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CLINICAL INVESTIGATION

Percutaneous Treatment of Malignant Jaundice Due to Extrahepatic Cholangiocarcinoma: Covered Viabil Stent Versus Uncovered Wallstents

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Abstract To compare clinical effectiveness of Viabil-covered stents versus uncovered metallic Wallstents, for palliation of malignant jaundice due to extrahepatic cholangiocarcinoma, 60 patients were enrolled in a prospective and randomized study. In half of the patients a bare Wallstent was used, and in the other half a Viabil biliary stent. Patients were followed up until death. Primary patency, survival, complication rates, and mean cost were calculated in both groups. Stent dysfunction occurred in 9 (30%) patients in the bare stent group after a mean period of 133.1 days and in 4 (13.3%) patients in the covered stent group after a mean of 179.5 days. The incidence of stent dysfunction was significantly lower in the covered stent group ($P = 0.046$). Tumor ingrowth occurred exclusively in the bare stent group ($P = 0.007$). Median survival was 180.5 days for the Wallstent and 243.5 days for the Viabil group ($P = 0.039$). Complications and mean cost were similar in the two groups. Viabil stent-grafts proved to be significantly superior to Wallstents for the palliation of malignant jaundice due to extrahepatic cholangiocarcinoma, with comparable cost and complication rates. Appropriate patient selection should be performed prior to stent placement.

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Introduction

Cholangiocarcinoma is the second most common primary cancer in the hepatobilliary region [1]. The location is intrahepatic in up to 5–10% of cases, hilar (Klatskin's tumor) in 60–70%, and extrahepatic in 20–30% [2]. Early diagnosis is usually difficult and therefore cholangiocarcinoma is fatal in most cases due to the late clinical presentation and lack of effective nonsurgical therapeutic modalities [3]. The only curative solution is complete surgical resection; nevertheless, in most cases the tumor is unresectable at presentation and the prognosis is limited to 12 months due to cachexia and rapid decline in performance status. Liver failure and sepsis, secondary to biliary obstruction, can also contribute to the high mortality [4]. Overall survival rate, including operated patients, is low, with <5% surviving up to 5 years [5].

Percutaneous or endoscopic stent insertion using metallic stents offers a valid palliation in the case of inoperable lesions and is considered the most "cost-effective" palliative treatment [6–9]. However, mesh metallic stents are frequently occluded due to tumoral ingrowth, leading to continuous medical reinterventions for the patient. In the effort to avoid this discomfort, covered metallic stents have been introduced over the last 10 years, with the use of various coverage materials [10–15]. Initial data on the efficacy of covered stents were limited and controversial. More recent studies directly comparing covered versus bare stents have shown promising results [16]. In previous studies Viabil-covered stents, due to their ePTFE/FEP coverage and their specific conformation, have

been shown to be safe and effective in the palliation of malignant biliary disease and efficient in preventing tumor ingrowth [17–20].

The purpose of this prospective randomized study was to compare the clinical results of Viabil stent-grafts versus Wallstents for the palliation of malignant biliary disease secondary to unresectable extrahepatic cholangiocarcinoma. The study hypothesis was that the use of covered stents in patients with the following selection criteria would improve the survival and patency rates without a higher complication rate. The composite endpoint was defined as patient death or endoprosthesis occlusion.

Materials and Methods

Study Design and Patients

The study design was prospective and randomized. Two medical centers were involved in the study, following the same protocol. The study protocol was both approved by local ethical committees and performed according to the guidelines described in the Declaration of Helsinki for biomedical research involving human subjects. Participating interventional radiologists had considerable experience with biliary interventions.

Inclusion criteria were obstructive jaundice caused by Bismuth type I unresectable extrahepatic cholangiocarcinoma, with a total serum bilirubin level <15 mg/dl, absence of hepatic metastasis, patient age ≤80 years, a satisfactory coagulation status (INR value ≤1.5 and platelet count value of ≥70,000), and a performance status >3 on the Eastern Cooperative Oncology Group scale [21 (Table 1). Absolute exclusion criteria were intrahepatic and hepatic bifurcation (Klatskin) tumors, presence of hepatic metastasis, patient age >80 years, previous surgical or radiotherapeutical palliative treatment, and very poor patient general condition. Presence of ascites was not a contraindication; in those cases a left-side approach was chosen. Prior to the procedure, written informed consent was obtained from all patients.

Sixty patients were included in the study: 36 men and 24 women, with an age range of 46–78 years (mean, 65.3 years). In half of the patients a bare stent was placed, whereas in the other half a covered stent was used. In patients assigned to the bare stent group, a Wallstent (Boston Scientific, Watertown, MA, USA) was inserted, and in patients assigned to a covered stent a Viabil-covered biliary stent (W. L. Gore & Associates, Flagstaff, AZ, USA) was used. Patients' characteristics are reported in Table 2.

Randomization was performed using a randomization envelope containing 30 mesh and 30 covered stent cards. The cards were divided at the two centers involved and each card was drawn after the diagnostic percutaneous transhepatic cholangiography (PTC) for patients who fulfilled the study's inclusion criteria.

Diagnosis of cholangiocarcinoma was based on pathological examination after needle/forceps biopsy or bile aspiration, cross-sectional imaging (computed tomography and magnetic resonance imaging findings of mass with delayed enhancement), and clinical findings (malignant jaundice with increased neoplastic markers).

Stent Type

The Wallstent is a self-expanding stent made from a biomedical stainless-steel alloy with a radiopaque core, filaments woven in a tubular fashion, and flexible construction. The Wallstent is mounted on a 6-Fr (RP Delivery System) or 7-Fr (Unistep Plus Delivery System) carrying catheter. The Unistep Plus Delivery System is made of coaxial tubes which allow reconstrainment as

Table 1 Study inclusion criteria

Bismuth classification	Type I
Total serum bilirubin level	<15 mg/dl
Hepatic metastases	Absence
Patient age	<80 years
Ascites	Absence
Coagulation status	
INR	<1.5
Platelet count	>70,000
Performance status	
Eastern cooperative Oncology group scale	>3

Table 2 Patient characteristics in the two groups

Patient characteristic	Wallstent group	Viabil group
No. of patients	30	30
Gender (M/F)	16/14	20/10
Age, mean years (range)	63.7 (46–73)	66.5 (52–78)
Stricture location		
Upper CHD (not confluence)	3	3
Lower CHD	8	8
Upper CBD	10	12
Lower CBD (not papilla)	9	7
Cystic duct condition		
Infiltrated	7	14
Clips	1	5
Patent	22	11
Histological/ cytological diagnosis	18/30	14/30
Total bilirubin before stenting, mean mg/dl	7.2	10.3

indicated by the limit marker and has radiopaque marker bands which aid in accurate placement of the stent. The endoprosthesis is available in a diameter of 10 or 12 mm and length of 6–9 cm. The stent diameter selected should be approximately 1–2 mm larger than the diameter desired. Deployed lengths reflect expansion to the desired diameter. Constricting the stent to a smaller diameter will cause a longer deployed length, depending on the degree of constriction. On average, a 0.5-mm change in diameter yields a 10–15% change in length. Once the desired diameter is reached, no additional reduction in stent length should occur. The Wallstent is a bare stent with an area that is not in contact with the biliary wall. The percentage free area (the area not in contact with the biliary wall) was calculated by the manufacturer for all stent diameters. The results found that the stent free area was approximately 80% fully open to nearly 50% constrained. In addition, the Wallstent endoprosthesis is magnetic resonance compatible, with the only disadvantage of some image artifacts.

The Viabil is a self-expanding covered stent made of an ePTFE/FEP tubular lining externally supported by a helical nitinol stent with radiopaque markers at both ends. The inner lining is made of low-porosity, ultrathin, 0.010-mm-thick, ePTFE/FEP. Multiple sections of the wires near each end of the nitinol stent project outward from the external surface of the tubular lining and act as anchoring fins. The presence of these lateral anchoring fins reduces the risk of stent migration and the delivery system consists of a 10-Fr outer sheath. Two versions are available on the market, one with transmural drainage side holes which are present in the lining for 2 cm along the proximal end, and a fully covered one. The purpose of these holes is to avoid obstruction of the intrahepatic side ducts or the cystic duct. If an endoprosthesis with transmural drainage holes is selected, the middle and hepatic end radiopaque rings demarcate the boundaries of the holed region. The endoprosthesis is available in a diameter of 8 or 10 mm and a length of 4, 6, 8 or 10 cm in both the holed and the fully covered version. According to the manufacturer the Viabil should extend at least 2 cm proximal and distal to the margins of the stricture. Due to the nitinol lining, total expansion is reached approximately 24 h after placement but the endoprosthesis length is not subject to variation. Positioning should not result in excessive length into the duodenum. There are not enough data at this moment regarding Viabil magnetic resonance compatibility. Finally, Viabil stents can be retrieved either percutaneously or endoscopically even several months after placement [22].

Methods

PTC was performed under local anesthesia (2% lidocaine) and conscious sedation. Antibiotic prophylaxis was administered before the procedure in all patients and continued for up to 5 days after the PTC procedure. A right-side access was chosen in most cases, reserving the left-side access to cases where there was a small amount of ascites that would not permit a right-side puncture. Stent placement for both types used was performed as either a one-step (primary stenting technique) or a two-step (secondary stenting technique) procedure. Primary stenting provides an immediate solution to the patient's problem, with a theoretical higher risk of complications. In the case of secondary stenting, there is more time to think about and organize the procedure, but the external catheter does not provide a wide-lumen internal drainage and may also be accidentally removed or even get infected. The decision for primary or secondary stenting was physician related and was based on the morphological evaluation of the lesion at the moment of initial PTC and/or from the presence or absence of hemorrhage. Particularly in cases where bleeding occurred during PTC, the stent was placed 3 to 4 days later in order to avoid stent obstruction from thrombus. When secondary stenting was performed, an 8- to 10-Fr (Flexima; Boston Scientific) biliary catheter was left in place for 2–6 days. In the case of tight strictures, balloon (6–8 mm in diameter) dilatation was performed before stent insertion or drainage catheter placement. When a covered stent was used, a 9- or 10-Fr-diameter and 25-cm-long introducer sheath (Radiofocus; Terumo, Tokyo) was advanced over a 0.035-inches, extrastiff Amplatz guidewire (William Cook Europe, Bjaeverskov, Denmark) across the stricture region into the duodenum in order to increase the diameter of the tract. When feasible, a biopsy specimen was taken with a flexible biopsy forceps (Radial Jaw 3; Boston Scientific) from the obstructed area before stent deployment. One or, occasionally, two endoprostheses were used in order to cover the entire extent of the lesion. Covered stents with side holes were placed in order not to obstruct the cystic duct or the intrahepatic ducts. In total, we used 36 Wallstents, 6–9 cm long and 10 mm wide, and 31 Viabil stent-grafts, 6–8 cm long and 8–10 mm wide. Eleven covered stents had side holes and 20 did not.

After stent placement, a 5-Fr catheter was left in the intrahepatic tract as an external access in all cases. In order to determine satisfactory stent deployment and contrast runoff, a final cholangiogram was performed 1–3 days later and catheter removal followed.

Follow-Up and Reintervention

Follow-up parameters consisted in blood laboratory exams, clinical findings, and imaging (ultrasound) on an outpatient basis. When the patient was presented with jaundice or cholangitis, stent occlusion was suspected. Imaging (ultrasound, computed tomography, or magnetic resonance imaging) and clinical evaluation confirmed stent occlusion

with dilatation of the biliary system; reintervention with endoscopic retrograde cholangiopancreatography (ERCP) or PTC followed. The use of MRI was limited to a few cases where ultrasound and contrast-enhanced computed tomography did not clearly exclude the presence of intrahepatic metastasis. Specifically, it was performed in one case in the Wallstent group and five cases in the Viabil group.

A biopsy specimen was taken with a flexible forceps from the occlusion site in order to characterize the obstruction cause. In most cases stent dysfunction occurs due to sludge formation, small stones, thrombus accumulation, or tumor in- or overgrowth. Occlusion due to sludge or stones usually occurs in cases where the endoprosthesis is not carefully deployed, kinks, or gets fractured or in cases where there is no satisfactory bile runoff toward the duodenum. Occlusion due to thrombus is seen if hemobilia occurs. Tumor ingrowth is the case where neoplastic tissue grows in between the stent struts or after cover membrane erosion in the case of covered stents. Tumor overgrowth is the case where occlusion is attributed to the growth of neoplastic tissue centrally to the proximal end of the endoprosthesis. Independent of the biopsy result, endoprosthesis revision and new cholangiography followed. Revision consisted in stent "cleaning" with a semi-inflated balloon, which was moved up- and downward in the endoprosthesis lumen. If "cleaning" was not successful or if stent kinking also occurred, bilioplasty followed (Fig. 1). If the patient's general condition was satisfactory (no hepatic metastasis and no serious comorbidities), new stent placement followed; otherwise reintervention was limited to drainage catheter insertion.

Study Endpoints and Definitions

Major study endpoints were the assessment of technical success, safety of stent implantation, patient survival, and

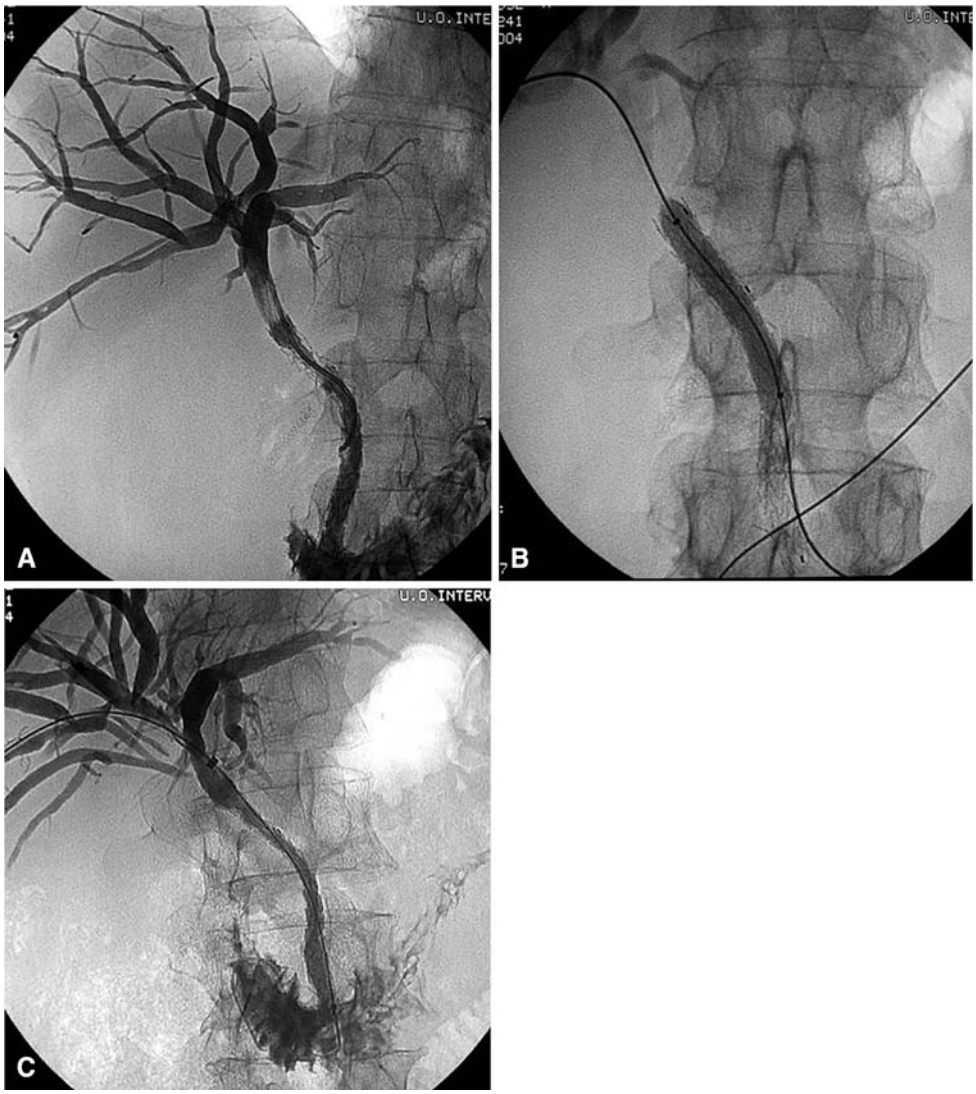

Fig. 1 **A** Stent dysfunction 102 days after placement of a 6 × 80-mm Viabil stent with side holes. **B** Reintervention in this case was performed with balloon dilatation. **C** The final cholangiographic result is satisfactory

stent patency for the patients in each study group and a comparison between the two groups. The minor study endpoints were characterization of the type of stent dysfunction in patients in each group and comparison between the two groups.

Technical success was achieved when the stent-graft was correctly deployed in the expected location, with residual stenosis at the end of the procedure <30%. Safety of stent implantation was correlated to the incidence of periprocedural and intraprocedural complications. Complications were considered early when they occurred in the first 30 days after stent placement; otherwise they were considered late and were classified as minor or major according to the SIR criteria on [23].

Stent patency corresponds to the absence of recurrent symptomatic biliary obstruction. Primary patency of the endoprosthesis was defined as the time interval between initial placement and recurrence of obstruction. If there was no evidence of obstruction during the patient's life, the patency period was considered to be equal to the survival period, but censored.

Cost-Effectiveness Analysis

The total procedure cost was calculated and compared between the two groups. Cost was subject to variation regarding the type and number of stents used, the total number of necessary sessions for stent placement, the duration of the hospital stay, and the cost associated with the number and kind of complications and reinterventions. An arbitrary mean cost was defined for each of the procedures in order to avoid differences between the two centers.

Statistical Analysis

Cumulative stent patency and patient survival were estimated by the Kaplan–Meier technique and supplemented by the log-rank test for comparisons between groups [24]. The unpaired *t*-test was used for comparison of quantitative variables, and Fisher's exact test for qualitative variables. Statistical analysis was done using the NCSS 97 statistical package (NCSS Statistical Software, Salt Lake City, UT, USA).

Results

A total of 72 patients with malignant jaundice and the diagnosis of cholangiocarcinoma were treated at our units between January 2005 and December 2007. Twelve of the patients did not meet the inclusion criteria (age, bilirubin levels) and were excluded from the study. The remaining 60 patients were included in the study, and on a randomized basis one of the two endoprostheses was used for palliation of malignant jaundice. Patients were followed up until May 2008. No patient was lost during the follow-up period.

A left-side access was used in four cases in the bare stent and two cases in the covered stent group. Stenting was performed on the same day as PTC (primary stenting) in 17 cases in the Wallstent group and 8 in the Viabil group, whereas secondary stenting was performed in the remaining 13 and 22 cases in these groups, respectively. Mean waiting time between PTC and stenting was 2.1 days for the Wallstent and 2.8 for the Viabil group. Control cholangiography and catheter removal were performed 3.3 days after stenting in the two groups, respectively.

Technical Success and Complications

All stents were successfully inserted and deployed, and no case of stent migration was observed in either group, with a technical success rate of 100% for both groups. Early complications were observed in four patients in the bare stent group (13.3%) and in three cases (10%) in the covered stent group (Table 3). In the uncovered stent group three cases of peritoneal irritation occurred immediately after stenting and were resolved with intravenous antibiotic therapy in less than 24 h. The catheter removal time was not influenced by this complication, which is considered minor (class B according to the SIR) [23]. In the same group a case of self-limited biliary hemorrhage occurred after primary stent placement. The patient remained hemodynamically stable and was not transfused or embolized, and the bleeding stopped spontaneously without influencing the hospitalization time (class A complication).

In the covered stent group two cases of peritoneal irritation occurred after primary stenting and were also resolved by intravenous antibiotic therapy in less than 24 h without any delay in the patient's management (class B complication). In the third complicated case in this group, bile leakage occurred after primary stenting that led to formation of a biloma. The hospitalization time was

Table 3 Complications in the two groups

Type of complication	Wallstent group	Viabil group
Peritoneal irritation (class B)	3/30	2/30
Self limited biliary hemorrhage (class A)	1/30	–
Biloma formation (class D)	–	1/30
Total	4/30 (13.3%)	3/30 (10%)

prolonged for a week, intravenous antibiotic therapy was administered, and percutaneous drainage was necessary (class D complication).

Patency and Survival

The mean follow-up after stent placement was 212 days (range, 45–675 days). All patients were dead at the end of the study. Thirty-day mortality rate was zero for both groups. Median survival time was 180.5 days (SE [standard error] = 15.8 days, SD [standard deviation] = 82.6 days) for the mesh stent group and 243.5 days (SE = 25.7 days, SD = 141.1 days) for the covered stent group. There was a significant difference in the two groups according to Kaplan–Meier survival analysis ($P < 0.05$) (Fig. 2).

Stent premature occlusion occurred in both groups. Mean patency rate was 166 days (SE = 16 days, SD = 87.7 days) for the mesh stent and 227.3 days (SE = 25.5 days, SD = 139.7 days) for the covered stent group. There was also a significant difference in the patency rates of the two groups according to Kaplan–Meier survival analysis ($P < 0.05$) (Fig. 3).

Endoprosthesis dysfunction occurred in nine (30%) patients in the mesh stent group, after a mean period of 133.1 days (SE = 16.1 days, SD = 48.4 years), and forceps biopsy was successfully performed in all. The cause of dysfunction was tumor ingrowth in eight (88.8%), in one of whom ingrowth was associated with tumor overgrowth. In one patient occlusion was found due to sludge formation and occurred 55 days after placement. Dysfunction occurred in four (13.3%) patients in the Viabil stent group, two with and two without side holes, after a mean period of 179.5 days (SE = 26.1 days, SD = 52.2 days) (Fig. 4). Forceps biopsy was successfully performed in all, and obstruction was attributed to tumor overgrowth in the two fully covered endoprostheses (Table 4). There was a significant difference ($P < 0.05$) between the two groups in tumor ingrowth (which occurred exclusively in the mesh stent group), whereas no significance was noted regarding tumor overgrowth (which occurred mainly in the covered stent group).

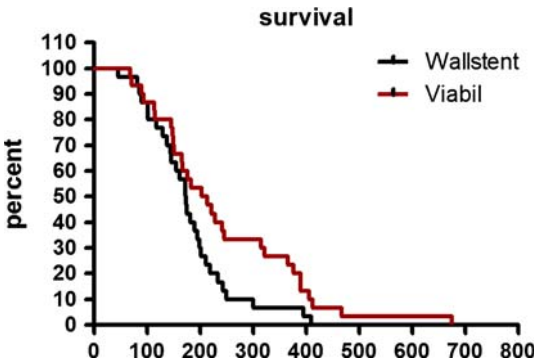

Fig. 2 Kaplan–Meier survival analysis of the patients in the two groups ($P = 0.037$)

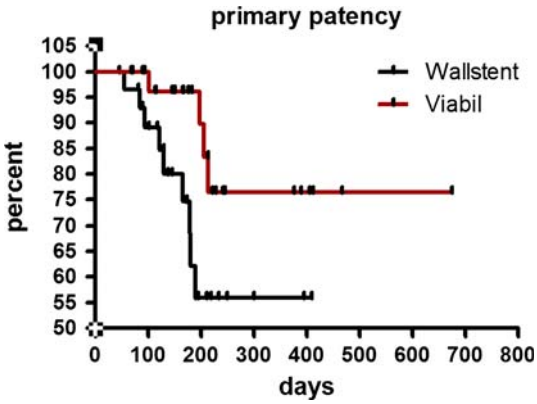

Fig. 3 Kaplan–Meier analysis of primary patency in the two groups ($P = 0.046$)

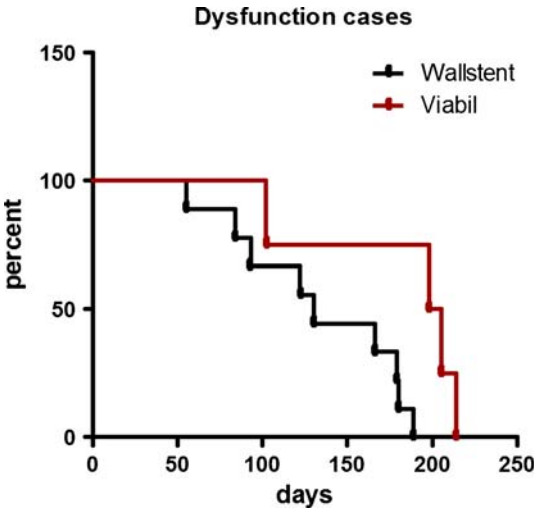

Fig. 4 Kaplan–Meier analysis of primary patency in cases where stent dysfunction occurred ($P = 0.024$)

Reintervention for stent obstruction was performed transhepatically in all cases in both groups due to the fact that patients were referred to the interventional radiology units. In four cases in each group, new mesh stent insertion was performed, whereas in three cases in the Wallstent group an 8-Fr drainage catheter was left in situ due to the patient's

Table 4 Causes of stent dysfunction in the two groups

Type of stent dysfunction	Wallstent group	Viabil group		*P*-value
		Holes	No holes	
Overgrowth	1/9	0/2	2/2	ns
Ingrowth	8/9	0/2	0/2	<0.05
Sludge formation	1/9	2/2	0/2	ns

ns nonsignificant

Table 5 Overall comparison of the two groups

	Wallstent group	Viabil group	*P*-value
Length of survival	180.5 days	243.5 days	<0.05
Incidence of complications	13.3%	10%	ns
Dysfunction	30%	13.3%	<0.05
Patency rate	133.1 days	179.9 days	<0.05

ns nonsignificant

impaired condition. Mean secondary patency was 48.5 days (SE = 11.2 days, SD = 33.7 days) for the mesh stent group and 121.8 days (SE = 31 days, SD = 15.5 days) for the covered stent group. Table 5 reports an overall comparison between the two groups.

Cost-Effectiveness Analysis

The cost difference between the two groups consisted in the type of device used initially, the total length of hospital stay, and the number and type of reinterventions needed. The mean Wallstent price amounted to 1897€ (range, 1430–3030€; SE = 94.8€; SD = 519.6€) and the mean Viabil price was 2419€ (range, 2310–4610€; SE = 76.3€; SD = 418.1€). The materials used for implantation of the two stents (puncture set, guidewires, catheters, contrast) were considered to be of equal cost in the two groups. The mean hospital stay for patients treated with a Wallstent was 6 days (SE = 0.3 days, SD = 1.8 days), and that for the Viabil group was 5.6 days (SE = 0.4 days, SD = 2.3 days). Considering a mean price for each hospital day of 600€, the total cost of the first intervention was 5504€ (range, 3887–8920€; SE = 203.6€; SD = 1115€) for the mesh stent group and 5223€ (range, 4710–11,910€; SE = 271.4€; SD = 1489€) for the covered stent group, without a significant difference between the groups ($P = 0.42$).

Considering the number and type of reinterventions and the total hospital stay, the mean cost for the Wallstent group amounted to 6875€ (range, 3980–11,460€; SE = 403.9€; SD = 2212€), and that for the Viabil stent group to 6352€ (range,: 4710–16,440€; SE = 458.2€; SD = 2510€), without a significant difference between the groups ($P = 0.39$). These results show that even though cost of the Viabil is higher, due to the fact that fewer reinterventions are needed, there is no significant difference in the total cost of patient management.

Discussion

Cholangiocarcinoma is a malignant tumor that arises from the intrahepatic and extrahepatic bile duct epithelium and is classified as an adenocarcinoma in more than 90% of cases [3, 25]. It is the second most common primary cancer in the hepatobiliary region, after hepatocellular carcinoma, with approximately 2500 cases annually in the United States, but still remains a relatively rare disease, accounting for <2% of all human malignancies [1, 26]. Cholangiocarcinoma may affect the common hepatic and distal common bile duct in 20–30% of cases, whereas in 60–70% it may arise at the bifurcation of the hepatic ducts (Klatskin's tumour) [2]. In 5–10% it may originate from the intrahepatic bile ducts [2, 7].

Patients suffering from Bismuth I cholangiocarcinomas may be in an operable condition, so they can be treated surgically. Complete surgical resection, when feasible, offers the best option of cure. Outcome and prognosis depend on growth pattern and stage [27–29]. However, 56–81% of patients have unresectable cholangiocarcinoma due to advanced tumor stage or inoperable condition due to bile duct obstruction and comorbidities [30–32]. There is also a group of patients thought to be operable who, during surgical exploration, turn out to be inoperable. Therefore, the surgical approach is more a center-based decision. In a recently published surgical study, Allen et al. summarize their 18-year experience with resection of distal cholangiocarcinoma disease and report a 5-year survival rate of 43% [33]. Their study included only patients in whom resection was performed after surgical exploration. In only 15% of these cases were positive resection margins detected, while the perioperative overall mortality rate was 3%. In another study, Nakeeb et al. report a median survival of 11.3 months for distal cholangiocarcinoma, including therapeutic and palliative surgery, with an operative mortality rate of 4% [34].

In our series, inoperability followed the local center's criteria, which include invasion to the adjacent vessels (portal vein and hepatic artery), the hepatoduodenal ligament, the proximal and distal biliary extent, and pancreatic invasion. We consider surgery to be the first treatment option when it can be assured that resection offers R0 surgical margins, considering the 3–4% mortality rate of surgical palliation. Nevertheless, the fact is that only a few patients are really in condition to benefit from surgery, because there is no guarantee that the preoperative inclusion criteria will be confirmed on the operation table and because of the relatively high intra- and postsurgical mortality and morbidity rate. There are patients who would obtain a better quality of life after nonsurgical palliation with stent placement but, because of the complications that may occur during a palliative surgical operation, do not recover and die earlier than might be expected.

Unfortunately there has no direct randomized comparison of stents and palliative surgery until now. In general, nonsurgical biliary drainage has been shown to offer similar palliation and survival with palliative biliary–enteric

bypass, but with a lower morbidity, mortality, cost, and recovery time [35]. In previous studies, percutaneous use of metallic stents has offered valid palliation in cases of malignant strictures from cholangiocarcinoma [6–8]. Endoscopic stent placement may also be considered an option, but in our experience percutaneous treatment is very effective for stent placement, without causing serious complications. Metallic stent placement is considered to be the most cost-effective treatment of inoperable malignant common bile duct strictures, especially for patients who are expected to live more than 6 months [9].

Bare stents may be occluded from tumor invasion through the stent's struts. In the effort to prevent tumor ingrowth, covered metallic stents have been developed over the last 10 years using various coverage materials [10–15, 36]. Nevertheless, early generations of covered stents did not show higher patency rates than uncovered stents because the coverage membrane was not always effective in preventing ingrowth, while in some cases they were more prone to migration or dislocation [10, 11]. ePTFE/FEP-covered stents are more likely to be safe and effective in the palliation of malignant biliary disease [17–20]. It has also been shown that the ePTFE/FEP membrane is efficient in preventing tumor ingrowth [19]. In addition, due to its conformation, the Viabil endoprosthesis is less prone to migration [37]. This prospective randomized study, has compared the Viabil endoprosthesis with Wallstents, which have been widely used during the last decade as a palliation option for malignant obstructive jaundice.

The fact that we treated only Bismuth type I lesions allowed us to use uncovered and covered stents in a randomized way. This would not have been feasible for Bismuth types II to IV, for which only bare endoprostheses should be used. In the case of type I lesions care should be taken with the location of the cystic duct. A fully covered endoprosthesis may be placed only when the cystic duct is occluded from tumor. A cystic duct that is free or partially infiltrated necessitates the use of a covered endoprosthesis with the presence of side holes in order to avoid cholecystitis, and this is a clear advantage of the Viabil in comparison to other biliary stents developed in the past that did not offer a version with side holes. According to the initial experience of our group [18, 20], acute cholecystitis may occur when a Viabil stent with side holes is not ideally positioned and covers the cystic duct. Our experience in this study shows that the Viabil stent, due to its flexible conformation, the presence of side holes, and the variety of lengths available (40–80 mm), may, in experienced hands, be safely placed almost anywhere in the common hepatic or common bile duct, keeping the cystic duct patent, and for this reason no cholecystitis occurred.

Ingrowth is an issue with bare stents as shown in a study by Tham et al. [38], who analyzed Wallstent occlusion after placement in malignant biliary strictures and concluded that its major cause was ingrowth in 64% of cases. Our results indicate that Viabil stents have a higher primary patency than Wallstents, with Kaplan–Meier survival analysis yielding a *P*-value of 0.04. The increased primary patency rate must be quite exclusively attributed to the fact that Viabil stents are covered with a material that is likely to be effective in preventing tumor ingrowth [19]. In our study, ingrowth occurred exclusively in the Wallstent group after a mean period of 142.9 days. The patency rate was influenced due to the fact that there was a very low early mortality rate in the population that we treated, due to the satisfactory condition of the patients that we selected to treat. In other words, the beneficial effects of ePTFE/FEP membranes may be noticed especially in cases with less advanced disease and no serious comorbidities, whereas if survival is <3 months, covered stents likely are not necessary.

Regarding tumor overgrowth, Viabil stents seem to have a disadvantage in comparison with Wallstents. Wallstents have been shown to be effective in preventing tumor overgrowth, and this may be explained by the fact that Wallstents, if not fully expanded, maintain a longer length than initially predicted. This characteristic is absent from Viabil stents, where, due to the nitinol skeleton, the endoprosthesis does not shorten after deployment, and tumor overgrowth may not always be prevented if the stent expands only 1–2 cm above the proximal tumor site. We did not experience the same thing regarding tumor growth in the papillary region, considering that the covered stent was advanced in the papilla toward the duodenum in all cases that we treated. It is interesting that we did not see any case of pancreatitis. Ideally the papilla should be kept open with a proximal bare extension but Viabil conformation does not offer this option.

There was also a statistically significant difference in survival rate between the two groups in this study. The higher survival rate of the covered stent group is probably a result of the quality of life that is offered to patients by the covered endoprosthesis, considering that they do not undergo frequent reinterventions and avoid frequent hospitalization and possible complications.

Another impact of the covered endoprosthesis was found in the cost analysis, where, even though the mean cost of a single session is higher for the Viabil stent than for the Wallstent, there is no significant difference in total procedure costs between the two groups. This finding is similar to the older study by Lammer et al., comparing plastic and metallic stents for palliation of malignant jaundice [39], and has to do with the fact that lower patency rates lead to new hospitalizations and reintervention, with a total cost increase. Cumulative costs per patient

to maintain improvement have been measured over several months, and although mesh stent placement is initially less expensive, costs over time increase due to repeat procedures to treat reocclusion. In the long run, placement of a more expensive but more durable covered stent is equal to placement of a cheaper mesh stent.

In conclusion, Viabil stents have been shown to be safe for palliation of malignant jaundice caused by extrahepatic cholangiocarcinoma. They also seem to be effective in preventing tumor ingrowth and may therefore reduce the rate of stent occlusion and increase patients' quality of life. The results of this study suggest that Viabil stents may be superior to conventional uncovered Wallstents in the management of malignant biliary obstruction due to Bismuth type I cholangiocarcinoma, with similar costs and complication rates, and therefore should be considered as the first option in the selection of an endoprosthesis, especially for inoperable patients in relatively good general condition.

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