Digital Gastroenterology

Alexander Kusnik^{1,2}, Timo Itzel¹, Steven Dooley¹, Anne Dropmann¹, Jan Stallkamp³, Thomas Ganslandt⁴, Matthias Ebert^{1,2}, Andreas Teufel^{1,2}

Department of Medicine
University Medical Center
Mannheim, Medical Faculty
Mannheim, Heidelberg
University, Mannheim;
Preventive Medicine Baden-Württemberg (CPMBW),
Medical Faculty Mannheim,
Heidelberg University,
Mannheim;

 Fraunhofer Institute for Manufacturing Engineering and Automation, Project Group for Automation in Medicine and Biotechnology, Mannheim;

4) Department of Biomedical Informatics of the Heinrich-Lanz-Center, University Medical Center Mannheim, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

Address for correspondence:

Prof. Dr. Dr. Andreas Teufel Section Hepatology, Section **Clinical Bioinformatics** Department of Medicine II, University Medical Center Mannheim Medical Faculty Mannheim, Heidelberg University Baden-Württemberg Center for Preventive Medicine and Digital Health Theodor-Kutzer-Ufer 1-3 68167 Mannheim Germany andreas.teufel@medma.uniheidelberg.de

Received: 07.09.2020 Accepted: 08.10.2020

The advent of digital technology is transforming health care in general, but also gastroenterology and hepatology. Electronic devices can automatically and precisely take measurements of physiological parameters or support an improved and less error-prone documentation. Mobile devices, such as smartphones or various wearables, e.g. smart watches, which can transmit ECGs live, open up new possibilities for monitoring and prevention, especially in rural areas (mHealth). Wearables, in particular, could be helpful in stimulating a change in lifestyle, if necessary. In addition to progress in treatment and prevention of diseases, digital medicine is also developing into a significant economic factor. A study by PricewaterhouseCoopers on the socio-economic impact of mHealth indicated that mHealthsolutions could save 99 billion EUR in healthcare costs in the European Union (EU) and add 93 billion EUR to the European gross domestic product [1].

In gastroenterology, considerable efforts are being made to improve medical care and prevention, by means of increased digital processes, particularly for gastrointestinal inflammatory and oncological diseases. The main developments are the documentation of gastroenterological patients in electronic health records (EHRs), use of artificial intelligence (AI) in endoscopy, automation and artificial intelligence (AI) in pathological diagnostics, development of smartphone Apps and use of wearables.

ELECTRONIC HEALTH RECORDS

Electronic health records are already the standard of clinical documentation in various countries. Their advantages are obvious. They offer direct and universal access to relevant patient information to both physician and patient. In a nationwide survey, 65% of all of Canadian general practitioners felt that patient care improved after the introduction of EHRs. The benefits were seen in the improved availability of laboratory results, warnings of potential medication errors and possible remote access to patient records. Only less than 5% reported that EHRs had a negative impact on the quality of care [2]. A study from the US reached similar conclusions as patients treated in hospitals with fully implemented EHRs, e.g. for acute myocardial infarction, had fewer heparin overdose errors (45.7% vs. 72.8%, p<0.01) than patients treated without EHRs. Also, they were more likely to be treated according to guidelines [3]. Finally, studies also showed that the increased use of EHRs can support physician productivity [4].

Electronic health records also offer enormous scientific potential. By evaluating a large number of EHRs, correlations of diseases with environmental factors, drugs and comorbidities can be assessed, potentially improving future patient management. A study conducted by Sidebottom et al. [5] compared the impact of primary and secondary prevention between two rural populations in New Ulm, Minneapolis/ USA (16,470 inhabitants). Almost the entire population was represented in one health care network and interventions were specifically planned based on the EHR (e.g. programs for weight control, algorithms for identifying persons at high risk for coronary heart disease etc.). As a result, the proportion of residents with controlled blood pressure significantly increased by 6.2 percent. Furthermore, as the age of the cohort increased, the 10-year Atherosclerotic Cardiovascular Disease risk scores (5.1) increased less than in the control population (5.9).

In adults with non-alcoholic fatty liver disease (NAFLD), about 25% of deaths are due to cardiovascular disease. Reducing this risk requires the identification and modification of appropriate risk factors such as hypertension. An American cross-sectional study [6] identified additional, non-traditional risk factors on the basis of EHRs. For example, a significantly increased MELD score was associated with an increased risk of cardiovascular disease. Furthermore, albumin and sodium were inversely associated with cardiovascular disease. Statistically, heart disease was more common in individuals with a NAFLD fibrosis score above 0.676 than in individuals with a lower score. These studies indicated that the use of computer-based algorithms to detect and possibly halt a negative course of a disease at an early stage is desirable.

Such algorithms may also be an aid to prevent the premature progression of liver disease. For example, a recent registry study on more than 130,000 European patients showed that diabetes mellitus was the strongest independent predictor of hepatocellular carcinoma or liver cirrhosis [7]. Such an observation may help to establish individual risk profiles for personalized prevention and improve both disease prevention and resources of the health care system.

Electronic health records may also be helpful for the identification of patients at risk for specific health conditions and inclusion of these patients in standardized surveillance programs. Colorectal cancer screening using automated messages linked to EHRs resulted in twice as many people being screened over two years [8].

Finally, the digitalization of medical documentation can also contribute to a closer networking of different health care providers. A study from England showed that liver enzyme tests were the third most frequently ordered laboratory tests in primary care since 2001 [9]. More than 20% of the patients had abnormal results [10]. However, very few patients, probably less than 5%, are being diagnosed with a liver disease [11].

ARTIFICIAL INTELLIGENCE

Artificial intelligence is currently discussed in many areas. However, there is no uniform definition. Artificial intelligence basically describes computer programs performing functions, such as learning and problem solving, that we associate with human intelligence. A further differentiation is made into machine learning and deep learning.

Machine learning has found its way into many areas of our daily life: Internet searches, identification of objects in pictures (e.g. face recognition) or the conversion of speech into text. These techniques require predefined patterns and algorithms to work, for example as a decision tree. In a second step, the algorithms gain the ability to differentiate specific patterns through constant repetition. However, machine learning techniques are limited in their ability to process natural data without prior training [12]. Deep learning is a subarea of machine learning, using neural networks and a constantly growing data representation by increasing levels of abstraction [13].

In gastroenterology, deep learning strategies are regularly applied in endoscopy. For example, additional use of AI technology significantly increased the adenoma detection rate and the average number of adenomas found per patient [14]. Artificial intelligence particularly helped with smaller adenomas. Furthermore, accuracy of polyp detection was estimated to be as high as 96.4% in other reports [15]. However, larger multicenter randomized studies are still needed.

Neural networks may also be a significant aid in the histological diagnosis of gastrointestinal tumours. Kather et al.

[16] illustrated that neural network might be used to determine the instability of microsatellites just from the conventional histology of a tumor, which was important with respect to (immuno-) therapeutic options.

For the visual assessment of radiological images AI may help to objectify the qualitative assessment and reduce the intra-/interobserver variability [17-19].

APPS AND TRACKERS

With new functions such as the recording of pulse and ECG, pedometer, sleep behavior and other options, smartphones are also ideal for more intensive and continuous monitoring and integration into medical care. The acceptance of most patients with chronic diseases for appropriate monitoring can be assumed. In a survey conducted in the USA on 40 patients with liver cirrhosis with an average MELD of 22 [22], 60% of those surveyed said that they would use a smartphone App for daily monitoring of their cirrhosis. Their wishes and expectations were being able to communicate with their physician (80.0%), to receive notification concerning their medication (63%), transmission of diagnostic results and appointment reminders (75%), more information regarding the clinical status (78%), low salt dietary recipes (63%).

Twenty one of 25 patients with liver cirrhosis and hepatic encephalopathy stated that they would also use smartphone games if they could clearly identify cognitive deterioration.

The smartphone App "EncephalApp Stroop" developed by Bajaj et al. [21] may be used for the screening of minimal hepatic encephalopathy. A time-controlled stroop test can be used to measure psychomotor speed. The test consists of two components: three hash marks (###) appear in three different colors (green, red, or blue) and also vary in size. The total time required to complete five correct runs of connecting hash marks size and color and the required number of attempts are monitored [22-24].

The "Patient Buddy" App [25] was designed particularly for patients with liver cirrhosis. An accompanying study by Ganapathy et al. [26] monitored patients for 30 days via the App after an inpatient stay due to liver cirrhosis. On a separate device, patients were also monitored for drug intake, salt intake and weight gain. In addition, weekly cognitive tests and cirrhosisrelated symptoms were obtained. The study demonstrated that the "Patient Buddy" App successfully prevented hospital admissions related to hepatic encephalopathy, by generating warning messages and encouraging early outpatient visits.

However, digital smartphone applications may also support physicians. For example, the mobile application "MyGIhealth" [27] systematically collects information on gastrointestinal symptoms and summarizes them in a regular report to the treating physician. Thus, the physician has a comprehensive overview prior to the first patient contact. Similarly, the "SonarMD" health platform exists for patients with chronic inflammatory bowel disease [28]. The platform sends regular questionnaires to the patient regarding current symptoms. All trends or signs of changes in the course of the disease are then presented to a physician for further assessment, who in turn can contact the patient at short notice and adjust the treatment strategy if necessary.

PORTABLE BIOSENSORS

Fitness trackers have become widely used in recent years and are currently the most popular portable biosensors. They are generally used to monitor the number of steps, sleep, and possibly heart rate. In gastroenterology, however, few applications for biosensors have been established so far. An already existing device is "AbStats" [29] consisting of a flat microphone that is attached to the abdominal wall measuring frequency of intestinal contractions. An initial study on 40 patients reported that abdominal acoustic monitoring may successfully postoperatively predict an ileus [30].

Overall, the development of clinically relevant Apps or portable biosensors is still in the early stages. A recently published meta-analysis of 550 studies [31] illustrated a lack of meaningful studies demonstrating a positive effect. In addition, there was no single effect of portable devices (without medical feedback) on reducing weight, blood sugar levels, blood pressure and cholesterol levels. However, such integrative developments would be clinically relevant for the future and therefore highly desirable.

OUTLOOK

Overall, digital strategies will increasingly be applied in clinical medicine and patient care. Smartphone applications and portable biosensors will lead to an improved and more integrated care among diverse health care providers. Thus, they may become an additive health care structure. Artificial intelligence will be of significant aid in improving diagnoses, increasing reliability and procedure rate in radiology and histology. Even though many of the strategies are still in their infancy, an increase in awareness among physicians is necessary in order to accompany the technological development, obtain medically meaningful study results, and further improve digital strategies in patient care. As the technological resources increasingly become available a successful digital transformation will advance gastroenterology and hepatology to a new level.

Conflicts of interest: None to declare.

Authors' contributions: A.K. and A.T conceived and wrote the editorial; J.S, T.G., M.E, T.I and A.D collected the data and revised the paper. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

Acknowledgments: A.K. and A.T. were supported by the Ministry of Science, Research and Arts of the State of Baden-Württemberg [funded project: Baden-Württemberg Center for Digital Detection and Prevention of common diseases (BW-ZDFP)].

REFERENCES

 Institute PHR. Socio-economic impact of mHealth: An assessment report for the European Union. 2017. Accessed 2020 22 Sep. Available from: https://www.pwc.in/assets/pdfs/consulting/strategy/socioeconomic-impact-of-mhealth-the-european-union.pdf

- Collier R. National Physician Survey: EMR use at 75%. CMAJ 2015;187:E17-E18. doi:10.1503/cmaj.109-4957
- Enriquez JR, de Lemos JA, Parikh SV, et al. Modest Associations Between Electronic Health Record Use and Acute Myocardial Infarction Quality of Care and Outcomes: Results From the National Cardiovascular Data Registry. Circ Cardiovasc Qual Outcomes 2015;8:576-585. doi:10.1161/ CIRCOUTCOMES.115.001837
- Adler-Milstein J, Huckman RS. The impact of electronic health record use on physician productivity. Am J Manag Care 2013;19(10 Spec No):SP345-SP352.
- Sidebottom AC, Sillah A, Vock DM, et al. Assessing the impact of the heart of New Ulm Project on cardiovascular disease risk factors: A population-based program to reduce cardiovascular disease. Prev Med 2018;112:216-221. doi:10.1016/j.ypmed.2018.04.016
- Corey KE, Kartoun U, Zheng H, Chung RT, Shaw SY. Using an Electronic Medical Records Database to Identify Non-Traditional Cardiovascular Risk Factors in Nonalcoholic Fatty Liver Disease. Am J Gastroenterol 2016;111:671-676. doi:10.1038/ajg.2016.44
- Alexander M, Loomis AK, van der Lei J, et al. Risks and clinical predictors of cirrhosis and hepatocellular carcinoma diagnoses in adults with diagnosed NAFLD: real-world study of 18 million patients in four European cohorts. BMC Med 2019;17:95. doi:10.1186/s12916-019-1321-x
- Green BB, Wang CY, Anderson ML, et al. An automated intervention with stepped increases in support to increase uptake of colorectal cancer screening: a randomized trial. Ann Intern Med 2013;158:301-311. doi:10.7326/0003-4819-158-5-201303050-00002
- O'Sullivan JW, Stevens S, Hobbs FDR, et al. Temporal trends in use of tests in UK primary care, 2000-15: retrospective analysis of 250 million tests. BMJ 2018;363:k4666. doi:10.1136/bmj.k4666
- McLernon DJ, Donnan PT, Ryder S, et al. Health outcomes following liver function testing in primary care: a retrospective cohort study. Fam Pract 2009;26:251-259. doi:10.1093/fampra/cmp025
- Lilford RJ, Bentham L, Girling A, et al. Birmingham and Lambeth Liver Evaluation Testing Strategies (BALLETS): a prospective cohort study. Health Technol Assess 2013;17(28). doi:10.3310/hta17280
- LeCun Y, Bengio Y, Hinton G. Deep learning. Nature 2015;521:436-444. doi:10.1038/nature14539
- Bengio Y. Learning Deep Architectures for AI. Found Trends Mach Learn 2009;2:1–127. doi:10.1561/2200000006
- Wang P, Berzin TM, Glissen Brown JR, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. Gut 2019;68:1813-1819. doi:10.1136/gutjnl-2018-317500
- Urban G, Tripathi P, Alkayali T, et al. Deep Learning Localizes and Identifies Polyps in Real Time With 96% Accuracy in Screening Colonoscopy. Gastroenterology 2018;155:1069-1078.e8. doi:10.1053/j. gastro.2018.06.037
- Kather JN, Pearson AT, Halama N, et al. Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer. Nat Med 2019;25:1054-1056. doi:10.1038/s41591-019-0462-y
- Zhou LQ, Wang JY, Yu SY, et al. Artificial intelligence in medical imaging of the liver. World J Gastroenterol 2019;25:672-682. doi:10.3748/wjg. v25.i6.672
- Ambinder EP. A history of the shift toward full computerization of medicine. J Oncol Pract 2005;1:54-56. doi:10.1200/JOP.2005.1.2.54
- Freedman M, Osicka T. Reader variability: what we can learn from computer-aided detection experiments. J Am Coll Radiol 2006;3:446-455. doi:10.1016/j.jacr.2006.02.025

J Gastrointestin Liver Dis, December 2020 Vol. 29 No 4: 493-496

- Bloom PP, Wang TJ, Green B, Marx M, Ha J, Richter J. Su1473 -Technology Utilization in Patients with Cirrhosis and Preferred Features of Digital Health Management Tools. Gastroenterology 2019;156:S1273-S1274. doi:10.1016/S0016-5085(19)40188-1
- 21. Bajaj JS, Thacker LR, Heuman DM, et al. The Stroop smartphone application is a short and valid method to screen for minimal hepatic encephalopathy. Hepatology 2013;58:1122-1132. doi:10.1002/hep.26309
- Zeng X, Li XX, Shi PM, et al. Utility of the EncephalApp Stroop Test for covert hepatic encephalopathy screening in Chinese cirrhotic patients. J Gastroenterol Hepatol 2019;34:1843-1850. doi:10.1111/jgh.14656
- Allampati S, Duarte-Rojo A, Thacker LR, et al. Diagnosis of Minimal Hepatic Encephalopathy Using Stroop EncephalApp: A Multicenter US-Based, Norm-Based Study. Am J Gastroenterol 2016;111:78-86. doi:10.1038/ajg.2015.377
- Bajaj JS, Heuman DM, Sterling RK, et al. Validation of EncephalApp, Smartphone-Based Stroop Test, for the Diagnosis of Covert Hepatic Encephalopathy. Clin Gastroenterol Hepatol 2015;13:1828-1835.e1. doi:10.1016/j.cgh.2014.05.011

- 25. Creative Information Technology I. Patient Buddy. Available from: https://www.citi-us.com/healthcare/patient-buddy
- Ganapathy D, Acharya C, Lachar J, et al. The patient buddy app can potentially prevent hepatic encephalopathy-related readmissions. Liver Int 2017;37:1843-1851. doi:10.1111/liv.13494
- 27. GiHealth. Chey BSW. MyGiHealth. Available from: https://mygi.health/
- SonarMD. Keep patients healthier by joining a VBC program designed for GI. 2020 June 30. Available from: https://sonarmd.com/forproviders/
- Alpha Logic I. Introducing AbStats The New Vital Sign*. 2020. Available from: http://gi-logic.com/products/abstats/
- Spiegel BM, Kaneshiro M, Russell MM, et al. Validation of an acoustic gastrointestinal surveillance biosensor for postoperative ileus. J Gastrointest Surg 2014;18:1795-1803. doi:10.1007/s11605-014-2597-y
- Jo A, Coronel BD, Coakes CE, Mainous AG 3rd. Is There a Benefit to Patients Using Wearable Devices Such as Fitbit or Health Apps on Mobiles? A Systematic Review. Am J Med 2019;132:1394-1400.e1. doi:10.1016/j.amjmed.2019.06.018