RESEARCH ARTICLE

Perioperative Liver Function after Hepatectomy in a Tertiary University Hospital in Damascus

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Abstract

Background: Liver resection is the only viable therapeutic treatment option for several neoplastic entities of the liver. Although, the number of resectable patients is increasing in Syria, liver failure is still a major complication affecting mortality and morbidity rates. **Methods:** Between 2009 and 2016, 104 patients undergoing liver resection in Damascus University Faculty of Medicine were retrospectively analyzed. Liver function tests were conducted before surgery (ps) and in the perioperative period (po) and comparisons were performed with division into anatomic VS non-anatomic or malignant VS non-malignant groups. **Results:** Liver synthetic, excretory and detoxifying functions deteriorated after liver resection (INR ps 'presurgery'=1.129 po 'perioperative'=1.426 P<0.001, TP ps=7.426 po=5.581 P<0.001, ALB ps=4.204 po=3.242 P<0.001, T-Bill ps=0.061 po=0.136 P<0.001) and liver cell necrosis increased after resection (ALT ps=27.597 po=200.221 P<0.001, AST ps=33.395 po=190.553 P<0.001). There was no significant difference in liver functions when we compared anatomic VS non-anatomic groups or malignant VS non-malignant groups, but liver cell necrosis was higher with malignancies (ALT malignant group=236.475 non-malignant group=89.5 P=0.002, AST malignant group=222.644 non-malignant group=101.125 P=0.001). **Conclusion:** Although liver resection affects liver function significantly, no differences in outcomes were found between anatomic VS non anatomic or malignant VS non-malignant groups.

Keywords: Peri-operative- liver function- hepatectomy- malignant- non-malignant- anatomical- nonanatomical- Syria

Introduction

Liver resection is the only therapeutic treatment option for several neoplastic entities of the liver (Simmonds et al., 2006; Van Cutsem et al., 2006). It becomes the routine aspect of administering certain liver conditions such as primary liver malignancies and secondary ones. Five-year survival is insignificant in un-treated patients compared with around 30% in those receiving hepatic resection (Simmonds et al., 2006). However, Hepatic resection is still among some of the most complex operative interventions performed and is full of risk and complications.

The most significant agent determining postoperative morbidity and mortality is the capacity of the remnant liver to regenerate (Clavien et al., 2007). Clinical inquiries, following removal of up to 50% of functional liver, found that there was usually only a gentle and short-lived rise in serum bilirubin and depression of serum proteins indicating sustained briefness of hepatocellular function (Iwatsuki and Starzl, 1988) (Savage and Malt, 1991; Nagasue et al.,

1987; Huguet et al., 1992; Yamanaka et al., 1993). While removing up to 75% of the liver was allowance in most patients. However, it would be advantageous to estimate the size of the liver vestige after partial hepatectomy to reduce chances of liver insufficiency.

Post hepatectomy liver failure (PHLF) remains one of the most severe complications of major liver resection, and occurs in up to 10% of cases (Paugam-Burtz et al., 2009; Ren et al., 2012). Several studies report a lower average of PHLF in East Asian countries (1-2%), but when present, PHLF represents a significant source of morbidity and mortality (Ren et al., 2012). The definition of PHLF has varied widely among groups making comparison of rates between studies challenging. Numerous definitions of PHLF are found in the literature, with variations by country and between hospitals within the same country (Eguchi et al., 2000).

In 2011, the International Study Group of Liver Surgery (ISGLS) proposed a standardized definition and graded the severity of PHLF. After evaluating more than 50 studies on PHLF after hepatic resection, the

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consensus conference committee realized PHLF as "a post-operatively acquired deterioration in the ability of the liver to maintain its synthetic, excretory, and detoxifying functions, which are characterized by an increased INR and concomitant hyperbilirubinemia on or after postoperative day 5" (Rahbari et al., 2011).

The comparison between liver function before, perioperative liver resection and the interplay of clinical factors that predispose to liver failure following anatomical/ non-anatomical or malignant/ nonmalignant hepatectomy is the topic of this review. We will examine a number of clinical situations, which might shed light on causes of liver failure following resection in patients admitted in Al-Assad University Hospital from 2009 to 2016.

Materials and Methods

All patients who underwent liver resection at Al-Assad University Hospital in Damascus, Syria between 1/1/2009 and 31/3/2016 were evaluated to be included in this study. Patients who were not resectable or had undergone Radio ablation were excluded.

The Research Ethics Committee, Faculty of Medicine, Damascus University had approved this retrospective study by its decision number 16-02-06.

A group of medical students supervised by working physicians in the same hospital collected data manually from patient's charts in Archive, Laboratory, and Pathology Departments.

Standard demographic and clinic pathologic data were obtained including: age, sex, pathology (malignant, non- malignant), history of smoking or alcohol use, days in intensive care unit (ICU) and days of hospitalization.

Laboratory values including: INR, ALT, AST, Total protein, ALB, Urea, Creatinine, total bilirubin, of all patients were taken at pre-surgery and perioperative time. Pre-surgery Lab values were obtained at the first day of administration. Perioperative period was defined as the first three days after surgery. Identical laboratory samples were drawn multiple times in the perioperative period, the worst value was used for the purpose of analysis.

Patients were divided into two categories

patients who had an anatomic resection and those who had non-anatomic resection, and into malignant and non-malignant categories. Anatomic resections involve two or more hepatic segments as described by (Couinaud, 1957)whereas non-anatomic involves the resection of metastases with a rim of uninvolved tissue (Strasberg, 2005).

Specific Technique

On administration, all patients underwent exclusive examinations and the decision to give neoadjuvant chemotherapy was taken according to each case. Resections were made by the same surgical technique, and performed under low central venous pressure general anesthesia. Surgical team performed only open resections with Pringle Manoeuvre used at the discretion of the surgeon. Intraoperative Ultra sound was used and hepatic parenchyma was divided by Clamp-Crush technique or energy-assisted devices. The patient's condition after surgery was used to admit patients in the ICU or in the Surgical Department.

Analysis

Statistical significance was defined as 2-tailed $P<0.05$. Data analyses were performed using SPSS and the missing data were excluded from analysis. Categorical variables were presented as percentage. Continuous variables were presented as mean or median (Range)

Chi-Square test was used to compare categorical variables whereas T-test was used to compare continuous variables.

Results

This study included 104 patients; 56 of them were female (53.8%) and 48 were male (46.2%). The mean age of the patients was 49.327 (range 9-74). There were 25 smokers (24%) and 7 alcoholic (6.7%) patients.

The median length of stay in the hospital was 11 days, while the median length of stay in the ICU was 3 days.

Table 1. Compare Liver Function Tests Between Pre-Surgery (PS) and Perioperative Period (PO)

	N	PS	PO	P Value
INR	81	1.1299	1.4267	<0.001
TP	68	7.426	5.581	<0.001
ALB	67	4.204	3.242	<0.001
ALT	77	27.597	200.221	<0.001
AST	76	33.395	190.553	<0.001
ALP	62	243.21	157.097	<0.001
T-Bill	78	0.0611	0.136	<0.001
Urea	83	28.49	27.986	0.681
Creatinine	83	0.8518	0.788	0.053
Na	86	141.264	141.688	0.662
K	86	4.384	4.1076	<0.001
Cl	71	103.461	107.137	<0.001

Table 2. Compare Liver Function Tests Between Pre-Surgery (PS) and Perioperative Period (PO) in Patients Underwent Anatomic Resection Only

	N	PS	PO	P Value
INR	54	1.1472	1.4507	<0.001
TP	44	7.536	5.627	<0.001
ALB	43	4.184	3.291	<0.001
ALT	50	26.88	213.52	<0.001
AST	50	32.74	209.48	<0.001
ALP	41	277.951	170.073	<0.001
T-Bill	52	0.5977	1.1208	0.005
Urea	53	27.862	28.302	0.787
Creatinine	54	0.8341	0.7711	0.132
Na	57	141.57	141.816	0.859
K	57	4.3156	4.1346	0.037
Cl	47	103.485	107.077	<0.001

Table 3. Compare Liver Function Tests between Pre-Surgery (PS) and Perioperative Period (PO) in Patients Underwent Non- Anatomic Resection Only

	N	PS	PO	P Value
INR	27	1.0952	1.3785	<0.001
TP	24	7.225	5.496	<0.001
ALB	24	4.242	3.154	<0.001
ALT	27	28.926	175.593	<0.001
AST	26	34.654	154.154	<0.001
ALP	21	175.381	131.762	0.002
T-Bill	26	0.4377	0.8842	0.028
Urea	30	29.6	27.427	0.238
Creatinine	29	0.8848	0.8193	0.234
Na	29	140.662	141.438	0.429
K	29	4.5183	4.0545	0.001
Cl	24	103.413	107.254	0.001

Table 4. Compare between Anatomic and Non-Anatomic Live Resection

	N	anatomic	N	non-anatomic	P Value
Hospitalization	67	12.925	37	12.541	0.832
ICU day	64	2.469	33	2.394	0.801
Sex					
(Female)	56	37	56	19	0.704
(Male)	48	30	48	18	
Age	67	49.791	37	48.486	0.667
After-Surgery					
INR	57	1.4511	29	1.3921	0.359
TP	56	5.611	28	5.482	0.427
ALB	56	3.264	27	3.148	0.232
ALT	55	206.418	29	178.966	0.548
AST	55	202.8	29	161.483	0.243
ALP	48	171.396	24	136.208	0.178
T-Bill	57	1.1491	27	0.8978	0.365
Na	61	142.044	33	141.106	0.474
K	61	4.1244	33	4.0539	0.553
Cl	57	107.17	28	107.354	0.88
Urea	59	28.22	33	27.752	0.852
Creatinine	60	0.7605	31	0.8271	0.332

Of 104 patients, 67 had anatomic resection (64.4%) and 37 had non-anatomic resection (35.6%). There were 71 patients submitted to hepatic resection for malignant tumors (68.3%) and 31 for non-malignant tumors (29.8%) 2 missing data.

Discussion

The purpose of this study was to identify the early change of liver function after liver resection. The liver is a multi-function organ with synthetic and metabolic functions, therefore no single test can assist its functions (Wagener, 2013; Mizuguchi et al., 2014). After resection, it begins to regenerate within 3 days and reaches its original size by 6 months (Nagasue et al., 1987; Gove and Hughes, 1991). Thus, we analyzed routine postoperative

Table 5. Compare between Patients Submitted to Hepatic Resection for Malignant and Non-Malignant Reasons

	N	malignant	N	non-malignant	P Value
Hospitalization	71	13.577	31	11.065	0.189
ICU day	66	2.621	29	2.069	0.073
Sex					
(Female)	55	32	55	23	0.007
(Male)	47	39	47	8	
Age	71	52.31	31	42.839	0.002
After-Surgery					
INR	61	1.4184	24	1.4542	0.599
TP	62	5.561	21	5.595	0.849
ALB	61	3.202	21	3.281	0.451
ALT	59	236.475	24	89.5	0.002
AST	59	222.644	24	101.125	0.001
ALP	51	158.078	20	160.9	0.919
T-Bill	59	1.049	24	1.0683	0.946
Na	66	141.7	27	141.659	0.977
K	66	4.1427	27	4.003	0.267
Cl	60	106.978	24	107.675	0.585
Urea	65	29.935	26	23.615	0.017
Creatinine	63	0.8095	27	0.7226	0.225

clinical practice and biochemical blood tests related to liver function.

Anatomic liver resection selection criteria are still expanding (Jarnagin et al., 2002; Imamura et al., 2003) due to development in anesthetic and surgical techniques. However, liver functions and hepatic insufficiency are still of a significant concern.

Liver synthetic functions are assessed by protein and coagulation factors synthesis. The decrease in protein synthesis affects albumin. Nevertheless; albumin is not specific or sensitive enough to detect compromised function. Protein loss with ascites might decrease albumin levels; so this decrease does not cop with the decrease in synthetic function. The increase of the international normalized ratio (INR) may refer to decrease in the synthesis of coagulation factors (Wagener, 2013). Transaminases are intracellular and intramitochondrial enzymes so they represent the degree of acute hepatic injury but not impairments of function (Wagener, 2013). The total bilirubin indicates to glucuronidation pathways (phase II) of metabolic hepatic function but it may give misleading result about liver function because it is insensitive to ischemic injury (Wagener, 2013).

Post-operative hepatic insufficiency defined as total serum bilirubin of >7 mg/dl and/or the formation of new ascites, while some studies find that PoD 3 bilirubin level of ≥3 mg/dl was the predictive measure for Post-operative hepatic insufficiency (Mullen et al., 2007; Etra et al., 2014). None of our patients developed a total serum bilirubin more than 6.02 even patients who died. Serum bilirubin and INR are also used as measures of liver function (Bismuth et al., 1983; Ettorre et al., 2001) and used in the score to predict liver sufficiency after liver resection (Child and Turcotte, 1964; Schindl et al., 2005). They are considered as early predictors of death from

postoperative liver failure (Balzan et al., 2005; Mullen et al., 2007). This study revealed significant differences in serum bilirubin and INR as shown in Table 1 but we found slight differences between them when we compared anatomic versus non anatomic resection and malignant versus nonmalignant resection.

This study revealed significant decrease in liver synthetic functions as serum bilirubin and INR values show in Table 1, this kind of surgery led to function deterioration after performing the operation despite of the type of resection (Table 2, 3). However, serum bilirubin and INR After the surgery were not different significantly when we compared anatomic versus non anatomic resection and malignant versus nonmalignant resection.

Renal function is affected by liver function, acute or chronic liver failure, (Gines et al., 2003) the postoperative renal function and non-renal complications are well known (Armstrong et al., 2009). The levels of serum creatinine and urea in patients who had an uncomplicated hepatectomy remained stable in normal range with little variant depending on the vast of resection and little increase of urea (Reissfelder et al., 2011). In this study the serum creatinine and urea levels in patients decreased as showed in Table 1. There was no significant change for both serum creatinine and urea levels when we compared anatomic versus non anatomic resection or serum creatinine when we compared malignant versus nonmalignant resection. However change happened in urea when we compared malignant versus nonmalignant resection.

Liver resection led to significant increase in transaminases as shown in Table 1. However, the type of resection (anatomic or non-anatomic) didn't affect that increase significantly. On the other hand, resection for malignant reasons showed significant higher increase in transaminases than resection for non-malignant reasons.

Limited concerns are the relatively small sample size, but our hospital is the central and major hospital for liver resection in Syria. Secondly, no primary analysis of postoperative complications, survival, or outcome prediction was performed because most of patients have followed up in their cities and there is no central patient record database in Syria. In the end, we could not analyze future liver remnant because it is not routinely calculated. We just presented the result of liver function during hospital stay and further study beyond 6 months should be proceeded to evaluate the late result.

In conclusion, we found no significant statistic differences (P > 0.05) although it vary significantly in clinical values, in anatomic versus non anatomic liver resection or liver resection for malignant versus benign lesions which indicate all patients after liver resection need the same level of caring. However, this result is for liver function during hospital stay and further study beyond 6 months should be proceeded to evaluate the late result.

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