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Research Article

Intra-Operative Assessment of Cardiac Power Index in Liver Transplantation: The Impact on Post-Operative Myocardial Injury and Short-Term Outcomes

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Keywords

- Liver transplantation
- Haemodynamic monitoring
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Abstract

Background and Objectives: Despite comprehensive preoperative cardiovascular assessment, cardiovascular events remain a leading cause of postoperative mortality, due to the complexity of liver transplantation surgery. Therefore hemodynamic monitoring during liver transplantation is crucial. With PICCO (Pulse Index Continuous Cardiac Output) technology, hemodynamic parameters such as cardiac power index (CPI) can be follwed during surgery. The aim of this study is to investigate the relationship between CPI and postoperative secondary myocardial infarction.

Method: A total of 53 patients were included in the study. Patients divided into two groups according to the presence or absence of myocardial injury following liver transplantation.

Results: Postoperative myocardial injury (PMI) was observed in 28.3%(n=15) of these patients. ΔCPI was significantly lower in patients with PMI (-0.27 ± 0.11 W/m²), than those without PMI (0.08 ± 0.18 W/m²) ($p<0.05$). The multivariate analysis showed that the only independent predictor of PMI was ΔCPI (HR: 2.245, 95% CI: 1.145 – 4.387, p: 0.032). ROC analysis that revealed ΔCPI values lower than -0.15 W/m² were significantly associated with PMI. Peak troponin level, hospital stay and myocardial infaction prevelance were significantly higher in ΔCPI ≤ -0.15 W/m² group (all $p < 0.05$).

Conclusion: Our data shows that ΔCPI which constitutes the decrease in CPI during transition from the anhepatic phase to the neohepatic phase, can be used as a marker of poor cardiac prognosis in patients who underwent liver transplantation

INTRODUCTION

Cardiovascular events are among the leading causes of mortality in liver transplant(LT) patients [1]. Thus, screening for cardiovascular diseases play a significant role in the pretransplant evaluation. However, as it is a complex procedure and is characterized by hemodynamic instability, even patients without cardiovascular pathology are at the risk of myocardial ischemia during the procedure.

With close hemodynamic monitoring using sophisticated devices and early intervention of patients during LT, cardiovascular collapse can be prevented. Arterial pulse contour analysis and the thermo-dilution technique (PICCO) is one of these devices and it has been proven to be a reliable monitoring technique that plays a significant role in decision making [2,3], With PICCO (Pulse Index Continuous Cardiac Output) technology, many hemodynamic parameters can be followed. One of them is the cardiac power index (CPI). The ability of cardiac pumping can be represented by cardiac power output (CPO) and it is the product of mean arterial pressure (MAP) and CO. Cardiac power index (CPI) is CPO indexed to body surface area. In clinical studies it has been found to be the strongest independent predictor of hospital mortality in cardiogenic shock patients [4].

Previous studies showed that the presence of postreperfusion syndrome independently predicted postoperative myocardial injury after LT. The diagnosis of post-reperfusion syndrome is determined by examining the changes in MAP. CPI, on the other hand, provides information about cardiac contractility beyond MAP. Therefore, we considered that CPI might be a better indicator of postoperative myocardial damage. As a result, in this study, it was planned to investigate the

relationship between intraoperative CPI and postoperative secondary myocardial infarction. Our hypothesis was that by retrospectively evaluating relationship between intraoperative CPI and postopreative cardiac troponin I(cTnI) levels, it may be possible to identify patients who are at the risk of postoperative myocardial injury in early stages.

METHODS

Patients who underwent coronary angiography as part of LT preoperative evaluation, from 2017 to 2021 at a single medical center and found not to have critical coronary lesion were included in this retrospective cohort study. The decision to proceed with angiography was based on a previously published protocol [5]. Patients with a history of coronary artery disease(CAD), coronary revascularisation, heart failure and significant arrythmia were excluded. Our aim was to investigate the impact of changes in CPI during the surgical procedure on myocardial perfusion, so we excluded patients already have cardiac disease or coronary artery disease, as we believed it could affect the results.

During surgery, in addition to noninvasive monitoring, patients were received invasive radial artery catheter and central venous catheter via internal juguler vein. For hemodynamic monitoring, a 5F catheter (Pulsiocath®; Pulsion Medical System, Munich, Germany) inserted through right femoral artery and connected to the PICCO2® system in all patients. The measurements were performed by transpulmonary thermodilution method by injecting 15 mL cold saline (8ºC) through the central venous line. It was indexed by each patient's estimated body surface area.

Data collection

Hemodynamic volumetric parameters monitored by the PiCCO system were collected simultaneously at four timepoints including after anesthesia induction (T1), anhepatic phase (T2), the 30th minute of the neohepatic phase (T3) and the end of the neohepatic phase (T4) with at least three measurements made in each phase. The average of these measurements was used. Parameters monitored by the PiCCO system were cardiac index (CI), extravascular lung water index (ELWI), systemic vascular resistance index (SVRI) and stroke volume variability (SVV) values. They were recorded together with mean arterial pressure (MAP) and central venous pressure (CVP) measurements.

Baseline demographical characteristics and mortality data were obtained from medical records. Cardiac mortality was defined as death attrituable to myocardial infarction, heart failure and/or arrhythmias. Demographics, pre-existing comorbid conditions and serum troponin levels were recorded manually. MELD (Model for End-stage Liver Disease), score and RCRI (Revised Cardiac Risc İndex), calculation were based on patients clinical and laboratory findings.

Postoperative MI was diagnosed as a rise and/or fall of cTnI values with at least one of the following: the presence of typical angina, the presence of new ischemic findings on the ECG and detection of wall motion abnormalities on echocardiography.

Ethics

This study protocol was approved by Medipol University Faculty Hospital ethics committee. Informed consent was obtained from all patients before any study-related procedures and the study was conducted in accordance with the latest version (2013) of Declaration of Helsinki. There isn't any ethical considerations related to the study.

Clinical outcome

The primary endpoint of the study was type 2 myocardial injury. Secondary end-points were duration of hospital stay, cardiac and all-cause mortality. The vital status of patients was ascertained by review of discharge summaries and death notes in the electronic health record.

Type 2 myocardial injury was defined as a rise and/or fall of cTn values with at least one value above the 99th percentile URL and evidence of an imbalance between myocardial oxygen supply and demand unrelated to acute coronary athero-thrombosis, requiring at least one of the following: Symptoms of acute myocardial ischaemia; New ischaemic ECG changes Development of pathological Q waves; Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic aetiology [6]. Cardiac mortality was defined as death attributable to myocardial ischemia and infarction, heart failure or cardiac arrest because of other or unknown causes.

ΔCPI is the difference between CPI-3(neohepatic phase) and CPI-1(pre-anhepatic phase). As ΔCPI is a negative value, lower ΔCPI indicates a large gap between CPI-3 and CPI-1.

STATISTICAL ANALYSIS

Statistical analyses were conducted with the use of SPSS (version 17.0; SPSS, Chicago, Illinois). Data were expressed as percentage for categorical variables and as mean ± SD for continuous variables. Shapiro-Wilk test was

conducted to test for normal distribution. Comparisons among continuous variables were performed by using the Student t test and Mann-Whitney U test for independent samples that show normal and non-normal distribution respectively. Associations of the categorical variables between groups were determined with the use of chi-square test. Statistical significance was defined as a p value < 0.05 for all comparisons. Pearson correlation analysis was used to test the relationship between the change in cardiac power index (ΔCPI) and the peak post-operative Troponin level, as well as the duration of hospital stay (days). The results of the correlations were shown on separate scatter-dot graphs with the corresponding r and p values. The predictors of post-operative myocardial injury were tested by univariate and multivariate logistic regression analyses. In univariate logistic regression analyses age, ΔCPI, operation time (OT), and vasopressor need (VN), found to be associated with myocardial injury following liver transplantation. These variables were tested in the multivariate analysis. Results were expressed as the p value and hazard ratio (HR), in CI of 95%. A receiver operating characteristic (ROC) curve was generated for discriminative ability of ΔCPI to predict myocardial injury after LT. Results were expressed as area under the curve (AUC), standard deviation (SD), p value, and 95% confidence intervals (CI). We divided patients into 2 groups based on the ΔCPI value derived from the ROC analysis. Post-operative outcome variables were compared according to the cut-off ΔCPI value. The results were expressed in a separate table.

RESULTS

A total of 53 patients were included in the study and postoperative secondary myocardial injury (PMI) was observed in 28.3% (n=15) of these patients. Basal characteristics of patients with and without PMI are summarized in Table. There was no significant difference between the two groups in terms of gender, etiology of liver failure, revised cardiac index and MELD scores, EF, sPAP, BSA, smoking status and the presence of comorbid diseases (diabetes mellitus, hypertension, arrhythmia, heart failure, cerebrovascular disease, renal disease, peripheral artery disease) (p>0.05 for all). The mean age of patients with PMI is significantly higher (61.2 ± 8.6 years) than for those without PMI (55.8 ± 7.1 years) (p<0.05). Also, there is a significant difference between the two groups in terms of postoperative NT-proBNP levels (832 ± 1751.1 pg/mL and 390 ± 514.5 pg/mL, respectively) (p<0.05).

Intra-operatively assessed hemodynamic parameters and surgical features of the liver transplant patients compared based on the occurrence of myocardial injury following surgery is shown in Table. ΔCPI was significantly lower in patients with PMI (-0.27 ± 0.11 W/m^2) than those without PMI (0.08 ± 0.18 W/m^2) (p<0.05). Also, intraoperative vasopressor need was significantly higher in patients with PMI (87% vs 24%, p<0.05). Furthermore, operation time was considerably longer in patients with PMI than those without PMI (505 ± 21 minutes vs 408 ± 31 minutes, p<0.05).

The mean ΔCPI was significantly lower in patients with PMI than those without PMI as shown on Figure. Also, Figure shows that there was a negative correlation between ΔCPI and peak Troponin levels (r=-0,645, p<0,001). Similarly, a negative correlation was present between ΔCPI and the duration of hospital stay (Figure) (r=-0,587 p=<0,001).

We performed univariate and multivariate logistic regression analyses to determine the independent predictors of PMI. Significant variables in the univariate model were found as ΔCPI (HR: 2.326, 95% CI: 1.511 – 3.716, p: 0,012) and operation time (HR: 2.651, 95% CI: 1.104 – 6.317, p< 0.001). The multivariate analysis showed that the only independent predictor of PMI was ΔCPI (HR: 2.245, 95% CI: 1.145 – 4.387, p: 0.032) following liver transplantation.

In order to establish a cut-off value for ΔCPI to determine post-operative myocardial injury, we performed ROC analysis that revealed ΔCPI values lower than -0.15 W/m^2 were significantly associated with PMI. According to the cut-off ΔCPI value, we devided patients into 2 groups as 1) ΔCPI ≤ -0.15 W/m^2 and 2) ΔCPI > -0.15 W/m^2. Table shows the comparison of the post-operative outcome variables between the groups defined according to the cut-off value for ΔCPI assessed during the surgical procedure. Peak troponin level, hospital stay and myocardial infarction prevalence were significantly higher in ΔCPI ≤ -0.15 W/m^2 group (all p < 0.05). Figure shows the graphical demonstration of the association of low ΔCPI (≤ -0.15 W/m^2) with cardiac and all-cause mortality, respectively.

DISCUSSION

In this study, the relationship between intra-operatively measured CPI and postoperative myocardial injury in liver transplantation patients was investigated. The main findings of the study can be listed as follows; there is a negative correlation between ΔCPI and postoperative secondary myocardial injury. Also hospital stay, cardiac and all-cause mortality is higher in patients with lower ΔCPI. Furthermore, it has been demonstrated that this relationship is independent of other factors.

With investment and updates in surgical techniques

and anesthetic management, mortality rates after LT have been significantly improved. However, as it is considered a complex procedure and is characterized by hemodynamic instability, significant instability challenges remain for LT. Especially transition from the anhepatic phase to neohepatic phase is the most critical time of the surgery. Abrupt hemodynamic and metabolic changes during that time may cause cardiovascular collapse, which is associated with adverse outcomes during the postoperative period [7].

To prevent cardiovascular collapse, close hemodynamic monitoring and early intervention of patients during LT are critical. Hence, sophisticated invasive monitoring with devices which offer crucial information for the successful management of patients is required during the surgery. Arterial pulse contour analysis and thermo-dilution technique (PICCO) is one of these devices and it has been proven to be a reliable monitoring technique which plays a significant role in making decisions [2]. With PICCO technology, many hemodynamic parameters can be followed. One of them is the cardiac power index (CPI). CPI represents the power of left ventricular cardiac output in Watt. It is the product of pressure (MAP) and flow (CO) [8]. In several studies it was shown that, CPI is associated with prognosis of heart failure patients [9-11]. Also, it has been found to be the strongest independent predictor of hospital mortality in cardiogenic shock patients [4].

In our study we planned to investigate the relationship between intraoperative CPI and postoperative secondary myocardial injury. For this reason, the relationship between CPI measured during the three phases (pre-anhepatic, anhepatic and neo-hepatic phase), of surgery and the presence of postoperative myocardial injury in patients who are evaluated with coronary angiography before LT and found not to have critical coronary lesion was investigated. Unlike other studies which indicate that, CPI is a predictor of worse prognosis after surgery, in our study there was no correlation between CPI measured during all phases of the surgery and PMI. The phase at which reperfusion syndrome occurs is when the transition from the anhepatic phase to the neohepatic phase takes place. We also raised the question of whether the change in CPI during this phase could be related to postoperative myocardial perfusion. At this point, we decided to investigate the relationship between postoperative MI and ΔCPI, which is the difference between CPI-3(neohepatic phase) and CPI-1(pre-anhepatic phase). It was found out that there is a negative correlation between postoperative secondary myocardial injury and ΔCPI. This finding supported our idea that, patients who experienced significant decrease in CPI during transition from the anhepatic phase to the neohepatic phase, which constitutes the reperfusion phase, were more prone to postoperative myocardial injury. That result is compatible with other studies which show that post-reperfusion syndrome (PRS), which means 30% decrease in the mean arterial pressure(MAP) for at least a minute and which appears in the first five minutes after graft reperfusion at neohepatic phase [12], is associated with adverse cardiovascular events [13]. As far as we know, this is the first study related to ΔCPI, which is not routinely used as a marker during surgeries.

In our study, none of patients experienced PRS. Although the relationship between MAP and poor outcomes was demonstrated previously by several studies [14,15] in our study there was not any correlation between MAP changes during phases of the surgery and PMI. However patients with lower ΔCPI, even did not experienced PRS, are more prone to PMI. Also their hospital stay was longer and their all-cause mortality and cardiac mortality rate were higher. As a result it can be suggested that ΔCPI is a more sensitive cardiovascular prognostic marker than MAP in liver transplantation patients.

Taking these findings into consideration, it can be stated that in patients undergoing liver transplantation, irrespective of the risks in preoperative assessment, postoperative adverse cardiac events could be reduced with effective intraoperative hemodynamic management. The significance of hemodynamic monitoring during liver transplantation has already been demonstrated through previous studies [16,17]. During the surgery hemodynamic status of the LT recipient can be monitored using MAP, CVP [18]. However it was shown that they are poor predictors of ventricular filling volume and fluid responsiveness during various conditions [19], PiCCO systems, altough have not been universally validated for LT surgery, promise hope for the future. We attributed this situation to the fact that they also provided information about cardiac output, which could indicate a better reflection of the cardiac condition, apart from blood pressure. However, in our study, we found an association with ΔCPI rather than CPI itself in relation to myocardial ischemia. Although we hypothesized that this could be a result of the significant decrease in cardiac output during the transition to the neohepatic phase, reaching a definitive conclusion is not possible due to the limited number of patients. We believe that this question may be answered in the future through more comprehensive studies.

CONCLUSION

ΔCPI which constitutes the decrease in CPI during transition from the anhepatic phase to the neohepatic

phase, can be used as a marker of poor cardiac prognosis in patients who underwent liver transplantation. However, due to the limitation in the number of patients in our study, we can not fully explain the mechanism and can not provide practical clinical applications for this finding, Close follow-up of the patients with lower ΔCPI may provide a significant benefit to reduce cardiovascular events by ensuring early diagnosis and treatment.

LIMITATIONS

The major limitation of our study was the small sample size, so the results should be validated in a larger population. Another drawback of the study was that although the post-surgery need for vasopressor therapy was investigated, a standardized vasopressor treatment during the surgical procedure was lacking, thus preventing a meaningful comparison. As a result, the impact of treatments administered during surgery on surgical outcomes remains unknown.

DATA STATEMENT

Due to the sensitive nature of the questions asked in this study, survey respondents were assured raw data would remain confidential and would not be shared.

Data not available / The data that has been used is confidential

AUTHOR CONTRIBUTION

A.Yazar, I.Oğuz Karaca, Tumay Yanaral had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. A. Yazar should be regarded as first author.

Drafting of the manuscript and ritical revision of the manuscript for important

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