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BRIEF REPORT

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Assessment of ventricular contractile function during orthotopic liver transplantation

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Abstract Hemodynamic alterations are a well-known phenomenon that influence the outcome of orthotopic liver transplantation (OLT). Whether or not myocardial dysfunction, which has various causes, contributes to this instability is still debated. Previous transesophageal echocardiography (TEE) studies have presented controversial data, not leading to final clarification. This is mainly because the impact of other contributing factors (inotropic support, alternating preload conditions and temperature) remained unaccounted for. We therefore measured the left ventricular shortening fraction (LVSF), a parameter reflecting myocardial contractility, in 10 consecutive patients undergoing OLT without veno-venous bypass. We measured during preparation (PP), during the anhepatic (AP) phase and the immediate reperfusion phase (RP). During the AP we observed a significant decrease of LVSF which never fell to subnormal levels in the majority of our patients, whereas during the RP, LVSF returned to PP values. These findings support the assumption that myocardial function is influenced by OLT, but that it plays only a minor role in the occurrence of hemodynamic instability, which could mainly be attributed to volume fluctuations.

Keywords Orthotopic liver transplantation · Ventricular function · Echocardiography-shortening fraction

Abbreviations *AP* Anhepatic phase · *CI* Cardiac index · *EF* Ejection fraction · *HR* Heart rate · *LVSF* Left ventricular fractional shortening · *MAP* Mean arterial pressure · *OLT* Orthotopic liver transplantation · *PP* Preparation phase at hemodynamic stability · *RP* Reperfusion · *TEE* Transesophageal echocardiography

Introduction

During orthotopic liver transplantation, (OLT) dramatic and acute hemodynamic instability may occur, especially during the anhepatic phase (AP) and immediately after reperfusion (RP) of the liver graft [1, 2]. These instabilities are said to have several causes, which are clinically marked by systemic hypotension, bradycardia, and pulmonary hypertension [2]. The most widely discussed of these is myocardial dysfunction.

There is evidence that the AP may lead to an accumulation of cardiodepressant substances in the circula-

tion, as it occurs in patients with end-stage hepatic failure [3, 4]. Furthermore, the cold, acidotic and hypercalemic fluid washed out of the liver graft after reperfusion contains inflammatory mediators, some of them identified as potential myocardial depressant factors [1, 3, 4, 5, 6, 7, 8]. Conventional systemic hemodynamic monitoring including cardiac output measurements also supported the hypothesis that myocardial function plays an influential role.

However, the possibility to analyze the changes in circulating volumes and the contractile function of the heart has reaped controversial results [2, 7, 8]. Transesophageal echocardiography (TEE), used as an intraoperative monitoring tool, provides direct visual access to the heart, thereby elucidating a few of the speculations about the contribution of myocardial dysfunction to hemodynamic instability during OLT. Impaired left ventricular function and alterations in ventricular compliance were found by Estrin et al. [7], whereas DeWolf et al. [1] and De La Morena et al. [2, 9] found no evidence of impaired myocardial function and attributed instability to other factors, such as insufficient increase in preload. However, none of these studies distinguish between loading conditions, ventricular diameter, or peripheral vascular resistance.

In patients undergoing coronary artery bypass grafting, left ventricular fractional shortening (LVSF) is a clinically established and reliable surrogate parameter of ventricular contractility independent of inotropic support, alternating preload conditions and temperature. We therefore aimed to evaluate left ventricular contractility during OLT in ten end-stage liver disease patients by examining the echocardiographically determined ejection fraction (EF) and LVFS during different various phases of grafting.

Materials and methods

After approval by the institutional review board and with the patients' informed consent, ten consecutive patients undergoing OLT surgery without veno-venous bypass were enrolled in the study. Preoperative echocardiographic assessment of heart function was performed according to a protocol. Patients with impaired cardiac function, valvular heart disease, obvious arrhythmies and evidence of pulmonary hypertension or preexisting pulmonary disease other than the common symptoms of end stage liver dysfunction were not enrolled. Anesthetic management was performed as described in detail previously [10]. Two anesthesiologists familiar with the study followed all the patients in order to decrease bias related to varying anesthetic management. After induction of anesthesia, routine TEE was performed using a 5 MHz two-dimensional transesophageal echo-probe (Hewlett Packard Sonos 2500, HP, USA). The probe was advanced through the esophagus to the position in which the cross sectional plane (short axis view) of the left ventricle was obtained at the level of the papillary muscles, as well as a longitudinal four-chamber view. The sequences were recorded on videotape during the various stages of the procedure: during preparation phase at hemodynamic stability (PP), at the anhepatic phase (AP) before opening of the anastomoses, and immediately after reperfusion (RP). After the procedure, blinded independent investigators analyzed the TEE tapes, calculated EF according to Simpson's rule and LVSF/Δ% from the left ventricular enddiastolic area – the left ventricular endsystolic area / left ventricular enddiastolic area *100.

Statistical analysis

Data are expressed as mean ± SD unless otherwise indicated. Data of the various time points were compared using ANOVA analysis for repeated measurements. $P \leq 0.05$ was considered statistically significant.

Results

Ten consecutive patients (7 male/ 3 female, mean age 48.2 + 6,) underwent OLT for posthepatitic cirrhosis ($n = 5$), alcoholic cirrhosis ($n = 3$), primary biliary cirrhosis ($n = 1$) or Morbus Wilson ($n = 1$). Systemic hemodynamic data and echocardiographic indices are shown in Table 1.

We observed an approximately 50% decrease in cardiac index (CI) during AP in accordance with a significant decrease in mean arterial pressure (MAP) and an increase in heart rate (HR) compared to PP values. These changes were paralleled by a significant increase in oxygen extraction rate as measured with SvO2. Systemic vascular resistance indices increased significantly during this period. Reperfusion led to an increased CI above baseline, increased central filling pressures (CVP, PAOP, MPAP), and significant decline in vascular resistance indices. Patients presented with high range ejection fractions, corresponding to their hyperdynamic situation, which remained statistically unchanged throughout the procedure.

Table 1 Hemodynamic data and echocardiographic indices of ventricular function during the three phases of orthotopic liver transplantation. *PP* Preparation Phase; *AP* Anhepatic Phase; *R* Reperfusion * statistically significant difference to PP

Hemodynamic data			
Heart rate beats.min^{-1}	91 ± 17	110 ± 22	98 ± 16
Cardiac output l.min^{-1}	3.8 ± 1.2	1.9 ± 0.7*	4.5 ± 1.6
Mean arterial pressure mmHg	77 ± 14	62 ± 9*	64 ± 14
Mean pulmonary arterial pressure mmHg	15 ± 5	13 ± 5	22 ± 5*
Central venous pressure mmHg	8 ± 4	7 ± 4	11 ± 5*
Pulmonary artery occlusion pressure mmHg	8 ± 3	6 ± 4	11 ± 4
Mixed venous oxygen satturation SvO2%	82 ± 67	71 ± 10	81 ± 10
Systemic vascular resistance SVRi dyn.s.cm^{-5}	790 ± 194	1271 ± 228*	612 ± 257
Echocardiographic indices			
Ejection fraction %	81 ± 9	71 ± 13	69 ± 11
Left ventricular fractional shortening %	51 ± 13	36 ± 10*	53 ± 15

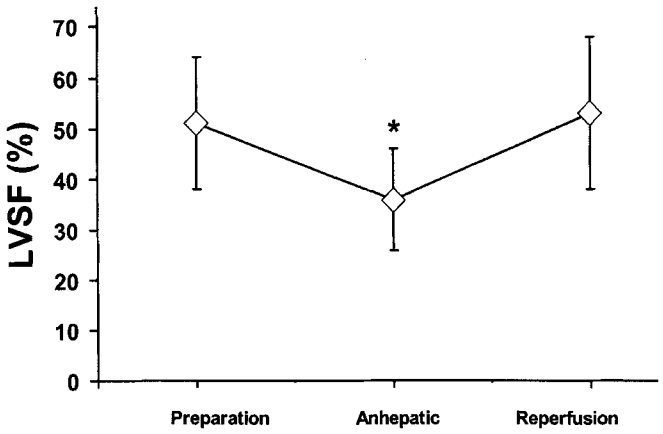

Fig. 1 *LVFS* Left ventricular fractional shortening as an indicator of ventricular contractility during three phases of orthotopic liver transplantation (OLT). *x-axis* phases of OLT, *y-axis* percentage (%) of LVFS

LVSF decreased significantly during AP without reaching subnormal or dramatic values. Reperfusion led to a restoration towards PP values (Fig. 1).

Discussion

The findings of our TEE study confirm previous evidence of maintained myocardial function during OLT [2]. We found significant alterations of systemic hemodynamics in accordance with minor changes of ventricular EF. LVSF reflecting myocardial contractility decreased significantly during AP but tended towards a subnormal value in only one patient.

With the introduction of TEE as a direct intraoperative monitor of the heart, some speculations as to whether altered left or right ventricular function play a role in the systemic hemodynamic changes during OLT have been solved [5, 9, 11]. Nevertheless, especially the analyses of contractile function and circulating volumes, which are of concern in the diagnosis of the ischemia-reperfusion syndrome, remain debated [4, 10, 11]. Despite significant alterations of systemic hemodynamics, we observed maintained EF values throughout the procedure that could at least be attributed to well-adjusted fluid and catecholamine management.

We found a normal LVSF during RP, but a significant drop during the AP, which returned to normal PP values during RP. This could be explained by one or a combination of the following: a reduced clearance of myocardial depressant factors during AP; secondly, the fall in MAP in combination with a reduced back-flow due to caval cross-clamping, which could have compromised blood flow to the coronary arteries as well.

With regard to experimental data showing a myocyte depression by plasma obtained during OLT and the reported clinical evidence of prolonged hemodynamic perturbation in combination with limited ventricular function in some patients after OLT [4, 7], direct effects of so-called myocardial depressant factors on myocardial function can not be completely excluded. Hence, we speculate that in vivo, sufficient mechanisms exist to mitigate these effects and/or that not all of the patients undergoing OLT are prone to such effects. Two findings would support this assumption: Firstly, we never observed discerning subnormal values, even during the significant AP decrease. Secondly, the remaining normal values of EF and LVSF during reperfusion contradict assumptions that myocardial dysfunction is a major cause of ischemia-reperfusion syndrome.

We are aware that the lack to clarify how released cytokines, undetected previous myocardial damage or inadequate volume management contributes to myocardial depression during OLT might be seen as a limitation of our study. Myocardial function assessment using contractility reflecting factors (unlike sole EF interpretation) could help to identify patients carrying a notable risk for hemodynamic disturbances potentially influencing surgical success and outcome negatively. Unfortunately, it would go far beyond the limits of this brief report to clarify this issue, but it could be an incentive for further studies.

In conclusion, our findings confirm the assumption that myocardial contractility is maintained during orthotopic liver transplantation in patients without pre-existing cardiac limitations. Observed hemodynamic alterations during OLT might be attributed to volume shifts during the procedure, although the release of myocardial depressant factors during certain phases of OLT might contribute. It may additionally underline that adequate intraoperative management can help to mitigate hemodynamic effects attributable to the release of myocardial depressant factors.

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