A unique type of fully covered metal stent for the management of post liver transplant anastomotic strictures

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Abstract

Background: We report our experience of treating anastomotic strictures using a novel type of fully covered metal stent (FCSEMS). This stent, known as the Kaffes Stent, is short-length with an antimigration waist and easily removable due to long retrieval wires deployed within the duodenum.

Methods: 62 patients who had this stent inserted were prospectively analysed.

Results: 81% of patients had long-term resolution of their stricture with a significant improvement in liver function tests. Complication rates were 15% with one patient requiring biliary reconstruction.

Conclusions: This type of FCSEMS is effective and safe at resolving anastomotic strictures.

Background

Anastomotic strictures are isolated, short-length strictures affecting 4–9% of patients post-liver transplantation, typically associated with technical factors such as bile leaks, the length of the donor bile duct, suture placement and size discrepancy [1, 2]. They typically develop 5–8 months after transplantation [3].

Stenting has historically been with plastic stents, on a 3-monthly basis for up to a year. Plastic stents are at risk of migration and stent occlusion, and their efficacy at resolving strictures is low, often leaving patients requiring multiple ERCPs or the need for a biliary reconstruction [4]. FCSEMS (fully covered self expanding metallic stents) have been shown to resolve benign strictures; however, stent migration can occur because the centre of the stent does not always overlie the stricture [5–7].

Kaffes stents (Taewoong Medical) are a novel type of FCSEMS that have a short-length, an antimigration waist, and long removal wires which lie within the duodenum for easy removal. The ends of the stents are larger in diameter than the mid-point. This unique design reduces stent migration by producing a radial force against the stricture, contributing to better outcomes. Previous randomised trials have illustrated their success with resolving anastomotic strictures when compared to plastic stenting [8].

Methods

Prospective data on Kaffes stents inserted from December 2016 through to February 2020 was analysed for stricture resolution, adverse event rates and improvements in both symptoms and liver function tests (LFTs). Ethics approval was not required as inserting this type of stent was standard care at our institution.

Inclusion criteria

This was a single centre study performed at King’s College Hospital, London. All patients included had duct-to-duct biliary anastomoses and were referred for ERCP based on a radiologically confirmed anastomotic stricture on MR (magnetic resonance) imaging. Patients with complex hilar strictures were excluded.

Method for insertion

Two types of Kaffes stent were inserted – a 40 mm by 10 mm stent and a 40 mm by 8 mm stent. All Kaffes stents were inserted over a HydraJAG guidewire, 0.035-inch (Boston Scientific). Stents aimed to be removed 12 weeks after insertion with stent forceps and a cholangiogram was performed to assess whether the stricture had resolved or whether further stenting was required. Decisions to perform a sphincterotomy or balloon dilatations were made by the endoscopist at the time of the procedure but followed no pre-determined protocol (Fig. 1).

Definitions

Initial resolution of a stricture was defined as either where there was no stricture demonstrated on the cholangiogram (at the time of the second ERCP), or if there was still a stricture, whether a 12 mm extraction balloon was easily able to pass through. Recurrence was defined as where the stricture occurred within the follow-up period. Long-term stricture resolution was defined by the absence of recurrence within the follow-up period. Complications were found from discharge summaries. LFTs were analysed before stent insertion and after removal in patients with resolved strictures only.

Statistical analysis

Categorical and continuous variables were analysed using the Fisher's exact test and independent samples t-test respectively. A paired sample t-test was used to assess for improvement in LFTs. 2 × 2 contingency tables assessed significant differences between categorical variables www.graphpad.com/quickcalcs/contingency1/.

Results

Sixty-two patients had a Kaffes stent inserted, mean age of 53 (SD 11.9, range 13–72) years; 1 patient had a living-related donor right lobe graft; of the remainder 68% were DBD (donation after brain death) grafts. The mean CIT (cold ischaemic time) was 8.4 hours (± 2.4) for the DBD group and 8.9 (± 2.5) for the DCD (donation after circulatory death) group (Table 1). The aetiologies for liver disease are shown in Table 2. 13 (21%) patients had previous plastic stenting and 1 patient had had the traditional type of longer-length FCSEMS (Wallflex™, Boston Scientific) without stricture resolution. The mean time between the transplant and Kaffes insertion was 41 months (SD 72, range 3 days – 327 months). 38 patients had balloon dilatations of strictures prior to stent insertion. 29 had a sphincterotomy at the time of stent insertion, whilst another patient had had a previous sphincterotomy.

Table 1
Highlights the main outcomes and specific factors of the Kaffes stent. DBD: Donation after brain death; CIT: Cold ischaemic time. * One patient died of frailty post-transplant 13 months after a Kaffes stent successfully resolved the stricture and another was re-transplanted for chronic rejection so for the purpose of this study, both were not included in the analysis for long-term stricture resolution.

No. of patients inserted	**62**
No. of patients removed	56
Immediate Stricture resolution	54/56 (96%)
Long-term stricture resolution (%)	42/52* (81%)
Complications (%)	9/62 (15%)
Biliary reconstruction	1
Mean age (years)	53
Females (%)	26 (42%)
Symptomatic (%)	16 (26%)
DBD (%)	36/53 (68%)
CIT (Hours) (± SD)	8.6 (2.4)

Table 2
The aetiologies of liver disease for patients stented. HCC: Hepatocellular carcinoma; Non-alcoholic steatohepatitis; PFIC: Primary Familial intrahepatic cholestasis.

Aetiology	FCSEMS	Aetiology	FCSEMS
Alcoholic liver disease	14	Drug-induced liver failure	1
Hepatitis C	4	Primary Hyperoxaluria	2
Primary biliary cirrhosis	4	Cystic Fibrosis related cirrhosis	1
Budd Chiari	3	NASH	4
Autoimmune hepatitis	3	Polycystic	2
Hepatitis B	2	PFIC	1
HCC	12	PSC	1
Acute liver failure, cause unknown	4	Paracetamol toxicity	3
Wilson's disease	1		

Immediate stricture resolution (Fig. 2)

To date, 56 patients have had their Kaffes stent removed, of whom 54 (96%) had immediate stricture resolution at the time of stent removal. There was no relationship between stent size, balloon dilatations (N = 33, P = 1.00) and/or sphincterotomies (N = 26, P = 1.00) and stricture resolution. Of the 2 patients in whom the Kaffes stent had failed to resolve stricturing, 1 went onto have stricture resolution with a plastic stent insertion, whilst the other had a traditional longer-type of FCSEMS inserted, both without successful stricture resolution.

Of the 54 patients in whom there was immediate stricture resolution, 1 died of frailty a year after transplant and another was re-transplanted due to chronic rejection, both having no relationship to their initial anastomotic stricture; these patients were excluded from the overall analysis.

Long-term stricture resolution

Overall, 42/52 (81%) patients went onto have long-term stricture resolution with no recurrence (mean follow-up period was 548 days (SD 256, range 13-1097 days). Of the 10 patients who had recurrence (mean time to recurrence was 224 days (SD 200, range 37–575 days), 1 patient became jaundice 3 months after stent removal, but instead of further stenting, a sphincterotomy was enough to improve drainage. 9 had asymptomatic recurrence on imaging (5 with cholestatic LFTs), of whom 5 had a further Kaffes placed, 1 had the traditional FCSEMS placement, another improved with sphincterotomy. Only 1 patient required biliary reconstruction as at their ERCP, the wire failed to pass through the stricture.

Improvement in symptoms

Forty-six patients were asymptomatic with an anastomotic stricture on imaging (18 with cholestatic LFTs). 16 patients were symptomatic (6 jaundiced, 4 pruritic, 6 cholangitic). Of these, symptoms resolved in 13 (3 jaundiced, 4 pruritic, 6 cholangitic). Of the 3 patients who also continued to be jaundice after stent insertion, 2 had their stent removed within 4 weeks of insertion, the 3rd after 86 days; all 3 were found to have stricture resolution. Two of these patients were found to have papillary stenosis and improved after sphincterotomy; the other patient required re-transplantation due to chronic rejection. Overall, there was a significant improvement in patients' LFTs following stent insertion (see Table 3).

Table 3
The mean and range of LFTs in patients before stent insertion compared to after removal in patients where stricture had resolved. LFTs: Liver function tests; SD: Standard deviation.

LFTs	Mean before stent (SD)	Range before	Mean after stent (SD)	Range after	P value
GGT (IU/L)	513 (538)	13-2008	193 (320)	11-2154	< 0.01
AST (IU/L)	101 (179)	13-1070	41.4 (32.1)	9-175	0.03
ALP (IU/L)	313 (322)	42-2088	169 (109)	58–622	< 0.01
Bili (μmol/L)	26.7 (46.1)	3-305	14.0 (13.6)	4–70	0.03

Complications

Overall, 9 (15%) of the 62 patients had a complication: 3 patients developed pancreatitis after the Kaffes stent insertion, 4 developed cholangitis, 1 after insertion and 3 following stent removal, 1 patient had a wire-guided perforation of the bile duct without complication, 1 had the retrieval wires uncoil. There was no associated mortality.

Of the stents that were removed at the time of writing, all were removed successfully (mean of 114 days (SD 70), range 3-345 days), although as above, 1 stent needed 2 attempts because the removal wires uncoiled. Stent removal for a patient 345 days after insertion was delayed due to pregnancy; the stent was removed easily without complications.

Discussion

Our results confirm that the Kaffes stent is effective at resolving anastomotic strictures with no patients requiring biliary reconstruction. This one case was due to the inability to achieve wire guided cannulation of the stricture and therefore, unable to place a Kaffes stent. This effectiveness appears to be due to its unique design (Fig. 3D).

Our experience, however, has highlighted a 'learning curve' with using the Kaffes stent. One issue is the delivery of the deployment wires into the duodenum. We recommend the use of forceps, inserted through the scope, to pull the wires out. Care should be taken not to just withdraw the scope with the wires inside it, as this could dislodge the stent. Another issue is that the stents can collect sludge and debris, and this is evident at the time of stent removal. This finding was associated with 3 of our patients developing cholangitis after removal; a balloon trawl is advised to remove any remaining debris after the stent has been removed. One patient became pregnant after her Kaffes stent was inserted. It was therefore not removed for over a year but was successfully removed without complication. However, the longer the stents are left in for, the more likely they are likely to collect sludge and debris. The use of prophylactic ursodeoxcholic acid may be of some benefit although we have not adopted this approach at the time of writing. 12 weeks is therefore the recommended maximum length of time they should be left for. Finally, the Kaffes stent should not be deployed for anastomotic strictures too close to the hilum (< 2 cm) as they tend to migrate distally resulting in biliary obstruction.

There was no relationship between the patients who had sphincterotomies or balloon dilatations, and successful resolution of the anastomotic stricture using the Kaffes stent. The stent is deployed from an 8.5 Fr delivery system so unless the stricture is very tight, the stents were mostly able to cross the stricture without dilatation.

Conclusion

In conclusion, our preliminary observations indicate that the Kaffes stent is highly effective at treating anastomotic strictures. Complication rates are low and stent migration is not a feature. These findings will improve the quality of life for post-transplant patients avoiding repeated ERCPs and potentially biliary reconstruction. Further multi centre data is required to understand the efficacy of this stent in the management of anastomotic biliary structures post liver transplantation.

Abbreviations

FCSEMS
Fully covered metal stent
LFTs
Liver function tests
MR
Magnetic resonance
CIT
Cold ischaemic time
DBD
Donation after brain death
DCD
Donation after circulatory death

Declarations

Ethics approval and consent to participate: Ethics approval was not required as insertion of the Kaffes stent was our normal standard of care – therefore deemed unnecessary by national regulations. We have consent for publication of images submitted. Consent from individual patients is not applicable as individual's data is not included.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests – None

Funding - None

Authors contributions – BW, PH, MH and DJ wrote the manuscript; MF, YE, KES collected the data; JD and DR performed the endoscopies; NH, KM, AP, PS, MC, HV, WJ performed the transplant surgery.

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References

1. Sharma S, Gurakar A, Jabbour N. Biliary strictures following liver transplantation: past, present and preventive strategies. Liver Transpl 2008;14:759-69.
2. Roos FJM, Poley JW, Polak WG et al. Biliary complications after liver transplantation; recent developments in etiology, diagnosis and endoscopic treatment. Best Pract Res Clin Gastroenterol 2017;31:227-235.
3. Zoepf T, Maldonado-Lopez EJ, Hilgard P et al. Balloon dilatation vs. balloon dilatation plus bile duct endoprostheses for treatment of anastomotic biliary strictures after liver transplantation. Liver Transpl. 2006 Jan;12(1):88-94.
4. Graziadei IW, Schwaighofer H, Koch R et al. Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation.Liver Transpl. 2006 May;12(5):718-25
5. Traina M, Tarantino I, Barresi L et al. Efficacy and safety of fully covered self-expandable metallic stents in biliary complications after liver transplantation: a preliminary study. Liver Transpl. 2009 Nov;15(11):1493-8.
6. Kahaleh M, Behm B, Clarke BW et al. Temporary placement of covered self-expandable metal stents in benign biliary strictures: a new paradigm? (with video). Gastrointest Endosc. 2008 Mar;67(3):446-54.
7. Park DH, Lee SS, Lee TH et al. Anchoring flap versus flared end, fully covered self-expandable metal stents to prevent migration in patients with benign biliary strictures: a multicenter, prospective, comparative pilot study (with videos). Gastrointest Endosc. 2011 Jan;73(1):64-70.
8. Kaffes A, Griffin S, Vaughan R et al. A randomized trial of a fully covered self-expandable metallic stent versus plastic stents in anastomotic biliary strictures after liver transplantation. Therap Adv Gastroenterol. 2014 Mar;7(2):64-71.

Figures

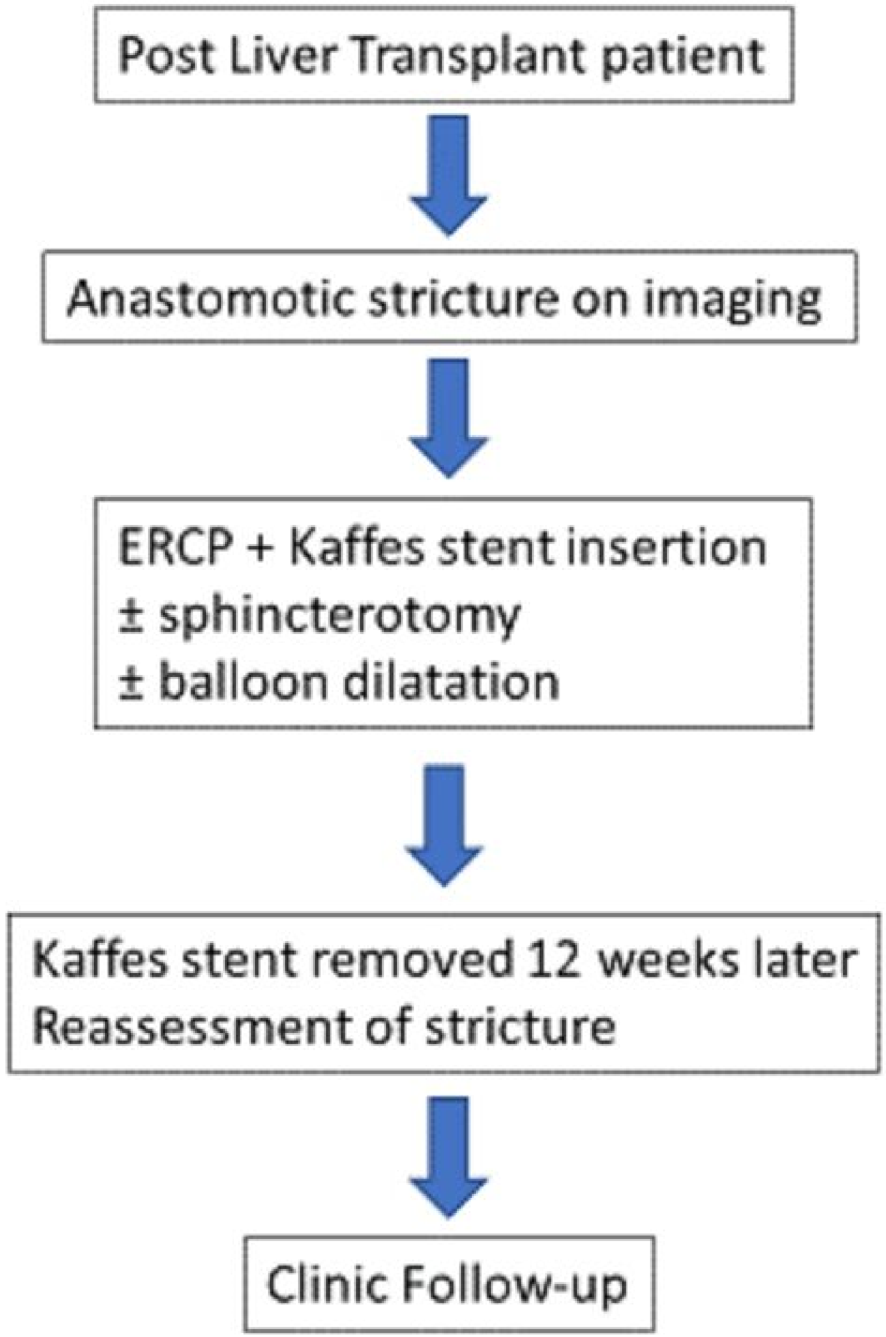

Figure 1

Protocol for Kaffes stent insertion. ERCP: Endoscopic retrograde cholangiopancreatography.

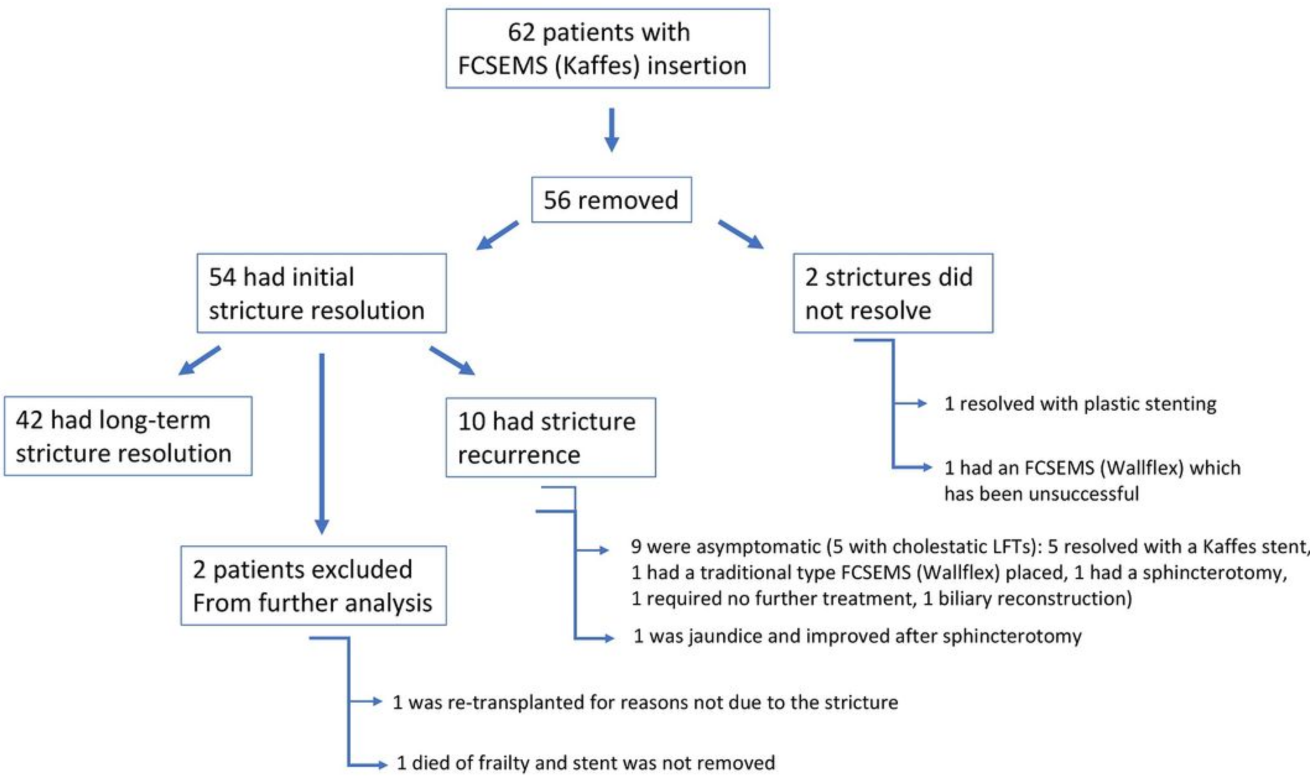

Figure 2

A flow chart of outcomes in the FCSEMS group

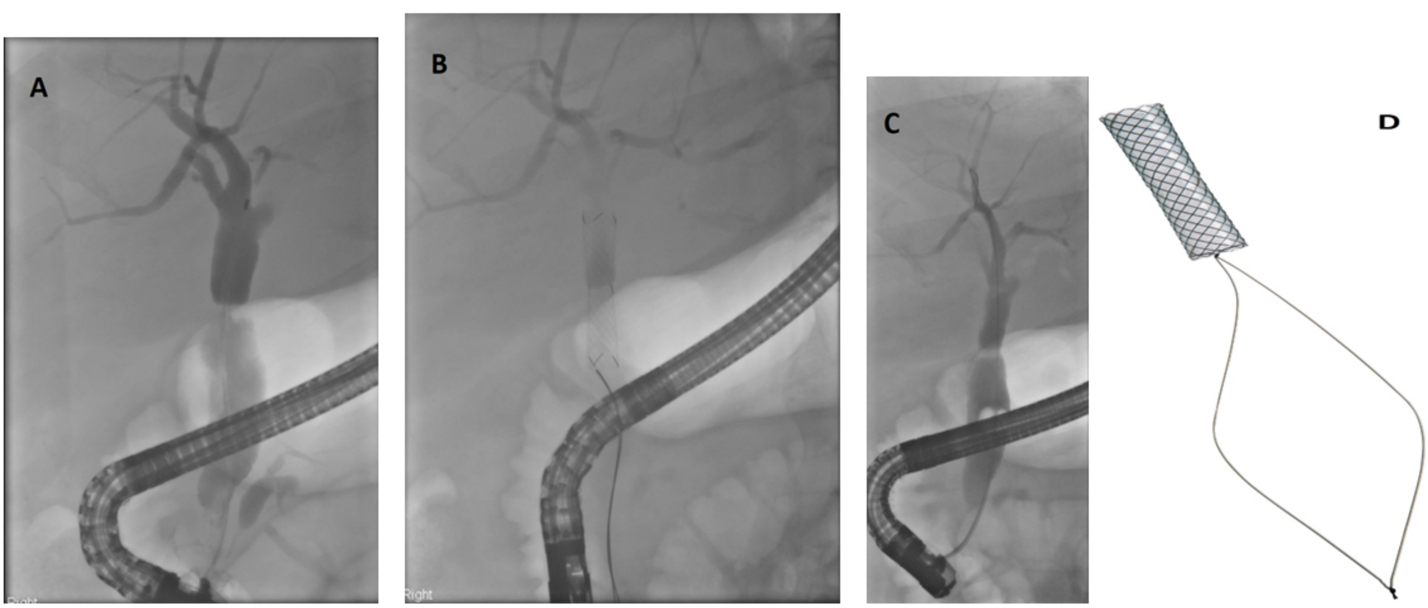

Figure 3

The cholangiograms are of a patient who underwent liver transplantation in 2014 for HCC with underling NASH cirrhosis (DBD graft, CIT 8 hours). 31 months later they developed cholestatic liver enzymes and imaging showed an anastomotic stricture. They underwent an ERCP and plastic stent insertion but the stent migrated. At the 2nd ERCP (Figure 3A), the cholangiogram demonstrated the persistence of this stricture. The stricture was dilated using an 8mm Hurricane Balloon (Boston Scientific) and an 8x40mm Kaffes Stent inserted (Figure 3B). 3 radiopaque markers on either side of the stent confirm the stent's position – the top markers represent where the stent begins to be deployed and the middle markers where it should sit over the stricture. Biochemistry immediately improved. The stent was removed 63 months later with complete resolution of the stricture as shown (Figure 3C). Figure 3D shows the unique design of the Kaffes Stent with its short-stent length, antimigration waste and long retrieval wires.