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WJG 20th Anniversary Special Issues (4): Irritable bowel syndrome

Breath tests and irritable bowel syndrome

Satya Vati Rana, Aastha Malik

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ARTICLE: FUNCTIONAL GI DISORDERS

Methanogens and Hydrogen Sulfide Producing Bacteria Guide Distinct Gut Microbe Profiles and Irritable Bowel Syndrome Subtypes

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IBS-C subjects had higher breath CH_4 that correlated with higher gut microbial diversity and higher relative abundance (RA) of stool methanogens, predominantly *Methanobrevibacter*, as well as higher absolute abundance of *Methanobrevibacter smithii* in stool. IBS-D subjects had higher breath H_2 that correlated with lower microbial diversity and higher breath H_2S that correlated with higher RA of H_2S-producing bacteria, including *Fusobacterium* and *Desulfovibrio* spp. The predominant H_2 producers were different in these distinct microtypes, with higher RA of Ruminococcaceae and Christensenellaceae in IBS-C/CH_4+ (which correlated with Methanobacteriaceae RA) and higher Enterobacteriaceae RA in IBS-D. Finally, microbial metabolic pathway analysis revealed enrichment of Kyoto Encyclopedia of Genes and Genomes modules associated with methanogenesis and biosynthesis of methanogenesis cofactor F420 in IBS-C/CH_4+ subjects, whereas modules associated with H_2S production, including sulfate reduction pathways, were enriched in IBS-D.

DISCUSSION:

Our findings identify distinct gut microtypes linked to breath gas patterns in IBS-C and IBS-D subjects, driven by methanogens such as *M. smithii* and H_2S producers such as *Fusobacterium* and *Desulfovibrio* spp, respectively.

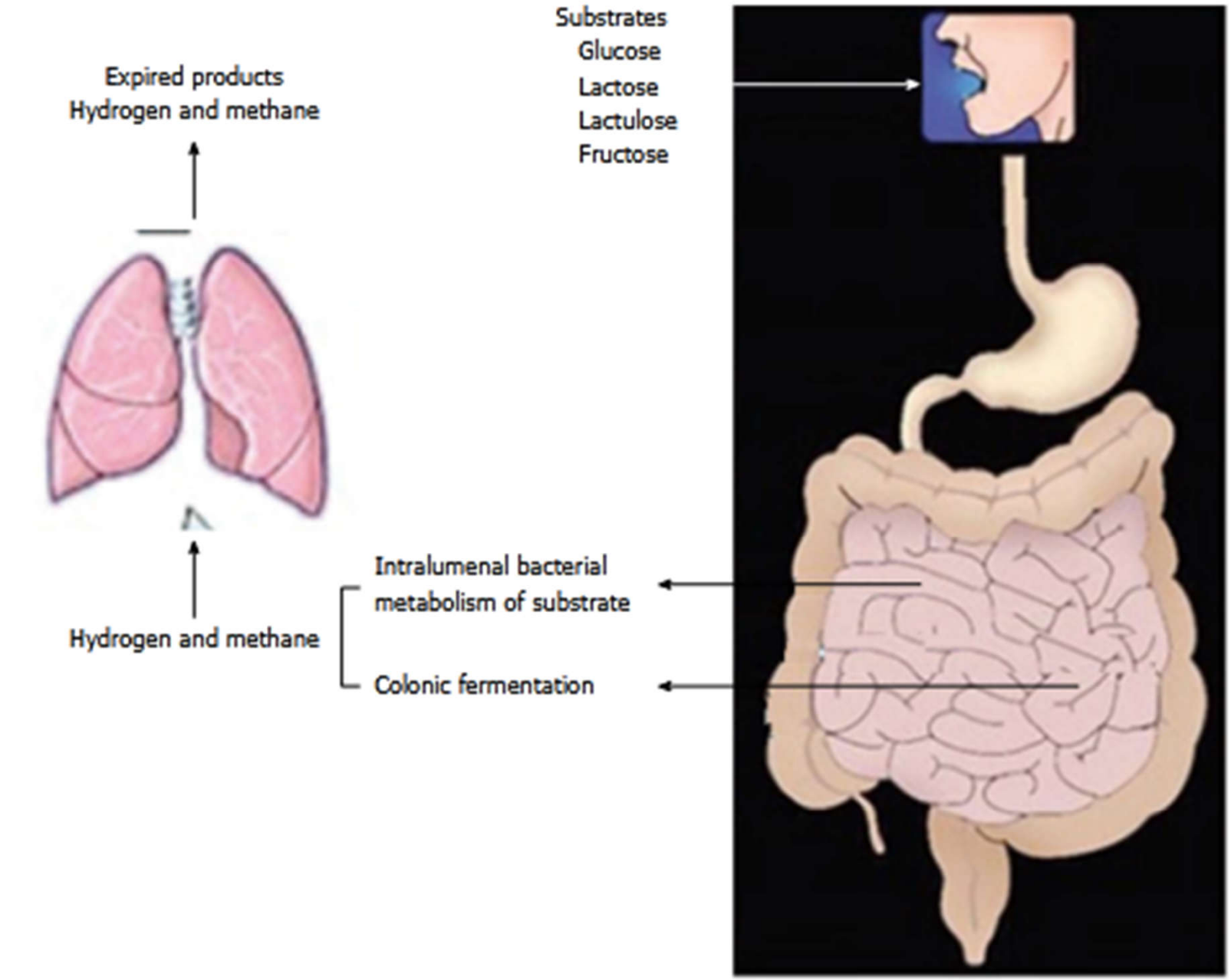

Figure 1 Principle of breath testing.

Figure 2 Gases released can be detected by Breath analyzer.

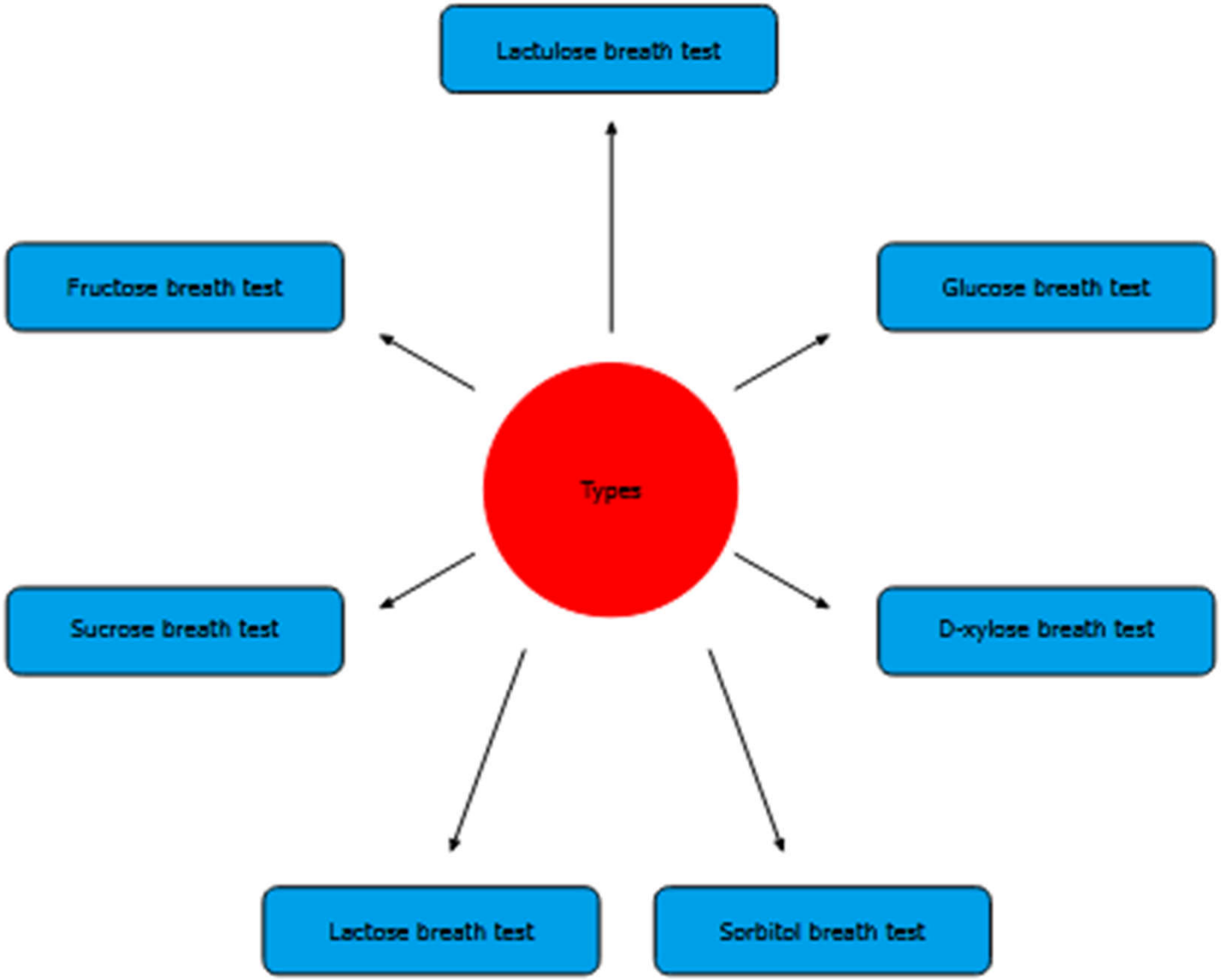

Figure 3 Types of breath tests.

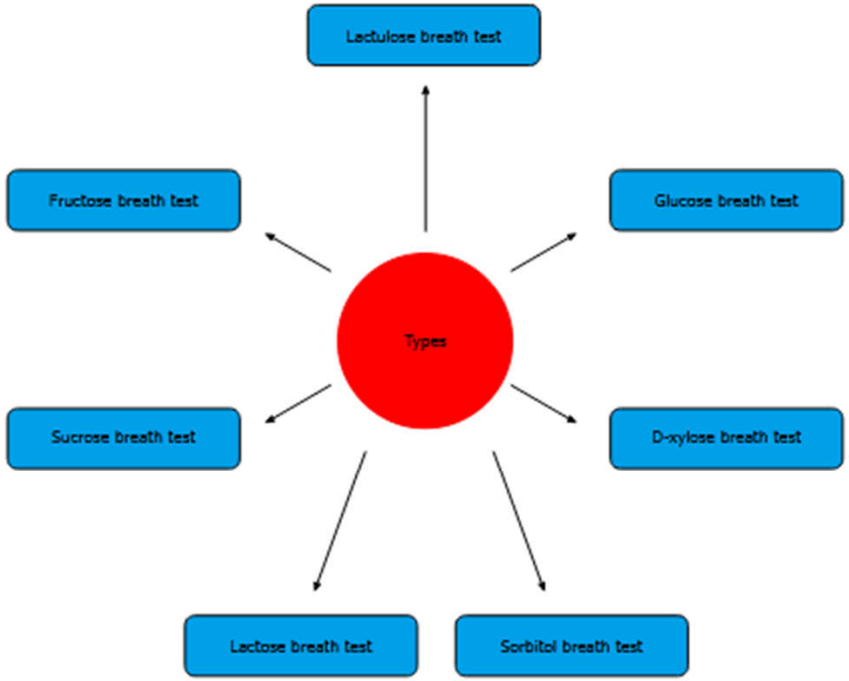

Figure 3 Types of breath tests.

CONCLUSION

This review summarizes the use of breath tests, not only to direct about dietary interventions but they also to provide prognostic information. These breath tests can help in the diagnosis of SIBO and carbohydrate malabsorption in IBS patients. Further studies analyzing H_2 and CH_4 concentrations in breath samples may improve diagnostic criteria for carbohydrate malabsorption in IBS patients. Moreover, area-under-the-curve analysis of the change in H_2/CH_4 concentration in breath samples over time after administering lactulose as a substrate may in future help to analyze the bacterial level in the bowel. Breath testing is also a useful to the low-FODMAP diet in IBS patients. In most cases of food intolerance, diagnosis is difficult. Thus, breath testing provides accurate, reliable and a non-invasive measure of absorption of a test sugar by assessment of breath H_2/CH_4 levels. Breath tests are performed to determine whether fructose and/or lactose and/or sorbitol are FODMAPs for an individual who has IBS symptoms. Thus, it can be shown whether an individual can or cannot completely digest fructose, lactose and sorbitol. This can be helpful to patients as well as physicians to formulate a particular diet which may help to reduce gastrointestinal symptoms present in IBS patients.

JOURNAL OF VIRAL HEPATITIS
JVH

ORIGINAL ARTICLE

Baseline and on-treatment HBcrAg levels as predictors of HBeAg seroconversion in chronic hepatitis B patients treated with antivirals

Soo Young Hwang, Sung Hwan Yoo, Hye Young Chang, Sora Kim, Jung Il Lee, Kwan Sik Lee, Young Youn Cho, Kim Hyung Joon, Hyun Woong Lee

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HBeAg seroconversion is an important treatment endpoint. We aimed to identify predictors of seroconversion using serum HBsAg and hepatitis B core-related antigen (HBcrAg) in HBeAg-positive patients treated with nucleos(t)ide analogs (NAs). Data and samples from 70 HBeAg-positive patients treated with entecavir or tenofovir between January 2007 and December 2017 were retrospectively analysed. The mean follow-up period was 11 years. The predictive power for HBeAg seroconversion of HBcrAg levels at baseline and 2 years after antiviral therapy was determined using receiver operating curve analysis. Twenty-one patients (30%) achieved HBeAg seroconversion at a mean of 28 (range, 12–84) months after antiviral treatment. The median baseline HBcrAg and HBsAg levels were 6.9(5.7–7.0) vs. 5.8(5.5–6.5) $\log_{10}$U/mL (p = .006), 4.9(4.5–5.1) vs. 4.5(4.1–5.0) $\log_{10}$IU/mL (p = .044) in the no seroconversion group and seroconversion group, respectively. In the multivariate analysis, the serum HBcrAg levels at baseline and 2 years after antiviral therapy were predictive factors for HBeAg seroconversion ([HR]; 0.326; [CI], 0.111–0.958; p = .042 and HR, 0.4555; CI, 0.211–0.984; p = .045). HBcrAg levels≤6.5$\log_{10}$U/mL at baseline and ≤5.3$\log_{10}$U/mL at 2 years after antiviral therapy had sensitivities of 53.1% and 69.8%, specificities of 95.2% and 70.6%, positive predictive values of 82.6% and 50.0%, and negative predictive values of 82.6% and 84.5%, respectively, with AUROCs of 0.712 (95%CI, 0.596–0.830) and 0.745 (95%CI, 0.599–0.891) for predicting HBeAg seroconversion. In chronic hepatitis B patients treated with NAs, HBcrAg levels≤6.5$\log_{10}$U/mL at baseline and ≤5.3$\log_{10}$U/mL at 2 years after antiviral therapy were useful predictive factors of HBeAg seroconversion.

New International Guidelines and Consensus on the Use of Lung Ultrasound

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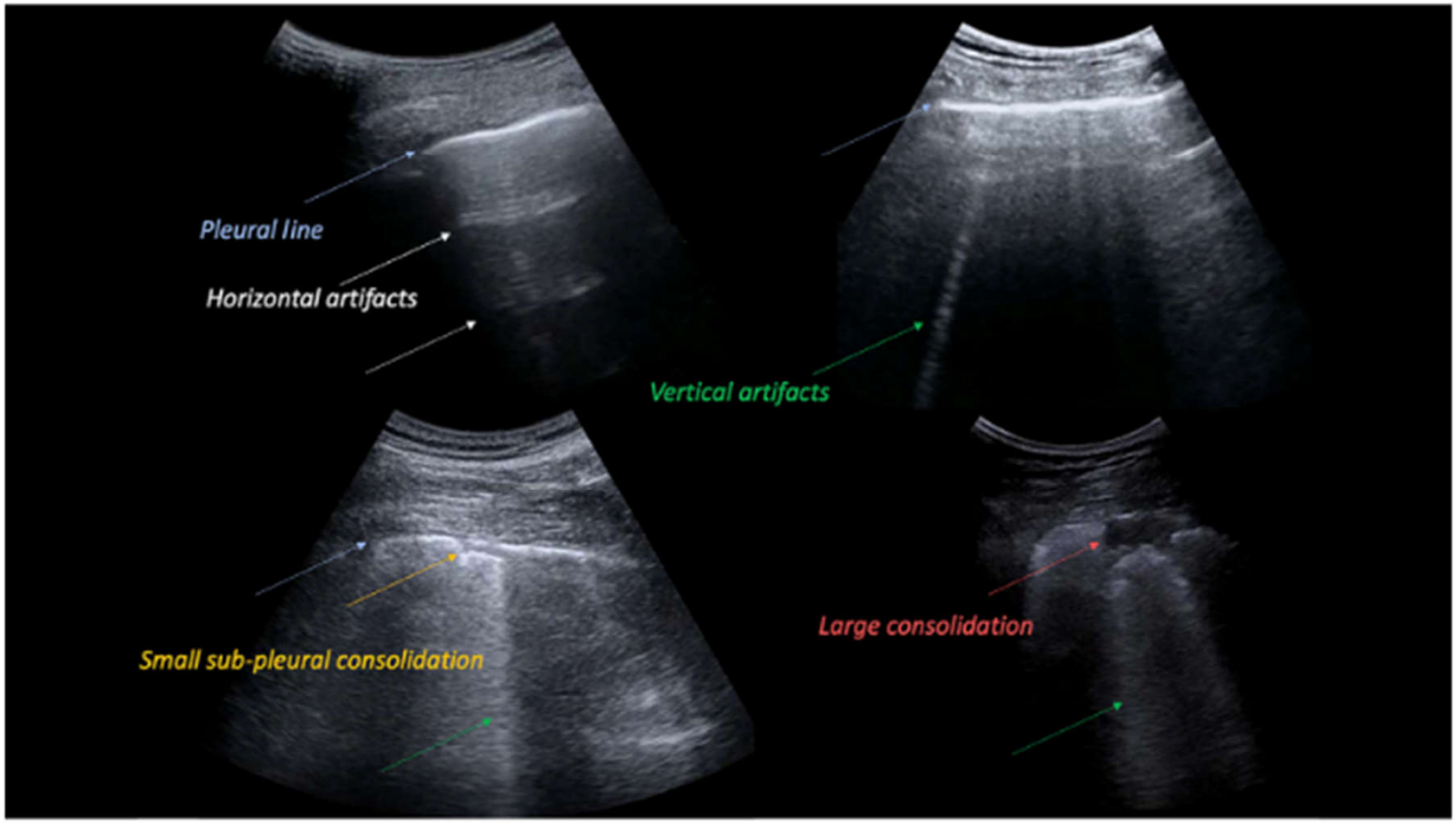
Following the innovations and new discoveries of the last 10 years in the field of lung ultrasound (LUS), a multidisciplinary panel of international LUS experts from six countries and from different fields (clinical and technical) reviewed and updated the original international consensus for point-of-care LUS, dated 2012. As a result, a total of 20 statements have been produced. Each statement is complemented by guidelines and future developments proposals. The statements are furthermore classified based on their nature as technical (5), clinical (11), educational (3), and safety (1) statements.

Key Words—A-lines; artificial intelligence; B-lines; COVID-19; lung ultrasound; lung ultrasound protocols; lung ultrasound standardization; LUS safety assurance; point of care ultrasound; post-COVID-19; quantitative ultrasound; SARS-CoV-2; sonographic interstitial syndrome; vertical artifacts

Table 1. Summarization of Statements and Guidelines

Statement ID	Statement Classification	Statement Text
1	Technical	As it is already happening in other areas of medical imaging, artificial intelligence (AI) is now being applied to the analysis of LUS data. Critical and well-detailed studies are fundamental to prevent over expectations and misuse of this technology.
2	Technical	Before new technologies will be mature, LUS will continue to be performed with standard ultrasound (US) imaging. In order to improve its reproducibility, standardization of imaging protocols is essential.
3	Technical	In the current definition, B-line artifacts represent a wide variety of patterns. It is crucial to understand the physical origin of their genesis and to characterize the signals responsible for their visualization. This is a fundamental step toward the development of quantitative US modalities dedicated to the diagnosis and monitoring of lung diseases
4	Technical	It is indispensable to find a consensus on objective parameters for the evaluation of regularity/ irregularity/thickening of the pleural line and the distinction of micro and macro subpleural consolidations, both for dimensional criteria and for US aspects.
5	Technical	It is necessary to improve the comprehension of the qualitative and quantitative characteristics of the artifacts currently called B-lines in relation to the physiological and pathophysiological changes of histology of the lung.
6	Safety	In animal models, there is evidence that lung ultrasound (LUS) in the diagnostic regime can induce pulmonary capillary hemorrhage. It is therefore required to investigate the need for specific safety limits for US technologies when applied to the monitoring and diagnosis of lung diseases
7	Clinical	There is a need for high quality studies (randomized, prospective) to achieve acceptance for the

Figure 2. Examples of ultrasound images displaying typical LUS patterns. Pleural line, horizontal artifacts (A-lines), vertical artifacts (B-lines), and consolidations are indicated by blue, white, green and red arrows, respectively.



We view this document as a starting point for further international collaborations and foresee the need to update this international consensus with a time frame of 5 years. Indeed, while statements and guidelines can be seen as a description of the state of the art in LUS, future developments should be considered as a forward-looking perspective on the most clinically relevant and scientifically challenging questions. We invite from now clinicians, engineers and physicists to join in the effort of expanding and strengthening the LUS community. Improving the reproducibility, accuracy, reliability, and awareness of LUS will in fact produce shared benefits for research, the health care sector, and patients.

REVIEW

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Is your patient at risk for NAFLD?

mately 37% of US adults. The progression from nonalcoholic fatty liver with no inflammation to steatohepatitis with inflammation and progressive fibrosis is associated with substantial morbidity and mortality. The epidemic of NAFLD requires that primary care providers recognize at-risk patients and screen them. The authors review identifying individuals at risk, treatment options founded on lifestyle modification, and when to consider referring patients to a hepatologist.

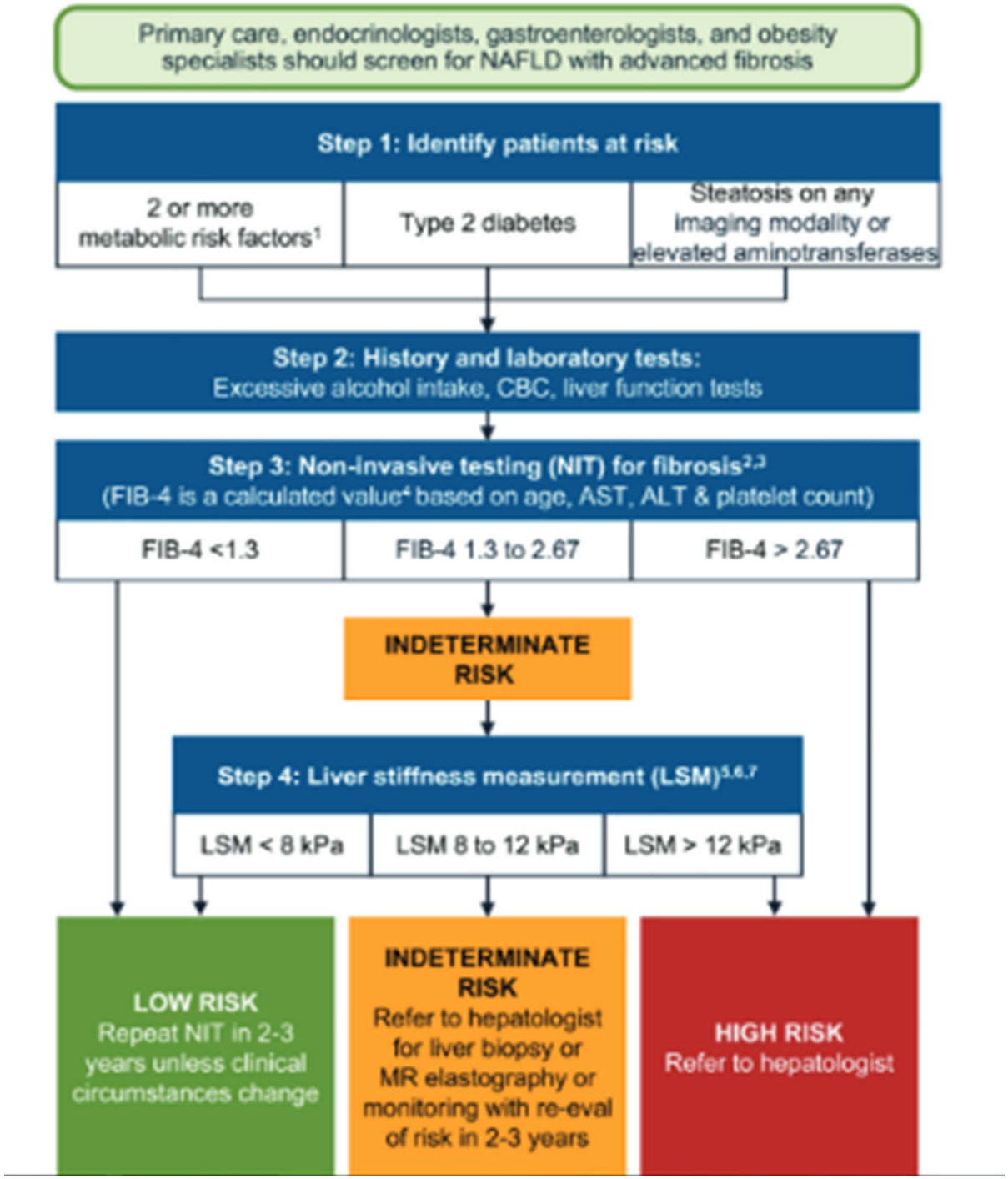
KEY POINTS

Screen for NAFLD in patients with diabetes, those with 2 or more metabolic risk factors, or those with fatty liver on imaging.

The Fibrosis-4 score is a noninvasive tool using age, aspartate aminotransferase and alanine aminotransferase values, and platelet count to identify patients at risk for fibrosis.

Vibration-controlled transient elastography measures liver stiffness and helps determine the presence and severity of fibrosis.

Intensive lifestyle modification with a calorie-restricted Mediterranean diet, exercise, and weight loss is the mainstay of treatment for NAFLD.


Primary care, endocrinologists, gastroenterologists, and obesity specialists should screen for NAFLD with advanced fibrosis
Step 1: Identify patients at risk
2 or more metabolic risk factors[1]
Type 2 diabetes
Steatosis on any imaging modality or elevated aminotransferases
Step 2: History and laboratory tests:
Excessive alcohol intake, CBC, liver function tests
Step 3: Non-invasive testing (NIT) for fibrosis[2,3]
(FIB-4 is a calculated value[4] based on age, AST, ALT & platelet count)
FIB-4 <1.3
FIB-4 1.3 to 2.67
FIB-4 > 2.67
INDETERMINATE RISK
Step 4: Liver stiffness measurement (LSM)[5,6,7]
LSM < 8 kPa
LSM 8 to 12 kPa
LSM > 12 kPa
LOW RISK
Repeat NIT in 2-3 years unless clinical circumstances change
INDETERMINATE RISK
Refer to hepatologist for liver biopsy or MR elastography or monitoring with re-eval of risk in 2-3 years
HIGH RISK
Refer to hepatologist

	LOW RISK FIB-4 < 1.3 or LSM < 8 kPa or liver biopsy F0-F1	INDETERMINATE RISK FIB-4 1.3 - 2.67 and/or LSM 8 - 12 kPa and liver biopsy not available	HIGH RISK[1] FIB-4 > 2.67 or LSM > 12 kPa or liver biopsy F2-F4
	Management by PCP, dietician, endocrinologist, cardiologist, others	Management by hepatologist with multidisciplinary team (PCP, dietician, endocrinologist, cardiologist, others)	
Lifestyle intervention[2]	Yes	Yes	Yes
Weight loss recommended if overweight or obese[3]	Yes May benefit from structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Greater need for structured weight loss programs, anti-obesity medications, bariatric surgery	Yes Strong need for structured weight loss programs, anti-obesity medications, bariatric surgery
Pharmacotherapy for NASH	Not recommended	Yes[4, 5, 6]	Yes[4, 5, 6, 7]
CVD risk reduction[8]	Yes	Yes	Yes
Diabetes care	Standard of care	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)	Prefer medications with efficacy in NASH (pioglitazone, GLP-1 RA)

Figure 2. Management of NAFLD and NASH.

was associated with a lower risk of liver fibrosis, cirrhosis, and hepatocellular carcinoma. The proposed mechanism for this decrease in liver injury associated with drinking coffee is the antioxidant effects of caffeine, as well as several other components found in coffee.[49]

Silymarin, an extract of milk thistle, was reported to reduce fibrosis without improvement in steatosis or inflammation, though larger studies are needed.[50] Resveratrol, a chemical found in red wine, may in conjunction with lifestyle modification improve inflammation in patients with NAFLD, though the benefits in NASH are inconsistent.[51]

CONCLUSION

In this era of a global epidemic of NAFLD, PCPs play an essential role in identifying patients with NAFLD and in screening them for advanced fibrosis using noninvasive techniques. The screening and management algorithms proposed by the AGA provide an opportunity to develop partnerships with gastroenterology or hepatology practices and avoid unnecessary referrals. There is no FDA-approved pharmacotherapy for NASH. Intensive lifestyle modification to manage weight, diet, and physical activity is the only approved therapy.

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DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

Lung scarring occurs in up to 11% of patients recovered from COVID, regardless of infection severity

Hannah Murphy | *December 05, 2022* | *COVID-19*

Researchers recently estimated that up to 11% of patients who recover from COVID could have lung scarring that may worsen over time.

This data was published recently in the *American Journal of Respiratory and Critical Care Medicine*, where experts used the follow-up CT imaging (completed within 240 days of discharge) from 209 patients hospitalized with COVID to stratify the risk of residual lung damage for a post-hospitalization cohort of almost 3,500 individuals without follow-up imaging.

Corresponding author Iain Stewart, PhD, of the Margaret Turner Warwick Center for Fibrosing Lung Disease and co-authors suggested that the team's work could have major implications for patients who are released from the hospital following a COVID infection, as a "substantial" number of these individuals could have fibrotic abnormalities of the lungs that need to be addressed and potentially managed.

Radiology

REVIEWS AND COMMENTAR

CT of Post-Acute Lung Complications of COVID-19

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Conflicts of interest are listed at the end of this article.

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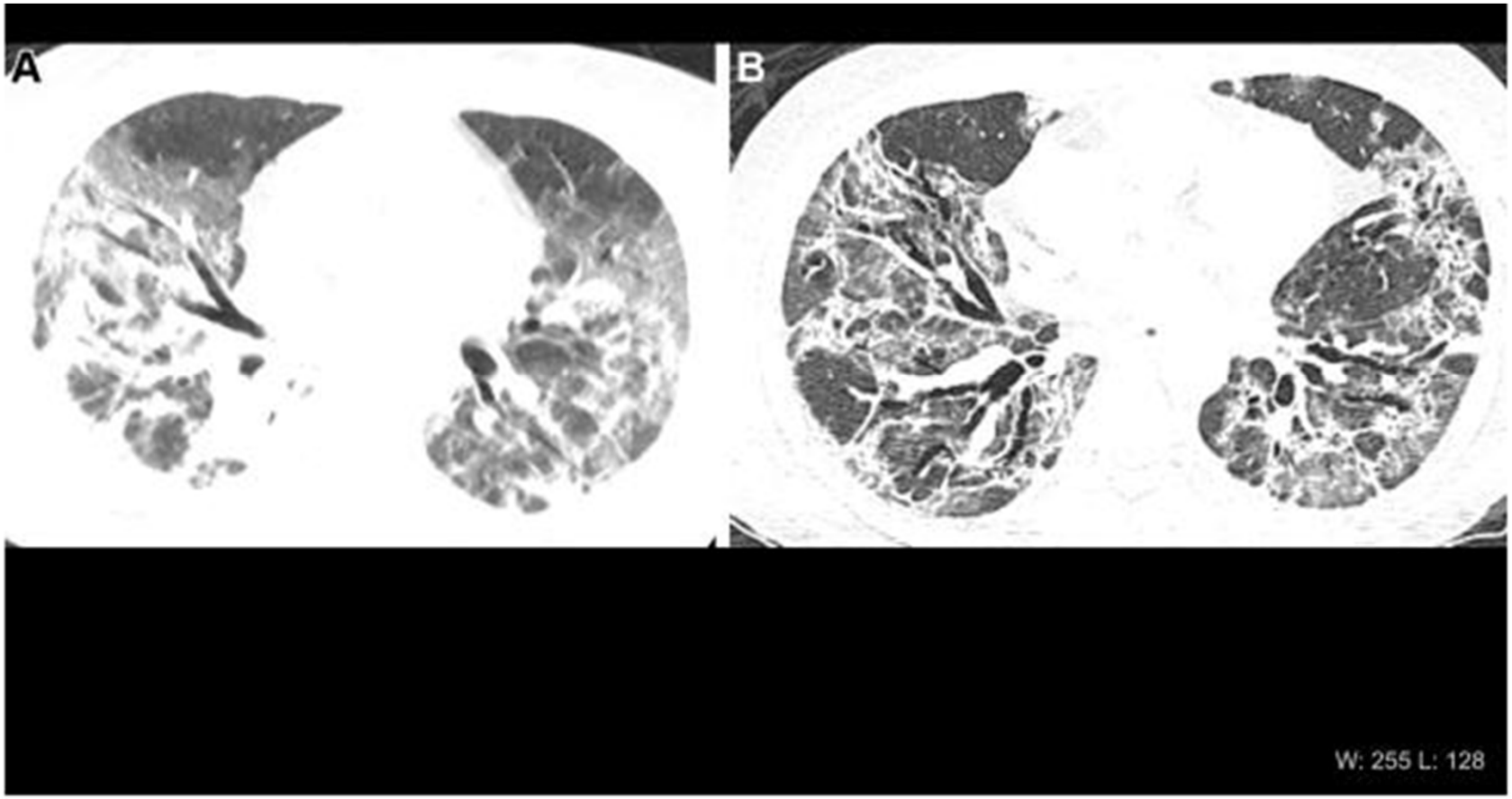
The acute course of COVID-19 is variable and ranges from asymptomatic infection to fulminant respiratory failure. Patients recovering from COVID-19 can have persistent symptoms and CT abnormalities of variable severity. At 3 months after acute infection, a subset of patients will have CT abnormalities that include ground-glass opacity (GGO) and subpleural bands with concomitant pulmonary function abnormalities. At 6 months after acute infection, some patients have persistent CT changes to include the resolution of GGOs seen in the early recovery phase and the persistence or development of changes suggestive of fibrosis, such as reticulation with or without parenchymal distortion. The etiology of lung disease after COVID-19 may be a sequela of prolonged mechanical ventilation, COVID-19–induced acute respiratory distress syndrome (ARDS), or direct injury from the virus. Predictors of lung disease after COVID-19 include need for intensive care unit admission, mechanical ventilation, higher inflammatory markers, longer hospital stay, and a diagnosis of ARDS. Treatments of lung disease after COVID-19 are being investigated, including the potential of antifibrotic agents for prevention of lung fibrosis after COVID-19. Future research is needed to determine the long-term persistence of lung disease after COVID-19, its impact on patients, and methods to either prevent or treat it.



Patient with severe, long-term lung damage from COVID. Images in a 54-year-old man with COVID-19–related acute respiratory distress syndrome and subsequent fibrosis. (A) Axial CT 2 weeks after admission shows diffuse ground-glass opacity (GGO) with reticular abnormality and traction bronchiectasis in right middle lobe, indicating organizing phase of lung injury

The findings revealed that although patients with the most severe cases of COVID (those requiring ventilation, etc.) were more likely to display residual lung abnormalities indicative of interstitial lung disease following their release, nearly 8% of patients with less severe cases were also found to be at high risk.

The researchers acknowledged that they cannot yet determine whether these changes will progress or resolve in the long-term, but they have planned a second phase of research that will reevaluate study participants at the 12-month mark.

“At that time, we will also use linked electronic health records of hospital admissions and mortality data to support our analyses. We expect to have the final results in early 2023,” the authors stated.

Journal of
Clinical Medicine

MDPI

Editorial

Special Issue "Prostate Cancer: Recent Advances in Diagnostics and Treatment Planning"

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This editorial of the Special Issue "Prostate Cancer: Recent Advances in Diagnostics and Treatment Planning" aims to draw more attention to the broad and diverse field of prostate cancer (PCa) diagnosis and the utilization of different diagnostic means to improve clinical decision-making and treatment strategy planning. PCa is the second most frequent malignancy in men [1]. Tumor aggressiveness varies, ranging from non-aggressive tumors that may be safely monitored to poor prognosis tumors only suited for palliative treatment. Undoubtedly, new imaging modalities such as magnetic resonance imaging (MRI) and positron emission tomography (PET) with targeted tracers are more sensitive than conventional imaging [2] and may result in stage migration and a natural inclination toward altering clinical management. In contrast to other cancers, the PCa community acknowledges that precision medicine has developed more slowly [3]. Genetic counseling and germline testing can aid in the early detection and management of PCa. Biomarkers based on urine, serum, and tissue increase PCa patient detection and facilitate risk stratification.

risk stratification.

Indications for prostate biopsy can be determined with the aid of MRI, which is also essential for local staging. When combined with clinicopathological information, MRI results in a more accurate prognosis, which may help with tailored patient care [4]. In the case of localized PCa, MRI findings are associated with clinically relevant long-term oncologic outcomes. The diagnosis of clinically significant PCa is improved by targeted biopsies, as routine transrectal ultrasonography is not always accurate. Additionally, the evidence supporting the addition of MRI-targeted biopsies to systematic biopsies necessitates a review of the active surveillance (AS) inclusion criteria and a shift in research focus away from one-size-fits-all protocols and toward more flexible and personalized risk-based AS approaches [5]. On the other hand, modern, less expensive ultrasound-based techniques can deliver high-quality imaging in the absence of an MRI [6–8].

Prostate-specific membrane antigen (PSMA) PET has been adopted for staging aggressive tumors. Compared with traditional imaging, PSMA PET offers a reasonably good sensitivity for detecting regional and extrapelvic metastases. Additionally, it can play a significant part in the early diagnosis of extraprostatic disease and help with surgical planning. Furthermore, PSMA PET has been shown to be a valuable technique for planning definitive radiation therapy in patients who have not yet received treatment [9]. Furthermore, even at low PSA levels, PSMA PET is highly effective at detecting and localizing post-treatment biochemical recurrence [10]. Molecular PET, in the post-radical prostatectomy setting, leads to management modifications to prepare patients for salvage radiotherapy by detecting lesions in anatomical locations not typically included in the usual postoperative radio-

Genetic alterations are associated with differential prognosis and clinical phenotypes in metastatic PCa. Blood biomarkers could assist clinicians in managing patients with localized disease and provide the most robust degree of evidence for predicting more aggressive Pca [13]. Liquid biopsies are valuable as a source of prognostic, predictive, and response biomarkers in PCa. Most clinical applications have been developed in the advanced metastatic setting. These minimally invasive tests can guide diagnosis and treatment selection [14]. However, before therapeutic adoption, newly discovered data on these putative predictive biomarkers must be confirmed in biomarker-driven randomized controlled trials [15].

Together, these methods produce risk calculators/nomograms that can predict the risk of developing cancer, the likelihood that the disease will be aggressive, and the likelihood that the patient will respond well to therapy [16,17]. However, we need to learn how to appropriately interpret them and to treat patients while keeping in mind the clinical objectives, such as overall survival, disease recurrence, and quality of life, that the treatment intended to attain. This can only be achieved with sufficiently large studies of patients who are followed up for a long time, even if they are observational studies. This can reduce side effects, expenses, and resource usage while minimizing the danger of over- or under-treating patients.

THE END