be warranted, as US may not be adequate to characterize large lesions.

So, what do we do? We do the best we can. We use published guidelines when they are available (and in the realm of adnexal lesions, we have guidelines on which to rely). We trust our gut that when something seems amiss, we look again and perhaps recommend a close follow-up. We try to be consistent, and if there are competing guidelines, it's okay to choose the one that we will be more likely to use. And in this case, the simplified approach to adnexal lesions that allows characterization of lesions into classic and nonclassic categories may be enough.

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CLINICAL and MOLECULAR HEPATOLOGY

Review

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Development of hepatocellular carcinoma in treated and untreated patients with chronic hepatitis B virus infection

Chih-Lin Lin[1,2] and Jia-Horng Kao[3,4,5,6]

Hepatitis B virus (HBV) is responsible for more than 50% of hepatocellular carcinoma (HCC) in HBV hyperendemic areas, such as the Asia-Pacific region. Several hepatitis B viral factors are involved in HBV-related hepatocarcinogenesis. Hepatitis B viral load is the most important risk factor of HCC development. In addition, HBV integration, HBV genotype C, and core-promoter mutations are also associated with a risk of HCC development. For untreated chronic hepatitis B (CHB) patients, the estimated HCC incidence rates per 100 patient-years were 0.03–0.17 in inactive carriers, 0.07–0.42 in asymptomatic carriers, 0.12–0.49 in chronic hepatitis, and 2.03–3.37 in cirrhosis. Complementary to HBV DNA, serum levels of the hepatitis B surface antigen and hepatitis B core-related antigen (HBcrAg) can predict the occurrence of HCC for untreated patients with low and intermediate viral loads, respectively. For patients receiving antiviral therapy, the risks of HCC occurrence 40–60% lower than those for untreated patients. Patients treated with residual detectable HBV DNA or intrahepatic cccDNA still have a risk of HCC. Serum levels of HBcrAg, M2BPGi and fibrosis-4 are predictive of the risk of HCC development in treated patients. Several well-developed HCC risk scores can help clinicians identify high-risk CHB patients for HCC surveillance, regardless of treatment status. These strategies can help minimize the threat of HCC and prolong survival in CHB patients. **(Clin Mol Hepatol 2023;29:605-622)**

Keywords: Chronic hepatitis B; Cirrhosis; Hepatocellular carcinoma

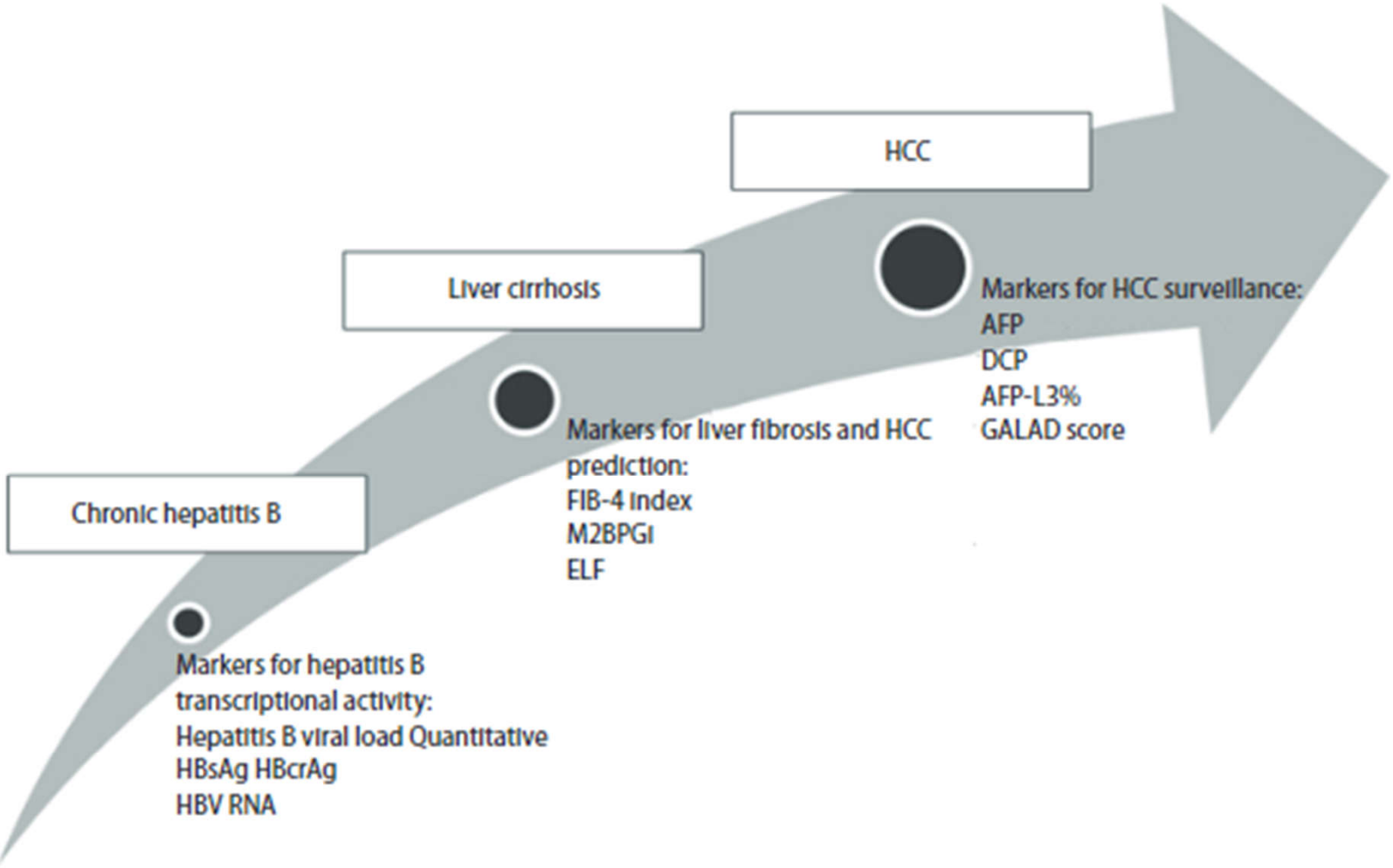

Figure 1. Serum biomarkers for the management of patients with chronic hepatitis B. AFP, α-fetoprotein; AFP-L3, lectin-bound AFP; DCP, des-gamma carboxy-prothrombin; ELF, enhanced liver fibrosis score; HBcrAg, hepatitis B core-related antigen; HCC, hepatocellular carcinoma; M2BPGI, mac-2 binding protein glycosylation isomer; HBV, hepatitis B virus.

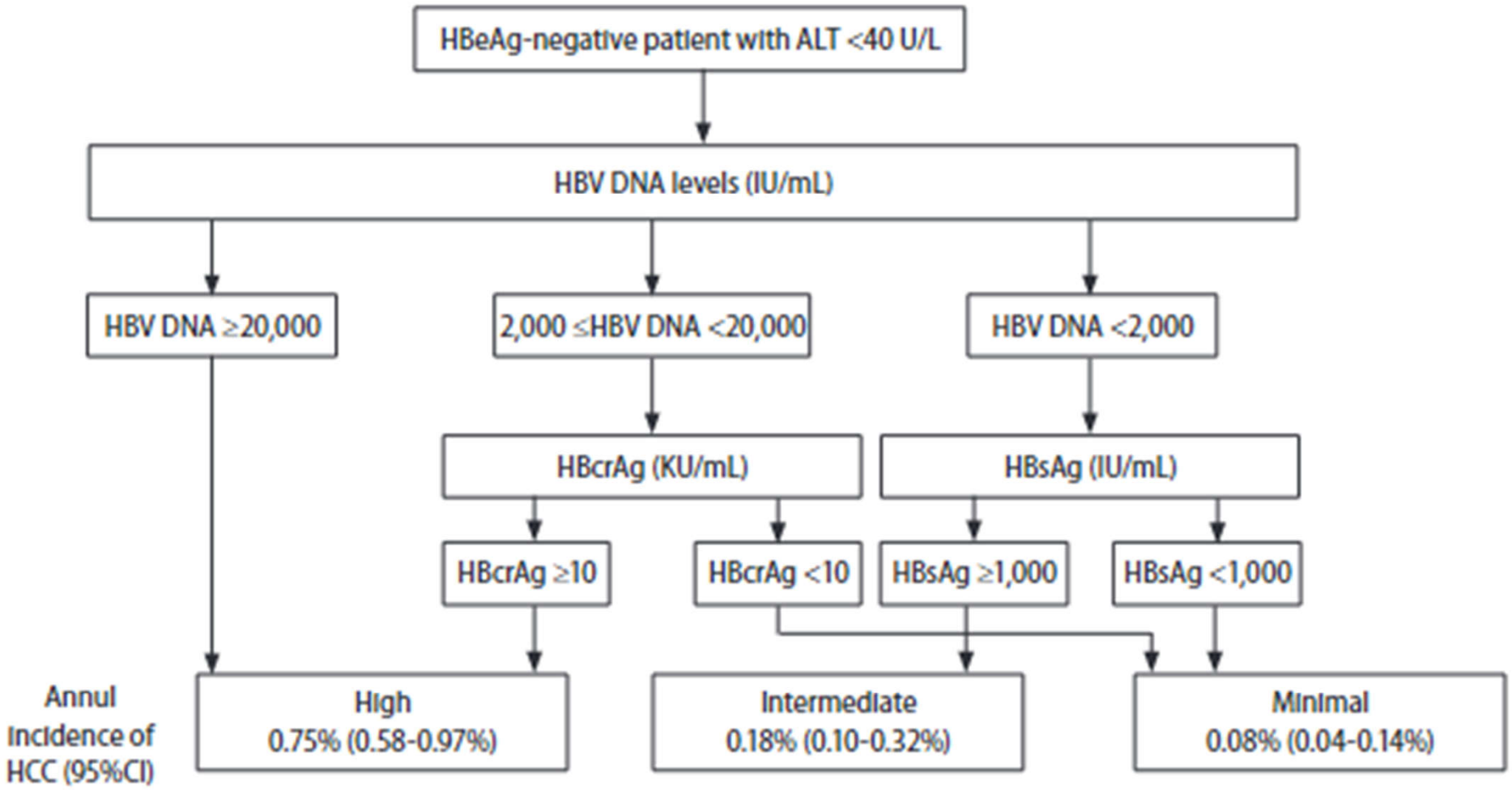

Figure 2. Hepatocellular carcinoma risk stratification of untreated HBeAg-negative chronic hepatitis B patients by HBV DNA, HBsAg and HBcrAg. HBcrAg, hepatitis B core-related antigen; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; ALT, alanine aminotransferase; HCC, hepatocellular carcinoma.

ment. However, several challenges remain before HBV-relat-

ed HCC can be eliminated. First, the benefit of antiviral treatment in HCC reduction remains unclear among patients with normal or minimally higher serum levels of ALT. In a randomized trial conducted by Hsu et al.[140], 160 treatment-naïve, non-cirrhotic patients with serum ALT levels between 1- and 2-fold the upper limit of normal were randomized to receive tenofovir disoproxil fumarate or placebo treatment for 3 years. Tenofovir disoproxil fumarate significantly reduced the risk of fibrosis progression (RR, 0.56; 95% CI, 0.35–0.88; P=0.013).[140] A multinational, multicenter, open-label, phase 4 trial (ATTENTION study; NCT03753074) is currently underway to clarify whether antiviral therapy decreases the risk of HCC development in this special clinical setting. Second, NAFLD or metabolic dysfunction–associated fatty liver disease (MAFLD) are associated with an increased risk of end–stage liver disease and HCC. The high prevalence of NAFLD/MAFLD

INTRODUCTION

Caring for the Liver: Updates on Global Prevalence, Cutting-Edge Diagnosis, and State-of-the-Art Management for Researchers and Clinicians, 2023 and Beyond

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Lai Wei[4]

Charles Kahi[5]

In 2015, *Clinical Gastroenterology and Hepatology* (*CGH*) published a special issue covering the then state-of-the-art approach to diagnosis and management of liver diseases. However, the pace of major advancements and paradigm shifts in the hepatology landscape has been such that an updated review became inevitable. Since 2015, direct antiviral agents for hepatitis C virus (HCV) have led to the cure of millions of people. In addition, direct antiviral agents have led to a decline in HCV as a cause of liver transplantation and hepatocellular carcinoma (HCC). However, alcohol-related liver disease (ALD) and nonalcoholic fatty liver disease (NAFLD) have become a significant global burden. These developments are not surprising, especially with the rise of ALD during the COVID-19 pandemic and the increasing rates of obesity and type 2 diabetes driving NAFLD.

Since 2015, hepatologists have gradually moved away from liver biopsy for most liver diseases, except for phase 2b and 3 clinical trials of nonalcoholic steatohepatitis D (HDV), has become another major research focus. Similarly, new medications for cholestatic liver disease have led to significant improvements in management. HCC treatment options have also expanded with the availability of new targeted therapy and immunotherapy, allowing the cure of many patients that could not be offered such options in 2015. All these developments and many others have led to changes in the treatment paradigms for cirrhosis and liver transplantation, which are covered in this special issue.

The hepatology field is now focused on new areas that were not at the forefront in 2015, such as artificial intelligence (AI), and the urgent and largely unmet needs in addressing health inequities and optimizing quality.

In this special issue celebrating the 20th anniversary of *CGH*, teams of experts address the current state-of-the-art approaches to diagnosing and managing liver diseases. The following is a snapshot of each article included in this edition.

importance of ongoing research.

Arab, Addolorato, Mathurin, and Thursz tackle the most common cause of cirrhosis and liver-related mortality, ALD. They review the multiple pharmacologic and nonpharmacologic therapies for alcohol use disorder, and advocate for an integrated approach to treatment. They also emphasize recent progress made in managing patients with severe alcoholic hepatitis, including improved survival prediction and the advent of early liver transplantation.

Singal, Kudo, and Bruix present a thorough review of major developments and therapies across multiple treatment paradigms for HCC. The authors prioritize treatment options, first describing those with curative intent that provide longer disease-free survival, followed by detailing noncurative locoregional and systemic therapy options. Most of these strategies and regimens constitute significant breakthroughs that have occurred in the past decade, making this review all the more timely.

Finally, Terrault, Francoz, Berenguer, Charlton, and Heimbach comprehensively review the current state of liver transplantation, focusing on the recent shift in the etiologic indications from HCV to ALD and NAFLD. The novations in the field, including bariatric surgery and the potential of xenotransplantation.

The articles in this special issue were intently written with *CGH*'s broad clinical gastrointestinal and hepatology audience in mind, spanning subspecialties and career stages. The overarching aim is to provide a state-of-the-art update and a broadly useful go-to resource, at least until the developments in this dynamic field mandate another update! We sincerely hope that you will find this special issue informative and engaging, and enjoy reading it as much as we did.

Conflicts of interest

These authors disclose the following: Mazen Noureddin serves on the Advisory Board for Altimmune, BI, BMS, Cytodyn, 89BIO, EchoSens, Gilead, GSK, Madrgial, Merck, Novo Nordisk, OWL, Prespecturm, Pfizer, Roche Diagnostic, Siemens, Terns, and Takeda; is Principal Investigator for a drug study at Allergan, Akero, BMS, Gilead, Galectin, Genfit, GSK, Conatus, Corcept, Enanta, Madrigal, Novartis, Novo Nordisk, Shire, Takeda, Terns, Viking, and Zydus; and is a stockholder with Anaetos, Rivus Pharma, CIMA, ChronWell, and Viking. Lai Wei has consulted for Novo Nordisk, Pfizer, and Roche; is a speaker for Gilead and Novo Nordisk; reports research grant to institution from Gilead, GSK, Pfizer, and Sanofi; and is Principal Investigator for a drug study at Boehringer-Ingelheim, Gilead, Haisco, HEC, Kaiyin, MSD, and Pfizer. Laurent Castera served as a consultant or advisory board member for Echosens, Gilead, Madrigal, MSD, Novo Nordisk, Pfizer, and Sagimet; and a speaker for Echosens, Gilead, Inventiva, and Novo Nordisk. The remaining author discloses no conflicts.

Section Editor: Prateek Sharma, MD

Potassium-Competitive Acid Blockers and Gastroesophageal Reflux Disease

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Having said this, I would not say that P-CABs are the next generation of PPIs. P-CABs are competing against PPIs, which revolutionized acid-suppression therapy. PPIs have a 30-year history of documented efficacy—and a level of efficacy that was unheard of prior to their existence—as well as a very good track record for safety, other than the concerns around acid suppression, which will apply equally to P-CABs at least for continuous therapy.

The overarching theme of our discussion is, I think, the fact that GERD should be viewed not as a single condition but as a range of underlying pathophysiologies and manifestations, which need tailored treatment. Once 60% to 80% of patients have improvement, the benefit beyond that comes down to understanding better what the disease is—understanding the nonresponders rather than the responders. The other point to highlight is that P-CABs as a class will exhibit common features but that they are likely, nonetheless, to show differences some of which may be clinically relevant. As in other areas, one will need to be careful to avoid the assumption that all P-CABs are exactly the same and that they will all produce identical outcomes.

MAYO CLINIC

Long-Term Effects of COVID-19

Shreeya Joshee, BS; Nikhil Vatti, MD; and Christopher Chang, M

Abstract

Shreeya Joshee, BS; Nikhil Vatti, MD; and Christopher Chang, MD, PhD, MBA

Abstract

Coronavirus disease 2019 (COVID-19) is the third deadly coronavirus infection of the 21st century that has proven to be significantly more lethal than its predecessors, with the number of infected patients and deaths still increasing daily. From December 2019 to July 2021, this virus has infected nearly 200 million people and led to more than 4 million deaths. Our understanding of COVID-19 is constantly progressing, giving better insight into the heterogeneous nature of its acute and long-term effects. Recent literature on the long-term health consequences of COVID-19 discusses the need for a comprehensive understanding of the multisystemic pathophysiology, clinical predictors, and epidemiology to develop and inform an evidence-based, multidisciplinary management approach. A PubMed search was completed using variations on the term post-acute COVID-19. Only peer-reviewed studies in English published by July 17, 2021 were considered for inclusion. All studies discussed in this text are from adult populations unless specified (as with multisystem inflammatory syndrome in children). The preliminary evidence on the pulmonary, cardiovascular, neurological, hematological, multisystem inflammatory, renal, endocrine, gastrointestinal, and integumentary sequelae show that COVID-19 continues after acute infection. Interdisciplinary monitoring with holistic management that considers nutrition, physical therapy, psychological management, meditation, and mindfulness in addition to medication will allow for the early detection of post-acute COVID-19 sequelae symptoms and prevent long-term systemic damage. This review serves as a guideline for effective management based on current evidence, but clinicians should modify recommendations to reflect each patient's unique needs and the most up-to-date evidence. The presence of long-term effects presents another reason for vaccination against COVID-19.

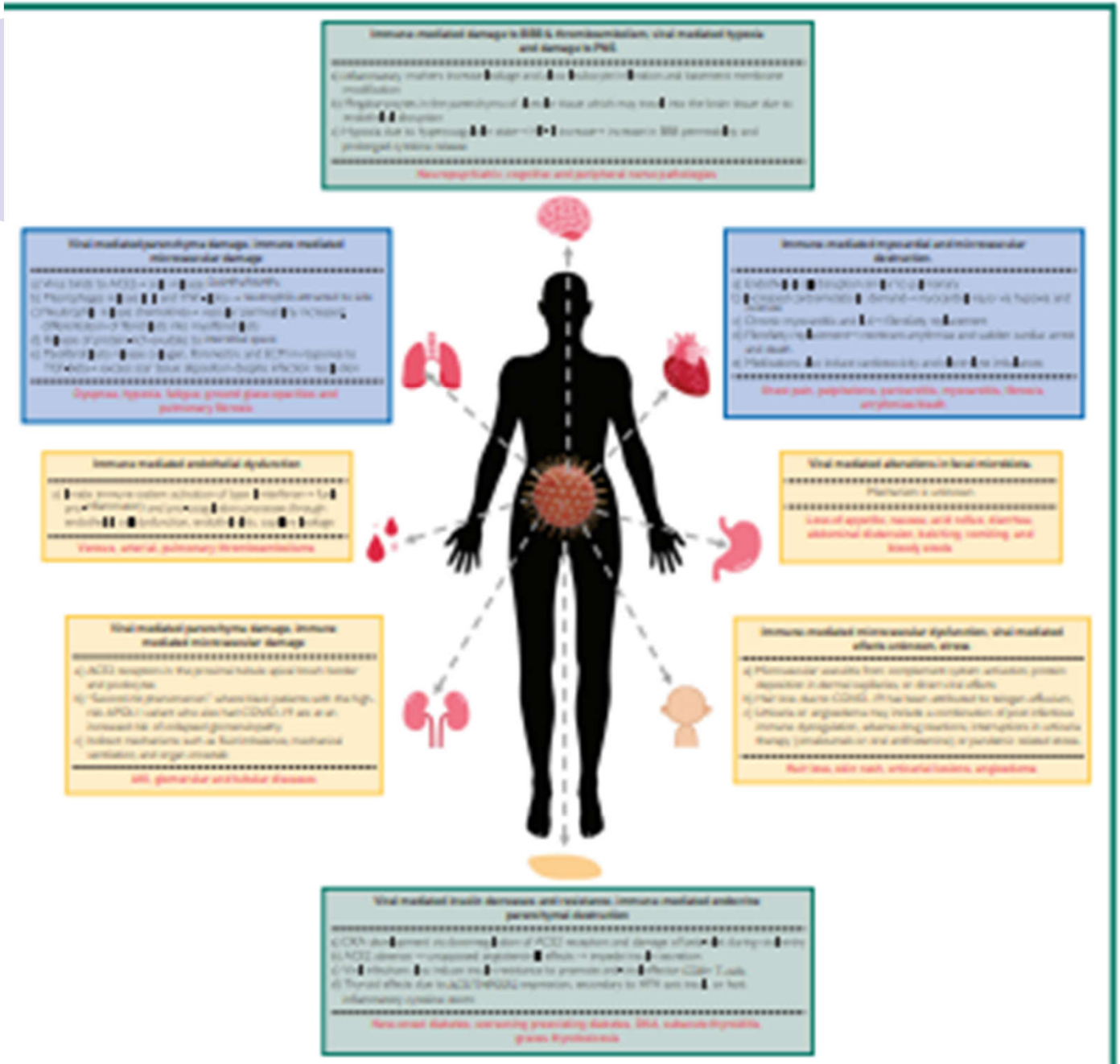

FIGURE 1. Pathophysiology of pulmonary, cardiac, neurological, hematological, renal, gastrointestinal, integumentary, and endocrine effects of post-acute coronavirus disease 2019 and its subsequent clinical manifestations. [1,5,17,28,29,48,78,94] BBB = blood brain barrier; ACE = angiotensin-converting enzyme; ACE2 = angiotensin-converting enzyme 2; AKI = acute kidney injury; APOL1 = apolipoprotein L1; COVID-19 = coronavirus disease 2019; DAMP = damage-associated molecular pattern; DKA = diabetic ketoacidosis; ECM = extracellular matrix; HIF-1 = hypoxia-inducible factor 1; HPA = hypothalamic-pituitary-adrenal; IL = interleukin; PAMP = pathogen-associated molecular pattern; PNS = peripheral nervous system; TGF = tumor growth factor; TMPRSS2 = type 2

THE END