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REVIEW ARTICLE

Harnessing magnetic forces: Discovery and development of biliary strictures treatment with compression anastomosis

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Abstract

Magnetic compression anastomosis (MCA) is emerging as a promising alternative that uses magnetic force to create an anastomosis bypassing the stenosis in biliary strictures (BSs) where techniques such as percutaneous transhepatic biliary drainage and endoscopic retrograde cholangiopancreatography with stent placement are inadequate in the presence of complete obstruction or severe stenosis. MCA offers potential benefits such as less operative trauma, shorter hospital stay and lower complication rates. By placing magnets proximal and distal to the stenosis, necrosis of fibrotic tissue occurs, creating a new anastomosis. Investigating the role of MCA in the treatment of BS is crucial because of its potential to revolutionize care, improve outcomes and reduce healthcare costs. It offers an alternative for patients who are not suitable for conventional surgery. A comprehensive review of the principles, techniques, outcomes and applications of MCA is essential to inform clinicians, researchers and policy makers and to guide future research and clinical practice to optimize patient care for BSs.

Keywords: Benign; malign; biliary strictures; magnetic compression anastomosis

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Introduction

Biliary strictures (BSs) cause significant difficulties in clinical management and often require invasive procedures with associated morbidity and mortality. The development of percutaneous transhepatic biliary drainage (PTBD) as an interventional radiological procedure has allowed recanalisation of severe BSs, whether due to benign or malignant strictures or postoperative strictures [1]. The placement of multiple plastic stents or metal stents with or without balloon dilatation via endoscopic retrograde cholangiopancreatography (ERCP) has also shown good results in the treatment of BSs [2]. However, endoscopic or percutaneous treatment is not successful when it is not possible to place a guidewire percutaneously or endoscopically due to complete obstruction and severe stenosis in the bile duct. In these cases, patients require the use of an external PTBD catheter to drain bile, which places a great burden on the patient by decreasing quality of life and creating a high risk of infection [3]. Traditionally, surgical interventions such as hepaticojejunostomy or endoscopic stenting have also been used to address these strictures. However, these approaches are not without limitations, including complications such as anastomotic leakage, stricture recurrence and patient discomfort. Consequently, there is a growing interest in exploring alternative, less invasive techniques for the treatment of BSs. One such promising approach is magnetic compression anastomosis (MCA), which has emerged as a novel and minimally invasive method for the creation of biliary anastomoses. MCA involves the use of magnetic force to create an anastomosis between two biliary segments, bypassing the area of stenosis. This technique offers several potential advantages over conventional surgical methods, including less operative trauma, shorter hospital stay and lower complication rates. For MCA, a daughter magnet is placed percutaneously at the proximal end of the stricture and a master magnet is placed endoscopically at the distal end of the stricture. The attraction force between the two magnets leads to necrosis of the fibrotic stricture tissue and formation of a new transmural anastomosis [4].

The importance of investigating MCA in the context of BSs is based on its potential to revolutionise the treatment of these challenging conditions. MCA has the potential to improve patient outcomes, enhance quality of life and reduce healthcare costs by offering a less invasive alternative to traditional surgical interventions. In addition, the development of MCA techniques holds promise for expanding the pool of patients who may benefit from biliary reconstruction, including high-risk or unsuitable candidates for conventional surgery.

In light of the growing interest and expanding clinical applications of MCA in the treatment of BS, a comprehensive review of the available literature on this topic is imperative. This review aims to provide a comprehensive overview of the principles, techniques, outcomes and current clinical applications of MCA in the treatment of BSs. By synthesising the available evidence, identifying areas of consensus and debate, and highlighting future directions for research and clinical practice, this article aims to inform clinicians, researchers and health policy makers about the potential role of MCA in optimising patient care for BSs.

Types and Causes of Biliary Stricture

BSs can be broadly divided into two categories: benign and malignant. Benign BSs can arise from various factors leading to secondary scarring and fibrosis due to inflammation in the affected area. The most common causes of benign strictures include those following surgery and inflammatory conditions. These include postoperative strictures and postoperative complications, especially after Roux-en-Y reconstruction, the most common anastomosis method in biliary surgery. Laparoscopic cholecystectomy stands out as the primary procedure associated with postoperative BSs, with a higher incidence observed in laparoscopic surgeries compared to open cholecystectomy [5]. The development of postoperative BSs during laparoscopic procedures can be attributed to factors such as inadvertent partial or complete incisions in the biliary duct, thermal injuries during tissue dissection, vascular injuries resulting in ischemic damage, or adhesions forming post-surgery. Additionally, anatomical variations, local inflammation, and inadequate surgical expertise are recognized as significant risk factors for the development of postoperative BSs [6]. Liver transplantation, especially living donor liver transplantation (LDLT), is the second most common surgical procedure associated with postoperative BSs [7]. The occurrence of benign BSs following LDLT surpasses that observed after orthotopic liver transplantation (OLT), with reported prevalence rates ranging from 8.3% to 31.5%. [8,9]. Cholangiocarcinoma is the predominant malignancy found in strictures affecting the proximal and middle sections of the bile ducts, in contrast to pancreatic adenocarcinoma, which typically leads to strictures in the

distal bile duct. Other less common causes of malignant BSs include metastatic cancer, lymphoproliferative disorders, gallbladder carcinoma, and hepatocellular carcinoma [10].

Historical Development

Denan pioneered the concept of compression anastomosis in 1826, describing the formation of sutureless anastomotic fistulae through ischaemic compression of tissue [11]. Murphy later refined Denan's spring device in 1892, resulting in the renowned Murphy's buton [12]. This device facilitated the creation of circular gastrointestinal anastomoses by applying ischaemic compression between two buttons held together by a spring. In 1991, compression buttons and modified Murphy buttons were utilized for endoscopy-assisted gastrojejunostomy in an animal study. The evolution of compression anastomosis continued with the introduction of magnetic attraction as a means of achieving tissue compression [13]. Jansen et al. conducted pioneering human experiments in 1980, demonstrating successful mucosa-to-mucosa anastomosis using magnetic attraction [14]. Subsequent studies by Saveliev et al. in 1993 further validated the clinical feasibility of MCA, establishing successful anastomoses in various gastrointestinal locations [15]. Yamanouchi et al. expanded the application of modern MCA in 1998, successfully creating bile duct-small bowel fistulae and introducing new avenues for its utilization [16].

MCA Mechanism and Process

MCA involves the use of magnetic force to create an anastomosis between two luminal structures. In the context of BSs, MCA typically involves the placement of magnetic rings or capsules across the stricture site using endoscopic or percutaneous techniques. Once positioned, the magnets exert a compressive force on the tissue, leading to apposition and eventual formation of a natural anastomosis. Unlike stent placement, MCA does not rely on the presence of luminal tissue to maintain patency, potentially reducing the risk of stent-related complications [17].

Preliminary evaluation before MCA is performed is essential for placement of magnets and prediction of outcomes. Success factors for MCA include the length and shape of the bile duct stricture, magnetic power and alignment of the bile duct axis. MCA may fail in long strictures or irregularly shaped and tortuous bile ducts. Longer strictures typically result in weaker magnetic forces between the magnets. Insufficient magnetic force can inhibit tissue necrosis and prevent the formation of a new fistula. Therefore, accurate assessment of stricture length and shape is imperative for optimal magnet alignment prior to MCA. For example, strictures are usually longer and more tortuous in LDLT recipients than in OLT recipients. The level of post-OLT strictures is more distal in the common bile duct compared to post-LDLT strictures. Post-OLT strictures are intermediate benign BSs, whereas post-LDLT strictures are high-grade benign BSs. Furthermore, the intrahepatic ducts are more dilated but less angulated and tortuous in post-OLT strictures than in post-LDLT strictures. Therefore, MCA is more feasible in post-OLT stenoses and has a high success rate. However, non-invasive radiologic modalities such as computed tomography, ultrasonography, and magnetic resonance cholangiopancreatography (MRCP) have limitations in identifying suitable candidates for MCA, as they cannot fully assess stenosis length, shape, and bile duct axis. ERCP or PTBD provide detailed information on stricture characteristics, including length, shape and duct alignment, but these are invasive methods [18].

Magnets and MCA Device

The strength of magnets plays a pivotal role in the success of MCA. Rare earth magnets, such as neodymium iron-boron and samarium-cobalt (Sm-Co) magnets, are commonly utilized due to their high magnetic flux densities and robust holding forces, which are crucial for MCA procedures. Notably, Sm-Co magnets exhibit a greater holding force compared to neodymium ironboron magnets, rendering them preferred in many cases [19, 20]. To assess magnetic strength accurately, studies often employ a magnetic force determination algorithm (MAGDA), which calculates the magnetic strengths of the magnets utilized in MCA. This calculation aids in predicting the likelihood of MCA success. MAGDA considers various factors including magnet shape, dimensions, magnetic material composition, degree of magnetization, and experimentally determined or estimated in vivo magnetic separation forces [21].

The MCA device typically comprises two identical nickel-coated NdFeB magnets (grade, N45), referred to as the main magnet and the daughter magnet. Each magnet is cylindrical in shape, featuring a tail at one end for silk thread attachment. Different magnet sizes (with diameters ranging from 2 to 5 mm and heights of

10 mm) can be manufactured to accommodate various clinical scenarios. Selection of an appropriate magnet for a specific patient depends on factors such as canal diameter and stenosis characteristics [22].

Procedure

MCA is a non-surgical alternative treatment method that can improve the long-term prognosis as a result of biliobiliary and bilioenteric anastomoses in the treatment of severe or completely obstructed benign BSs that cannot be resolved by conventional endoscopic or percutaneous methods [23]. The feasibility and safety of biliobiliary and bilioenteric anastomoses created using MCA have been confirmed in both human and animal studies [18]. MCA is not normally indicated to treat malignant biliary strictures, which can usually be treated with conventional peroral or percutaneous methods [24]. In the literature, Avaliani et al [25] reported the use of magnets for bilioenteric anastomosis in patients with malignant obstruction in contrast to other investigators. However, these investigators used magnets to create a fistula between the intact bile duct and the duodenal wall, not for recanalisation of malignant obstruction.

Biliobiliary Anastomosis

The MCA procedure can be divided into four steps as follows:

- 1. Tract formation for magnet delivery: Common routes of magnet delivery are percutaneous and peroral. Using a 16 or 18 Fr catheter, the PTBD tract is created for magnet delivery. The PTBD catheter is replaced with a 16 or 18 Fr sheath prior to the MCA approach to allow proper magnet placement through the PTBD tract and reduce duct damage. In the common bile duct route, full endoscopic sphincterotomy and balloon dilatation or temporary placement of a retrievable, fully covered, self-expandable metal stent (FCSEMS) is used to facilitate magnet delivery and dilate the papilla [18, 24].
- 2. Magnet approach: A thread attached to a magnet is fixed to a polypectomy trap and the magnet is transported via the PTBD pathway to the anastomosis site. The polypectomy trap is passed through the channel of an ERCP scope and the other magnet is fixed in front of the scope. The magnet is moved to the anastomosis site via FCSEMS and the attraction between

the two magnets results in the approach of the MCA. A balloon catheter can be used to advance the magnets through both PTBD and ERCP pathways to better approximate the magnets. Approximation of the two magnets is confirmed radiographically. The distance between the approximated magnets is 2-15 mm for biliobiliary anastomoses. The long sheath tube is then removed and the indwelling PTBD catheter is placed. The FCSEMS placed in the common bile duct is removed immediately after the magnet is approximated. Doppler ultrasound-based scanning and follow-up is frequently performed because of the possibility of rupture during MCA if blood vessels are placed between two magnets [26, 27].

- 3. Magnet removal: When a fistula forms due to ischaemic necrosis caused by approximated magnets, the magnets migrate spontaneously into the duodenum. However, if spontaneous migration does not occur after about 8-10 weeks, the magnets can be pushed out using a guide wire or catheter. Magnets can also be removed from the PTBD duct via percutaneous transhepatic cholangioscopy (PTCS). The median time to successful magnet removal after the magnet approach has been reported to be 53.3 days (range, 9-181 days) for biliobiliary strictures [24]. Factors for successful magnet removal include the distance between the two magnets, the magnetic strength of the two magnets and the histological characteristics of the stenosis site.
- 4. Maintenance and removal of the internal catheter: After removal of the magnet, a 12-16 Fr internal catheter, FCSEMS or double pigtail plastic stents are inserted into the fistula. The recanalised fistula is endoscopically confirmed under fluoroscopy after magnet removal. The average length of stay of the PTCS catheter or FCSEMS to maintain the new fistula tract is 4-6 months. The PTCS catheter and FCSEMS have demonstrated similar safety and efficacy for fistula maintenance. However, FCSEMS is more convenient for patients because the PTCS catheter has a longer indwelling time and requires a greater number of replacements [28].

Table 1. Results of Market State	Magnetic	Compression Ana	stomosis for Beni	ign Biliary	Strictures after Li	ver Transplantation
Study	Year	Type of article	Reason for operation	Patients (n)	Number of successful patients (n)	Complication/ Restenosis (n)
*Muraoka et al. ^[27]	2005	Case report	LDLT	2	2	-
Okajima et al. ^[30]	2005	Case report	LDLT	1	1	-
Akita et al. ^[31]	2008	Case report	LDLT	1	1	-
Matsuno et al. ^[32]	2009	Case report	LDLT	1	1	-
Itoi et al. ^[26]	2010	Case report	LDLT	1	1	-
Jang et al. ^[33]	2011	Retrospective study	LDLT	12	10	Cholangitis (1) Restenosis (1)
Oya et al. ^[34]	2012	Case report	LDLT	1	1	-
Akira et al. ^[35]	2014	Case report	LDLT	1	1	-
Ersoz et al. ^[36]	2016	Case report	LDLT	6	6	-
Jang et al. ^[37]	2017	Retrospective study	LDLT	39	35	Cholangitis (1) Restenosis (1)
*Ryusuke et al. ^[38]	2017	Case report	LDLT	1	1	-
Parlak et al. ^[39]	2017	Retrospective study	LDLT	7	6	-
Parlak et al. ^[39]	2017	Retrospective study	OLT	2	1	-
Nakaseko et al. ^[40]	2017	Case report	LDLT	1	1	-
*Masahiko et al.	2018	Case report	LDLT	1	1	-
Li et al. ^[22]	2020	Retrospective study	OLT	9	9	Cholangitis (1) Biliary bleeding (1)
Bülent et al. ^[23]	2022	Retrospective study	LDLT	6	5	Cholangitis (1) Magnet migration (1) Magnet entrapment (1)
Bülent et al. ^[23]	2022	Retrospective study	OLT	2	2	-
Erkan et al. ^[41]	2022	Retrospective study	LDLT	26	20	-

Those marked with * indicate patients who underwent bilioenteric anastomosis. The other patients are those who underwent biliobiliary anastomosis.

Table 2. Results of M	lagnetic	Compression Ana	astomosis in Postopera	tive Benig	n Biliary Strict	ures
Study	Year	Type of article	Reason for operation	Patients (n)	Number of successful patients (n)	Complication/ Restenosis (n)
*Takao et al. ^[19]	2001	Case report	Gastric cancer	1	1	-
Mimuro et al. ^[43]	2003	Case report	Pancreatic cancer	1	1	-
Itoi et al. ^[44]	2005	Case report	Bile duct cancer	1	1	-
*Yukawa et al. ^[45]	2008	Case report	Gastric and gallbladder cancer	1	1	-
*Suyama et al. ^[46]	2010	Case report	Gallbladder cancer	1	1	-
*Itoi et al. ^[47]	2011	Case report	CCC	1	1	-
Itoi et al. ^[47]	2011	Case report	Liver metastasis from colon cancer	1	1	-
*Jang et al. ^[3]	2014	Case report	Pancreatic NET Choledochal cyst Pancreatic NET	3	3	-
Jang et al. ^[3]	2014	Case report	Abdominal trauma (1) Gallbladder stone (2) Hepatic CAC (1)	4	2	-
Jiang et al. ^[48]	2018	Case report	Liver metastasis from rectal cancer	1	1	-
*Liu et al. ^[49]	2019	Case report	Peri-ampullary carcinoma	4	4	Restenosis (1)
Bülent et al. ^[23]	2022	Retrospective study	Cholecystectomy	11	10	Magnet migration (1) Magnet entrapment (2)
Min Young et al. ^[50]	2022	Case report	Cholecystectomy	1	1	-

Those marked with * indicate patients who underwent bilioenteric anastomosis. The other patients are those who underwent biliobiliary anastomosis.

CCC, cholangiocellular carcinoma; NET, neuroendocrine tumor; CAC, cystadenocarcinoma.

Table 3. Results of Magnetic Compression Anastomosis in Malignant Biliary Strictures							
Study	Year	Type of article	Causes of stricture	Patients (n)	Number of successful patients (n)	Complication (n)	
Avaliani et al. ^[25]	2009	Retrospective study	Tumors of VA (7) Pancreatic cancer (21) CCC (6)	34	34	Cholangitis (2) Restenosis (3)	

VA, Vater's ampulla; CCC, cholangiocellular carcinoma.

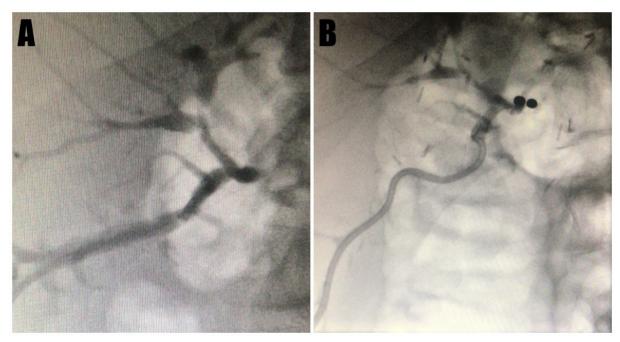


Figure 1. Cholangiogram showing indications for MCA. MCA is applicable for refractory benign biliary stricture that cannot be resolved using conventional endoscopic or percutaneous methods due to complete obstruction (A and B) where neither a guidewire nor dye can pass.

Bilioenteric Anastomosis

In both biliary-enteric and biliary-biliary anastomosis procedures, the methods and principles of MCA share similarities. However, the approach for delivering magnets varies depending on the specific route chosen. Options include surgically created percutaneousjejunum, percutaneous-percutaneous, or percutaneousperoral routes, with the latter being the most commonly employed [27]. The process of magnet delivery via the percutaneous route mirrors the previously described method, albeit utilizing a forward-facing endoscope in peroral approaches. Notably, endoscopic delivery may pose challenges in patients with elongated afferent loops, necessitating an alternative approach through a surgically established skin/intestinal fistula [3]. In the context of biliary-enteric anastomoses, magnets are typically spaced 2-7 mm apart [18]. The average duration for successful magnet removal post-approach in cases of biliary-enteric strictures ranges from 7 to 40 days [24].

Follow-up after MCA

After 4-6 months post-MCA, patients undergo a comprehensive evaluation including assessment

of clinical symptoms, laboratory parameters and Complications



Figure 2. Magnetic compression anastomosis for stricture after cholecystectomy. (A and B) A percutaneous transhepatic biliary drainage (PTBD) catheter was placed and dilated to 16 Fr. One magnet was passed through the PTBD duct and the other magnet was passed through the common bile duct using an endoscopic retrograde cholangiopancreatography (ERCP) scope. Approximation of the magnets was successful. C and D show the approximated magnets. After adhesion was completed on day 5, percutaneous 10 Fr and endoscopic 7 Fr double pigtail plastic stents were implanted after removal of the magnets.

(Pictures taken from Associate Professor Dr. Emre Unal from Hacettepe University Department of Interventional Radiology).

abdominal ultrasonography imaging following removal of the PTCS catheter or transcutaneous FCSEMS. The reported recurrence rate of post-MCA stenosis is very low compared to recurrence rates after ERCP and PTBD [8, 29]. If recurrence is suspected, further diagnostic procedures such as MRCP or cholangiographic examination may be required [18]. In cases of restenosis, recanalization can be achieved by PTBD or balloon dilatation [27]. The primary adverse event associated with MCA is typically mild cholangitis, which can usually be effectively managed with conservative treatment [3]. To mitigate the risk of cholangitis, ensuring adequate biliary drainage before and after the procedure is essential. Additionally, there is a possibility of bile hemorrhage resulting from PTBD duct injury by the sheath [22]. The only adverse event reported to occur from magnet approach to indwelling catheter removal was mild fever [24]. Follow-up assessments have not revealed any

late adverse events or mortality directly linked to the MCA procedure. Given that magnets are aseptic devices that do not trigger inflammatory or immune responses within the bile duct, only cases of magnet migration and entrapment in the bile or hepatic ducts during magnet placement have been reported. In such cases, balloon or bougie dilation distal to the magnets, percutaneous pressurization, manipulation of the magnets with various tools, and percutaneous cholangioscopic intervention can solve the problem in most cases. When magnets cannot be removed with all these attempts, surgery may be considered [23]. Consequently, MCA appears to be a safe option even for patients undergoing liver transplantation or those who are immunocompromised [18].

Clinical Evidence and Results

In 107 patients with benign BS after LDLT, 93 (86.9%) successful anastomoses were performed, 89 biliobiliary and 4 bilioenteric anastomoses. In 13 patients with benign BS after OLT, 12 successful (92.3%) biliobiliary anastomoses were performed. In 15 patients with benign BS after liver transplantation, 14 of which were LDLT and 1 OLT, the anastomosis was unsuccessful. In 31 patients with postoperative benign BS other than liver transplantation, 28 successful (90.3%) anastomoses, 17 biliobiliary and 11 bilioenteric, were performed. In 34 patients with malignant BS, bilioenteric anastomosis was performed successfully (100%) in all patients. In total, 167 of 185 patients with biliary stricture were successful (90.2%).

After successful biliobiliary anastamosis in 118 patients with benign strictures, cholangitis was observed in 4 patients, biliary bleeding in 1 patient, magnet migration in 2 patients and magnet entrapment in 3 patients. Restenosis developed in 2 patients. In 15 patients with benign BS who underwent bilioenteric anastomosis, no complications were observed and restenosis developed in only 1 patient. After successful bilioenteric anastomosis in 34 patients with malignant strictures, cholangitis was observed in 2 patients. Restenosis occurred in 3 patients during follow-up. In total, cholangitis was observed in 6 patients (3.5%), biliary bleeding in 1 patient (0.5%), magnet migration in 2 patients (1.1%) and magnet entrapment in 3 patients (1.7%) after successful MCA in 167 patients. In 6 patients, restenosis (3.5%) developed during follow-up. The results of our extensive literature review are shown in tables 1, 2 and 3.

In result, many studies investigating the efficacy and safety of MCA in the treatment of enignant and malignant BSs have shown promising results, and the clinical feasibility, safety and usefulness of MCA have been proven in many cases of stenosis and obstruction without the need for surgery.

Challenges and Future Directions

While MCA holds great promise, several challenges remain to be addressed. Technical considerations such as optimal magnet design and placement technique require further refinement to improve outcomes and minimize complications. Additionally, comparative studies are needed to directly compare the efficacy of MCA with traditional interventions, particularly in specific patient populations such as those with benign vs. malignant strictures. Future research should also explore the potential role of adjunctive therapies, such as tissue engineering or drug-eluting coatings, to further enhance the efficacy of MCA in biliary stricture management.

Conclusion

MCA represents a promising and innovative approach for the treatment of BSs, offering advantages such as durable patency, reduced risk of stent-related complications, and feasibility in complex anatomies. While further research is needed to optimize technique and clarify long-term outcomes, MCA holds the potential to revolutionize the management of BSs and improve patient outcomes. Since MCA is an interventional procedure, the burden on the patient is extremely low and it can be performed in elderly patients or those with poor systemic status. MCA is emerging as a non-surgical alternative for recanalisation of biliobiliary and bilioenteric strictures and offers a safe and feasible option with high success rate, minimal stricture recurrence and reduced trauma.

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