

**REVIEW**

# Watch out for the Saurkraut: *Weissella confusa* endocarditis in a liver transplant candidate

Karn Wijarnpreecha  | Robert J. Fontana

Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, Michigan, USA

**Correspondence**

Robert J. Fontana, Division of Gastroenterology and Hepatology, University of Michigan, 3912 Taubman Center, 1500 E. Medical Center Dr., SPC 5362, Ann Arbor, MI 48109-5362, USA.

Email: [rfontana@med.umich.edu](mailto:rfontana@med.umich.edu)**CASE REPORT**

A 65-year-old Caucasian male with alcohol associated cirrhosis, Child-Pugh Classification C, a MELD-sodium score of 18, and currently undergoing liver transplant evaluation, presented to the hospital with confusion, weakness, and weight loss. He reported a gallbladder stent placement 19 months ago for chronic cholecystitis, endoscopic resection of an ampullary adenoma 10 months ago, and a transjugular intrahepatic porto-systemic shunt (TIPS) placement for refractory ascites 17 months ago. His initial temperature was 36.6 Celsius, blood pressure 109/65 mmHg, respiratory rate 16 per minute, and regular heart rate of 60 beat per minute. Initial physical exam showed systolic murmur grade 3, abdominal exam with slightly distended abdomen, alert and oriented to person but not place or time, and presence of asterixis. He denied a history of recreational drug use, smoking, or recent alcohol intake. His home medications included furosemide 20 mg daily, spironolactone 25 mg daily, rifaximin 550 mg twice daily, lactulose 30 gram twice daily, zinc sulfate 50 mg twice daily, ursodiol 300 mg twice daily, and ropinirole 0.25 mg at bedtime.

Pertinent admission laboratory findings included a white blood cell count (WBC) of 13.3k/ml with a left shift and stable liver biochemistries with aspartate aminotransferase 40 U/L, alanine aminotransferase 17 U/L, alkaline phosphatase 133 U/L, total bilirubin 1.4 mg/dl, albumin 2.0 g/dl, sodium 132 mmol/L, platelet 133K/ $\mu$ l, and international normalized ratio (INR) 1.4 (calculated MELD score 14). He had a negative chest x-ray and urinalysis (Table 1) but blood cultures grew gram-positive rods in less than 24 hours that were speciated as *Weissella confusa*. Vancomycin was started following

the blood culture results. However, repeat blood cultures the following day showed persistent *Weissella confusa* bacteremia. On further questioning, he reported eating sauerkraut on a weekly basis for several years but had no unusual new food exposures, sick contacts, or recent travel. An infectious disease consultant recommended to switch from vancomycin to ampicillin 2 gram every 6 hours. Repeat blood cultures on day 4, 6, and 7 were negative. A transthoracic echocardiography (TTE) showed evidence of thickened aortic and mitral valve likely degenerative calcification. A transesophageal echocardiography (TEE) was recommended with the suspicion of infective endocarditis (IE) from the association between *Weissella confusa* bacteremia and IE per previous literature. In comparison of TEE versus TTE, TEE has higher sensitivity to detect IE in those with prolonged bacteremia, unknown source of bacteremia, persistent fever, and pre-existing valvular disease.<sup>1,2</sup> Because of the need for TEE, the gastroenterology team was consulted for upper endoscopy to screen for esophageal varices prior to the TEE. After discussion with the cardiology team, the TEE was completed without the need for a preoperative upper endoscopy. The TEE demonstrated new moderate aortic regurgitation, a thickened aortic valve consistent with aortic stenosis, but no obvious mobile vegetation. However, a multidisciplinary team conference recommended to proceed with a positron emission tomography to look for disseminated disease since positive findings would strongly support the diagnosis.<sup>3</sup> Interestingly, the positron emission tomography scan showed a metabolically active focus adjacent to the aortic valve consistent with IE but no extracardiac foci indicative of dissemination.

The patient was treated with penicillin V 4 million units every 4 hours for 2 weeks followed by oral

amoxicillin-clavulanate 875mg every 12 hours for 4 more weeks. The infectious disease consultant recommended to switch from ampicillin to penicillin given the successful treatment with penicillin V reported in the literature.<sup>4</sup> However, 1 week later, he was readmitted with hemorrhagic shock due to a 2cm bleeding duodenal ulcer that was treated with endoscopic therapy. A repeat echocardiogram at day 48 showed thickened aortic valve and mild to moderate aortic insufficiency consistent with healed endocarditis. The patient completed a 6-week course of antibiotics and remains asymptomatic 4 months later with a MELD-Na score of 13.

Cardiac surgery was not recommended for the patient given high risk of mortality in cardiac surgery procedure in the setting of Child Pugh Classification C combined with renal impairment.<sup>5</sup> Furthermore the clearance of bacteria from blood culture, healing of aortic valve demonstrated from TTE, and clinical course improving suggested that surgery was not needed. Unfortunately, the patient was readmitted on day 147 with confusion from *Gemella sanguinis* bacteremia and found to have a multifocal stroke from septic emboli from MRI brain. TEE showed mitral and aortic valve endocarditis with severe destruction but no abscesses. He was started on vancomycin and penicillin G for the treatment of recurrent IE. Although the patient had a surgical indication for valve replacement surgery with progressive heart failure and valve destruction, he was deemed not to be a good cardiac surgical candidate due to underlying liver disease severity, and he passed away from severe sepsis secondary to endocarditis on day 157.

## DISCUSSION

Patients with cirrhosis are at increased risk of bacterial infections due their impaired host immune function and reduced integrity of the gut mucosal barrier in the setting of portal hypertension and enteric dysbiosis. IE is a serious infection with high morbidity and mortality in patients with cirrhosis.<sup>6</sup> Currently, information regarding the incidence, etiologies, and outcomes with IE in liver transplant (LT) candidates remains limited. In addition, there is no specific recommendation for the type or duration of antibiotic therapy for IE in patients with decompensated cirrhosis awaiting LT. Herein, we report a patient with decompensated alcohol associated cirrhosis who presented with acute IE from a rare organism, *Weissella confusa*, presumably acquired from ingestion of fermented sauerkraut.

Patients with cirrhosis have significantly greater morbidity and mortality with IE compared to patients without cirrhosis.<sup>7</sup> In case series of consecutive IE cases, the proportion of patients with cirrhosis ranges from 5 to 17 percent. The aortic valve was the most

commonly infected site, followed by the mitral valve in cirrhotic patients. A study from Taiwan reported a higher risk of IE in patients with cirrhosis (0.30%) compared to general population (0.17%) with odds ratio (OR) 2.04  $p < 0.0001$ .<sup>8</sup> The causal microorganisms of IE in cirrhosis tend to be more gram-positive bacteria (74%–100%), predominantly *Staphylococcus aureus* (26%–80%) (general population 23%–27%), less Streptococci (10%–39%) (general population 32%–58%), and rare gram negative bacilli (3%–5%), or fungi (0%–3%). Nosocomial infection was estimated to arise in 45% of cirrhosis patients versus 17% in non-cirrhosis patients.<sup>7</sup> Previous studies reported that some IE can occur after procedures such as TIPS, upper endoscopy, or liver biopsy. Potential sources of infections are from oral, gut, urogenital, and skin sites.

Although prior guidelines in 2013 consider esophageal varices a relative contraindication to pursue TEE, the evidence to support this recommendation are limited.<sup>9</sup> The most recent retrospective multicenter analysis investigated the risk of overt gastrointestinal bleeding (primary outcome), likelihood of 2g/dl decline in hemoglobin or the need of blood transfusion within 48 hours after TEE (secondary outcome) among patients with cirrhosis with and without esophageal varices documented by upper endoscopy.<sup>10</sup> Interestingly, there was no overt bleeding in the study of 191 cirrhotic patients (79 (41.4%) had esophageal varices (30.4% large varices) and no significant difference in likelihood of decline in hemoglobin or blood transfusion requirement between cirrhosis with and without varices after controlling for confounders.<sup>10</sup> Moreover, the risk of secondary outcome was similar between patients who had upper endoscopy before (27.5%) versus after TEE (26.7%,  $p = 1.00$ ).<sup>10</sup> The finding is supported by the recent systematic review and meta-analysis that showed that the incidence of post-TEE bleeding in patient with varices was low (0.84%, 95% confidence interval [CI] 0.34%–1.56%) and the bleeding risk was comparable between patients with and those without varices (risk difference, 0.26%; 95% CI, –0.80% to 1.32%;  $I^2 = 0\%$ ;  $p = 0.88$ ).<sup>11</sup> Based on the current findings, the presence or suspicion of esophageal varices should not delay urgent TEE and does not warrant upper endoscopy before procedure.<sup>12</sup>

To date, there is no specific treatment recommendation regarding the preferred antibiotic or duration for IE treatment in cirrhosis, particularly in LT candidates. A systematic review reported that aminoglycosides, vancomycin, and cephalosporins were the antimicrobials most frequently used for treatment of IE in cirrhosis.<sup>13</sup> A previous study reported no difference in duration of treatment for IE in cirrhosis (mean  $40 \pm 28$  days) versus no cirrhosis (mean  $42 \pm 22$  days).<sup>14</sup> However, it should be noted that previous studies demonstrated an approximately six-fold increased risk of death from IE in cirrhosis compared to non-cirrhotic control patients.<sup>7</sup> Cardiothoracic surgery

**TABLE 1** Timeline of events in 65-year old liver transplant candidate with *Weissella confusa* endocarditis

Day 1	Presented with altered mental status, weakness, fatigue with 20 pounds weight loss  Temperature 36.6 Celsius; Physical exam – asterixis, slightly distended abdomen, systolic murmur  <i>Key Labs:</i> White blood cells 13,400/ $\mu$ l (H) with neutrophil (75.2%) (high) Hemoglobin 10.1 g/dl Creatinine 1.24 mg/dl Aspartate transaminase 43 IU/L (H) Alanine aminotransferase 18 IU/L Alkaline phosphatase 138 IU/L (H) Total bilirubin 1.4 mg/dL (H) MELD sodium score = 18 MELD score = 14 Child-Pugh Classification C Liver ultrasound showed an unremarkable gallbladder with no ascites
Day 2	Blood culture x 2 positive for <i>Weissella confusa</i>  Started IV vancomycin
Day 3	Repeat blood culture positive for <i>Weissella confusa</i>  Switched IV vancomycin to IV ampicillin
Day 4	Repeat blood culture negative.  Switched ampicillin to penicillin for 2 weeks due to suspected endocarditis  Transthoracic echocardiogram – thickened aortic and mitral valve
Day 6	Transesophageal echocardiogram showed new thickened aortic valve stenosis with moderate aortic regurgitation.  PET showed minimally elevated FDG activity adjacent to the aortic valve favored to be adjacent myocardial activity. No focal hyperintense uptake at TIPS or gallbladder region.  Repeat blood culture negative on day 8
Day 16	Hospitalized with hemorrhagic shock due to duodenal bleeding.  Endoscopy showed a 2 cm flat based ulcer in the second part of the duodenum.
Day 19	Switched to oral amoxicillin-clavulanate for 4 weeks per infectious disease team
Day 46	Completed 6 weeks of antibiotic treatment
Day 48	Hospitalized with abdominal pain and leukocytosis presumably from a splenic infarct seen on CT abdomen.  Repeat echocardiogram showed thickened aortic valve (healed endocarditis) and mild to moderate aortic insufficiency  Patient discharged next day without antibiotics

**TABLE 1** (Continued)

Day 147	Hospitalized with <i>Gemella sanguinis</i> bacteremia complicated by aortic and mitral valve endocarditis with valvular destruction, and multifocal stroke from septic emboli  Started on penicillin G and vancomycin  Patient deemed not to be a cardiac surgical candidate due to underlying liver condition
Day 157	Death

Abbreviation: MELD; Model For End-Stage Liver Disease, PET; positron emission tomography, FDG; fluorodeoxyglucose, CT; computed tomography.

was also offered less frequently in cirrhosis patients due to the high risk and mortality in decompensated cirrhosis. A recent multicenter study reported that Child-Pugh Class B/C was associated with significant increase in mortality with adjusted hazard ratio of 3.1 (95% CI 1.47–6.56,  $p = 0.003$ ) and renal impairment with adjusted hazard ratio of 1.10 (95% CI 1.03–1.17,  $p = 0.005$ ).<sup>5</sup> In general, the mortality of patients with cirrhosis undergoing cardiothoracic surgery increased with the severity of liver dysfunction with MELD score  $\geq 13.5$  or CTP score  $> 7$  is considered contraindication.<sup>15–17</sup> Nonetheless, clinical cure of IE was reported in 68.2% of cirrhosis patients with an overall mortality of 41.4%.

*Weissella confusa*, is a gram-positive commensal coccobacillus that can be isolated from the gut and skin of both children and adults. This organism is a lactic acid fermenter and previously classified as member of *Leuconostoc* and *Lactobacillus* genera. Among the 19 recognized species of *Weissella*, *Weissella confusa* is the most frequently associated with human infection. It has also been used as a key ingredient in fermented food products due to its ability to ferment lactose to lactic acid. Previous literature reported clinical manifestations of *Weissella confusa* infection ranging from soft tissue infection to severe sepsis, osteomyelitis, meningitis, and rare instances of IE. Our review of the published literature found only three cases reports<sup>4,18,19</sup> of IE from *Weissella confusa* (Table 2). The first case was a 49-year-old male with chronic alcohol use who presented with rash, weakness, and 100-pound weight loss in 6 months period, and found to have mitral valve endocarditis with blood culture positive for *Weissella confusa*.<sup>18</sup> However, the patient declined the treatment and died 4 days after being discharged. The source of his infection was suspected to be from dental caries. Interestingly, another case was reported in a patient from Ghana where *Weissella confusa* is commonly used in fermenting food. In the current case, it is speculated that the patient contracted *Weissella confusa* bacteremia from chronic consumption of fermented sauerkraut in the setting of a denuded duodenal mucosa due to the endoscopic mucosal resection (EMR) procedure he had previously undergone for his ampullary adenoma. Bacterial translocation is a well-known phenomenon in patients with cirrhosis and portal hypertension, and

**TABLE 2** *Weissella confusa* endocarditis reported in the literature and the current case

Author (year)	Age/Sex	Presentation	Medical history	Antibiotic (days)	Outcome
Flaherty et al. (2003)	49/Male	Weight loss, fatigue, poor nutrition and dentition	Alcohol use disorder	Patient declined	Died 4 days after discharge
Shin et al. (2007)	65/Male	Incidental finding of vegetation from echocardiogram from regular check up	Aortic insufficiency	Penicillin (28) Gentamicin (35) Cefoperazone (28) (total 5 weeks)	Survived at 1 year follow up
Hurt et al. (2021)	63/Male	Chest tightness, palpitation, chronic consumption of fermented food from Ghana	Congenital bicuspid aortic valve, diabetes, hypertension, dyslipidemia	Amoxicillin (28) Gentamicin (17) (total 4 weeks)	Aortic valve replacement (day 36) Survived on day 62 and discharged
Wijarnpreecha et al. (2022)	65/Male	Weight loss, confusion, weakness, chronic consumption of fermented food	Alcohol cirrhosis, chronic cholecystitis, ampullary adenoma	Penicillin (14) Amoxicillin-clavulanate (28) (total 6 weeks)	Died 157 days after initial presentation

we presume that the saurkraut he chronically ingested likely had some residual *Weissella confusa* organisms present. Previous study demonstrated that lactic acid bacteria are the dominant microorganisms in the final fermented saurkraut product, which is considered to act as probiotics to promote human health and microbial stability.<sup>20</sup> To date, no previous literature ever reported saurkraut ingestion with development of IE.

In summary, *Weissella confusa* endocarditis in cirrhosis can be severe or even fatal if delayed diagnosis or left untreated. The temporal relationship between fermented food consumption and *Weissella confusa* endocarditis is difficult to establish from published case series. Nonetheless, we recommend avoiding consumption of fermented food in those who had *Weissella confusa* endocarditis to minimize the risk of recurrent infection. Finally, transplantation providers should be aware of the high mortality and morbidity of IE in cirrhosis, particularly those with undergoing LT evaluation. TTE is insensitive to detect native valve IE compared with TEE. Urgent TEE for investigation of IE in patients with decompensated cirrhosis should not be delayed. The current evidence does not support the need for upper endoscopy prior to TEE to screen for varices.

## KEY POINTS

- Patients with cirrhosis and IE have a higher morbidity and mortality than those without cirrhosis.
- TEE should not be delayed for investigation of valvular vegetation and routine upper endoscopy screening for varices prior to TEE is not supported by the current evidence nor the American society of Echocardiography guidelines.
- Risk of mortality from cardiac surgery is prohibitively high among cirrhosis with Child Pugh score >7 or MELD score ≥ 13.5.
- The optimal type and duration of antibiotics in liver transplant candidates with IE and time prior to listing are not established.

What is your recommendation regarding the need for upper endoscopy for variceal screening prior to the TEE?

- Proceed with TEE without the need of upper endoscopy
- Perform upper endoscopy before TEE given the risk of variceal bleeding is high in decompensated cirrhosis and delay TEE for few weeks after variceal banding if banding indicated
- Perform upper endoscopy to check for varices but will not delay TEE given the urgent need to investigate for IE

**Answer: A.** The recent meta-analysis showed that the incidence of post-TEE bleeding in patient with

varices was low (0.84%, 95% CI 0.34%–1.56%) and the bleeding risk was comparable between patients with and those without varices.<sup>11</sup> Based on the current evidence, the presence or suspicion of esophageal varices should not delay urgent TEE and does not warrant upper endoscopy before procedure.

How do clinical outcomes and treatment options differ in patients with and without cirrhosis who have IE?

- Patient with cirrhosis have similar mortality rate but higher risk of recurrent IE after treatment when compared with those without cirrhosis
- Patient with cirrhosis have similar mortality rate but higher risk of renal impairment and prolonged hospitalization when compared with those without cirrhosis
- Patient with cirrhosis had higher mortality rate with higher risk of renal impairment when compared with those without cirrhosis
- Patient with cirrhosis have higher mortality rate but lower risk of renal impairment when compared with those without cirrhosis

**Answer: C.** A previous study clearly demonstrated that patients with cirrhosis and IE had higher mortality (OR 4.95, 95%CI 1.89–12.91), with higher risk of renal impairment (OR 8.23, 95%CI 3.06–22.2) when compared with those with IE without cirrhosis.<sup>7</sup>

Should valvular replacement surgery be performed in addition to antibiotic treatment for IE in patients such as this case with decompensated cirrhosis?

- The patient should undergo valvular replacement due to high risk of recurrent IE.
- The patient should undergo valvular surgery due to the need of valvular replacement before LT
- The patient should not undergo valvular replacement due to high risk of morbidity and mortality in valvular replacement surgery given his Child Pugh Class C status.

**Answer: C.** In general, the mortality of patients with cirrhosis undergoing cardiothoracic surgery increased with the severity of liver dysfunction with MELD score  $\geq 13.5$  or CTP score  $> 7$  is considered contraindication.<sup>15–17</sup> The patient has MELD score of 14 and CTP score of 10 (total bilirubin 1.4 mg/dl (1 point), albumin 2.0 g/dl (3 points), INR 1.4 (1 point), Slight ascites/distended abdomen/History of refractory ascites with TIPS (2 points), Grade 3–4 encephalopathy (3 points)).

## FUNDING INFORMATION

Karn Wijarnpreecha receives funding from the AASLD Advanced/Transplant Hepatology Award. Robert J. Fontana received grants from Gilead and Abbvie.

## CONFLICTS OF INTEREST

We do not have any financial or non-financial conflicts of interest. Case studies such as ours defined as “experiences or observations associated with one or two individuals” are exempt from institutional review board approval at the University of Michigan.

## ORCID

Karn Wijarnpreecha  <https://orcid.org/0000-0002-6232-6343>

## REFERENCES

- Reynolds HR, Jagen MA, Tunick PA, Kronzon I. Sensitivity of transthoracic versus transesophageal echocardiography for the detection of native valve vegetations in the modern era. *J Am Soc Echocardiogr.* 2003;16(1):67–70.
- Sekar P, Johnson JR, Thurn JR, Drekonja DM, Morrison VA, Chandrashekhar Y, et al. Comparative sensitivity of transthoracic and transesophageal echocardiography in diagnosis of infective endocarditis among veterans with staphylococcus aureus bacteremia. *Open Forum Infect Dis.* 2017;4(2):ofx035.
- Ten Hove D, Slart R, Sinha B, Glaudemans A, Budde RPJ. (18)F-FDG PET/CT in infective endocarditis: indications and approaches for standardization. *Curr Cardiol Rep.* 2021;23(9):130.
- Shin JH, Kim DI, Kim HR, Kim DS, Kook JK, Lee JN. Severe infective endocarditis of native valves caused by *Weissella confusa* detected incidentally on echocardiography. *J Infect.* 2007;54(3):e149–51.
- Tirado-Conte G, Rodes-Cabau J, Rodriguez-Olivares R, Barbanti M, Lhermusier T, Amat-Santos I, et al. Clinical outcomes and prognosis markers of patients with liver disease undergoing transcatheter aortic valve replacement: a propensity score-matched analysis. *Circ Cardiovasc Interv.* 2018;11(3):e005727.
- Shah ASV, McAllister DA, Gallacher P, Astengo F, Rodriguez Perez JA, Hall J, et al. Incidence, microbiology, and outcomes in patients hospitalized with infective endocarditis. *Circulation.* 2020;141(25):2067–77.
- Fernandez Guerrero ML, Gonzalez Lopez J, Gorgolas M. Infectious endocarditis in patients with cirrhosis of the liver: a model of infection in the frail patient. *Euro J Clin Microbiol Infect Dis.* 2010;29(10):1271–5.
- Hung TH, Hsieh YH, Tseng KC, Tsai CC, Tsai CC. The risk for bacterial endocarditis in cirrhotic patients: a population-based 3-year follow-up study. *Int J Infect Dis.* 2013;17(6):e391–3.
- Hahn RT, Abraham T, Adams MS, Bruce CJ, Glas KE, Lang RM, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. *J Am Soc Echocardiogr.* 2013;26(9):921–64.
- Sack JS, Li M, Zucker SD. Bleeding outcomes following transesophageal echocardiography in patients with cirrhosis and esophageal varices. *Hepatol Commun.* 2021;5(2):283–92.
- Hui RW, Leung CM. Incidence of gastrointestinal bleeding after transesophageal echocardiography in patients with gastroesophageal varices: a systematic review and meta-analysis. *J Am Soc Echocardiogr.* 2022;35(4):387–94.
- Sack JS, Zucker SD. Safety of transesophageal echocardiogram in patients with cirrhosis and esophageal varices. *J Am Soc Echocardiogr.* 2022;35(4):444–5.
- Ioannou P, Savva E, Kofteridis DP. Infective endocarditis in patients with liver cirrhosis: a systematic review. *J Chemother.* 2021;33(7):443–51.

14. Allaire M, Ollivier-Hourmand I, Garrioud A, Dao T, Cadranel J. Infectious endocarditis in patients with cirrhosis: epidemiology, characteristics and outcome. *JSM Gastroenterol Hepatol*. 2017;5(1):1077.
15. Northup PG, Friedman LS, Kamath PS. AGA clinical practice update on surgical risk assessment and perioperative management in cirrhosis: expert review. *Clin Gastroenterol Hepatol*. 2019;17(4):595–606.
16. Thielmann M, Mechmet A, Neuhauser M, Wendt D, Tossios P, Canbay A, et al. Risk prediction and outcomes in patients with liver cirrhosis undergoing open-heart surgery. *Euro J Cardiothoracic Surg*. 2010;38(5):592–9.
17. Suman A, Barnes DS, Zein NN, Levinthal GN, Connor JT, Carey WD. Predicting outcome after cardiac surgery in patients with cirrhosis: a comparison of Child-Pugh and MELD scores. *Clin Gastroenterol Hepatol*. 2004;2(8):719–23.
18. Flaherty JD, Levett PN, Dewhirst FE, Troe TE, Warren JR, Johnson S. Fatal case of endocarditis due to *Weissella confusa*. *J Clin Microbiol*. 2003;41(5):2237–9.
19. Hurt W, Savarimuthu S, Mughal N, Moore L. A rare case of *Weissella confusa* endocarditis. *Clin Infect Practice*. 2021;12:100078.
20. Zabat MA, Sano WH, Wurster JI, Cabral DJ, Belenky P. Microbial community analysis of sauerkraut fermentation reveals a stable and rapidly established community. *Foods*. 2018;7(5):77.

**How to cite this article:** Wijarnpreecha K & Fontana RJ. Watch out for the Saurkraut: *Weissella confusa* endocarditis in a liver transplant candidate. *Clinical Liver Disease*. 2022;20:188–193. <https://doi.org/10.1002/cld.1256>