



Publication List LiMAx[®] Test

Last update September 2024

Selected publications on the LiMAx[®] test, compiled by Humedics GmbH
The list does not contain all available publications, other publications are available on request

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Liver Surgery – Conventional

1. Stockmann M., Lock J. F., Vondran F. W. R., Seehofer D.
[Comparison of the LiMAX test vs. the APRI+ALBI score – Incorrect comparison parameters lead to questionable results](#)
Eur J Surg Oncol. 2024 Sep 17;50(12):108697. doi: 10.1016/j.ejso.2024.108697.
We read with great interest the recent article of Santol et al. comparing the LiMAX test with APRI + ALBI score in a multicenter retrospective analysis. We appreciate the validation of an easily available and inexpensive score for preoperative risk-assessment in liver surgery. However, the static LiMAX cut-off for a normal liver function (<315 µg/kg/h) is the wrong comparison parameter for an otherwise statistically correct analysis. Therefore, the drawn conclusions are misleading so far, and they have to be supported with additional data.
2. Santol J., Ammann M., Reese T., et al.
[Comparison of the LiMAX test vs. the APRI+ALBI score for clinical utility in preoperative risk assessment in patients undergoing liver surgery – A European multicenter study](#)
Eur J Surg Oncol. 2024 Apr;50(4):108048. doi: 10.1016/j.ejso.2024.108048.
APRI+ALBI outperformed LiMAX measurement in the preop prediction of PHLF B+C and postoperative mortality, at a fraction of the costs, manual labor and invasiveness.
3. Primavesi F., Maglione M., Cipriani F., et al.
[E-AHPBA-ESSO-ESSR Innsbruck consensus guidelines for preoperative liver function assessment before hepatectomy](#)
Br J Surg. 2023 Sep 6;110(10):1331-1347. doi: 10.1093/bjs/znad233.
Volumetry of the future liver remnant represents the foundation for assessment, and can be combined with indocyanine green clearance or LiMAX® according to local expertise and availability.
4. Anger F, Klein I, Löb S, Wiegering A, Singh G, Sperl D, Götze O, Geier A, Lock JF
[Preoperative Liver Function Guiding HCC Resection in Normal and Cirrhotic Liver](#)
Visc Med 2021;37:94-101. doi: 10.1159/000508172
Preoperative determination of liver function by the LiMAX test enables effective and safe patient selection for HCC resection in both cirrhotic and noncirrhotic liver.
5. Bluethner E, Jara M, Shresta R, et al.
[Future liver remnant function as a predictor of postoperative morbidity following liver resection for hepatocellular carcinoma – A risk factor analysis](#)
Surgical Oncology, Volume 33, June 2020, Pages 257-265 doi: 10.1016/j.suronc.2020.02.004
Future remnant liver function is a major predictor of postoperative ascites, haemorrhage, and wound healing disorders in cirrhotic and non-cirrhotic patients whereas future remnant liver volume failed to show significant correlations. Preoperative calculation of future remnant

liver function may augment surgical decision-making in high-risk patients and thereby improve perioperative outcome.

6. Blüthner E, Pape UF, Stockmann

[Assessing Non-Invasive Liver Function in Patients with Intestinal Failure Receiving Total Parenteral Nutrition—Results from the Prospective PNLiver Trial](#)

Nutrients **2020** Apr 26;12(5):E1217. doi: 10.3390/nu12051217

The aim of this longitudinal study is to evaluate the ability of non-invasive liver function tests to assess liver function following the initiation of PN. Our results suggest that the liver function over time is primarily determined by the degree of intestinal failure. Furthermore, the LiMAx test appeared more sensitive in detecting early changes in liver function in comparison to other liver function tests.

7. Bluethner E, Bednarsch J, Malinowski M, et al.

[Dynamic liver function is an independent predictor of recurrence-free survival after curative liver resection for HCC - A retrospective cohort study](#)

Int J Surg. **2019** Sep 5. pii: S1743-9191(19)30225-0. doi: 10.1016/j.ijisu.2019.08.033

This study shows that preoperative dynamic liver function assessed by LiMAx test as well as severity of underlying liver disease have a significant impact on recurrence-free survival after curative hepatectomy. Patients presenting with impaired liver function should be evaluated for other treatment e.g. liver transplantation or receive closer oncological follow-up.

8. Heise D, Neumann UP

[Commentary on: "Dynamic liver function is an independent predictor of recurrence-free survival after curative liver resection for HCC - a retrospective cohort study"](#)

Int J Surg. **2019** Nov;71:82-83. doi: 10.1016/j.ijisu.2019.09.022. Epub 2019 Sep 24

In conclusion, combining pathological characteristics, clinical data and tests to estimate the degree of the underlying liver dysfunction should be in the focus of research on the risk of recurrence after curative-intent surgery for HCC. Of note, Bluethner et al. have shown results of a novel liver function test which might be transferable into clinical practice.

9. Takaoka M

[Commentary on: "Dynamic liver function is an independent predictor of recurrence-free survival after curative liver resection for HCC - a retrospective cohort study"](#)

Int J Surg. **2019** Nov;71:168. doi: 10.1016/j.ijisu.2019.09.027. Epub 2019 Sep 28

Although a retrospective study like the current one is prone to limitations and should be repeated prospectively, it clearly shows that an evaluation of liver function by the LiMAx method may have an impact on the recurrence free time after curative hepatectomy. LiMAx therefore has the potential to become an effective preoperative liver functional evaluation.

10. Wuensch T, Heucke N, Wizenty J, et al.

[Hepatic CYP1A2 activity in liver tumors and the implications for preoperative volume-function analysis](#)

Am J Physiol Gastrointest Liver Physiol. **2019** May 1;316(5): G608-G614. doi: 10.1152/ajpgi.00335.2018

The study aims to assess the remaining CYP1A2 activities in different hepatic tumor lesions and its consequences for the preoperative volume-function analysis in patients undergoing liver surgery. Hepatocellular adenomas but not hepatocellular carcinomas or colorectal liver metastasis contain significant residual CYP1A2 activity. These findings are important for an improved preoperative volume-function analysis and an accurate surgical risk assessment in hepatocellular adenoma cases.

11. Stockmann M, Bednarsch J, Malinowski M, et al.

[Functional considerations in ALPPS - consequences for clinical management](#)

HPB. **2017** Nov;19(11):1016-1025. doi: 10.1016/j.hpb.2017.07.010. Epub 2017 Aug 23

Since perioperative morbidity and mortality in ALPPS are extraordinarily high, a deeper understanding of actual liver function during the procedure is essential. The study provides evidence that liver function capacity is significantly impaired due to ALPPS step I. The data also shows that the portal ligated liver lobe still continues to contribute significantly to overall liver function. Therefore, future liver remnant function measured by the LiMAx test after step II is still predictable by volume/function analysis.

12. Cammann S, Oldhafer F, Ringe KI, et al.

[Use of the liver maximum function capacity test \(LiMAx\) for the management of liver resection in cirrhosis - A case of hypopharyngeal cancer liver metastasis](#)

Int J Surg Case Rep. **2017**; 39:140-144. doi: 10.1016/j.ijscr.2017.08.003. Epub 2017 Aug 10

The LiMAx-test enables determination of liver function at a so far unavailable level (metabolism via cytochrome P450 1A2) and hence might provide crucial additional diagnostic information to allow for safe liver resection even in cirrhotic patients.

13. Bednarsch J, Blüthner E, Malinowski M, et al.

[Regeneration of liver function capacity after partial liver resection is impaired in case of postoperative bile leakage](#)

World J Surg. **2016** Sep;40(9):2221-8. doi: 10.1007/s00268-016-3524-z

Liver regeneration after partial liver resection is impaired by postoperative bile leakage. However, a nearly normal recovery is possible if the bile leak is diagnosed early and immediately treated. LiMAx was the only parameter to assess differing liver regeneration continuously.

14. Oldhafer F, Ringe KI, Timrott K, et al.

[Monitoring of liver function in a 73-year old patient undergoing 'Associating Liver Partition and Portal vein ligation for Staged hepatectomy': case report applying the novel liver maximum function capacity test](#)

Patient Saf Surg. **2016** Jun 10;10:16. doi: 10.1186/s13037-016-0104-y. eCollection 2016

Case report describing the use of LiMAX for two-stage liver resection (ALPPS). LiMAX can be applied to monitor the liver function postoperatively and hence could be a useful tool for decision-making regarding the timing of the second stage of ALPPS.

15. Jara M, Bednarsch J, Lock JF, Malinowski M, et al.

[Enhancing safety in liver surgery using a new diagnostic tool for evaluation of actual liver function capacity - The LiMAX test](#)

Dtsch Med Wochenschr. **2014** Feb;139(8):387-91. doi: 10.1055/s-0033-1360061. Epub 2014 Feb 11

Article in German language: A review describing the LiMAX test methodology, volumetric resection planning, and a therapy algorithm based on LiMAX values.

16. Müller SA, Tarantino I, Corazza M, et al.

[A rapid and accurate new bedside test to assess maximal liver function: a case report](#)

Patient Saf Surg. **2013** Apr 25;7:11. doi: 10.1186/1754-9493-7-11. eCollection 2013

In the presented patient, residual liver function was accurately predicted preoperatively using a combination of the LiMAX test with CT-volumetry. This test may significantly improve preoperative evaluation and postoperative outcomes in liver surgery.

17. Lock JF, Malinowski M, Seehofer D, Hoppe S, et al.

[Function and volume recovery after partial hepatectomy: influence of preoperative liver function, residual liver volume, and obesity](#)

Langenbecks Arch Surg. **2012** Dec;397(8):1297-304. doi: 10.1007/s00423-012-0972-2

Partial hepatectomy leads to fast and complete functional recovery, while volume recovery is delayed and remains often incomplete. Functional recovery is mainly influenced by preoperative liver function, residual liver volume, and by obesity.

18. Stockmann M, Lock JF, Malinowski M, et al.

[The LiMAX test: a new liver function test for predicting postoperative outcome in liver surgery](#)

HPB. (Oxford) **2010** Mar;12(2):139-46. doi: 10.1111/j.1477-2574.2009.00151.x

The LiMAX test can validly determine liver function capacity and is feasible in every clinical situation. Combination with virtual resection enables calculation of the residual liver function. The LiMAX decision tree algorithm for hepatectomy may significantly improve preoperative evaluation and postoperative outcome in liver surgery.

19. Stockmann M, Lock JF, Riecke B, et al.

[Prediction of postoperative outcome after hepatectomy with a new bedside test for maximal liver function capacity](#)

Ann Surg. **2009** Jul;250(1):119-25. doi: 10.1097/SLA.0b013e3181ad85b5

Residual liver function is the major factor influencing the outcome of patients after hepatectomy and can be predicted preoperatively by a combination of LiMAX and CT volumetry.

Liver surgery – Laparoscopic

20. Rahimli M, Perrakis A, Gumbs A A, Andric M, Al-Madhi S, Arend J, Croner R S

[The LiMAX Test as Selection Criteria in Minimally Invasive Liver Surgery](#)

J. Clin. Med. **2022**, 11(11), 3018; <https://doi.org/10.3390/jcm11113018>

The LiMAX test is a helpful and reliable tool to precisely determine the liver function capacity. It aids in accurate patient selection for major or minor liver resections in minimally invasive liver surgery, which consequently serves to improve patients' safety. In this way, liver resections can be performed safely, even in patients with reduced liver function, without negatively affecting morbidity, mortality and the resection margin status, which is an important predictive oncological factor.

21. Haber P.K., Wabitsch S., Krenzien F., et al.

[Laparoscopic liver surgery in cirrhosis - Addressing lesions in posterosuperior segments](#)

Surg Oncol. **2019**; 28:140-144. doi: 10.1016/j.suronc.2018.12.001. Epub 2018 Dec 14

Patients with liver cirrhosis and a lesion in the posterosuperior liver segments are amenable to the minimal-invasive approaches as no significant differences can be observed with regard to safety and oncologic sufficiency. The LiMAX test was used to evaluate liver function and perioperative risk prior to surgery.

22. Kaffarnik M, Stoeger G, Liebich J, et al.

[Liver function, quantified by LiMAX test, after major abdominal surgery. Comparison between open and laparoscopic approach](#)

World J Surg. **2018** Feb;42(2):557-566. doi: 10.1007/s00268-017-4170-9

Hepatic dysfunction after major abdominal surgery is evident and underestimated. The LiMAX test provides an adequate tool to determine liver dysfunction. Open and laparoscopic approaches appeared similar in terms of liver dysfunction and postoperative SIRS.

23. Seehofer D, Sucher R, Schmelzle M, et al.

[Evolution of laparoscopic liver surgery as standard procedure for HCC in cirrhosis?](#)

Z Gastroenterol. **2017** May;55(5):453-460

Liver resection for HCC in patients with severely impaired liver function was carried out laparoscopically. No severe complications and especially no decompensation of cirrhosis was observed, as shown by the LiMAX test.

Liver Transplantation

24. Schurink I. J., de Goeij F. H. C., van der Heijden F. J., et al.

[Liver function maximum capacity test during normothermic regional perfusion predicts graft function after transplantation](#)

EPMA J. 2024 Jul 16;15(3):545-558; <https://doi.org/10.1007/s13167-024-00371-7>

This study shows for the first time the feasibility to assess liver function during aNRP in individual donor livers. LiMAx presents an objective tool to predict donor liver function and risk of complications in the recipient, thus enabling individualized matching of donor livers for an individual recipient. The LiMAx test may present a valuable test for the prediction of donor liver function, preventing post-transplant complication, and personalizing the selection of donor livers for individual recipients.

25. Minor T, von Horn C, Zlatev H, Saner F, Grawe M, Lüer B, Huessler E-M, Kuklik N, Paul

[A Controlled oxygenated rewarming as novel end-ischemic therapy for cold stored liver grafts. A randomized controlled trial](#)

Clin Transl Sci. 2022;00:1–10. DOI: 10.1111/cts.13409

Functional liver recovery after transplantation was evaluated by the LiMAx test, performed on the first postoperative day, while the patient was still intubated. Liver function was found to be significantly increased after COR treatment by more than one third of the values obtained in the cold storage group.

26. Raschzok N, Schott E, Reutzel-Selke A, et al.

[The impact of directly acting antivirals on the enzymatic liver function of liver transplant recipients with recurrent hepatitis C](#)

Transpl Infect Dis. 2016 Dec;18(6):896-903. doi: 10.1111/tid.12606. Epub 2016 Nov 1

The new directly acting antivirals enable all-oral interferon-free treatment of chronic hepatitis C virus infection. In this study such antiviral treatment enabled sustained elimination of recurrent hepatitis C in liver transplant recipients and was associated with a significant improvement of the enzymatic liver function as measured by the LiMAx test.

27. Jara M, Malinowski M, Lüttgert K, Schott E, et al.

[Prognostic value of enzymatic liver function for the estimation of short-term survival of liver transplant candidates: a prospective study with the LiMAx test](#)

Transpl Int 2015 Jan;28(1):52-8. doi: 10.1111/tri.12441. Epub 2014 Sep 29

Liver function of chronic liver failure patients without hepatocellular carcinoma was prospectively investigated when they were evaluated for liver transplantation. LiMAx provides good prognostic information of liver transplant candidates, patients who are not at risk of death can be identified reliably by measuring actual enzymatic liver function capacity.

28. Stockmann M, Lock JF, Malinowski M, et al.

[How to define initial poor graft function after liver transplantation? - a new functional definition by the LiMAx test](#)

Transpl Int **2010** Oct;23(10):1023-32. doi: 10.1111/j.1432-2277.2010.01089.x

Initial poor graft function is a frequent complication after liver transplantation, but there is no consensus on its definition. The LiMAx test might provide the first adequate functional parameter to assess and classify liver graft performance from the beginning.

29. Lock JF, Schwabauer E, Martus P, et al.

[Early diagnosis of primary nonfunction and indication for reoperation after liver transplantation](#)

Liver Transpl **2010** Feb;16(2):172-80. doi: 10.1002/lt.21973

Initial graft function is a major factor influencing the clinical outcome after liver transplantation, but a reliable method for assessing and predicting graft dysfunction is not available so far. The LiMAx test might be effective for identifying critical complications that could threaten graft survival within 24 hours after LTX.

Interventional Liver Therapy

30. Senk K., Rio Bartulos C., Wilcke J., et al.

[Peri-interventional LiMAx test for liver ablation - A feasibility study](#)

Clin Hemorheol Microcirc **2023** Aug 25. doi: 10.3233/CH-238107

The LiMAx test may be a valuable tool in liver ablation for both peri-interventional monitoring of liver function and preintervention risk assessment.

31. Fischer J, Wellhöner S, Ebel S, et al.

[The Liver Maximum Capacity Test \(LiMAx\) Is Associated with Short-Term Survival in Patients with Early Stage HCC Undergoing Transarterial Treatment](#)

Cancers **2022**, 14, 5323. <https://doi.org/10.3390/cancers14215323>

The liver maximum capacity test (LiMAx) represents a useful tool to estimate liver function in patients with chronic liver disease. LiMAx results correlate with short-term survival in patients with early stage HCC after transarterial chemo- or radioembolization. Low LiMAx levels might enable the identification of patients with poor hepatic function and decreased short-term survival after treatment.

32. Leyh C, Heucke N, Schotten C, et. Al.

[LiMAx Prior to Radioembolization for Hepatocellular Carcinoma as an Additional Tool for Patient Selection in Patients with Liver Cirrhosis](#)

Cancers **2022**, 14, 4584. <https://doi.org/10.3390/cancers14194584>

Patients with lower LiMAx® values at baseline have a significantly increased risk for hepatic decompensation after RE, despite being categorized as Child–Pugh A. Therefore, LiMAx® can be used as an additional tool to identify patients at high risk of post-interventional hepatic failure.

33. Rashidi-Alavijeh J, Kahraman A, Gerken G, Theysohn JM, Willuweit K, Hoyer DP, Lange CM, Buechter M

[Enzymatic liver function measured by LiMAx is superior to current standard methods in predicting transplant-free survival after TIPS implantation](#)

Scientific Reports (**2021**) 11:13834; doi: 10.1038/s41598-021-93392-5

A total number of 30 patients were included, of whom seven received liver transplantation (N = 2) or died (N = 5) during follow-up. LiMAx values after [...] TIPS implantation and MELD score [...] were significantly associated with transplant-free survival according to univariate logistic regression. In AUROC analysis, LiMAx at day one after TIPS (sensitivity 85.7%, specificity 78.3%, AUROC 0.85, cut-off ≤ 165 $\mu\text{g}/\text{kg}/\text{h}$), LiMAx value at the day before TIPS (sensitivity 100%, specificity 73.9%, AUROC 0.82, cut-off ≤ 205 $\mu\text{g}/\text{kg}/\text{h}$) and MELD score (sensitivity 71.4%, specificity 73.9%, AUROC 0.82, cut-off ≥ 15) had the highest prognostic accuracy. LiMAx values prior and after TIPS procedure seem to be good prognostic parameters regarding prediction of transplant-free survival of patients undergoing TIPS implantation.

34. Reichert MC, Schulz A, Massmann A, et al.

[Predictive Power of Liver Maximum Function Capacity Test in Transjugular Intrahepatic Portosystemic Shunt Patients: A Pilot Study.](#)

Dig Dis. **2019** Oct 16:1-8. doi: 10.1159/000503098

This is a pilot study in patients prior TIPSS placement to investigate whether the risk of liver function associated complications correlates with the functional reserve of the liver, as assessed by liver maximum function capacity (LiMAX) test. In multivariate regression models and AUROC analysis, a drop in LiMAX predicted the development of liver function associated complications after TIPSS placement.

35. Barzakova ES, Schulze-Hagen M, Zimmermann M, et al.

[Monitoring Liver Function of Patients Undergoing Transarterial Chemoembolization \(TACE\) by a ¹³C Breath Test \(LiMAX\)](#)

Cardiovasc Intervent Radiol. **2019** Sep 18. doi: 10.1007/s00270-019-02325-3. [Epub ahead of print]

LiMAX is capable of detecting changes in liver function, even modulations caused by superselective TACE procedures. Accordingly, it could be used as a tool for patient selection and monitoring of transarterial therapy. In comparison, Child-Pugh and ALBI scores did not reflect any of these changes.

36. Alizai PH, Haelsig A, Bruners P, et al.

[Impact of liver volume and liver function on posthepatectomy liver failure after portal vein embolization – A multivariable cohort analysis](#)

Ann Med Surg (Lond) **2017** Dec 7;25:6-11. doi: 10.1016/j.amsu.2017.12.003. eCollection 2018 Jan

The future liver remnant is the only preoperative factor with a significant impact on post hepatectomy liver failure after previous portal vein embolization. Assessment of preoperative liver function with LiMAX test may additionally help in the identification of patients at risk to develop postoperative liver failure. Conventional liver biochemistry parameters, as well as MELD and Child-Pugh scores were not able to detect patients at risk.

37. Malinowski M, Lock JF, Seehofer D, et al.

[Preliminary study on liver function changes after trisectionectomy with versus without prior portal vein embolization](#)

Surg Today **2016** Sep;46(9):1053-61. doi: 10.1007/s00595-015-1293-1

Volume-function analysis using LiMAX and CT scan enables reliable prediction of early postoperative liver function. LiMAX values did not change after portal vein embolization, confirming that liver function distribution in the liver stays constant after embolization.

38. Malinowski M, Geisel D, Stary V, et al.

[Portal vein embolization with plug/coils improves hepatectomy outcome](#)

J Surg Res **2015** Mar;194(1):202-11. doi: 10.1016/j.jss.2014.10.028. Epub 2014 Oct 30

Portal vein embolization with plugs or coils has become the standard of care before extended hepatectomy. The procedure is a safe and efficient method to increase future liver remnant volume as measured by the LiMAX test. The additional central embolization with plug or coils led to an increased hypertrophy, due to lower recanalization rates, and subsequently decreased incidence of postoperative liver failure.

39. Brinkhaus G, Lock JF, Malinowski M, et al.

[CT-guided high-dose-rate brachytherapy of liver tumors does not impair hepatic function and shows high overall safety and favorable survival rates](#)

Ann Surg Oncol **2014** Dec;21(13):4284-92. doi: 10.1245/s10434-014-3835

Computed tomography-guided high-dose-rate brachytherapy (CT-HDRBT) is an emerging therapeutic option for irresectable liver tumors. However, its potentially negative effect on liver function has not yet been investigated. CT-HDRBT for local tumor treatment has little impact on total liver function capacity as measured by the LiMAX test, by high patient safety, and encouraging survival rates.

40. Malinowski M, Stary V, Lock JF, et al.

[Factors influencing hypertrophy of the left lateral liver lobe after portal vein embolization](#)

Langenbecks Arch Surg. **2015** Feb;400(2):237-46. doi: 10.1007/s00423-014-1266-7. Epub 2015 Jan 6

No recanalization, small initial FLR and longer time were assessed with better FLR hypertrophy. More sufficient PVE techniques and postponed hepatectomy might improve the outcome. Small initial FLR should not be a disclosure for curative hepatectomy.

Hepatology – Acute Liver Failure

41. Kreimeyer H, Buechter M, Best J, Gieseler RK, Katsounas A, Sowa JP, Gerken G, Canbay A, Manka P, Bechmann LP

[Performance of the LiMAx test, fibrinogen, and transient elastography in patients with acute liver injury](#)

Dig Dis **2022** Feb 22. doi: 10.1159/000523696

Decision-making in ALF remains challenging. LiMAx and fibrinogen might predict the prognosis in patients with non-acetaminophen-induced ALF and in combination could be feasible tools to decide if LT is necessary.

42. Buechter M, Gerken G, Hoyer DP, et al.

[Liver maximum capacity \(LiMAx\) test as a helpful prognostic tool in acute liver failure with sepsis: a case report](#)

BMC Anesthesiol **2018** Jun 20;18(1):71. doi: 10.1186/s12871-018-0538-0

Acute liver failure is a life-threatening entity particularly when infectious complications worsen the clinical course. Estimating prognosis is challenging by use of the established scores. Improvement of enzymatic liver function measured by the LiMAx test was the first parameter predicting beneficial outcome in a patient with ALF complicated by sepsis.

43. Vondran FW, Schumacher C, Johanning K, et al.

[Application of the liver maximum function capacity test in acute liver failure: a helpful tool for decision-making in liver transplantation?](#)

Case Rep Transplant **2016**; 2016:7074636. doi: 10.1155/2016/7074636. Epub 2016 May 4

Acute liver failure is associated with a critical state of the patient that requires almost immediate decision-making regarding further therapy. Application of a noninvasive liver function test might help to determine the prognosis of acute liver failure and support decision-making for or against transplantation as well as acceptance of a critical donor organ in case of a critically ill patient.

44. Lock JF, Kotobi AN, Malinowski M, et al.

[Predicting the prognosis in acute liver failure: results from a retrospective pilot study using the LiMAx test](#)

Ann Hepatol **2013** Jul-Aug; 12(4):556-62

Acute liver failure is a rare but potentially life-threatening condition and liver transplantation remains frequently the only effective therapy. Nevertheless, some patients recover without transplantation but the individual indication for or against transplantation remains difficult. The LiMAx test might be effective in predicting the individual prognosis and the need for transplantation in acute liver failure.

Hepatology - Chronic Liver Failure

45. Schleiger A, Kramer P, Sallmon H, Jentsch N, Pileckaite M, Danne F, Schafstedde M, Müller H-P, Müller T, Tacke F, Jara M, Stockmann M, Berger F, Ovroutski S

[Functional hepatic deterioration determined by 13C-methacetin breath test is associated with impaired hemodynamics and late Fontan failure in adults](#)

Front. Cardiovasc. Med. 9:952080 (2022). doi: 10.3389/fcvm.2022.952080

We herein demonstrate that maximum liver function capacity measured by the LiMax® test is impaired in patients with impaired Fontan hemodynamics and Fontan failure. Hence, the LiMax® test represents a valuable complementary diagnostic modality for FALD and might be useful in evaluating the indication for combined heart and liver transplantation.

46. Schleiger A, Kramer P, Sallmon H, Jentsch N, Pileckaite M, Danne F, Schafstedde M, Müller HP, Müller T, Tacke F, Jara M, Stockmann M, Berger F, Ovroutski S

[Morphologic Alterations Precede Functional Hepatic Impairment as Determined by 13C-Methacetin Liver Function Breath Test in Adult Fontan Patients](#)

Front Cardiovasc Med. 2021; 8: 764009. Publ. online 2021 Dec 23. doi: 10.3389/fcvm.2021.764009

To the best of our knowledge, this is the first study to evaluate maximal liver function capacity using LiMax® test in Fontan patients, which is a useful complementary diagnostic instrument to assess chronic hepatic injury. Maximal liver function capacity was preserved in most of our adult Fontan patients despite morphologic evidence of FALD. Moreover, maximal liver function capacity does not correlate with the extent of FALD severity evaluated by sonography or laboratory analysis. Thus, the development and progression of FALD in Fontan patients is not a uniform process and diagnostics of chronic hepatic injury during follow-up should encompass various modalities.

47. Dziondzio T, Öllinger R, Schöning W, Rothkäppel A, Nikolov R, Juraszek A, Ritschl PV, Stockmann M, Pratschke J, Jara M

[Validation of a new prognostic model to predict short and medium-term survival in patients with liver cirrhosis](#)

BMC Gastroenterol. 2020 Aug 12;20(1):265. doi: 10.1186/s12876-020-01407-8. PMID: 32787947; PMCID: PMC7425128

The CreLiMax risk score appears to be a competitive and valid tool for estimating not only short- but also medium-term survival of patients with end-stage liver disease. Particularly in patients with Child-Pugh Class B cirrhosis the new score showed a good ability to identify patients not at risk of death.

48. Buechter M, Kersting S, Gerken G, et al

[Enzymatic liver function measured by LiMAX – a reliable diagnostic and prognostic tool in chronic liver disease](#)

Scientific Reports **2019**, 9:13577. doi.org/10.1038/s41598-019-49746-1

LiMAX was superior to TE and serum biomarkers in predicting patients' outcome by 90-day mortality (AUROC 0.811, $p < 0.001$). Enzymatic liver function measured by LiMAX was closely associated with different severity stages of CLD and was a reliable diagnostic and prognostic tool with an accuracy comparable to current standard methods.

49. Blüthner E, Bednarsch J, Pape UF, et al.

[Advanced liver function assessment in patients with intestinal failure on long-term parenteral nutrition](#)

Clin Nutr **2019** Mar 5. pii: S0261-5614(19)30093-7. doi: 10.1016/j.clnu.2019.02.039

The LiMAX test is significantly associated with widely accepted risk factors for intestinal failure associated liver disease by multivariable analysis, whereas ICG test and FibroScan failed to show significant correlations. Liver function assessment by LiMAX test may therefore have the potential to early detect alterations in liver function and identify patients at risk for the development of liver disease.

50. Jara M, Dziódzio T, Malinowski M, et al.

[Prospective assessment of liver function by an enzymatic liver function test to estimate short-term survival in patients with liver cirrhosis](#)

Dig Dis Sci **2019** Feb;64(2):576-584. doi: 10.1007/s10620-018-5360-5. Epub 2018 Nov 7

Apart from serum creatinine levels, enzymatic liver function measured by LiMAX was found to be an independent predictor of short-term mortality risk in patients with liver cirrhosis. A risk score combining both determinants allows reliable prediction of short-term prognosis considering actual organ function.

51. Buechter M, Thimm J, Baba HA, et al.

[Liver maximum capacity: a novel test to accurately diagnose different stages of liver fibrosis](#)

Digestion **2019**;100(1):45-54. doi: 10.1159/000493573. Epub 2018 Oct 2

Enzymatic liver function measured by LiMAX showed strong correlation with histology in patients with CLD irrespective of its underlying etiology and was superior to TE and serum biomarkers, possibly making it useful as a novel and noninvasive tool for the determination of hepatic disease severity.

52. Malinowski M, Jara M, Lüttgert K, et al.

[Enzymatic liver function capacity correlates with disease severity of patients with liver cirrhosis: a study with the LiMAx test](#)

Dig Dis Sci **2014** Dec;59(12):2983-91. doi: 10.1007/s10620-014-3250-z. Epub 2014 Jul 4

Assessment and quantification of actual liver function is crucial in patients with chronic liver disease to monitor disease progression and predict individual prognosis. LiMAx appears to provide reliable information on remnant enzymatic liver function in chronic liver disease and allows graduation of disease severity.

NASH and Obesity

53. Blank V, Petroff D, Boehlig A, Heinze A, Karlas T, Berg T, Wiegand J

[Clinical implications of hepatic structure and function evaluation based on vibration-controlled transient elastography and liver maximum function capacity test in patients with nonalcoholic fatty liver disease](#)

Eur J Gastroenterol Hepatol **2022** Jan 31. doi: 10.1097/MEG.0000000000002347

There is a significant correlation between the functional liver capacity (LiMAx) and the structural liver assessment by VCTE. In cases with high liver stiffness or FAST-score, low LiMAx results may identify NAFLD patients at risk for disease progression and reduce the risk of false-positive categorization.

54. Schmitz S MT, Kroh A, Koch A, Brozat JF, Stier C, Neumann UP, Ulmer TF, Alizai PH

[Comparison of Liver Recovery After Sleeve Gastrectomy and Roux-en-Y-Gastric Bypass](#)

Obesity Surgery **2021**, <https://doi.org/10.1007/s11695-021-05390-1>

Bariatric surgery, especially sleeve gastrectomy, leads to an improvement of liver function. However, in some patients with T2DM, higher preoperative weight and male sex postoperative deterioration of liver function capacity may occur.

55. Schmitz SM, Kroh A, Ulmer TF, Andruszkow J, Luedde T, Brozat JF, Neumann UP, Alizai PH.

[Evaluation of NAFLD and fibrosis in obese patients - a comparison of histological and clinical scoring systems](#)

BMC Gastroenterol. **2020** Aug 5;20(1):254. doi: 10.1186/s12876-020-01400-1. PMID: 32758151; PMCID: PMC7405451.

APRI allows screening of NAFLD as well as fibrosis in obese patients. This score is easy to calculate and affordable, while conveniently only using routine clinical parameters. Using the NAS histologic scoring system bears the risk of underdiagnosing NASH in comparison to SAF score.

56. Alizai PH, Lurje I, Kroh A, et al.

[Noninvasive evaluation of liver function in morbidly obese patients](#)

Gastroenterol Res Pract **2019**, 4307462, <https://doi.org/10.1155/2019/4307462>

The aim of this study was to assess alterations in liver function in obese patients with a noninvasive liver function test. The liver function capacity correlates with histological and clinical scoring systems. The LiMAx test may be a valuable tool for noninvasive screening for NASH in obese patients.

57. Alizai PH, Wendl J, Roeth AA, et al.

[Functional liver recovery after bariatric surgery - a prospective cohort study with the LiMAx test](#)

Obes Surg **2015** Nov;25(11):2047-53. doi: 10.1007/s11695-015-1664-0

Bariatric surgery provides long-term weight loss and improvement of obesity-associated diseases such as nonalcoholic steatohepatitis. Histologic improvement has been reported in some studies after bariatric surgery. Bariatric surgery leads to a significant functional recovery of the liver as measured by the LiMAx test. An initial marked weight loss may negatively influence functional liver recovery.

58. Lodewick TM, Roeth AA, Olde Damink SW, et al.

[Sarcopenia, obesity and sarcopenic obesity: effects on liver function and volume in patients scheduled for major liver resection](#)

J Cachexia Sarcopenia Muscle **2015** Jun;6(2):155-63. doi: 10.1002/jcsm.12018. Epub 2015 Apr 28

Preoperative liver function of sarcopenic, obese and sarcopenic-obese patients as measured by the LiMAx test might be reduced, possibly leading to more post-operative morbidity. Sarcopenia and sarcopenic obesity did not seem to influence liver size and function negatively. However, obese patients had larger, although less functional, livers, indicating dissociation of liver function and volume.

59. Hoppe S, von Loeffelholz C, Lock JF, et al.

[Nonalcoholic steatohepatitis and liver steatosis modify partial hepatectomy recovery](#)

J Invest Surg **2015** Feb;28(1):24-31. doi:10.3109/08941939.2014.971206. Epub 2014 Nov 13

The impact of nonalcoholic fatty liver disease comprising simple steatosis and steatohepatitis on liver recovery after partial hepatectomy has not been evaluated. This study suggests that nonalcoholic fatty liver disease impairs functional recovery assessed by LiMAx after partial hepatectomy.

60. Fierbinteanu-Braticevici C, Plesca D, Tribus L, et al.

[The role of ¹³C-Methacetin breath test for the non-invasive evaluation of nonalcoholic fatty liver disease](#)

J Gastrointestin Liver Dis **2013** Jun;22(2):149-56

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in many parts of the world. Due to the impairment of microsomal function which occurs in NAFLD, ¹³C-Methacetin breath test could be a reliable diagnostic and follow-up test for NAFLD patients.

Chemotherapy and Drug Dosing

61. Gairing S J, Kuchen R, Müller L, Cankaya A, Weerts J, Kapucu A, Sachse S, Zimpel C, Stoehr F, Pitton M B, Mittler J, Straub B K, Marquardt J U, Schattenberg J M, Labenz C, Kloeckner R, Weinmann A, Galle P R, Wörns M-A, Foerster F

[13C-Methacetin Breath Test Predicts Survival in Patients With Hepatocellular Carcinoma Undergoing Transarterial Chemoembolization](#)

Clinical and Translational Gastroenterology **2022**;13:e00529. DOI: 10.14309/ctg.0000000000000529

Baseline and longitudinal 13 C-MBT values predict survival of patients with HCC undergoing TACE. The relative change in 13 C-MBT values predicts short-term mortality and may assist in identifying patients who will not benefit from further TACE treatment.

62. Senk K, Wilcke J, Haimerl M, Verloh N, Rio Bartulos C, Bäuml W, Stroszczyński C, Wiggermann P

[Prediction of Transarterial Chemoembolization \(TACE\) - Outcome by pre- and postinterventional 13C-Methacetin breath test](#)

Clin Hemorheol Microcirc. **2021** Aug 28.; doi: 10.3233/CH-219118

For the first time, we were able to show in our study that patients who are scheduled for TACE could benefit from a LiMAX test to be able to estimate the benefit of TACE. The higher the pre-interventional LiMAX values, the higher the benefit of TACE. On the other hand, laboratory parameters summarized in the form of the MELD score, had significantly less descriptive correlation with the TACE outcome

63. Bednarsch J, Czigany Z, Loosen SH, Heij L, Ruckgaber L, Maes H, Krause JP, Reen M, Toteva B, Vosdellen T, Bruners P, Lang SA, Ulmer TF, Roderburg C, Luedde T, Neumann UP

[Perioperative rifaximin is not associated with enhanced functional and volumetric recovery after major liver resection](#)

Sci Rep. **2021** Sep 9;11(1):17936; doi: 10.1038/s41598-021-97442-w

The objective of this randomized controlled trial (RCT) was to assess the impact of rifaximin on the course of liver function, liver regeneration and volumetric recovery in patients undergoing major hepatectomy. Between 2016 and 2020, 45 patients were randomized and 35 patients (16 individuals in the rifaximin and 19 individuals in the control group) were eligible for per-protocol analysis. The median relative increase in liver function from POD 4 to POD 7 was 27% in the rifaximin group and 41% in the control group ($p = 0.399$). Further, no significant difference was found in terms of any other endpoints of functional liver- and volume regeneration or perioperative surgical complications following the application of rifaximin versus no intervention. Perioperative application of rifaximin has no effect on functional or volumetric regeneration after major hepatectomy.

64. Reichert MC, Massmann A, Malinowski M, et al.

[Volume–Function Analysis \(LiMAx Test\) in Patients with HCC and Cirrhosis Undergoing TACE—A Feasibility Study](#)

Digestive Diseases and Sciences **2020** Aug 20

In our prospective pilot study in patients with HCC and cirrhosis undergoing multiple TACE, robust and reliable LiMAx measurements were demonstrated. Lower LiMAx levels before TACE were associated with surrogate markers (bilirubin) of liver failure after TACE. Specific subgroups at high risk of PTHF should be investigated. This might facilitate the future development of strategies to prevent occurrence of PTHF.

65. Wellhörner S, Gerhardt F, Berg T, et al.

[¹³C-methacetin breath test for the prediction of liver damage caused by transarterial chemoembolization in patients with hepatocellular carcinoma](#)

Journal of Hepatology **2020** vol. 73 | S653–S915

Measuring liver function using a ¹³C-methacetin breath test is a helpful method for early identification of patients at risk of liver function deterioration by TACE.

66. Parmar KL, O'Reilly D, Renehan AG, et al.

[Prospective study of change in liver function and fat in patients with colorectal liver metastases undergoing preoperative chemotherapy: protocol for the CLiFF Study](#)

BMJ Open **2020** Sep 23;10(9):e027630

This prospective study will assess changes in liver function longitudinally, measured by the LiMAx test, and liver fat, measured by advanced MRI using both MR spectroscopy and the modified Dixon method, in up to 35 patients undergoing preoperative chemotherapy for CLM. The primary outcomes will be the changes in liver function and fat compared with baseline prechemotherapy measurements. Secondary outcome measures include: routinely measured liver function blood tests, anthropometric measurements, postoperative histology and digital quantification of fat, postoperative complications and mortality and quality of life.

67. Berndt N, Eckstein J, Holzhütter HG, et al.

[Metabolic heterogeneity of human hepatocellular carcinoma: implications for personalized pharmacological treatment](#)

The FEBS Journal 288(7) Oct **2020**

Taken together, our study revealed a large heterogeneity of metabolic changes in HCC, which do not follow a single 'master program' but instead may result from a plethora of simultaneously operative influencing factors, such as the availability and quality of nutrients, the medication history of the patient, comorbidities (e.g., diabetes), random mutations in proteins of regulatory pathways, metabolic responses to virus load, humoral signals received from inflammatory immune cells, cell–cell and cell–matrix contacts, and the extension and differentiation of the tumor. This situation calls for personalized treatment options that are based on a careful analysis of the tumor-specific metabolic capabilities. Our approach may serve as a promising step in this direction.

68. Alraish et al.

[Pharmacokinetics of tigecycline in critically ill patients with liver failure defined by maximal liver function capacity test \(LiMAX\)](#)

Ann Intensive Care. **2020**; 10: 106

The present study demonstrates a high variability of TGC plasma concentrations in critically ill patients. The results show a significant correlation between the degree of liver dysfunction, measured by the LiMAX test, and TGC Cmax. LiMAX test may be a helpful tool beyond others for adjusting the required dosage of hepatic metabolized antibiotics in critically ill patients.

69. Kirchner C, Sibai J, Schwier E, et al.

[Dosing of Antimycotic Treatment in Sepsis-Induced Liver Dysfunction by Functional Liver Testing with LiMAX](#)

Case Rep Crit Care. **2019** Dec 26;2019:5362514. doi: 10.1155/2019/5362514. eCollection 2019

In patients with septic shock, liver function is often significantly impaired and therefore also hepatic drug metabolism is altered. We provide a new approach for sepsis treatment considering liver function capacity to optimize dosage of hepatically metabolised drugs with potential hepatotoxic effects.

70. Lock JF, Sponholz C, Hoppe S, et al.

[Visfatin/NAMPT is unrelated to nonalcoholic fatty liver histology but correlates with liver recovery after partial liver resection: Data from a pilot study](#)

Integr Mol Med, **2018** Volume 5(3): 1-4doi: 10.15761/IMM.1000331

Circulating visfatin/NAMPT was measured by enzyme linked-immunosorbent assay, mRNA by RT-PCR. Postoperative liver recovery was studied in a subset of subjects using the LiMAX-method. Visfatin/NAMPT is related to markers of oxidative stress, inflammation and liver recovery after hepatic surgery, but not to NAFLD histology or insulin resistance.

71. Lock JF, Westphal T, Rubin T, et al.

[LiMAX test improves diagnosis of chemotherapy-associated liver injury before resection of colorectal liver metastases](#)

Ann Surg Oncol **2017** Sep;24(9):2447-2455. doi: 10.1245/s10434-017-5887-2. Epub 2017 May 17

The LiMAX test enables non-invasive preoperative diagnosis of chemotherapy-associated liver injury. Preoperative performance of the LiMAX test can augment surgical strategy and timing of surgery after previous chemotherapy, thus avoiding increased postoperative morbidity.

72. Jara M, Bednarsch J, Malinowski M, et al.

[Effects of oxaliplatin-based chemotherapy on liver function-an analysis of impact and functional recovery using the LiMAX test](#)

Langenbecks Arch Surg **2016** Feb;401(1):33-41. doi: 10.1007/s00423-015-1352-5. Epub 2015 Oct 27

Enzymatic liver function (LiMAX) is significantly reduced after oxaliplatin-based chemotherapy and subsequently recovers within 8 weeks after cessation of chemotherapy. However, pace of regeneration appears to be highly different among patients suggesting patient individual chemotherapy-free interval monitored by LiMAX.

73. Bednarsch J, Jara M, Lock JF, et al.

[Noninvasive diagnosis of chemotherapy induced liver injury by LiMAx test – two case reports and a review of the literature](#)

BMC Res Notes **2015** Mar 26;8:99. doi: 10.1186/s13104-015-1055-6

The LiMAx test might be a sensitive tool to diagnose mild functional impairment after chemotherapy when standard liver function tests have remained within normal ranges and might be capable to assess the course of regeneration after chemotherapy. This could be useful to optimize individual chemotherapy-free interval before liver surgery can be carried out safely.

74. Rayes N, Pilarski T, Stockmann M, et al.

[Effect of pre- and probiotics on liver regeneration after resection: a randomized, double-blind pilot study](#)

Benef Microbes **2012** Sep;3(3):237-44. doi: 10.3920/BM2012.0006

Liver regeneration is a prerequisite for extended liver surgery. Several studies have shown that the bacterial gut flora is able to modulate liver function. The effect of synbiotics on liver function after hepatic resection has not been analyzed yet. Synbiotics might be able to increase liver function capacity in patients after liver resection as measured by the LiMAx test.

75. Lock JF, Malinowski M, Schwabauer E, et al.

[Initial liver graft function is a reliable predictor of tacrolimus trough levels during the first post-transplant week](#)

Clin Transplant **2011** May-Jun;25(3):436-43. doi: 10.1111/j.1399-0012.2010.01264.x

The narrow therapeutic range of tacrolimus requires careful management after liver transplantation. Initial graft function is a major factor influencing the pharmacokinetics of tacrolimus and can be validly determined by the LiMAx test.

Intensive Care Medicine and Sepsis

76. Alraish R, Wicha SG, Frey OR, Roehr AC, Pratschke J, Stockmann M, Wuensch T, Kaffarnik M
[Liver function, quantified by the LiMAx test, as a predictor for the clinical outcome of critically ill patients treated with linezolid](#)
Technol Health Care **2022**;30(2):309-321. doi: 10.3233/THC-191847
The LiMAx test predicts clinical failure more precisely than linezolid trough levels in critically ill surgical patients. Therefore liver failure may have a stronger impact on the outcome of critically ill surgical patients than low linezolid Cmin. While linezolid Cmin failed to predict patient's outcome, LiMAx results were the only independent predictor of clinical failure.
77. Köhler T, Pletz MW, Altmann S, Kirchner C, Schwier E, Henzler D, Winde G, Eickmeyer C
[Pericarditis Caused by Enterococcus faecium with Acute Liver Failure Treated by a Multifaceted Approach including Antimicrobials and Hemoadsorpt](#)
Case Reports in Critical Care Volume **2021**, Article ID 8824050, <https://doi.org/10.1155/2021/8824050>
This case shows how complex infectious diseases with an atypical infectious focus resulting in septic shock can be successfully treated. A combination of antimicrobial (tigecycline and caspofungin) and long-term adjunctive hemoadsorption therapy was administered while hepatotoxic antibiotic medication was monitored by liver function testing.
78. Nee J, Schroeder T, Vornholt F, et al.
[Dynamic determination of functional liver capacity with the LiMAx test in post-cardiac arrest patients undergoing targeted temperature management-A prospective trial](#)
Acta Anaesthesiol Scand. **2019** Dec 12. doi: 10.1111/aas.13523
Transiently increased transaminases is a common finding after cardiac arrest but little is known about the functional liver capacity during the post-cardiac arrest syndrome and treatment in the intensive care unit. Liver functional capacity is impaired in patients after cardiac arrest undergoing targeted temperature at 33°C. More data are needed to determine if liver functional capacity may add relevant information, especially in the context of pharmacotherapy, to individualize post-cardiac arrest care.
79. Kaffarnik MF, Ahmadi N, Lock JF, et al.
[Correlation between plasma endothelin-1 levels and severity of septic liver failure quantified by maximal liver function capacity \(LiMAx test\). A prospective study](#)
PLoS One. **2017** May 23;12(5):e0178237. doi: 10.1371/journal.pone.0178237. eCollection 2017
Sepsis-related hepatic dysfunction is associated with elevated plasma levels of endothelin-1, TNF- α and IL-6. Low LiMAx results combined with increased endothelin-1 and TNF- α and a favorable correlation between LiMAx and cytokine values support the findings of a crucial role of Endothelin-1 and TNF- α in development of septic liver failure.

80. Bednarsch J, Menk M, Malinowski M, et al.

[13-C breath tests are feasible in patients with extracorporeal membrane oxygenation devices](#)

Artif Organs. **2016** Jul;40(7):692-8. doi: 10.1111/aor.12634. Epub 2015 Nov 3.

The LiMAx test as a (13) C-breath test accessing liver function might be of particular predictive interest if patients with ECMO therapy develop multiorgan failure.

81. Kaffarnik MF, Lock JF, Vetter H, et al.

[Early diagnosis of sepsis-related hepatic dysfunction and its prognostic impact on survival: a prospective study with the LiMAx test](#)

Crit Care **2013** Oct 31;17(5):R259. doi: 10.1186/cc13089

Sepsis-related hepatic dysfunction can be diagnosed early and effectively by the LiMAx test. The extent of LiMAx impairment is predictive for patient morbidity and mortality. The sensitivity and specificity of the LiMAx test was superior to that of ICG-PDR regarding the prediction of mortality.

82. Wicha SG, Frey OR, Roehr AC, et al.

[Linezolid in liver failure: exploring the value of the maximal liver function capacity \(LiMAx\) test in a pharmacokinetic pilot study](#)

Int J Antimicrob Agents **2017** Oct;50(4):557-563. doi: 10.1016/j.ijantimicag.2017.06.023

Patients in the intensive care unit frequently require antibiotic treatment, liver impairment poses substantial challenges for dose selection in these patients. This is the first pilot application of the LiMAx test in a pharmacokinetic study demonstrating its potential to explain pharmacokinetic variability in linezolid clearance.

Technology and Methodology

83. Buechter M, Gerken G

[Liver Function - How to Screen and to Diagnose: Insights from Personal Experiences, Controlled Clinical Studies and Future Perspectives](#)

J. Pers. Med. **2022**, *12*, 1657. <https://doi.org/10.3390/jpm12101657>

To conclude, we have a bouquet of different diagnostic and prognostic tools to screen and estimate liver function in patients with acute and chronic liver diseases. These entities should be applied carefully and thoughtfully to our patients. With the LiMAX test, we have a strong and robust additional assay that offers the unique opportunity of specific, semiquantitative and dynamic measurement of actual enzymatic liver function, which we included in our novel diagnostic algorithm to screen patients with presumptive acute or chronic liver disease

84. Verloh N, Fuhrmann I, Fellner C, Nickel D, Zeman F, Kandulski A, Hornung M, Stroszczynski C, Wiggermann P, Haimerl M

[Quantitative analysis of liver function: 3D variable-flip-angle versus Look-Locker T1 relaxometry in hepatocyte-specific contrast-enhanced liver MRI](#)

Quantitative Imaging in Medicine and Surgery *12*(4); January **2021**, DOI:10.21037/qims-21-597

Both T1 relaxometry sequences are suitable for the evaluation of liver function based on 13C-MBT. However, the Look-Locker sequence is less susceptible to artifacts and might be more advantageous, especially in patients with impaired liver function.

85. Schurink IJ, de Haan JE, Willemse J, Mueller M, Doukas M, Roest H, de Goeij FHC, Polak WG, Ijzermans JNM, Dutkowski P, van der Laan LJW, de Jonge J

[A proof of concept study on real-time LiMAX CYP1A2 liver function assessment of donor grafts during normothermic machine perfusion](#)

Sci Rep **11**, 23444 (2021). <https://doi.org/10.1038/s41598-021-02641-0>

No single reliable parameter exists to assess liver graft function of extended criteria donors during ex-vivo normothermic machine perfusion (NMP). The liver maximum capacity (LiMAX) test is a clinically validated cytochromal breath test, measuring liver function based on 13CO₂ production. As an innovative concept, we aimed to integrate the LiMAX breath test with NMP to assess organ function. Eleven human livers were perfused using NMP. After one hour of stabilization, LiMAX testing was performed. Injury markers (ALT, AST, miR-122, FMN, and Suzuki-score) and lactate clearance were measured and related to LiMAX values. We demonstrate, as proof of principle, that liver function during NMP can be quantified using the LiMAX test, illustrating a positive correlation with traditional injury markers. This new breath-test application separates livers with adequate cytochromal liver function from inadequate ones and may support decision-making in the safe utilization of extended criteria donor grafts.

86. Heise D, Schulze-Hagen M, Bednarsch J, Eickhoff R, Kroh A, Bruners P, Eickhoff SB, Brecheisen R, Ulmer F, Neumann UP

[CT-Based Prediction of Liver Function and Post-PVE Hypertrophy Using an Artificial Neural Network](#)

J. Clin. Med. **2021**, 10(14), 3079; <https://doi.org/10.3390/jcm10143079>

This study aimed to evaluate whether hypertrophy after portal vein embolization (PVE) and maximum liver function capacity (LiMAx) are predictable by an artificial neural network (ANN) model based on computed tomography (CT) texture features. Our study shows that an ANN model based on CT texture features is able to predict the maximum liver function capacity and may be useful to assess potential hypertrophy after performing PVE.

87. Oldhafer F, Wittauer E-M, Beetz O, Weigle CA, Sieg L, Eismann H, Braubach P, Bock M, Jonigk D, Johanning K, Vondran FWR

[Supportive Hepatocyte Transplantation after Partial Hepatectomy Enhances Liver Regeneration in a Preclinical Pig Model](#)

Eur Surg Res **2021** doi: 10.1159/000516690

HTx can be performed safely and effectively immediately after a partial (50%) hepatectomy as well as 3 days postoperatively, with comparable results regarding the enhancement of liver function and regeneration.

88. Theilig D, Tsereteli A, Elkilany A, et al.

[Gd-EOB-DTPA-enhanced MRI T1 relaxometry as an imaging-based liver function test compared with ¹³C-methacetin breath test](#)

Acta Radiol **2019** Jul 19:284185119861314. doi: 10.1177/0284185119861314. [Epub ahead of print]

Gd-EOB-DTPA (Gadolinium) enhanced magnetic resonance imaging (MRI) and especially MRI T1 relaxometry is a procedure allowing the assessment of spatial distribution of liver function without ionizing radiation and can be easily integrated into preoperative clinical routine. All MRI T1 relaxometry parameters showed a correlation to the LiMAx value. It should be noted that in context of this study predominantly the excretory liver function has been investigated.

89. Blüthner E, Jara M, Shrestha R, et al.

[The predictive value of future liver remnant function after liver resection for HCC in noncirrhotic and cirrhotic patients](#)

HPB (Oxford) **2019** Jul;21(7):912-922. doi: 10.1016/j.hpb.2018.11.012. Epub 2019 Feb 4

Future remnant liver function using the LiMAx algorithm is superior to future remnant liver volume for the prediction of hepatectomy-related morbidity in patients with hepatocellular carcinoma.

90. Heucke N, Wuensch T, Mohr J, et al.

[Non-invasive structure-function assessment of the liver by 2D time-harmonic elastography and the dynamic Liver MAXimum capacity \(LiMAx\) test](#)

J Gastroenterol Hepatol **2019** Feb 13. doi: 10.1111/jgh.14629. [Epub ahead of print]

Accurate assessment of structural and functional characteristics of the liver could improve the diagnosis and the clinical management of patients with chronic liver diseases. However, the structure-function relationship in the progression of chronic liver disease remains elusive. Findings show that structural changes in the liver due to progressing liver diseases and reflected by increased tissue stiffness correlate with a functional decline of the organ as reflected by a decreased metabolic capacity of the liver measured by the LiMAx test.

91. Fuhrmann I, Brünn K, Probst U, et al.

[Proof of principle: Estimation of liver function using color coded Doppler sonography of the portal vein](#)

Clin Hemorheol Microcirc **2018**;70(4):585-594. doi: 10.3233/CH-189323

The diagnostic value of Doppler ultrasonography of the portal vein for the evaluation of liver function is still contradictory. Aim of this study was to test the relationship between clinical liver function tests based on MRI and breath testing and blood flow in the portal vein. The results of this proof-of-principle study indicate that color coded doppler ultrasound-based assessment of portal velocity is of only limited value for the evaluation of liver function.

92. Major RD, Kluge M, Jara M, et al.

[The predictive value of the maximal liver function capacity test for the isolation of primary human hepatocytes](#)

Tissue Eng Part C Methods **2018** Mar;24(3):179-186. doi: 10.1089/ten.TEC.2017.0369. Epub 2018 Feb

The need for primary human hepatocytes is constantly growing, for basic research as well as for therapeutic applications. However, the isolation outcome strongly depends on the quality of liver tissue but a preoperative test that allows prediction of the hepatocyte isolation outcome is lacking. The LiMAx test might be a useful tool to predict the quantitative outcome of hepatocyte isolation, as long as underlying liver disease is taken into consideration.

93. Haimerl M, Brünn K, Poelsterl S, et al.

[Quantitative evaluation of real-time maximum liver capacity \(LiMAx\) and time intensity curve \(TIC\) analysis in CEUS-based microperfusion](#)

Clin Hemorheol Microcirc **2017**;67(3-4):373-382. doi: 10.3233/CH-179217

The main purpose of this experiment was to compare the diagnostic performance of real-time maximum liver capacity (LiMAx) with dynamic contrast enhanced ultrasound (CEUS)-based liver microcirculation. Within the framework of this study, CEUS-based perfusion parameters were not able to assess severity of liver disease, assessed with current standard of diagnostic care LiMAx test.

94. Rubin TM, Heyne K, Luchterhand A, et al.

[Kinetic validation of the LiMAx test during 10,000 intravenous ¹³C-methacetin breath tests](#)

J Breath Res **2017** Nov 29;12(1):016005. doi: 10.1088/1752-7163/aa820b

The aim of this study was to analyze the recorded DOB kinetics in a large population for further refinement of the test protocol. Two new methods of kinetic analysis are proposed in this article: the time dependency of the DOB kinetics and the time interval until half of the DOB maximum. Both, the specific patterns and proposed kinetic analysis, have the potential to further improve the sensitivity and specificity of the test and its clinical applicability by shortening its duration.

95. Lodewick TM, Alizai PH, van Dam RM, et al.

[Effect of age on liver function in patients undergoing partial hepatectomy](#)

Dig Surg **2017**; 34(3):233-240. doi: 10.1159/000452494. Epub 2017 Feb 15

Postresection liver failure is the most frequent cause of fatal outcome following liver surgery. Diminished preoperative liver function in the elderly might contribute to this. LiMAx values were not significantly different between patients aged <60 and >70 years. Liver function did not seem to differ between younger and older patients.

96. Rubin T, Haimberger T, Helmke A, et al.

[Liver Status Assessment by Spectrally and Time Resolved IR Detection of Drug Induced Breath Gas Changes](#)

Photonics **2016**, 3, 31; doi:10.3390/photonics3020031

The LiMAx value is successfully used in clinical routine to reduce the mortality rate upon liver resections by more than 70%. A variety of other application areas have been reported. The combination of the LiMAx test with the QCL-based FLIP device presented here will revolutionize liver therapy and medical fields in which the liver plays a vital role.

97. Jara M, Bednarsch J, Valle E, et al.

[Reliable assessment of liver function using LiMAx](#)

J Surg Res **2015** Jan;193(1):184-9. doi: 10.1016/j.jss.2014.07.041. PubMed PMID: 25150081

¹³C-liver function breath tests can facilitate the assessment of hepatic function in-vivo and may help surgeons to identify candidates for safe liver surgery. However, their acceptance into clinical practice is dependent on evaluation of technical efficacy and repeatability. The LiMAx test shows excellent reproducibility in subjects with normal liver function. General anesthesia has no effect on test results.

98. Rubin T, von Haimberger T, Helmke A, et al.

[Quantitative determination of metabolism dynamics by a real-time \$^{13}\text{CO}_2\$ breath test](#)

J Breath Res **2011** Jun;5(2):027102. doi: 10.1088/1752-7155/5/2/027102. Epub 2011 Apr 19

We have developed a flow-through fast liver investigation packet (FLIP) to quantitatively measure the amount of exhaled $^{13}\text{CO}_2$, as a result of liver metabolism processes. Detection of the complete breath volume and the spectrally fully resolved line shape allows sensitivity in the ppb range with a standard deviation of approximately 80 ppb, a prerequisite to quantitatively analyze liver metabolism processes.

99. Lock JF, Taheri P, Bauer S, et al.

[Interpretation of non-invasive breath tests using \$^{13}\text{C}\$ -labeled substrates – a preliminary report with \$^{13}\text{C}\$ -Methacetin](#)

Eur J Med Res **2009**; 14:547-50

Non-invasive breath tests can serve as valuable diagnostic tools in medicine as they can determine particular enzymatic and metabolic functions in vivo. However, methodological pitfalls have limited the actual clinical application of those tests till today. This analysis compares the breath recovery of a ^{13}C -Methacetin breath test (LiMAX) with the actual serum kinetics of the substrate. It is shown, that breath and serum kinetics of the same test are significantly different over a period of 60 minutes.

Health Economics

100. Stockmann M, Vondran FWR, Fahrner R, et al.
[Randomized clinical trial comparing liver resection with and without perioperative assessment of liver function](#)
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