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Authors

Moein, Hamid-Reza
Arteaga, Elvis J
Sarkar, Souvik

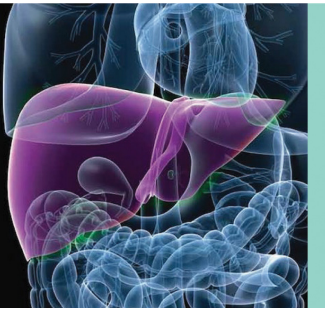
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Using Telehealth for Diagnosis and Management of Non-Alcoholic Fatty Liver Disease

Hamid-Reza Moein, M.D.,  Elvis J Arteaga, M.D.,† and Souvik Sarkar, M.D., Ph.D.†,‡ *

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in the Western World.¹ In the United States, NAFLD prevalence is estimated at 25-30%, and is growing with increasing prevalence of obesity and type 2 diabetes (T2DM), thus becoming an economical and clinical burden for health-care systems.^{1,2} NAFLD or non-alcoholic steatohepatitis (NASH), more advanced type of fatty liver disease, can lead to liver cirrhosis, hepatocellular carcinoma, cardiovascular disease, and chronic kidney disease.³⁻⁵ Despite all these complications and high burden on health care, it is underdiagnosed by primary care providers (PCPs) and referral to hepatologist is not well-established, thus leading to delays in diagnosis and care.⁶⁻⁸ Therefore, it is essential to develop modalities for early linkage-to-care pathways to reduce risks of adverse outcomes. Establishing triage pathways for PCPs, as the pillars of the health care, to determine patients most at-risk for future complications and easy to refer modalities can improve linkage-to-care to specialists.

In the age of information technology, telemedicine has the potential to play an effective role in management of diseases for patients in rural areas with less access to specialists and potentially decrease the gap-in-care.⁹⁻¹¹ Telemedicine has been used successfully in the field of hepatology around the world,^{10,12-15} but data on fatty liver disease is limited. There are only few reports on successful utilization of telehealth in lifestyle modification for NAFLD.^{16,17} In this review, we will highlight the potential for using telehealth in diagnosis and management of fatty liver disease and review the feasibility in reducing disparities in care.

APPLYING TELEHEALTH IN DIAGNOSIS AND MANAGEMENT OF NAFLD/NASH

Coronavirus disease 2019 (COVID-19) pandemic accelerated telehealth utilization [2020_Telehealth_Benchmark_Survey_Results.pdf (ctfassets.net); Accessed

From the *Division of Gastroenterology and Hepatology, Carolinas Medical Center, Atrium Health Wake Forest Baptist, Charlotte, NC; †Department of Internal Medicine, University of California, Davis, Sacramento, CA; and ‡Division of Gastroenterology and Hepatology, University of California, Davis, Sacramento, CA.

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on March 3, 2021] and expanded its use to urban populations. Upon successful experience with the Extension for Community Healthcare Outcome (ECHO) project,¹⁸ similar models have been adopted across the globe, not only for treatment of chronic liver diseases but also for multiple clinical conditions, enabling access to care for rural patients.¹⁹

Studies to determine role of telehealth specifically for NAFLD/NASH patients remain few and far between.^{16,17} But opportunities abound for the use of telehealth to improve diagnosis and management of fatty liver disease. There is a significant unmet need to guide and educate PCPs in rural areas or during a pandemic at community hospitals without access to gastroenterologists/hepatologists, in diagnosis and management of NAFLD/NASH. PCPs have a crucial role in diagnosis and management of NAFLD; however, lack of understanding remains an important barrier to link-to-care at-risk patients.^{8,20} Analysis of referrals trends at a tertiary care center showed that only 44/31934 (0.1%) of diabetic patients were referred to hepatology clinic for NAFLD.⁶ This was much less than what is expected based on the pooled prevalence of NAFLD among diabetic patients in the United States (59.6%)²¹ and can be attributed to lack of standardized referral algorithm and under recognition by PCPs or endocrinologists. Furthermore, a significant proportion of the referrals were low-risk patients (Fibrosis-4 [FIB-4] score < 1.3) who could essentially be managed by their PCPs.⁶ Srivastava et al. demonstrated that using a non-invasive risk stratification model (FIB-4) and subsequent transient elastography reduced unnecessary referrals by 80% and increased detection of advanced fibrosis by five5-fold.⁷

Telehealth encompasses a wide gamut of modalities^{12,13} that can be potentially harnessed for the management of patients with NAFLD/NASH.

Interactive Telemedicine

It encompasses direct interaction with the consultant (teleconsultation) or with PCP (televisit).¹⁸ Teleconsultation provides the opportunity for the consultant hepatologist and other collaborators such as nutritionist, pharmacists, or bariatric surgeons to interact with the patient directly, after receiving a referral from patient's PCP. This feature enables a multidisciplinary care and can potentially advances care in patients with fatty liver disease.

Telementoring

This has been applied in ECHO® model, where a team of experts hepatologists and pharmacists (hub) educate the PCPs and then they deliver the care to their patients.¹⁸ In addition, a similar model of telementoring termed ECHO-Plus was developed as a joint endeavor between University of California (UC), San Francisco and UC, Davis.¹³ In this model, in addition to the established one-to-many model of ECHO®, there was a focus on one-to-one telementoring to create hepatitis C treatment champions in Northern California. The 'mentor' site (consultant) and pharmacist connected with the 'mentee' site, which was attended by the PCP and the patient. This intense one-to-one telementoring created early hepatitis C treaters.²² As NAFLD awareness among PCPs increase, so will increase the need for specialty care for education as well as patient care, especially in rural settings. Both the one-to-many (ECHO®) and the one-to-one telementoring model has shown pathways for developing models-of-care for NAFLD patients.

Teleeducation

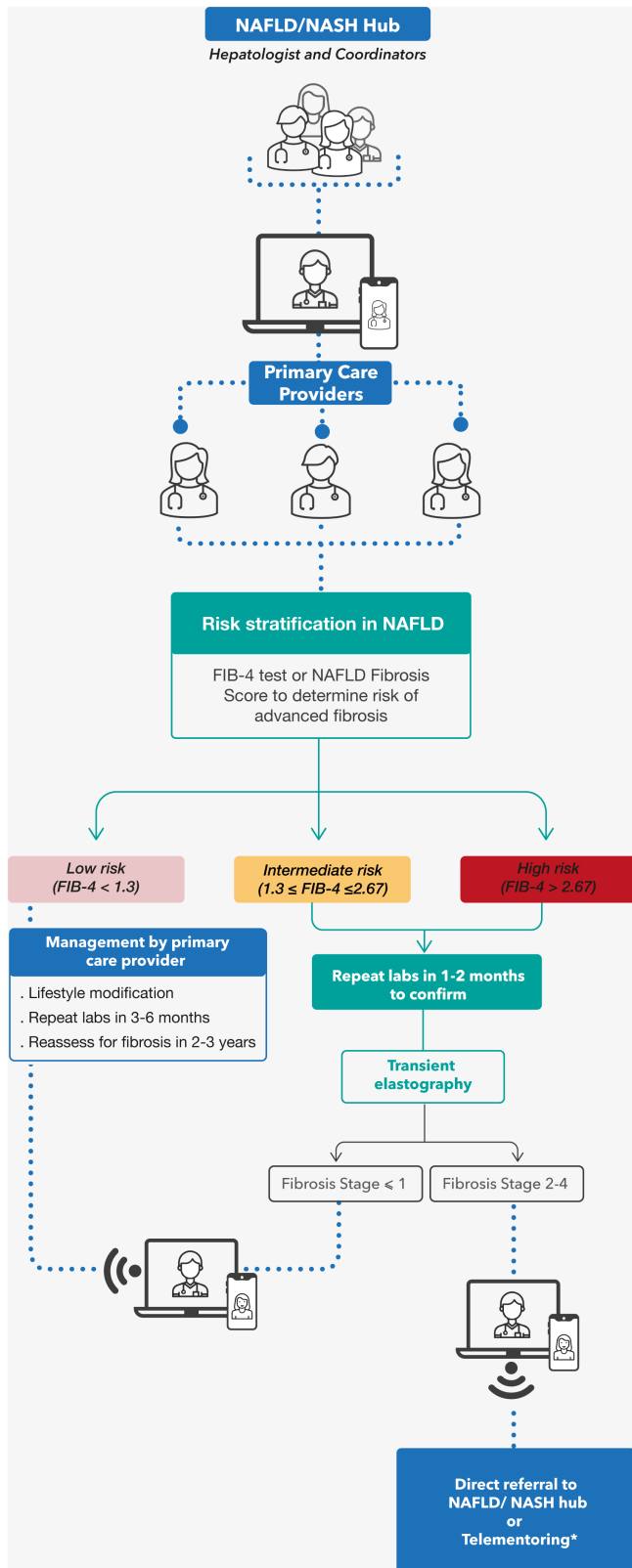
Educational materials about NAFLD provided by hepatologists and a multidisciplinary team such as nutritionists or pharmacists or endocrinologists can be stored and subsequently accessed by PCPs or patients at their convenience anywhere with Internet access.

Telemonitoring

Weight loss has been associated with slowing the progression of NAFLD and decreasing inflammation in the liver.¹⁶ Mazzotti et al. demonstrated that web based lifestyle modification of NAFLD patients was not inferior to in person interventions and they both resulted in similar weight loss and normalization of liver enzymes.¹⁶ Using wearable devices can help monitor simple measures such as step count, daily weights and even diet. Motz et al. demonstrated improvements in physical, laboratory, and imaging findings of 3 NASH patients by applying telemonitoring and supervised exercise training.¹⁷

Store and Forward

This feature may be useful for fatty liver disease patients who developed cirrhosis. These patients can share pictures from their eyes, skin, abdomen to their physicians for evaluation of ascites and jaundice. Patients may



also be able to share a picture of their laboratory results with physicians in case of no access to patients' lab results through electronic medical records, which can facilitate the management.

FIG 1 A multitude of telehealth tools will facilitate academic centers become 'hubs', as defined in the ECHO® model. The hubs will provide access to knowledge and support to primary care providers (PCPs) for triage and management of NAFLD/NASH. Trained PCPs then can utilize the non-invasive screening tools (i.e., FIB-4 score and/or NAFLD fibrosis score) to risk stratify patients with high clinical suspicion for NAFLD. PCPs will be able to manage the low risk NAFLD patients and further risk stratify them based on transient elastography. Patients with fibrosis stage 2-4 can be either directly referred to NAFLD 'hub' by teleconsultation or can be managed by telementoring (individualized (one-to-one) education of PCPs by specialists).

PROPOSED MODEL OF TELEHEALTH FOR NAFLD/NASH

The growing burden of NAFLD/NASH and the distance of majority of these patients from urban centers of care, demands the need for establishing telehealth-based models to deliver care to these patients. The successes from well-established ECHO® model,¹⁸ and one-to-one telementoring^{13,22} provides pathways to developing a NAFLD/NASH model-of-care. Using these two models and incorporating stepwise risk-stratification method,^{7,23} guided proposal of a pathway for telehealth-based management of NAFLD/NASH patients (Fig. 1). A key focus of the proposed model is in educating PCPs while selectively increasing access-to-care to consultants for advanced NAFLD/NASH patients.

Education of PCPs and other care providers remain key to the early detection and appropriate linkage-to-care of patients at-risk for advanced NASH. The tertiary care centers can become 'hubs,' as defined in the ECHO® model and provide access to knowledge and support for triage and management of NAFLD/NASH. Srivastatva et al. showed a real-world data about practicality of their proposed NAFLD referral pathway with 88% reduction in unnecessary referrals.⁷ While practice guidelines do not yet recommend routine screening for NAFLD/NASH among diabetic patients,²⁴ new data shows benefit in screening for NAFLD in these at-risk patients.²⁵ Those with clinical suspicion for NAFLD will undergo the non-invasive lab-based test, as shown in Fig. 1, and if indicated to pursue imaging-based fibrosis assessment test based on local availability.

PROS AND CONS OF TELEHEALTH FOR NAFLD/NASH PATIENTS

One of the most desirable advantages of telehealth is easier access to patients, even those in rural areas. Positive

TABLE 1. POTENTIAL PROS AND CONS OF TELEHEALTH TOOLS IN NAFLD

Pros	Cons
More access for diverse group of patients and especially in remote areas with limited access to hepatologists	Cannot be used for acute and very sick patients with complications of NAFLD such as decompensated cirrhosis
Allows expanding the education among more patients and PCPs	Older age and low socioeconomic populations cannot optimally access telemedicine
Potentially earlier detection of NAFLD and its complications by PCPs after being educated	Technical challenges such as lack of strong Internet, smartphones
Potentially less unnecessary referrals and health-care costs	Billing issues, not all insurances cover the telehealth/telemedicine charges

patient and clinician satisfaction from teleconsultations in gastroenterology and liver disease including NAFLD patients has been reported.^{10,15}

Telemedicine helps to increase PCPs' knowledge and attention to NAFLD, which not only increases the timely detection of NAFLD but also can potentially decrease its complications. In addition, inappropriate referrals to hepatologists, which ultimately can decrease the health-care costs.^{7,26}

One of the barriers in telemedicine has been insurance re-imburements.^{11,14} However, COVID-19 pandemic clearly showed the benefits of telehealth/telemedicine and helped inform policy decision to remove barriers of insurance coverage. The current rule does not require patients to be far from large facilities to be qualified for the telemedicine service; this increased the population who can benefit from telemedicine.¹¹ Possible pros and cons of telemedicine in fatty liver disease are summarized in Table 1.

ADDRESSING DISPARITIES IN FATTY LIVER DISEASE CARE USING TELEHEALTH

Health and health-care inequities and disparities exist in the United States and impacted morbidity and mortality in the nation.²⁷ A recent meta-analysis by Rich et al. showed that prevalence of NAFLD and risk of its progress to NASH are significantly higher in Hispanics as compared to other ethnicities.²⁸ Telehealth is potentially a great tool to overcome current disparities and extending the best possible care to everyone even in far rural areas. However, disparities in use of technology also exists.^{29,30} The more-educated urban and suburban residents tend to have more access to Internet compared to less-educated and rural residents. Older patients are less likely to choose telemedicine over in office visits for primary care visits.³⁰ Moreover, based on a survey in 2019 by Pew Research Center only 53% of US seniors had smart phones. In accordance with these findings,

Wegermann et. al showed a suboptimal use of telehealth for chronic liver diseases in older, blacks and those with Medicare/Medicaid health insurances.²⁹ The main question here is that considering all current disparities can telemedicine improve diagnosis and early referral of those high-risk NAFLD patients? The answer is not clear as this model has not been tested before, but one can speculate that the proposed model may be effective since this proposed model is mainly focused on educating the PCPs and also offers individualized telementoring. This model can potentially overcome the issue of no access to smart phone or tablets by some elderly or low socioeconomic patients, as they can connect to the NAFLD/NASH 'hub' in the PCP office.

CONCLUSION AND FUTURE DIRECTIONS

Accumulation of data over years has shown that telemedicine is highly effective in management of various medical problems.⁹ Currently, there is no standardized algorithm for early diagnosis, management, and referral of patients with NAFLD, especially with the use of a combination of telemedicine tools. Controversy remains regarding cost effectiveness,⁹ of telehealth approaches and its uptake among providers and patients. The COVID-19 pandemic showed the clear benefit of telehealth as a sustainable and beneficial model with significant benefits for patients and providers. Thus, more recent analysis will be needed post-pandemic to understand the benefits of telemedicine on economics and clinical outcomes especially in the setting of NAFLD, NASH, and its complications. Based on Telehealth Benchmark Survey in 2020, telehealth adoption and use will sustain, and health-care systems will expand their telehealth programs (2020_Telehealth_Benchmark_Survey_Results.pdf [ctfassets.net]; Accessed on March 3, 2021). In view of this encouraging news and with the development of pharmacological treatments for NASH, studies are warranted to understand and implement telemedicine-based approaches to provide access to care to all patients at-risk.

CORRESPONDENCE

Souvik Sarkar, M.D., Ph.D., Gastroenterology and Hepatology, University of California Davis, 4150 V St; PSSB 3500, Sacramento CA 95817. E-mail: ssarkar@ucdavis.edu

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