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Dynamics of change in coagulation parameters in carcinoma patients with epidural analgesia following liver resection

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Abstract

Background and Purpose: *Liver resection is associated with postoperative coagulopathy. There is a risk of occurrence fatal epidural anaesthesia (EA) complications. The purpose of this study is to monitor the dynamics of change in coagulation parameters with regard to the resected mass of the liver tissue in patients with continuous thoracic epidural analgesia.*

Materials and Methods: *The retrospective study included 57 patients, with liver resection performed due to metastases of colon carcinoma with normal preoperative coagulation status, that underwent the technique of continuous thoracic epidural analgesia (TEA) and general anaesthesia. The patients were divided into two groups depending on the number of resected liver segments. The Small Resections' group (SR) included patients that had one or two liver segments removed while the Major Resection (MR) group included patients that had three of more liver segments removed. Resected liver tissue mass, prothrombin time (PT) values and platelet count were analyzed during five postoperative days (PODs).*

Results and Conclusions: *There is a statistically significant difference of PT value ($p<0.001$) during five days within each of the tested groups, as well as between both groups ($p<0.001$). During all five PODs there is a negative correlation between PT values and removed liver tissue mass in both patient groups. The analysis showed that by removing liver mass larger than 165 g we can expect PT<0.7. TEA application after liver resection is a technique that demands individual assessment of the expected patient postoperative coagulation status. Resected liver tissue mass can be an effective predictor of postoperative coagulopathy.*

INTRODUCTION

Continuous EA is a technique that ensures quality analgesia for surgery in the upper abdomen. The advantages of EA are reduced opioid consumption, lower incidence of cardio and pulmonary complications, shorter duration of postoperative ileus and early mobilization of patients *(1, 2)*.

Postoperative coagulopathy can occur after a simple hepatectomy regardless of the normal patient's preoperative coagulation status *(3)*. Perioperative blood transfusion can additionally influence coagulopathy due to large intraoperative blood loss and excessive electrolyte consumption.

Consequently, EA can provoke in patients suffering from coagulopathy the occurrence of epidural and spinal hematoma, as a fatal complication *(4)*. Therefore, it is of vital importance to determine optimal postoperative time for the extraction of epidural catheter (EC). Therapy cannot always achieve the recovery of coagulation function, additionally complicating the decision on EA application. In spite of the guidelines for neuroaxial analgesia in patients with coagulopathy, there are no guidelines for patients with liver resection *(5)*. Medical resources show controversial data on determining the optimal timing, i.e. precise POD for the extraction of EC *(6, 7, 8, 9)*. Some authors claim that EA application should be limited to so-called small liver resection in patients that have preoperative normal liver and coagulation function *(7)*.

The aim of this study was to determine the dynamics of changes in postoperative coagulation parameters during five days with regard to the mass of resected liver tissue and establish the sensitive predictors of coagulopathy in these patients.

MATERIAL AND METHODS

After obtaining institutional review board approval, we conducted a retrospective study including 57 patients of both gender, American Society of Anaesthesiologist Physical Status I-III (ASA), that underwent liver resection with combined technique of continuous TEA and general anaesthesia, and postoperative EA due to metastases of colorectal carcinoma during the period from 2007 to 2009 at the University Hospital Center *Sestre milosrdnice* – Clinic for Tumors.

All patients that were included in the study had normal coagulation parameters during the preoperative period and received neither blood nor blood preparation (blood derivatives). Patients who took vitamin K and fresh frozen plasma during the preoperative period were not included in the study.

Patients were divided into two groups depending on the number of resected liver segments. Small Resection (SR) group included 32 patients who had one or two liver segments removed. Major Resection (MR) group included 25 patients who had 3 or more liver segments resected.

Blood tests, including platelet count (PLT), prothrombin time (PT), International Normalized Ratio (INR), activated partial thromboplastin time (aPTT) and fibrinogen were determined before surgery, immediately after surgery, and daily until values returned within the normal range (5 days).

All patients received premedication midazolam 0.1 mg/kg orally 1 h prior to the induction into anaesthesia. They were monitored with electrocardiogram, pulse oxmetry, capnography, inspired and expired oxygen, anaesthetic vapor concentration, systemic (radial) arterial blood pressure, and central venous pressure through the right jugular vein and bispectral index analysis (BIS).

An epidural catheter was inserted into epidural space of all patients at the T8-T11 level using the loss of resistance technique after local anaesthesia. Lidocaine 2% 2 mL, plus 2 mL after 5 min was used to exclude the subarachnoid placement of the catheter. Levobupivacaine 0.5% 5–7 mL and 100 mcg fentanyl were injected before the induction of anaesthesia, and following that a combination of 0.25% bupivacaine and fentanyl was continuously administered (2 mcg/mL) in the dosage of 4–6 mL/h.

Anaesthesia was introduced by Propofol 1–2 mg/kg, fentanyl 2–3 μg/kg and vecuronium 0.1 mg/kg. After endotracheal intubation, anaesthesia was maintained by sevofluran 1.5–2.0% in 50% oxygen-air mixture, and repeated by relaxant vecuronium 0.5 mg/kg, and if necessary fentanyl 50–100 μg.

The weights of resected specimen was measured by weighing scales after liver resection, and correlations among mass of resected liver, PLT, INR, PT, aPTT and fibrinogen were also investigated.

All patients were awakened after surgery in the operating room and subsequently transferred to the intensive care unit (ICU).

Continuous monitoring of hemodynamic and respiratory functions, VAS, neurological status, laboratory results (acid-basic status, red blood cell count, and liver enzymes) and coagulation parameter results was retained in the ICU. Postoperative analgesia was administered by continuous application of a combination of 0.125% bupivacaine and 2 mcg/ mL fentanyl in the dosage of 5–8 mL/h. In case of insufficient analgesia VAS ≥4, a patient received on request 1–2 mg Morphine iv by titration up to satisfactory analgesia.

Differences between the two groups were compared by using the Student´s *t-test*. The differences between average PT values during five days using t-test were statistically significant ($p<0.001$). A significance test with sensitivity and specificity was used to establish the correlation between the mass of the resected liver sample and PT.

RESULTS

SR and MR groups did not statistically differ with regard to demographic characteristics.

The average weight of resected liver tissue in patients from SR group was 147.7 ± 110.2 g, and in patients from MR group 440.7 ± 181.7 g.

There was a statistically significant difference in five-day PT values within SR group ($p<0.001$) and within MR group ($p<0.001$), as well as between both groups of patients ($p<0.001$). The patients from SR group had higher PT median values on average in relation to MR group (Figure 1).

Statistically significant negative correlation was found between PT median values and mass (gram) of removed tumor ($p<0.001$).

The analysis of obtained results during five days showed that PT median values in SR group were the lowest

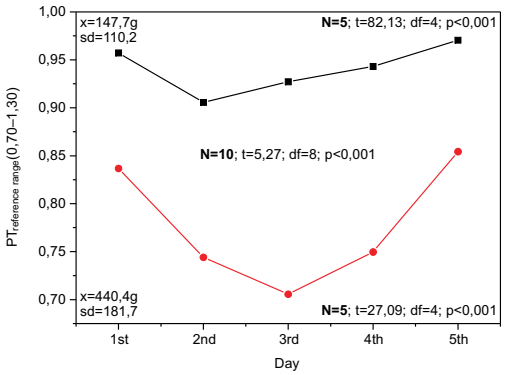

Figure 1. *Changes in five days postoperative PT in patients undergoing major or minor liver resections p<0.001.*

on the second and in MR group on the third POD (Figure 1).

The significance test with sensitivity and specificity demonstrated that with 95% sensitivity and 52.2% specificity the optimal cut off of removed liver with expected PV≤0.7 was 165 g (Figure 2).

Statistically significant correlation between PT median values and platelet count values (p<0.002) was identified on 4th postoperative day. The increase of PT median value is accompanied by higher platelet count median value. Not a single patient in both groups had the value of platelet count lower than 100000/mL during 5 PODs.

DISCUSSION

Our study describes the use of EA and coagulation changes in 5 PODs that occur in small and major liver resection. All included patients had normal preoperative coagulation status and did not receive any transfusion neither before nor during operative procedure.

The results of our study pointed out a negative correlation of change in PT median values and mass of resected liver parenchyma in both groups of patients, which is in agreement with the results of research of other authors so far *(6, 7, 8, 10)*.

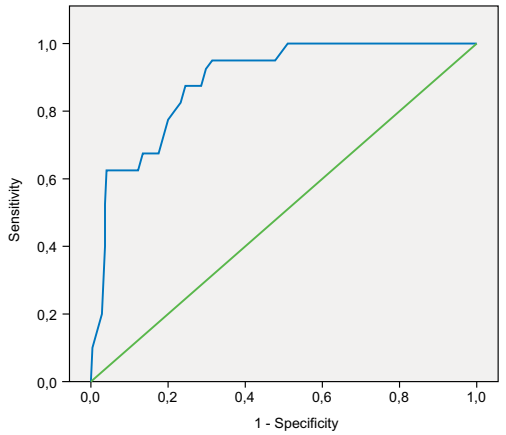

Figure 2. *Significance test with sensitivity and specificity was used to establish correlation between the mass of the resected liver sample (g) and PT. sensitivity is 95%, specificity 52.2% and optimal cutoff is 165 g.*

Matot et al. came to a conclusion that patients with small liver resection had the highest decrease of PT value (PV<0.7) occurring 24 hours after surgery, and it was already during following 24 hours that their PT recovered *(9)*. Our study showed exactly the same dynamics of change in PT median value in patients from SR group as in the mentioned study. In comparison with the study by Matot *et al.,* PT values in our study during 5 PODs were not <0.7 in SR group. According to the same author, the dynamics of change in MR group were the same as those in our study. The lowest PT values in both studies were 48 hours after surgery, but opposed to Matot et al, our study showed that PT median values were not above normal (PV>0.7).

Our results demonstrated that the dynamics of value of platelet count followed the changes in PT increase after 48 hours in patients from MR group, and PLT value was not below 100000/mL.

On the basis of the results of our study and the results of Matot et al, a conclusion can be drawn that EA is safe for small liver resection because recovery (24–48h) from the new coagulopathy is rapid. This recovery occurs up to 72 hours after surgery, which enables safe extraction of EC, as recommended in the guidelines for EA.

There have been no published data on the optimal cut off of resected tissue that can be used as a sensitivity predictor for the choice of technique of postoperative analgesia in patients with liver resection. Statistical analysis of sensitivity and specificity of the relation between the mass of liver resection and PT in all 57 patients showed that after the removal of liver tissue >165 g we can expect PT values <0.7 with 95% sensitivity and 52% specificity during postoperative period. Borderline value obtained in our study can be a new predictor of coagulopathy in patients after liver resection.

In our study, average weight of resected liver tissue amounted to 147,7 ± 110,2 g, i.e. even within this group of patients that are »safe« for the introduction of EC, according to the majority of authors, we can expect a disorder in PT value and postponement of catheter extraction or other adverse complications according to the result of borderline resection heavier than 165 g.

The decision on the choice of analgesia technique is necessary to be made individually for each patient in cooperation with the surgeon with regard to the expected mass of liver resection. Further research is necessary on a more extensive sample of patients in order to select optimal technique of analgesia in patients with liver resection. A draft of guidelines for neuroaxial anaesthesia in patients with liver resection would enhance safety, as well as facilitate the choice of optimal technique of analgesia.

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