11   The Preoperative Coagulation Pattern in Liver Transplant Patients

Franklin A. Bontempo, M.D.

Jessica H. Lewis, M.D.

Margaret V. Ragni, M.D.

Thomas E. Starzl, M.D., Ph.D.

INTRODUCTION

The liver plays a central role in the maintenance of adequate hemostasis. Among its many functions is the synthesis and degradation of clotting factors I, II, V, VII, IX, X, XI, XII, Fletcher, and Fitzgerald; clotting inhibitors α-1-antitrypsin (α1-AT), α-2-macroglobulin (α2-M), and antithrombin III (AT-III); and plasminogen. Only F VIII is an exception—both F VIIIR:Ag and F VIIIR:vW are synthesized in vascular endothelium, while the site of production of F VIII:C is unknown. When the liver suffers functional damage, particularly in advanced cirrhosis, clotting abnormalities frequently occur, and may result in serious bleeding (1,3). When such a patient requires surgery, the presence and severity of preoperative coagulation abnormalities may lead to intraoperative bleeding (2).

In liver transplantation, because the liver disease is often advanced and transfusion requirements are usually high, the evaluation of preoperative coagulation patterns may be of use in predicting blood loss, gauging severity of liver disease, and initiating

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TABLE 11.1. Categorization of Patients

Diagnosis		No.	F	M	Age range
PNC	(post necrotic cirrhosis)	22	8	14	18–48
PBC	(primary biliary cirrhosis)	18	18	0	36–59
CA	(carcinoma/neoplasia)	11	7	4	21–54
SC	(sclerosing cholangitis)	8	2	6	17–45
MISC	(miscellaneous)	11	3	8	25–47
Totals		70	38	32	17–59

therapy. We have analyzed preoperative coagulation profiles and categorized patients according to diagnosis. In addition, we have correlated data on blood product usage with preoperative coagulation abnormalities and patient survival in an attempt to predict which patients are at risk for massive bleeding during transplantation and for early demise.

Patient Categories

Patients were categorized by group as shown in Table 11.1. The post necrotic cirrhosis (PNC) group included patients with chronic active hepatitis and those with a history of hepatitis B or nonA, nonB hepatitis. The carcinoma/neoplasia (CA) group consisted of patients with a variety of malignant tumors and one with multiple adenomas. In the miscellaneous (MISC) category, several patients had fulminant hepatitis and the others had rare or combined disorders that fit neither of the previous groups.

Coagulation Parameters

Standard coagulation tests were performed on 64 patients preoperatively, and a coagulation abnormality score (CAS) was devised by assigning one point for each definite abnormality in the eight different test categories shown in Table 11.2. The CAS was based on a slightly more narrow definition of abnormal so that only distinctly abnormal values would be counted. The mean CAS, the mean values of the coagulation tests, and the percent abnormal for each test in each diagnostic group and for all patients are also shown in Table 11.2.

F	M	Age range
8	14	18–48
8	0	36–59
7	4	21–54
2	6	17–45
3	8	25–47
8	32	17–59

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TABLE 11.2. Mean CAS, Mean Values of Coagulation Tests, and Percentage of Patients Abnormal in Each Category and in Entire Group

Group	No.	CAS	TT (sec)	(%)	AT-III (U/ml)	(%)	APTT (sec)	(%)	Platelet Count (×/10³µl)	(%)	PT (sec)	(%)	I (mg/dl)	(%)	FSP (%)	Lysis (%)
PNC	20	5.3	30.3	(85)	0.36	(95)	40.9	(79)	92	(90)	16.8	(95)	182	(40)	* (25)	* (20)
MISC	10	4.8	29.2	(80)	0.49	(90)	48.3	(80)	199	(70)	28.9	(80)	183	(50)	* (11)	* (33)
SC	8	2.75	21.2	(63)	0.82	(50)	39.8	(75)	189	(63)	13.0	(25)	473	(0)	0 (0)	0 (0)
PBC	16	1.94	21.7	(56)	0.94	(25)	35.7	(38)	249	(38)	12.3	(25)	389	(0)	* (13)	0 (0)
CA	10	0.80	20.1	(55)	0.97	(22)	30.9	(10)	308	(0)	11.9	(0)	455	(0)	0 (0)	0 (0)
All	64	–	25.3	(67)	0.67	(60)	39.0	(59)	188	(55)	16.3	(52)	313	(20)	* (13)	* (11)
Normal			20 or<		0.70 or >		36.0 or<		150 or >		13.5 or<		150 or >		0	0

*Mean values for + or 0 tests not meaningful.

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TABLE 11.3. Mean Values (U/ml) for Coagulation Factors for Patients in Each Category and Entire Group

Group	No.	II	V	VII	IX	X	XI	XII
PNC	20	0.33	0.35	0.27	0.43	0.56	0.44	0.65
MISC	10	0.46	0.45	0.52	0.45	0.64	0.46	0.67
SC	8	1.13	0.64	1.42	1.02	1.43	0.63	1.00
PBC	16	0.95	1.00	1.00	0.90	0.95	0.76	1.07
CA	10	0.81	1.10	0.92	1.05	0.80	1.00	1.11
Total	64	0.68	0.68	0.74	0.73	0.81	0.63	0.87

Normal for all factors = 0.50–1.50 U/ml

The most frequently abnormal tests were the thrombin time (67%), antithrombin III (60%), and activated partial thromboplastin time (59%). In Table 11.3, several coagulation factors are shown to have been in the low normal range preoperatively. As can be seen in both tables, the PNC and MISC groups had more frequently abnormal tests than the other groups of patients.

Intraoperative Blood Use

Table 11.4 shows that intraoperative blood product usage was highest in the PNC group, followed by the SC group. The PBC and CA groups used significantly lower amounts probably because the hepatocytes are usually less abnormal in these diseases.

TABLE 11.4. Blood Product Usage During 70 First Liver Transplants. Mean Values for Each Disease Category and All

Group	No. of Patients	RBC	FFP	Plat	Cryo
PNC	22	58.0	55.0	31.3	9.8*
MISC	11	43.7	42.1	23.0	12.5
SC	8	58.1	47.6	21.6	24.3
PBC	18	23.0	23.4	10.9	3.9
CA	11	32.6	28.5	11.5	3.3
All	70	42.8	39.9	20.5	9.3*

*Excluding the hemophiliac.

	IX	X	XI	XII
	).43	0.56	0.44	0.65
	).45	0.64	0.46	0.67
	1.02	1.43	0.63	1.00
	).90	0.95	0.76	1.07
	1.05	0.80	1.00	1.11
	).73	0.81	0.63	0.87

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	Plat	Cryo
	31.3	9.8*
	23.0	12.5
	21.6	24.3
	10.9	3.9
	11.5	3.3
	20.5	9.3*

TABLE 11.5 Correlation (r) and Significance (p) Between CAS, RBC Usage, and Survival for Individuals in Entire Group and in Each Category

	CAS vs RBC			CAS vs Survival*			(Postop)† CAS vs Survival			RBC vs Survival			(Postop)† RBC vs Survival		
	n	r	p	n	r	p	n	r	p	n	r	p	n	r	p
All	64	.454	=.001	64	-.281	<.02	56	-.203	<.07	70	-.408	=.001	62	-.310	<.01
PNC	20	.380	<.05	20	-.480	<.02	16	-.504	<.03	22	-.619	=.001	18	-.550	<.01
MISC	10	.280	NS	10	-.355	NS	9	-.317	NS	11	-.112	NS	10	-.044	NS
SC	8	.461	NS	8	-.257	NS	7	-.161	NS	8	-.378	NS	7	-.316	NS
PBC	16	-.077	NS	16	-.174	NS	14	.000	NS	18	-.126	NS	16	-.189	NS
CA	10	.261	NS	10	.000	NS	10	.000	NS	11	-.174	NS	11	-.174	NS

*Survival for 6 months = 1; nonsurvival = 0.
†Not including 8 deaths during first liver transplants.

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The mean usage for all first liver transplantations was 43 units for red cells, 40 for FFP, 21 for platelets, and 9 for cryoprecipitate.

Survival Correlation

Correlation of RBC usage and CAS with survival was significant for the patients as a group and for the PNC group specifically. Additionally, the CAS correlated significantly with RBC usage as shown in Table 11.5. The two postoperative groups in the table exclude patients who died in the operating room.

DISCUSSION

These findings support the contention that when widespread parenchymal liver damage occurs, as in many of the patients in the PNC and MISC groups, severe clotting abnormalities result. When large areas of normal hepatic parenchyma remain, as in bile duct disease (PBC and SC) or malignancy, normal amounts of coagulation factors may still be produced.

The correlation between the degree of coagulation abnormality (CAS) and RBC usage is highly significant ($p = .001$); in addition, patients who died in the operating room and had a higher mean CAS used more blood than those surviving the procedure. With these results in mind, immediate preoperative correction of coagulation defects by various means may be helpful in decreasing blood usage intraoperatively and possibly increasing survival. Studies to evaluate this are presently underway.

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