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BRIEF ARTICLE

Ischemic preconditioning-induced hyperperfusion correlates with hepatoprotection after liver resection

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Abstract

AIM: To characterize the impact of the Pringle maneuver (PM) and ischemic preconditioning (IP) on total blood supply to the liver following hepatectomies.

METHODS: Sixty one consecutive patients who underwent hepatic resection under inflow occlusion were randomized either to receive PM alone (n = 31) or IP (10 min of ischemia followed by 10 min of reperfusion) prior to PM (n = 30). Quantification of liver perfusion was measured by Doppler probes at the hepatic artery and portal vein at various time points after reperfusion of remnant livers.

RESULTS: Occlusion times of 33 ± 12 min (mean ± SD) and 34 ± 14 min and the extent of resected liver tissue (2.7 segments) were similar in both groups. In controls (PM), on reperfusion of liver remnants for 15 min, portal perfusion markedly decreased by 29% while there was a slight increase of 8% in the arterial blood flow. In contrast, following IP + PM the portal vein flow remained unchanged during reperfusion and a significantly increased arterial blood flow (+56% *vs* baseline) was observed. In accordance with a better postischemic blood supply of the liver, hepatocellular injury, as measured by alanine aminotransferase (ALT) levels on day 1 was considerably lower in group B compared to group A (247 ± 210 U/I *vs* 550 ± 650 U/I, $P < 0.05$). Additionally, ALT levels were significantly correlated to the hepatic artery inflow.

CONCLUSION: IP prevents postischemic flow reduction of the portal vein and simultaneously increases arterial perfusion, suggesting that improved hepatic macrocirculation is a protective mechanism following hepatectomy.

Key words: Ischemic preconditioning; Reperfusion injury; Liver; Surgery; Liver blood flow

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INTRODUCTION

The common strategy to reduce intraoperative blood loss in human liver resection consists of temporary clamping

of the portal triad (Pringle maneuver, PM)[1]. The extent of bleeding during surgery is associated with higher postoperative complication rates[2], and the need for autologous blood transfusion may correlate with earlier recurrence of malignancies[3]. The length of the ischemic time strongly determines the release of liver enzymes after hepatectomy[4] indicating considerable hepatocellular injury caused by PM[5]. After declamping of the portal triad, reperfusion of the remnant liver causes additional damage to its parenchymal and non-parenchymal cells[6] which may cause the loss of functional integrity and consecutive hepatic failure[7,8].

Several strategies against the deleterious ischemia-reperfusion (I/R)-induced complications have been suggested[9-11], but these were not routinely introduced in the field of hepatic surgery in humans. This is mainly because of the complex mechanisms involved in I/R, including metabolic, immunological, and microvascular changes which exhibit numerous interactions, rendering the liver a difficult target for preventive strategies.

A new experimental approach to reduce I/R-related injury in the myocardium was firstly presented by Murry[12] who referred to "ischemic preconditioning" (IP) as an adaptation of the myocardium to ischemic stress induced by repetitive short periods of ischemia and reperfusion. Meanwhile, it could also be demonstrated that IP prior to sustained warm ischemia can protect parenchymal and non-parenchymal liver cells by increasing the tolerance against I/R-related organ hypoxia under experimental as well as clinical conditions[13-16]. An important observation was also that IP in human liver surgery was associated with better intraoperative hemodynamic stability, particularly on reperfusion of warm ischemic livers[17].

Although the underlying protective mechanisms of IP are still not fully understood[18], some studies have shown that the activation of Kupffer cells, leucocytes and the release of cytotoxic mediators on reperfusion may lead to a substantial breakdown of the hepatic microcirculation, an event which seems to play a key role following warm and cold ischemia[19-21]. For example, Klar *et al*[22] observed an inverse correlation between the hepatic microvascular blood flow rate and the maximum postoperative enzyme release from the liver. On the other hand, in healthy livers, a balanced portal vein (PV) and hepatic artery (HA) inflow are significantly dependent on the arterial buffer response, an autoregulation system which influences the whole blood supply to the liver at the level of the hepatic arterioles and portal venules, and which is assumed to be predominantly the result of adenosine action[23,24].

At this time, there is evidence that IP improves the hepatic microcirculation after warm as well as cold ischemia, but the influence of PM and IP on macrocirculatory parameters have not been elucidated as yet. In this study, we therefore investigated the hepatic inflow in patients undergoing liver resections with special regard to postischemic liver injury and patient outcome.

MATERIALS AND METHODS

Patients and randomization

The study was approved by the local Ethics committee and written informed consent was obtained from each patient before randomization. We investigated 116 consecutive patients at our institution who were subjected to liver resection (time period 12 mo). Of these, only 68 patients could randomly be assigned according to the inclusion criteria. These were defined as "significant" hepatectomies, i.e. removal of at least one segment. A total of 48 patients were excluded from randomization for the following reasons: (1) extent of liver resection less than one segment according to Couinaud (n = 16); (2) anticipated necessity of total vascular exclusion (n = 8); (3) necessity of additional surgical procedures such as bilioenteric anastomosis or associated gastrointestinal procedures (n = 3); (4) laparoscopic liver resection (n = 10); (5) underlying liver cirrhosis (n = 9); and (6) emergency surgery (n = 2). Of the 68 randomized patients, 7 were withdrawn from the analysis because of intraoperative detection of inoperability. Finally, 61 patients were randomized to a control group (A, n = 31), receiving PM, and to a study group (B, n = 30), who received IP by cross-clamping the portal triad for 10 min followed by 10 min of reperfusion prior to PM. Determination of blood flow of the common HA and PV was carried out simultaneously before starting PM or IP (baseline) as well as 10 min after IP (only group B), and at 15 min of reperfusion as well as before abdominal closure (group A, 32 ± 4 min; group B, 29 ± 6 min after declamping the portal triad) using the transit-time flowmeter (CardioMed CM 2005; MediStern AS, Oslo, Norway). This device measures the difference in travel time between pulses transmitted in the direction of, and against, the flow. The blood flow velocity is directly proportional to the measured difference between upstream and downstream transit times. Because the cross-sectional area of the probe/vessel was known as the probes were individually adapted to the vessel diameter, the product of that area and the flow velocity provided a measure of volumetric flow. The calculations were easily performed by a microprocessor-based converter and displayed online on a computer during surgery.

Study design

The targeted endpoints were the occurrence of IP- and PM-related flow changes of the HA and PV at defined time points. Secondary endpoints were serum levels of alanine aminotransferase (ALT) on postoperative day 1 and complication rates. Operations were performed by 4 experienced abdominal surgeons in a routine clinical setting. Transection was started immediately after inducing PM which was maintained until the transection was finished. Parenchymal transection was performed using a water jet cutter (Saphir Medical, Lyon, France). The volume of the resected liver was determined by the quantity of displaced fluid in a pre-filled trough.

All anesthetic procedures were performed by the same team of experienced anesthesiologists ensuring a standardized protocol. To meet intraoperative fluid demand and to compensate for blood loss, crystalloids and colloidal solutions, respectively, were infused as described elsewhere[17]. Adequate mean arterial pressure (MAP >

Table 1 Baseline data of study patients

Group	Age (yr)	Sex (*n*) M/F	Tumor (*n*) mal/non mal	Fibrosis (*n*) none/mod/sev	Steatosis (*n*) none/min/mod/sev
Control (A) (*n* = 30)	57 ± 14 (26-81)	18/12	26/4	10/15/5	8/16/5/1
IP (B) (*n* = 31)	55 ± 13 (28-77)	19/12	28/3	12/14/5	10/14/5/2
P-value	0.61	0.92	0.65	0.39	0.39

There were no significant differences between the control and ischemic preconditioning (IP) groups. Fibrosis: min (≤ 10%); mod (≤ 40%); liver steatosis: min (≤ 25%); mod (≤ 50%); sev (≥ 50%); mal: malignant. Examination by pathologist of non-cancerrous adjacent liver tissue; all patients included.

Table 2 No differences in the intraoperative data of the 2 groups of patients

Group	OP time (min) mean/range	PM time (min) mean/range	LR time (min) mean/range	LV resected (mL) mean/range	Segments resected (*n*) mean/range
Control (A) (*n* = 30)	260 ± 63 (170-420)	34 ± 14 (15-82)	30 ± 10 (10-50)	390 ± 303 (80-1400)	2.7 ± 1.3 (1-5)
IP (B) (*n* = 31)	271 ± 58 (180-420)	33 ± 12 (8-67)	31 ± 11 (15-56)	426 ± 453 (30-2000)	2.7 ± 1.1 (1-5)
P-value	0.36	0.70	0.83	0.77	0.69

OP: Operation; PM: Pringle maneuver; LR: Liver resection; LV: Liver volume.

65 mmHg), central venous pressure (CVP 9-14 mm Hg), and diuresis (> 100 mL/h) were maintained throughout the operation by fluid infusion and, when necessary, by administration of vasopressors (dopamine 2-3 μg/kg per hour and/or norepinephrine) as appropriate.

Laboratory parameters of hepatocellular injury (ALT) and liver function (bilirubin) were obtained before surgery and on postoperative days 1, 2 and 7. Transient liver failure was defined as bilirubin levels > 5 mg/dL and/or prothrombin activity < 40% for at least 3 postoperative days. Fatal liver failure was defined as death from irreversible hepatic dysfunction in the absence of other causes.

Statistical analysis

Numerical values are presented as mean and standard deviation unless otherwise noted. All significance tests were 2-sided and a *P*-value < 0.05 was considered statistically significant. Data analysis was performed using SPSS 11.0 (SPSS Inc., Chicago, USA). Comparison between the 2 groups (with/without IP) was performed using the Mann-Whitney *U* test, the χ^2 test or the Fisher exact test, as appropriate. The association between flow parameters and peak levels of postoperative ALT (day 1) was evaluated by the Pearson Product Moment Correlation. Multivariate analysis of complications was performed by means of logistic regression (backward selection). A multivariate analysis was performed by entering parameters that appeared to be of significance on the univariate analysis into a Cox proportional hazard model to test for significant effects while adjusting for multiple factors.

RESULTS

Baseline data

The analysis of collected data was based on the criteria of the CONSORT group[25]. There were no differences in demographic data and liver histology between the 2 groups (Table 1). Intraoperative parameters were also comparable between the controls and the study population (Table 2).

Flow characteristics

The perfusion data of the HA and PV prior to any intervention (baseline) did not differ between groups (Table 3). Patients who did not receive IP (controls), showed a markedly decreased PV flow by 29% at 15 min reperfusion and by 26% before abdominal closure (32 ± 4 min after declamping). Simultaneously, a slight increase in HA flow of 8% and 3.5% was observed after 15 and 32 min, respectively, of reperfusion of the liver remnants (Figure 1A). In contrast, patients who received IP (group B), maintained stable PV flow during the IP procedure as well as at 15 and 29 min after declamping the portal triad (Figure 1B). In addition, IP induced a more than 200% increase in HA perfusion immediately after IP and the significantly elevated arterial flow was maintained at 15 min (+56%) as well as at 29 min (+38%) after starting reperfusion of the liver remnants, demonstrating a continuing influence of IP on the postischemic blood supply (Table 3, Figure 1B). This results in a total increase in liver perfusion *via* HA and PV of 27% when patients underwent the IP procedure ($P < 0.01$, Table 3).

Laboratory parameters

Postischemic liver damage was measured by ALT levels during the postoperative course. In controls, we observed a significant ALT increase from 28 ± 12 U/L to 550 ± 659 U/L on day 1 when compared to preoperative values, which clearly suggests the PM as the cause of enzyme release. In contrast, IP-treated patients showed markedly reduced ALT levels of about 50% (247 ± 210 U/L, $P < 0.05$), indicating substantial hepatoprotection by this procedure (Table 4). In the further course, postischemic elevated ALT levels in both groups returned to normal within 7 d of hepatectomy. Serum bilirubin levels were determined as a parameter of hepatocellular function, but did not show notably different values at any time during the postoperative course (days 1-7, Table 4).

Intraoperative parameters and postoperative course

Blood loss as well as the need for autologous transfusion

Table 3 Flow characteristics of patients undergoing PM (control, *n* = 30) and IP + PM (study group, *n* = 31)

Group	Vessel	Baseline (mL/min)	After IP (mL/min)	15 min (mL/min)	Before abd. closure (mL/min)
Control	HA	141 ± 24	-	152 ± 29	146 ± 18
IP	HA	126 ± 19	263 ± 51	196 ± 38[a]	174 ± 22[a]
Control	PV	1023 ± 130	-	726 ± 121	757 ± 58
IP	PV	930 ± 94	920 ± 81	919 ± 75[a]	949 ± 62[a]
Total (Co)	HA + PV	1164 ± 72	-	878 ± 77	903 ± 37[c]
Total (IP)	HA + PV	1056 ± 53	1183 ± 64	1115 ± 49[b]	1123 ± 58[b]

There were significantly enhanced PV, HA, and total flows in IP-treated patients. PM: Pringle maneuver; HA: Hepatic artery; PV: Portal vein; abd: Abdomen; Co: Control. [a]$P < 0.05$, [b]$P < 0.01$ *vs* control; [c]$P < 0.05$ *vs* baseline.

Table 4 Outcome data of patients undergoing liver resection with PM (A) or with IP + PM (B)

Group	RPC (units) mean/range	ALT (U/L) mean/range	Bilirubin (mg/dL) mean/range	LF (*n*) transient/fatal[a]	Biliary compl. (*n*) major/minor
Control (A) (*n* = 30)	0.90 ± 1.24 (0-5)	550 ± 650 (54-2888)	1.73 (0.40-9.83)	2 (2)	2[b] (4)
IP (B) (*n* = 31)	0.47 ± 1.31 (0-6)	247 ± 210 (45-852)	1.40 ± 1.26 (0.23-5.59)	0 (1)	1 (2)
P-value	0.014	0.04	0.69	0.04	0.04

[a]Death; [b]Requiring re-operation. Total complication rate was 14/30 (45%) in controls (A) and 6/31 (20%) in the IP group (B). One death in the study group (B) resulted from a perforated duodenal ulcer (postoperative day 21). RPC: Red packed cells; ALT: Alanine aminotransferase; LF: Liver failure; compl.: Complications.

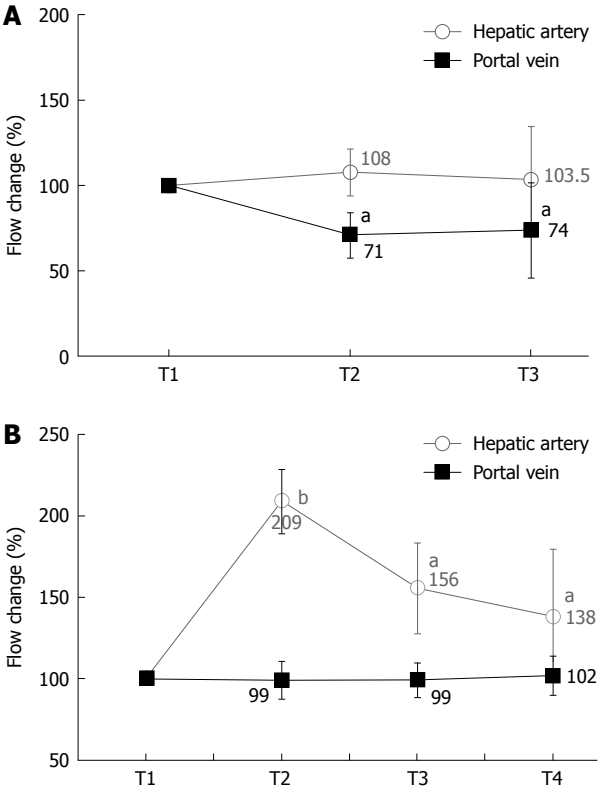

Figure 1 Changes in portal vein (PV) and hepatic artery (HA) inflow (100% = baseline) at operation (mean ± SD) in the control group (A) and study population (B). T1: Before starting the Pringle maneuver; T2: At the end of the IP procedure, i.e. 10 min ischemia and 10 min of reperfusion; T3: One minute of simultaneous reperfusion of PV and HA; T4: Immediately before abdominal closure (29 ± 6 min and 32 ± 4 min after stopping portal triad crossclamping in group A and B, respectively). [a]$P < 0.05$, [b]$P < 0.01$ *vs* baseline.

were significantly lower in the IP-treated group with 17% of patients receiving blood transfusion *vs* 48% in the control group ($P < 0.05$, Table 4). The postoperative course was uneventful in 24/30 (80%) patients in group B but only in 17/31 (53%) patients in group A ($P < 0.05$). Liver dysfunction, as previously defined, occurred in 2 patients of group A, but only in one patient of the IP-treated group (Table 4). Biliary leakage ceased spontaneously in 4 of the 6 patients (67%) of controls, but the other two patients required re-operation and bilioenteric anastomosis. In the study group, 2 patients had transient bile secretion and one patient of this group needed re-operation (bilioenteric anastomosis) (Table 4).

Blood supply to the liver and hepatocellular injury

With regard to earlier work, demonstrating a strong correlation between microcirculatory failure and postischemic enzyme release[22,26], it was of particular interest to determine whether there were changes in macrohemodynamic parameters, i.e. the PM and IP may have an impact on parenchymal cell damage. Firstly, we analyzed the correlation between PV flow and ALT levels on day 1. Interestingly, by applying the Pearson Product Moment Correlation we did not find a significant association between the amount of the hepatocellular injury and quality of PV perfusion, either in controls ($r = -0.38$, $P = 0.3$) or in IP-treated patients ($r = -0.41$, $P = 0.2$). In contrast, when the HA flow of patients with PM (controls) and the corresponding ALT values on day 1 were analyzed, we found a weak, but significant inverse correlation, indicating a substantial influence of the macrocirculation at reperfusion on postischemic liver injury ($r = -0.62$, $P = 0.042$, Figure 2A). This correlation was even more evident, when patients underwent IP prior to PM as shown in Figure 2B ($r = -0.73$, $P = 0.024$), suggesting the HA perfusion was more susceptible to the procedure of IP in warm liver I/R.

Predictors of postoperative morbidity

Parameters which were predictive for the development of

Table 5 Factors predicting occurrence of postoperative complications by multivariate logistic regression (backward selection) of factors of importance or significance on univariate analysis

Analysis (*P*-value)	IP treatment	Length of PM	Resected LV	HA flow	PV flow	Liver steatosis	Liver fibrosis
Univariate	0.038	0.043	0.067	0.044	0.72	0.81	0.94
Multivariate	0.047	0.022	NS	NS	NS	NS	NS

Treatment with IP and length of the PM are the only independent predictors of complications. NS: Not significant.

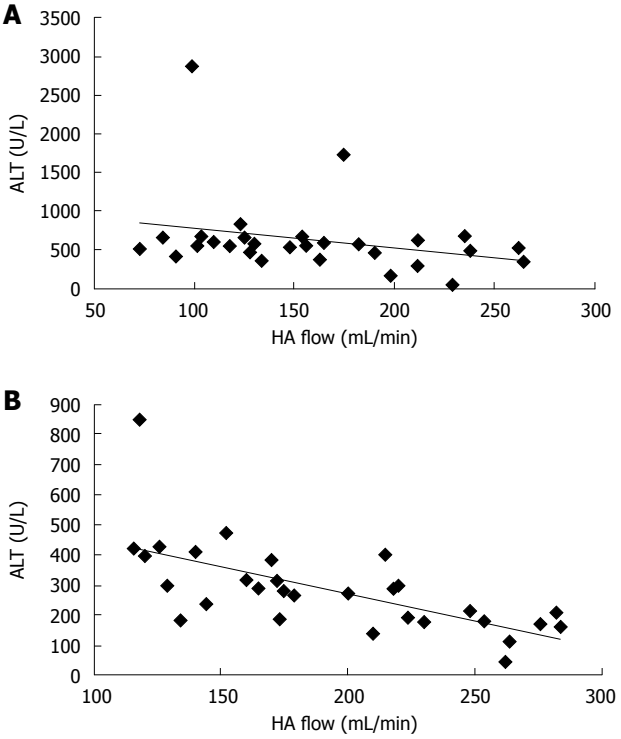

Figure 2 The Pearson product moment correlation between HA flow and alanine aminotransferase (ALT) levels. On day 1, there is an inverse correlation ($P < 0.05$) in the control group (A) undergoing PM ($r = -0.62$). In patients undergoing IP prior to PM (B), an even stronger correlation ($r = -0.73$, $P < 0.01$) was found. Straight lines represent regression analysis; data include values of all patients.

postoperative complications (ALT release, hepatic failure, biliary complications) are given in Table 5. Of 7 investigated parameters only the length of the PM and the procedure of IP were factors independently influencing the outcome of patients after hepatic resection. In particular, it was also found that the quality of HA perfusion was not predictive of complications, presumably reflecting the complex downstream mechanisms of liver I/R which might only in part be related to macrohemodynamic changes of blood flow to the postischemic liver.

DISCUSSION

This study presents the first assessment of human hepatic macrocirculation in response to I/R injury after the PM and IP in human hepatectomy. The main results obtained are: (1) that IP significantly improves hepatic macrocirculation upon reperfusion of liver remnants; (2) that the HA contributes most to the improved blood supply of the liver; and (3) that the quality of HA flow exhibits a strong correlation with postischemic ALT release.

During liver surgery in humans clamping of the portal triad (PM) is practiced to minimize intraoperative blood loss, but can lead to serious liver dysfunction[2,7,27]. Consequently, it has been generally accepted that periods of warm and cold ischemia of the liver should be shortened as much as possible[4,28]. Some experimental and clinical studies suggested that intermittent clamping of the portal triad reduced the negative effects of prolonged continuous warm ischemia on hepatic reperfusion injury[7,29]. However, the most important problems associated with that procedure are an increased blood loss during the episodes of reperfusion[7,30] and a marked prolongation of the operation time[30,31]. Ischemic preconditioning may combine the beneficial effects on reperfusion injury with the avoidance of additional blood loss during surgery[30,32].

In animal experimental studies, hepatic I/R is associated with perfusion failure of sinusoids due to significant hemoconcentration, reduced perfusion pressure, pressure-related sinusoidal leukostasis, as well as sinusoidal narrowing caused by hypoxia-induced endothelial swelling[33]. The impaired restoration of hepatic microvascular flow correlates also with the extent of liver injury after hemorrhagic shock and resuscitation[34]. Prevention of microcirculatory failure may largely protect the liver from parenchymal cell necrosis after I/R, suggesting that the degree of microvascular failure determines the extent of lethal hepatocyte injury[34]. Similar relationships between liver perfusion and injury could be observed in humans after warm and cold ischemia[26,35]. Interestingly, Puhl *et al*[26] could demonstrate a significant inverse correlation of the quality of the microvascular perfusion with postoperative liver enzyme release as well as bilirubin elimination in human liver transplants. This indicates that the observed (relative) hyperemia in the sinusoids might confer protection against postischemic liver injury. Another study by Klar *et al*[22] could also demonstrate in patients an inverse correlation between the intraoperatively measured hepatic microvascular blood flow rate and the maximum postoperative enzyme release from the liver. However, neither study included data on macrohemodynamic parameters, i.e. flows in the HA and PV in these clinical settings. Therefore, it cannot be concluded that the preservation of the sinusoidal blood flow after I/R can be the result of preservation of the HA and PV inflow during the reperfusion period.

While changes in the nutritive sinusoidal blood flow are the result of complex humoral, cellular, and immunologic interactions, the mechanisms leading to microcirculatory shutdown after liver I/R are related, at least in part

also to upstream mechanisms, i.e. regional macrocirculation of the liver[23,36]. Consequently, efforts should also focus on the preservation of an optimal blood supply to the liver under different pathological conditions at the levels of the HA and PV. In line with this, it was demonstrated that hepatosplanchnic blood flow was still reduced in humans at 60 min of reperfusion after severe hypovolemia, even though arterial blood pressure, cardiac output, and blood flow to other organs was already fully restored[37].

In the present study, we observed a severely decreased portal blood flow and a minimal increase in the HA flow on reperfusion of livers undergoing more than 30 min of portal crossclamping, a time period which is known to induce significant hepatocellular injury in humans[16]. We also found that IP could abolish the postischemic PV flow decrease and, *vice versa,* IP induced a significantly better HA flow throughout the reperfusion period, resulting in a markedly improved overall blood supply to the liver. This might be of substantial importance with regard to the nutritive sinusoidal perfusion, given that the autoregulatory capacity of the HA to maintain a constant flow rate in the presence of pathological conditions is limited, known as the hepatic arterial buffer response[23,24]. Therefore, IP effectively restored the total hepatic flow to almost normal values during reperfusion whereas in the control group the minimal increase of the HA flow failed to compensate for the postischemic perfusion deficit at the PV (Table 3). Because hemodynamic parameters, like MAP, CVP, and heart rate were kept stable upon reperfusion, and IP-treated patients did need significantly lower norepinephrine administration to maintain an adequate MAP, this observation can only be explained by an IP- mediated effect[17]. However, the exact mechanisms for that observation cannot be answered in the present study, although it was reported that both the hepatic arterial pressure-flow autoregulation and buffer response are mediated through changes in the washout of locally produced adenosine[38], and that IP may effectively increase the formation of the vasodilator adenosine while the unwanted degradation of adenine nucleotides to purines caused by the PM can be attenuated by IP[39].

Interestingly, we observed also a significant correlation between the postischemic ALT release on day 1 and the HA flow in controls, and this was even more pronounced in IP-treated patients, which clearly demonstrates that local macrohemodynamic changes at the HA may play an important role in the prevention of hepatic I/R injury. Because in our study hepatocellular damage was independent of postischemic PV flow changes, one can only speculate about the relevance of this observation, in particular with regard to the "small for size" problem in living related donor liver transplantation. This phenomenon, referred to as portal venous hyperperfusion of the partial liver allograft and associated with severe transplant dysfunction is thought to be the result of an imbalanced autoregulation of the arterial buffer response, resulting in a low concentration of adenosine-mediated HA branch constriction in the presence of increased portal perfusion[40]. Because hepatectomies with the loss of up to 5 liver segments as in our study may be compared to the above-mentioned situation, it was interesting that we found a substantial decrease of the PV flow upon reperfusion in controls which was not adequately compensated by an increase in the HA flow whereas in IP-treated patients the HA flow was significantly enhanced while the PV flow was kept stable during the reperfusion period, suggesting an impact of IP on the empirically observed reciprocal regulation between PV and HA inflow[37]. However, the previously described substantial alterations of nutritive sinusoidal flow impairments may occur, even in the absence of overt macrohemodynamic changes, as a result of an I/R-induced heterogeneity of hepatic microvascular downstream mechanisms[36,37]. In addition, despite postischemic ALT release being a well- established parameter for the estimation of hepatic injury following I/R, ALT levels alone are not predictive of the occurrence of postoperative liver failure following liver resection or transplantation[14,41].

In summary, this study provides some new insights into macrohemodynamic changes during liver resection under inflow occlusion and on treatment with IP in humans. As we could not simultaneously investigate the hepatic microcirculation in this setting, the impact of HA and PV perfusion alterations on the nutritive blood supply in sinusoids remains speculative. Further studies are necessary to clarify this aspect, and in particular, the impact of macro- and microhemodynamic changes on postischemic liver function in humans.

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COMMENTS

Background

Liver surgery has become a safe procedure in the past years and is mainly done because of malignant tumors. A common strategy to reduce blood loss during surgery is to temporarily shut down the blood supply to the liver [pringle maneuver (PM)], which, however may be associated with severe hepatocellular injury and consequent enhanced morbidity.

Research frontiers

Many efforts were undertaken to overcome the deleterious effects of ischemia-reperfusion injury of the liver caused by the PM. A new method of hepatocellular protection comprises ischemic preconditioning (IP), i.e. an additional short ischemia and reperfusion period prior to sustained ischemia, as set by the PM. However, mechanisms of protection by IP are still largely unknown.

Innovations and breakthroughs

Recent reports have highlighted numerous mechanisms which are involved in the protection of ischemic livers, including humoral, cellular, and immunologic interactions. Furthermore, an improved hepatic microcirculation seems to play a key role in liver protection following IP. However, no data were available which comment on hepatic macroperfusion under different conditions, such as IP.

Applications

By understanding how changes of blood flows of the portal vein and hepatic artery under inflow occlusion or IP may influence hepatocellular damage, this

study may provide some strategies for therapeutic intervention during liver surgery, such as selective portal triad clamping.

Terminology

IP of the liver consists of a short ischemia-reperfusion period (e.g. 10 min/10 min) immediately prior to longer periods of liver ischemia, which are often necessary during extended liver resections. Although it seems paradoxical, this additional short ischemia-reperfusion period confers protection on the liver by different mechanisms.

Peer review

This is a good study from a well-known liver surgery group with excellent methodology and adequate data analysis. The group expanded on their previous investigations on the role of IP in liver protection following resection. In the current study, the authors intuitively studied the effect of IP on hepatic artery and portal vein blood flow and demonstrated that IP prevented postischemic flow reduction of the portal vein and significantly increased the arterial perfusion.

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