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ORIGINAL ARTICLE

Blood salvage autotransfusion during transplantation for hepatocarcinoma: does it increase the risk of neoplastic recurrence?

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Summary

Impact of intraoperative blood salvage autotransfusion (IBSA) on neoplastic recurrence. during liver transplantations for hepatocellular carcinoma (LT-HCC). Between January 1989 and February 2003, 16 patients received a LT-HCC without IBSA. This group was compared with 31 patients who received the same surgical procedure during the same period, but with IBSA. Data were prospectively collected. All patients had at least a 1-year postoperative follow up. Pairing was made according to the size of the largest nodule. The percentage of recurrence observed in the two groups was similar: 6.4% in the IBSA group vs. 6.3% in the group without IBSA. The median amount of transfused salvage blood was 1558 ml. The differences observed between the two groups concerned the Child score which was A in 58% patients of the IBSA group vs. 80% in the other group; the percentage of severe portal hypertension was 55% in the IBSA group vs. 31%; the median number of packed red blood cell units transfused intraoperatively was 7 in the IBSA group vs. 0, and the median number of frozen fresh plasma units transfused intraoperatively was 11 in the IBSA group vs. 4.5. It appears that IBSA, essentially used during the most haemorrhagic transplantations, could be used in the case of HCC because it does not modify the risk of neoplastic recurrence.

Introduction

Liver transplantation (LT) still remains a major surgical procedure, in which a intraoperative haemorrhage is one of the vital risks [1,2]. Therefore, most LTs require the transfusion of homologous blood products, sometimes in large amounts. This requirement may be reduced if a system of intraoperative blood salvage autotransfusion (IBSA) is used. The latter, however, could present the theoretical risk of reintroducing neoplastic cells when it is used in cancer surgery. At present, this risk is only theoretical because few studies have yet been published; these studies are mostly experimental, with contradictory results on the risk of malignant cell dissemination [3–7]. The few clinical studies that are available concerning, mostly urological and thoracic tumours have not shown that this risk is higher after IBSA [8–11]. So far, no study has been carried out on the use of IBSA in LTs for hepatocellular carcinoma (HCC).

The aim of the present study was to evaluate the risk of neoplastic recurrence after IBSA during LT-HCC on patients with cirrhosis.

Materials and methods

Patients

This study included 47 patients who received a LT-HCC associated with cirrhosis, between January 1989 and

February 2003, all in the same centre. This represented 15% of all LTs during this period (47 of 309) and 52% of the LT-HCC (47 of 90). The other 48% of LT-HCC did not respond to our matching criteria or the follow up was to short. Among these 47 patients 16 did not receive an IBSA and 31 received an IBSA during their LT-HCC.

Methods

All data were prospectively collected for each patient until 1 March 2003 with overall analysis on 1 June 2004. A minimum follow up of 1 year after transplantation was required for all patients. Thus, most possible recurrences could be detected, because in 95% of the cases they occur during the first year.

Pairing the two groups was made on the basis of the largest HCC nodule, which was the major risk factor of tumour recurrence in our population of LT-HCC patients. The number of patients included in the IBSA group was twice that of the control group, in order to identify possible recurrences. Statistical analyses were made with the chi-square and Fisher's tests for qualitative variables and the Student's *t*-test for the quantitative variables (STATVIEW 5.0*).

Surgical procedure

Each patient received an orthoptic liver transplant with conservation of the inferior vena cava (IVC). The eavo-caval anastomosis was made between the IVC of the graft and a plasty of the three hepatic veins of the recipient [12]. No temporary portacaval anastomosis was made [12]. The salvaged autologous blood was collected intraoperatively and its autotransfusion was made with the help of a CELL-SAVER 5* (Haemonetics*) to which an antiaggregate filter was added (the same filter as the one used during massive homologous transfusion). The rest of the procedure and of the surgical management was as usual.

Results

Preoperative characteristics of the patients

The patients who received an IBSA had a more advanced liver cirrhosis, with more Child C and less Child A type (Table 1). Similarly, the portal hypertension was more often considered as severe by the surgeon in the IBSA group. Appreciation of the level of portal hypertension was left to the surgeon during the operation and was appreciated on splanchnic veins dilatation. In this group, fewer patients placed on the waiting list were treated for a HCC.

Intraoperative characteristics

The intraoperative data indicate that the number of transfusions of homologous blood [packed red blood cell (PRBC) and fresh-frozen plasma (FFP) units] was significantly lower than in the group without IBSA (Table 2). The number of patients who did not receive an intraoperative transfusion of PRBC (56% vs. 10%; $P = 0.0009$) and FFP units (44% vs. 13%; $P = 0.02$) was also significantly higher than in the group without IBSA.

In this series, no death was observed within the month following the LT, and the percentage of postoperative complications in the same period was 36%.

Characteristics of the tumour

No statistically significant histological difference in the HCC characteristics was found between the two groups (Table 3).

Follow up and cancer recurrence

The median follow up of the whole population (47 patients) was 34 months (range: 12–169) with a median follow up of 48 months (range: 12–169) in the IBSA group, and 15 months (range: 12–40) in the group without IBSA.

The percentage of neoplastic recurrence was the same in both groups: 6.4% in the IBSA group vs. 6.3% in the group without IBSA ($P = 0.9$).

Discussion

This study shows that using IBSA in LT-HCC associated with cirrhosis does not seem to modify the risk of postoperative neoplastic recurrence. To our knowledge, no study has yet been published on this subject in association with LT. Nevertheless, our conclusion is similar to that of clinical studies carried out after urological and hepatic surgery for malignant tumours, which found no difference in both metastatic dissemination and medium- and long-term survival [8–11].

It has been observed that the population of patients with IBSA differs from that which did not receive it. In fact, our results show that in these patients the cirrhosis of the liver was more progressive with more Child C types, and more severe portal hypertension. The differences observed in both criteria are close to being statistically significant ($P = 0.08$ and $P = 0.1$), which can probably be explained by the small population included in our study. Furthermore, the number of patients who received a preoperative transfusion of homologous blood products (PRBC and FFP) was significantly higher in the

Table 1. Preoperative characteristics of the patients.

	IBSA group, *n* (%; *n* = 31)	Non-IBSA group, *n* (%; *n* = 16)	*P*-value
Age (years)	53 ± 12	58 ± 6	0.1
Sex			
Men	26 (84)	14 (87.5)	0.8
Women	5 (16)	2 (12.5)	
Cirrhosis			
Alcoholic	12 (39)	4 (25)	0.9
Viral	18 (58)	9 (56)	
Hemochromatosis	1 (3)	3 (19)	
Child Pugh Score			
A	18 (58)	12 (80)	0.08
B	7 (22..5)	3 (20)	
C	6 (18.5)	0	
Portal hypertension			
None	2 (6.5)	1 (6)	0.1
Moderate	12 (38.5)	10 (62)	
Severe	17 (55)	5 (32)	
Pretransplantation treatment of HCC			
Yes	6 (19)	7 (44)	0.1
No	25 (81)	9 (56)	
Macroscopic vascular lesions	2 (6.5)	0	0.4

HCC, hepatocellular carcinoma; IBSA, intraoperative blood salvage autotransfusion.

Table 2. Intraoperative characteristics.

	IBSA group (*n* = 31)	Non-IBSA group (*n* = 16)	*P*-value
Number of PRBC units (median)	7 (0–35)	0 (0–13)	0.005
Number of FFP units (median)	11 (0–50)	4.5 (0–20)	0.01
IBSA (median)	1558 ml (400–20 000)	–	–

PRBC, packed red blood cells; FFP, fresh-frozen plasma; IBSA, intraoperative blood salvage autotransfusion.

Table 3. Tumour characteristics.

	IBSA group (*n* = 31)	Non-IBSA group (*n* = 16)	*P*-value
HCC size (median)	3 cm (2–4)	3 cm (1–8)	0.1
Number of HCC nodules (median)	2 (1–7)	1 (1–6)	0.2
Vascular thrombi			
Yes	4 (13%)	3 (19%)	0.6
No	27 (87%)	13 (81%)	
Tumour differentiation			
Good	16 (53%)	6 (37.5%)	0.5
Average	13 (40%)	8 (50%)	
Poor	2 (7%)	2 (12.5%)	
Milan criteria*			
Yes	18 (58%)	11 (68%)	0.3
No	13 (42%)	5 (32%)	

*Milan criteria: one nodule ≤5 cm or three nodules at most, with size under 3 cm (mazzafero 96).
HCC, hepatocellular carcinoma; IBSA, intraoperative blood salvage autotransfusion.

group that received an IBSA, while there were less patients in the group that received no blood product during surgery. This means that IBSA was used in transplantations with a major risk of haemorrhage (whether it could be foreseen or not before surgery).

On the contrary, it has been noted that the characteristics of HCCs were similar in both populations. In fact, the IBSA group had more patients with a macroscopic neoplastic vascular thrombosis, a well-known factor of malignant recurrence [13,14] as well as more patients who received no treatment while they were on the waiting list for treatment of their cancer.

The use of IBSA during LT-HCC with cirrhosis is a transfusion technique, which, without increasing the risk of postoperative neoplastic recurrence, does not carry the risk of a viral or bacterial transmission, or that of haemolytic complications that can be observed after homologous blood transfusions [15], or after a differed autologous transfusion, all methods that have also a higher cost (due to freezing and conservation of the blood products) and

the possible risk of red blood cell destruction [16]. Furthermore, the IBSA technique also has several advantages: it is easy to use, even in an emergency: it recovers a large amount of blood, provides good quality red blood cells, without viral or bacterial risk, avoids the danger of a haemolytic accident, and is economical after the loss of 1 l of blood [7]. In addition, this type of transfusion may perhaps stimulate the immune system, contrary to deferred homologous or autologous transfusions [17].

In conclusion, the autotransfusion of salvaged blood may be used in LT-HCC. Therefore, we recommend it, all the more when the risk of haemorrhage during transplantation seems to be higher (progressive cirrhosis and/or severe portal hypertension) because the amount of transfused homologous blood products can then be reduced.

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