



## Publication List LiMAX<sup>®</sup> Test

Last update July 2020

Selected publications on the LiMAX<sup>®</sup> 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. 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.*

2. 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.*

3. 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.ijvsu.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.*

4. 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.ijvsu.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.*

5. 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.ijvsu.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.*

6. 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.*

7. 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.*

8. 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.*

9. 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.*

10. 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.*

11. 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.*

12. 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.*

13. 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.*

14. 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.*

15. 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

16. 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.*

17. 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.*

18. 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

19. 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.*

20. 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.*

21. 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.*

22. 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

23. 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.*

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

[Monitoring Liver Function of Patients Undergoing Transarterial Chemoembolization \(TACE\) by a <sup>13</sup>C 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.*

25. 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.*

26. 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.*

27. 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.*

28. 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.*

29. 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

30. 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.*

31. 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.*

32. 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

33. 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.*

34. 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.*

35. Jara M, Dziodzio 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.*

36. 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.*

37. 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

38. 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.*

39. 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.*

40. 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.*

41. 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.*

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

[The role of <sup>13</sup>C-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, <sup>13</sup>C-Methacetin breath test could be a reliable diagnostic and follow-up test for NAFLD patients.*

## Chemotherapy and Drug Dosing

43. 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.*

44. 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.*

45. 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.*

46. 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.*



47. 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.*

48. 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.*

49. 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

50. 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.*

51. 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- $\alpha$  and IL-6. Low LiMAx results combined with increased endothelin-1 and TNF- $\alpha$  and a favorable correlation between LiMAx and cytokine values support the findings of a crucial role of Endothelin-1 and TNF- $\alpha$  in development of septic liver failure.*

52. 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.*

53. 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.*

54. 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

55. Holzhütter HG, Wuensch T, Gajowski R, et al.

[\*\*A novel variant of the <sup>13</sup>C-methacetin liver function breath test that eliminates the confounding effect of individual differences in systemic CO<sub>2</sub> kinetics\*\*](#)

Arch Toxicol **2020** Feb;94(2):401-415. doi: 10.1007/s00204-020-02654-0. Epub 2020 Feb 4

*The novel test revealed that a significant portion of the drug is not immediately metabolized, but transiently taken up into a storage compartment. Intriguingly, not only the hepatic detoxification rate but also the storage capacity of the drug, turned out to be indicative for a normal liver function. We thus used both parameters to define a scoring function which yielded an excellent disease classification (AUC = 0.95) and a high correlation with the MELD score (RSpearman = 0.92). The novel test variant 2DOB promises a significant improvement in the assessment of impaired hepatic detoxification capacity. The suitability of the test for the reliable characterization of the natural history of chronic liver diseases (fatty liver—fibrosis—cirrhosis) has to be assessed in further studies.*

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

[\*\*Gd-EOB-DTPA-enhanced MRI T1 relaxometry as an imaging-based liver function test compared with <sup>13</sup>C-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.*

57. 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.*

58. 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.*

59. 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.*

60. 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.*

61. 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.*

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

[Kinetic validation of the LiMAx test during 10,000 intravenous <sup>13</sup>C-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.*

63. 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.*

64. 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.*

65. 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

*<sup>13</sup>C-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.*

66. Holzhütter HG, Lock JF, Taheri P, et al.

[Assessment of hepatic detoxification activity: Proposal of an improved variant of the <sup>13</sup>C-Methacetin breath test](#)

PLoS One **2013** Aug 15;8(8):e70780. doi: 10.1371/journal.pone.0070780. eCollection 2013

*Breath tests based on the administration of a <sup>13</sup>C-labeled drug and subsequent monitoring of <sup>13</sup>CO<sub>2</sub> in the breath are important tools in liver function diagnostics. The capability of such breath tests to reliably indicate hepatic CYP performance is limited by the fact that <sup>13</sup>CO<sub>2</sub> is not exclusively exhaled but also exchanged with other compartments of the body. Computer simulations suggest that the predictive power of the proposed 2DOB breath test to reliably quantify the CYP-specific hepatic detoxification activity should be significantly higher compared to the conventional breath test.*

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

[Quantitative determination of metabolism dynamics by a real-time <sup>13</sup>CO<sub>2</sub> 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 <sup>13</sup>CO<sub>2</sub>, 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.*

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

[Interpretation of non-invasive breath tests using <sup>13</sup>C-labeled substrates – a preliminary report with <sup>13</sup>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 <sup>13</sup>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

69. Stockmann M, Vondran FWR, Fahrner R, et al.

**[Randomized clinical trial comparing liver resection with and without perioperative assessment of liver function](#)**

BJS Open **2018** Jun 14;2(5):301-309. doi: 10.1002/bjs5.81. eCollection 2018 Sep

*Perioperative use of the LiMAx test improves postoperative management and reduces the incidence of severe complications, postoperative ICU stay, and postoperative hospital stay after liver surgery.*

70. Jara M, Reese T, Malinowski M, et al.

**[Reductions in post-hepatectomy liver failure and related mortality after implementation of the LiMAx algorithm in preoperative work-up: a single-center analysis of 1170 hepatectomies of one or more segments](#)**

HPB (Oxford) **2015** Jul;17(7):651-8. doi: 10.1111/hpb.12424

*Postoperative liver failure and postoperative liver failure-related mortality decreased in patients undergoing hepatectomy following implementation of the LiMAx algorithm.*

71. Lock JF, Reinhold T, Malinowski M, et al.

**[The costs of postoperative liver failure and the economic impact of liver function capacity after extended liver resection – a single center experience](#)**

Langenbecks Arch Surg **2009** Nov;394(6):1047-56. doi: 10.1007/s00423-009-0518-4. Epub 2009 Jun 16

*Postoperative liver failure is a relatively frequent and life-threatening complication after extended liver resection. This study describes the economic burden of PLF from the hospitals' perspective and explores the role of liver function capacity measured by the LiMAx test. Liver function capacity does not only predict postoperative liver failure but also correlates with total costs in general.*