Breast cancer risk characteristics of women undergoing whole-breast ultrasound screening versus mammography alone

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invasive cancer and advanced cancer were determined using BCSC prediction models. High interval invasive breast cancer risk was defined as heterogeneously dense breasts and BCSC 5-year breast cancer risk ≥2.5% or extremely dense breasts and BCSC 5-year breast cancer risk ≥1.67%. Intermediate/high advanced cancer risk was defined as BCSC 6-year advanced breast cancer risk ≥0.38%.

Results: A total of 95.3% of 38,166 ultrasounds were among women with heterogeneously or extremely dense breasts, compared with 41.8% of 825,360 screening mammograms without supplemental screening ($p < .0001$). Among women with dense breasts, high interval invasive breast cancer risk was prevalent in 23.7% of screening ultrasounds compared with 18.5% of screening mammograms without supplemental imaging (adjusted odds ratio, 1.35; 95% CI, 1.30–1.39); intermediate/high advanced cancer risk was prevalent in 32.0% of screening ultrasounds versus 30.5% of screening mammograms without supplemental screening (adjusted odds ratio, 0.91; 95% CI, 0.89–0.94).

Conclusions: Ultrasound screening was highly targeted to women with dense breasts, but only a modest proportion were at high mammography screening failure risk. A clinically significant proportion of women undergoing mammography screening alone were at high mammography screening failure risk.

Awards.

Dieter Oesterhelt (Max Planck Institute of Biochemistry), Peter Hegemann (Humboldt University of Berlin) and Karl Deisseroth (Stanford University) will receive the Albert Lasker Basic Medical Research Award.

Katalin Karikó (BioNTech) and Drew Weissman (University of Pennsylvania) will be honored with the Lasker-DeBakey Clinical Medical Research Award.

David Julius (California Institute of Technology) will receive the Lasker-Koshland Special Achievement Award in Medical Science.

The Lasker Awards carry an honorarium of $250,000 for each category. Due to the pandemic, the Foundation will not be presenting the Awards this year in a traditional in-person ceremony.

Optogenetics

Dieter Oesterhelt, Peter Hegemann, and Karl Deisseroth receive the Albert Lasker Basic Medical Research Award for the discovery of light-sensitive microbial proteins that can activate or silence individual brain cells and for their use in developing optogenetics, a revolutionary technique for neuroscience.

The work of Dieter Oesterhelt, Peter Hegemann, and Karl Deisseroth has advanced technologies for probing brain function and opened pathways for the better understanding of neurodegenerative diseases and mental illnesses.

Read more: Optogenetic therapy partially restored visual function in a blind patient

Scientists can now study neurons and their circuitry with stunning clarity and probe their functional underpinnings with unprecedented resolution. Hundreds of laboratories around the

The winners of the Lasker Awards 2021

MALIN OTMANI · SEPTEMBER 28 2021

KARL DEISSEROTH, PHOTO: JIM GENSHEIMER, DIETER OESTERHELT AND PETER HEGEMANN, PHOTO MARCUS WA

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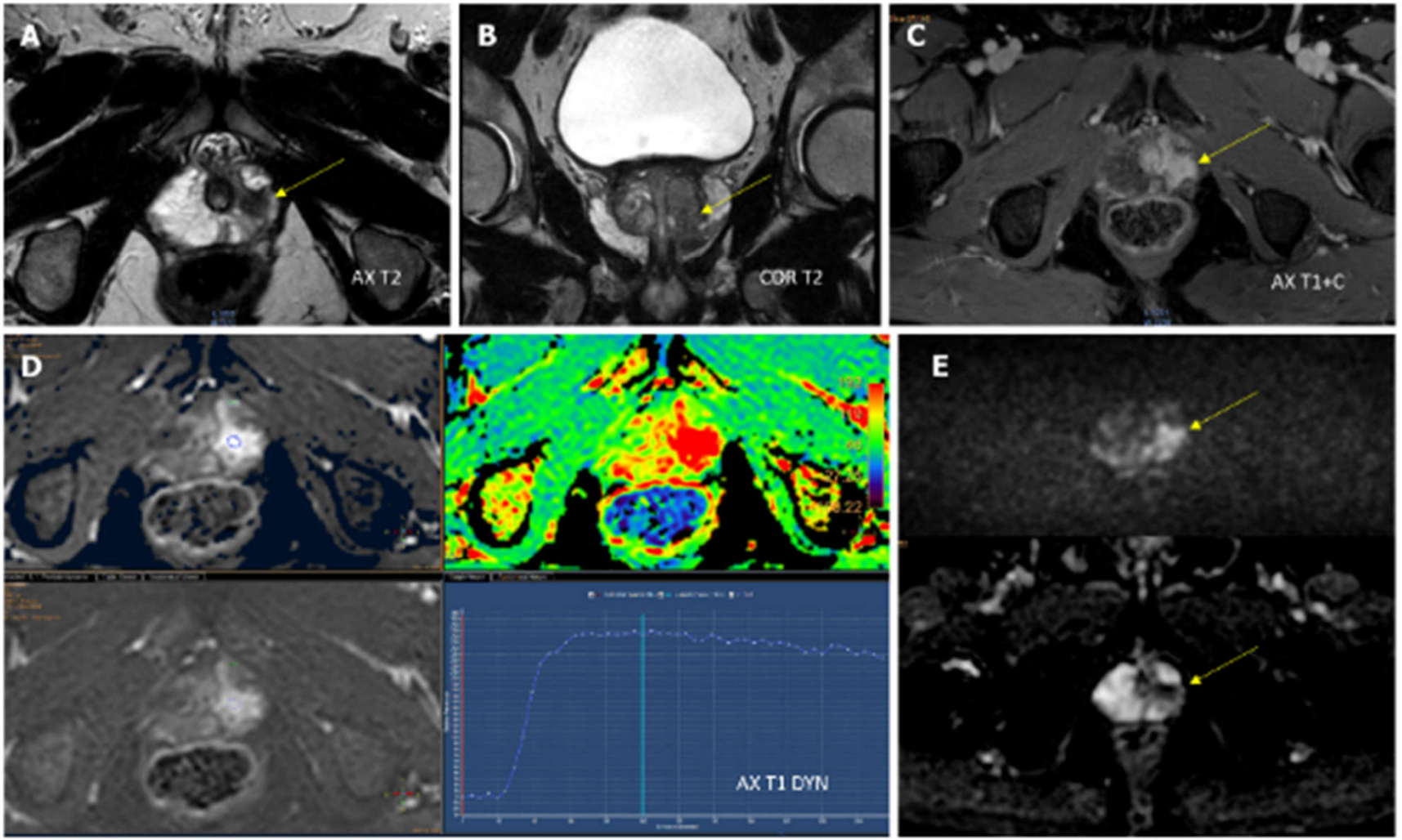
MINIREVIEWS

Future of prostate imaging: Artificial intelligence in assessing prostatic magnetic resonance imaging

Lyubomir Chervenkov, Nikolay Sirakov, Gancho Kostov, Tsvetelina Velikova, George Hadjidekov

Abstract

Prostate cancer (Pca; adenocarcinoma) is one of the most common cancers in adult males and one of the leading causes of death in both men and women. The diagnosis of Pca requires substantial experience, and even then the lesions can be difficult to detect. Moreover, although the diagnostic approach for this disease has improved significantly with the advent of multiparametric magnetic resonance, that technology has certain unresolved limitations. In recent years artificial intelligence (AI) has been introduced to the field of radiology, providing new software solutions for prostate diagnostics. Precise mapping of the prostate has become possible through AI and this has greatly improved the accuracy of biopsy. AI has also allowed for certain suspicious lesions to be attributed to a given group according to the Prostate Imaging-Reporting & Data System classification. Finally,



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Core Tip: The peer reviewed literature has provided sufficient support for the continued application and development of artificial intelligence (AI) in prostate cancer clinical care. In addition, the expanding introduction of various AI-based software products created by leading companies is providing practical benefits to radiologists for improved prostate cancer diagnosis. Certainly, the known complexity of the disease and its consequential difficult diagnosis supports the continued development of new approaches for earlier and more accurate detection, such as could be provided through AI technologies.

REVIEW ARTICLE OPEN

Host-microbiome interactions: Gut-Liver axis and its connection with other organs

Swadha Anand[1]✉ and Sharmila S. Mande[1]✉

An understanding of connections between gut microbiome and liver has provided important insights into the pathophysiology of liver diseases. Since gut microbial dysbiosis increases gut permeability, the metabolites biosynthesized by them can reach the liver through portal circulation and affect hepatic immunity and inflammation. The immune cells activated by these metabolites can also reach liver through lymphatic circulation. Liver influences immunity and metabolism in multiple organs in the body, including gut. It releases bile acids and other metabolites into biliary tract from where they enter the systemic circulation. In this review, the bidirectional communication between the gut and the liver and the molecular cross talk between the host and the microbiome has been discussed. This review also provides details into the intricate level of communication and the role of microbiome in Gut-Liver-Brain, Gut-Liver-Kidney, Gut-Liver-Lung, and Gut-Liver-Heart axes. These observations indicate a complex network of interactions between host organs influenced by gut microbiome.

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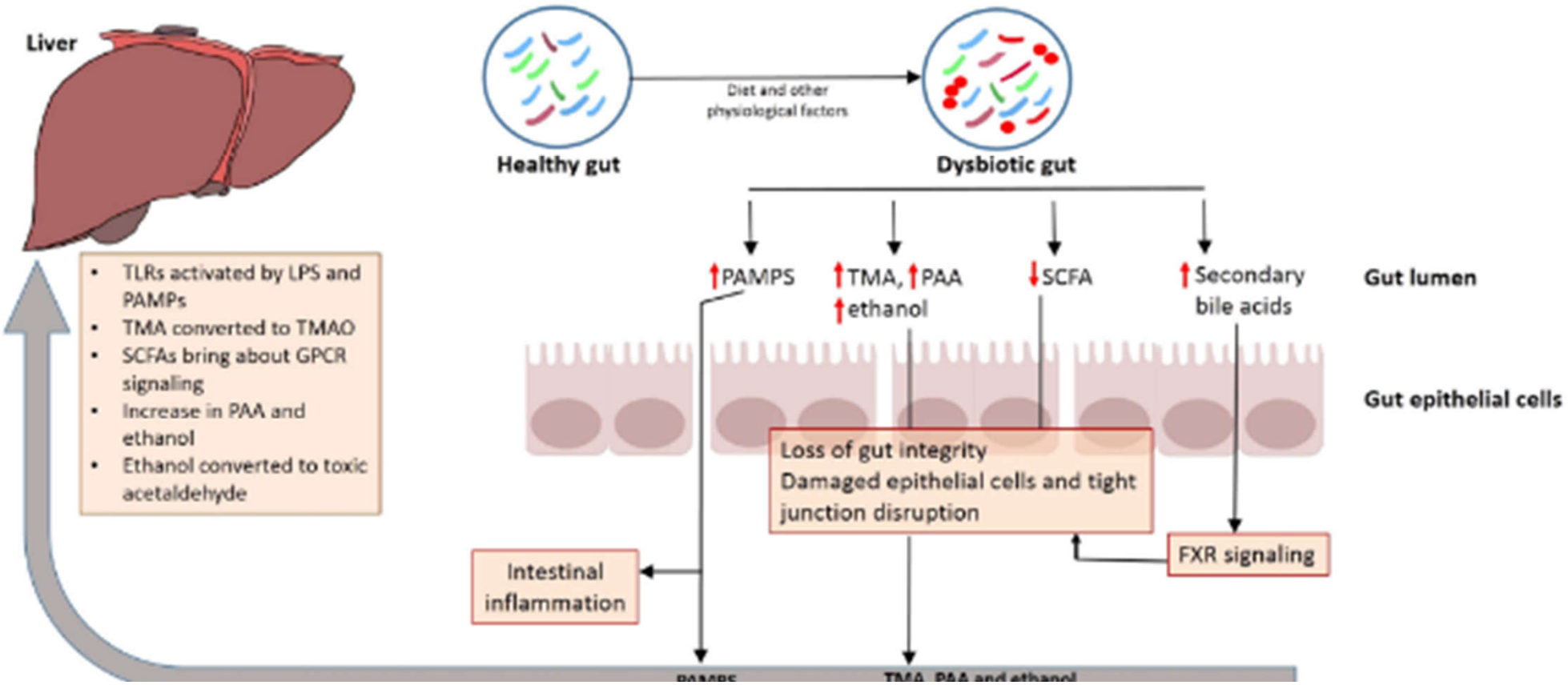
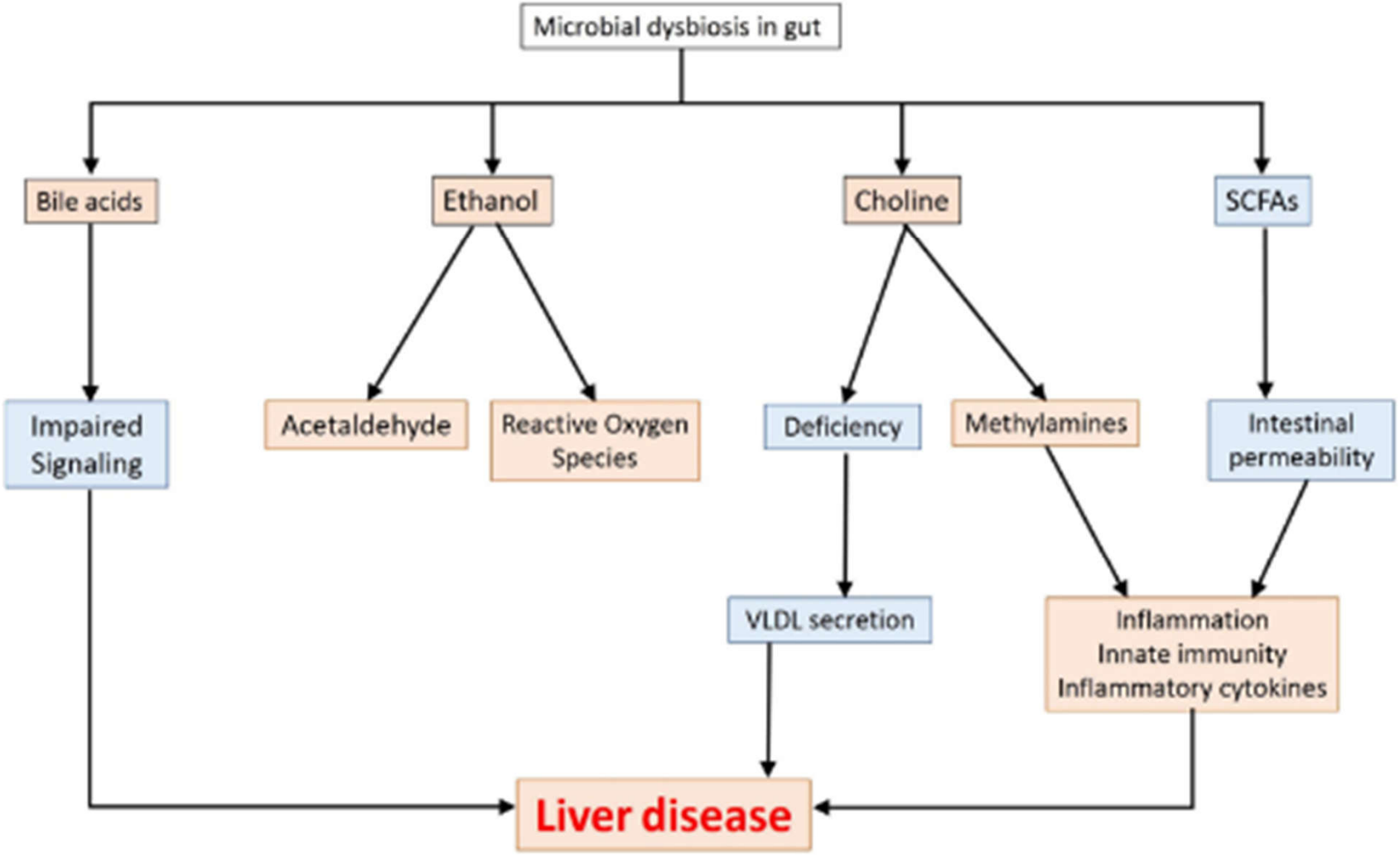

Liver
Healthy gut
Diet and other physiological factors
Dysbiotic gut
TLRs activated by LPS and PAMPs
TMA converted to TMAO
SCFAs bring about GPCR signaling
Increase in PAA and ethanol
Ethanol converted to toxic acetaldehyde
PAMPS
TMA, PAA
ethanol
SCFA
Secondary bile acids
Gut lumen
Gut epithelial cells
Loss of gut integrity
Damaged epithelial cells and tight junction disruption
FXR signaling
Intestinal inflammation


Microbial dysbiosis in gut
Bile acids
Ethanol
Choline
SCFAs
Impaired Signaling
Acetaldehyde
Reactive Oxygen Species
Deficiency
Methylamines
Intestinal permeability
VLDL secretion
Inflammation
Innate immunity
Inflammatory cytokines
Liver disease

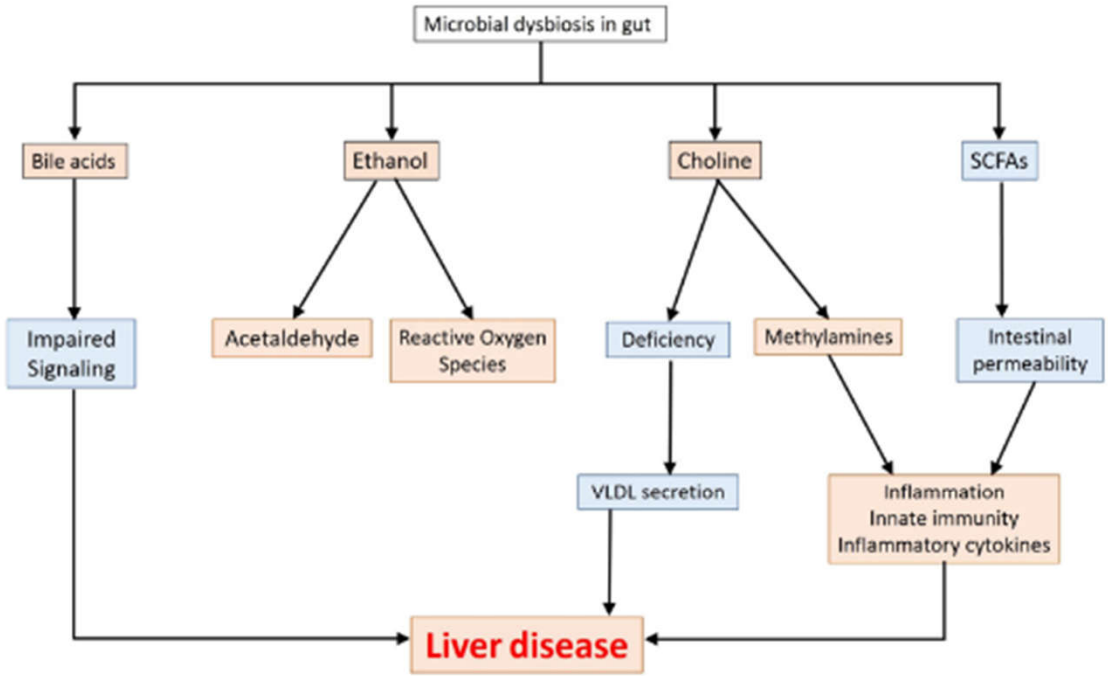
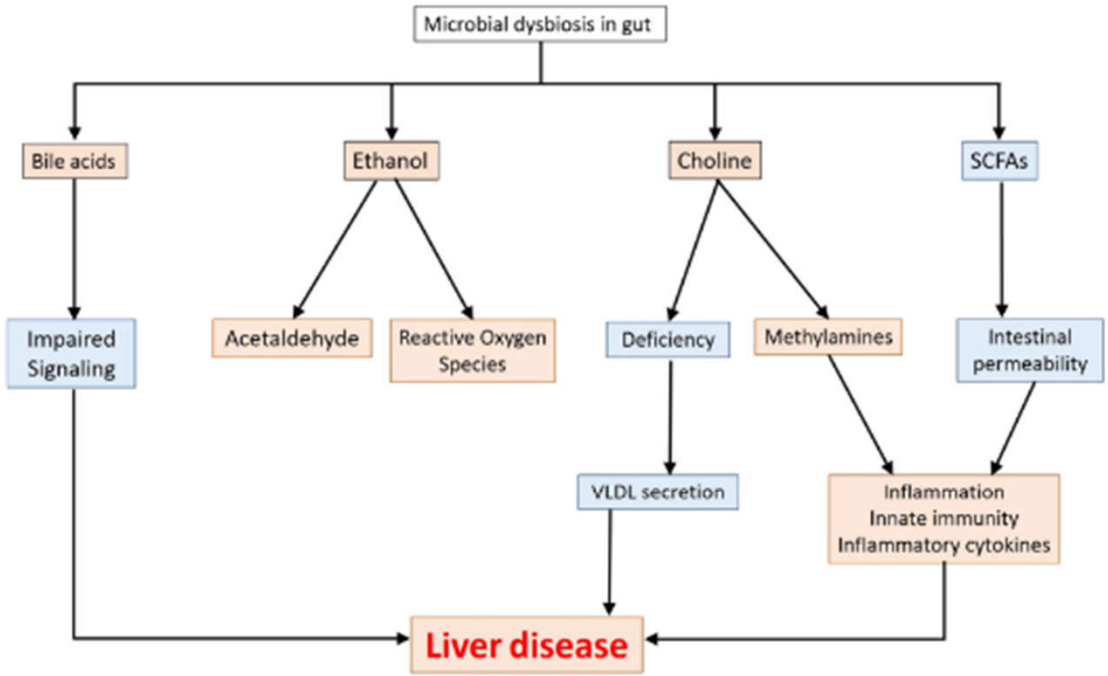


Fig. 2 Gut metabolites and liver disease. Metabolites biosynthesized by the microbiome and their impact on onset of liver disease.

This leads to induction of pattern recognition receptors (PRR) like TOLL-like receptors and NOD-like receptors in liver cells, which results in activation of pro-inflammatory signaling cascades, which

resistant to 'Choline Deficient Amino Acid' (CDAA) induced steatohepatitis and have reduced expression of pro-inflammatory cytokines[35]. In contrast, TLR2-deficient mice on



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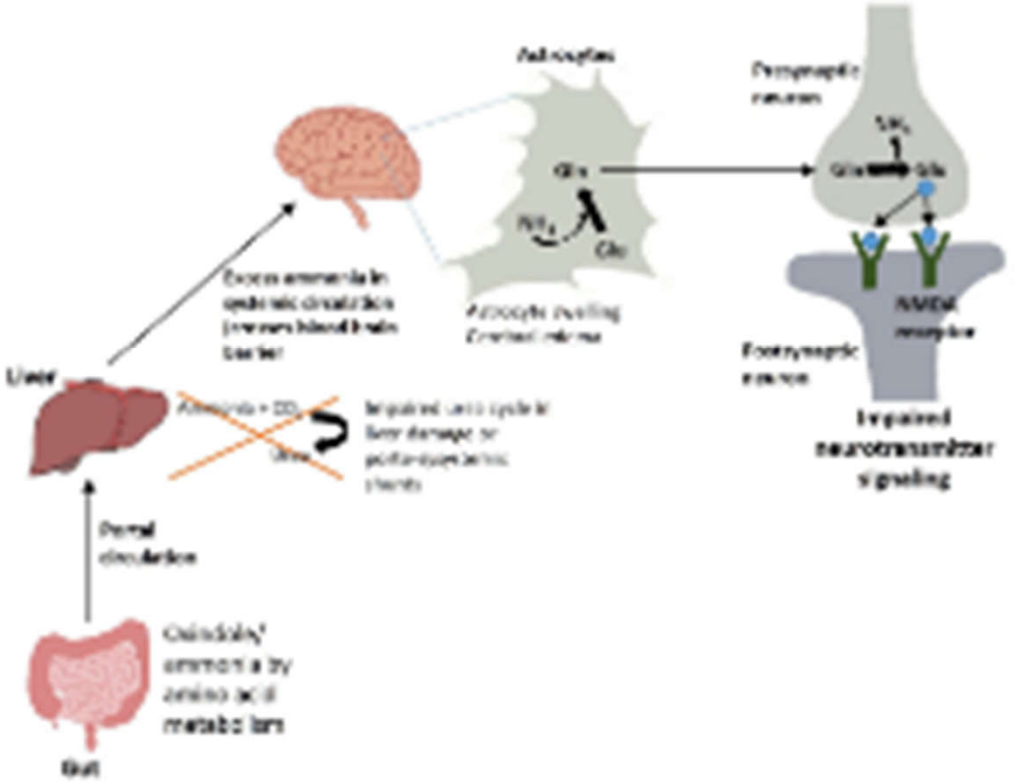

Fig. 1 Gut–Liver–brain axis. Impairment of liver urea cycle in liver disease condition leads to increase in serum lactate and ammonia which reach the brain and affect neurotransmitter signaling and astrocyte swelling.

which has been associated to neurological symptoms (Fig. 1). This may result in formation of brain derived proinflammatory

and inflammation of adipose tissue[xxx].

In summary, the Gut-Liver axis refers to bidirectional communication between gut, its microbiome and the liver. The metabolites produced by gut microbiome are connected with liver through systemic circulation, portal circulation and the bile duct. While the metabolites produced in the gut influence immunity, metabolism and bile acid production, the bile acids produced in liver in turn regulate the gut microbial composition as well as gut epithelial barrier integrity. Therefore, a dysbiosis in gut microbiome not only leads to a change in the bile acid pool within the host, but also often been observed in liver related pathophysiologies like NAFLD, NASH, ALD, etc. Further, since some gut bacteria are capable of metabolizing bile acid, the bile acid pool determines and influences the composition of gut microbiome. The shifting level of bile acids impacts the microbial integrity and metabolism by affecting FXR signaling. Exposure of liver immune cells to metabolites like LPS produced by gut bacteria can increase liver inflammation. Further, the liver regulates the innate immunity as well as metabolism of various toxins and metabolites in other organs. In other words, a deterioration in liver condition can also impact the metabolism signaling and immunity in other important host organs. Hence, the Gut-Liver axis can be extended to distal organs like Gut-Liver-Brain, Gut-Liver-Kidney, Gut-Liver-Heart and Gut-Liver-Lung axes.

Findings from the Gut-Liver X (X being Brain or Kidney or Heart or Lung) axes indicate potential of utilizing gut microbiome as diagnostic and therapeutic strategy for early detection and management of not only liver diseases, but also diseases affecting other organs (e.g., chronic kidney disease, hepatic encephalopathy, cardiovascular ailments, respiratory dysfunctions, etc.). Identifying microbiome signatures which can be indicative of different health conditions is an active area of research. An understanding of Gut-Liver axis and interactions with distal organs can further help in

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identifying probiotic and fecal transplant strategies as preventive therapeutic regimes for liver ailments. Although certain studies have indicated potential use of probiotics as a therapy for chronic liver diseases, long-term impacts as well as effects on host-microbiome balance have yet to be elucidated (Supplementary Table 1). Clinical trials with standardized dosage of probiotics and extended duration of administration along with regular follow-ups are necessary to confirm the efficacy of the probiotics in manipulating the Gut–Liver axis as well as understanding their impacts on other organs like brain, kidney, lung and heart.

ORIGINAL ARTICLE

JVH WILEY

Mortality and morbidity related to hepatitis C virus infection in hospitalized adults—A propensity score matched analysis

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Abstract

The World Health Organization (WHO) aims to reduce HCV mortality, but estimates are difficult to obtain. We aimed to identify electronic health records of individuals with HCV infection, and assess mortality and morbidity. We applied electronic phenotyping strategies on routinely collected data from patients hospitalized at a tertiary referral hospital in Switzerland between 2009 and 2017. Individuals with HCV infection were identified using International Classification of Disease (ICD)-10 codes, prescribed medications and laboratory results (antibody, PCR, antigen or genotype test). Controls were selected using propensity score methods (matching by age, sex, intravenous drug use, alcohol abuse and HIV co-infection). Main outcomes were in-hospital mortality and attributable mortality (in HCV cases and study population). The non-matched dataset included records from 165,972 individuals (287,255 hospital stays). Electronic phenotyping identified 2285 stays with evidence of HCV infection (1677 individuals). Propensity score matching yielded 6855 stays (2285 with HCV, 4570 controls). In-hospital mortality was higher in HCV cases (RR 2.10, 95%CI 1.64 to 2.70). Among those infected, 52.5% of the deaths were attributable to HCV (95%CI 38.9 to 63.1). When cases were matched, the fraction of deaths attributable to HCV was 26.9% (HCV prevalence: 33%), whilst in the non-matched dataset, it was 0.92% (HCV prevalence: 0.8%). In this study, HCV infection was strongly associated with increased mortality. Our methodology may be used to monitor the efforts towards meeting the WHO elimination targets and underline the importance of electronic cohorts as a basis for national longitudinal surveillance.

THE END