ORIGINAL ARTICLE

A non-randomized study in consecutive patients with postcholecystectomy refractory biliary leaks who were managed endoscopically with the use of multiple plastic stents or fully covered self-expandable metal stents (with videos)

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Background: Endoscopic management of postcholecystectomy biliary leaks is widely accepted as the treatment of choice. However, refractory biliary leaks after a combination of biliary sphincterotomy and the placement of a large-bore (10F) plastic stent can occur, and the optimal rescue endotherapy for this situation is unclear.

Objective: To compare the clinical effectiveness of the use of a fully covered self-expandable metal stent (FCSEMS) with the placement of multiple plastic stents (MPS) for the treatment of postcholecystectomy refractory biliary leaks.

Design: Prospective study.

Setting: Two tertiary-care referral academic centers and one general district hospital.

Patients: Forty consecutive patients with refractory biliary leaks who underwent endoscopic management.

Interventions: Temporary placement of MPS (n = 20) or FCSEMSs (n = 20).

Main Outcome Measurements: Clinical outcomes of endotherapy as well as the technical success, adverse events, need for reinterventions, and prognostic factors for clinical success.

Results: Endotherapy was possible in all patients. After endotherapy, closure of the leak was accomplished in 13 patients (65%) who received MPS and in 20 patients (100%) who received FCSEMSs ($P = .004$). The Kaplan-Meier (log-rank) leak-free survival analysis showed a statistically significant difference between the 2 patient populations (χ^2 [1] = 8.30; $P < .01$) in favor of the FCSEMS group. Use of <3 plastic stents ($P = .024$), a plastic stent diameter <20F ($P = .006$), and a high-grade biliary leak ($P = .015$) were shown to be significant predictors of treatment failure with MPS. The 7 patients in whom placement of MPS failed were retreated with FCSEMSs, resulting in closure of the leaks in all cases.

Limitations: Non-randomized design.

Conclusion: In our series, the results of the temporary placement of FCSEMSs for postcholecystectomy refractory biliary leaks were superior to those from the use of MPS. A randomized study is needed to confirm our results before further recommendations. (Gastrointest Endosc 2015;■:1-9.)

Abbreviations: FCSEMS, fully covered self-expandable metal stent; MPS, multiple plastic stents.

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Biliary leaks can occur after laparoscopic cholecystectomy in 0.3% to 2.7% of patients.[1] ERCP has emerged as a minimally invasive method for the primary treatment for bile leaks.[2-11] The outcome of sealing the leak can be accomplished by a variety of endoscopic techniques. These methods include biliary sphincterotomy alone, biliary stenting with or without sphincterotomy, and nasobiliary drainage.[2-10] All of these methods of endotherapy seem to be equally effective in allowing the leak to heal in most cases, but the approach of choice remains controversial.[2,8-10] Although there is no consensus regarding the optimal endoscopic intervention, recent data suggest that a combination of biliary sphincterotomy and the placement of a transpapillary biliary stent has a better outcome for the treatment of high-grade and more complex biliary leaks.[3] However, despite the high success rate and safety of endotherapy for bile leaks, there are reports of difficult-to-treat refractory bile leaks that require multiple endoscopic interventions and sometimes require surgery.[3,4,9,10,12] In recent years, the temporary placement of a fully covered self-expandable metal stent (FCSEMS) has emerged as an effective rescue therapy for refractory biliary leaks.[12-20] However, in patients with persistent biliary leaks, instead of using FCSEMSs, the endoscopist could place >1 plastic stent at a lower cost to further decrease the transpapillary pressure gradient and to seal the leak. However, costs also should be considered as far as rescue therapy is concerned. In our country, the cost of an ERCP with placement of multiple plastic stents (MPS) is U.S. $2200, and the cost of an ERCP in which a FCSEMS is used is U.S. $3200. The price of the ERCP is the same for both treatments, but the placement of an FCSEMS increases the price by $1000, and this issue can be included in the treatment decision. Further, in the United States the problem is similar, being that the price of the ERCP is the same, but the cost of the stents is different, increasing the price by >$1000. Until now, there have been no comparative studies between these 2 types of endoscopic treatment, and the decisions regarding treatment of a refractory biliary leak must be made on an individual basis.[12,16-18] Therefore, it is not known whether the MPS used for the closure of a refractory biliary leak are as successful as the use of an FCSEMS. We conducted a non-randomized study aiming to compare the clinical effectiveness of the use of an FCSEMS with the placement of MPS for the treatment of postcholecystectomy refractory biliary leaks. Additionally, we compared the technical success, adverse events, need for reinterventions, and prognostic factors for clinical success.

METHODS

Patients and setting

This work was a prospective clinical study. Between May 2010 and September 2013, 2 consecutive cohorts of patients with refractory biliary leaks were enrolled in the study and followed prospectively. The patients were referred for ERCP if they had a postcholecystectomy biliary leaks that failed to close after endotherapy, specifically a combination of biliary sphincterotomy and the placement of a 10F transpapillary biliary stent. Patients were submitted to endotherapy in 2 consecutive cohorts of 20 patients each. The first 20 patients were treated with MPS, and the next cohort of 20 patients was treated with the temporary placement of FCSEMSs. In each group of consecutive patients, the treatment was done at the discretion of the endoscopist, meaning that the endoscopist was allowed to choose the number, type, and size of the plastic stents in the MPS group or the size and type of the metal stent in the FCSEMS cohort. Further, this decision was done accordingly with the diameter of the duct and the location of the leak. Patients with refractory bile leaks with an etiology other than postcholecystectomy were excluded from the study. This study was conducted at 3 institutions (2 tertiary-care referral academic centers and 1 general district hospital). All of the patients provided informed written consent before their procedures. Each institutional review board involved approved this study.

Outcomes and definitions

The primary outcome was the clinical success of each type of endotherapy, defined as closure of the leak. The secondary outcomes included the determination of prognostic factors associated with closure of the leak, technical success, safe removal of the stents, duration of treatment, adverse events, and the need for reinterventions. Refractory biliary leaks were defined as leaks that failed to close after endoscopic intervention with a combination of biliary sphincterotomy and the placement of a 10F transpapillary biliary stent, regardless of the biliary leak location (cystic stump, common bile duct and/or common hepatic duct, Luschka).[17] All of the plastic stents used were at least 7 cm long. High-grade biliary leaks were defined as leaks observed fluoroscopically before intrahepatic opacification.[3] Closure of the leak was considered after the cessation of bile output, which was defined as biliary drainage of <5 mL/day in the percutaneous drains[17] and confirmed at follow-up ERCP. Failure of endotherapy was defined as the persistence of biliary drainage through the percutaneous drain or the persistence of a bile leak at follow-up ERCP. Reintervention was defined as the need for further intervention to control the leak after the initial endotherapy for the refractory leak, including repeat ERCP for additional stenting or surgery. Adverse events were defined as any adverse event related to the ERCP or stent placement, and adverse events were carefully monitored by using previously determined definitions.[13,14,17,21]

Intervention, stents, and follow-up

The ERCP procedures were performed with the patient in the prone position under sedation with propofol

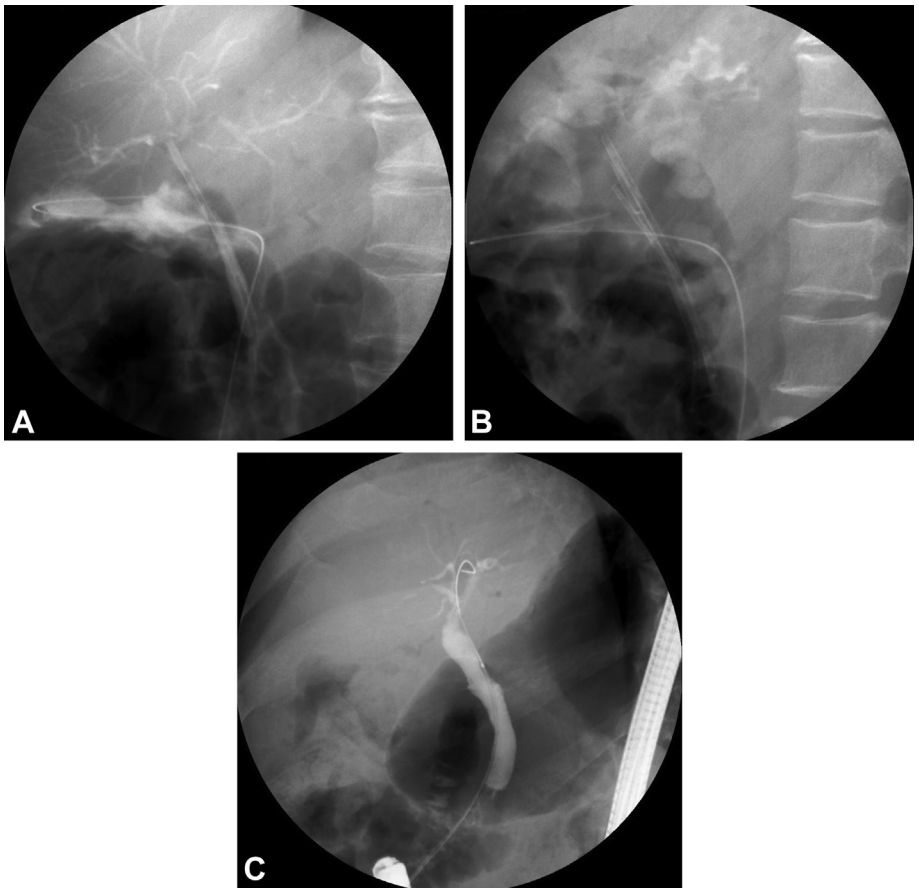

Figure 1. Endoscopic management of a refractory biliary leak by using multiple plastic stents. **A,** Fluoroscopic image showing persistence of a bile leak and persistence of biliary drainage through the percutaneous drain after 15 days of plastic stenting. **B,** Radiograph immediately after endoscopic placement of 3 plastic stents for endotherapy of a refractory bile leak. **C,** Follow-up cholangiography after plastic stents removal. No contrast media extravasation is seen.

administered by an anesthesiologist. All procedures were performed by 2 experienced pancreatobiliary endoscopists (J.C., M.L.). During the study, J.C. performed the endoscopic procedures at the 3 participating centers, and M.L. performed most of the endoscopic examinations in center 1 (Cuf). Patients were considered eligible to enter the study if, after the first treatment for the biliary leak, the output of the drain was $\geq$600 mL/day at the sixth day, $>$500 mL/day after the 10th day, or $\geq$400 mL/day at day 15 in association with maintenance or worsening of the bilious fluid collections on abdominal US or on a CT scan. During the initial ERCP procedure, a diagnostic cholangiogram was obtained for documenting the site and grade of the refractory biliary leak. For treatment with MPS, the endoscopist determined the number and diameter of the stents to be inserted on the basis of the diameter of the bile duct (Fig. 1). Although this decision was left to the discretion of the endoscopist, there was always an effort to place the maximum number of stents allowed by the size of the duct. Smaller ducts were treated with a combination of a lower number of stents (eg, a small duct with a diameter of 5 mm was treated with 2 stents—1 of 10F + 1 of 8.5F; a large duct with a diameter of 10 mm was treated with $\geq$3 stents of 10F). For this treatment, polyethylene stents were used in all cases (Advanix biliary stent; Boston Scientific, Natick, Mass. Cotton-Huibregtse biliary stent; Cook Medical, Winston-Salem, NC). For FCSEMS treatment, the guidelines of the study included the following: (1) Patients in whom the bile duct had a diameter of $\leq$5.0 mm were treated with FCSEMSs having an 8-mm luminal diameter and a length that varied from 40 to 80 mm to allow the stent to be placed above the leak site in all cases. (2) Patients in whom the bile duct diameter was $>$5.0 mm were treated with FCSEMSs having 10-mm luminal diameters (Video 1, available online at www.giejournal.org). In the FCSEMS approach, 2 types of stents were used: WallFlex (Boston Scientific) and the Niti-S (TaeWoong Medical, Seoul, South Korea). All of the patients were treated and monitored with a percutaneous drain, and the drainage output was used to evaluate the success of stent placement in closing the bile leak. The placement of a percutaneous drain was an inclusion criterion for the study. The drains were placed at 2 different times:

TABLE 1. Demographics and baseline characteristics of patients

Characteristic	Metal stents	Plastic stents	*P* value
Sex, no. (%)			.204
Male	9 (45)	13 (65)	
Female	11 (55)	7 (35)	
Age, median (range, mean), y	62 (32-89, 59.8)	61.5 (23-84, 59.8)	.914
Site of bile leak, no. (%)			.490
Cystic duct stump	15 (75)	13 (65)	
Common bile duct/common hepatic duct	5 (25)	7 (35)	
Type of leak, no. (%)			.507
High grade	14 (70)	12 (60)	
Low grade	6 (30)	8 (40)	
Time interval until first rescue ERCP, median (range, mean), d	10 (7-24, 10.6)	10.5 (6-16, 11.1)	.390
Output of the percutaneous drain 1 d before patient entered the study, median (range, mean), mL/d	620 (780-590, 644.2)	650 (800-450, 666.1)	.630

during surgery when injury was suspected or before the first ERCP when a bilious fluid collection was found. The drains stayed in place during the study until cholangiographic documentation of clinical success of the rescue therapy was obtained. After clinical evidence of complete resolution of the initial condition, the patients were scheduled for a second ERCP in which the stents were removed by using rat-toothed forceps or a cold snare at the discretion of the endoscopist (Video 2, available online at www.giejournal.org). During the second ERCP, a new cholangiogram was obtained for documenting the closure of the leak. However, after the first treatment for the refractory biliary leak, patients with drain outputs >300 mL/day after the 10th day in association with maintenance or worsening of the bilious fluid collections on abdominal US or on a CT scan were considered to be treatment failures and were subjected to a second ERCP. After confirmation of a persistent bile leak, patients previously subjected to treatment with MPS were retreated with FCSEMSs, and the patients initially treated with FCSEMSs were considered for surgery.

For all patients, the follow-up continued for at least 6 months after the end of treatment and closure of the leak. The patients were followed-up with blood analyses and upper abdominal US at 3 and 6 months after discharge from the hospital.

Statistical analysis

The intention-to-treat method was used in all of the analyses. The χ^2 test, the Mann-Whitney *U* test, and the Fisher exact test were used to calculate the statistical significance of different demographic and clinical variables when appropriate. The cumulative leak-free survival (clinical success) was evaluated by using the Kaplan-Meier method, and the groups were compared by using the log-rank test. The 95% confidence interval (CI) for long-term, leak-free survival was calculated with the Clopper-Pearson (exact) method. The potential prognostic factors associated with closure of the leaks were assessed by using a univariate analysis that was conducted by using the Fisher exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. All of the reported *P* values were for a 2-tailed test, and $P < .05$ was considered statistically significant. All of the statistical analyses were performed by using the software package SPSS, version 22 (Statistical Package for the Social Sciences, IBM Corporation, Armonk, NY).

RESULTS

Between May 2010 and September 2013, 40 patients (22 male and 18 female) with a median age of 62 years (range 23-89 years) were enrolled in the study. Twenty patients were included in each group. All of the patients had a refractory biliary leak located at the cystic stump or at the common bile duct and/or common hepatic duct. The patient demographics, bile leak location, type of leak characteristics, output of the percutaneous drain before the study was begun, and interval between the first ERCP and second endoscopic intervention for the refractory biliary leak are summarized in Table 1. There were no significant differences in the demographics and baseline characteristics of the 2 groups defined in the Methods section. The 40 patients included were treated as follows: In center 2 (Pulido Valente) J.C. performed 19 cases (9 in the MPS group and 10 in the FCSEMS group). In center 3 (Beja) J.C. performed 11 cases (7 in the MPS group and 4 in the FCSEMS group). In center 1 (Cuf) M.L. performed 9 cases (4 in the MPS group and 5 in the

TABLE 2. Comparative outcomes between plastic stents and metal stents after endoscopic management of refractory biliary leaks, including adverse events

Outcome	Plastic stents	Metal stents
Clinical success of rescue endotherapy, no. (%)	13/20 (65)	20/20 (100)*
Cessation of bile output in percutaneous drains, time, median (range), d	11 (8-17)	3.5 (2-9)
Duration of stenting, time, median (range), d	56 (26-82)	17 (8-29)
Adverse events, stent-related, no. (%)	0 (0)	2 (10), mild pancreatitis

*$\chi^2 = 8.485$; $P = .004$.

FCSEMS group), and J.C. performed 1 case (FCSEMS group).

First endoscopic treatment for refractory biliary leaks

Stent implantation was technically successful in all patients. The endoscopic management of refractory biliary leaks is shown in Table 2. Regarding the clinical success of the first rescue endotherapy, 33 of 40 patients (82.5%) who received temporary placement of MPS or FCSEMSs had their bile leaks closed. In the group of patients subjected to the temporary placement of MPS, 13 of 20 patients (65%) experienced closure of the biliary leak. In the 13 patients with clinical success, ceased bile output in the percutaneous drains was seen after a median time of 11 days (range 8-17 days), and the plastic stents were removed after a median period of 56 days (range 22-82 days). In this group of 13 successfully treated patients, the median value of the maximum number of stents simultaneously inserted was 3 (range 2-5), and the median maximum stent diameter was 25.5F (range 20F-35.5F). In the remaining 7 patients without clinical success, the median value for the maximum number of stents simultaneously inserted was 2 (range 2-2), and the median maximum stent diameter was 20F (range 18.5F-20F). The range of French gauge for MPS placement was calculated from the sum of the French gauges of the stents implanted at the same procedure (eg, 2 × 10F and 1 × 8.5F would be 2 × 10 = 20 + 1 × 8.5 = 8.5, which would be 28.5) as suggested elsewhere.[11] Clinical success was achieved in all of the 20 patients treated with FCSEMSs. In this group, cessation of bile output in the percutaneous drains was observed after a median time of 3.5 days (range 2-9 days), and the metal stents were removed after a median period of 17 days (range 8-29 days). In the 20 patients submitted to the temporary placement of an FCSEMS, 8 patients were treated with the Niti-S stent and 12 with the WallFlex stent. There were no differences in clinical success, median time of stenting, adverse events (namely pancreatitis), and safe removal of the stents among the 2 groups of patients. Regarding the clinical success, there was a significant difference between the 2 types of endotherapy in favor of the use of the FCSEMS ($\chi^2 = 8.485$; $P = .004$).

Follow-up, reinterventions, and adverse events

The remaining 7 patients in whom the placement of MPS was unsuccessful were considered clinical failures because of similar or increased levels of percutaneous drainage and maintenance of the bilious fluid collections on abdominal US or on a CT scan. In this group of 7 patients, the output of the percutaneous drain 1 day before the placement of the FCSEMS was as follows: median 395 mL/day (range 345-520 mL/day). The follow-up ERCP with the removal of the plastic stents confirmed the persistence of a biliary leak. All 7 of the patients were treated again with the placement of an FCSEMS. At the end of this new endoscopic management, clinical success was obtained in all of the patients. In this group of 7 patients treated again with an FCSEMS, cessation of bile output in the percutaneous drains was observed after a median time of 5 days (range 4-10 days), and the metal stents were removed after a median period of 28 days (range 14-30 days). Further, in this group of 7 patients, 3 were treated again with the Niti-S, and 4 were treated again with the WallFlex stent. There were no differences in clinical success, median time of stenting, adverse events, and safe removal of the stents among the 2 groups of patients. Overall, in the 27 patients treated with an FCSEMS, the stent removal attempts were achieved without difficulty. In this group of 27 patients, the mid bile duct diameter was initially measured, with values ranging from 5.3 mm to 13.2 mm. After FCSEMS placement, the bile duct assumed the shape and diameter of the stent (for bile ducts <10 mm), returning to normal after FCSEMS removal. At the end of the study, none of the patients was referred for surgery, and endotherapy proved to be successful in all cases.

In the MPS group, there were no adverse events related to the ERCP or stents. In the group of patients treated with an FCSEMS, no adverse events related to the ERCP were observed. However, in 2 of 20 patients (10%) subjected to FCSEMS placement, mild pancreatitis was observed, and this adverse event was considered to be stent related. In these 2 cases, the patients were managed conservatively. There were no cases of metal stent migration, duodenal ulcerations, or de novo choledocholithiasis and bile duct strictures found within the FCSEMSs or bile ducts at the time of stent removal.

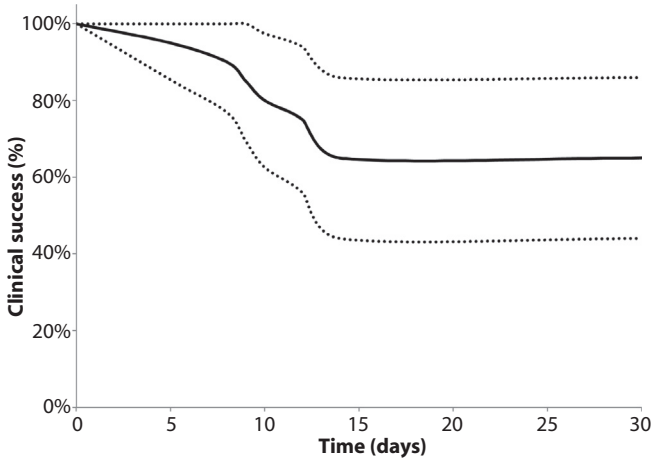

Figure 2. Kaplan-Meier analysis of leak-free survival rates (*clinical success*) after first rescue endoscopic treatment with multiple plastic stents for a refractory biliary leak (*solid line*) and 95% confidence interval (*dashed line*).

Leak-free survival and univariate analysis of prognostic factors associated with closure of the leak

After endoscopic treatment with MPS, the Kaplan-Meier analysis showed that the estimated cumulative mean time of clinical success was 23.1 days (95% CI, 18.9-27.3 days). By the end of endotherapy with MPS, the leak-free survival rate was 65% (95% CI, 44.0%-86.0%) at 30 and 60 days (Fig. 2). The comparison of leak-free survival between the patients treated with MPS and the patients subjected to FCSEMS placement by using a log-rank test showed a statistically significant difference between the 2 patient populations (χ^2 [1] = 8.30; $P < .01$), and this result was in favor of the patients who underwent FCSEMS stenting. The univariate analysis of treatment failure with MPS is shown in Table 3. Of the 7 evaluated variables (sex, age, maximum number of stents inserted, maximum stent diameter, biliary leak location, type of leak, and interval between first endoscopic treatment and second ERCP for refractory bile leak), the use of <3 plastic stents, a low plastic stent diameter (<20F), and a high-grade biliary leak proved to be statistically significant predictors of treatment failure of a refractory biliary leak with MPS ($P < .01$).

DISCUSSION

According to our findings in this prospective, nonrandomized study of 2 consecutive cohorts of patients with refractory biliary leaks after the combination of biliary sphincterotomy and the placement of large-bore (10F) plastic stents, the temporary placement of an FCSEMS is the treatment of choice. The use of MPS seems to be less preferable, leading to fewer cases (65%) of clinical success. Additionally, the use of <3 plastic stents, a plastic stent diameter <20F, and a high-grade biliary leak were associated with treatment failure by using MPS.

With the era of laparoscopic approaches, the number of biliary leaks after cholecystectomy has increased, creating the necessity for minimally invasive procedures to manage these leaks and potentially reduce morbidity and mortality.[1,9,10] ERCP has emerged as the primary treatment; the goal of ERCP is to reduce the pressure gradient between the bile duct and duodenum, therefore creating a preferential flow of bile into the duodenum and allowing the defect to heal.[1,2,8] A variety of ERCP techniques have been used, including biliary stenting, nasobiliary drainage, biliary sphincterotomy, or a combination of these procedures.[2-10] All of these techniques have proven to be effective in most cases, and the approach of choice remains controversial because each type of endotherapy has merits and limitations.[2,9,10] For simple leaks such as small cystic duct leaks (low-grade leaks) and Luschka duct leaks, the success rate of endotherapy is high. However, in a small subset of patients with more complex leaks (high-grade cystic stump leaks, common bile duct and/or common hepatic duct leaks, bile leaks after liver transplantation, or large leaks after partial cholecystectomy), successful closure can be more problematic.[3,4,12,16,17] In a retrospective study of 207 patients who had high-grade leaks, Sandha et al[3] reported that these leaks could be managed better with a combination of biliary sphincterotomy and stenting, suggesting that this modality has the highest potential for sealing a biliary leak. In the current study, we chose a standard and homogeneous approach to try to maximize the benefits of the first endoscopic treatment. Therefore, all patients with a leak were initially treated with a combination of biliary sphincterotomy and placement of a large-bore (10F) plastic stent.

However, even after the combination of stenting and sphincterotomy, refractory biliary leaks can occur, and recently, the temporary placement of an FCSEMS has been shown to be an efficacious rescue therapy, with success rates ranging from 90.5% to 100%[14-20] (Table 4). The large stent diameter diverts more flow away from the leak site, causing a significant decrease in the pressure gradient at the papilla. Furthermore, in biliary ducts where the diameter at the site of the leak is <10 mm, the FCSEMS directly covers the leak site, increasing the potential for sealing the leak. This would be true only of cystic duct and common bile duct and/or common hepatic duct leaks. Refractory bile leaks above the bifurcation are usually poor candidates for FCSEMS placement as the placement of the metal stent across the bifurcation as the potential of obstructing drainage from the other side of the liver. Baron and Poterucha[12] first reported the use of partially covered (n = 2) and fully covered (n = 1) self-expandable metal stents in 3 patients with complex biliary leaks of the gallbladder bed after open subtotal cholecystectomy procedures. That study reported a 100% rate of clinical success. Wang et al[14] reported

TABLE 3. Univariate analysis of prognostic factors associated with closure of leaks in patients treated with placement of ≥2 biliary plastic stents (MPS)

Factor	Closure of leak		*P* value
	No	Yes	
Sex, no. (%)			.658
Male	5 (38.5)	8 (61.5)	
Female	2 (28.6)	5 (71.4)	
Age, median (range, mean), y	64 (23-84, 59.0)	64 (39-79, 61.1)	.874
Site of bile leak, no. (%)			.174
Cystic duct stump	3 (23.1)	10 (76.9)	
Other than cystic duct stump	4 (57.1)	3 (42.9)	
Maximum no. plastic stents inserted, median (range, mean)	2 (2-2, 2.0)	3 (2-5, 2.9)	.024*
Maximum plastic stent diameter reached, median (range, mean), F	20 (18.5-20, 19.6)	25.5 (20-35.5, 25.4)	.006*
Time interval until first rescue ERCP, median (range, mean), d	8 (6-15, 9.6)	13 (7-16, 11.9)	.130
Type of leak, no. (%)			.015*
High grade	7 (58.3)	5 (41.7)	
Low grade	0 (0)	8 (100)	

*$P < .05$.

TABLE 4. Studies reporting the use of fully covered self-expandable metal stents for endoscopic management of benign biliary disease including bile leaks

First author	Patients, no.	Biliary leaks, no.	Etiology	Closure of leaks, no. (%)	Duration of stenting, median (range), d	Adverse events, no. (%), type of adverse event (no.)
Wang[14]	13	13	Chole and OLT	13/13 (100)	103 (67-493)	3/13 (23) Bile duct strictures (2) ampullary adenoma (1)
Canena[17]	25	17	Chole	17/17 (100)	16 (7-28)	0
Akbar[18]	37	21*	Chole	19/21 (90.5)	NA	NA
Lalezari[19]	17	5	Chole	5/5 (100)	92 (48-251)	2/5 (40) Hepatic abscess and sepsis (1) occluded stent (1)
Phillips[22]	17	17	OLT	16/17 (94.1)	102 (35-427)	6/17 (35) Bile duct strictures (6)

Chole, Postcholecystectomy; *OLT,* orthotopic liver transplantation; *NA,* not available related with the bile leak group.
*Some patients had a partially covered self-expandable metal stent.

the first case series with the use of FCSEMSs to treat a heterogeneous group of 13 patients with complex leaks. Although the bile leaks resolved in all patients, several adverse events were reported, and the prolonged FCSEMS placement was associated with the majority of the adverse events. However, a recent study evaluated 17 patients with refractory biliary leaks. All patients were successfully treated with an FCSEMS placed for ≤30 days without adverse events, suggesting that short-term stenting is efficacious and is not associated with adverse events.[17] However, some authors speculate that a refractory biliary leak could eventually be managed by upsizing the existing plastic stent or adding additional plastic stents, avoiding the costs of an FCSEMS.[12,16-18] In this study, we compared the placement of an FCSEMS with MPS, and we found significant differences. FCSEMS placement sealed the leak in 100% of patients compared with a clinical success rate of 65% in the patients subjected to MPS placement. Furthermore, in the 13 cases of success by using the MPS treatment, cessation of bile output in the percutaneous drains was observed after a median time of 11 days, which compares poorly with the results of the FCSEMS group, in which cessation of bile output in the percutaneous drains was observed after a median time of 3.5 days. These results suggest that even in cases of success, the MPS strategy is associated with a longer time to seal the leak and prolonged hospital stays compared with the temporary placement of an FCSEMS. More reinterventions were required in the MPS group because 7 of the patients did not achieve clinical success. These patients were retreated with an FCSEMS, which proved to be successful even in the cases refractory to the initial rescue therapy

by using MPS. Taken together, the results of FCSEMSs were superior to those of MPS in terms of several variables, including the clinical success rate, duration of treatment, and need for reinterventions.

The use of <3 plastic stents, a plastic stent diameter <20F, and a high-grade biliary leak were significant predictors of treatment failure with MPS. These observations suggest, with caution, the following: (1) All patients with refractory high-grade bile leaks should be treated with FCSEMSs, and (2) if treatment of a refractory bile leak by using MPS is considered, at least 3 stents with a diameter >20F should be used. In our series, all patients with low-grade refractory biliary leaks were successfully treated with MPS. We could eventually suggest that patients with refractory, low-grade, biliary leaks could be treated with MPS, reducing costs and decreasing the incidence of pancreatitis. However, as previously mentioned, a successful outcome by using MPS is associated with a longer treatment time compared with the placement of an FCSEMS, and this should be evaluated carefully in terms of costs and quality of life in future studies before this recommendation is made.

The temporary placement of an FCSEMS is safe. Several adverse events have been described in small series with long-term duration of stent placement[14,18,19,22] (Table 4), but these adverse events can be avoided by short-term stenting. Further, in most of the studies concerning benign biliary diseases, including strictures, the migration rate was >30%. In a recent study of 17 patients with postcholecystectomy refractory biliary leaks, short-term stenting (<30 days) was clinically efficacious and was associated with the absence of early and late adverse events, including migration, after a median follow-up of 125 weeks.[17] In this study, short-term stenting was associated with a low adverse event rate, and we believe that the shorter the duration of stenting the lower the probability of migration. Special concerns have been raised concerning de novo biliary strictures after temporary FCSEMS placement (especially after long-term stenting),[14] in liver transplant patients[22] and after oversizing (placement of a 10-mm stent in a duct with a smaller diameter).[23] At the end of the study, the oversizing in bile ducts with luminal diameters >5.0 mm was safe, and none of our 27 patients who had FCSEMSs placed developed de novo stricture formation. This was related to the short-term stenting as suggested in the previously mentioned report.[17] Finally, in our study, as suggested elsewhere,[23] the removal of an FCSEMS was safe and easily accomplished.

The present study has several limitations. First, our nonrandomized design could have introduced sampling bias. However, there were no major differences in the demographics, bile leak location, type of leak characteristics, and interval between first ERCP and the second endoscopic intervention between the 2 groups studied. We suggest that a prospective multicenter randomized study should be performed to confirm our results in a larger population and to allow a multivariate analysis, which would give much stronger conclusions. In this proposed future study, the length of the hospital stay and the costs should be carefully evaluated. Another potential weakness of our study is the fact that this study was performed only by very experienced endoscopists, and we cannot exclude the possibility of obtaining a poorer outcome in community hospitals. Strengths of our study include the prospective design, the relatively large sample size (refractory bile leaks are uncommon), and the newly reported findings. To our knowledge, this is the first study to compare the 2 types of rescue endoscopic management techniques available for the treatment of postcholecystectomy refractory biliary leaks.

In conclusion, in our series and in our centers the results of using an FCSEMS as rescue endotherapy for postcholecystectomy refractory biliary leaks were superior to those with the use of MPS. We suggest that a randomized clinical trial is needed before the temporary placement of an FCSEMS is recommended as the treatment of choice.

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