Fully covered self-expandable metal stents in biliary strictures caused by chronic pancreatitis not responding to plastic stenting: a prospective study with 2 years of follow-up

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Chronic pancreatitis can be complicated by benign biliary stricture in about 5-40% of the patients[1]. The severity of this biliary narrowing varies with patients having a wide range of presentation ranging from asymptomatic elevation of liver enzymes to deep jaundice and cholangitis. It is important to treat biliary obstruction, as long standing biliary stricture can lead on to secondary biliary cirrhosis[1,2]. Surgery, because of effective long lasting results, is the treatment of choice for benign biliary strictures due to chronic pancreatitis[3]. However, surgery is associated with significant morbidity and hence there have been increasing attempts to develop non surgical methods of relief of obstruction of the biliary tract[4]. Endoscopic biliary stenting is an attractive, minimally invasive, non surgical method of relief of biliary obstruction. The stenting in benign diseases has been traditionally done with plastic stents and they have been demonstrated to offer satisfactory short term biliary drainage, but long term results are not so impressive because of stent clogging or migration and thus poor long term efficacy[1,5]. To improve upon the long term results of plastic stents, insertion of multiple plastic stents have been suggested as an option. Although it results in more durable response, it requires multiple endoscopic sessions[6]. Uncovered self-expandable metallic stents (SEMS), although result in a longer and effective relief of biliary obstruction, are not considered in benign disease because of technical difficulties associated with its removal. Hence, partially covered SEMS were developed and one of their important attributes was the ability of removability, which could offer the possibility of removal of the stent once the stricture has resolved. Partially covered SEMS may also clog because of tissue in growth, thereby decreasing its patency rates. To overcome this problem of tissue in growth, fully covered biliary SEMS (FC SEMS) have been developed. They seem to be an attractive therapeutic modality in patients with benign biliary stricture due to chronic pancreatitis, but limited data is available.

The authors conducted a prospective, single-center trial to investigate the durability of resolution of benign biliary stricture due to chronic pancreatitis after temporary insertion of FC SEMSs with unfIared ends (UEs) and flared ends (FEs) in 17 patients (mean age 52 years; 16 males). The patients included had symptomatic biliary stricture that persisted after 3 months or more after insertion of a single 10 Fr plastic stent (mean 2.18 stent exchanges per patient, range 1-6) and were unfit for surgery or had refused surgery. They used Nitinol FC SEMSs 10 mm in diameter (Niti-S; Taewoong Medical Co, Gyeonggi-do, Korea). The inner part of the stent is covered by silicone at both ends (3 cm) and by polytetrafluoroethylene (PTFE) in the central part. Initially (for first seven patients) they used FCSEMSs with UEs for easier removal. However, as these stents migrated more than expected, the authors later on started using FC SEMS with a 14 mm flared ends (in subsequent 10 patients). The stents were placed below the orifice of the cystic duct in the common bile duct so as to avoid cholecystitis. The stents were planned to be removed 6 months after the insertion and the follow up was done at 6 months interval (liver function tests [LFT] and telephone interview) for a period of 2 years.

The migration rate was 100% for UE-SEMSs and 40% for FE-SEMSs. The stents could be successfully removed in all the 6 patients with stent in situ as well as in all the 3 patients with intrabiliary migrated UE-SEMSs. No patient had incomplete distal stent migration. And in all of the removed stents, the inner PTFE covering was intact. The resolution of biliary stricture at the 6 month scheduled stent removal was observed in 70.6% patients (43% of patients with UE SEMS and 90% patients with FE SEMS). After 24 months, 8 of 15 patients (53%) had normal LFT results and two patients died after 18 and 24 months, respectively, because of acute myocardial infarction and lung cancer and none of these two patients had recurrence of biliary stricture. Stent-related cholangitis caused by migration was more frequent in patients with UE-SEMSs and shorter stents (4 cm and 5cm in length), and proximal migration was seen in patients with UE-SEMSs only. On follow-up, 1 patient developed cholangitis 18 months after stent removal and underwent placement of a partially covered SEMS. The authors concluded that durable asymptomatic resolution of benign biliary stricture due to chronic pancreatitis

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**NEWS AND VIEWS**
with normalization of LFT results can be achieved more likely by using FE-SEMSs in almost half of the patients after 2 years of follow-up.

**Commentary**

In comparison to plastic stents, SEMS have prolonged patency and thus have an established role in the management of malignant biliary obstruction. But, because of stent associated endoluminal hyperplasia and extreme difficulty with potential of damage to the bile duct during removal after stent deployment, they are not usually considered as an option in benign biliary disease like benign biliary stricture due to chronic pancreatitis. However, as the fully covered SEMS are usually removable and have a prolonged patency, they may be considered in the treatment of benign biliary strictures. In the current study, the authors have demonstrated that successful long-term resolution of benign biliary stricture due to chronic pancreatitis can be achieved in with temporary fully covered SEMS placement. These results are encouraging but high rates of migration are a matter of concern. Even earlier studies with fully covered SEMS had reported higher migration rates[7,8]. Cahen et al[9] used fully covered SEMS in 6 patients benign biliary stricture due to chronic pancreatitis and found stricture resolution in 67% of patients at the time of the stent removal. However, they also reported migration in 33% patients and complications in 67% patients with impossibility to remove proximally migrated SEMS in 2 patients. Although in the current study the authors were able to remove all the proximally migrated SEMS, the complication in the form of SEMS related cholangitis because of migration of the stent was observed in 5 patients.

To decrease the migration rates, the authors used FC SEMS with a 14 mm flared ends which led on to no proximal migration and lower distal migration rates. However, these flared ends can cause duct injuries or de novo strictures because of tissue hyperplasia caused by excessive outward radial pressure of a flared stent end[10,11]. Moon et al have recently described a modified fully covered SEMS that is covered on both sides with a silicone membrane and has a convex margin at both ends to prevent tissue hyperplasia. Also to prevent migration, the central portion of 1 to 2 cm of has a cross-wired structure and smaller-diameter waist, whereas the remainder has a fixed hook and cross wired structure[11]. They used this stent in 21 patients with benign biliary stricture with varying etiologies (6 had chronic pancreatitis) and reported marked improvement or resolution of the biliary stricture in 20 of 21 patients. Stent migration was seen in 4 of 21 patients (19.0%) and no new de novo stricture was reported in any patient.

We still are in the learning phase of using metal in benign biliary disease and the results of this current study re emphasize the same. Although the results are encouraging, a number of technical issues like decreasing the migration rates and preventing stent induced damage to the bile duct need to be settled before fully covered SEMS can be accepted as a treatment of choice for benign biliary stricture due to chronic pancreatitis. Till that time surgery remains the treatment of choice and fully covered SEMS may be considered for patients who are unfit or refuse surgery.

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**Capsule endoscopy in nonresponsive celiac disease**

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Celiac disease (CD) is a chronic autoimmune enteropathy occurring in genetically predisposed individuals following ingestion of gluten that leads on to villous atrophy causing malabsorption. The treatment of this complex immunological disease is simple and that is gluten-free diet. The adherence to the gluten free diet improves symptoms in majority of the patients with celiac disease. However, 7% - 30% of patients may not respond to gluten free diet (GFD) and these subset of patients present a diagnostic dilemma[12,13]. Although the differential diagnosis in such situation include the complications of long standing celiac disease like lymphoma, ulcerative jejunitis, and adenocarcinoma, the most common cause of non response to gluten free diet is inadvertent gluten ingestion[12,13]. Capsule endoscopy (CE) has enabled us to evaluate the small bowel completely and it gives magnified imaging of the small bowel mucosa. It is an important investigation for evaluating patients with gastrointestinal disease is simple and that is gluten-free diet. CE has been shown to be having better sensitivity than the conventional upper gastrointestinal (GI) endoscopy in detecting villous atrophy[15]. It has also been evaluated as a tool to assess the extent of the damage to the small bowel mucosa as well as response to GFD[16,17]. It has also been evaluated in patients with nonresponsive CD and refractory CD and villous atrophy or ulcerations have been reported as features of complicated CD[18,19]. The authors of the current study determined the prevalence of mucosal abnormalities on CE in patients with nonresponsive CD and compared them with those found in CD-free controls and a group with treated uncomplicated CD so as to determine the accuracy of these CE findings in predicting refractory or complicated CD.

The authors performed CE in 42 consecutive patients with biopsy proven non responsive CD who had persistent...
symptoms even after at least 6 months of GFD. They were compared with a control group of 84 age and sex-matched
patients with normal duodenal histology who underwent CE concurrently with the evaluation of nonresponsive CD
patients. Also a post hoc analysis, with a blinded retrospective re-reviews of CE in 30 consecutive asymptomatic patients with
biopsy-proven CD who underwent follow-up CE after at least 6 months of treatment with a GFD was also done. The features
on CE that were considered indicative of villous atrophy were (scalloping, fissuring or mosaic pattern of the mucosa and
absence of villi. The time until the appearance of the first villi and time with features of atrophy were also recorded. Other
abnormalities such as erosions (defined as small mucosal break with or without exudates or surrounding red color), ulcers
(defined by a large pale or yellow base with a pink or red surrounded border of elevated mucosa), submucosal lesion,
and stenosis were also recorded. Because of magnification in CE, it is difficult to accurately distinguish erosions from ulcers
and therefore for analytical purposes, authors combined ulcers with erosions.

On comparison with controls, the small-bowel transit time was significantly longer in nonresponsive CD patients
(5.0 ±1.6 hours vs 4.3±1.7 hours, p = .019), but was not significantly different from that of the uncomplicated CD
patients (4.9 ±1.4 hours, p = .79) and there was no capsule retention. The macroscopic features of villous atrophy on CE
were detected in 15 patients (31%) with nonresponsive CD and 14 patients with uncomplicated CD (47%) [p=0.132]. None
of the controls had macroscopic features of villous atrophy. The villous atrophy was confirmed on histology in 16 patients with
nonresponsive CD (13 had partial villous atrophy and 3 had total villous atrophy). CE and histology agreed on examina-
tions with negative findings in 22 patients and examinations with positive findings in 9 patients. Seven patients who had
negative findings on CE had histological evidence of villous atrophy and 4 patients who had positive findings on CE had
negative findings on histology. However, all 3 patients with total villous atrophy had positive findings on CE compared
with 6 of 13 patients with partial villous atrophy. There was weak agreement of capsule endoscopy findings and
histology in the patients with nonresponsive celiac disease (k=0.44) and overall sensitivity and specificity of CE for the
detection of any degree of villous atrophy as graded by histology was low being 56% and 85%, respectively. The most frequent
diagnosis in nonresponsive CD was inadvertent gluten ingestion in 20 patients found out by a positive CD-specific serology
during follow-up.

Single or multiple erosions / ulcerations of the small bowel were observed in 19% of patients with nonresponsive CD, 18% controls, and 31% of patients with uncomplicated CD and neither the rate nor quantity of erosion/ulcerations was significantly different among the study groups (p=0.35). One of the patients with non responsive CD had deep ulceration in the jejunum and this patient was diagnosed as refractory celiac disease type II. A tumor (adenocarcinoma) with active bleeding was detected on CE in the jejunum of another patient with nonresponsive CD. No cases of ulcerative jejunitis, lymphoma, or cancer were detected in either the CD-free controls or patients with uncomplicated CD.

**Commentary**

Small bowel ulcerations in a patient with celiac disease and on GFD have been believed to indicate non response and
suggest a possibility of refractory sprue or ulcerative jejunitis or lymphoma. This study dispels this notion by demonstrating
that the small-intestine erosions/ ulcerations are no more common in nonresponsive CD than the patients with treated
responded uncomplicated CD and thus not all small-bowel ulcerations suggest refractory disease, ulcerative jejunitis, or
significant pathology. Also as large number of erosions/ulcerations in patients with nonresponsive CD were associated with increased aspirin / non steroidal anti inflammatory drugs (NSAID) use, it is prudent to take a detailed medication history in patients with celiac disease undergoing CE. Also in this study, majority of the patients with non responsive CD had inadvertent gluten ingestion, a detailed dietary history with an expert dietician should be taken before patients undergo expensive evaluation with tests like CE. Another important fact deduced from this study is the persistence of the mucosal damage despite being asymptomatic on GFD. In this study, macroscopic features of villous atrophy were detected in 47% of patients with treated uncomplicated CD, suggesting persistent mucosal damage despite a GFD. Lee et al had also demonstrated failure to normalize the mucosal inflammation and villous atrophy in celiac disease, even in patients who are clinically asymptomatic.20 Although these results are encouraging, CE has limitations like subjective interpretation, incomplete examination of the small bowel, lack of appreciation of partial villous atrophy and inability to obtain the biopsy specimens.

**References**

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