Different Modus Operandi Analysis of Liver Function in Liver Transplantation Perioperation

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[Abstract]

Objective: To approach different modus operandi liver function metergasis regularity in liver transplantation perioperation.

Method: We finished 103 patients liver transplantation in 2004 – 2007. According to modus operandi, they were randomly draw and divided classic (include 16 patients in malignant tumor) and piggyback (include 18 patients in benign lesion) group, we compare liver function metergasis regularity in liver transplantation perioperation.

Results: Except 9 patients pulmonary infection, 9 patients renal inadequacy, 1 patient cerebral infarction, other patients were healed without graft nonfunction, biliary tract complication, hepatic artery embolism, stricture, acute excluded, and so on abnormal occurrence. Different modus operandi have obvious statistical effects on liver function after operation, but piggyback modus operandi have more obvious statistical effects on liver transplantation than classic in operation. But after operation piggyback modus operandi recovery is faster than classic.

Conclusion: Changes of liver function is regularity in liver transplantation perioperation period. According to regularity, we may judge all kinds of influence factors and avoid to puncture liver biopsy repeatedly.

Keywords: Intraoperative period; Liver transplantation; Liver function

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Liver transplantation is an effective method in healing terminal liver illnesses. After a patient goes through liver resection, period without the liver, and transplantation of the new liver, light symptoms include unhealthy liver function (increase in liver enzymes and bilirubin), serious symptoms include loss of function. Now we conduct a retroactive analysis of clinical data, for liver transplantation patients in our hospital from July 2004 to 2007. We present observations on changes of liver function in classic and piggyback modus operandi.

1. Materials and Methodology
   1.1 General Information

Our hospital treated 46 cases of benign liver illnesses (38 cases of piggyback operations and 8 classic operations), and 57 cases of malignant tumor (7 cases of piggyback operations and 50 cases of classic operations). 16 cases of piggyback operations were randomly selected from the benign illness cases, all male, aged 2 – 68 years old, average (48.3 ± 6.9) years old. Among these, there are 11 cases of hepatitis B with cirrhosis, 3 cases of hepatitis C with cirrhosis, 1 case of large cavernous hemangioma, 1 case of autoimmunity hepatitis. 18 cases of classic operations were randomly selected from the malignant tumor cases (classic operations group), among which 14 were male patients, and 4 were female patients, aged 35 – 55 years old average (47.7 ± 13.9) years old. Among these, there are 12 cases of complicating cirrhosis, 4 cases of liver recession prior to operation, 8 cases of liver artery embolism chemotherapy, among those diagnosed with cancer after the operations, there are 9 cases of combined gate合并门 vein thrombus 静脉癌栓, and 1 case of precancerous pathological changes. Liver function classification, according to Child Classification: 10 cases of class A (6 cases of piggyback operations, 4 cases of classic operations), 8 cases of class B (3 cases of piggyback operations, 5 cases of classic operations), 16 cases of class C (9 piggyback operations, 7 classic operations).

1.2 Modus Operandi

The donors in the two groups were both healthy young people, among which 1 was a brain dead donor. Standard liver harvesting method was used (piggyback group); others were corpus donors of the same blood type. Rapid liver harvesting method was used, 2500ml 4˚C UW fluid perfusion of abdomen aortic artery, portal vein, and biliary. Hot ischemia is 0 – 5 min, cold ischemia 180 – 570 min. Resection of the ill liver in classic original position operations followed techniques introduced by Starzl. First dissect the first hilar, separating common bile duct, liver artery and portal vein. Separate left triangular ligament, liver and stomach ligament, separate vein in the lower chamber behind liver, block the first liver gate, and vein in the upper and lower chamber, resect the ill liver. Vein bypass was not conducted. In piggyback liver transplantations, method of dissecting the first liver gate, and separating ligaments around the liver are the same as classic transplantations. The key is to partially block the vein in the lower chamber behind the liver, when separating vein in the lower chamber behind liver and dissecting the second liver gate. When resecting the ill liver, we usually shape up the left and middle liver vein common trunk and part of the vein, for use in mating. Methods to rebuild the bile duct: bile duct end to end mating 32 cases （15 in the piggyback group, 17 in the classic group）, bile duct jejunum 空肠 Reux-en-Y mating 2 cases (1 case in piggyback group, 1 in classic group), drainage with T-hose after operation 27 cases, no drainage with T-hose 7 cases. None with vein bypass.

1.3 Process in Perioperative Period

The two groups of patients all received oxygen in the ICU ward. Central vein pressure, artery pressure and changes in other blood flow dynamics were monitored. Balance of water and

electrolyte was maintained. Nutrition support and prevention of infection were provided. Anticoagulant, blood vessel activation, and liver protection drugs were administered. Patients of hepatitis B were administered with oral intake of lamivudine regularly, and intramuscular injection of hepatitis B immunoglobulin. Triple immunosuppressive plan with Tacrolimus (FK506) + CellCept (MMF) + Prednisone (Pred) was administered regularly after operation, jointly used with Zenapax, Solae or neither. For patients with incomplete kidney function, FK506 is delayed or reduced. Peak and trough value of FK506 are monitored every other day (perioperative period concentration 10 – 15 ng/L). 3d before operation regular inspect blood vessel ultrasonic scan and chest X-Ray, to grasp the situation of portal vein, lower chamber vein, liver artery and lung. 10d after re-inspect abdomen CT. For the 9 cases with incomplete kidney functions (3 cases in the piggyback group, 6 cases in the classic group), after administering Furosemide, all showed quite good improvements. 9 cases with lung infections (5 cases in the classic group, 4 cases in the piggyback group), 9 cases of infarction (2 cases in the piggyback group, 7 cases in the classic group), all healed before leaving hospital after symptomatic treatment. No patient showed acute rejection after operation, no function from donor liver, narrow bile duct, bile leakage, or narrow liver artery. Liver function, coagulation, blood flow dynamics, and blood gas were monitored daily.

1.4 Measurement

At various time points (1, 2, 3, 4, 5, 6, 7, 10, 14 d after operation), these measures were taken for the two groups: levels of alanine aminotransferase (ALT), total bilirubin (TBiL). Measurements were taken and recorded on donor liver hot and cold ischemia, operation time, amount of blood loss and blood infusion during operation, which all have impact on liver function.

1.5 Statistical Method

For the two groups, before operations, the last test measurements were used, after operations, 1, 2, 3, 4, 5, 6, 7, 10, 14 d test measurements were used. ALT and TBiL changes are presented using box charts. SPSS 11.5 statistical software was used to conduct Mann-Whitney μ test on liver function measures before and 1 d after operations. A level of $P<0.05$ is used to indicate difference being significant. Risk factors impacting liver function (operation time, hot and cold ischemia time, amount of blood loss and blood infusion) are presented in convention of ($\bar{X} \pm s$). The t test was adopted, using $P<0.05$ to indicate difference is significant.

2. Results

2.1 Between the two groups, blood loss and blood infusion shows significant difference ($P<0.05$). The two groups of patients, operation time, period without a liver, cold preservation time, and hot ischemia time showed no significant difference ($P>0.05$, see table 1).

2.2 The two groups of patients, ALT, TBiL before and after operation showed significant difference ($u=29.68, 5.09, P<0.05$, see table 2, 3). 1d after operation, piggyback group's ALT and TBiL were both higher than the classic group, however, the recovery times were faster than the classic group. Peaks of ALT and TBiL are not synchronous, with rise of ALT happening earlier than that of TBiL, but the trends of increase are about the same. The ALT's speed of decrease is faster than that of TBiL. There was no obvious relapse during decrease (see Figures 1, 2).

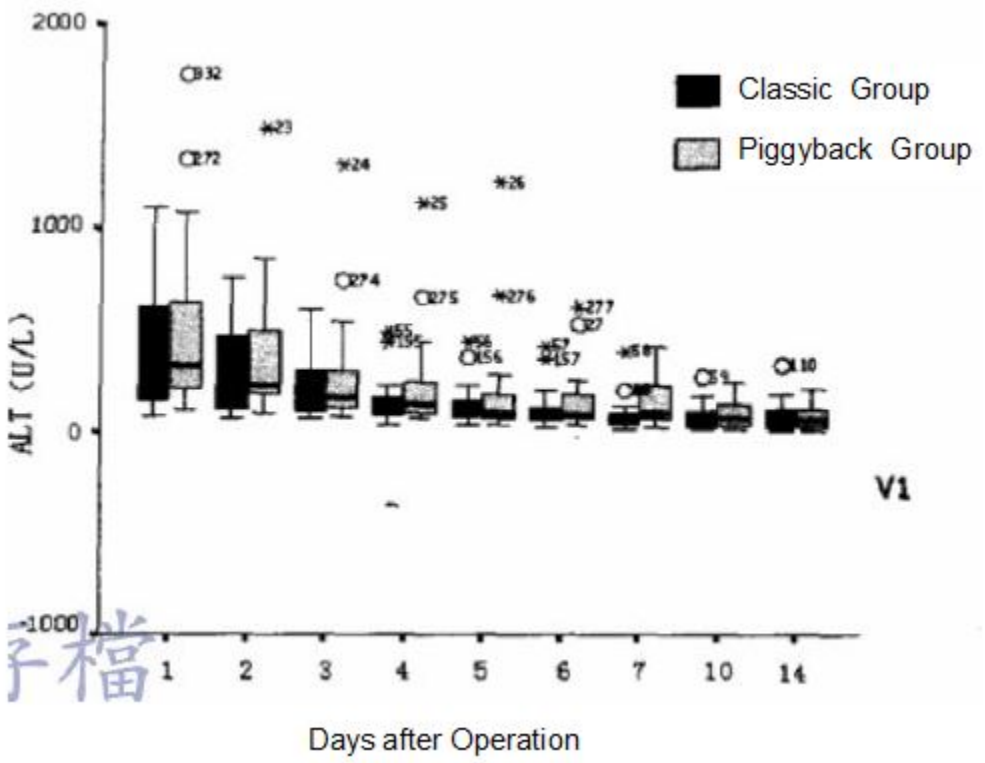

Figure 1 ALT dynamic state change in perioperation

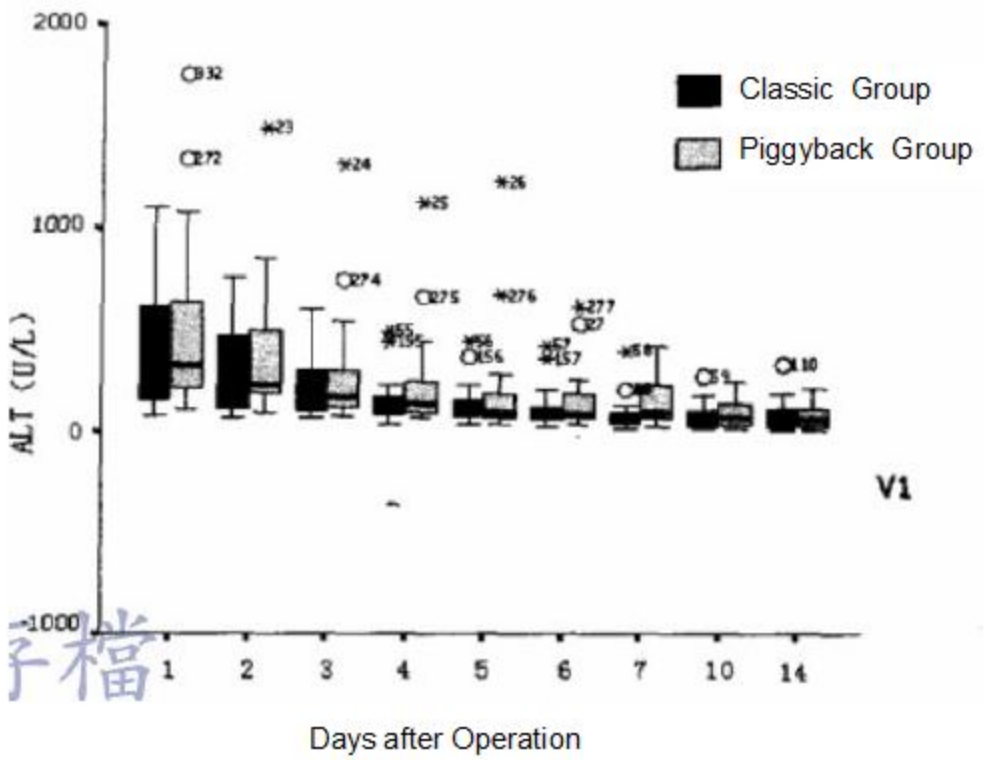

Figure 2 TBiL dynamic state change in perioperation

Table 1 Influence liver function factor in preoperation and midstoperation between classic and pigyyback ($\bar{x} \pm s$)

	# cases	operation time (min)	No liver time (min)	blood loss (ml)	blood infusion (ml)	cold preserve time (min)	hot ischemia time (min)
Classic Group	18	551.1 ± 131.3	79.1 ± 15.8	9941.3 ± 8462.6	9831.3 ± 7356.5	392.8 ± 97.1	4.0 ± 0.8
Classic Group	16	509.2 ± 96.0	75.2 ± 27.8	4758.6 ± 3286.8	4894.4 ± 3072.9	389.2 ± 110.6	3.9 ± 1.0
t value		1.05	0.49	2.30	2.50	0.10	0.32
P value		>0.05	>0.05	<0.05	<0.05	>0.05	>0.05

Table 2 ALT change in different operation group perioperatively

Piggyback Group		Classic Group	
ALT difference	Ranking	ALT difference	Ranking
1022. 9	31	647. 3	28
666. 1	29	598. 0	26
384. 9	23	52. 0	2
250. 0	19	858. 3	30
192. 0	16	165. 4	11
151. 5	9	98. 4	5
88. 0	4	169. 0	12
103. 1	6	130. 0	8
600. 0	27	1044. 2	32
225. 0	18	207. 0	17
164. 0	10	569. 0	25
330. 0	20	61. 0	3
1122. 0	33	107. 1	7
189. 0	15	357. 0	22
346. 0	21	179. 0	13
181. 9	14	44. 0	1
1612. 3	34		
522. 0	24		
N1 = 18	T1 = 353	N2 = 16	T2 = 242

Table 3 Change in different operation group perioperatively

Piggyback Group		Classic Group	
TBIL difference	Ranking	TBIL difference	Ranking
5. 19	6	13. 49	9
80. 05	27	57. 50	24
-204. 75	-33	47. 00	22
61. 30	25	41. 58	17
-42. 90	-18	-4. 60	-5
45. 70	20	39. 38	16
74. 00	26	35. 07	14
32. 33	12	7. 00	7
0. 00	1	100. 82	29
-3. 00	-2	-161. 79	-32
-245. 00	-34	-4. 00	-3
35. 20	15	26. 47	11
125. 88	31	3. 79	4
45. 33	18	52. 00	23
106. 00	30	45. 80	21
91. 28	28	21. 30	10
7. 05	8		
35. 00	13		
N1 = 18	T1 = 173	N2 = 16	T2 = 167

3. Discussions

Recovery of liver function after liver transplantation is critical in evaluating the success of liver transplantation. Liver function changes during the perioperative period is especially important. It is critical to grasp the changes in liver functions, and to distinguish sequential order and casual relationship among different factors affecting liver functions.[1]

3.1 Hot and cold ischemia and factors in preservation also cause different degrees of damage to liver and the bile duct system[2]. ALT mainly exist in the liver cytoplasm. Its increase is a sensitive measure of liver damage. After operation and perfusion, early tests can reveal damage of liver during harvesting, cold preservation, and re-

perfusion, as well as predict and evaluate the function of the transplanted liver. Piratvisuth et al. [4] believe that re-perfusion without blood is the most important risk factor causing liver function damage. Temperature recovery without blood can cause ALT level increase after liver transplantation. ALT levels for both groups of patients reached peak within 24 h after the operations. And the main cause of ALT increase is the damage from re-perfusion without blood of the donor organ. Preservation time of the donor organ is a critical factor in damages from re-perfusion without blood [5]. The two groups hot and cold ischemia time had no difference, and yet post-operation ALT levels showed difference. Considering that during piggyback operations, when second liver gates were exposed, the stretch and squeeze of liver are clearly larger than in the classic operations, it is relevant to worsening of the liver damage. ALT shows the degree of damage from re-perfusion without blood. It normally requires 5 – 7 d for recovery [6]. Some academic reports show that levels can reach 2 – 4 times of normal person within 10 d of operation, and later restores to normal levels gradually [7]. If during the first few days after transplantation, the ALT level increase was not obvious, then the patient is in bad condition. Bilirubin rapid increase indicates bad liver function. Attention must be paid to various causes of vast liver function death. If after a few days of the operation, ALT level increases again, urgent attention must be paid to acute rejection reaction, blood vessel incomplete function or solution. Liver puncture can reveal the root cause.

3.2 Bilirubin level changes is a key factor to watch during the perioperative period. The medium level of bilirubin level fluctuations at different time intervals after the operation indicate that TBiL does not recover with change of time. Rather, different factors present mixed impacts at different time intervals. The two modus operandi showed significant impact on TBiL changes. Excluding the difference of hot and cold ischemia, blood loss and blood infusion showed significant impacts. Huge blood flow dynamics change and damage of large number of red blood cells cause fluctuations in TBiL. TBiL is highly sensitive in judging pathological changes in the liver, but it lacks specificity. This is because too many factors affect the recipient patient in liver transplantations. These factors could exist individually, but in operations, they more often present joint impacts. TBiL alone has limited effect in judging the specific root causes [8].

3.3 Advantages and drawbacks from classic and piggyback modus operandi have been a focus of arguments in recent years. The majority of transplantation experts believe, that piggyback style shows more advantages than the classic style. Hosein [9] compared 90 cases of original position liver transplantations, and showed that piggyback style can reduce the operation time and time period without a liver, reduce the blood loss and use of blood products during operation, and reduce in-hospital time and ICU time. Ye Qifa et al. [10] compared improved piggyback style with classic piggyback style. The improved style showed clear advantage over the classic style, in

terms of liver function recovery. After 2 weeks of operation, liver function basically recovered in the improved style. This is 2 weeks faster than the classic style. This study shows, that the piggyback and classic styles show difference in terms of ALT and TBiL recovery after operations. This is basically consistent with the above observation. In piggyback operations stretch and squeeze of liver is much larger than in the classic style. The operational differences in the two styles is the root cause that piggyback style shows larger fluctuation in liver functions after operations, compared to the classic style. However, the piggyback style does not block the lower chamber vein, the patient's blood flow dynamics is steady, and reduced blood congestion in stomach, intestine and lower limbs. Impact to kidney function is relatively low. Red blood cell damage is low. This may be a reason for reduced fluctuation in TBiL and faster ALT recovery. Therefore, if piggyback style is chosen for patients with high TBiL or unstable blood flows before operations, TBiL recovery becomes more stable after the operation. But which style should be adopted, must depend on the type of illness, position of tumor, liver function status, operator's skill, and blood flow dynamics during operation.

To summarize, through analyzing liver functions during the perioperative period for different modus operandi, and understanding the trend and magnitude of liver function changes, if the patient's liver function shows abnormal behavior, exclusive diagnosis can be obtained in order to guide clinical treatment. However, to clarify the specific root cause, liver puncture must be performed. Piggyback style has more impact on liver function, but showed faster recover after operations. Therefore from the liver functions prospective, impact to operations must be considered when choosing the modus operandi.

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