Original Article

Malignant Biliary Obstruction: Percutaneous Biliary Intervention Versus Its Combination with Arterial chemoinfusion and chemoembolization

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ABSTRACT **Objective:** To evaluate the long-term outcomes and its relative influenced factors of percutaneous transhepatic catheter drainage and biliary stent implantation combination with Arterial chemoinfusion or /and chemoembolization in dealing malignant biliary obstruction.

Method: Fifty-five cases with malignant biliary obstruction were analyzed retrospectively including 27 males and 28 females with a mean age of 70.58+/- 12.19 yrs. The causes of obstruction were primary heptocellular carcinoma (n=2), cholangiocarcinoma (n=18), pancreatic carcinoma (n=17),periampullary tumor (n=6),gallbladder carcinoma(n= 5),liver metastasis tumor (n=7). In this series, 25 patients received PTCD treatment, the other 30 cases, bile duct stents were implanted into treat the bile duct obstruction. Etiological treatments were adopted by 30 cases following one to four weeks after PTCD or stent implantation, such as hepatic arterial chemotherapy and embolism (HACE). Data were analyzed according to both the intention-to-treat principle and the treatment actually administered. Univariate (Kaplan-Meier method) and multivariate (Cox model) analyses were performed.

Results: Technique successful rate was 100% in this series, including 37 case by PTCD and 35 cases by stenting-released. The cumulative mean survival time was 23.62+/-18.85weeks, meanwhile times for two groups were 25.17+/-20.12 weeks and 21.99+/-17.55 weeks respectively. The mean survival times were 13.85+/-11.01weeks and 37.31+/-19.14weeks($P<0.0001$), in which 30 cases followed etiological treatment and 42 cases only by PTCD or stenting-released . The treatment effective rate was 86.11%(62/72,), to whom of 62 cases in this series, the total serum bilirubin, direct bilirubin and glutamic-pyruvic transaminase (GTP) level were decreased obviously during one-week after therapy, the symptoms such as skin itch, poor appetite were relieved and improved by various degrees.

Conclusion: Placement with self-expanding stenting is an alternative to percutaneous catheter drainage in patients with malignant biliary obstruction, with potential favorable advantages for survival. Combining arterial chemoinfusion and chemoembolization play an important role in long-term outcome, these results argue against the merely use of percutaneous catheter drainage or stenting route.

KeyWords: Malignant biliary obstructive ; Interventional therapy; Curative Effects

Usually, as a life-threatening symptom, malignant biliary obstruction (MBO) was accompanied with in many late-stage malignant tumor, such as hepatocellular carcinoma, pancreas carcinoma and liver metastasis tumor. Patients with MBO have poor prognoses and median survival of only 3-10 months(1- 6), surgical curable treatment is limited seriously for malignant obstructive obstruction.

Since Molnar and Stockum (7) described the percutaneous transhepatic biliary drainage procedure in 1974,Substantial advances have been made in percutaneous therapy to treat biliary obstructions. Experiences with the insertion of expandable stents into the extrahepatic bile duct in five mongrel dogs were reported in 1985 (8). For nearly two decades, the percutaneous biliary catheter drainage and percutaneous biliary stent implantation has become a standard palliative treatment for inoperable malignant biliary obstructions. Despite widespread experience in percutaneous drainage or stenting in malignant biliary obstructions, articles comparing the outcomes of merely percutaneous biliary intervention versus combing transcatheter arterial chemoinfusion and chemoembolization (TACE) in lesions caused malignant jaundice are limited in number.

We present the results of percutaneous biliary catheter drainage and stenting versus its combing TACE in patients with inoperable malignant biliary obstruction. This is a retrospective nonrandomized studies intended to compare long-term survival rate of two methods and to evaluate its relative factors.

Materials and Methods

The authors have no commercial, proprietary, or financial interest in the products or companies described in this article.

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Submitted December 20, 2008. Accepted for publication February 25, 2009.
Available at www.lymphologyandoncology.com

ISSN: 1538-5124/$ - see front matter

Patient Population

From August 1998 to August 2005, fifty-five patients with inoperable MBO were evaluated in this retrospective study, including with 27 males and 28 female with an average age of 70.58+/-12.19yrs. All patients were considered for surgery but could be re jected due to disease extent (metastases, portal vein or hepatic arte rial obstruction, or invasion of both hepatic lobes) or severe disa bility due to age or associated diseases. The cause of MBO was pancreatic carcinoma in 17 patients, primary hepatocellular carci noma in 2 patients, cholangiocarcinoma in 18 patients, gallbladder cancer in 5 patients, periampullary tumor in 6 patients, liver metas tases tumor in 7 patients The stricture was located in the upper third of the common bile duct (CBD) in 30 patients, in the middle third in 18, and in the lower third in 7.

All patients were diagnosed as malignant biliary obstruction by abdominal spiral enhanced CT or/and enhanced MR, combing with percutaneous cholangiography findings, meanwhile based on symptoms at presentation, with pathologic confirmation whenever possible. The main clinical symptoms of malignant biliary obstruction included anodynia icteric sclera, skin itching, flavourina in different some degree. The main results of laboratory examination in our series before treatment are shown as Table 1.

The inclusion criteria were the presence of malignant obstruction of the CBD below the hilar confluence caused by unresectable malignant disease for which palliative treatment was indicated. Exclusion criteria were previous biliary surgery, previous insertion of other metallic endoprostheses, and uncontrollable coagulopathy (international normalized ratio > 3.0). Patients were also excluded from the trial if they were confirmed massive tumoral hepatic infiltration (multiple nodules in both lobe or diffuse infiltration).

The protocol of the clinical trial was approved by the ethics committee of the Shanghai 10th People's Hospital of Tongji University, and written informed consent was obtained from each patient. Of 55 patients, 23 cases who had MBO received arterial chemoinfusion or/and embolization after percutaneous transhepatic interven-

Table 1

Baseline Characteristics of 55 Patients with malignant biliary obstruction

Patient Characteristics	Treatment		P
	PTCD(n=25)	STENT(n=30)	
Mean age (y)	74.64± 12.17	69.03± 11.81	0.090
SEX			0.500
male	11 (44.0)	16 (53.3)	
female	14 (56.0)	14 (46.7)	
Clinical Diagnosis			0.618
liver cancer	1 (4.0)	1 (3.3)	
cholangiocarcinoma	8 (32.0)	10 (33.3)	
pancreatic carcinoma	8 (32.0)	9 (30.0)	
ampullary carcinoma	3 (12.0)	3 (10.0)	
carcinoma of gallbladder	3 (12.0)	2 (6.7)	
metastatic carcinoma	2 (8.0)	5 (16.7)	
Level of biliary obstruction			0.355
upper 1/3	13 (52.0)	17 (56.7)	
middle 1/3	7 (28.0)	11 (36.7)	
lower 1/3	5 (20.0)	2 (6.7)	
Child-Pugh scale (median)	8 (7-11)	9 (7-11)	0.770
GPT (IU/L) (median)	129.00 (29.00-381.00)	101.50 (31.00-448.00)	0.306
TB (umol/L) (median)	321.20 (114.80-573.60)	319.95 (46.00-537.00)	0.465
DB (umol/L) (median)	176.00 (53.60-398.20)	168.65 (28.50-378.30)	0.333
AKP (IU/L) (median)	368.00 (153.00-841.00)	534.00 (104.00-2490.00)	0.017
r-GT (IU/L) (median)	447.00 (84.00-1162.00)	481.50 (51.00-1641.00)	0.362
Alb (g/L) (median)	30.0 (19.0-39.0)	27.5 (18.0-38.0)	0.249
PT (second) (median)	0.50 (-1.0-4.7)	0.65 (-2.2-3.6)	0.820

Data are numbers of patients, unless otherwise indicated. Numbers in parentheses are percentages.

Child–Pugh scale–Child–PUgh scale for hepatic function

GPT–glutamic pyruvic transaminase

TB–serum total bilirubin DB–serum direct bilirubin

AKP–alkaline phosphatase r–GT–glutamyltranspeptidase

Alb–serum albumin PT–prolong of prothrombin time than standard control

tion in this retrospective study.

Percutaneous technique Initially, standard percutaneous transhepatic cholangiography with a thin 21-gauge Chiba minimally invasive needle (William Cook Europe, Denmark) was performed under local anesthesia with 2% lidocaine HCl (Zhaohui Pharmaceuticals Inc., Shanghai, China) and analgesia with 50 mg pethidine HCl (Huayuan Pharmaceuticals Inc., Shanghai, China),and then a guide wire was placed through the stenosis (single-needle technique). At that time, first a 5-F catheter (Cordis, Johnsion& Johnsion, USA) and thereafter a 8.3F drainage catheter (William Cook Europe, Denmark) by a 0.35 inch stiff hydrophilic wire (Terumo, Tokyo, Japan), with its distal end in the duodenum for internal-external drainage, was placed. The catheter was fixed to the skin and connected to a sealed bag, where bile was collected for the first 24-72 hours. A self-expanding metal stent mounted on a delivery system was then placed. The stent was dilated if stent expansion at the level of the stricture was less than or equal to 50% of the diameter of the unconstrained stent ends (as measured on the anteroposterior view of the cholangiogram). Thereafter, imaging was repeated via the drainage catheter to check patency, function, and stent position. An external drainage catheter was left in place for 1-3 day after stent release. The catheter was removed if free bile flow into the duodenum was documented or the drainage quantity of bile in a sealed bag collected less than 100 ml in 24 hours for stenting patients.

Transcatheter Arterial Chemoinfusion or /and Chemoembolization (TACE) Clinical assessment in the interventional radiologist and serum bilirubin and liver enzyme assays were conformed the recovery of hepatic function. The baseline characteristics before TACE in 55 patients with MBO were shown in Table 2.After PTCD or stenting 7-28 days later(median 15days,mean,15.74 days), arterial Chemoinfusion or /and Chemoembolization were adopted as etiological therapy for the patients who had signed written informed consent approved by the ethics committee of the Hospital . The arterial proposal we used included as following: 5-fluorodeoxyuridine (5-fluoro-2'-deoxy-β -uridine, FUDR, Zhejiang Haizheng Pharmaceuticals Inc., Zhejiang, China) 1000-1250mg and carboplatin 300mg were infusioned by common hepatic artery and superior mesenteric artery with a half of total infusion dosage respectively, thereafter, pirarubicin 20mg (Shenzhen Main Luck Pharmaceuticals Inc., Shenzhen, China) and iodized oil 5-10ml (Shanghai Xudong Pharmaceuticals Inc., Shanghai, China) were administered for chemoembolization according to focus size and its arterial supply（iodized oil dosage usually as 1ml per 1.0 cm tumor diameter in its CT shown maxim diameter）. The arterial interventional treatment would be repeated from 6 -8 weeks (median, 6 weeks; mean, 6.72 weeks.)

Follow up

All patients' clinical and radiological data were recorded on standard forms. Follow-up evaluation included assessment of serum bilirubin and liver enzyme levels (alkaline phosphatase, alanine aminotransferase, and r-glutamyl transpeptidase) performed before percutaneous drainage and before arterial interventional treatment. Clinical assessment in the interventional radiology outpatient facility and serum bilirubin and liver enzyme assays were also performed every 10 weeks after treatment unless there was clinical evidence of jaundice, cholangitis, or other complications. Between these assessments, monthly control examinations were also performed by telephone interviews with patients until the jaundice reoccured or the patient died.

Complications such as cholangitis, cholecystitis, and pancreatitis were diagnosed by clinical signs and symptoms, by laboratory tests, and when indicated by imaging studies. When the patients had signs of jaundice, ultrasonography or computed tomography (CT) of the liver was performed to determine whether the jaundice was caused by advanced metastatic disease or if the intrahepatic ducts were dilated and repeat intervention was indicated. Percutaneous transhepatic cholangiography was performed before repeat percutaneous biliary intervention to determine the type and level of obstruction.

Study Endpoints and Definitions

Major study endpoints were assessment of technical and therapeutic success, stent and drainage patency, hepatic function level changes transarterial interventional effects and patients' survival.

Biliary intervention was considered technically successful if a stent was deployed in the expected location and the degree of stent expansion after balloon dilation, when necessary, was at least 80% of the diameter of the unconstrained stent ends (as measured on the anteroposterior view of the cholangiogram). Safety was judged on the basis of the incidence of complications. Events directly related to stent placement that resulted in admission to the hospital for therapy, an unplanned increase in the level of care, permanent adverse sequelae, or death were classified as major complications. Minor complications were events that required nominal therapy or observation and resulted in no sequelae.

The definition of a stent remaining patency and the arterial treatment being clinically successful in the follow-up period were the absence of recurrent biliary obstruction and the focus caused obstruction keeping reduce in size and number than its occurred before treatment . Primary patency of the stents was defined as the time interval between initial placement and recurrence of obstruction.

To evaluating patients' hepatic function changes, data are remarked as TB、Alb、PT prolong、ascites and hepatic encephalopathy scale, according to Child-Pugh classification scale of hepatic function (Class A: score 5-7; Class B: score 8-10; Class C: score 11-15) .

If serum bilirubin and GPT, r-GT level after treatment equate to or more than preoperation level, not-relief should be considered in this research for whom received percutaneous transhepatic inter-

ventional treatment. If there was no evidence of obstruction during a patient's life, the patency period was considered equal to the survival period but censored. Survival of patients was defined as the time interval between initial biliary intervention and the patient's death.

Statistical Methods

All data observed from laboratory examination, clinical appearance and imaging results were imputted into (version 13.0; SPSS, Chicago, IL, 2004) for statistic analysis. Continuous variables were expressed as medians. Statistical methods we used are as following, Kaplan-Meier survival analysis for divided groups as percutaneous and arterial methods, univariate analysis was performed and included any potential prognostic factor: age, sex, tumor type, biliary obstruction level, duodenal invasion, comorbid medical conditions, performance status, serum bilirubin level, alkaline phosphatase level, r-glutamyltranspeptidase and serum creatinine concentrations, and prothrombin activity. Meanwhile independent sample t test is adopted between TACE therapy group and controlled group. The variance is significant when P<0.05 in this studies.

Probability curves of overall survival and freedom from biliary obstruction were calculated according to the Kaplan-Meier method and compared by performing the log-rank test. Probability data were expressed as medians. The biliary patency and survival predictor factors were analyzed by COX regression model form patient's baseline characteristics to treatment performance status.

Results

This long-term analysis was performed after including 55 patients with inoperable malignant biliary obstruction. After successfully percutaneous transhepatic treatment, all patients were informed to receive further TACE treatment as an etiological therapy. According to patient's status and willing, 23 patients received TACE treatment (TACE group), the other 32 patients refused further TACE treatment(controlled group), the baseline characteristic of 55 patients before TACE management in two groups showed no statistical significance as in Table 2 .

Technical Success

Stent insertion or catheter drainage were technically successful in all 55 patients (100%), including a percutaneous self-expanding metal stent (n =30) and catheter drainage (n =25) in this study. Table 3 shows the characteristics of the patients included in the analysis, both groups were identical or nearly identical, except for alkaline phosphatase activity (percutaneous, 94.5 IU/L vs. stenting, 176.0 IU/L; P=0.029< .005). In addition to the 6 patients in whom neither a percutaneous drainage nor a stenting was successfully placed, treatment failure was due to procedure-related complications (multiple organ failure (MOF) in four patients and hemorrhage in two) that resulted in death. On the other hand, the median decline of serum total bilirubin(TB) and serum direct bilirubin(DB) concentration level at 1week after percutaneous intra-hepatic interventional treatment were 95.40 umol/L, 53.10 umol/L in the percu-

Table 2
Patient characteristics after drainage in 55 patients with MBO

Patient characteristics	Treatment		P
	PTCD(n=25)	STENT (n=30)	
Technical success rate	25 (100)	30 (100)	
Therapeutic effective rate	22 (88.0)	27 (90.0)	0.132
Child-Pugh scale (median)	9 (6-10)	9 (7-11)	0.664
GPT decline (IU/L) (median)	45.00 (-188.00-269.00)	58.00 (-60.00-253.00)	0.928
TB decline (umol/L) (median)	95.40 (3.40-308.50)	107.80 (-112.00-450.00)	0.576
DB decline (umol/L) (median)	53.10 (2.00-211.30)	57.65 (-83.00-253.00)	0.422
AKP decline (IU/L) (median)	94.50 (-329.00-474.00)	176.00 (-387.00-1979.00)	0.029
r-GT decline (IU/L) (median)	168.50 (-224.00-903.00)	172.50 (-245.00-912.00)	0.456
Alb change (g/L) (median)	-2.0 (-11.0-7.0)	-1.0 (-15.5-8.0)	0.692
PT (second) (median)	0.8 (-0.5-2.8)	1.2 (0.3-3.6)	0.080

Data are numbers of patients, unless otherwise indicated. Numbers in parentheses are percentages.
Theraputic effective means the TB value after drainage is lower than that of before drainage
Child–Pugh scale–Child–PUgh scale for hepatic function
GPT–glutamic pyruvic transaminase
TB–serum total bilirubin DB–serum direct bilirubin
AKP–alkaline phosphatase r–GT–glutamyltranspeptidase
Alb–serum albumin PT–prolong of prothrombin time than standard control

taneous drainage group and 107.80 umol/L,57.65 umol/L in the stenting group (P=0.576,P=0.422).

Therapeutic Success

Therapy was successful in 22 patients of the percutaneous drainage group and 27 patients of the stent-release group. When therapeutic success was calculated according to the treatment actually applied, there were no differences between groups (percutaneous, 22 [88%] of 25 patients; stenting, 27 [90%] of 30 patients; P =0.132). Similarly, there were no statistical significance in the concentration decline of GPT,AKP and r-GT level after percutaneous treatment (Table 3) .

Table 3
Baseline characteristics before HACE in 55 patients with MBO

Baseline characteristics	Treatment		P
	HACE (n=23)	Controll (n=32)	
Mean age (y)	71.47± 12.41	71.17± 12.13	0.936
SEX			0.876
male	11 (47.8)	16 (50.0)	
female	12 (52.2)	16 (50.0)	
Clinical Diagnosis			0.034
liver cancer	0 (0.0)	2 (6.3)	
cholangiocarcinoma	6 (26.1)	12 (37.5)	
pancreatic carcinoma	8 (34.8)	9 (28.1)	
ampullary carcinoma	3 (13.0)	3 (9.4)	
carcinoma of gallbladder	1 (4.3)	4 (12.5)	
metastatic carcinoma	5 (21.7)	2 (6.3)	
Level of biliary obstruction			0.167
upper 1/3	10 (43.5)	20 (62.5)	
middle 1/3	9 (39.1)	9 (28.1)	
lower 1/3	4 (17.4)	3 (9.4)	
Child-Pugh scale (median)	9 (6-10)	9 (7-11)	0.288
GPT (IU/L) (median)	63.00 (16.00-569.00)	55.00 (6.00-209.00)	0.156
TB (umol/L) (median)	161.00 (19.20-415.30)	170.70 (48.40-437.60)	0.227
DB (umol/L) (median)	97.50 (9.70-278.60)	116.50 (27.50-287.10)	0.277
AKP (IU/L) (median)	244.00 (135.00-572.00)	329.00 (87.00-1020.00)	0.089
rGT (IU/L) (median)	198.00 (48.00-923.00)	216.00 (75.00-786.00)	0.669
Alb (g/L) (median)	28.0 (14.0-39.0)	27.0 (15.0-37.0)	0.395
PT (second) (median)	0.8 (0.4-1.9)	1.2 (-0.5-3.6)	0.031

Data are numbers of patients, unless otherwise indicated. Numbers in parentheses are percentages.
Child–Pugh scale–Child–PUgh scale for hepatic function
GPT–glutamic pyruvic transaminase
TB–serum total bilirubin DB–serum direct bilirubin
AKP–alkaline phosphatase r–GT–glutamyltranspeptidase
Alb–serum albumin PT–prolong of prothrombin time than standard control

As Table 4 showing, after TACE treatment, there were statistical differences between TACE group and controlled group in Child-Pugh scale, TB and DB level, including PT changes. The decline level of GPT, AKP and r-GT level after vascular interventional management were no statistically significant.

Biliary Patency and Obstruction Relief Time

After a median follow-up of 112.43 weeks (range, 4-311 weeks), the cumulative biliary patency of overall patients in 10, 20, 30, 40, 50, 60 weeks were 91%,60%,39%,32%,23% and 10% respectively. The cumulative patency of TACE treatment group and controlled group was shown in Fig. 1A, the patency rate of TACE treatment group versus controlled group by independent samples test, P value was equal or less than 0.05 between 20-40 weeks. By Kaplan-Meier analysis for biliary patency, estimate mean patent time was 32.58 weeks vs. 28.31 weeks according to PTCD and stenting grouping (log-rank test, P=0.530>0.05), as by TACE inter-

Table 4
Patient characteristics after HACE in 55 patients with MBO

Patient characteristics	Treatment		P
	HACE (n=23)	Control (n=32)	
Child-Pugh scale (median)	7 (5-10)	8 (3-12)	0.026
GPT decline (IU/L) (median)	32.20 (-20.00-318.00)	9.00 (-14.00-75.00)	0.071
TB decline (umol/L) (median)	73.40 (4.40-264.00)	40.60 (-174.00-166.10)	0.008
DB decline (umol/L) (median)	47.80 (4.20-190.30)	26.00 (-33.50-112.20)	0.010
AKP decline (IU/L) (median)	106.00 (-82.00-1979.00)	163.00 (-387.00-1473.00)	0.656
r-GT decline (IU/L) (median)	72.00 (-486.00-672.00)	73.00 (-530.00-245.00)	0.695
Alb change (g/L) (median)	4.0 (-8.0-16.0)	1.0 (-6.0-5.0)	0.078
PT (second) (median)	0.6 (0.1-2.8)	1.2 (0.0-3.4)	0.014

Numbers in parentheses are range of variance
Child–PUgh scale–Child–PUgh scale for hepatic function
GPT–glutamic pyruvic transaminase
TB–serum total bilirubin DB–serum direct bilirubin
AKP–alkaline phosphatase r–GT–glutamyltranspeptidase
Alb–serum albumin PT–prolong of prothrombin time than standard control

vention factor, estimate mean patent time was 41.58 weeks vs. 16.62 weeks for TACE group and controlled group (log-rank test, P=0.000<0.05) (Fig. 1B) .

Biliary obstruction recurred in 11 (50%) patients in the percutaneous group and in 18 (66.7%) patients in the stenting group. In fact, the Cox regression model, including both the percutaneous transhepatic procedure and vascular performance status score, was used to identify vascular performance status score as an independent predictor of biliary patency (relative risk, 7.005; 95% CI: 2.686, 18.269; P =0.000<0.05).

Periprocedural Morbidity and Mortality

The major complication rate was higher in the percutaneous group than in the stenting group, although this difference was not statistically significant (12% vs. 6.7%, respectively; P=0.219),.By the end of follow-up, forty-eight patients were died. The mortality rate of TACE group in 10,20,30, and 40 weeks were 4%, 19%, 12%, 37%, respectively, meanwhile, 36%,50%,33% and 75% respectively of controlled group, there was obvious difference between groups with respect to cumulative number of died cases (Independent t-test P=0.028<0.05) .

Patient Survival

By the end of follow-up, seven patients were alive. After a median follow-up of 112.43 weeks (range, 4-311 weeks), the cumulative survival rate of overall patients in 10, 20, 30, 40, 50, 60 weeks were 78%,53%,43%,24%,15% and 10% respectively.There was no difference in the probabilities of survival (percutaneous drainage 26.97 weeks; stent-release, 26.09 weeks; log-rank test, P=0.902 >0.05)(Fig. 1C), meanwhile the probability of overall survival was significantly higher in the TACE group than in the controlled group (38.30 vs.16.22 weeks; log-rank test, 5.13; P=0.000)(Fig. 1D) . At univariate analysis, vascular performance status score and preoperation DB level at entry were the additional variable associated with patient survival. The Cox regression model, including both the percutaneous transhepatic procedure and vascular performance status score, was used to identify vascular performance status score as an independent predictor of survival (relative risk, 3.982; 95% CI: 1.92, 8.23; P =0.000<0.05).

Discussion

Self-expanding stents were introduced in an attempt to overcome the limitation of external biliary drainage catheters and plastic endoprostheses. Metal stent have high expansion ratio, provide a larger lumen for drainage, permit stent placement in multiple ducts. Since Klaus A .et al (1992)(9) published the histological analysis results of bile duct tissue from 15 patients who underwent treatment for MBO with stenting-placement, the most important factors contributing to occlusion biliary stent had sludge formation, tumor overgrowth and ingrowth, not foreign body reaction or mucosal hyperplasia. More and more papers report that incrustation of sludge and bile and tumor progression in the form of ingrowth and overgrowth that result in stent occlusion are ongoing primary mechanisms of failure (4, 10-13).

An average survival time of less than 9 months is characteristic of patients who have MBO. By stenting-release, Boguth et al [14] observed recurrent obstructive jaundice in 20% (n =12) of 59 patients

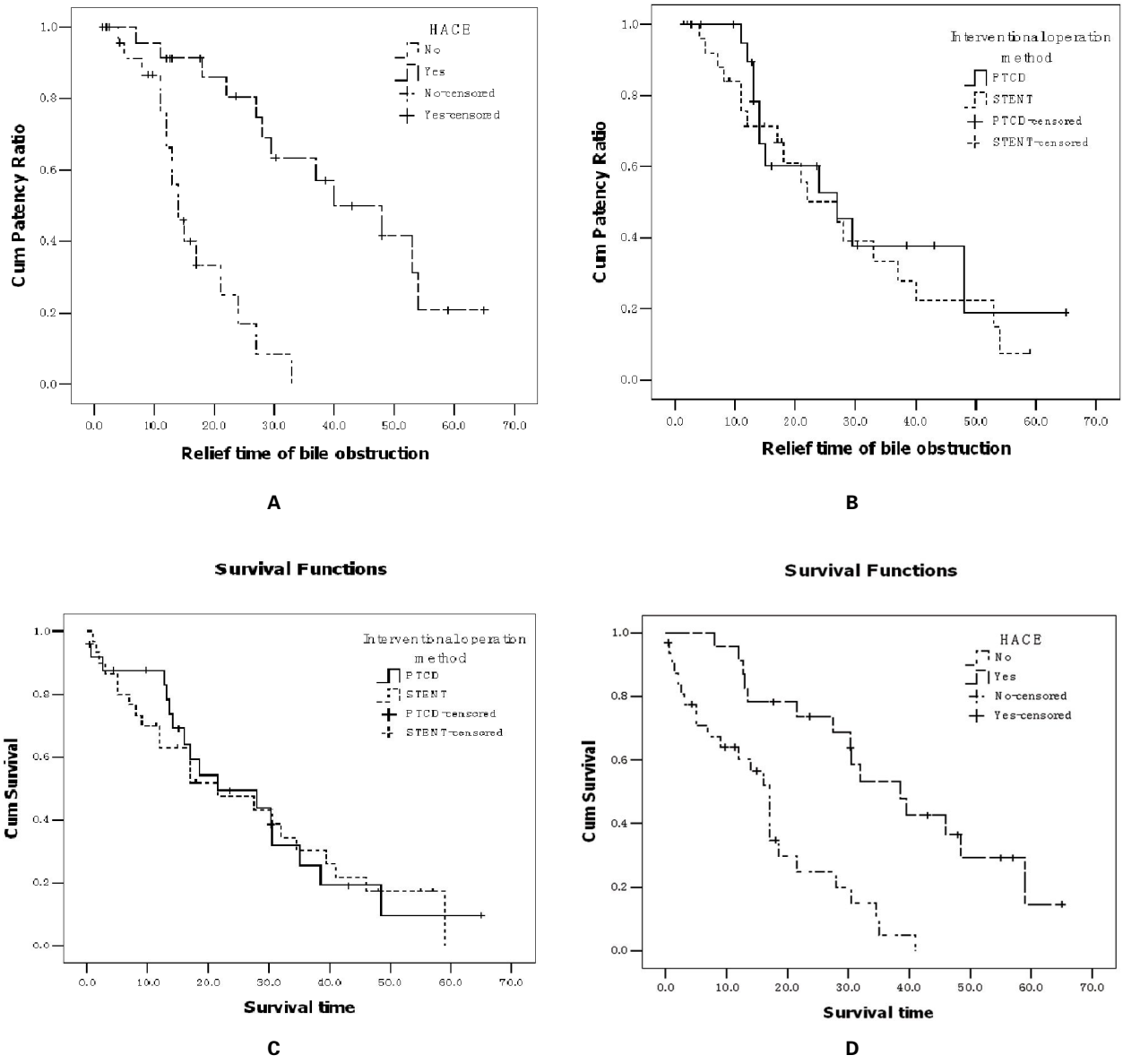

Fig. 1 A. Cumulative patency of TACE treatment group and controlled group; B. Cumulative patency of PTCD group and stenting group; C. Cumulative survival of PTCD group and stenting group; D. Cumulative survival of TACE treatment group and controlled group.

after treatment of malignant obstructions with placement of self-expanding stainless steel stents, the mean survival time in their series was less than 6 months. In the long-term survival time, our results suggest that there was no difference in the probabilities of freedom from biliary obstruction, but the probability of overall survival was significantly higher in the TACE group than in the controlled group. Vascular performance status score is an independent predictor of survival form univariate analysis, namely etiologic therapy for caused MBO should play very important role for survival after liver function become or approach normal.

For etiologic therapy, adjuvant radiotherapy including local, external and intra-luminal method have been advocated since Johnson DW (1985) reported treatment with external-beam and intracavity radiotherapy for malignant obstruction jaundice (15) . In 1995, Whittington R et al.(16) published the results of protracted fluorourail infusion with radiation in management of localized pancreaticobiliary carcinoma. Meanwhile, the results of treatment with intra-luminal radio-therapy of proximal biliary neoplasm were reported by Eschelman DJ et al(17) in 1988. As to vascular intervention for malignant biliary obstruction, a few articles were found in our nation and East- Asian countries. Lu ZM et al (18) reported 45 cases who received treatment for local tumor had an average survival of 15.2 months. Miura Y et al (19) treated 23 of the 29 patients by expanding stent, including seventeen patients underwent radiotherapy, and 16 patients received various systemic chemotherapies, significant increase was seen in the median survival time in

the chemo-radiation group: 261 days versus 109 days in controlled groups. In this retrospective trial, the median survival time of TACE group and controlled group was 38.30 weeks versus 16.22 weeks. The survival result of controlled group is almost identical with the results of other articles reported. The main reason of relative long-term survival time of TACE group is treatment of primary tumor which induced malignant biliary obstruction. Fig.2 intuitionistically demonstrates the Great influence done by HACE to the prolongation of survival time.

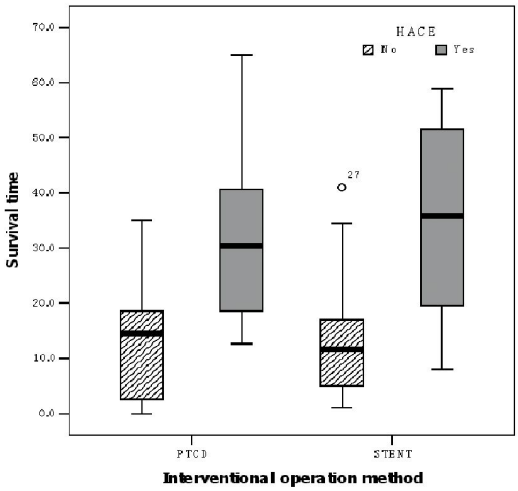

Fig.2 Great influence done by HACE to the prolongation of survival time

To improve the patency rate achieved with metallic stents, a few studies (6,20-24) to investigate polyurethane-covered metallic stents have been performed. However, in these studies, the patency duration was not prolonged compared with the duration achieved with noncovered stents. In the three studies (6,20,24) in which polyurethane-covered metallic stents were used, each of the authors reported defects in the polyurethane-covered stents, with tumor ingrowth and consequent stent obstruction; these findings suggest that polyurethane degrades over time. Lee et al (25) observed 25- and 50-week patency rates of 81% and 53%, respectively, in a study cohort of 100 patients treated with various metallic stents.. In an European multicenter study that included 42 patients (26), significant difference in the patency rate of four types of metallic stents was observed. Self-expandable nitinol and Ni-Co-Ti alloy stents had 25-week patency rates of 78% and 67%, respectively, whereas Z-stents and balloon-expandable tantalum stents had 25-week patency rates of 30% and 20%, respectively. In this retrospective nonrandomized studies, By Kaplan-Meier analysis for biliary patency, according to PTCD and stenting grouping, estimate mean patent time had no statistic difference (32.58 weeks vs. 28.31 weeks, P=0.530),as by TACE intervention factor, estimate mean patent time shown obviously statistic difference (41.58 weeks vs.

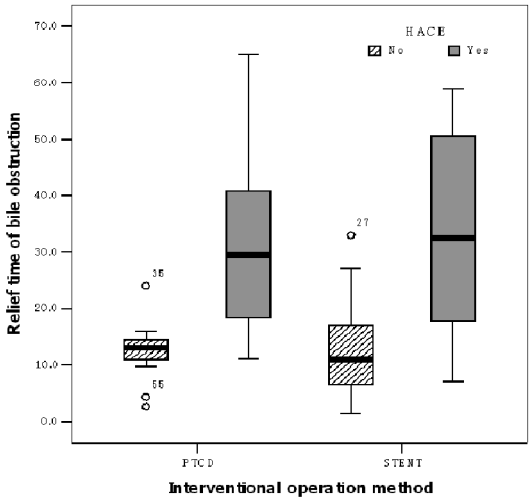

Fig. 3 Great influence done by HACE to the prolongation of biliary patency

16.62 weeks , P=0.000). Namely, treatment for focus which caused malignant biliary obstruction would play very important role in keeping biliary patency, although many investigators in those studies concluded that metal stents offered a higher success rate and longer prosthesis patency than did polyethylene prostheses. Fig.3. intuitionistically demonstrates the Great influence done by HACE to the prolongation of biliary patency.

As to overcome recurrent obstruction after stent implantation, there has been a considerable range of reported rates of restenosis of different stents including covered, uncovered and radiation stents. It is difficult to compare the patency rates with different stents because most patients died before their stents had been in place long enough to become occluded. Lammer et al (27) treated 53 patients who had malignant biliary obstructions with self-expanding stainless steel stents, and only six (11%) of these patients experienced recurrent obstructive jaundice. The mean observation period, however, was 4.5 months. O'Brien et al (13) treated 28 patients with malignant obstruction by means of endoscopic implantation of self-expanding stainless steel stents. During a survival time of 1.0-38.5 months (median,15.1 months), they observed a 46% (13 patients) re-occlusion rate. In our series, biliary obstruction occlusion rate is coincidence with the other reports, but in the Cox regression model analysis, vascular performance status was only an independent predictor of biliary patency (relative risk, 7.005; 95% CI: 2.686, 18.269; P =0.000<0.05).

As Jiang Weijian (28) reported, the main causes of death in MBO patients are bleeding of congestive tract, hepatic failure and multiple organ function failure. Although the PTCD and stenting can relieve the symptoms and improve the life quality, they both do no effect on the growth of carcinoma, so it shows no significant difference in survival time between the two groups. This viewpoint is also demonstrated in the statistic analysis for the etiologic therapeutic factor: whatever in PTCD or stenting group, the survival

time of etiologic-therapied sub-group significantly exceeded that of controlled sub-group ($P < 0.001$). So it is important and essential to give effective and in-time etiologic therapy after biliary intervention for prolonging the patients' survival time.

By analysing the data of the patients who died in short-term (less than 4 weeks and 8 weeks), we observed that the direct serum bilirubin of these patients are significantly higher than the others ($P > 0.05$). Direct serum bilirubin is the metabolic product of indirect serum bilirubin in hepatic cells and excreted into intestinal tract through biliary system, the higher level it remains in blood, the more serious degree of bile duct obstruction and more harmful effect on hepatic function and other system presents. The indications of such cases for intervention should be more strict. Whether and at which level the direct serum bilirubin could be regarded as a criteria of patient exclusion still requests further research..

In conclusion, our results suggest that placement with self-expanding stents is an alternative to percutaneous catheter drainage in patients with malignant biliary obstruction, with potential favorable advantages for survival. With consideration that combining arterial chemoinfusion and chemoembolization is seemd to play an important role in long-term outcome, these results argue against the merely use of percutaneous catheter drainage or stenting route. In that sense, this study provides a rationale for comparing merely percutaneous and combining with TACE to define the better approach to this important clinical issue.

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