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Combining Liver Function Parameters Identifies Patients with an Increased Risk for Complications after LVAD Implantation – A Pilot Study

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Abstract

Serious complications after Left Ventricular-Assist-Device (LVAD) implantation include Liver Dysfunction (LDF) and ultimately liver failure. Transaminases and bilirubin, which are commonly used, are poor indicators of successful outcomes. We sought to identify better suited parameters as successful outcome indicators in end-stage chronic heart failure patients with an LVAD-implantation indication.

This prospective controlled observational pilot study analyzed liver-function-tests in 58 patients with end-stage chronic heart failure and an LVAD-implantation indication. The primary endpoint was death from multiple organ failure (mostly liver dominated) within 30 days after LVAD-implantation. The secondary endpoint was risk-factor-evaluation for liver-associated death preoperatively and on day 3 after LVAD-implantation.

We found significant differences at baseline between survivors and non-survivors in gamma-Glutamyl Transferase (γ-GT), albumin as well as fibrosis and cirrhosis ($p \leq 0.039$). Alkaline-Phosphatase (AP) tended to be higher in non-survivors ($p=0.058$). We assigned these parameters points and calculated patients' LDF-risk. At least 3 abnormal parameters at baseline indicated a 50% death-risk after implantation. A high number of abnormal parameters suggested a high liver-associated mortality-risk. After LVAD-implantation, the abnormal parameter constellation differed from the preoperative one. On day 3, non-survivors had higher bilirubin and Glutamate-Dehydrogenase (GLDH) levels and MELD-XI-scores than survivors ($p \leq 0.014$). These are potential markers for disease assessment. All but one patient with a high-risk LDF prognosis died, but patients with low-risk survived LVAD-implantation.

Thus, combining preoperative γ-GT, AP, albumin, fibrosis, and cirrhosis and postoperative bilirubin, GLDH, and MELD-XI scores is promising to identify patients with an increased risk for severe liver-associated complications after LVAD-implantation.

Keywords: Ventricular assist device; Liver dysfunction; Chronic HF; VAD; LVAD; Heart failure

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Introduction

Heart Transplantation (HTx) is the gold standard treatment for end-stage Heart Failure (HF) [1]. However, there is a discrepancy between the number of donor organs available and the number of patients needing HTx, leading to some patients dying while on the waiting list. Therefore, the short- and long-term implantation of mechanical ventricular support systems (Ventricular-Assist-Device: VAD) are gaining importance to maintain end organ perfusion [1,2]. While VAD-implantation improves quality of life, physical performance, and patient's survival [3], severe postoperative complications including bleeding, infections, thromboembolic events, and multiple organ failure are a major concern [3-5]. A severe complication, which significantly worsens patients' outcome, is Liver Dysfunction (LDF) and ultimately liver failure [6,7]. Hepatic dysfunction is characterized by elevated transaminases, elevated bilirubin, and impaired coagulation and is often triggered by hepatic ischemia [8,9]. These disrupted parameters are a consequence of impaired perfusion due to

low cardiac output and elevated right-sided cardiac pressures. This in turn, results from vasoconstriction of the complete splanchnic nerve area causing insufficient oxygenation of centrilobular hepatocytes and, thus, cell necrosis [10].

Currently, it is impossible to preoperatively identify, which patient will develop LDF. Only few and inconsistent published data exist on this topic [11]. Liver function testing has mainly been studied in patients with stable chronic HF [11-15] and some in patients with VAD [16,17], while tests in patients with acute decompensated chronic HF are scarce [18-20]. The parameters that are used regularly to determine LDF are bilirubin and liver enzymes. However, their normal cut-off values are poorly suited to define liver function in cardiac insufficient patients, because in these patients the values are often already elevated at baseline. Additionally, bilirubin and liver enzymes do not adequately reflect the organ's complexity. Therefore, it is difficult to evaluate patients' outcome reliably and to initiate the necessary therapies using these parameters. In this study, we looked for more suitable parameters or helpful combinations to predict the outcome after LVAD-implantation.

Materials and Methods

Patients and study design

This prospective controlled observational pilot study included patients with end-stage chronic HF, who were treated with a LVAD-implantation. Patients age ≥ 18 years were electively admitted to our hospital or transferred from other hospitals. Patients were recruited from October 28th, 2011 to January 31st, 2013. We recruited as many patients as possible within this period. Sixty-one patients gave written informed consent. One patient died during aneurysm-surgery parallel to LVAD implantation and two died because of Right Heart (RH) failure and loss of vascular resistance during initiation of temporary RH-bypass-support on days 1 and 10. As these deaths were not liver-associated, these patients were excluded. The study conforms to the ethical guidelines of the Declaration of Helsinki and was approved by the Hannover Medical School ethics committee.

The primary endpoint was death from multiple organ failure (mostly liver dominated) within 30 days after LVAD-implantation. The secondary endpoint was evaluation of risk factors for liver-associated death preoperatively and on day 3 after LVAD-implantation.

Implantation of heart-assist-devices

A HeartWare Ventricular Assist Device (HVAD; HeartWare Inc., Miramar, FL, USA) or a HeartMate II Device (HM II; Thoratec, Pleasonton, CA, USA) was implanted by the surgeons of the department of cardiothoracic, transplantation and vascular surgery at the Hannover Medical School, Germany according to standard procedures.

Transjugular liver biopsy

If the patients' condition allowed, a Transjugular Liver Biopsy (TJLB) was performed. The liver was accessed *via* the right jugular vein and the superior vena cava. Biopsies were taken using an 18G Quick-Core biopsy set (Merit Medical Systems, South Jordan, UT, USA). The tissue was examined according to histologic standard procedures.

Liver function tests

Liver function was evaluated before and after LVAD-implantation. The tests included Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), ɣ-Glutamyl Transferase (ɣ-GT), Alkaline Phosphatase (AP), Total Bilirubin, total protein, albumin, Serum Cholinesterase (CHE), Glutamate Dehydrogenase (GLDH), Hyaluronic Acid (HA) [5], Indocyanine Green Plasma Disappearance Rate (ICG-PDR) and Retention Rate (ICG-R15; LiMON test system (Pulsion Medical Systems, Munich, Germany), as well as a score calculation according to the Model of End-Stage Liver Disease (MELD-XI-score). The MELD-XI-score (without INR values) was used because heart disease patients are often treated with anticoagulants, which leads to increased INR values [21]. Parameters were assessed as part of standard routine testing at baseline between days -1 to -7 before and days 1 to 21 after LVAD-implantation. Exceptions were albumin, ICG-PDR, and ICG-R15, which were measured at baseline and on days 7 and 21.

Ultrasound examination

Liver congestion was determined using ultrasound [22]. Ultrasonographic hepatic examinations were routinely performed in all patients at baseline and on days 7 and 21 by a "Deutsche Gesellschaft für Ultraschall in der Medizin" certified physician (www.degum.de) using the C4-1-array (Siemens Acuson S2000, Munich, Germany). The sonographer was blinded to all clinical data.

Sonographic signs of right-sided HF were assessed by measuring the diameter of the inferior vena cava and its associated respiratory fluctuation. Hepatic congestion was evaluated by measuring diameter, flow direction, flow velocity, and flow volume in the hepatic and the portal veins. Congestion was defined as the calculated diameter in the right hepatic vein >10 mm in combination with flow velocity from ≥ -10 cm/sec, flow pattern and velocity of the portal vein, and signs of portal hypertension.

Statistics

Statistical analysis was done using SPSS Version 26 (SPSS Inc., Chicago, IL, USA). P-values of ≤ 0.05 were considered significant. Means ± SD or SEM and medians were calculated. Difference between groups was assessed using the Chi-square- or Mann-Whitney-U-test, because no parameters followed a normal distribution. Effect size was analyzed according to Pearson. Values of r ≥ 0.3 were defined as moderate and values of r ≥ 0.5 as strong. Categorical data were compared with Fisher's exact test. Cut-offs was determined using ROC-Analysis (maximized Youden Index). The statistical methods of this study were reviewed by a biostatistician.

Results

Preoperative assessment

Fifty-eight patients were analyzed. Their baseline characteristics are given in Table 1. Patients were predominantly male, the mean age was 53 years, and about half had dilated cardiomyopathy. All patients had NYHA scores III or IV. Cardiac, renal, and lung parameters were not statistically significant for liver-associated mortality (p ≥ 0.080). Six patients demonstrated severe tricuspid insufficiency, of which three died of liver failure. Of the 31 patients with right HF, seven died.

The only clinical laboratory parameter that differed significantly preoperatively between survivors and non-survivors was the preoperative liver condition (p=0.012). Patients with a history of ECMO (not shortly before implantation) had an increased risk of liver-associated mortality (p=0.047). There were no significant differences in previous lung, kidney, thyroid, metabolic, or cardiac diseases nor in diabetes (p=0.457-0.950) (for details see Table A).

Table 1: Baseline characteristics[#].

	Survivors		Non-survivors				
		N	% of patients	N	% of patients	P-value	Effect size r
Gender	male	42	82.40%	6	85.70%	0.827	
	female	9	17.60%	1	14.30%		
Admission type	elective	47	92.20%	6	85.70%	0.572	
	urgent	4	7.80%	1	14.30%		
	emergency	0	0.00%	0	0.00%		
Ward pre-OP	ICU	12	23.50%	2	28.60%	0.787	
	intermediate Care	15	29.40%	2	28.60%		
	normal	24	47.10%	3	42.90%		
Mobility pre-OP	immobile	16	31.40%	4	57.10%	0.081	
	partially mobile	20	39.20%	3	42.90%		
	mobile	15	29.40%	0	0.00%		
Underlying liver disease.	none	50	98.00%	7	100.00%	0.711	
	virus hepatitis	1	2.00%	0	0.00%		
Most recent liver histology	normal	42	91.30%	4	57.10%	0.012	0.34
	fibrosis	2	4.30%	1	14.30%		
	cirrhosis	2	4.30%	2	28.60%		
Liver congestion	no	15	37.50%	0	0.00%	0.071	
	yes	25	62.50%	6	100.00%		
BMI (≤ 18 or ≥ 30)		17	33.30%	5	71.40%	0.053	0.25
NYHA	NYHA III	25	49.00%	1	14.30%	0.086	0.23
	NYHA IV	26	51.00%	6	85.70%		
ECMO history	no	48	94.10%	5	71.40%	0.047	0.26
	yes	3	5.90%	2	28.60%		
Laboratory tests*		Median	Min-Max	Median	Min-Max	P-value	Effect size r
AST (U/l)		32	16-125	31	24-52	0.99	
ALT (U/l)		25	4-494	22	9-62	0.474	0.3
ɣ-GT (U/l)		101	13-466	184	11-500	0.022	0.25
AP (U/l)		88	36-530	122	80-321	0.058	
Bilirubin (µmol/l)		18	4-92	22	17-58	0.214	
CHE (kU/l)		5	1.41-11.50	3.7	2.35-5.53	0.107	
GLDH (U/l)		3	1-19	3	2-8	0.844	
Albumin (g/l)		32	18-44	28	19-32	0.039	0.27
Protein (g/l)		63	45-81	60	48-72	0.227	
HA (mg/dl)		114	6.2-1127.8	144	98.5-654.4	0.21	
MELD-XI		13	6-33	12	10-26	0.533	
ICG-PDR (%/min)		8.4	2.1-28.2	7	2.1-14.0	0.4	
ICG-R15 (%)		28.4	1.5-66.9	35	12.2-73.0	0.359	

[#]Significant differences between survivors and non-survivors are shown in bold print and are highlighted in grey. Borderline significant differences, where the significance would become clear if a larger patient collective were analyzed, are depicted in bold print.
Mobility is defined as: immobile = patient is bedridden, partially mobile = patient can leave the bed, and mobile = patient can leave the room; *n=51 for all parameters except AP (n=50) as well as ICG-PDR and ICG-R15 (both n=49).
Pre-OP: Preoperative, BMI: Body Mass Index, ICU: Intensive Care Unit, tox.: Toxic, NYHA: New York Heart Association; ECMO: Extra Corporal Membrane Oxygenation; Min: Minimum; Max: Maximum

Mobility, liver congestion, NYHA, and extreme BMI (≤ 18 or ≥ 30) (all <0.100) approached significance.

When taking laboratory values into account, surviving and deceased patients differed significantly in their ɣ-GT (p=0.022) and albumin (p=0.039) levels; AP was close to significance (p=0.058).

Cut-offs was obtained *via* ROC-Analysis: ɣ-GT ≥ 109 U/l (p=0.012), AP ≥ 96.5 U/l (p=0.045), albumin ≤ 30.5 g/l (p=0.042), which led to 0 or 1 point in risk stratification (Figure 1A). The state of the liver also affects the prognosis. Therefore, 1 point was added for fibrosis and 2 points for cirrhosis. Thus, a maximum of 5 risk points was possible (ɣ-GT, AP, albumin, and fibrosis or cirrhosis).

Table A: Sensitivity and specificity for ROC curve analysis (maximized Youden-Index).

Parameter	Cut-off	Sensitivity	Specificity
Pre-OP			
AP	96.5	0.857	0.431
γ-GT	109	1	0.471
Albumin	30.5	0.857	0.412
Post-OP			
Bilirubin	28.5	1	0.314
GLDH	3.5	1	0.294
MELD-XI	17	1	0.392

All deceased patients had at least 3 points. Consequently, a result of 3 or more points meant that the patients' risk of death was about 50% (Figure 1B).

Twenty-one patients received a TJLB of whom 18 patients had a successful biopsy. Sixteen patients (89%) had liver congestion, of who two died. Six patients (33%) demonstrated moderate fibrosis, and one died. Only one patient (6%) was diagnosed with cirrhosis and this patient died.

Postoperative assessment

Deceased patients showed significantly greater changes in bilirubin, AST, ALT, LDH, ICG-PDR, ICG-R15, HA, MELD XI, GLDH, protein, and creatinine during the course of 21 days after the LVAD-implantation than surviving patients (Table 2).

When analyzing the postoperative course, the third day was the earliest time point at which survivors and non-survivors demonstrated a clear and consistent difference between parameters. Thus, the subsequent results refer to day 3.

The liver function test values on day 3 are shown in Table 3. Surviving and deceased patients differed significantly in their bilirubin, AST, γ-GT, GLDH, MELD XI, and HA values.

Cut-offs was obtained *via* ROC-Analysis: Bilirubin ≥ 28.5 µmol/l (p=0.001), AST ≥ 64.5 U/l (p=0.010), γ-GT ≥ 95.0 U/l (p=0.019), GLDH ≥ 3.5 U/l (p=0.001), MELD XI ≥ 17 (p=0.003), and HA ≥ 318.0 mg/dl (p=0.000), which led to 0 or 1 point in risk stratification (Figure 2 A). Of these, HA was excluded, because it is not a standard routine test, AST, because a definite cut-off could not be determined, and γ-GT as well as LDH, because their r-values were below 0.3. Thus, a maximum of 3 points was possible (bilirubin, GLDH, and MELD-XI). All deceased patients showed 3 points. A result of 3 indicated a death risk of about 50% (Figure 2B).

Fifteen patients were considered preoperatively as patients at risk of not surviving the LVAD-implantation (≥ 3 risk points). After reevaluation of these patients, the abovementioned parameter constellation (bilirubin, GLDH, and MELD-XI) on postoperative day 3, indicated a correct prognosis in 14 patients (p=0.009). One patient who had a high-risk prognosis survived. None of the patients with preoperative scores less than 3, thus belonging to the group with low risk, died after the operation.

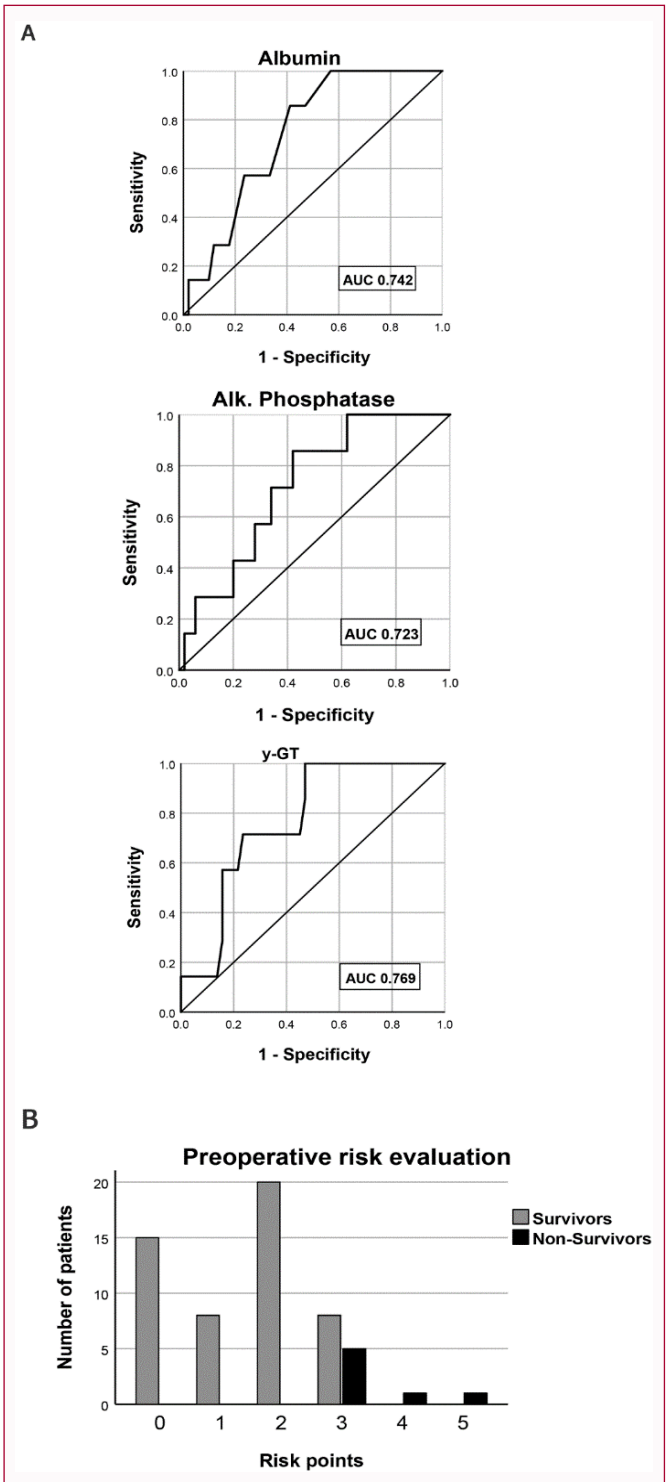

Figure 1: Preoperative analysis: A) ROC curve for AP, γ-GT, and albumin (for details see Table A in Supplemental online material) and B) a diagram depicting the number of patients with scores from 0 to 5. Survivors are shown in grey and non-survivors in black.
AUC: Area Under the Curve

Discussion

Patients with a high risk of LDF show an increased mortality after LVAD-implantation despite a successful surgical procedure [16,17]. Therefore, we studied whether the LDF-risk can be identified while planning the LVAD-indication. We ultimately decided to use routine tests as risk parameters where the results are easily and rapidly available.

Our results show that there is not a single prognostic factor

Table 2: Clinical parameters for survivors *vs.* non-survivors over the postoperative course of 21 days*.

	Survivors			Non-survivors			P-value	Effect size r
	Median	Minimum	Maximum	Median	Minimum	Maximum		
Bilirubin (µmol/l)	33	10	191	185	36	744	0.002	0.41
AST (U/l)	86	34	997	3920	55	7234	0.002	0.41
ALT (U/l)	36	13	1506	782	23	1975	0.004	0.38
γ-GT (U/l)	158	35	1051	133	73	385	0.685	
AP (U/l)	164	84	518	118	93	339	0.364	
CHE (kU/l)	3.48	1.64	7	2.93	1.83	4.34	0.334	
LDH (U/l)	574	278	1370	3106	503	5469	0.001	0.43
ALT/LDH	0.04	0	0.09	0.04	0.01	0.11	0.747	
ICG-PDR (%/min)	12.85	3.4	33.1	3.35	1.9	4.3	0.002	0.41
ICG-R15 (%)	14.9	0.7	73	61	52.5	75.2	0.003	0.39
HA (mg/dl)	184.5	35.58	2596.45	1239.8	325	13988	0.001	0.43
MELD-XI	17	9	38	38	24	45	0	0.51
GLDH (U/l)	5	2	623	289	6	982	0.001	0.44
Protein (g/l)	49	36	62	43	39	48	0.015	0.28
Albumin (g/l)	23	15	29	22	17	26	0.179	
Creatinine (µm/l)	135	55	907	222	147	297	0.008	0.35

*Significant differences between survivors and non-survivors are shown in bold print and are highlighted in grey. Only the most abnormal values measured from each patient were included

Table 3: Postoperative clinical parameters of survivors *vs.* non-survivors on day 3*.

	Survivors			Non-survivors			P-value	Effect size r
	Median	Minimum	Maximum	Median	Minimum	Maximum		
Bilirubin (µmol/l)	20	6	191	65	29	194	0.004	0.37
AST (U/l)	53	24	367	151	54	395	0.004	0.38
ALT (U/l)	25	10	644	46	19	246	0.152	
γ-GT (U/l)	60	18	197	105	55	277	0.032	0.28
AP (U/l)	79	42	225	91	56	289	0.608	
CHE (kU/l)	4.13	1.85	8.59	4.48	3.23	6.25	0.535	
GLDH (U/l)	3	1	470	6	4	55	0.001	0.43
LDH (U/l)	445	197	768	757	328	969	0.041	0.27
Protein (g/l)	54	41	67	54	45	62	0.765	
Creatinine (µm/l)	102	40	522	132	59	220	0.34	
HA (mg/dl)	151.17	23.54	2459.65	443.72	321.93	13988	0.006	0.36
MELD-XI	12.8	9.44	35.02	23.1	17.02	38.16	0.014	0.32
AST/ALT	2.14	0.53	4.7	3.1	1.46	5.64	0.201	
ALT/LDH	0.06	0.02	0.98	0.06	0.04	0.3	0.808	

*Significant differences between survivors and non-survivors are shown in bold print and are highlighted in grey

that can predict liver-associated mortality preoperatively. This fact is also confirmed by many publications, which have included clinical parameters [12,14,21]. In our study, there was a preoperative tendency for BMI (≤ 18.5 or >30), impaired mobility, NYHA IV, history of ECMO, or other parameters with p-values <0.09 to indicate an increased risk. Ultimately, it is the number of abnormal parameters that is important, not an individual one. If the number of these existing parameters is high, there is an increased risk of liver-associated postoperative mortality-risk. We will first discuss the individual parameters we analyzed.

Two enzyme profiles have been reported previously in patients with end-stage chronic HF: Increased hepatocellular enzymes (AST, ALT) or increased cholestatic enzymes (γ-GT, AP) and bilirubin [23]. Sometimes a mixed profile is observed [13]. In our study, the deceased patients demonstrated mainly a cholestatic enzyme profile in combination with decreased albumin levels before VAD-placement, supporting previous studies [10,17,19,22-24]. This suggests that γ-GT and AP played a more important role in our collective than transaminases, indicating cell integrity.

An increase in γ-GT and AP induced by enzyme synthesis is reported to be accompanied by an increase in bilirubin [26]. This was only partially confirmed in our cohort at baseline. We saw a more pronounced increase in γ-GT than in AP, reflecting that biliary epithelial cells and bile ducts are sensitive to elevated liver vein

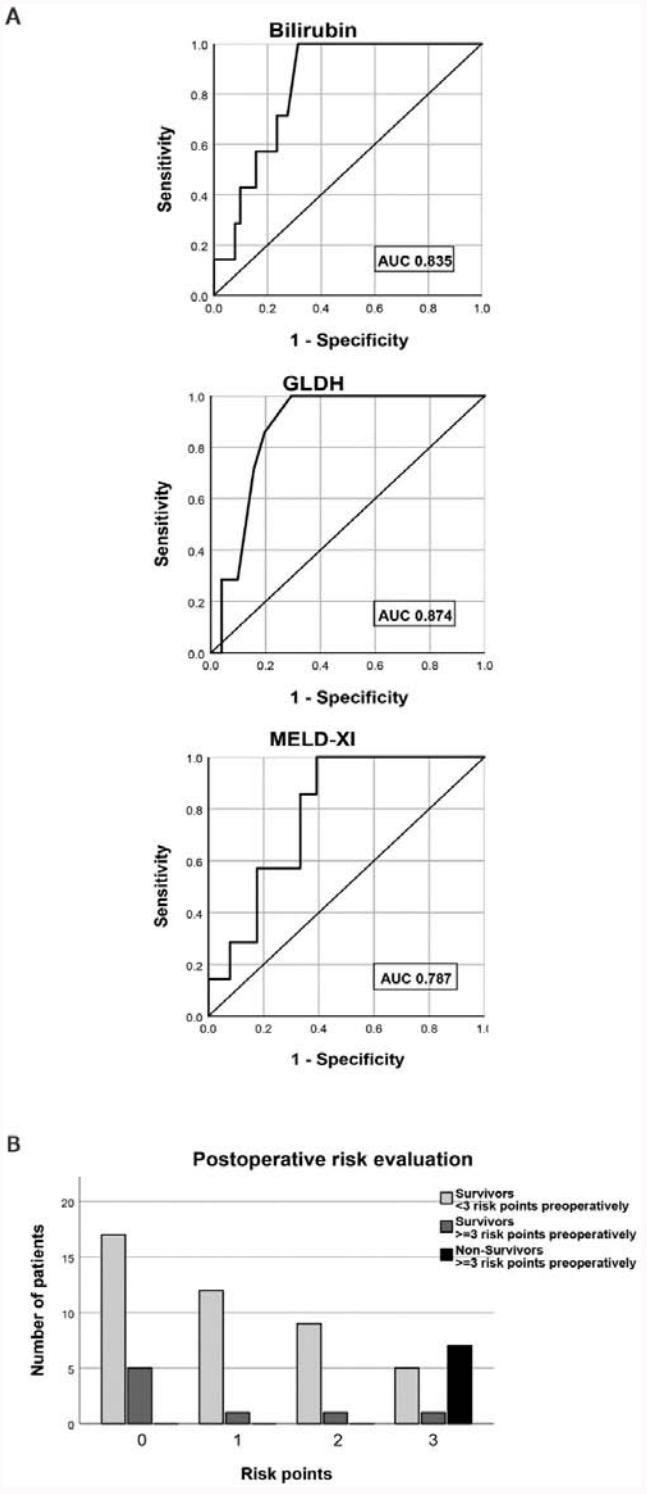

Figure 2: Postoperative analysis on day 3: A) ROC curve of bilirubin, GLDH, and MELD-XI (for details see Table A in Supplemental online material) and B) a diagram depicting the number of patients with risk points from 0 to 3 postoperatively. Survivors are shown in grey and non-survivors in black. AUC: Area Under the Curve

pressure and the resulting congestion.

Right HF with backward failure that causes systemic congestion has been reported to be associated with an increase of cholestatic parameters [27]. Most of our patients demonstrated hepatic congestion, which is in line with these findings.

In our study, three of seven non-survivors had severe tricuspid insufficiency, indicating that this parameter may be a risk factor of postoperative mortality. However, the number of patients is too small to demonstrate statistical significance.

Albumin is considered an independent outcome predictor after LVAD-implantation, and is included in preoperative risk scores [9,28,29]. Lau et al. [26] found that reduced albumin concentrations are not influenced by hemodynamic parameters. In our study, 80.3% of all patients had preoperative hypoalbuminemia, but there were no significant differences in hemodynamic parameters between survivors and non-survivors, confirming Lau et al. [26] findings.

The ICG-PDR was below the limit given in the literature in 86% of our patients (data not shown). Survivors as well as non-survivors showed reduced ICG-PDR at baseline, but values were not significantly worse in the latter. Other studies in critically ill patients found similar values [20-32]. ICG-PDR values were different postoperatively between survivors and non-survivors over the course of the study (p=0.002; Table 2). Unfortunately, we did not assess ICG-PDR on day 3. Therefore, additional studies are needed to elucidate whether it is suitable as a prognostic factor. Vos et al. [33] report that reduced ICG-elimination may be caused by cholestasis [33]. Thus, ICG-PDR does not seem to give additional preoperative information for the risk assessment in comparison with the simple determination of cholestatic parameters (bilirubin and γ-GT), and it is not a routine test.

HA is reported to be a fibrotic conversion biomarker in chronic liver disease [5,34]. Kalay et al. [35] demonstrated increased HA levels in chronic HF patients. Most of our survivors and non-survivors had elevated HA levels, although most of them showed no fibrosis or cirrhosis. The reason for this could be liver congestion. However, high HA levels are also found in other diseases. Therefore, HA is not suitable as a preoperative risk factor. In addition, it is not a routinely performed test.

Our study indicates that a TJLB before LVAD-implantation does not give additional information on the patient's prognosis. The results of the histopathologic examination for fibrosis and cirrhosis merely confirmed the diagnosis that had already been made using other clinical methods (sonography, acoustic radiation forced impulse imaging). In addition, the TJLB technique has interventional risks such as bleeding or coagulation problems and requires greater technical efforts and expenses.

The MELD-XI score is an independent predictor for cardiac and overall mortality [36]. A retrospective analysis by Yang et al. [21] showed that 38.4% of the patients with advanced HF had a preoperative MELD-XI score ≥ 17 and that this predicts patients' outcome. We saw no differences in the MELD-XI scores before the LVAD-implantation. However, on day 3 after surgery, survivors and non-survivors differed significantly. The MELD-XI score increased continuously in non-survivors. Several studies also showed that patients with high postoperative scores have a higher postoperative mortality-risk [21,37]. Thus, MELD-XI is only suitable as a postoperative predictor.

Preoperative and postoperative parameters must be evaluated separately, because aside from the underlying chronic HF, the LVAD-implantation itself can induce LDF or can worsen an already existing LDF [6]. This results in different preoperative and postoperative risk parameter constellations.

Nishi et al. [38] reported that day 3 after surgery is a suitable time point to reevaluate patients and assess their further prognosis. After analyzing the course of important parameters in our cohort, day 3 was confirmed as the first day after surgery at which significant parameters (GLDH, bilirubin, and MELD-XI) differed clearly between survivors and non-survivors. The combination of bilirubin, GLDH, and MELD-XI on day 3 postoperatively was best suited to identify a critical clinical course early on. Although an artificial heart improves the patient's hemodynamics, up to 94% of patients develop LDF [10]. It is often diagnosed with delay [39], is difficult to treat, and frequently leads to multi-organ failure [40]. LDF was the main cause of death in our cohort. It seems that the detoxification function, as indicated by hyperbilirubinemia, remains impaired. The severity of the liver damage is shown by the increased release of GLDH from the mitochondria of the cells in the centrilobular area. This region is very vulnerable to hypoxia, particularly severe circulation failure and right heart insufficiency [41].

Especially the combination of preoperative reduced liver function and the additional postoperative inflammation could mean an increased risk for liver-associated multi-organ failure after LVAD-implantation.

Our results demonstrate that hepatic congestion is not a general contraindication for VAD-implantation. However, the LDF warning signs at baseline should be taken seriously. The risk stratification for patients with cardiac-induced hepatopathy is only possible if selected parameters are combined. The combination of liver function tests (γ-GT, AP, albumin) and the preoperative diagnosis of an existing liver fibrosis or cirrhosis help to identify patients with an increased risk for hepatic deterioration and mortality after LVAD-implantation. When the LVAD indication is assessed, liver function may help to decide, whether a permanent (RH-bypass-therapy, Venoarterial 3) or temporary (biventricular assist device) right ventricle support may be necessary. This could avoid further right ventricular deterioration with additional burden for the liver (e.g., through high doses of vasopressors and through venous congestion in combination with low cardiac output) and prevent jeopardizing the outcome. After LVAD-implantation, other parameters are more important for risk assessment (bilirubin, GLDH, and MELD-XI). Day 3 after surgery proved to be the best time point to identify a potential liver failure with the chance to choose a successful intervention for prevention.

Our study has some limitations. The number of patients is small due to the limited number of LVAD-implantations that are done to bridge heart transplantations. In addition, patients' underlying diseases were heterogeneous, which is also owed to the fact that the collective is small. Our patient collective and the devices that were implanted are dated. However, the data are comparable to implantations with the new generation HeartMate III. The latter is said to cause less thrombosis and is smaller. However, at the Hannover Medical School, thrombosis was not a problem with the HeartMate II device. In addition, the new generation HeartMate can simulate a pulse, which we believe does not play a crucial role for liver failure risk. This could be looked at in a future study. Also, the study does not look at the heart, which would be directly affected by the type of device.

Conclusion

Combining different routine parameters preoperatively and close postoperative monitoring of patients at risk starting on day 3 could improve the success of LVAD-implantations. This is a potentially promising approach that needs further investigation in a larger patient cohort.

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