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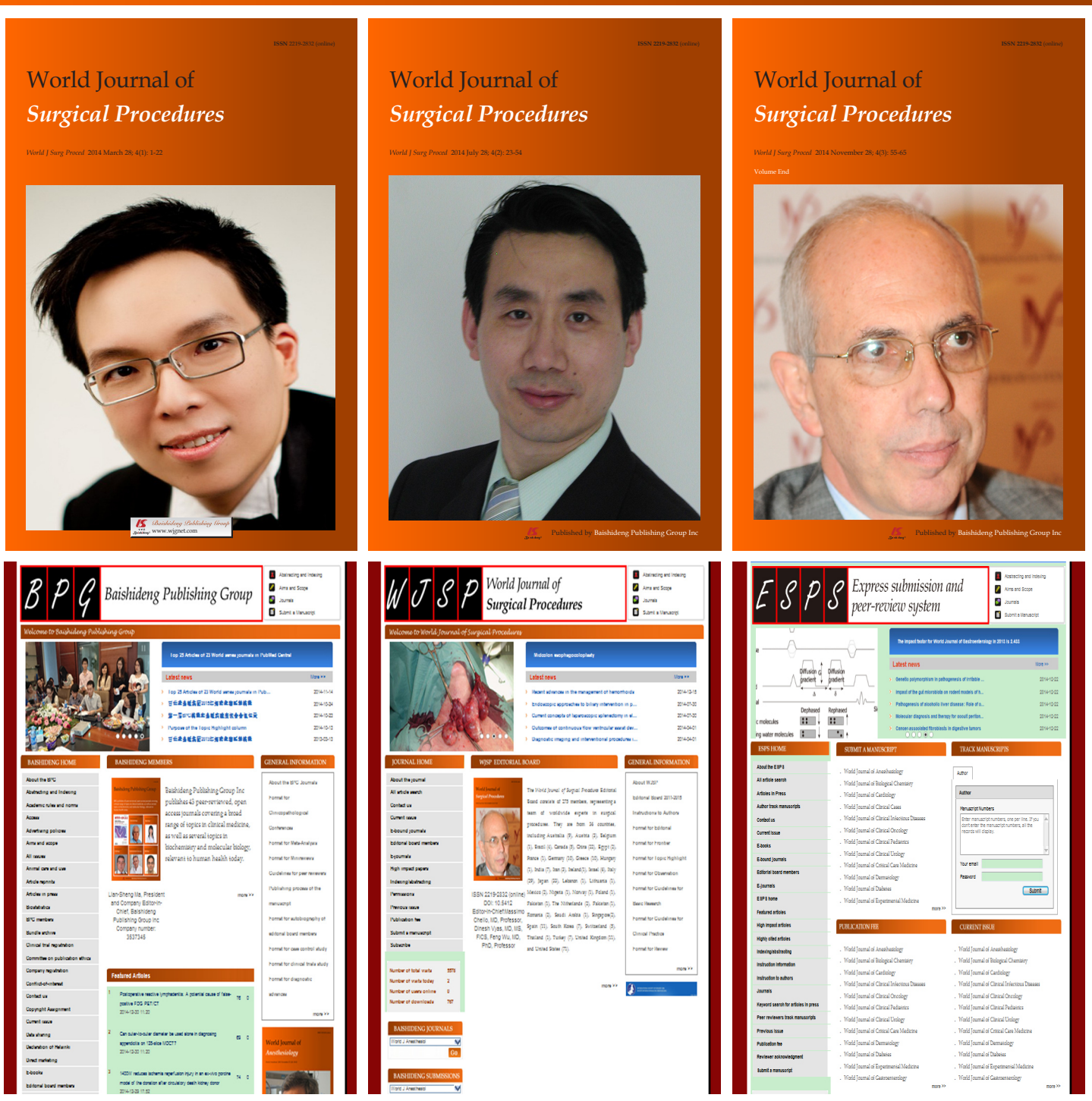

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World Journal of Surgical Procedures (*World J Surg Proced*, *WJSP*, online ISSN 2219-2832, DOI: 10.5412) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

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MINIREVIEWS

Outcomes of continuous flow ventricular assist devices

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Abstract

Heart transplantation is commonplace, the supply is limited. Many exciting changes in the field of mechanical circulatory support have occurred in the past few years, including the axial flow pump. Left ventricular assist device (LVAD) therapy is ever evolving. As the use of LVAD therapy increases it is important to understand the indications, surgical considerations and outcomes.

Key words: Left ventricular assist device; Axial flow; Mechanical circulatory support; Heart failure; Continuous flow

Core tip: Left ventricular assist devices provide a durable, long-term alternative to heart transplant for those with end-stage heart failure. In an era of limited transplant donor supply, axial flow pumps are a viable alternative.

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INTRODUCTION AND OVERVIEW

It is estimated that 5 million individuals are affected by heart failure. In general patients with heart failure have a poor prognosis and while cardiac transplantation is an effective long-term therapy for a select group of patients, the number of transplants have plateaued[1]. While pharmacologic therapy and cardiac resynchronization have improved symptoms and survival in heart failure patients, the survival for patients on inotropes is approximately 6% at 12 mo[2,3]. Due to the severe organ shortage and marginal improvements in outcomes with medical management alternate therapies such as mechanical circulatory support have developed. Since the first generation pulsatile pumps were developed approximately 50 years ago, improvements have been made to the design and have largely been replaced by axial pumps[4]. This article will review mechanical circulatory support, specifically left ventricular assist device (LVAD) axial flow pumps, and indications for use, surgical considerations and outcomes.

History of axial pumps

The first sets of pumps were developed over fifty years ago at the National Heart, Lung and Blood institute[4]. First generation pumps were pulsatile and included the Heartmate XVE and Novacor device. Originally placed as a bridge to transplant, the REMATCH trial showed an unprecedented improvement in early survival compared to conventional therapy and they were approved for destination therapy[5]. In 2009, Slaughter *et al*[6] showed

significantly better survival for axial flow pumps, 68% at 1 year and 58% at 2 years. These findings resulted in a significant change in practice and increased the use of axial flow pumps by tenfold[4].

Pump mechanics

Compared to pulsatile devices, axial flow pumps are smaller in size and easier to implant. In addition they have a singular moving part, making axial flow pumps more reliable with a lower adverse event profile. Axial flow pumps have a blood inlet and an outlet. A single internal rotor or impeller continuously unloads the left ventricle propelling blood in the axial direction. The impeller is kept within a rigid house. There are several bearing designs that drive the impeller, which include mechanical/pivot design, hydrodynamics, electromagnetic or a permanent magnet[7].

In an axial flow pump, mechanics are based on preload, speed at which the impeller rotates and afterload. For example, as the blood volume decreases, such as in hemorrhagic shock, the pump will continue to flow and the ventricle will collapse and result in inlet obstruction. In contrast, the patient might be volume overloaded and the speed of the pump might be inadequate to unload the ventricle resulting in signs and symptoms of heart failure.

Axial flow pumps are sensitive to afterload and this can have a profound impact on the flow mechanics. As the blood pressure increases the impeller has to increase its power to generate rotation in an attempt to maintain the constant rotations per minute (rpm). With an increased afterload, even at a set rpm, the increased afterload causes decrease in flows and hemodynamic support[8]. In this scenario the pulsatility index (PI) will be elevated and the flows will be decreased. It is therefore important to control blood pressure in the acute and outpatient setting.

Axial flow pumps run by setting the speed of the impeller, or rpm. Pump speeds are based on the patient's clinical status, volume status and echocardiographic findings[8]. The monitor provides information on speed, power, PI and calculated flows. The monitor can alert clinicians about proper pump function and changes in the PI or power may be a result of pump malfunction or a change in clinical status.

To summarize, axial flow pumps are durable pumps with a 58% survival at 2 years for destination therapy. Long term durability is attributed to minimal friction and heat production. Pump function is based on the patient's clinical status and pump speed. And finally due to continuous blood flow patients lack a pulse and may require Doppler blood pressure measurement.

How long have they been used

Axial flow pumps went into trial in 2003. Primary endpoints for bridge to transplant (BTT) patients included rate of survival to transplant or survival at 180 d. The primary endpoint for destination therapy patients was a composite endpoint at 2 years that included survival, adverse events and pump durability. The study found improved survival rates, improvement in quality of life and functional status in both groups. Axial flow devices, specifically the Heartmate Ⅱ, were approved by the Food and Drug Administration in 2008 as a bridge to transplant and in 2010 as destination therapy[9]. Since then a more recent review of outcomes for destination therapy demonstrates 74% survival at one year[10].

TYPES OF USE

Second generation and third generation axial flow devices have a high degree of reliability. This has resulted in a tenfold increase in their use[4]. Current indications include, myocardial recovery, BTT, bridge to decision and destination therapy. Device strategy is dependent on the patient's clinical status, co morbidities, end organ dysfunction and social support.

Bridge to recovery

Very few patients after LVAD placement will have myocardial recovery. A recent analysis of approximately 1100 Heartmate Ⅱ patients showed a 1.8% rate of recovery[11]. In a few, long term left ventricular unloading may provide reversal of atrophy in the cardiomyocytes and recovery of left ventricular geometry and function[12]. One such strategy includes the addition of pharmacological therapy to patients with continuous flow devices, to promote reverse remodeling. Birks *et al*[13] showed in a small group of patients the addition of high dose ACE inhibitors, beta blockers plus clenbuterol promotes myocardial recovery. While much is unknown about myocardial recovery after LVAD implantation, a considerable amount of research is being performed in this area.

Bridge to decision

Patients receiving mechanical circulatory support prior to determining eligibility for transplant are considered bridge to decision. In these patients end organ dysfunction including pulmonary hypertension, renal failure, obesity, medical compliance, tobacco abuse can be absolute or temporary contraindications for heart transplant. For a few of these patients, organ dysfunction will be reversible with mechanical circulatory support or afford them the opportunity to modify lifestyle making them eligible for transplantation.

Bridge to transplant

Bridges to transplant are patients who are eligible for cardiac transplant but have had progression of their disease. On any given day, there are 3000 patients on the waitlist per day, since survival is poor, approximately 43% will require mechanical circulatory support to "bridge" them until an organ is available[14]. The goal is to prevent end organ dysfunction for continued eligibility. Additionally, during that wait-list time, the patient is able to be out of the hospital, enjoying a reasonable quality of life and gaining strength and conditioning.

The use of LVAD therapy in candidates for heart

transplant is not benign and careful consideration should be made regarding the risks and benefits. While LVAD therapy will support end-organ function and improve quality of life, LVAD therapy will require an additional sternotomy for placement and redo sternotomy at the time of transplant. Additional concerns include blood transfusions at the time of placement, infections, stroke, and complications with the pump.

Destination therapy

Most patients in heart failure are not candidates for transplantation. Without advanced therapy, many will die within a year or continue to have poor function and quality of life.

The REMATCH trial was the first study to compare mechanical circulatory support to medical management. In this landmark trial the survival rate was 52% in the patients receiving mechanical circulatory support and 23% in the medical management group[5]. In 2002 the first generation pumps were approved and in 2010 the second-generation pump was approved for destination therapy. Since then the survival rates have improved and mechanical circulatory support provides patients equivalent survival to transplant patients at one year[6,15].

With the support of LVAD's, destination therapy patients have improved quality of life and improvement in their function. A study from Rogers *et al*[16] reported on functional capacity and quality of life of patients under long-term LVAD support. NYHA functional class, 6-min walk distance, patient activity scores as well as quality of life (Minnesota Living With Heart Failure and Kansas City Cardiomyopathy Questionnaires) were collected before and after LVAD implantation. Following implant, 80% of destination treatment patients at 6 mo and 79% at 24 mo improved to NYHA functional class I or Ⅱ. Mean 6-min walk distance in these patients was 204 m in patients able to ambulate at baseline, which improved to 350 and 360 m at 6 and 24 mo. There were also significant and sustained improvements from baseline in both quality of life scores. The relative bridge to recovery is minimal between indications.

TYPES OF PUMPS

Heartmate Ⅱ

The Heartmate Ⅱ is a continuous axial flow device. It contains an internal rotor with helical blades that curve around a central shaft. As blood enters the chamber the internal blade rotates and converts the radial velocity of the blood flow to an axial direction, hence the term axial pump. The pump weighs 350 g and can flow up to 10 L/min. The inflow cannula is placed in the left ventricle apex and the outflow graft is connected to the ascending aorta. Due to pump size the pump housing is placed in the left upper quadrant in the pre-peritoneal pocket. The device is connected to controller *via* a driveline that is tunneled thru the subcutaneous tissue and brought out to the skin.

Jarvik 2000

The Jarvik 2000 is a continuous flow pump that unlike the Heartmate Ⅱ is placed within the left ventricle. It weighs approximately 85 g. A single impeller is housed within titanium housing completely inside the ventricle. Interestingly the outflow can be connected to either the ascending or descending aorta. The pump flows up to 7 L/min. One added benefit of the Jarvik pump is the skull mounted driveline. Unlike other pumps the skull implant is designed to be resistant to infection and allows patients to shower, bath or swim[17].

INCOR

The INCOR is a continuous axial flow pump developed by Berlin Heart. The INCOR design is slightly different in that the impeller is levitated by an electromagnetic bearing and therefore the parts do not come in contact with each other. The lack of contact improves long-term durability by decreasing heat and friction. The pump can flow up to 6 L/min. The INOR is currently not available in the United States[18].

Micromed debakey

The Micromed Debakey is a fully implantable electromagnetic axial flow pump. The pump weighs 93 g. Due to its small size it can be placed in the intra-pericardial position. The pump consists of an inflow cannula, apical ring, the pump, and outflow graft. A flow probe encircles the outflow graft providing real-time cardiac output. The pump can flow up to 5 L/min. The pump is connected thru a driveline to a controller module and runs off 12-volt DC batteries for 4 to 6 h[19].

TECHNICAL CONSIDERATIONS

Aortic insufficiency

Pre-operative aortic insufficiency (AI) is important to identify in LVAD patients. Patients with greater than moderate aortic insufficiency prior to implant should be surgically treated at the time LVAD implant. Since the ventricle does not contract the ventricle fills during the cardiac cycle creating a circular loop[20]. Since the left ventricle does not have time to unload this may affect the long term durability of the pump. More importantly aortic insufficiency leads to high pump flows and low total cardiac output[21]. For patients with mild AI who are undergoing LVAD placement for long term support the AI may progress over time and should be monitored. Cowger *et al*[22] found that patients supported at 18 mo had moderate or worse AI and half the individuals with moderate or worse AI required readmission for heart failure or an arrhythmia. They pointed out that while the long-term significance is not known increase in AI might have real clinical impact on long-term mechanical support.

A second group of patients develop AI over time due to degeneration or fusion of the leaflets. Since patients with LVAD's have minimal or no pulse in the native LV,

although contracting the LV may not generate enough pressure to open the aortic valve. The lack of pulse is implicated in postoperative AI[23]. Decreasing pump speed may reduce the transvalvular gradient and temporarily improve systemic perfusion especially in patients who develop AI after LVAD placement. But this may be temporary solution. More durable options include the Park stitch, over sewing of the valve with patch, or replacement with a tissue valve, but come with increased morbidity.

Surgical options for the treatment of aortic insufficiency include repair or replacement of the aortic valve. The Park stitch is described as a central coaptation stitch has been shown to be a durable option up to two years after LVAD placement[24]. Another option includes over sewing of the outflow tract and keeping the valve leaflets intact. Patients with an over sewn aortic valve are completely dependent on the LVAD. If an aortic valve replacement is needed, a tissue valve is preferred. Mechanical valves leave patients with increased risk of thromboembolic phenomena, since the lack of ventricular contraction leads to sub valvular thrombus formation and stasis around the struts.

Mechanical aortic valve

Preexisting mechanical aortic valves are considered a relative contraindication to LVAD placement. Leaving a mechanical aortic valve leaflets patients at higher risk of thromboembolic complications and the possibility that the valve could remain in the open position. Replacement of mechanical valve at the time of LVAD operation increases pump times and may not be tolerated in sicker patient. Therefore careful consideration should be made when placing LVAD's in this patient population[25].

Mitral regurgitation

In most cases mitral regurgitation does not need to be corrected at the time of implantation. Once the LV is decompressed, in most cases mitral insufficiency can be managed by increasing or decreasing pump speed. In a few patients, specifically BTT candidates, the addition of a mitral valve regurgitation may result in a decrease in pulmonary vascular resistance (PVR) and may permit certain patients thought to be ineligible for transplantation to become candidates[26]. It should be noted that patients with myocardial recovery who undergo LVAD explanation might need an additional operation for mitral insufficiency at the time of device explant.

Tricuspid regurgitation

Tricuspid regurgitation in patients with right heart dysfunction is associated with poor prognosis[27]. Continued tricuspid regurgitation after LVAD may progress after LV decompression, resulting in further annular dilatation and right ventricular (RV) failure. Also there is increased operative mortality in patients undergoing isolated redo tricuspid valve (TV) operation especially in the face of worsening right heart failure. While there are increased cardiopulmonary bypass times in patients who undergo concomitant TV repair/replacement, repair/or replacement of the TV at the time of implantation results in improved short term results including less RV failure and may promote remodeling of the RV[23,28].

Patent foramen ovale

Investigations for a patent foramen ovale (PFO) should be performed prior to LVAD implantation. Imaging studies include surface or trans esophageal echocardiography combined with "bubble study" and concurrent color Doppler. Patients can perform a Valsalva maneuver with release to identify hidden PFO's. Doppler echocardiography may show a left to right shunt, but the bubble study may not reveal a PFO in the setting of high elevated left atrial pressures[21]. After LVAD implantation, unloading of the left ventricle may uncover a PFO. Patients may present with stroke or pump thrombosis. One of more common consequences of a PFO includes the development of severe hypoxia due to a right to left shunt, making it important to identify prior to LVAD implantation[21].

Mitral stenosis

Mitral stenosis is a bigger problem for patients undergoing LVAD placement[29]. Mitral stenosis limits left ventricular filling and limit pump flows[30]. In addition, the persistently elevated left atrial pressure lead to continued pulmonary hypertension. Treatment options include commisurotomy or tissue replacement[8].

Ventricular tachycardia

Ventricular tachycardia (VT) is common in patients with heart failure. Most patients undergoing LVAD's already have an implantable defibrillator at the time of the surgery. Despite ventricular unloading many patients continue to have VT. Reversible and non-reversible causes of VT should be determined since continued VT after LVAD placement can lead to inadequate systemic perfusion. Reversible causes include suction events or cannula position. Patients with irreversible causes should be managed with pharmacological therapies and or catheter ablation[31]. A unique option includes scar mapping and ablation for resistant ventricular arrhythmias. A recent series by Cantillon *et al*[32] showed that out of 32 diagnostic and ablation procedures out of 611 LVAD implantations, the dominant mechanism was intrinsic myocardial scar, with only 14% of VT circuits involving the apical inflow cannulation site. Ablation was acutely successful (VT non-inducible) in 86% of patients, with freedom from recurrent VT of 67% during a mean duration of LVAD support of 120 d.

DURABILITY OF PUMP

Pump technology has improved significantly since the original pulsatile devices. The current second generation pumps have an estimated clinical life of greater than 5 years. Due to improved durability we are now seeing a different number of adverse events.

Complications

Thrombosis and bleeding are common complications in patients with mechanical circulatory support. Patients with LVADs are prone to thrombosis due to the blood device interaction. In order to prevent this patients are maintained on a regimen of coumadin and antiplatelet agents. The current rates of pump thrombosis is anywhere from 0.014 to 0.03 events per patient-year and actually may be increasing in incidence[33]. Pump thrombosis is a difficult problem to diagnose and even more difficult to treat. Laboratory monitoring of lactate dehydrogenase, plasma free hemoglobin and increased pump power alert physicians to pump thrombus but additional studies such as RAMP protocols help to diagnose thrombus. The question remains how best to treat the problem. Increase in pump speed, change in international normalized ratio goals, or additional antiplatelet agents may help to resolve the pump thrombosis. Ultimately some patients will have to their pump changed out due to the thrombosis; which comes with and increased morbidity and mortality.

Bleeding

Bleeding is another common problem seen in patients with LVAD's. The combination of anticoagulation and acquired hematologic problems due to device flow characteristics results in a bleeding diathesis. Bleeding is a significant problem and results in 3% mortality from bleeding complications[34]. Gastrointestinal bleeding is a long been recognized complication of axial flow pumps. Acquired von Willebrand syndrome or distention of submucosal venous plexus from diminished pulsatility is thought to be a key event. An attempt at decreasing pump speeds to restore pulsatility and stop the destruction of large von willebrand factor multimers may be of benefit[34]. Other treatment options include epinephrine or octreotide. For patients with recalcitrant bleeding, long-term cessation of anticoagulation or surgical management of the culprit gastrointestinal tract lesion has also been used.

Stroke

The incidence of stroke after LVAD placement is reported to be 8.0% to 25.0%[35]. Depending on the anticoagulation regimen, antiplatelet regimen and device type the stroke rates will vary[36]. Approximately a third of ischemic strokes will convert to a hemorrhagic stroke.

Infection

Infection remains a considerable complication with LVAD patients. Infections can be grouped into three categories; VAD specific, VAD related or non-VAD related infections[37]. Of the VAD specific infections, pocket infections occur in ten percent of the population. Driveline infections are a much larger problem in the LVAD population. The rate of infection is somewhere between 0.37-0.58 events per patient year. Driveline infections are generally related to driveline movement. Chronic movement prevent in growth of tissue into the external velour layer of the driveline. Once a driveline infection is suspected, treatment should include both systemic and local antibiotics. It is important to note that infections in the LVAD patients may lead to pump infections, bacteremia and even more worrisome pump thrombosis[33].

Pump failure

The newer second generation are estimated to have long-term clinical durability; greater than 5 years[7]. But with increased wear and tear it exposes the LVAD to device related problems. Failure of the controller and power source are rare. The most susceptible to damage is the external driveline due to tugging, twisting or kinking. The estimated rate is approximately 0.03 events per patient year[38]. In most cases of pump failure, patients are trained on trouble shooting the controller and power source.

Brief comparison compared to heart failure

The REMATCH trial evaluated the efficacy and safety of long-term left ventricular assist device support chronic end-stage heart failure patients. Compared with optimal medical management, LVAD implantation significantly improved the survival and quality of life. Favorable results in this bridge to transplant population encouraged the design of the multicenter REMATCH trial to evaluate the efficacy and safety of long-term LVAD support. Compared with optimal medical management (n = 61), LVAD implantation (n = 68) doubled the 1-year survival rate (from 25% to 51%). While the original trial compared first generation pumps to medical management, the outcomes with LVADS were superior. At two years the survival was 23% compared to 8% in the medical therapy group. Functional status and quality of life were improved at one year in the LVAD group[5]. A second study comparing first generation devices to the current axial flow devices showed improved survival. One-year survival was 68% and 58% at the second year compared to original REMATCH trial results[6].

EFFECTS ON PHYSIOLOGY

End organ perfusion

An animal study using the Terumo DuraHeart LVAD, an axial flow device, found an increase in the plasma renin levels without a significant increase in the blood pressure despite the up regulation[39]. But the clinical relevance is unknown. More work is needed to evaluate and closely study the effect of continuous-flow devices in select populations of heart failure patients, such as those with baseline severe multisystem organ failure. In addition, longer-term studies are needed to assess end-organ function with continuous-flow devices, which may have important implications for use as destination therapy[40].

Renal failure

Forty five percent of patients with heart failure have associated renal dysfunction. Cardiorenal syndrome is related to low output and low flow to the kidneys and venous hypertension. Since chronic kidney disease is a relative contraindication to heart transplant, patients with heart failure and renal dysfunction may be candidates for

destination therapy. LVAD therapy improves forward flow and improves renal function in a large proportion of patients. Initial improvements can be seen in the first month, but plateaus thereafter. The implantation of LVAD therapy might help differentiate reversible and irreversible renal dysfunction in heart failure[41].

PA pressures

Fixed pulmonary hypertension is a contra indication for patients with heart failure. Many times it is unclear if pulmonary hypertension is due to left ventricular failure or intrinsic lung disease. Generally these patients will have a transpulmonary gradient greater than 14 mmHg and a pulmonary vascular resistance greater than 3 Wood units. For patients with reversible pulmonary hypertension, unloading of the left ventricle may decrease pulmonary hypertension. A study from John *et al*[42] showed improvement in mean pulmonary pressures and improvement in PVR. While the improvements in pulmonary artery pressures are seen in the first 6 mo, the changes in pulmonary pressures plateau. The hemodynamic changes in pulmonary artery pressures appear to persist after heart transplant.

Right ventricle

After LVAD placement, end organ perfusion improves and there may be a drastic decrease in afterload of the pulmonary circulation. In some patients this is beneficial, but in a third of patients this will result in right ventricular failure. Hannan *et al*[37] looked at the outcomes of right ventricular failure after LVAD placement. Overall, 30 (6%) patients receiving left ventricular assist devices required a right ventricular assist device, 35 (7%) required extended inotropes, and 33 (7%) required late inotropes. A significantly greater percentage of patients without right ventricular failure survived to transplantation, recovery, or ongoing device support at 180 d compared with patients with right ventricular failure. They concluded that right ventricular failure is associated with worse outcomes than without. An extremely difficult problem to manage both medically and surgically, acute RV failure comes with high short and long term mortality. Predicting RV failure is difficult. Optimizing volume status, decreasing pulmonary pressures and the addition of inotropes is important. Post operatively the use of inhaled nitric oxide and pulmonary vasodilators will help to augment right ventricular function.

Coagulation

Recent reports have indicated that there may be an increase in the relative rate of thrombosis of axial flow devices[43]. The exact etiology of this observation is unknown but does make one more aware of the need for meticulous attention to anticoagulation in these implantable devices with a continuous blood interface.

SUMMARY/OVERVIEW

Although heart transplantation is commonplace, the supply is limited. Many exciting changes in the field of mechanical circulatory support have occurred in the past few years, including the axial flow pump. LVAD therapy is ever evolving. As the use of LVAD therapy increases it is important to understand the indications, surgical considerations and outcomes.

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MINIREVIEWS

Review of (acquired) incidental, rare and difficult tracheoesophageal fistula management

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Abstract

Acquired benign tracheoesophageal fistula is a rare condition and a difficult problem. The rarity and unpredictable presentation of this condition makes the design and setting of randomized prospective trials impossible. Guidelines on this matter are also difficult to establish. Based on a comprehensive evaluation of published literature and their experience, the authors review the etiology and best options for treatment, either surgical and non surgical, according to present knowledge.

Key words: Tracheoesophageal fistula; Esophageal stents; Tracheal stents; Surgical treatment

Core tip: Acquired nonmalignant tracheoesophageal fistula is a rare life-threatening condition. Several management approaches have been proposed, without a real consensual approach. The authors review the published literature and discuss the different options.

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INTRODUCTION

Acquired benign tracheoesophageal fistula (TEF) is a rare condition and a difficult problem that simultaneously compromises the respiratory and digestive functions. Morbidity is very high and, in untreated patients, mortality is probably close to one hundred percent. Similarly, treatment is also very difficult and published collective experience scarce. The rarity and unpredictable presentation of this condition makes the design and setting of randomized prospective trials impossible and is a limiting factor for the quality of information derived from the very few retrospective series published so far. Guidelines on this matter are also difficult to establish since the few published data differ significantly in issues like fistula etiology and location and the clinical expertise of surgeons (thoracic, general, ear, nose and throat) and gastroenterologists.

Therefore, for surgeons facing this difficult issue, a full and comprehensive evaluation of the literature should consider all the published data and the specificities of the information provided, such as the correct assessment of hospital resources, namely, the collective experience of a mandatory multidisciplinary approach. In such a difficult and rare condition, to reach a large and sound clinical experience is very challenging. At best, the concurrent experience in other clinical fields will hopefully provide the skills to deal with acquired benign tracheoesophageal fistulas. Due to the complexity of this condition, a clinical surgeon uncomfortable with the management of this disease should refer these patients to an experienced center.

THE SURGICAL APPROACH

Five important papers published on this subject can be

identified[1-5], coming from experienced surgical groups with a sound reputation and experience and reporting clinical good outcomes. However, none of those groups were able to treat more than 75 patients and only over a long period of 30 to 35 years could those numbers be reached. Published scientific evidence is, at best, on the expert opinion range (level 3). Hilgenberg *et al*[1] were probably the first to publish a systematic review on this complication based in their personal experience with 20 patients. Lesions were caused by tracheal intubation (14), blunt trauma (3), orthopedic cervical spine procedures (2) and foreign body ingestion (1). Almost all of these lesions involved the proximal esophagus and the surgical approach relied on tracheal resection and anastomosis with either a direct suture of the esophageal perforation (16 patients) or an end to end reconstruction (3). Mortality reached 10% and fistula recurrence 5%. The most useful recommendations were the importance of preoperative mechanical ventilation weaning and the use of interposition of healthy muscular tissue buttressing the tracheal and esophageal suture lines.

Mathisen *et al*[2] reported their results in 1991 with a series of 38 patients treated for tracheoesophageal fistulas over a 16 year period, later completed with another 36 patients operated on from 1992 to 2010[3]. Interestingly in this series, the largest published until now, the etiology changed, with a decreasing incidence of post intubation injuries (71.1% to 47.2%) whilst other causes, like esophageal surgery and laryngectomy complications, increased in prevalence (5.3% to 27.8%). Reported fistulas were mostly located in the mid and upper trachea (61% and 36%). The majority (92%) were less than 3 cm long. Surgical approach was mostly cervical or cervical plus upper sternotomy. There was a clear trend change, from tracheal resection and anastomosis to direct and simple repair of the tracheal lesions, during the time span of this study, which the authors attributed to the increase of complications of esophageal and laryngeal surgery as the cause of tracheoesophageal fistulas. In this setting, compared with post intubation injury, the destruction of tracheal tissue was found less disruptive and more suitable for a conservative approach. Although mortality decreased from over 10% to 2.8% in the second period, fistula recurrence more than doubled, general complications remained the same, the number of patients requiring a tracheal procedure increased more than four fold, and the patients that were not able to recover oral intake were in excess of 17.1%, a five fold increase over the first time period. The authors established a relationship between these events and the minor tracheal lesions, TEF occurring after resection of the esophagus or larynx, and they considered that the later conditions were more challenging problems with a higher rate of fistula recurrence. They also reinforce the statement for the use of healthy muscular tissue to protect suture lines, underlining the importance of mechanical ventilation weaning before endeavouring tracheal reconstruction. For ventilator dependent patients, the authors emphasize the need for an adequate endotracheal tube cuff placement distal to the fistula opening. They also sustain the need for optimization of the overall medical condition prior to any definitive surgical approach, through placement of a feeding jejunostomy and a decompression gastrostomy, the removal of nasogastric feeding tubes (which adds further damage to tissues), and control of sepsis. They argue against the use of temporary or definitive esophageal stents because, in their opinion, they do not contribute to the treatment of established lesions and may also enlarge TEF, creating giant fistulas.

Another very interesting study comes from Italy with Baisi *et al*[4] reporting 31 patients operated on for tracheoesophageal fistulas over a period of 18 years. In this series, two thirds of the fistulas were caused by endotracheal intubation. The other significant cause was orthopedic cervical spine surgery (4 patients). Laryngeal surgery was not identified as a cause and esophageal surgery accounted with only one case of a Zenker's diverticulectomy as the primary procedure. Fistulas were all proximal in the trachea and surgical approach was mainly cervical. Again, they agree with previous authors on the need for weaning the patient from mechanical ventilation and obtaining an optimal general and medical condition with endoscopic percutaneous gastrostomy, feeding jejunostomy and sepsis control. In their experience, tracheal resection and reanastomosis was rarely needed since 26 patients were treated with tracheal and esophageal direct suture. This approach is contradictory to Mathisen's claim that post intubation lesions are more disruptive of tracheal tissue and more often require tracheal resection. These last authors also emphasize the need for muscular tissue interposition. Mortality was low, with only one reported death.

A very important series comes from the Mayo Clinic in Rochester, with Deschamps[5] presenting the results from a-30-year retrospective review including 35 patients. In this series, fistula etiology differs significantly from previous data, with most TEFs related to post-esophagectomy complications, while the post-intubation lesions accounted for less than 6% of the cases. Other important differences were the presence of trauma (17.1%), mediastinal tuberculosis (14.3%), radiation therapy (5.7%) and the *de novo* reported presence of an indwelling airway or esophageal stents as a cause for TEF (11.4%). All these etiologies were previously unreported. Not surprisingly, fistula location was more widely distributed, the majority being located distally in the carina (9) and main bronchus (14). This modified the surgical approach and strategy, with most patients being operated on through a thoracotomy or a thoracotomy plus a cervicotomy or laparotomy. In some patients, segmental bronchial resection was needed. The number of TEF requiring a multistaged repair was also important (7) and reoperations for complications (esophageal leak, bleeding, recurrence of TEF and tracheal dehiscence) reached almost 22.8%. Despite those figures, mortality was only 5.7% and 29 patients (82.9%) were able to return to an oral diet. Still, a great number of patients were treated with single stage division of the fistula and direct repair of both the tracheal and esophageal defect. These authors concur with previous

reports on the importance of buttressing the suture lines and weaning the patients from mechanical ventilation, although they do not equally emphasize these procedures, particularly in cases where tracheal resection and anastomosis is not needed.

Bartels *et al*[6] presented a report on tracheobronchial lesions (including 4 TEF) exclusively as morbidity of post esophageal resections. They were more frequent with the transthoracic approach than with the transmediastinal route and all cases were evident up to one month after the original operation. Prevalence was 3.9%. Factors closely related to the occurrence of those lesions were neoadjuvant radiotherapy, extensive thoracic linfadenectomy and dissection, as well as insufficiently drained local sepsis (mostly from anastomotic leaks). Despite this surgical group experience and expertise in Siewert's report, mortality averaged 33% and was correlated with the above risk factors. The authors found no positive contribution for fibrin glue or stents use and underscored the importance of weaning the patient from mechanical ventilation and of the use of buttressing of suture lines.

THE CONSERVATIVE APPROACH

For many years, esophageal stenting has been used in the management of malignant and benign dysphagia and tracheoesophageal fistulas[7]. Tracheal[8] and combined (tracheal and esophageal) stenting[9-12] were also reported, including combined surgical and endoscopic approaches. The results from these studies are difficult to analyze due to the mixed nature of the pathologies involved (benign, malign, strictures, isolated esophageal or tracheal fistulas) and the diversity of stents used (plastic, metallic, covered or uncovered, retrievable or not). Major criticisms on this type of solutions for benign TEF are the low rate of fistula sealing without a real cure[13], the unnecessary and deleterious delay of definitive treatment and the potential for further damage of already traumatized tissue[14,15]. In fact, it is unlikely that the artificial surface of an esophageal prosthesis might allow, without the natural matrix provided by natural healthy tissue (muscle or other tissue buttressing), the healing of the *pars membranosa* of the trachea, the anterior wall of the native or interponate esophagus or both. This is mostly true in a patient dependent on mechanical ventilation because positive pressure will fuel the conditions for a perpetual tracheal leak. The same holds true for tracheal prosthesis alone. In this case, despite effective sealing of the airway, the esophageal leak will be responsible for local sepsis and persistent fistula. However, we found that a tracheal prosthesis that seals the airway defect might be temporarily useful, protecting the tracheal suture and tissue buttressing during unavoidable mechanical ventilation in the post operative period[8]. Its temporary and cautious use might also correct (modulate) late tracheal stenosis after surgical procedures. Recently, we used this approach with good results on a patient successfully operated on for TEF (post tracheal intubation) that subsequently developed isolated tracheal stenosis (unpublished data).

In our personal series, we also registered 2 TEF after esophageal resection for cancer (3.1% of the esophagectomies performed) with both patients submitted to neoadjuvant radiotherapy. Both patients were operated on through a thoracic approach and both suffered from long lasting cervical anastomotic leaks. The risk factors were identical to the ones reported in the Siewert[6] series but, in these cases, the TEF presented late, at 3 and 9 months after esophagectomy and cervical anastomotic leaks closure (unpublished data). A conservative approach was initially selected, with esophageal or tracheal prosthesis, but this approach failed and both patients were later operated on (tracheal and esophageal suture and sternocleidomastoid muscle interposition). One recovered uneventfully from the surgical procedure. The other patient suffered from recurrence of the fistula, reoperation, and finally, transsternal definitive tracheostomy followed by death from sepsis and multiple organ failure.

Finally, a 5th patient was operated on with a TEF resulting from a long lasting (1 year) tracheal stent initially inserted to treat a post intubation stenosis. This case underlines the indwelling esophageal or tracheal prosthesis risk of TEF.

CONCLUSION

Treating benign TEF is challenging and a very difficult problem due to the potential devastating complications, patient suffering and death. Personal or institutional experience is scarce and even "high volume" centers face this problem at most once a year. There are no randomized studies or guidelines and only expert opinion is available[1-6,16]. Furthermore, published series differ significantly over important issues like fistula etiology and location, hospital resources and specificities of surgical and gastroenterology training. Therefore, for the occasional surgeon facing this problem, there are "off the shelf" solutions. Thus, these cases should be referred to experienced centers.

TEF patients require a multidisciplinary approach, encompassing the cooperation not only of surgical specialties (general, thoracic, ear, nose and throat), but also anesthesiologists and intensivists who in the end will have to manage and secure the airway in a complicated and difficult acute setting. This is a very important statement and only Baisi *et al*[4] report briefly and incompletely state this need. There are in fact a few studies published by anesthesiologists[17,18] reporting the difficulties they faced and the imaginative solutions that they used to overcome these uncommon situations. Some of these reports deserve to be carefully consulted, discussed and made available to all surgical teams as in some cases the reported "tricks" may make a substantial difference.

From the surgical point of view, some important issues are consensual. Almost all groups agree on the advantage of unsupported ventilation before any major surgical procedure. An optimal medical condition also should be pursued, namely through a gastric decompression and feeding jejunostomy tube placement. If at all

possible, the simpler surgical solution is certainly the best, that is, use of a single surgical approach (cervical or thoracic), a direct suture of the tracheal and esophageal lesions and the placement muscle interposition between suture lines. In fact, only Camargo *et al*[19] seems to minimize the importance of this simple, harmless and effective step. In spite of the complexity and etiology of TEF, a recent trend for less frequent tracheal resections, less frequent use of multistage procedures and esophageal exclusion or diversion is apparent.

Every surgeon must be prepared for complex and demanding procedures like tracheal resection and reconstruction, laryngotracheal resection and reconstruction eventually associated with major esophageal surgery.

The use of stents in benign situations must be cautious, temporary, tailored for specific situations, and should not be considered as a definitive approach. However, during the post operative period when a distal to the suture line tracheal tube placement is not possible, they may have a role as an adjunct, either as a short bridge for a definite surgical approach or as an airway protection procedure in a mechanical ventilation dependent patient.

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MINIREVIEWS

Diagnostic imaging and interventional procedures in a growing problem: Hepatic alveolar echinococcosis

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Abstract

Alveolar echinococcosis (AE) of the liver is caused by the metacestode of the fox tapeworm *Echinococcus multilocularis* (*E. multilocularis*), which is endemic in many parts of the world. AE is a very aggressive and potentially fatal infestation which always affects the liver primarily and metastasizes to any part of the body. Without timely diagnosis and therapy, the prognosis is dismal, with death the eventual outcome in most cases. Diagnosis is usually based on findings at radiological imaging and in serological analyses. The alveolar cysts grow by exogenous proliferation and behave like a malignant neoplasm. Since AE lesions can occur almost anywhere in the body, familiarity with the spectrum of cross-sectional imaging appearances is advantageous. Therefore, AE lesions can cause physicians to generate a long list of differential diagnoses, including malignant tumors. Disseminated parasitic lesions in unusual locations with atypical imaging appearances may make it difficult to narrow the differential diagnosis. For diagnosis, ultrasonography (US) remains the first line examination. For a more accurate disease evaluation, aiming to guide the surgical strategy, computed tomography (CT), magnetic resonance imaging (MRI), including magnetic resonance cholangiography (MRC) imaging, are of importance, providing useful complementary information. However, making the correct diagnosis is possible if imaging findings are correlated with appropriate clinical findings. We present an overview of the radiological patterns produced by *E. multilocularis* lesions as seen on US, CT and MRI and discuss the interventional procedures in hepatic AE lesions.

Key words: Alveolar echinococcosis; Liver; Diagnosis; Intervention; Imaging; Review

Core tip: Diagnosis and treatment of alveolar echinococcosis remains a challenge for clinicians. Most patients suffering from a chronic carrier status need continuous medical treatment and follow-up examinations. Diagnosis of alveolar echinococcosis is supported by results from imaging studies, histopathology and/or serological analyses. The present review summarizes current understanding of imaging features and knowledge of interventional procedures.

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INTRODUCTION

Alveolar echinococcosis (AE) is a rare parasitic disease due to the intra-hepatic development of the larva of the small metacestode *Echinococcus multilocularis* (*E. multilocularis*). Metacestode cells of *E. multilocularis* proliferate in the liver, inducing slowly progressive, life-threatening tumor like growths[1,2]. The prognosis is generally poor

and liver transplantation may be required in patients with inoperable lesions, chronic liver failure[2,3]. Most patients suffering from a chronic carrier status need continuous medical treatment and follow-up examinations[1,4]. In addition to anti-infective therapy with benzimidazoles, early diagnosis by imaging techniques, radical surgery, transplantation, radiological interventional procedures and long term medical care of the patients have contributed to the success of treatment and increase in patient survival time[5].

This article provides an epidemiological, pathophysiological, diagnostic profile of the disease as background for a detailed review of the clinical, interventional approach, and radiological features of hepatic AE. The current roles of specific imaging modalities are described to aid radiologists in the timely detection and characterization of AE infestations.

EPIDEMIOLOGICAL AND PATHOPHYSIOLOGICAL CHARACTERISTICS

Most human cases of *E. multilocularis* infection have been reported in endemic areas of western and central Europe, including Turkey, the former Soviet Union, Iran, Iraq, western and central China, and northern Japan[6]. Definitive hosts are foxes and, less commonly, cats and dogs. Intermediate hosts are wild rodents. Humans are infested either by direct contact with definitive hosts or indirectly by intake of contaminated water or contaminated plants, such as wild berries[6,7]. Humans are accidental intermediate hosts, becoming infected after ingesting contaminated foods, including fruits and vegetables[8]. The walls of the parasite eggs are destroyed in the host digestive system, after which the embryos penetrate the intestinal wall and reach the liver, by way of the portal or lymphatic system, where the larvae develop. In the liver, *E. multilocularis* larvae grow as tumor-like buds that evolve into multiple vesicles containing a germinal layer surrounded by a laminar membrane[4]. The liver parenchyma near the mass is typically atrophic with capsular retraction due to biliary or vascular invasion. Necrosis is observed in the center of the lesions; moreover, these lesions may become superinfected with bacteria and fungi, possibly leading to complications such as liver abscesses and septicemia. The larva causes invasive and destructive changes in the human host that often lead to complications[7-9].

Hepatic AE is a chronic disease with a latent stage that may last for years before signs and symptoms develop. If left untreated, the disease is usually fatal. Death eventually results from hepatobiliary complications, such as biliary obstruction with bacterial or fungal superinfection or secondary biliary cirrhosis, bleeding from esophageal or duodenal varices due to portal hypertension, Budd-Chiari disease or obstruction of the vena cava[9,10].

CLINICAL FEATURES

The liver is the most common site of *E. multilocularis* infection, with more than 90% of patients having infected livers. The lesions may be single or multiple[4]. Alveolar echinococcosis of the liver behaves like a slow growing liver cancer. Symptoms of hepatic alveolar echinococcosis are principally cholestatic jaundice and epigastric pain[3,7]. Involvement of the bile ducts and blood vessels leads to severe complications, such as cholangitis, portal hypertension, liver abscesses, septic shock and Budd-Chiari syndrome[11].

DIAGNOSIS

Clinical diagnosis of hepatic AE is based on the patient's medical history, clinical features, morphological characteristics of lesions, determined at radiological imaging, and results of serological and histopathological analyses[7,8,12]. A diagnosis of alveolar echinococcosis is based on the presence of at least two of the following findings[4,12]: (1) a lesion or lesions with the typical appearance, detected in the usual sites at cross-sectional imaging; (2) echinococcus species-specific serum antibodies detected in blood tests with high diagnostic sensitivity and confirmed in immunoassays with high specificity; and (3) histopathological features suggestive of *E. multilocularis* and nucleic acid of *E. multilocularis* detected in a clinical specimen.

The World Health Organization Informal Working Group on Echinococcosis classification system, based on imaging findings, has been established as the international benchmark for standardized evaluation of diagnostic and therapeutic measures[13]. This PNM-system denotes the extension of the primary mass in the liver (P), the involvement of neighboring organs including lymph nodes (N), and metastases (M)[14] (Table 1).

IMAGING METHODS FOR DETECTING THE HEPATIC AE LESIONS

Abdominal ultrasonography (US) is the first line imaging examination for evaluation of patients in whom the presence of alveolar echinococcosis is suspected. Computed tomography (CT) and magnetic resonance (MR) imaging performed with cholangiopancreatography and diffusion-weighted techniques, as well as standard sequences, typically are required for preoperative evaluation[4,8,10]. Recently, we have performed CT perfusion imaging for demonstration of the perfusion characteristics of the hepatic AE lesions and to make a differential diagnosis between AE and other malignant liver lesions.

US

US is the initial investigative modality of choice for detection of hepatic AE lesions[4,12]. Typical findings at abdominal US (in approximately 70% of cases) include a large hepatic mass with juxtaposed areas of internal hyper- and hypo-echoic, irregular margins and scattered foci of calcification, and a pseudocyst with a large area of central necrosis surrounded by an irregular ring like region of hyperechoic representing fibrous tissue[15] (Figure 1A).

Table 1 PNM classification of alveolar echinococcosis

P	Primary lesion localized to the liver
PX	Primary lesion cannot be assessed
P0	No detectable hepatic lesion
P1	Peripheral hepatic lesion with no proximal hepatic vascular or biliary involvement
P2	Central hepatic lesion with proximal involvement of vessels or biliary ducts in one lobe[1]
P3	Central hepatic lesion with involvement of hilar vessels or biliary ducts in both lobes or with involvement of two hepatic veins
P4	Hepatic lesion with extension along the vessels[2] and biliary tree
N	Extrahepatic involvement of neighboring organs or tissues [diaphragm, lung, pleura, pericardium, heart, gastric or duodenal wall, adrenal gland, peritoneum, retroperitoneum, parietal wall (muscles, skin, bone), pancreas, regional lymph nodes, hepatic ligaments, kidney]
NX	Cannot be evaluated
N0	No regional involvement
N1	Regional involvement of contiguous organs or tissues
M	Absence or presence of distant metastasis (in lung, distant lymph nodes, spleen, central nervous system, orbits, bone, skin, muscle, kidney, distant peritoneum, and retroperitoneum)
MX	Not completely evaluated
M0	No metastasis[3]
M1	Metastasis

[1]For purposes of PNM classification, the liver is considered to be divided into two lobes by a plane projecting between the gallbladder bed and the inferior vena cava; [2]Vessels include the inferior vena cava, portal vein and arteries; [3]Absence of metastases is considered to be indicated by negative findings at chest radiography and computed tomography of the brain.

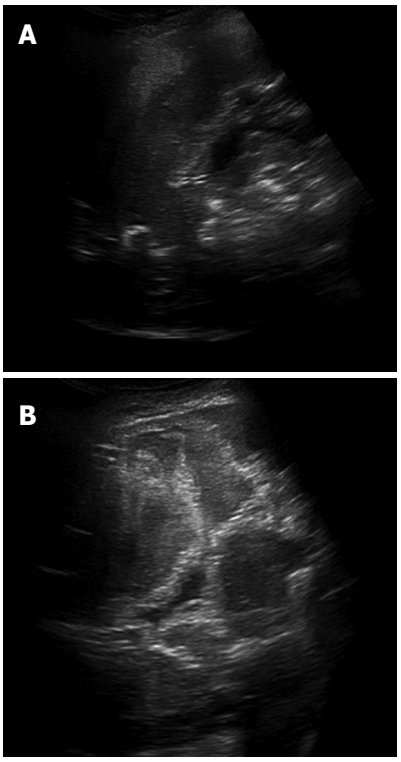

Figure 1 Alveolar echinococcosis in a 41-year-old woman. Abdominal gray-scale ultrasonography (US) image shows a heterogeneous mass lesion in the right lobe of the liver. The mass is generally hypoechoic but contains hyperechoic foci of calcifications (A). Alveolar echinococcosis in a 38 year old woman. Abdominal gray-scale US image shows a heterogeneous, hyperechoic lesion without calcifications (B).

Less typical appearances (in approximately 30% of cases) include multiple clustered hemangioma-like hyperechoic nodules (Figure 1B). These lesions usually show a "hail-storm pattern". This pattern represents the histopathologically heterogeneous stroma containing microscopic metacestode vesicles, areas of non liquefactive necrosis, entrapped host tissue and microcalcifications, which account for the stroma's relatively increased echogenicity[16]. Irregular borders and a lack of enhancement are suggestive of AE; the other liver lesions usually enhance and are rarely calcified. A pseudocyst appearance might also be seen in recurrent foci of AE after percutaneous drainage of primary lesions[11,16]. Doppler US images can show distortion and displacement of the hepatic veins, portal vein and biliary tree resulting from mass effect, invasion of the inferior vena cava, hepatic or portal vein walls, and intrahepatic bile duct dilatation[8].

CT

CT reveals anatomical and morphological features of lesions and best detects the characteristic pattern of calcification. It also allows to help determine the number, size and location of lesions in the liver and allows a comprehensive preoperative evaluation of vascular, biliary and extrahepatic extension, which is an important consideration when assessing lesion resectability[4,16,17]. Non-contrast enhanced CT images show an infiltrating tumor like hepatic mass with irregular margins and heterogeneous contents with varied attenuation, including scattered hyperattenuating calcifications and hypoattenuation areas corresponding to necrosis and parasitic tissue (Figure 2A); these findings are characteristic findings of alveolar echinococcosis (18). Calcifications are found approximately in 90% of all infected patients. Apart from the typical peripheral irregular calcifications, large homogeneous, multiple punctiform or scattered calcifications might be seen[4,8,9,16].

Large areas of central necrosis can be difficult to differentiate from abscesses. However, there is poor or no enhancement after bolus administration of intravenous contrast agent, emphasizing poor vascularization of the parasitic lesion (Figure 2B). Usually, no lymphadenopathy occurs[18,19]. Secondary pyogenic infection may occur at any time during the course of disease, resulting in abscess formation. Hilar infiltration occurs in approximately 50% of all patients, resulting in dilatation of the intrahepatic bile ducts and invasion of the portal vein, the portal branches and the hepatic veins. These conditions lead to hypoperfusion and subsequent atrophy of the affected liver segments[4,8,19]. CT findings of the hepatic AE lesions may be indistinguishable from primary hepatic neoplasms, such as cholangiocarcinoma, biliary cystadenoma and biliary cystadenocarcinoma, as well as hepatic metastases[4,9,20]. However, hypoattenuation, calcification and absence of contrast enhancement in a hepatic lesion can help identify it as hepatic AE.

CT perfusion, a non-invasive method that has been increasingly used in recent years, allows for functional

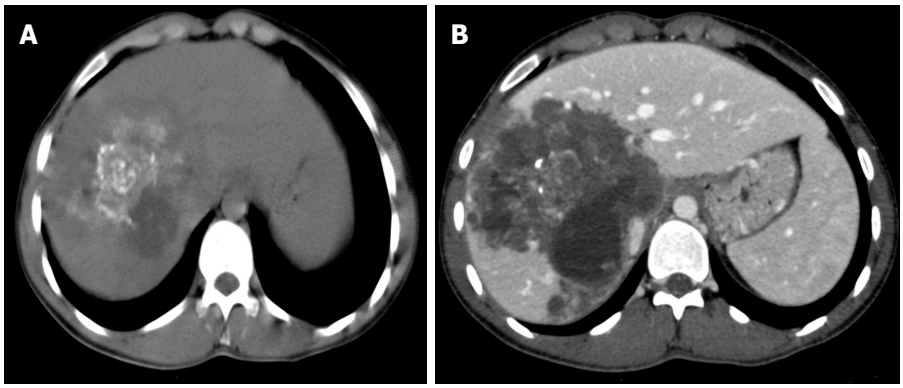

Figure 2 Alveolar echinococcosis in a 34-year-old man. Axial unenhanced computed tomography (CT) image demonstrates an infiltrating tumor-like hepatic mass with irregular margins and heterogeneous contents, including scattered hyperattenuating foci of calcification and areas of hypoattenuation corresponding to necrosis and parasite tissue (A). Alveolar echinococcosis in a 29 year old man. Abdominal CT images obtained after the administration of intravenous contrast medium show a poor enhancement, hypoattenuating lesion in the portal venous phase (B).

assessment of the perfusion of normal and pathological tissues by means of parameters such as the blood flow (BF), blood volume (BV), mean transit time (MTT), arterial liver perfusion (ALP), portal liver perfusion (PLP) and hepatic perfusion index (HPI). This technique allows for quantitative determination of lesion characteristics, enabling differentiation between malignant lesions and benign ones. Many studies have reported the use of this method to assess hepatocellular carcinoma, cirrhotic nodules and normal liver parenchyma[21]. Our experience suggests that CT perfusion is a feasible method to quantitatively assess angiogenesis of AE lesions of liver. We determined lower BF, BV, ALP and PVP values in AE lesions compared with normal liver parenchyma by using CT perfusion imaging (Figure 3). The above results demonstrated that CT perfusion can be used in hepatic AE lesions of liver that are confusable, especially with malignant lesions such as hepatocellular and cholangiocellular carcinoma.

MRI

MRI is a good modality for detection of the components of parasitic lesions and depicting vascular or biliary tree involvement and extrahepatic extension. Therefore, it should be added to preoperative evaluations, particularly evaluations of patients who are to undergo extensive hepatic resection or liver transplantation[8]. MRC has been used to detect the relationship between hepatic AE lesions and the biliary tree before surgical treatment or liver transplantation[4]. However, non-contrast enhanced CT imaging is superior to MRI in detecting calcifications. The MRI characteristics are a heterogeneous infiltrative mass with irregular margins and a necrotic center that exhibits low to intermediate signal intensity on T1-weighted images and heterogeneous signal intensity (areas of low and high signal intensity) on T2-weighted images. Areas of high T2 signal intensity correspond to small cystic or necrotic components, whereas areas of low T2 signal intensity correspond to fibrotic or collagenous components (Figure 4). T2-weighted images are useful for detecting small hepatic cysts and extrahepatic cysts[22,23].

Hepatic AE lesions are categorized on the basis of their imaging manifestations into five types. Type 1 (4%) lesions consist of multiple small cysts without a solid tissue component; type 2 (40%) lesions include a solid tissue component associated with multiple small cysts; type 3 (46%) lesions consist of a solid tissue component associated with irregular large cysts; type 4 (4%) lesions consist of solid tissue without cystic components; and type 5 (6%) lesions consist of a single large cyst without solid tissue components[22]. For lesions with characteristics not often seen in AE (especially types 1, 4 and 5), serological analyses can be helpful[8]. In particular, MRC can detect biliary dilatation, a reduced number of bile ducts within the lesion, invasion of the biliary wall, distortion and compression of the biliary tree, and communication of intrahepatic bile ducts with necrotic cystic regions[8,23].

Signal intensity at diffusion-weighted imaging can be quantified by calculating the apparent diffusion coefficient (ADC), a valuable indicator for the diagnosis and characterization of focal hepatic lesions[24]. Our experience suggests that AE lesions can be reliably identified on diffusion-weighted images obtained with *b* values of 50400800 and 1000 sec/mm^2 and qualitatively assessed on ADC maps. These lesions usually result in a subjectively higher ADC in the lesion than in liver parenchyma on diffusion-weighted images obtained with a *b* value of 800 sec/mm^2 (Figure 5). Restricted diffusion due to a superinfection (especially an abscess) may be observed in the necrotic central part of particularly large AE lesions. The general lack of diffusion restriction in hepatic AE lesions is an important finding that helps differentiate them from malignancies that have similar clinical features and imaging findings, including invasion and metastases. Table 2 summarizes characteristic imaging features that are helpful for diagnosing hepatic AE lesions.

INTERVENTIONAL PROCEDURES

In hepatic AE, radical surgical excision is followed by short-term antihelmintic therapy for resectable lesions and long-term aggressive antihelmintic therapy for par-

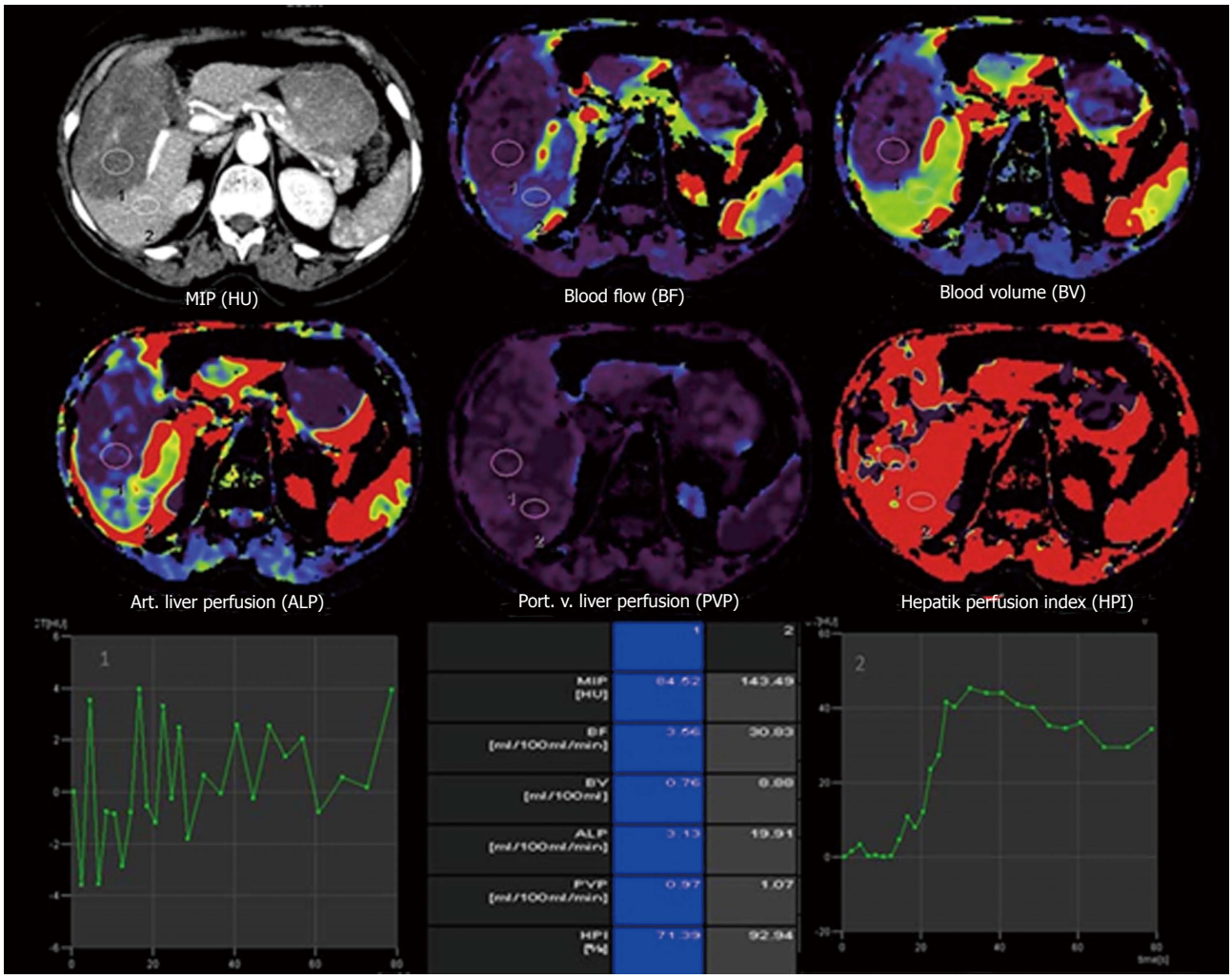

Figure 3 Transverse computed tomography perfusion functional maps of the blood volume, blood flow, portal-venous perfusion, arterial liver perfusion and hepatic perfusion index in a 49-year-old woman show a large alveolar echinococcosis lesion in the right lobe of the liver that has a distinct range of colors compared with the background liver parenchyma. Perfusion values from an ROI drawn in the solid component without calcification of alveolar echinococcosis (ROI 1) and normal tissue (ROI 2) show lower blood flow, blood volume, arterial liver perfusion and portal-venous perfusion values compared with normal liver parenchyma.

Table 2 Morphological characteristics of hepatic alveolar echinococcosis lesions

Modality	Hepatic AE lesions
US	Mass with irregular margins, scattered foci of calcification, central necrosis, and vascular and biliary involvement
CT	
Unenhanced	Mass with irregular margins, hyperattenuating foci of calcification, and hypoattenuating regions of necrosis and parasitic tissue
Contrast- enhanced	Mass with no substantial enhancement and peripheral fibroinflammatory components with slight but long-lasting enhancement
CT perfusion	Lower BF, BV, ALP and PVP values in AE lesions compared with normal liver parenchyma
MRI	
T1-weighted	Heterogeneous mass with irregular margins and a necrotic center that exhibits low to intermediate signal intensity
T2-weighted	Heterogeneous mass with irregular margins, a necrotic center that exhibits high signal intensity, and low-signal-intensity fibrotic and collagenous components
Contrast-enhanced	Mass with no substantial enhancement and peripheral fibroinflammatory components with slight but long-lasting enhancement
Diffusion-weighted	Mass with hypointense signal and high ADC on images obtained with high *b* values

AE: Alveolar echinococcosis; CT: Computed tomography; US: Ultrasonography; BF: Blood flow; BV: Blood volume; ALP: Arterial liver perfusion; PVP: Portal-venous perfusion; ADC: Apparent diffusion coefficient.

tially resectable or unresectable lesions. Patients with hepatic AE have a poor prognosis and high fatality rate; curative treatment of AE is possible only with early detection and complete surgical excision or liver transplantation[7,11]. Liver transplantation should only be considered in patients with very severe hilar extension, leading

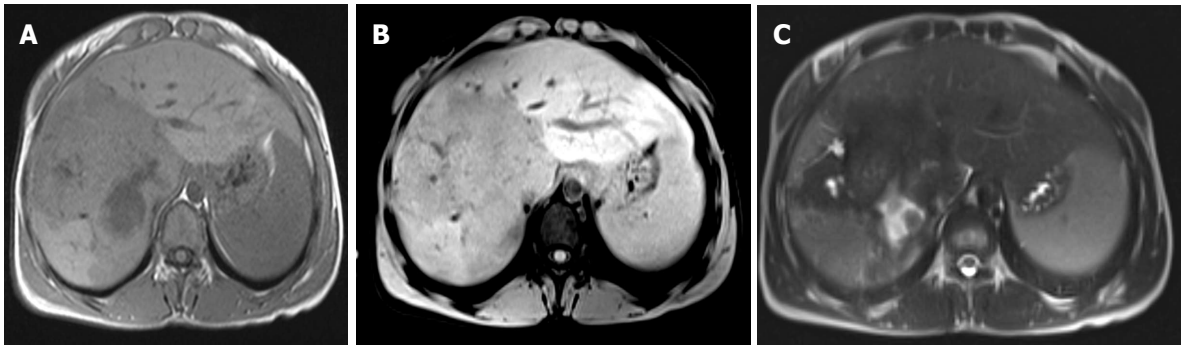

Figure 4 Alveolar echinococcosis in a 39-year-old man. Axial unenhanced T1-weighted image show an infiltrating hypointense mass in the right lobe of the liver (A). Axial magnetic resonance imaging obtained after the administration of intravenous contrast medium show no contrast enhancement within the mass (B). Axial T2-weighted image show an infiltrating hypointense mass in the right lobe of the liver (C).

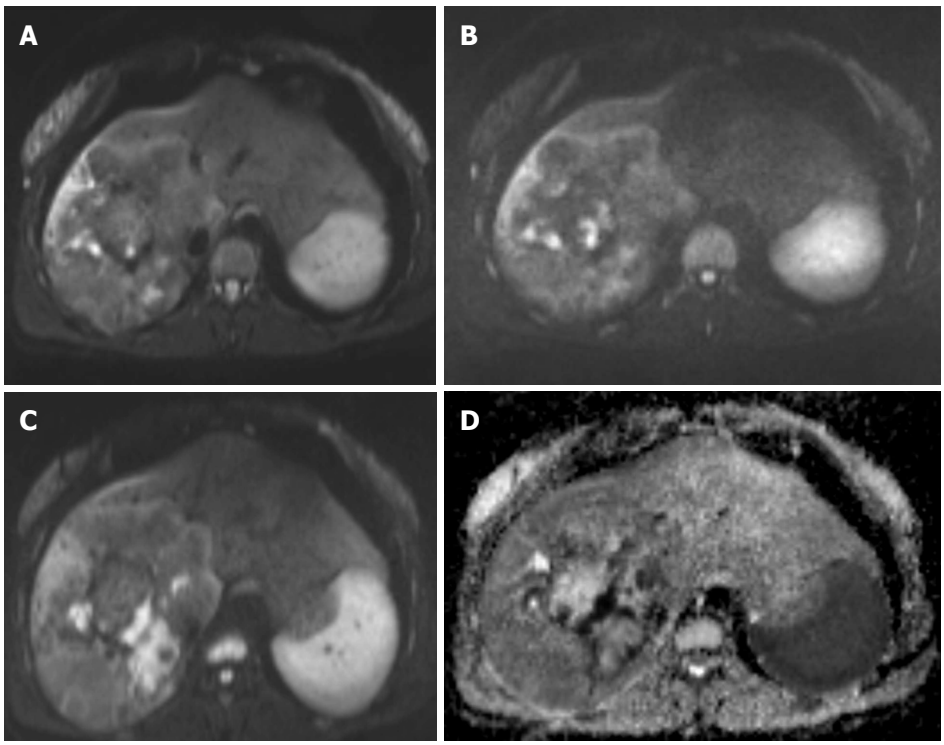

Figure 5 Alveolar echinococcosis in a 44-year-old man. Diffusion-weighted magnetic resonance images obtained with *b* values of 400 sec/mm^2 (A), 800 sec/mm^2 (B), and 1000 sec/mm^2 (C) and corresponding apparent diffusion coefficient map (D) show signal hyperintensity in a hepatic mass.

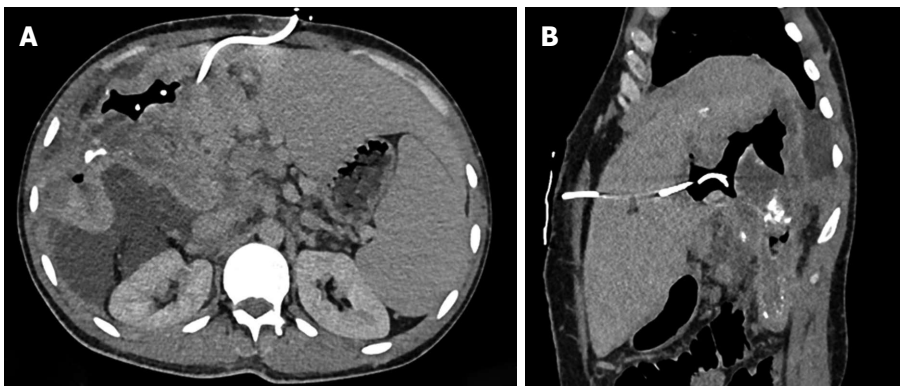

Figure 6 Non-contrast enhanced axial (A) and sagittal (B) computed tomography images show the percutaneous drainage of an infected parasitic cyst in a 43 year old woman with hepatic alveolar echinococcosis.

to uncontrolled biliary infections, symptomatic secondary biliary cirrhosis with ascites and/or severe variceal bleeding owing to portal hypertension[25].

Cases of late diagnosis require lifelong pharmacological treatment with benzimidazoles and thorough follow-up because benzimidazoles are assumed to exert only a parasitostatic effect on hepatic AE lesions. Albendazole is a broad spectrum anthelmintic agent. Perioperative treatment with albendazole can decrease the recurrence rate and increase the success rate of the operation[17,26]. Management of the septic complications of alveolar echinococcosis of the liver, such as cholangitis or liver abscesses, should prioritize interventional radiology[4,25]. The liver abscess is usually treated by percutaneous catheterization, which may lead to complete disappearance of the hepatic alveolar echinococcus lesion[11] (Figure 6). Additionally, treatment of portal hypertension in alveolar echinococcosis of the liver is also problematic. In patients without cirrhosis, percutaneous stent placement in the hepatic veins is a promising treatment alternative[27].

CONCLUSION

Hepatic AE lesions mimic slow-growing tumors of the liver parenchyma that tend to infiltrate adjacent structures, especially the portal hilum, hepatic veins, inferior vena cava and biliary system. For effective service to referring clinicians and their patients, radiologists should be familiar with the cross-sectional imaging findings of hepatic AE. Therefore, radiologists should depict in detail the relationships between the mass and the portal bifurcation, especially any evidence of invasion or extension into the main portal vein, hepatic veins, inferior vena cava and bile ducts. Additionally, if liver transplantation is contemplated, the remaining functional hepatic parenchymal mass and reserve should be calculated and septic complications should be treated by percutaneous drainage until performing the radical surgical excision or liver transplantation.

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CASE REPORT

Notaras procedure for incarcerated rectal prolapse

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Abstract

Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. The traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating incarcerated or strangulated rectal prolapses associated with severe edema. Herein we report a case of an incarcerated rectal prolapse treated with the Notaras procedure.

Key words: Notaras procedure; Rectal prolapse; Incarcerated; Perineal rectosigmoidectomy

Core tip: Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. So, the traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating an incarcerated or strangulated rectal prolapse associated with severe edema. Herein we report a case of an incarcerated rectal prolapse treated with the Notaras procedure.

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INTRODUCTION

Rectal prolapse is defined as intussusception of the rectum through the anal canal. Although known and described as early as 1500 BC[1], there is still uncertainty concerning its clinical definition, course and pathophysiology, which justifies the numerous therapeutic modalities and operations proposed[2]. Commonly, in many centers a single stage perineal rectosigmoidectomy is performed to treat patients with a reducible rectal prolapse. Patients with an incarcerated rectal prolapse usually present in the emergency department where manual reduction is first attempted. Reduction of a large prolapse may be difficult because of significant edema that collects in the rectal tissues. If reduction is unsuccessful, an emergency laparotomy and internal reduction is required. If patients with an acute incarcerated or strangulated rectal prolapse are treated with perineal rectosigmoidectomy, anastomotic leak risk is 25% during the postoperative period[3,4]. Edema in the rectal and perineal tissues and impaired blood flow are the main factors for a high percentage of anastomotic leaks. The traditional single stage perineal rectosigmoidectomy is not a safe surgical procedure for treating an incarcerated or strangulated rectal prolapse associated with severe edema[4].

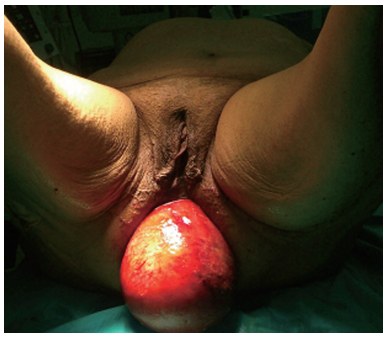

Figure 1 Edematous and incarcerated rectal prolapse without gangrenous areas.

CASE REPORT

In this report, we present a 59-year-old woman with a three year history of Alzheimer's disease. She checked in to the emergency department with a strangulated rectal prolapse which had appeared 3 h prior to consultation. Physical examination revealed a severely edematous and irreducible rectal prolapse without gangrenous areas (Figure 1). Despite sedation, the Trendelenburg position and topical application of sucrose to decrease bowel edema, all attempts for manual reduction were unsuccessful. As a result, we decided to perform a laparotomy. During the laparotomy, we tried internal reduction with external manual reduction again. The last attempt was successful. The prolapsed section was not necrotic, there were no gangrenous areas and blood flow increased. A piece of monofilament synthetic mesh was sutured behind the rectum, covering approximately one-third of its posterior circumference. The upper edge was then sutured to the sacral promontory, as described by Notaras[5]. The patient's postoperative course was uneventful and she was discharged on the 8th postoperative day. At the 6 mo follow-up, there was no recurrence in the rectal prolapse other than a minor constipation problem.

DISCUSSION

If the incarcerated or strangulated rectal prolapse cannot be manually reduced, a few techniques may help the bowel return to its anatomic position, such as sedation, Trendelenburg position and/or topical applications of salt and sucrose which may decrease bowel edema and enable a natural reduction[6]. The use of an elastic compression wrap can be practiced[7]. Perineal rectosigmoidectomy is a good surgical option in cases complicated by necrosis and poor intestinal blood flow. However, patients with an acute incarcerated or strangulated rectal prolapse have an increased risk of an anastomotic leak compared to other elective operations. After internal and external reduction, waiting a few minutes for a better blood supply if the patient has no complications with necrosis is an excellent option. With a good blood flow, the Notaras procedure, in effect rectopexy, suspends the rectum and the presence of the mesh additionally results in thickening of part of the rectal wall with the result that prolapse of the rectum will be prevented. In conclusion, with a good blood supply and the absence of necrosis, the Notaras procedure can be performed safely in patients with an incarcerated or strangulated rectal prolapse.

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COMMENTS

Case characteristics

The patient had pain in the rectum.

Clinical diagnosis

The patient had an irreducible rectal prolapse.

Differential diagnosis

It was a certain diagnosis with no differential diagnosis.

Laboratory diagnosis

Laboratory tests were in the normal range.

Treatment

The patient underwent emergency surgery (Notaras procedure).

Related reports

The second and the fifth references are about the repair of rectal prolapses. These studies may help to understand emergency repair of a rectal prolapse and this case.

Term explanation

Notaras procedure: a piece of monofilament synthetic mesh is sutured behind the rectum, covering approximately one-third of its posterior circumference.

Experiences and lessons

The Notaras procedure can be performed safely in patients with an acute incarcerated or strangulated rectal prolapse in the absence of necrosis.

Peer review

This is an interesting case report suggesting the use of a surgical procedure usually not described in the acute phase.

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16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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REVIEW

Endoscopic approaches to biliary intervention in patients with surgically altered gastroduodenal anatomy

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Abstract

Over the past decade the ability of endoscopists to access the biliary tree in patients with surgically altered gastroduodenal anatomy has significantly advanced. Much of the progress has occurred as a result of the development of better tools to navigate the deep small bowel, such as single-balloon- (SBE), double-balloon- (DBE), and spiral-enteroscopy-assisted endoscopic retrograde cholangiopancreatography (ERCP). However, despite using a cap, accessing the papilla or bile duct using these forward-viewing enteroscopy platforms remains challenging, even in expert hands. In patients with Roux-en-Y gastric bypass (RYGB) anatomy, the excluded stomach is a potential point of access for either a delayed transgastric- or immediate laparoscopy-assisted-ERCP approach. However, the parallel advancement of therapeutic endoscopic ultrasound (EUS) also provides alternative approaches through which the biliary system can be accessed and intervened on in patients with surgically altered anatomies. Generally speaking, in patients with short gastro-jejunal "Roux" and bilio-pancreatic limbs, ideally less than 150 cm in length, starting with a (cap-assisted) push-enteroscopy or balloon-enteroscopy approach would offer reasonable diagnostic and therapeutic ERCP success. When available, short-SBE or short-DBE scopes should be used, as they allow the use of conventional ERCP equipment, are associated with shorter procedure times, and are easier to manipulate. In patients with RYGB who have longer Roux and/or bilio-pancreatic limbs (> 150 cm in total length), or in patients who have failed prior attempts at deep enteroscopy-assisted ERCP, transgastric laparoscopy-assisted-ERCP is associated with higher rates of diagnostic and therapeutic success as compared to deep-enteroscopy-assisted ERCP. Finally, EUS-guided biliary access for antegrade biliary intervention or for rendezvous enteroscopy-assisted ERCP is possible. While percutaneous transhepatic biliary drainage and surgical bile duct exploration remain viable alternatives, these methods are not without significant morbidity and mortality and should only be considered if less invasive endoscopic interventions are not feasible or appropriate.

Key words: Endoscopic retrograde cholangiopancreatography; Bile duct; Roux-en-Y; Gastric bypass; Surgically altered anatomy

Core tip: In patients with short gastrojejunal "Roux" and bilio-pancreatic limbs, ideally less than 150 cm in length, starting with a (cap-assisted) push-enteroscopy or balloon-enteroscopy approach should offer reasonable diagnostic and therapeutic endoscopic retrograde cholangiopancreatography (ERCP) success. When available, short-single-balloon or short-double-balloon enteroscopes should be used, as they allow the use of conventional ERCP equipment, are associated with shorter procedure times, and are easier to manipulate. In patients with Roux-en-Y gastric bypass who have longer Roux and/or bilio-pancreatic limbs, or in patients who have failed prior attempts at deep enteroscopy-assisted ERCP, transgastric laparoscopy-assisted-ERCP should be considered, which is associated with high rates of diagnostic and therapeutic ERCP success.

Cosgrove ND, Wang AY. Endoscopic approaches to biliary intervention in patients with surgically altered gastroduodenal anatomy. *World J Surg Proced* 2014; 4(2): 23-32 Available from: URL: http://www.wjgnet.com/2219-2832/full/v4/i2/23.htm DOI: http://dx.doi.org/10.5412/wjsp.v4.i2.23

INTRODUCTION

According to the National Center for Health Statistics, 35.7% of United States adults were classified as obese in 2009-2010, and there is a rising linear trend in obesity rates[1]. As a result, many patients in the United States have been undergoing bariatric surgery, such as Roux-en-Y gastric bypass (RYGB)[2] (Figure 1). The increasing prevalence of patients with surgically altered gastroduodenal anatomy (most notably RYGB, but also including Billroth Ⅱ gastrojejunostomy, pancreaticoduodenectomy, and Roux-en-Y hepaticojejunostomy, which is used in liver transplantation) has posed a unique challenge for the endoscopic management of biliary and pancreatic issues. In patients with Roux-en-Y (RY) anatomy, endoscopic retrograde cholangiopancreatography (ERCP) is typically impossible *via* an oral route using a duodenoscope, as the scope must be passed from the gastrojejunostomy through the jejunojejunostomy and into the afferent bilio-pancreatic limb to the papilla. Furthermore, the gastrojejunal Roux limb is typically made longer than 100 to 150 cm in order to produce weight loss, and the sharp angulation into the afferent bilio-pancreatic limb also poses a technical challenge to reaching the papilla. It is therefore no surprise that the primary reason for ERCP failure in patients with altered gastroduodenal anatomy is failure to reach the biliary-enteric anastomosis or ampulla[3,4]. As obese, post-bariatric surgery patients are at an increased risk for developing gallstones and other associated complications that require biliary intervention[5,6], new technologies and approaches have been developed to manage these issues in patients with surgically altered anatomies.

USE OF A DUODENOSCOPE FOR "CONVENTIONAL" ERCP

Duodenoscopes have been optimized for performing ERCP in patients with normal gastroduodenal anatomy. Duodenoscopes possess an elevator and have side-viewing imaging to enable visualization of the major and minor papillae. Therapeutic duodenoscopes possess large accessory channels that allow for the use of a broad array of instruments and stents sizes, typically up to 10 French (Fr). However, the short working length (about 124 cm) of the duodenoscope is a limitation when attempting ERCP in patients with long-limbed small bowel anastomoses. For patients with shorter afferent limbs, such as those who have undergone a Billroth Ⅱ gastrectomy, ERCP using a duodenoscope remains a potentially feasible technique. In a retrospective study by Hintze *et al*[7] that included 59 patients with Billroth Ⅱ anatomy, the papilla was reached in 92% of patients using a duodenoscope. Once the duodenal stump was reached, therapeutic success was achieved in 100% of patients. For patients with gastrojejunal limbs 100 cm or longer, such as patients with RYGB anatomy, ERCP using a duodenoscope is rarely possible. Hintze *et al*[7] reported reaching the ampulla using a duodenoscope in only 33% of patients with RY reconstructions.

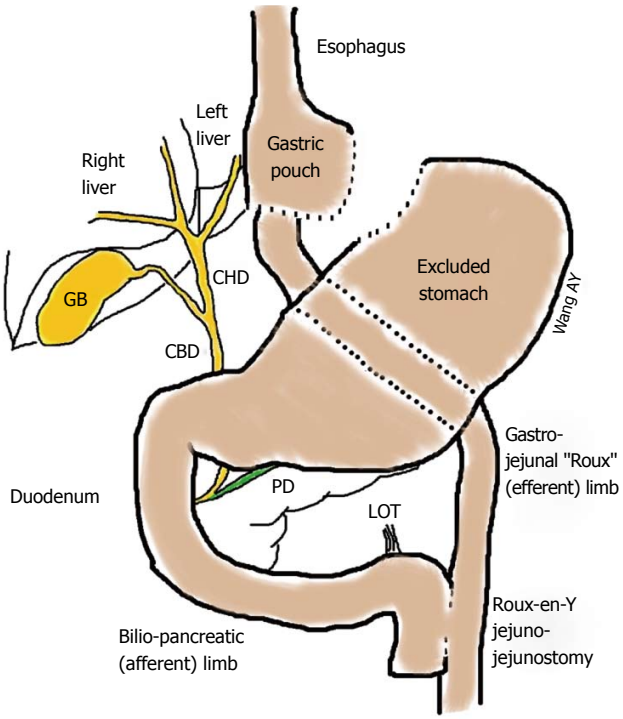

Figure 1 Surgically altered gastroduodenal anatomy found after Roux-en-Y gastric bypass.

PUSH ENTEROSCOPY FOR ERCP

In patients with surgically altered gastroduodenal anatomies with long small bowel limbs, push enteroscopy using a standard forward-viewing enteroscope or a pediatric colonoscope without an overtube has the potential to reach the ampulla, bile duct, or pancreatic duct orifices (such as in patients with pancreaticoduodenectomy) (Figure 2). However, the forward viewing optics and lack of an elevator make cannulation of a native papilla (in the case of RYGB patients) and therapeutic ERCP very challenging. In a study of 15 patients with RY anatomy who underwent ERCP using a colonoscope, ERCP was successful in only 2 patients, despite successfully reaching the papilla in 12 of these patients[8]. Furthermore, in a prospective study of 37 patients by Raithel *et al*[9], 91.8% of whom had RY anatomy, push enteroscopy was only able to reach the enteo-enteral anastomoses in 16.2% of patients. Other limitations of push-enteroscopy-assisted ERCP are high rates of loop formation and perforation[10].

In 2002, Wright *et al*[8] described using a colonoscope to reach the ampulla or desired ductal orifice, at which point the colonoscope was exchanged over a guidewire

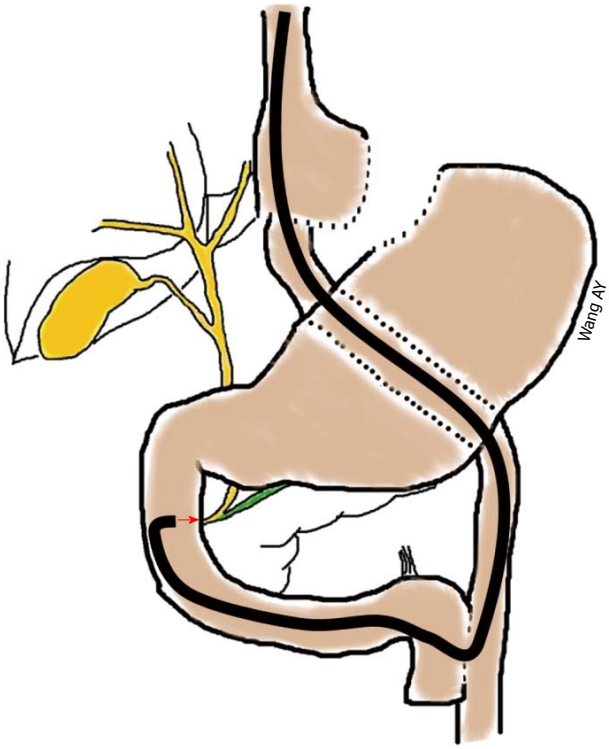

Figure 2 Using a long forward-viewing endoscope, such as an enteroscope with or without a spiral- or balloon-overtube or a pediatric colonoscope, endoscopic retrograde cholangiopancreatography can be performed in patients with Roux-en-Y gastric bypass anatomy or other surgically altered gastroduodenal anatomies. However, this technique is challenging due to forward-viewing optics, lack of an elevator, a smaller accessory channel, and need for specialized long catheters and guidewires in order to accomplish endoscopic retrograde cholangiopancreatography.

for a duodenoscope, which was passed in to the afferent bilio-pancreatic limb using a "Hansel and Gretel" technique. In some cases, the duodenoscope was pulled into the afferent limb using counter-traction from a wire-guided balloon that was passed retrograde into the afferent limb or stomach; this might be the first description of a single-balloon technique to facilitate small bowel passage of an endoscope. Using these techniques for patients who failed attempted ERCP using a colonoscope, the ampulla was ultimately reached in 67% of patients, and biliary access was achieved in 84% after exchange for a duodenoscope. The complication rate was 12% in this series[8].

BALLOON-ENTEROSCOPY-ASSISTED ERCP

Balloon-assisted enteroscopy can be performed using a single-balloon enteroscopy (SBE) or a double-balloon enteroscopy (DBE) platform. DBE uses an enteroscope with a balloon at its distal tip and an overtube with an anchoring balloon, while SBE uses a standard enteroscope with an overtube with an anchoring balloon. Using a "push-pull" method of scope advancement and successive inflation of one or both balloons (depending on the platform) to pleat the small bowel, a significant distance of small bowel may be traversed.

Balloon-assisted enteroscopy was originally developed to aid in the diagnosis and treatment of small bowel diseases that were previously out of reach of push enteroscopy using a dedicated enteroscope or a pediatric colonoscope. However, balloon-assisted enteroscopy also enables accessing the bilio-pancreatic afferent limb in patients with surgically altered gastroduodenal anatomy. In 2005, Sakai *et al*[11] described using DBE to reach the bypassed stomach in five out of six (83.3%) patients with RYGB anatomy.

In the abovementioned study by Raithel *et al*[9], when DBE was performed in the patients who failed ERCP *via* push enteroscopy (91.8% with RY anatomies), luminal access to the biliary tract was achieved in 74.1%, with diagnostic or therapeutic ERCP success in 87.2% of cases[9]. However, even with balloon-enteroscopy-assisted ERCP (BEA-ERCP), procedure success remains limited by the length of the Roux limb. Schreiner *et al*[12] calculated the summed (total) length of the Roux limb and the length from the ligament of Treitz to the jejunojejunal anastomosis in patients undergoing DBE-assisted ERCP (DBE-ERCP). They reported therapeutic success in 88% of cases with a total small bowel length less than 150 cm, but only 33% success for lengths from 150 to 225 cm, and 0% success for lengths greater than 225 cm.

While the efficacy of BEA-ERCP can also be limited in patients with extensive abdominal adhesions and fixed bowel segments that limit small bowel manipulation and pleating, SBE-assisted ERCP (SBE-ERCP) and DBE-ERCP have a growing track record of significant diagnostic and therapeutic success (Table 1). Procedure times for SBE- and DBE-ERCP are long, with average total procedure times of 72 to 78 min reported for SBE-ERCP[4,13] and 93 to 128 min for DBE-ERCP[9,14,15]. Complication rates for SBE-ERCP and DBE-ERCP appear to be similar (Table 2).

LIMITATIONS OF SBE- AND DBE-ASSISTED ERCP

Like colonoscopes and push enteroscopes, the enteroscopes used for SBE and DBE also lack an elevator and have forward-viewing optics. Additionally, these scopes typically have small accessory channels (2.8 mm, which can accommodate only up to 7-Fr devices). Furthermore, their long working lengths (of around 200 cm) prevent the use of conventional ERCP accessories. Longer accessories (600-cm-long guidewires, long papillotomes, and long retrieval balloons) are now available for use in SBE- and DBE-ERCP when long enteroscopes are used. These long wires and devices make SBE- and DBE-ERCP possible, but exchanging devices is challenging given the long distances that need to be traversed.

Various methods have been developed to circumvent the issue of using a long enteroscope to perform ERCP. Exchanging the single- or double-balloon enteroscope

Table 1 Data from studies that evaluated the efficacy of single-balloon and double-balloon enteroscopy-assisted endoscopic retrograde cholangiopancreatography in patients with surgically altered gastroduodenal anatomy

Ref.	Method	Cases (*n*)	Cases with RY-anatomy	Reached ampulla/ orifice	Diagnostic ERCP success	Therapeutic ERCP success
Wang *et al*[22]	SBE	16	12	81.3%	100%	90%
Saleem *et al*[13]	SBE	56	56	75%	92.8%	91%
Itoi *et al*[17]	SBE[1]	13	11	92.3%	N/A	83.3%
Shah *et al*[3]	SBE	45	N/A	69%	87%[2]	87%[2]
Yamauchi *et al*[16]	Short SBE	31	23	90%	89%	96%
Shah *et al*[3]	DBE	27	N/A	74%	85%[2]	85%[2]
Aabakken *et al*[41]	DBE	18	18	94.4%	88%	100%
Emmett *et al*[42]	DBE	20	20	85%	94.1%	100%
Pohl *et al*[43]	DBE	25	25	95.5%	N/A	88.0%
Raithel *et al*[9]	DBE	86	29	74.1%	91.3%[2]	91.3%[2]
Shimatani *et al*[44]	Short DBE	103	81	97.1%	98.0%	100%
Itoi *et al*[15]	Short and Long DBE[3]	13[4]	13	100%	66.7%	100%
Cho *et al*[45]	Short DBE	29	13	86.2%	96%	100%
Osoegawa *et al*[14]	Short DBE	47	29	96%	89%	100%
Siddiqui *et al*[46]	Short DBE	79	51	89.9%	90%	100%

[1]After the papilla was reached with the single-balloon enteroscope, it was replaced with a conventional forward-viewing upper gastrointestinal endoscope; [2]Reported success was for both diagnostic and therapeutic procedures; [3]For long double-balloon enteroscopy (DBE) cases, after the papilla was reached with the balloon enteroscope, it was replaced with a conventional forward-viewing gastroscope; [4]Of 13 total cases, 5 patients underwent long DBE and 4 patients underwent short DBE. Diagnostic success rates were calculated only for those patients in whom the ampulla/orifice was reached. Therapeutic success rates do not include those patients in whom the ampulla/orifice was not reached and/or diagnostic endoscopic retrograde cholangiopancreatography (ERCP) failed or patients who did not require any therapeutic intervention. SBE: Single-balloon enteroscopy. RY: Roux-en-Y.

Table 2 Reported rates of adverse events in patients with surgically altered gastroduodenal anatomy who underwent deep-enteroscopy-assisted endoscopic retrograde cholangiopancreatography

Ref.	Method	Cases (*n*)	Cases with RY anatomy	Pancreatitis	All adverse events
Wang *et al*[22]	SBE	16	12	12.5%	12.5%
Saleem *et al*[13]	SBE	56	56	0%	0%
Itoi *et al*[17]	SBE	13	11	0%	0%
Yamauchi *et al*[16]	Short SBE	31	23	7.7%	N/A
Emmett *et al*[42]	DBE	20	20	0%	0%
Raithel *et al*[9]	DBE	86	34	2.3%	N/A
Shimatani *et al*[44]	Short DBE	103	81	0%	4.9%
Itoi *et al*[15]	Long and short DBE	13	13	0%	7.7%
Siddiqui *et al*[46]	Short DBE	79	51	4%	5%
Lennon *et al*[4]	Spiral	29	29	0%	0%
Wagh *et al*[47]	Spiral	57	6 of 7 pts	0%	0%

DBE: Double-balloon enteroscopy; SBE: Single-balloon enteroscopy; RY: Roux-en-Y.

over a guidewire for a duodenoscope or conventional forward-viewing gastroscope, after the papilla has been reached, allows for the use of conventional ERCP equipment and can circumvent some of the limitations of long enteroscopes[15]. A short-DBE enteroscope with a working length of 152 cm is available that allows the use of standard ERCP accessories. A small retrospective study of patients with RY anatomy who underwent ERCP with either short DBE or long DBE reported 100% success in reaching the papilla in both groups. The collective therapeutic success rate for short- and long-DBE-ERCP during the first session was 67%. The short-DBE scopes reached the papilla more quickly (29 ± 19.2 min) as compared to the long-DBE scopes (64.8 ± 24.7 min)[15].

A short-SBE platform was recently described in a retrospective Japanese study of 22 patients. This scope has a working length of 152 cm, a large accessory channel with a diameter of 3.2 mm, and a water jet channel. Advantages of this scope include the ability to use more conventional ERCP devices, including duodenoscope-length wire-guided devices for stone extraction and stents up to 8.5 Fr in size, shorter setup time than for short DBE, and the ability to perform wire-guided intraductal ultrasonography. Despite its shorter length, these investigators reported a short-SBE-ERCP success rate of 90% for reaching the end of the afferent limb, and diagnostic and therapeutic ERCP success rates of 89% and 96%, respectively. Reported procedure times averaged at 40.2 min, which appears shorter than for most other BEA-

Table 3 Studies that evaluated the efficacy of spiral-enteroscopy-assisted endoscopic retrograde cholangiopancreatography in patients with surgically altered gastroduodenal anatomy

Ref.	Method	Cases (*n*)	Cases with RY anatomy	Reached ampulla/ orifice	Diagnostic ERCP success	Therapeutic ERCP success
Shah *et al*[3]	Spiral	57	N/A	72%	90%[1]	90%[1]
Lennon *et al*[4]	Spiral	29	29	N/A	40%	87.5%
Wagh *et al*[47]	Spiral	13	6 of 7 patients	77%	89%	90%

[1]Reported success was for both diagnostic and therapeutic procedures. Diagnostic success rates were calculated only for those patients in whom the ampulla/orifice was reached. Therapeutic success rates do not include those patients in whom the ampulla/orifice was not reached and/or diagnostic endoscopic retrograde cholangiopancreatography (ERCP) failed or patients who did not require any therapeutic intervention. RY: Roux-en-Y.

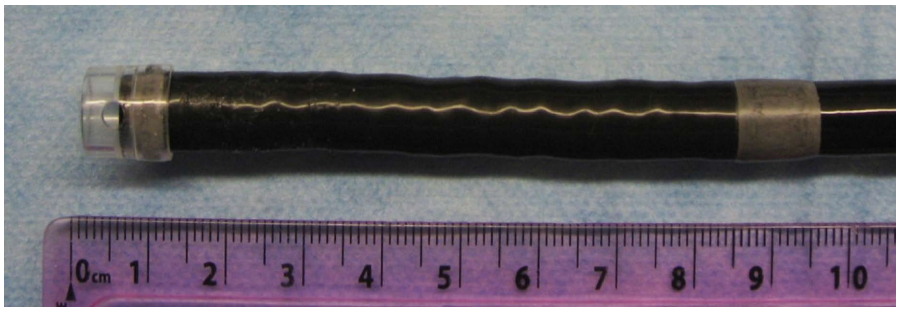

Figure 3 Low-profile, soft, distal attachment cap (D-201-10704, Olympus America, Center Valley, PA) is shown affixed to an enteroscope (SIF-Q180, Olympus America) for use in single-balloon-enteroscopy-assisted endoscopic retrograde cholangiopancreatography.

ERCP platforms[16].

Itoi *et al*[15,17] have described in two publications a novel modification that can be performed on either the single- or double-balloon overtubes so as to enable ERCP using a diagnostic gastroscope. Using SBE or DBE, a long enteroscope is passed to the papilla or ductal orifice. The overtube balloon is inflated anchoring the overtube in the afferent limb, and the enteroscope is withdrawn. A hole is then made in the overtube at 100 cm from the distal end and a diagnostic gastroscope can then be passed through this "shortened" overtube to perform ERCP using standard length instruments. Success rate of therapeutic ERCP on the first session was 76.9% for SBE[17] and 66.7% for DBE[15], by using this method. The drawback to this technique is that a distal attachment cap cannot be used, as it cannot be passed through the overtube.

SPIRAL-ENTEROSCOPY-ASSISTED ERCP

Spiral enteroscopy (SE) uses a spiral overtube and rotational movement to advance the enteroscope deep into the small bowel. Unlike SBE and DBE, SE does not require a balloon inflation system[18]. A retrospective study comparing SE-assisted ERCP (SE-ERCP) to SBE-ERCP reported similar diagnostic yields (48.3% for SBE-ERCP *vs* 40% for SE-ERCP, $P = 0.59$) and comparable rates of therapeutic success (100% for SBE-ERCP *vs* 87.5% for SE-ERCP, $P = 1.0$). No diagnostic benefit was seen when changing from one technique to another[4].

A multi-centered retrospective study of 129 patients (93 of whom had RY anatomy) who underwent 180 enteroscopy-assisted ERCPs reported similar success rates among SBE- (87%), DBE- (85%), and SE-ERCP (90%), when the papilla or ductal orifice was reached[3]. Procedure times for SE-ERCP also appear to be similar to those of BEA-ERCP, with mean times of 72 ± 34 min for SBE-ERCP and 81.9 ± 34.6 for SE-ERCP reported in another study[4]. Complication rates for SE-ERCP appear to be low (Table 2). In a large retrospective study of 2950 patients who had SE for various reasons, 0.3% of patients sustained severe complications, including 0.27% small bowel perforations[19]. Overall, studies of SE-ERCP report reasonable diagnostic and therapeutic success rates (Table 3), which are comparable to those published for SBE- and DBE-ERCP.

ADJUNCTIVE TECHNIQUES TO FACILITATE ENTEROSCOPY-ASSISTED ERCP

A soft, low-profile, distal attachment cap, similar to those used for endoscopic mucosal resection and endoscopic submucosal dissection, can improve visualization during enteroscopy-assisted ERCP and can be applied to SBE-, DBE-, or SE-platforms (Figure 3). The presence of a cap allows the scope to have an approximately 2-mm distance from the wall of the GI lumen, thereby improving visualization. The cap can also be used to manipulate small bowel folds enabling easier scope insertion. Furthermore, the cap can manipulate the ampulla so as to facilitate ductal cannulation and papillotomy (Figure 4). In a study of 10 patients with Billroth Ⅱ anatomy undergoing ERCP

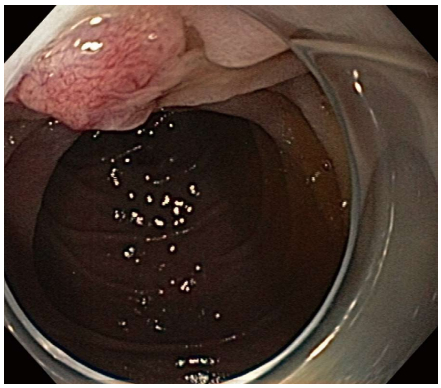

Figure 4 Low-profile, distal attachment cap was used in this case to push back duodenal folds to enable better visualization of the Ampulla of Vater during single-balloon-enteroscopy-assisted endoscopic retrograde cholangiopancreatography.

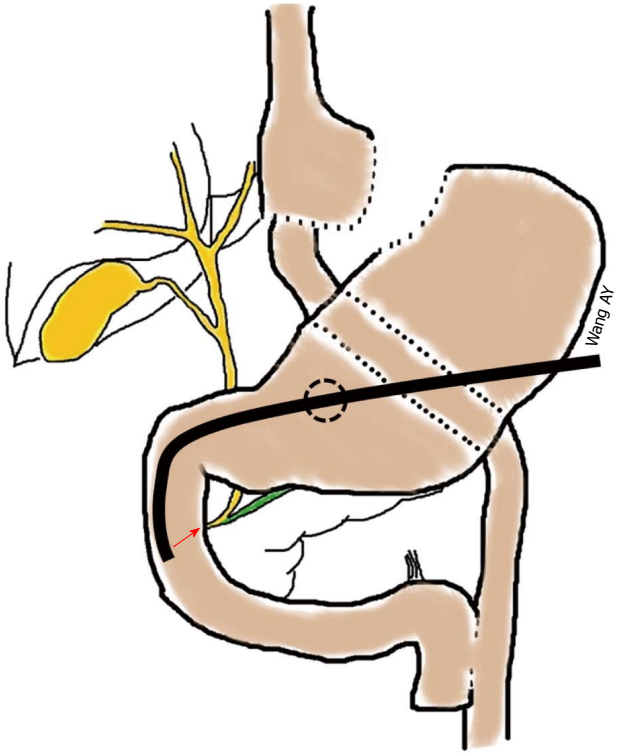

Figure 5 Endoscopic retrograde cholangiopancreatography using a duodenoscope can be performed in patients with Roux-en-Y gastric bypass anatomy by using a gastrostomy, which can be created surgically or endoscopically, to access the remnant stomach. Depending on the manner in which the gastrostomy is created, immediate or delayed endoscopic retrograde cholangiopancreatography can be performed.

with a forward-viewing endoscope, ampullary cannulation and sphincterotomy were successful in 100% of the patients when a cap-fitted enteroscope was used[20].

Intraluminal indigo carmine has been used to aid in the identification of the afferent bilio-pancreatic limb in patients with RY anatomies. Indigo carmine is a surface stain and can be injected through the enteroscope accessory channel to coat the mucosa at the RY anastomosis. Small bowel peristalsis moves the indigo carmine distally through the bowel, which will theoretically identify the efferent jejunal limb, as little (if any) indigo carmine should move by peristalsis into the afferent bilio-pancreatic limb. In a prospective study of 52 patients undergoing DBE-ERCP, application of indigo carmine correctly identified the afferent bilio-pancreatic limb in 80% of the patients[21]. Patient positioning and gravity filling of the afferent limb were attributed to the cases of incorrect identification. Once the bilio-pancreatic limb is identified, tattooing of the afferent limb can simplify future identification.

Failure to ascend into the afferent limb, typically due to sharp angulation at the anastomosis, is another common reason for ERCP failure[3]. Passing a biopsy forceps into the accessory channel to stiffen a long and floppy enteroscope can help in cannulation of the afferent limb. Passage of a long guidewire and a long retrieval balloon into the afferent limb has also been described to facilitate scope passage into the afferent limb[22]. In cases where the afferent limb cannot be accessed despite use of all available maneuvers, an endoscopic ultrasound (EUS)-guided rendezvous procedure has been described using a guidewire passed in an antegrade manner to pull an enteroscope to the papilla or duct of interest[23].

GASTROSTOMY-ASSISTED DELAYED (TRANSGASTRIC) ERCP

In patients with RYGB anatomy, the excluded stomach may be accessed, thus enabling antegrade passage of a duodenoscope to the ampulla for conventional ERCP. One method of accessing the bypassed gastric remnant is *via* a surgically created gastrostomy (Figure 5), which was first described in 1998[24]. Typically, a surgical Stamm gastrostomy is created using a 32- to 36-Fr Malecot tube, and the gastrostomy track is allowed to mature 2 to 4 wk prior to transgastric (TG) ERCP (Figure 6). The advantage of a surgical Stamm gastrostomy is that the gastrostomy tube may be replaced following transgastric ERCP, in case subsequent procedures are required (*e.g.*, for stent removal, to treat potential post-sphincterotomy bleeding, *etc.*).

A retrospective study of 59 cases of patients with surgically altered gastroduodenal anatomy reported higher success rates of reaching the ampulla/duct orifice for TG-ERCP (100%) compared to SBE-ERCP (77%, $P < 0.02$)[25]. This study also showed that TG-ERCP had a superior rate of therapeutic ERCP success (96% *vs* 64%, $P < 0.01$) as compared to SBE-ERCP. However, TG-ERCP was associated with a higher rate of complications (38% *vs* 9%, $P < 0.08$) as compared to SBE-ERCP, which trended towards statistical significance[25]. Reported complications of TG-ERCP include bleeding at the gastrostomy site, post-ERCP pancreatitis, and bowel perforation[26]. The main drawback of this technique is the need to allow the gastrostomy track to mature prior to ERCP, which obviates the use of this method in patients who require more urgent ERCP.

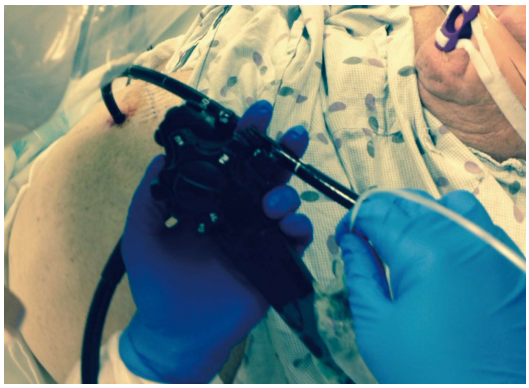

Figure 6 Example of transgastric endoscopic retrograde cholangiopancreatography in a patient with Roux-en-Y gastric bypass anatomy who underwent laparoscopic cholecystectomy and had an intraoperative cholangiogram that was suspicious for small, non-obstructing, bile duct stones. A 36-Fr Malecot tube had been left across a surgical Stamm gastrostomy. Endoscopic retrograde cholangiopancreatography in the supine position (under general anesthesia) was performed two weeks after surgical gastrostomy using a therapeutic duodenoscope. Despite an awkward scope position requiring the stabilization of the duodenoscope shaft using the left hand (as might be seen during complex colonoscopic polypectomy), biliary sphincterotomy and stone removal were successful.

LAPAROSCOPY-ASSISTED ERCP

Again, in patients with RYGB anatomy, ERCP may be accomplished by passing a duodenoscope through a gastrostomy *via* the excluded stomach. In contrast to TG-ERCP, which requires a mature gastrostomy track, laparoscopy-assisted ERCP (LA-ERCP) uses a laparoscopically created track that enables immediate ERCP in the operating room. The stomach is first secured to the abdominal wall, and the excluded stomach is then accessed laparoscopically. Using this method, a large trocar can be placed into the bypassed stomach through which a therapeutic duodenoscope can be passed to perform ERCP. Use of a trocar is not mandatory to perform ERCP; as long as the stomach has been sutured or tacked to the abdominal wall, a duodenoscope can also be passed through a fresh gastrostomy track. A large Malecot tube (32- to 36 Fr) can be inserted to keep the track patent if repeated ERCP is required.

LA-ERCP provides similar success rates as compared to delayed TG-ERCP, but LA-ERCP offers the advantage of being able to perform same-day ERCP[27-29]. A study of 30 patients reported a 93% rate of successful laparoscopic gastrostomy creation with a 100% therapeutic LA-ERCP success rate. While there was a 10% surgical re-exploration rate, no mortalities were reported[27]. A retrospective study comparing LA-ERCP to BEA-ERCP (SBE or DBE) reported that LA-ERCP had statistically superior rates of papillary identification (100% *vs* 72%) and therapeutic success (100% *vs* 59%)[12]. LA-ERCP also has a statistically significant advantage over SE-ERCP, with bile duct cannulation rates in one retrospective study reported at 57% for SE-ERCP versus 100% for LA-ERCP[29]. However, LA-ERCP has a somewhat high complication rate of 13%-14.5%[27,28], which is not dissimilar to that found following delayed TG-ERCP. Other disadvantages include prolonged procedure times (with mean operative time of 172-200 min[12,27]), the requirement to coordinate both endoscopy and surgical teams for the procedure, the need to maintain surgical sterility during the procedure, the need for post-surgical patient admission, and higher cost[29]. LA-ERCP costs substantially more than BEA-ERCP, with mean total hospital charges of $9529 for LA-ERCP versus $6574 for BEA-ERCP. A cost analysis by Schreiner *et al*[12] found that by performing LA-ERCP only after BEA-ERCP was attempted saved $1015 compared with starting with LA-ERCP.

Non-surgical, endoscopic methods of gastrostomy tube placement into the remnant stomach for subsequent ERCP have been described. *Via* EUS-guided puncture, the gastric remnant can be maximally insufflated to allow for percutaneous access guided by fluoroscopy. In a study of 10 patients, this procedure was 100% successful for gastrostomy tube placement with no complications[30]. Another non-surgical method involves percutaneous endoscopic gastrostomy (PEG) tube placement using DBE (or any deep enteroscopy approach) to reach the excluded stomach. A small study of 4 patients using this technique reported a 75% success rate for PEG placement, with only 1 case failing due to lack of abdominal transillumination[31]. No major complications were observed in any of these patients. Lastly, percutaneous computed tomography-guided gastrostomy placement has a reported success rate of 91%[32]. Although these methods are less invasive than open surgical gastrostomy tube placement, their requirement for tract maturation following gastrostomy tube placement and before ERCP can be performed limits these procedures from being utilized in patients who require urgent ERCP.

Baron *et al*[33] devised a novel endoscopic approach to enabling same-day ERCP in patients with RYGB *via* a technique known as percutaneous-assisted transprosthetic endoscopic therapy (PATENT)[34]. The PATENT method uses SBE or DBE to access the remnant stomach and facilitate gastrostomy creation using a trocar, with gastric apposition secured by T-tags. An 18-mm-wide esophageal-type fully covered self-expandable metal stent (FC-SEMS) is then deployed across the gastrostomy and a high-burst pressure (16 ATM) balloon is used to expand the stent, through which ERCP using a duodenoscope can be performed. Following ERCP, a gastrostomy tube is placed through the stent and inflated to prevent leakage of gastric contents. The transgastric FC-SEMS may be sectioned and removed over the gastrostomy tube or left in place for repeated ERCP in the future. Although gastrostomy tube placement for this procedure can be performed percutaneously or *via* retrograde balloon enteroscopy, balloon enteroscopy is recommended for this procedure, as it allows direct visualization during PEG placement and FC-SEMS deployment[33]. A case series of 5 patients who underwent ERCP *via* a transgastric FC-SEMS reported successful biliary sphincterotomy performed in all patients, and only 1 minor adverse event

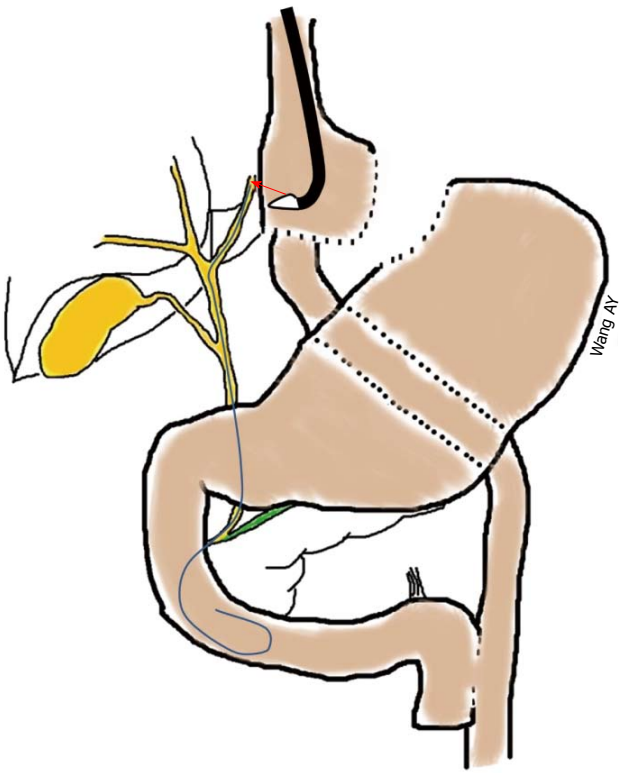

Figure 7 Using a therapeutic linear-array echoendoscope, a 19 G fine-needle-aspiration needle can be directed into dilated intrahepatic bile ducts in the left lobe of the liver. Once biliary access is established, up to an 0.035" guidewire can be passed antegrade across the extrahepatic bile duct and into the duodenum so as to facilitate rendezvous endoscopic retrograde cholangiopancreatography or antegrade bile duct therapy, such as large papillary balloon dilation to create sufficient space to push stones out of the bile duct and into the duodenum.

was observed. Median procedure time for this novel procedure was 97 min[34].

USE OF GASTRO-GASTRO FISTULA FOR ERCP

In patients with RYGB, defects in the staple line between the gastric remnant and the excluded stomach do occur; this "problem" can be used to patients' advantage to enable ERCP, when indicated. Case reports have described (1) the passage of a duodenoscope through a fistulous communication between the gastric pouch and the excluded stomach to perform ERCP[35]; and (2) the dilation of a defect in a gastric staple line through which a FC-SEMS was deployed, thus enabling antegrade passage of a duodenoscope into the excluded stomach to perform ERCP[36].

EUS-GUIDED ERCP

Therapeutic EUS is another method by which biliary access may be obtained in patients with surgically altered gastroduodenal anatomy (Figure 7). Weilert *et al*[23] used a therapeutic linear echoendoscope to direct a 19-gauge fine-needle-aspiration needle into the intrahepatic ducts of the left liver in order to perform transgastric-transhepatic, antegrade biliary interventions in patients with RYGB who had choledocholithiasis. Once guidewire access across the biliary system and the papilla was obtained, balloon sphincteroplasty followed by push-through of biliary stones was accomplished. This procedure was done in six patients and had a 67% rate of successful antegrade removal of biliary stones. Two patients in whom dilation catheters could not be advanced across the puncture site underwent successful rendezvous ERCP and stone extraction, by using a long guidewire that was passed across the gastrohepatic puncture site into the afferent limb to facilitate rendezvous DBE-ERCP. One patient sustained a subcapsular hematoma that resolved with conservative management; no cases of pancreatitis were reported. In a single operator, prospective, but non-randomized study, Park *et al*[37] performed EUS-guided biliary drainage in 45 patients. Fourteen of these patients had surgically altered anatomy and underwent EUS-guided, transhepatic, antegrade stenting or balloon dilation with a success rate of 57%. In the 6 patients who failed this approach, EUS-guided hepaticogastrostomy with transluminal stenting was performed, and one patient required percutaneous transhepatic biliary drainage. The overall adverse event rate for EUS-guided biliary drainage procedures was 11%.

CONCLUSION

Over the past decade the ability of endoscopists to access the biliary tree in patients with surgically altered gastroduodenal anatomy has significantly advanced. Much of the progress has occurred as a result of the development of better tools to navigate the deep small bowel, namely through SBE-, DBE- and SE-ERCP. Despite using a cap, accessing the papilla or bile duct using these forward-viewing platforms remains challenging, even in expert hands. In patients with RYGB, the excluded stomach is a potential point of access for either a delayed TG-ERCP or an immediate LA-ERCP approach. However, the parallel advancement of therapeutic EUS also provides alternative approaches through which the biliary system can be accessed and intervened on in patients with surgically altered anatomies.

Adequate training and experience in deep enteroscopy, ERCP, and therapeutic EUS would be ideal for endoscopists who are frequently referred patients with altered gastroduodenal anatomies. However, combination procedures done in tandem by endoscopists with strengths in different skills are also feasible (*i.e.*, a deep enteroscopist gets to the papilla and a biliary endoscopist does the ERCP, or an EUS specialist accesses the biliary tree and then an ERCP specialist does the transgastric-transhepatic biliary intervention).

Generally speaking, in patients with short gastro-jejunal "Roux" and bilio-pancreatic limbs, ideally less than 150 cm in total length, starting with a (cap-assisted) push-enteroscopy or BEA-ERCP approach would offer reasonable diagnostic and therapeutic ERCP success. When

available, short-SBE or short-DBE scopes should be used, as they allow the use of conventional ERCP equipment, are associated with shorter procedure times, and are easier to manipulate than their longer counterparts. In patients with RYGB who have longer Roux and/or pancreatico-biliary limbs (> 150 cm in total length), or in patients who have failed prior attempts at deep-enteroscopy-assisted ERCP, LA-ERCP (or delayed TG-ERCP if immediate ERCP is not required) is associated with higher rates of diagnostic and therapeutic success as compared to deep-enteroscopy-assisted ERCP. Finally, EUS-guided biliary access for antegrade biliary intervention or for rendezvous enteroscopy-assisted ERCP is possible. While percutaneous transhepatic biliary drainage[38] and surgical bile duct exploration[39,40] remain viable alternatives, these methods are not without significant morbidity and mortality and should only be considered if less invasive endoscopic interventions are not feasible or appropriate.

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REVIEW

Current concepts of laparoscopic splenectomy in elective patients

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Abstract

Formerly, open splenectomy represented the conventional surgical treatment for many hematologic diseases. Currently, thanks to permanent technical development and improved skills, also laparoscopic splenectomy (LS) has become a recognized procedure in the treatment of spleen diseases, even in case of splenomegaly. A systematic review was performed with the aim of recalling the proved concepts of this surgical treatment and to browse new devices and techniques and their impact on the surgical outcome. The literature search was initially conducted in PubMed by entering general queries related to LS. The record identified through PubMed searching (*n* = 1599) was then screened by applying several criteria (study published in English from 1991 to 2013 with abstract available, by excluding systematic/non-systematic reviews, meta-analysis, practice guidelines, case reports, and study involving animals). The articles assessed for eligibility (*n* = 160) were primarily evaluated by excluding studies that did not report operative time and conversion to open surgery. For articles that treated multiport LS we included only clinical trials with patients > 20. The studies included in qualitative synthesis were 23. The search strategy carried out in PubMed does not allow to obtain an overview of the items returned by the main queries. With this aim we replicated the search in the Web of Science™ database, only including the studies published in English in the period 1991-2013 with no other filter/selection criteria. The full records (*n* = 1141) and cited references returned by Web of Science™ were analyzed with the visualization of similarities (VOS) mapping technique. Maps of title/abstract text corpus and bibliographic coupling of authors obtained by applying the VOS approach were presented. If in normal-size or moderately enlarged spleens the laparoscopic approach is unquestionable, in massive splenomegaly the optimal technique remain to be determined. In this setting, prospective randomized trials to compare open *vs* LS are needed. Between the new techniques of LS the robotic single port splenectomy has the ability to join all the positive aspects of both techniques. Data about this topic are too initial and need to be confirmed with further studies.

Key words: Spleen; Splenectomy; Laparoscopy; Minimally Invasive; Splenic Diseases; Splenic Neoplasms; Visualization of similarities mapping

Core tip: Laparoscopic splenectomy (LS) has progressively become the "gold standard" for the surgical treatment of benign hematologic diseases, regardless

of the presence or absence of splenomegaly. The majority of previous published data reflects a substantial recognition of the laparoscopic method, although several areas still remain controversial. This review aims to update the current procedures and emerging technologies concerning minimally invasive splenectomy. The main indications and concerns for LS, as well as pre- and intraoperative potential problems in case of massive splenomegaly are reviewed. An evaluation of the techniques and clinical results of multiport laparoscopic splenectomy, hand-assisted laparoscopic splenectomy, robotic splenectomy, and single-port splenectomy is carried out. Moreover, postoperative outcomes of LS are examined, together with the procedure-specific complications.

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INTRODUCTION

Since 1991, when Delaitre and Maignien performed their first splenectomy procedure by laparoscopy, laparoscopic splenectomy (LS) has gained worldwide popularity as a feasible surgical option[1]. Currently, splenectomy is carried out either as causal or symptomatic treatment for many indications, and especially for benign hematologic disorders[2-4]. In the past, open splenectomy was the conventional treatment for both normalizing platelet count or for staging malignant diseases.

Many series suggest that LS may be considered the "gold standard" for surgical approach to benign hematologic diseases, even when not accompanied by splenomegaly. The majority of previous published data returns a substantial acceptance of the laparoscopic method, although some potential disadvantages are known (the length of operative time, or the technical difficulty in patients with splenomegaly). Even though splenomegaly has been considered for a long time a critical contraindication for LS, subsequent studies suggest that laparoscopic approach is practicable and should be used for spleens of almost any size[5,6].

Many previous series have shown that LS treatment of splenomegaly may be related with longer operative times, increased blood loss, additional perioperative complications, protracted hospital stay, and more conversion rates in comparison with LS for normal-sized spleens[7,8]. At present, technical developments as well as improved skills have generated an increase in the number of LS indications for splenic malignancies, thus demonstrating the appropriateness of laparoscopy in maintaining oncologic surgical principles. Furthermore, recent advancements in minimally invasive splenectomy has lead to the development of new laparoscopic techniques such as the robotic splenectomy and splenectomy through a single access[9,10].

SEARCH STRATEGY, OUTCOMES AND MAPS OF KNOWLEDGE

The selection of publications was performed using the PubMed and Web of Science™ search engines during the second half of March 2014. The search was initially conducted in PubMed by entering the following queries: "laparoscopic splenectomy", "single port splenectomy", "hand assisted splenectomy", and "robotic splenectomy". Each item was enter in PubMed by using the "(MeSH Terms)" and "(All Fields)" tag. For each query, the search was then refined by applying several additional filters: (1) study published in English ["(lang)" tag], applied at the pre-screening phase}; (2) publication dates from 1991 to 2013 ["(PDAT) tag"]; (3) publication type ["(ptyp)" tag], excluding systematic/non-systematic reviews, meta-analysis, practice guidelines, case reports, letters/editorials, and study involving animals; and (4) abstract available ["(text)" tag]. The articles assessed for eligibility (n = 160) were primarily evaluated by excluding studies that did not report operative time and conversion to open surgery (as number or percentage). For articles that treated multiport LS, further selection criteria were applied: (1) number of enrolled patients > 20 in clinical trials/randomized control trials (RCT); (2) no comparison between multiple accesses; and (3) no hand assisted conversion. The cut-off for enrolled patients was not applied in the records returned by the other main queries. The filter for clinical trials/RCT did not return any record in the "single port splenectomy" query, and it was not then being applied. The records processed in PubMed are showed according to PRISMA flow diagram for systematic reviews[11] (Figure 1). The studies included in qualitative synthesis (n = 23) are reported in Table 1. Differently from recent reviews on minimally invasive splenectomy[12], we used more strict criteria to select studies. Moreover, the number of patients/procedure for each study included in qualitative synthesis has been clearly indicated, avoiding to report the cumulative sample size (Table 1).

The search strategy carried out in PubMed as described above does not allow to obtain an overview of the items returned by the main queries. With this aim we replicated the search by entering the main queries in the Web of Science™ search engine (records identified = 1381). By screening for the studies published in English in the period 1991-2013, without applying any other criteria, 1141 records were included. The search was performed by selecting the following citation indexes: Science Citation Index Expanded (SCIEXPANDED), Conference Proceedings Citation Index-Science (CPCI-S), and Book Citation Index-Science (BKCI-S). All records published in journals with impact factor were sharing between PubMed and Web of Science™. The full records and cited references returned by Web of Science™ were exported as a multifields tab-delimited files, suitable to be analyzed with the visualization of similarities (VOS) map-

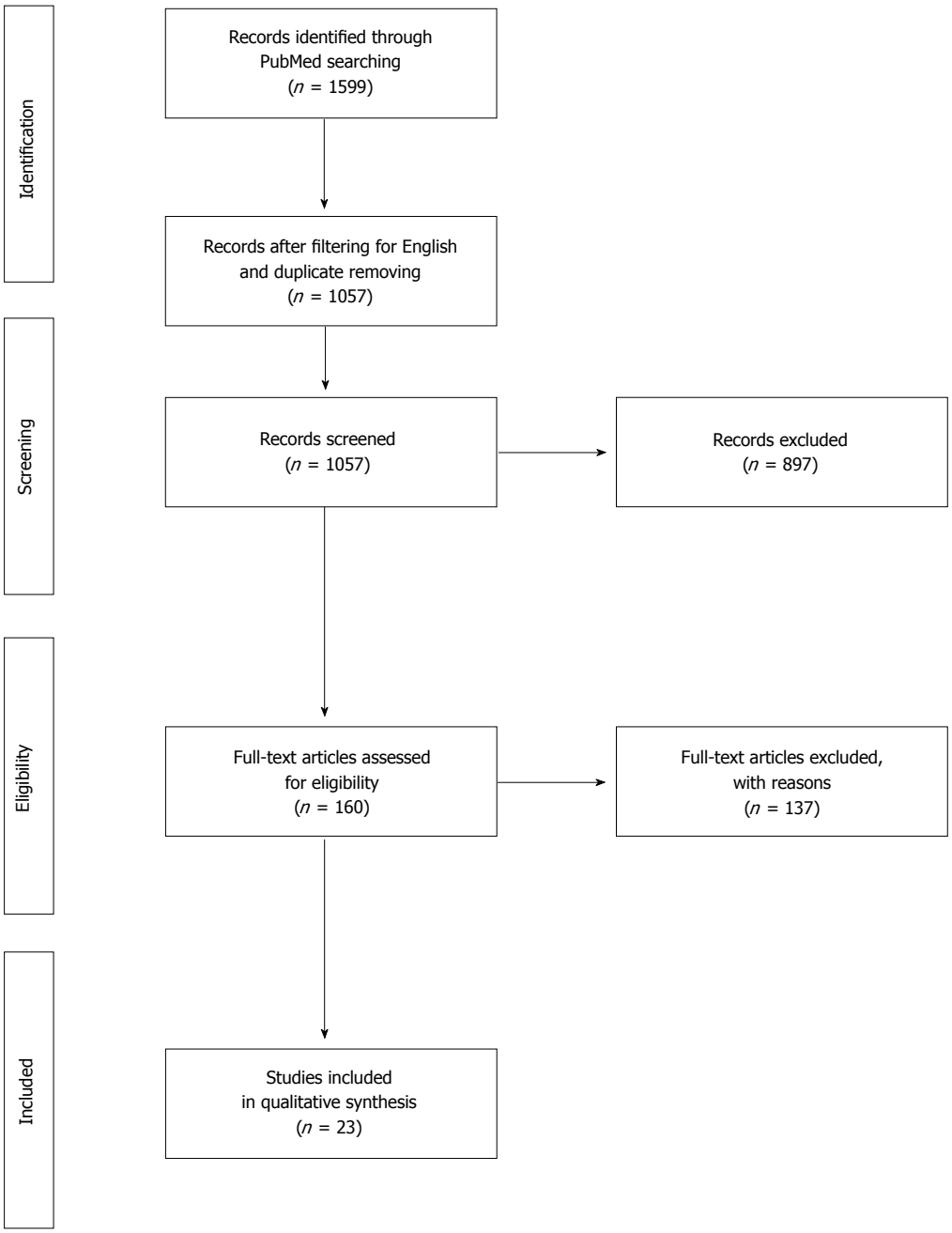

Figure 1 PRISMA flow diagram for the search strategy in PubMed database.

ping technique. The VOS method allows to construct maps based on a co-occurrence matrix[13,14], by applying a normalization method[15,16]. In this way, items with a high similarity are located close to each other, while items with a low similarity are located far from each other, allowing to detected clusters of related items. The records returned by the Web of Science™ searching were used to construct several VOS-based maps. In Figure 2 is showed the map created with the title/abstract text corpus of each record. For this map a binary term counting was used: only the presence/absence of a term in a record was retained, whereas the number of occurrences of a term in a single record was not taken into account. By assuming 5 as the minimum number of term occurrences, from 18145 terms 729 meet the threshold; of these, 420 terms with higher relevance/occurrence were selected. In Figure 3 is presented a bibliographic coupling of authors, assuming 5 as the minimum number of records/author. Of the 5017 authors, 126 meet the threshold.

OPERATIVE INDICATIONS

LS represents the main surgical indication for both benign and malignant diseases. Indications for LS are similar to open splenectomy (OS) (Table 2). Splenectomy can be useful to avoid the enhanced elimination of the blood's corpuscular elements and to alleviate symptoms related to an enlarged spleen, as well as a supplementary

Table 1 Characteristics of published studies on minimally invasive splenectomy included in qualitative synthesis

Ref.	Indication	Procedures	Patient No	Patient age	Operation time	Conversion	Class
Multiport LS							
Bo *et al*[56]	PI-LC	LS, OS	40/40	Adult	150	2	Retrospective
Ji *et al*[50]	Diverse	LS	105	Adult	100	2	Prospective
Zhou *et al*[112]	Diverse[1]	LS	81	Adult	163	3	Retrospective
Nobili *et al*[36]	GD	LS	30	Adult	150	1	Retrospective
Murawski *et al*[21]	Diverse	LS	159	Pediatric	149	8	Retrospective
Barbaros *et al*[51]	Diverse	LS	29	Adult	71	1	Retrospective
Park *et al*[114]	Diverse	LS	197	All	145	6	Prospective
Park *et al*[110]	Diverse	LS, OS	147/63	All	77	4	Prospective
Targarona *et al*[37]	Diverse[1]	LS, OS	105/81	Adult	166	8[2]	Retrospective
Lozano-Salazar *et al*[109]	ITP	LS, OS	22/27	Adult	270	2	Retrospective
Katkhouda *et al*[20]	HD	LS	103	Adult	161	4	Prospective
Rescorla *et al*[111]	HD	LS, OS	50/32	Pediatric	115	0	Retrospective
Szold *et al*[44]	Diverse	LS	59	All	79	1	Retrospective
Brunt *et al*[108]	Diverse	LS, OS	26/20	All	202	1	Retrospective
Katkhouda *et al*[23]	Diverse	LS	33	Adult	242	1	Prospective
Single port LS							
Monclova *et al*[85]	Diverse	SPLS, LS, RPAS	8/15/10	Adult	83	0	Retrospective
Misawa *et al*[94]	Diverse	SPLS	10	Adult	230	1	Prospective
Targarona *et al*[84]	Diverse	SPLS	8	Adult	97	2	Retrospective
Hand-assisted LS							
Swanson *et al*[73]	Diverse[1]	HALS, OS	20/19	Adult	135	1	Retrospective
Barbaros *et al*[71]	Diverse	HALS, OS	14/13	Adult	90	0	Prospective
Targarona *et al*[69]	Diverse	HALS, LS	20/36	Adult	135	1	Retrospective
Robotic splenectomy							
Vasilescu *et al*[98]	HS	RS, LS	10/22	Adult	107	1	Retrospective
Giulianotti *et al*[10]	Diverse	RS	24	Adult	199	2	Prospective

[1]Patients with massive splenomegaly; [2]Convertion rate estimated by calculating for patient No. and %; LS: Laparoscopic splenectomy; OS: Open splenectomy; PI: Portal hypertension; LC: Liver cirrhosis; GD: Gallbladder diseases; ITP: Idiopathic thrombocytopenic purpura; BHD: Benign hematologic disorders; HD: Hematologic disorders; RPAS: Reduced port access splenectomy; SPAS: Single port access splenectomy; HS: Hereditary spherocytosis; RS: Robotic splenectomy.

technique for staging malignant diseases[1]. Idiopatic thrombocytopenic purpura (ITP) is the most common indication among benign hematologic diseases, and the main cause for surgery (50%-80%) in the patients treated by laparoscopic splenectomy[17,18]. Spleens in patients with ITP may be only slightly enlarged, and thus they benefit from the minimally invasive surgery[1]. Also thrombotic or HIV-related thrombocytopenic purpura may be treated by splenectomy[19,20]. In addition, splenectomy is clinically indicated for hemolytic anemia (including hereditary spherocytosis), major and intermediate thalassemia with secondary hypersplenism or severe anemia, and refractory autoimmune hemolytic anemia[21].

Splenectomy may be required for therapeutic or diagnostic reasons in malignant diseases that are able to affect the spleen[7]. Indications include hematologic malignancies such as myeloproliferative disorders (myelofibrosis), as well as lymphoproliferative diseases (hairy cell leukemia, splenic lymphoma, chronic lymphocytic leukemia)[22-24]. Among malignancies, non-Hodgkin lymphoma (NHL) is by far the most represented pathology. In the patients with NHL, retroperitoneal lymphadenopathy and/or hypersplenism may occur without peripheral lymphadenopathy. Hematologic manifestations of hypersplenism consist of thrombocytopenia, neutropenia, and anemia, all difficult to treat medically. Primary splenic lymphoma may result as a lymphoma limited to the spleen, in presence or absence of hilar adenopathy. This uncommon NHL occurs in about 1% of patients with malignant lymphoma[4]. In this occurrence, splenectomy is also indicated to mitigate symptoms and to recover tissue samples for immunohistochemical and cytogenetic assays. Splenectomy alone for primary splenic lymphoma is associated with a better survival than diffuse NHL and splenomegaly.

When splenectomy is carried out for diagnostic or staging purposes, removal of the intact organ for histologic examination may be needed. This requires to perform an extra incision of 8-10 cm[25]. Conversely, no accessory incision is carried out during hand-assisted laparoscopic splenectomy (HALS), when the spleen can be directly removed via the hand port device[7]. Contraindications to LS include severe portal hypertension, uncorrectable coagulopathy, severe ascites, and traumatic spleen injuries.

PREOPERATIVE EVALUATION AND PREPARATION

All adult patients planned for splenectomy should be examined preoperatively by ultrasound to evaluate both spleen size and volume. Thin-slice spiral computed to-

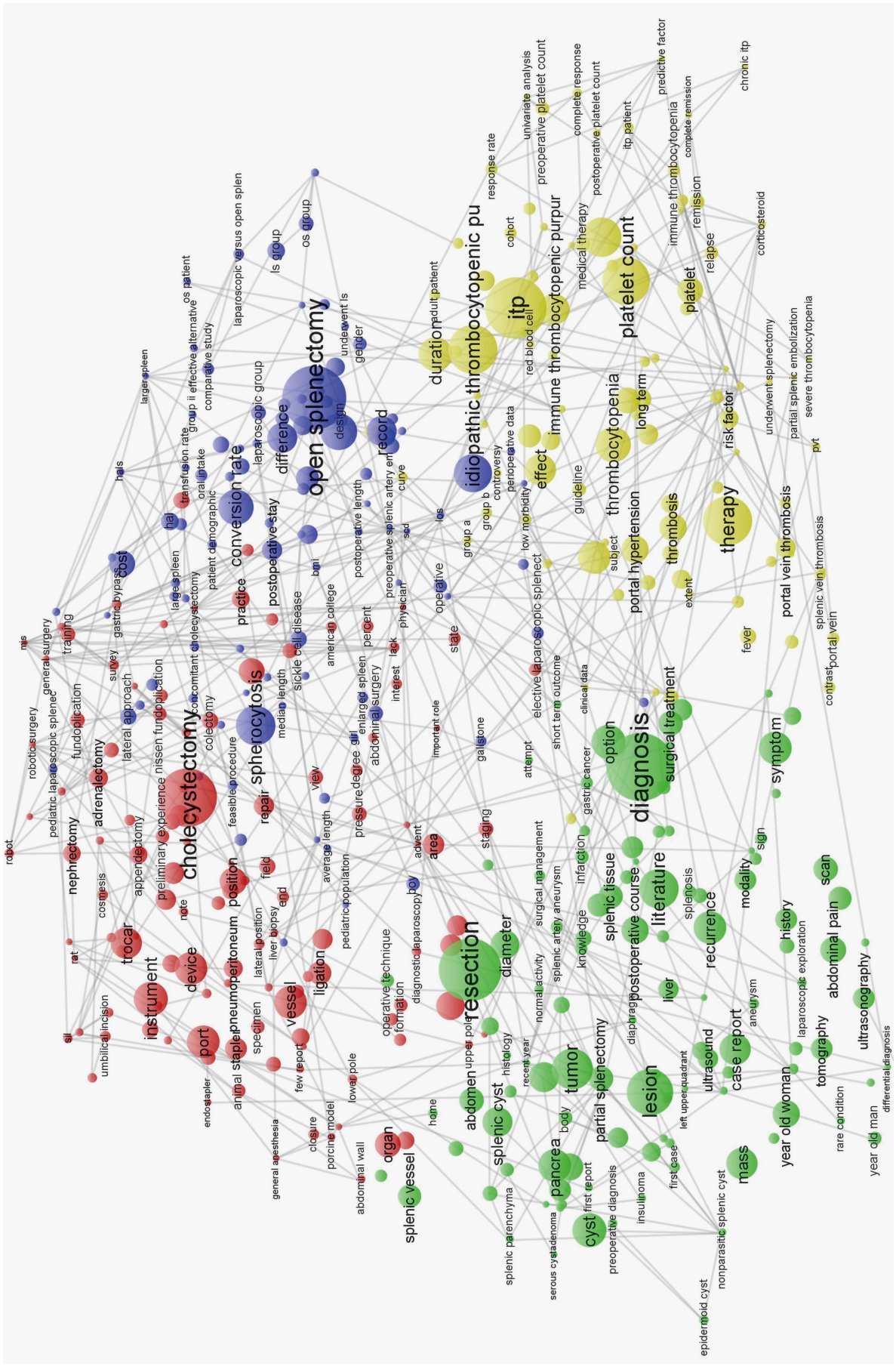

Figure 2 Map of the terms selected (*n* = 420) from the records included (*n* = 1141) after searching in web of science™ (records published in English during 1991-2013). The map was built by using the visualization of similarities approach. The terms in the title/abstract text corpus of each record were selected from 18145 terms by assuming the minimum number of term occurrences = 5; only the presence/absence of a term in a record was retained. The colors define the clusters of related items. The size of each circle is related to the number of occurrences.

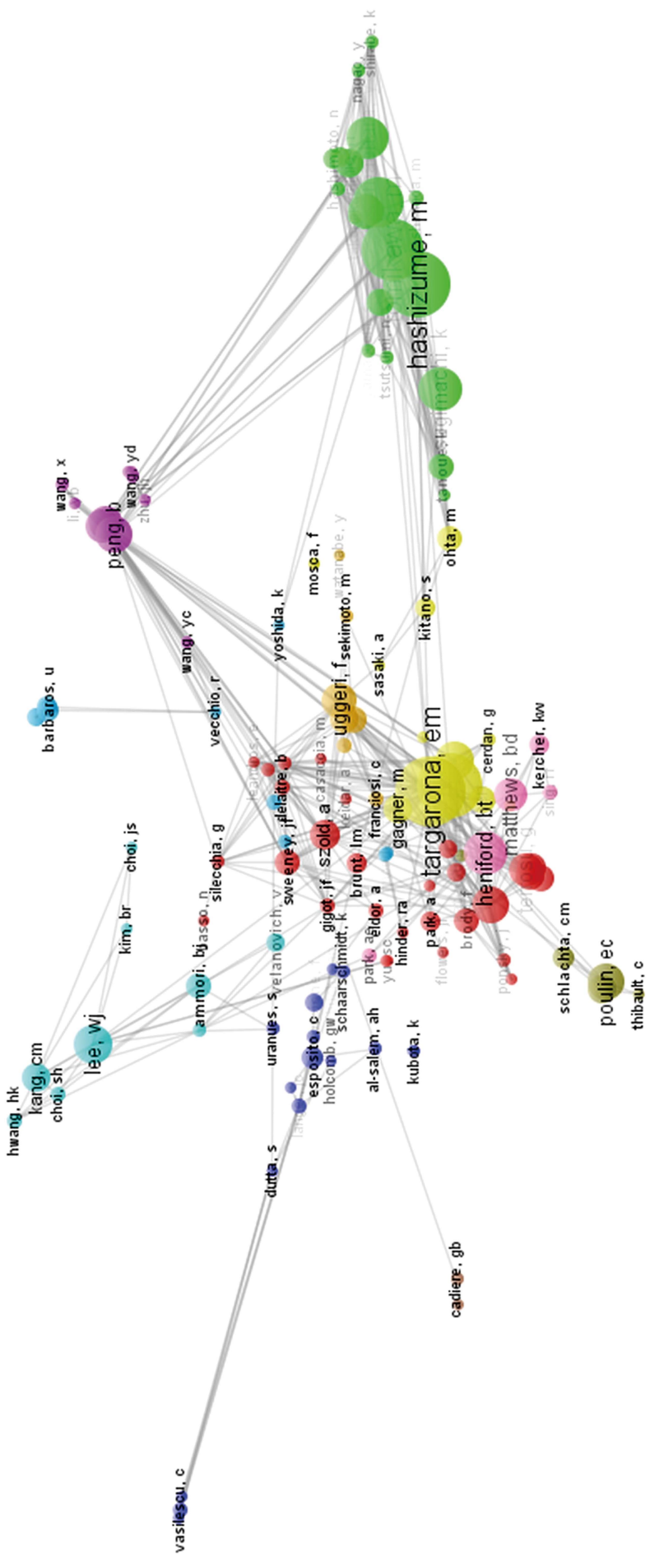

Figure 3 Bibliographic coupling of authors (*n* = 126) from the records included (*n* = 1141) after searching in web of science™ (records published in English during 1991-2013). The map was built by using the visualization of similarities approach. The selection was performed from a pool of 5017 authors, assuming the minimum number of records/author = 5. The colors define the clusters of related authors. The size of each circle is related to the number of links.

mography (TSSCT) should be utilized with the aim to obtain further anatomical information, or if malignancy is suspected. For autoimmune or hemolytic disease associated to massive splenomegaly, TSSCT may be useful to discover accessory spleens[26-27]. In patients affected by malignant hematologic diseases, computed tomography (CT) scan is able to provide reliable information about splenic size and volume[7]. Moreover, CT scan may be useful to detect splenic hilum lymphadenopathy, as well as to discover conditions that may responsible for critical intraoperative complications such as perisplenic inflammation or splenic infarction[7]. CT scan with three-dimensional reconstruction of the spleen and vessels may add an interesting vascular mapping useful to guide the surgical dissection in case of magistral or distributed type of vascular supply. Although recent magnetic resonance imaging techniques are able to provide excellent results in the detection of pathologic spleen states, they do not have an important part for preoperative evaluation of splenic size owing to elevated cost and/or minor accessibility in some countries.

In case of hypersplenism-induced cytopenia, a preoperative management is due to correct this state. The risk of harmful intraoperative bleeding is high when a low platelet count occurs. Treatment with prednisone (1 mg/kg per day, starting from 5 to 7 d before surgical treatment) is suggested to obtain a preoperative platelet count over 50×10^9/L. For therapy-resistant patients, platelet transfusions performed at some point in surgery, in any case following separation of the splenic pedicle, should be utilized[28]. Administration of immunoglobulins is made exclusively in case of autoimmune thrombocytopenia. Preoperative transfusions of packed erythrocytes should be considered in anemic

Table 2 Clinical indications of laparoscopic splenectomy in elective patients (data from Italian Registry of Laparoscopic Surgery of the Spleen; period: 1993-2007; *n* = 676) Clinical indication %

TP	
Idiopathic thrombocytopenic purpura	25
Thrombotic thrombocytopenic purpura	5.47
HIV-related thrombocytopenia	0.29
Other thrombocytopenia	5.62
HM	
Non-Hodgkin's lymphoma	20.71
Hodgkin's lymphoma	5.62
Idiopathic myelofibrosis	1.77
Chronic lymphatic leukemia	1.03
Hairy-cell leukemia	1.03
Other HM	2.66
HA	
Hereditary spherocytosis	9.17
Major beta-thalassemia	4.43
Autoimmune hemolytic anemia	1.77
Other HA	5.62
OP	
Splenic cyst	2.81
Splenic angioma	1.47
Splenic artery aneurysm	0.44
Unknown	5.03

IRLSS: Italian Registry of Laparoscopic Surgery of the Spleen; HM: Hematologic malignancy; TP: Thrombocytopenic purpura; HA: Hemolytic anemia; HIV: Human immunodeficiency virus; OP: Other pathologies.

patients. Vaccination against pneumococcal, meningococcal, and *Haemophilus influenzae* type B is recommended in elective cases at least 15 d before surgery[29]. For patients who underwent splenectomy, the risk of overwhelming postoperative infection able to become critical sepsis is a well-documented scenario. Preoperative antibiotic prophylaxis (PAP) is suggested to decrease infection rates. In LS procedures, PAP is conventionally based on cefazolin or clindamycin at once previous to surgery, continued by postoperative intravenous administration of amoxicillin or erythromycin.

In case of massive spleens, embolization of the preoperative splenic artery may be considered with the aim to prevent severe intraoperative bleeding and to decrease splenic size, even if no obvious advantage has been reported following this approach[30].

LS TECHNIQUE

Once the indication to the surgical operation is posed, concerns remain on the most suitable approach, since in case of enlarged spleens laparoscopic splenectomy becomes more technically challenging. The laparoscopic seems to be preferable to the conventional open approach in many cases, in view of the lower complication rate and shorter hospitalization times. Although OS and LS were compared in only one RCT[31], there is a widespread consensus on the superiority of the LS for almost all diseases that requires splenectomy. On the other hand, some restrictions persist for patients with splenic trauma, massive splenomegaly, and severe comorbidities.

The operating times may be longer in LS than OS. This finding has been reported as directly related to the spleen mass[8]. Many studies report that LS is accompanied by a lower intraoperative blood loss, whereas the intraoperative complication rate seems to be comparable between LS and OS. The length of postoperative hospital stay is less in LS than OS[19]. The time awaiting to return to everyday activity is considerably shorter in patients treated with LS[32], and better cosmetic outcomes are also achieved. The surgery costs include operating room, hospitalization time, and costs to society (*e.g.*, caused by lost workdays). Although operating room costs are usually higher with LS than OS as a result of more expensive equipment and the utilize of not reusable pieces, the whole cost for hospitalization is not appreciably higher for LS[33,34]. Conversely, whole hospitalization costs may be even lower in LS patients because of the shorter postoperative hospital stay[35]. Other studies have reported as the costs seemed to be related to patient age, spleen size, and major complications instead of surgical technique[19].

LS may be carried out by using several approaches (lateral, hemilateral, or supine) on the basis of surgeon preferences, spleen mass, patient characteristics, and the need to associated procedures. The supine position permits a fine access to the omental pouch and a favorable view of the splenic hilum, a good condition to be searched as the first step of the procedure in massively enlarged spleens[1]. This position is used also for LS-associated procedures (cholecystectomy, biopsies of the lymph nodes and/or other organs)[36]. On the other hand, the full lateral decubitus position is not recommended in case of splenomegaly, as the organ may drop into the right upper quadrant, getting too close to the ports and making spleen manipulation impossible[37]. In the hemilateral approach the patient is positioned with the left side elevated up to a 40° to 45° angle from the table surface. Following this approach the patient position can be regulated to surgical requirements, resulting preferred by many authors for the most common indications[38]. Usually, four trocars and are used. A pneumoperitoneum up to 12 mmHg represents the standard. Trocar position should reflect patient anatomy, being able to be adjusted for both spleen size and splenic attachments. A routine exploration for accessory splenic tissue is recommended to avoid potential disease recurrence[39-43]. Use of the endovascular stapler has been reported to make easy hilar dissection compared to previous ligation or clipping techniques[44,45]. In addition, electrothermal bipolar vessel sealer (LigaSure TM) or ultrasonic coagulating shears (Ultracision Harmonic ScalpelTM, Ethicon Endosurgical, Cincinnati, OH) have been utilized for dissection of smaller polar vessels and gastric vessels[22,37,46,47], as well as for the greater hilar vessels[48]. Some authors reported the safe use of LigaSureTM for hilar vessels with a diameter up to 7 mm in patients with normal or slightly enlarged spleens, being accompanied to lower blood loss and shorter time of surgery[46,49-52]. They concluded as the utilize of the LigaSureTM vessel sealing system following

a LS semilateral approach may be secure and useful, by reducing both blood loss and operating time, representing a reasonably priced alternative to endostaplers.

The spleen removal from the abdominal cavity may be a technical challenge, being a time-consuming procedure, especially in case of massive splenomegaly. In patients where a careful pathological analysis is not needed, the sample is morcellated in a commercially available bag using ring forceps or a tissue morcellator. For manifestation of lymphoma or splenic malignancy, as well as for staging reasons, the spleen should be recovered *in toto*, making a further incision necessary[41,44]. Scrupulous care must be used to avoid capsular tear and cell spillage. An undetected implantation of splenic cells may cause splenosis, as well as recurrence of benign/malignant diseases.

MASSIVE SPLENOMEGALY, TECHNICAL CONSIDERATIONS

Although there is no agreement in literature about the terms "splenomegaly" or "massive splenomegaly", the former should be characterized by using preoperative imaging. From a surgical point of view, splenomegaly is defined when a maximum splenic diameter results over 15 cm. A maximum splenic diameter more than 20 cm should be used to define a massive splenomegaly[53]. Besides spleen longitudinal diameter, clinical parameters in predicting the feasibility of laparoscopic splenectomy include a palpable margin that does not traverse the midline or extend over the iliac crest[8]. Given that LS represents the "gold standard" approach in normal-size and moderately enlarged spleens, HALS or OS should be considered for massive splenomegaly, since the need for open surgery is directly related to the increase in spleen size[22,54,55].

Very outsized spleens represent a critical finding that tests the current confines of laparoscopic surgery. If we have chosen a totally laparoscopic approach for massive splenomegaly, no further adjustment in patient position is required. With the hemilateral approach the tilt of the table can be varied during the procedure in order to better expose the spleen. The full lateral decubitus is not achievable, as the ports are frequently placed at the midline or even on the patient's right. Similarly, a supine approach is not favorable as it can be hard to move the large spleen outside from retroperitoneum. The decisive practical variation is that the place of the ports must be adapted to the spleen position, rather than placed in the typical subcostal position[39,56]. Ports must be positioned below and medial to the spleen that is palpable to physical examination; this often pushes them away from the costal margin. It is often impracticable to position the lateral port under the lower splenic pole, which may be profound in the pelvis and best placed as low as possible. Dissection and mobilization may be performed in the standard fashion with ultrasonic coagulation or radiofrequency devices. Care must be taken for not completely detaching the large spleen from the diaphragm too early, as the heavy organ may drop into the pelvis or right upper quadrant, becoming difficult to handle.

One providential aspect of the massive spleens is that the hilar vessels are elongated and separated from the organ, as well as from stomach and retroperitoneum, making them effortless to isolate and divide early. On the other hand, difficulties can be encountered in splenic malignancy if a lymphadenopathy at the hilum is present. All the nodes macroscopically enlarged must be harvested, giving a precise contribution in disease staging[25]. Sometimes their tight relation with the splenic vessels prevents the surgeon from a correct visualization and make the hilum extremely thick, so that the tissue cannot be included in the jaws opening of the linear stapler.

Another concern arising during spleen extraction is the bag's dimension. In fact, several bags obtainable for laparoscopic surgery are unfit to provide accommodation for the massive spleens. Spleens measuring up to 25 cm in craniocaudal lenght can be extracted laparoscopically using the 15-mm Endo Catch Ⅱ (Covidien/US Surgical, Norwalk, CT) sterile bag[57]. In case of larger spleens there are not commercially available bags conceived for splenic retrieval and the surgeon has to adapt other devices for this purpose, such as organ retrieval bags or "intestinal" bags[58].

When the spleen has to be recovered *in toto*, the incision has to be extended realizing a short subcostal incision, eventually joining the incisions of the lateral trocars. Otherwise, a Pfannenstiel incision may be performed: it has an aesthetic improvement over upper abdominal incisions, it is less painful and may result in fewer pulmonary complications.

HAND-ASSISTED LAPAROSCOPIC SPLENECTOMY

Hand-assisted laparoscopic splenectomy (HALS) may be considered as a modified LS. For this technique, the majority of authors suggest for the patient decubitus a semilateral or 45° right lateral position on the operating table[59]. A supplementary incision of 7-8 cm is made, great adequately for allowing the movement to surgeon's hand/forearm. It may be positioned in the above midline, in the right upper abdomen[6,60-62], or instead at the McBurney or Pfannenstiel site[63]. The incision place can be changed in relation to spleen size. At the chosen site the surgeon may use a hand port device for introducing into the abdomen the nondominant hand, while maintaining pneumoperitoneum. The introduced nondominant hand permit a tactile control, being useful during both many steps of the standard surgical procedure and in sudden hemorrhage or adhesions. Finally, the spleen can be taken away through the supplementary incision, frequently with no morcellation. Potential drawbacks consist in the hindrance caused by the surgeon hand/forearm, as well as in the progressively hand weakness during the procedure, as described by 21% of the surgeons[64,65]. Many splenectomy series have reported as HALS may be accompanied

by a decrease in operating times, conversion rates, and peri/postoperative complications with respect to the merely laparoscopic approach[60,62,66-70]. Although HALS requires a supplementary incision, so causing a further trauma to the abdominal wall, this approach preserves the advantages of typical laparoscopic surgery in term of short hospitalization time, early return to oral diet, and limited postoperative pain[6,55,71,72]. In particular, HALS is able to make easy the surgical management of massive splenomegaly, permitting a traumatic manipulation of huge organs. In a RCT that compared HALS *vs* OS, median spleen weight was 1200 g for the patients enrolled in the HALS group, with no need for conversion to OS[26]. Furthermore, massive spleens weighting over 3000 g may be removed in safety by HALS[5,37,39,61,71]. In comparison with OS, HALS is associated to small abdominal incisions, fewer postoperative pain, and shorter hospitalization times. In comparison with LS, HALS results with smaller amounts in conversion rate to OS[31,53,71,73].

SINGLE INCISION LAPAROSCOPIC SPLENECTOMY

Single-incision laparoscopic surgery (SILS) represents a specific variation to laparoscopic surgery, by using the same instruments and requiring only minor modifications when compared to conventional multiport technique. SILS has so far been used for a variety of procedures such as cholecystectomy, appendectomy, colectomy, and thyroidectomy[74-78], and more recently also for splenic surgery[9]. Differently from standard laparoscopy, SILS is associated to less incisional pain, avoiding complications related to port site, with a finer aesthetic appearance. In single incision lasparoscopic splenectomy (SILSp), the patient is placed in the right lateral decubitus, with the table flexed to provide a reverse Trendelenburg positioning to provide a better access the left hypochondrium[79-81]. In emaciated patients with normal-sized livers, a transumbilical approach may be considered. For patients with splenomegaly, a left-sided incision of 2 cm is carried out umbilicus area, following the midclavicular line. Two SILSp techniques have been described. A first technique requires to employ multiple trocars, introducing them one at a time through a single skin incision, after pneumoperitoneum has been obtained with a Veress needle[82,83]. A second option consists in insufflating the abdomen to realize pneumoperitoneum and introducing a multiport device[84]. The rest of the procedure is comparable to conventional multiport LS. Difficulties encountered during procedure are normally faced by inserting additional ports, by a conversion to multi-port splenectomy or to OS, with a whole conversion rate of 4.8%. Only four reports[84-88] compared the outcomes of SILSp and multi-port LS. The most frequent indication for SILSp is idiopathic thrombocytopenia followed by splenic cystic disease and hereditary spherocytosis, witnessing a prevalence of benign pathologies in normal-size spleens. Results comparing operative blood loss, hospital stay, pain medication requirements, are not univocal but analysis are accomplished on small series.

SILS has some technical weakness in comparison to multiport laparoscopic surgery. Although SILSp can be carried out with a standard rigid laparoscope and straight instruments, crowding above the access port/site usually may lead to clashing of surgical instruments. The parallel arrangement of instruments, as well as the interference between the surgeon and the camera operator, are able to increase the difficulty during the procedure. Moreover, lack of tissue triangulation considerably increases the complexity of splenic exposure and dissection. With the aim to obtain a better surgical exposure, the majority of surgeons applies 30° laparoscopes, while others use articulating or curved graspers and/or scissors[83,87,89-92]. Some investigators suggest to utilize longer laparoscopes to avoid cluttering of instruments[90]. Meanwhile, gastric suture and "tug-exposure" technique are suggested by several authors to make easy exposure during SILSp[87,93,94]. Targarona *et al*[80] suggest as although less trauma and better aesthetic results are reached throughout a standard single-access laparoscopy when the incision is performed in the navel, some dissection manoeuvres can be particularly difficult or even impossible, owing to the oblique dissection line between the umbilicus and the upper part of the spleen. Podolsky *et al*[95] describe as a low extension and length of the incisions is accompanied by a minor risk for both hernia site infections and intra-abdominal adhesions. Conversely, a bigger incision may increase the occurrence of seroma and umbilical hernia. A critical difficult for reaching a common use of SILSp is represented by the need of an extra learning curve. Moreover, there are concerns for increased complication rates that occurred when low-experienced surgeons in laparoscopic surgery tried to apply this technique.

ROBOTIC SPLENECTOMY

Laparoscopy has some limits, such as two-dimensional (2D) visualization and stiff instrumentation, which can make whole or partial splenectomy demanding. With the aim to overcome these restrictions, robotic surgery (da Vinci®, Intuitive Surgical, Sunnyvale, CA, United States) has been developed with "wrist-like" action of the instruments and with three-dimensional (3D) visualization, producing an high-resolution binocular view of the surgical field. These robotic devices seem to be able to open the way for more complex and advanced surgical procedures. Published studies on robot-assisted splenectomy include only case reports or small series. In the literature that compares robotic splenectomy *vs* LS, no significant difference is reported about conversion rate, drain removal, hospitalization times, and occurrence of complications[96-98]. On the other hand, operative times and overall costs are higher in robotic splenectomy. Currently, robotic splenectomy does not offer any apparent advantage in terms of clinical outcome[10,97]. Giulianotti suggests that the best indications for a robotic approach

are in cases of a large and friable spleen with a bulky and intrasplenic pancreatic tail, or when a partial splenectomy is planned. In fact, a partial splenectomy needs an accurate dissection of the splenic branches and the robotic technology with 3D vision and "wrist-like" instruments is particularly functional to this condition. Robotic splenectomy is performed through a multiport approach. The most recent update of this approach is robotic single-site splenectomy through the new Da Vinci Single-Site® robotic surgery platform. The Da Vinci Single-Site® robotic surgery platform could reduce the disadvantages related to the single-access surgery, such as instrument clashing, lack of triangulation, odd angles and need of space[99]. This surgical platform seems to overcome the previous robotic surgical platform for two main reasons. First, the surgeon inserts the instruments through the cannula, so that the hook (introduced on the left) intersects with the grasping forceps (introduced on the right). After tool recognition on the part of the robotic console, the surgeon can check the hook with his right hand and the forceps with his left. In addition, the new robotic tools are semiflexible and reach the surgical field in a more natural way and closer than that of standard single-access laparoscopy. These characteristics, as also described by Morelli *et al*[100], restore the normal triangulation, making surgical procedures easier than standard single-access laparoscopy.

POSTOPERATIVE CARE

Postoperative care after laparoscopic splenectomy is usually simple but it sometimes has to be more attentive because malignant spleens are frequently observed in older and more physiologically frail patients. Postoperative pain medication is given on an individualized basis. Most patients will not require further narcotics. Intravenous acetaminophen is administered during the first night. When pain is not adequately controlled, coanalgesia with a nonsteroidal anti-inflammatory drug (ketorolac tromethamine) may be added, producing the best clinical results[28]. The patient is allowed to drink clear fluids on the first post-operative morning; when clear fluids are well tolerated, the patient is allowed to continued to a diet if amylase and lipase levels are normal. Antibiotic administration is sustained by postoperative intravenous amoxicillin or erythromycin. Patients receiving *iv* cortisone are given oral steroids on postoperative day 1 after an overlap *iv* injection; thereafter, steroids are gradually tapered. Perioperative anticoagulant prophylaxis is recommended for all patients (low-molecular-weight heparin 100 U/kg per day) upon verification that bleeding is not occurring. Platelet count has to be monitored closely postoperatively and then with more delayed controls up to 3-6 mo for possible thrombocytosis making an antiplatelet therapy (i.i., acetylsalicylic acid) necessary.

PROCEDURE-SPECIFIC COMPLICATIONS

Post-splenectomy related complications embrace hemorrhage, left lower lobe atelectasis/pneumonia, left pleural effusion, subphrenic collection, iatrogenic pancreatitis, gastric, and colonic injury, and venous thrombosis[101]. The occurrence of these complications increase after conversion[8]. Treatment of post-splenectomy complications should be performed following the standard clinical protocols. An incidence of 15% for pancreatic injury has been reported[55]. It is characterized by peripancreatic fluid collections, pancreatic abscess, and/or atypical postoperative pain, as well as hyperamylasemia and amylase-rich drain fluid. For this reason, a routine assay for amylase on day 1 after surgery is suggested to alert the surgeon and change postoperative management if necessary. Thrombosis of portal or splenic vein is a potentially life-threatening complication that can take place after several weeks/months after surgery. It can lead to intestinal infarction and portal hypertension. The reported rate of venous thrombosis ranges from 0.7% to 14%[102,103]. In all patients a perioperative anticoagulant prophylaxis based on subcutaneous heparin should be carried out. In particular, subjects at elevated risk for portal and/or splenic vein thrombosis should be treated with anticoagulant prophylaxis for 4 wk. High-risk factors for the occurrence of this complication are the presence of myeloproliferative disorders associated with hypercoagulopathy, hemolytic anemia, hypersplenism or hematologic malignancy and splenomegaly. Diagnostic difficulties may delay the optimal treatment. Diagnosis can be obtained by color Doppler ultrasonography or contrast-enhanced CT[103].

Among the long-term postoperative complications, an overwhelming infection with the features of a life-threatening sepsis is well-documented. It is caused generally by infection from encapsulated organisms that are eliminate by the spleen[104,105]. The risk of infection is highest within the first 2 years post-splenectomy, but one-third of all infections may happen until 5 years after surgery. Although the whole incidence of post-splenectomy infections is quite low (3.2%), the mortality rate is particularly high (40%-50%)[29]. As mentioned before, vaccination against *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and *Neisseria meningitidis* infections at least 15 d prior to surgery, or in case of emergency, within 30 d after splenectomy is highly recommended. Antibiotic prophylaxis should be performed before surgery, when the patient is in the operating room. The patient must be informed as the risk for post-splenectomy infections will be increased lifelong.

CRITICAL EVALUATION

The good outcome of LS procedures is mainly conditioned by a correct preparation. As observed with other laparoscopic procedures, the key points are represented by the need to avoid complications and to reduce the probability that technical accidents may occur. Long-term outcome of the hematologic disease treated by LS has not been extensively studied. In literature, only reports

about idiopathic thrombocytopenic purpura demonstrate as the long-term outcomes between LS and OS may be comparable[106,107]. In case of lymphoproliferative and myeloproliferative disease, the advantages of a minimally invasive approach on this typically immunoincompetent population have a positive impact on the postoperative morbidity and mortality rate. Furthermore, these patients are frequently subjected to adjuvant chemo- and radiotherapy, which can be done within a shorter time from the intervention. However, many studies report about the outcome of the LS procedure, comparing initially the laparoscopic approach to the open procedure[108-111].

When large series and nonrandomized clinical trials have recorded better results for LS than OS, the interest has shifted to the right splenic dimension to be treated safely by a laparoscopic approach. The clinical guidelines drawed by the European Association for Endoscopic Surgery (EAES) suggest that in case of massive splenomegaly, HALS or OS should be considered, although this statement is based on a low-quality evidence[53]. As pointed by the EAES guidelines, laparoscopic resection for massive splenomegaly represents a challenging task because of the restricted abdominal working space, as well as for the complexity to execute intraabdominal manipulation and recovery a very large organ. The conventional parameters to set the operative difficulties are represented by the extension of surgery time, the amount of blood loss, and the level of conversion rate. These parameters are directly related to increase in splenic weight and size. In a recent multicentric study[8], the underlying hematologic malignancy (HM) and body-mass index (BMI) were found indipendent factors related to surgical conversion at multivariate analysis. It has to be retained that HM patients had a 4-fold higher conversion rate if compared to the benign group (11.7% *vs* 3.2%). This suggests that besides splenic size that is constantly enlarged in malignancies, body habitus of the patient plays a relevant part for both assessing the practicability of laparoscopic surgery and predicting the early results[57,112]. With the progressive extension of technical feasibility, also morbid obesity (BMI > 35) is no longer an absolute contraindication for LS, although remains unquestionable difficulties due to limited intraabdominal working space and poor viewing[113].

There is a general consensus among authors about LS may be a safe procedure in the hands of a skilled surgeon. On the other hand, is widely accepted the need for a learning period, as demonstrated by the higher conversion rates during the first LS procedures[114]. Thus, most surgeons suggest to deal with massive splenomegaly once the procedure on smaller size spleens is mastered. If in normal-size or moderately enlarged spleens the laparoscopic approach is unquestionable, in massive splenomegaly the laparoscopic surgery creates great defiance, where the most advantageous technique and its reasons remain to be established. In this setting, it appears ethically justifiable to perform prospective randomized trials with the aim to compare OS *vs* LS. One of the large appeal of minimally invasive surgery is the expectation of a considerable decrease in full costs. While operating room costs may be higher in LS than in OS, whole hospital charges results as a rule lower with LS, mainly due to the lower hospitalization time[33]. Analogously, societal costs are reported to be lower due to fewer lost workdays[19]. In any case, a systematic cost-effectiveness analysis still is required.

The literature regarding the single-access splenectomy and robotic splenectomy is still at an earlier state. Early experiences report as both techniques are practicable and secure in experienced hands. The potential benefits associated with SILSp with respect to multi-port LS is yet to be demonstrated. Unfortunately, many publications about SILSp are case reports or small series. Similarly, larger series and prospective studies are also required to evaluate the robotic *vs* laparoscopic approaches. Robotic single-site splenectomy with the new dedicated platform seems to be practicable and secure, going beyond the restrictions of earlier robotic or conventional SILSp. On the other hand, further studies should be performed also for exploring the potential cost-effectiveness of this new high-tech based approach.

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What makes a gastric bypass a good gastric bypass? Opinion and hypothesis

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Abstract

Gastric bypass is widely accepted as the gold standard bariatric operation. It was first reported 1967 and has been the subject of many technical alterations and variations since that time. Each of these variations has the potential to confer different outcomes, in terms of such things as weight loss, ease of surgery, risk, complications and durability of weight loss. All variations being performed these days should be accomplished with high levels of safety, in which case the primary interest of those undergoing surgery is the degree of weight loss that can be expected and the durability of that weight loss. Broadly speaking these two features will also determine the degree to which all co-morbidities are improved, which is also a goal of those undergoing surgery. In this article the authors describe the features of the Fobi Pouch gastric bypass which make it the most predictable and reliable variant of gastric bypass and report such evidence in the literature as exists for their contentions.

Key words: Gastric Bypass; Roux Y gastric bypass; Bariatric surgery; Weight loss surgery

Core tip: Gastric bypass surgery represents a family of operations. The details of how the surgery is performed will determine the success and durability of the weight loss achieved. The Fobi Pouch Gastric Bypass has been shown to be the most reliable in this respect. This article describes the details that make this the reliable gastric bypass it is.

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INTRODUCTION

Gastric bypass was first described in the literature by Mason *et al*[1] in 1967 and soon replaced jejuno-ileal bypass as the surgical procedure of choice for severe obesity. Roux-en-Y gastric bypass survives to this day as the gold standard bariatric operation for individuals with body mass index (BMI) > 40 or BMI > 35 in the presence of significant comorbidities, despite challenges from vertical banded gastroplasty in the 1970s and 80s, laparoscopic adjustable banding in the 1990s, and laparoscopic sleeve gastrectomy in the last five years. Its superiority in terms of degree and reliability of weight loss and durability of weight loss has been well documented[2-6]. However, Roux-en-Y gastric bypass does not describe a single operation, but rather a family of operations. There are many variants, and each one is probably performed a little differently by each and every surgeon who carries it out. The same is also true of other types of bariatric surgery, and distinguishes these operations from most other abdominal procedures. Unlike so much of abdominal surgery, where resection is undertaken to remove tumours or

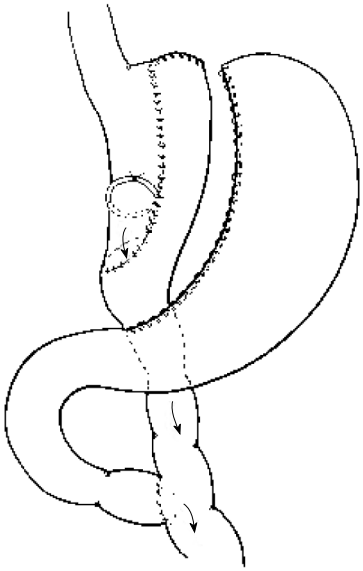

Figure 1 Schematic diagram of Fobi Pouch Gastric Bypass.

other offending organs, bariatric surgery aims to achieve weight loss and metabolic benefits, through anatomical changes undertaken to alter physiology or function. There is a real need to standardise the key features of the gastric bypass. Concepts regarding how these operations achieve their goal are changing, and will continue to change as our understanding of the drivers of obesity and metabolic disease also changes.

Gastric bypass, gastroplasty, gastric banding and sleeve gastrectomy have all been primarily regarded as restrictive operations, meaning the operation achieves weight loss, through restriction to eating resulting in an enforced reduction in energy intake. But as we have learned more over the years, we begin to appreciate other less obvious mechanisms by which each or some of these operations may achieve their goal[7,8]. In the 1980s Gastric bypass was recognised as having a greater impact on food choice than gastroplasty (or the subsequent variant of adjustable gastric banding), because of its propensity to induce dumping following the intake of sugar and fat[9]. This distinction remains and certainly contributes to the superior results of gastric bypass over the other restrictive operations. More recently, following intense interest in the metabolic benefits of bariatric surgery, there is compelling, though not yet conclusive evidence that duodenal bypass confers its own benefit, distinct from that brought about by reduction in the size of the gastric reservoir, and the slowing of gastric emptying[7,8].

Notwithstanding our knowledge of subtle mechanisms by which gastric bypass may achieve major weight loss, the restrictive component remains an essential feature of a successful gastric bypass operation. Significant weight regain after gastric bypass is invariably related to increased energy intake, which may come about through one or more of the following: (1) diminished restriction; (2) increased intake of energy dense foods; or (3) increased frequency of eating ("grazing"). While the latter two of these are largely beyond the control of the surgeon, the first can be minimised by attention to technical detail in the performance of gastric bypass. Variation in weight loss following gastric bypass does occur and is to be expected. One of the major factors accounting for such variation is the degree of restriction imposed by the surgery and the degree to which that restriction is permanent. It is the purpose of this paper to outline the authors' view on those features of a gastric bypass which may optimise weight loss and enhance the prospect of that loss being durable. These opinions have been developed through a 28 year experience of around 1500 gastric bypass operations, and review of such literature as can provide a basis to the recommendations. As many of the recommendations have never been subjected to rigorous testing, they might best, at this time, be considered opinion or "hypothesis".

BACKGROUND TO THE RECOMMENDATIONS

The weakness and disappointments of all bariatric operations rest largely with long-term weight regain. Reports of long-term weight loss outcomes are rare in the literature, and there exist no randomised trials comparing weight loss beyond around 5 years for any of the commonly and currently performed operations. Yet it is well recognised that the differences between operations may not become apparent for at least 5 years. At the present time the most mature and useful comparative data on various operations comes from the systematic review conducted by O'Brien *et al*[10] and reported in Obesity Surgery in 2006. In this report comparative data was presented for laparoscopic adjustable banding, BPD procedures, gastric bypass and banded gastric bypass. To be included in the systematic review, individual series had to have at least 100 patients with minimum 3-year follow-up. A total of over 1500 gastric bypasses were reported on and over 700 banded gastric bypasses. The former were a mix of open and laparoscopic bypasses and included the experience of a number of leading gastric bypass surgeons at the time, including the large experiences of Wittgrove *et al*[11] and Higa *et al*[12]. The Banded bypasses were all open procedures coming from three groups around the World reported by Fobi *et al*[13], Capella *et al*[14] and my own group[15]. In essence, all three groups performed a very similar procedure shown schematically in Figure 1, and referred to in this paper as the Fobi Pouch gastric bypass. The summary weight loss data, taken from the systematic review of O'Brien *et al*[10] is shown in Figure 2. The best early and late results were achieved by the banded gastric bypass and BPD procedures, which both yielded very similar results, and which were both clearly superior to those of the non banded gastric bypass group. Although the early results of the gastric bypass group were superior to those of the adjustable gastric banding group, there was significant weight regain in the standard gastric bypass group with time, meaning much of the advantage

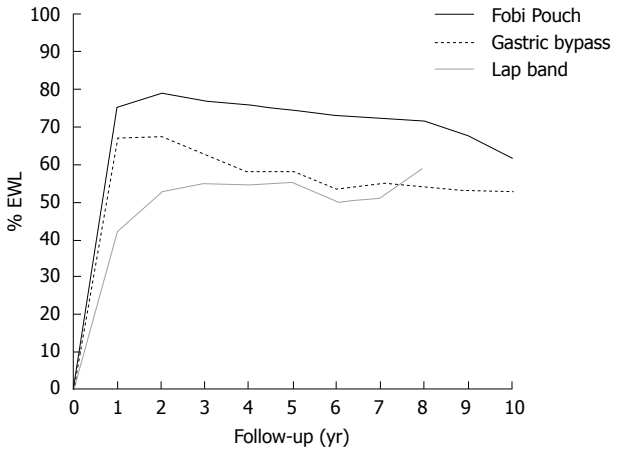

Figure 2 Medium - long-term weight loss data for banded gastric bypass (Fobi Pouch), standard gastric bypass and Laparoscopic adjustable banding. Data from systematic review by O'Brien *et al*[10] 2006. (%EWL on the x axis refers to the percentage of pre-operative weight in excess of ideal body weight, which has been lost at any one point in time, shown on the y axis.

over the gastric banding group was subsequently lost.

Having contributed 342 of the 779 patients to the banded gastric bypass group reported by O'Brien *et al*[10], we feel justified in proposing possible explanations for the superiority of this operation over the standard gastric bypass, performed by acknowledged expert surgeons, whether by open or laparoscopic surgery. In essence the difference rests with the size and shape of the pouch which possibilities are shown diagrammatically in Figure 3 and the presence of a silastic ring to define the size of the outlet[16]. These issues underpin the basis of our recommendations.

FOOD RESTRICTION AND GASTRIC BYPASS

Restriction to eating is achieved through the size and integrity of the gastric pouch and the size of the gastric outlet. We learned many years ago that simple stapling to create the pouch was unreliable, and the integrity of the pouch could be lost, and weight regained through so-called, "staple-line" disruption[17,18]. The problem persisted despite the development of better staplers. Gastric transection was required and over time became an integral part of all modern gastric bypass operations[19]. However, despite gastric transection, gastro-gastric fistulae may develop as staple lines adhere to one another and recanalisation occurs. This occurrence has been described in up to 6% of cases[20]. The consequence will depend on the size of the gastro-gastric fistula and may include gastric ulceration[17,21], bleeding and weight regain[22,23]. Prevention of this occurrence can be achieved by interposition of small bowel as described and proposed by Capella *et al*[23] and Fobi[22] and is to be recommended. We have never seen a gastro-gastric fistula develop following Fobi Pouch gastric bypass in over 1000 such operations performed by us since 1997.

POUCH SIZE

Much time and effort has been given to thinking about the optimal size of the gastric pouch. In the 1980s this was thought to be about 30 mL. Today, we believe it should be rather smaller. We learned through the 1980s that horizontal pouches, made across the upper portion of the greater curve of the stomach, as originally proposed, were very prone to dilatation. The recognition that vertical pouches based on the lesser curve of the stomach were much less prone to dilatation than the horizontal pouches based on the greater curve was an important one[24]. In addition to being less liable to dilatation, such vertically oriented pouches preserved a more reliable blood supply for the gastro-enteric anastomosis. Regardless of size, gastric pouches that include even a little of the greater curve of the stomach are more likely to dilate over time, and lead to weight regain, than those which begin at the angle of His. This is an important point, particularly in the age of laparoscopic gastric bypass. Gastric pouches should begin close to the angle of His rather than include any portion of greater curve and should be oriented down the lesser curve for a variable distance. The one caveat here is that the stapling should be carried out through stomach wall not lower oesophagus, to ensure more reliable healing.

POUCH LENGTH

It is both of interest and instructive to note empirically that weight loss after a Roux-en-Y gastric bypass operation is considerably greater than would be expected following total gastrectomy. There are likely two reasons for this. The pattern of motility in the oesophagus and jejunum are quite different from that of the stomach. Both propel food forward relatively quickly. The stomach does not, acting rather to churn its content. Inclusion in the food stream of a portion of stomach therefore acts to slow the passage of food from the oesophagus to the jejunum and hence contribute to the restriction imposed by the operation. If this tube (or lesser curve pouch) is too short (as shown in Figure 3C), strong peristalsis in the oesophagus may allow food to pass quickly to the jejunum and hence lead to reduced "restriction". For this reason small pouches based immediately below the gastro-oesophageal junction are not likely to function optimally, and weight loss may be disappointing. Ideally, the pouch should incorporate a length of lesser curve of the stomach (as shown in Figure 3A). Poiseuille's Law tells us that the flow rate through a tube is inversely proportional to its length. Slow flow or emptying of the pouch is desirable after gastric bypass and contributes to the restriction. In the Fobi pouch variant of gastric bypass the length of the gastric pouch is typically up to 8-10 cm[14,15] which is rather more than would commonly be achieved in the construction of a laparoscopic Roux-en-Y gastric bypass.

SHAPE OF THE POUCH

Much has been written and discussed over the years con-

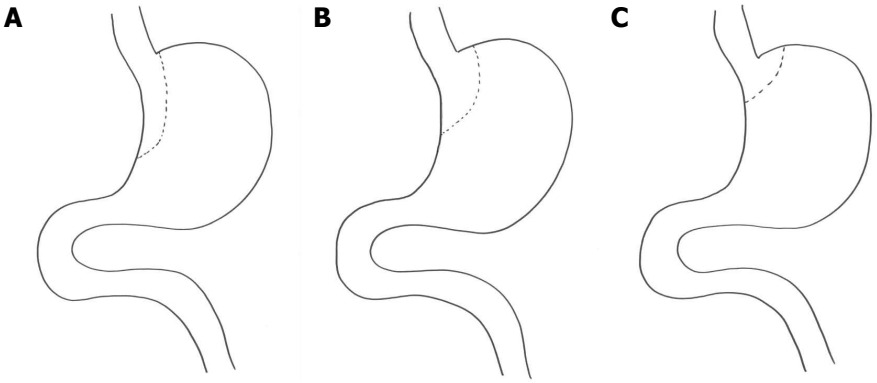

Figure 3 Schematic representations of possible configurations of gastric pouch. A: Shows a long narrow pouch based on the lesser curve; B: Shows a rather wider and shorter pouch based on the lesser curve; C: Shows a very small pouch formed by stapling just beyond the oesophago-gastric junction.

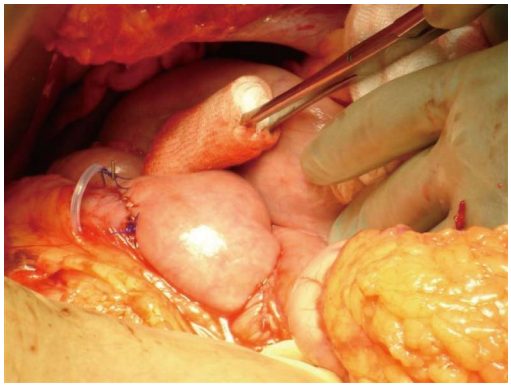

Figure 4 Operative photo showing the loose placement of a 6.5 cm silastic ring proximal to the gastro-jejunal anastomosis.

cerning the optimal size of the gastric pouch. Much less has ever been said or written regarding its shape. Yet it is likely that the shape (length and diameter) may be rather more important than the size itself[16]. LaPlace Law tells us that the pressure required to distend a structure (tube) is inversely proportional to its radius. Poiseuille's Law, mentioned above, tells us that resistance to flow through a tube is proportional to the length of the tube and inversely proportional to the 4th power of the radius. These two laws of physics suggest that for optimum function (viz. no dilatation with time, and slow emptying) the gastric pouch should be made long and narrow, as is the case with Fobi Pouch gastric bypass(as demonstrated in Figure 3). There is a tendency in the creation of a laparoscopic gastric bypass for the pouch to be made wider and therefore shorter (to accomplish the small volume) in order to allow the anastomosis to be performed using stapling devices, which will not fit into a long and narrow gastric pouch (such as is schematically shown in Figure 3B). The weight regain not uncommonly seen 3-5 years following laparoscopic gastric bypass[25] is certainly often explained by enlargement of the pouch. For durable restriction and therefore weight loss, a long narrow pouch is required.

GASTRIC OUTLET

For many years there has been general agreement that diameter of the gastric outlet should be around 1cm. This was the recommended size for gastric bypass operations when these became popular in the 1980s, and seemed confirmed by the 5.0 or 5.5 cm circumference size of the ring or band placed around the vertical banded gastroplasty[26,27]. However, from the early days of gastric bypass, it became clear that one of the reasons for late weight regain was enlargement of the gastric outlet, or gastro-jejunal anastomosis and more rapid emptying of the pouch as a result. This led Linner *et al*[28] and later Fobi[22] to describe the importance of placement of a ring around the gastric pouch to define the outlet size, once and for all. Unfortunately restrictive rings and bands gained a very bad reputation during the time of vertical banded gastroplasty, and most surgeons were disinclined to use such a device in the context of gastric bypass because of concern regarding possible ring/band erosion. Our experience and that of Fobi was however quite different. Ring erosion is a very infrequent occurrence and in our experience of over 1400 operations has never been seen except in the context of gastric ulceration. Further, again in our experience, gastric ulceration is largely related to staple-line disruption (gastro-gastric fistula)[17,21] or NSAID usage. As practiced in the setting of Fobi Pouch gastric bypass we have never seen a ring erosion in over 1000 operations carried out since 1997. Recent reports from others concur with this experience[29]. We however do emphasise that the ring should fit loosely around the gastric pouch rather than create a constriction around the pouch. This is likely to be the defining difference between the ring of the Fobi Pouch and the ring/band placed on a gastroplasty, which undoubtedly was more prone to erosion. Placement of a ring/band around the gastric pouch certainly contributes to the restriction and the nature of food that can be tolerated. The recommended ring size in the Fobi Pouch gastric bypass setting is 6.5 cm length[30] which gives an outside maximum diameter of the pouch of 1.9 cm. That such a ring should sit loosely around the gastric pouch as shown in Figure 4 demonstrates the narrow nature of the pouch formed.

There is now a growing recognition of the role played by the ring in weight loss maintenance[29-33], and surgeons undertaking gastric bypass are being encouraged to place

a ring for this reason. In a non randomised study recently reported by Awad *et al*[29] they compared the weight loss in their hands of 260 patients who underwent gastric bypass with a band and 218 patients who underwent the same gastric bypass but without a band. Percentage excess weight loss was equivalent for the first 24-36 mo and thereafter the %EWL was superior in the banded group. Weight loss was maintained through to 10 years in the banded group and by 7 years there was almost a 20% EWL difference between the banded and non banded groups, which difference was them maintained.

LENGTH OF ROUX LOOP

There remains a view held by some that the length of the biliary and alimentary limbs of the Roux loop are of importance. There is little evidence that this is the case. It is true that the length of the alimentary limb may determine the degree of malabsorption that occurs following the operation, however, unless this is extreme the degree to which this augments weight loss, and the degree to which such a contribution is durable is highly variable and unpredictable[34,35] because of adaptation occurring within the common channel of small bowel. In our opinion the length of the biliary limb should simply be determined by the convenience of the point for mesenteric division, such that the loop passes without tension to be anastomosed to the stomach. This is commonly in the vicinity of 50-60 cm from the duodeno-jejunal flexure. There is little reason to extend the length of the alimentary limb beyond 75 cm, which is quite sufficient to prevent bilio-pancreatic secretion reflux into the gastric pouch. Lengths in excess of half the small bowel, risk conferring troublesome diarrhoea, and should not be necessary in the vast majority of circumstances.

COMMENTARY ON LAPAROSCOPIC GASTRIC BYPASS

The ability to undertake gastric bypass laparoscopically, as opposed to by open surgery, clearly confers advantage in terms of hospital stay and recovery time. This has been well shown in a number of comparative studies which have only ever examined short-medium term weight loss, recovery time and complications. While rates of serious complications are similar, the specifics of the complications are different and weight loss in the first 1-5 years has been comparable[36-38]. However, the more important and meaningful comparison needs to be between standard gastric bypass (laparoscopic or open) and Fobi Pouch gastric bypass, as was made in the systematic review of O'Brien *et al*[10]. While randomised data on this point is scant, both this[39] and non-randomised data certainly point to the advantage of including a ring[29].

We believe that the majority of surgeons performing laparoscopic gastric bypass make the gastric pouch too short, too wide and without a ring to dictate the size of the gastric outlet. This lends itself perfectly to pouch dilatation, outlet enlargement and enhanced gastric emptying. The way in which laparoscopic staplers are used to create the pouch and particularly the way in which the anastomosis is performed using staplers (circular or linear)[25] is in large measure to blame. A long narrow pouch can certainly be performed with existing staplers, but an anastomosis between the Roux loop and a gastric pouch of no more than 1cm diameter dictates that a hand-sewn anastomosis be performed. This is a challenge for many surgeons, but should be regarded as the goal. A ring can undoubtedly be added with relative ease, particularly using the now commercially available devices such as the GaBP Ring®[33].

SUMMARY OF RECOMMENDATIONS

The superiority of the medium and long-term weight loss of the Fobi Pouch gastric bypass over more standard forms of gastric bypass, whether performed open or laparoscopically, provides the basis for the opinion and hypothesis expressed in this paper. We propose that for optimum reliability and sustainability in terms of weight loss a gastric bypass should include the following: (1) a vertical pouch of approximately 1 cm diameter, approximately 7-8 cm in length, originating close to the angle of His; (2) a transected stomach with interposition of a small bowel loop between staple lines; (3) a loose fitting silastic rubber ring of 6.5 cm circumference placed approximately 1cm proximal to the gastro-jejunal anastomosis; and (4) an alimentary limb length to the Roux loop of 75-100 cm.

At the present time, few if any of these suggestions have been reliably settled through thorough randomised prospective study. However, support for the comments from uncontrolled clinical experience and the systematic review reported by O'Brien *et al*[10] in 2006 does exist. It is common to see significant late weight regain after standard gastric bypass as demonstrated in the systematic review of O'Brien *et al*[10] and unfortunately some individuals regain all the weight they lost. This is most often attributable to pouch enlargement or rapid gastric pouch emptying, neither of which seem to occur after Fobi Pouch Gastric bypass. In my own experience of over 1000 Fobi Pouch gastric bypass operations, performed since 1997, we have never seen significant weight regain from technical failure due to pouch enlargement, gastro-gastric fistula or gastric outlet enlargement. We have never seen a single individual regain all of the weight lost, and we have never performed a revision procedure because of inadequate weight loss. The only individuals who have regained significant weight (usually no more than 50% of expected weight loss), have done so because of poor food choices or grazing throughout the day. This number represents 5%-10% of those who have undergone the surgery. With the 6.5 cm circumference silastic ring, we have reported removal of the ring in 1.8% of instances, because of severe intolerance to food with very frequent and troublesome regurgitation[30]. When this has

been done, some weight regain has been universal, and longer term control of weight has been compromised.

CONCLUSION

A great deal has been learned by those practicing bariatric surgery from the early days of gastric bypass. The challenge for today's surgeons is to embrace these lessons and test them, if they feel so inclined. There need not be such a thing as a technical failure following gastric bypass - but there will continue to be, if we ignore the lessons learned from the past. Gastric bypass is a thoroughly reliable procedure, when performed well. The success and durability of the weight loss achieved depends on the details of the operation performed. Not all gastric bypasses are the same - make your next one, a good one!

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REVIEW

Recent advances in the management of hemorrhoids

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Abstract

Hemorrhoids are considered one of the most common anorectal diseases with a prevalence of 4.4% up to 36.4% of the general population, and a peak incidence between 45 and 65 years. Hemorrhoidal disease presents with a prolapsed lump, painless bleeding, discomfort, discharge, hygiene problems, soiling, and pruritus. Sliding anal canal lining theory is the most accepted theory as a cause of hemorrhoidal disease; however, it is also associated with hyper-vascularity, and, recently, with several enzymes or mediators involved in the disintegration of the tissues supporting the anal cushions, such as matrix metalloproteinase. A comprehensive search in published English-language literature till 2013 involving hemorrhoids was performed to construct this review article, which discusses advances in the management of hemorrhoids. This includes conservative treatment (life style modification, oral medications, and topical treatment), office procedures (rubber band ligation, injection sclerotherapy, infrared and radiofrequency coagulation, bipolar diathermy and direct-current electrotherapy, cryosurgery, and laser therapy), as well as surgical procedures including diathermy hemorrhoidectomy, LigaSure hemorrhoidectomy, Harmonic scalpel hemorrhoidectomy, hemorrhoidal artery ligation, stapled hemorrhoidopexy (SH), and double SH. Results, merits and demerits of the different modalities of treatment of hemorrhoids are presented, in addition to the cost of the recent innovations.

Key words: Hemorrhoids; Rubber band; Infrared; Photocoagulation; Cryosurgery; LigaSure; Harmonic; Anopexy; Hemorrhoidal artery ligation; Stapled hemorrhoidopexy

Core tip: Patients with Grades Ⅰ-Ⅱ hemorrhoids can be treated with medical treatment or office procedures. For Grades Ⅲ-Ⅳ, surgical treatment should be offered and individually tailored to each patient. Conventional hemorrhoidectomy is the gold-standard, albeit with severe post-operative pain. LigaSure and harmonic scalpel hemorrhoidectomy offer shorter operative time, less post-operative pain and less time off work. Stapled hemorrhoidopexy provides similar results. However, though rare, devastating complications may occur, and so, should be performed only by experienced surgeons. Hemorrhoidal artery ligation is a potential non-excisional technique for the treatment of Grades Ⅱ-Ⅲ hemorrhoids with minimal postoperative pain and quick recovery.

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INTRODUCTION

Hemorrhoids are one of the most common anorectal disorders with a reported prevalence of 4.4% up to 36.4% of general population[1]. The peak prevalence occurs between 45 and 65 years of age[2,3]. Approximately one-third of patients affected by hemorrhoids seeks medical advise[4,5]. Different studies showed that about 5%-10% of patients suffering from hemorrhoids do not respond to conservative treatments, so surgical procedures become the treatment of choice in such cases[6].

LITERATURE SEARCH

A comprehensive search in the literature for English-language articles dealing with hemorrhoids published till 2013 was performed. The Databases searched included MEDLINE, preMEDLINE, the Cochrane Database of Systematic Reviews, meta-analysis, and the Cochrane Database of Registry of Controlled Trials. Additional appropriate references were also retrieved from the bibliographies of selected recent articles.

CLINICAL PICTURE AND CLASSIFICATION

Hemorrhoids are presented clinically by a prolapsed lump which may require manual reduction or is constantly prolapsed. Other clinical manifestations include painless bleeding, discomfort, discharge, hygiene problems, soiling, and pruritus[7-9].

Hemorrhoids can be classified according to their location and degree of prolapse. Internal hemorrhoids are located above the dentate line and covered by columnar epithelium. On the other hand, external hemorrhoids, are located below the dentate line and covered with squamous epithelium. Mixed hemorrhoids are known as "interno-external" hemorrhoids and are located both above and below the dentate line[10].

Internal hemorrhoids are further graded according to Goligher's classification which depends on the degree of prolapse into: (1) Grade Ⅰ hemorrhoids: Anal cushions bleed without prolapse; (2) Grade Ⅱ hemorrhoids: Anal cushions prolapse on straining but reduce spontaneously; (3) Grade Ⅲ hemorrhoids: Anal cushions prolapse on straining or exertion and require manual reduction; and (4) Grade Ⅳ hemorrhoids: The prolapse is irreducible and remains out all the time[11].

PATHOGENESIS

Although hemorrhoidal cushions are normal anatomic structures, they are infrequently referred to until issues arise, and then the term hemorrhoid is meant as a pathologic process. The pathogenesis of hemorrhoids is not completely clear[12]. Aigner *et al*[13,14], concluded that there is an association between hypervascularization and the incidence of hemorrhoidal disease as they reported that the terminal branches of the superior hemorrhoidal artery in patients with hemorrhoidal disease had a significantly larger diameter and greater blood flow, as well as higher peak velocity and acceleration velocity, when compared to those of healthy controls.

However, the sliding anal canal lining theory, which is the most accepted theory, stated that hemorrhoidal disease develops upon disintegration of the supporting tissues of anal cushions leading to their downward displacement. A number of possible contributing factors leading to migration of the hemorrhoidal cushions have been suggested, including lack of dietary fiber, prolonged straining, spending excess time on the commode, constipation, diarrhea, pregnancy, sedentary lifestyle, and a family history. Apart from pregnancy, none of these etiologies are supported by good evidence[15-17].

Recent studies examined the role of several enzymes or mediators which may be involved in the degradation of supporting tissues in the anal cushions like matrix metalloproteinase, which was found to be over-expressed in hemorrhoids. Since the discovery of increased microvascular density in hemorrhoidal tissue, neovascularization has been suggested as an important phenomenon in the pathogenesis of hemorrhoidal disease[18,19].

TREATMENT OF GRADE I AND GRADE II HEMORRHOIDS

Conservative treatment

Life style modification: The first item of conservative treatment of hemorrhoid is to modify life style so that the patient can avoid prolonged straining mainly by decrease formation of hard stool, which can be achieved by increasing the intake of dietary fiber and oral fluids. Other factors that may help to decrease straining include improving anal hygiene, avoiding unnecessary straining and medications, which cause either constipation or diarrhea[20-22].

Oral medications: The role of the drugs in management of hemorrhoids is either a defensive treatment for early grades where prolapse is not significant, or as a primary control of the acute bleeding till definitive office procedures or surgery can be done. Micronized Purified Flavonoid Fraction is composed of 90% Diosmin and 10% Hesperidin, and has demonstrated efficacy in the treatment of hemorrhoids. Although it has a phlebotonic activity, vasculo-protective effects, and antagonism of the biochemical mediators of inflammation, its precise mechanism of action remains unclear. Although flavonoid is the most commonly used drug for treatment of hemorrhoid, a meta-analysis of 14 randomized clinical trials (RCTs) regarding the role of flavonoids in the treatment of hemorrhoidal disease concluded that limitations in methodological quality, heterogeneity and potential publication bias raise questions about the apparent beneficial effects of flavonoids in the treatment of hemorrhoidal disease[23-28]. Another venotonic drug is Calcium Dobesilate. It improves the response of symptomatic acute attacks of first- and second-degree internal hemorrhoids when added to life style modification[29,30].

Topical treatment: Chong *et al*[26] noted that well-designed studies have found no evidence to support the use of any of the myriad of over-the-counter topical preparations that contain low-dose local anesthetics, corticosteroids, keratolytics, protectants, or antiseptics. These agents are widely used to relieve symptoms; however, their long-term use, particularly steroid preparations, may be detrimental and should be discouraged.

Office procedures

According to ASCRS Guidelines for Management of Hemorrhoids (2010), there is a strong recommendation based on moderate-quality evidence 1B that early grades including grade Ⅰ, Ⅱ and even Ⅲ that do not respond to conservative treatment can be managed with office procedures, which aim to decrease blood flow to the hemorrhoid, reduce the redundant tissue and fix the hemorrhoid to the underlying tissue to reduce prolapse. Office procedures include the following: (1) rubber band ligation (RBL); (2) sclerotherapy; (3) infrared coagulation; (4) radiofrequency coagulation; (5) bipolar diathermy and direct-current electrotherapy; (6) cryosurgery; and (7) laser therapy. Although these procedures are all relatively well tolerated and cause minimal pain, they have variable rates of recurrence. A meta-analysis of 18 randomized trials showed that RBL is the most effective of all office procedures as it is associated with a lower rate of recurrence, albeit with a more overall pain than other procedures[31].

RBL: RBL is the most commonly used office procedure in treating not only first- and second-degree hemorrhoids, but also selected cases with third-degree hemorrhoids. It represents about 80% of the office procedure with a successes rate of 99% on short-term and 80% on long-term follow-up, and a low complication rate ranging from 1% to 3%. The banding process causes necrosis and sloughing of the banded tissue resulting in an inflammatory reaction that causes refixation of the mucosa and elimination of the hemorrhoidal prolapse. A single hemorrhoid or multiple hemorrhoids may be treated with RBL per session. In one study, multiple ligations per session were reported to have more vagal symptoms, more post-procedural pain, and a higher rate of recurrence. However, no increase in complications with multiple ligations was reported in other large series. The cause of intra- or post-procedural pain, which is rare, has been attributed to strangulation of the anoderm, inflammation and edema[32,33]. Nazir *et al*[34], in their study of 1500 patients with 2nd and 3rd degree hemorrhoids, found a significant increase of post-procedural pain when using multiple ligations in one session, which was also associated with increased incidence of spasm of the anal sphincter. In agreement with this, Mattana *et al*[35], reported that, compared with multiple ligations, single RBL in one sitting was followed by a lower complication rate including pain. They also reported a significantly lower recurrence rate noted in patients with normal bowel habits, when compared with constipated subjects whose symptoms recurred in 85% probably due to prolonged straining. Thus, constipation may be considered a predictable factor for the outcome of RBL In such cases, the rubber band may be removed. Other complications of RBL include late hemorrhage, thrombosed external hemorrhoid, ulceration, rubber band slippage, pelvic sepsis, and, though rare, Fournier's gangrene[32,33].

Banding should be avoided in patients with coagulation disorders, either intrinsic, such as those with thrombocytopenia, or acquired, as seen with antiplatelet therapy (Plavix), or anti-coagulated with warfarin (Coumadin), or heparin products, because it may lead to bleeding. Such patients may be treated by other procedures including sclerotherapy and infrared coagulation. Immunocompromised patients or those with some cardiac disease like prosthetic cardiac valves, congenital cardiac malformation, and valvular dysfunction need special preparation with prophylactic antibiotics to avoid sever septic complications[36].

Banding can be performed with a suction apparatus or a forceps ligator. Flexible endoscope used for banding allowed better visibility and yielded comparable results, albeit with increased time and cost and a higher incidence of pain[37-43]. In a systematic review of RCTs comparing RBL with excisional hemorrhoidectomy[31], the authors reported that hemorrhoidectomy has a better long-term efficacy for the treatment of third-degree hemorrhoids than RBL, but at the expense of more post-operative pain, a higher rate of complications, and more time required to return back to normal physical activity.

Injection sclerotherapy: Injection sclerotherapy has been used long ago for treatment of bleeding hemorrhoids. Several materials including Ethanolamine Oleate, 5% Phenol in Almond oil, Sodium Tetradecyl Phosphate, and Sodium Morrhuate have been used as sclerosant that obliterates the hemorrhoid vascularity and induces inflammation, which ends with fibrosis that fixes the hemorrhoids to the surrounding tissue. After injection sclerotherapy, the patient requires only mild analgesics. Proper education regarding the appropriate diet, bulking agents and stool softeners as well as sitz baths should also be provided to the patient.

Complications of this procedure include mainly anorectal abscess and other rare complications, which may be fatal like necrotizing fasciitis, retroperitoneal sepsis, oleogranuloma (with oil-containing solutions), and pulmonary allergic reaction. Some studies found that these complications can be reduced with keeping good results by using more physiological agents such as hypertonic saline and 50% dextrose[44-47]. Concomitant anal diseases such as fistulas, tumors, anal fissures, and skin tags are a contraindication to treatment with sclerotherapy. Numerous studies that compared different treatment modalities for hemorrhoids showed that sclerotherapy seems to be a less effective option[48,49].

Infrared coagulation: Infrared coagulation depends on applying a flat tip probe proximal to the hemorrhoidal tissue, not the hemorrhoid itself, giving three to four pulses of infrared energy to the normal mucosa to cause tissue destruction, protein coagulation, and inflammation, which then leads to scarring and tissue fixation. This procedure may need several visits at monthly intervals as only one section of the hemorrhoids is treated per visit. Advantages of infrared coagulation include being quick, painless, effective with a low rate of complications, and

with a rapid return to work[50-53]. Two RCTs reported success rates of 67% and 96% of this procedure[54,55]. A meta-analysis of 5 clinical trials evaluated the results of 862 patients presenting with grades I and to II hemorrhoids and treated with 3 different modalities; namely, infrared coagulation, RBL, or sclerotherapy. Although RBL showed the best long-term efficacy, it had a significantly higher incidence of post-procedural pain. The authors considered infrared coagulation the most appropriate procedure for the management of grades I and II hemorrhoids[49].

Radiofrequency coagulation: The radiofrequency coagulation unit uses a disposable probe with an electrical current flowing between two flat electrodes (positive and negative) aligned at the tip, activating the unit for two seconds in three or four areas of hemorrhoid complex. This method results in reduction and subsequent fixation of the vascular components of the hemorrhoids to the underlying tissue by means of fibrosis. Acute urinary retention, wound sepsis, and peri-anal thrombosis are the most frequent complications reported after radiofrequency coagulation. Although it is a painless procedure, yet, it has been reported to have a higher recurrence rate of both bleeding and hemorrhoidal prolapse[52,56,57].

Bipolar diathermy and direct-current electrotherapy: Bipolar diathermy and direct-current electrotherapy use local heat application to induce coagulation and fibrosis that results in hemorrhoidal fixation. The success rates of both methods have been reported by several studies to be comparable to those of infrared coagulation, and to have a relatively low rate of complications[55,58].

Cryosurgery: Cryosurgery uses very low temperature to create water crystals within the cells resulting in destruction of the cell membrane and eventually the tissue. It was expected that cryosurgery will lead to less pain by freezing the sensory nerve endings and causing an immediate anesthetic effect, but clinical results have proved the opposite[59]. In addition to being a lengthy procedure, other disadvantages included profuse discharge, prolonged recovery, and late return to work. Thus, cryosurgery does not seem offer the patient with hemorrhoidal disease any advantages over other treatment options[5]. There are no recent publications in the literature assessing cryosurgery as a treatment option for hemorrhoidal disease.

Laser therapy: The Nd:YAG laser was first utilized in anorectal surgery in the 1960s. Senagore *et al*[60], in their study on 86 patients, concluded that there are no patient care advantages associated with the use of the Nd:YAG laser for excisional hemorrhoidectomy compared with scalpel excision. However, outcomes have improved later with the advent of the CO_2 laser and the development of the pulsed and the scanned laser[61,62]. Plapler *et al*[63], in their study of 350 patients treated with CO_2 laser open hemorrhoidectomy reported that laser therapy resulted in less postoperative pain and a better cosmetic scar when compared with conventional surgery. Similar results were also reported by Zahir *et al*[64] in 2000 on 50 patients. Plapler *et al*[65], studied 15 patients who underwent intra-hemorrhoidal laser therapy for grades Ⅱ and Ⅲ hemorrhoids, and reported that partial to complete resolution was associated with little pain and a shorter time as compared to open hemorrhoidectomy.

Giamundo *et al*[66], in 2010, used Doppler-guided hemorrhoidal laser for thermal occlusion of the hemorrhoidal arteries and reported that, at their institution, the total cost of the hemorrhoidal laser procedure is Eur700 per patient. These figures included the cost of the disposables, the fees of the health care workers, and the office occupancy. They also reported that the cost of EBL is approximately Eur230 per patient; however, without taking into consideration the potential need for multiple sessions per patient.

TREATMENT OF GRADE III AND GRADE IV HEMORRHOIDS

Standard treatment (Conventional hemorrhoidectomy)

Although some studies reported that RBL is a safe and effective method compared to open technique in third-degree symptomatic hemorrhoids[67], it is stated in the revised practice parameters for the management of piles that patients with grades Ⅲ-Ⅳ hemorrhoids should receive surgical treatment[68].

Excisional hemorrhoidectomy is considered to be the most effective treatment modality for hemorrhoids with the lowest recurrence rate as compared to other modalities; however, the main drawbacks are the marked post-operative pain and the highest complication rate[48]. Worldwide, the open (Milligan-Morgan) and closed (Ferguson) hemorrhoidectomy are the most commonly used procedures.

Post-operative pain is the most distressing concern for the patient after hemorrhoidectomy and may lead to delay of surgical treatment. Post-operative pain may results from sphincter spasm, damage to nerve endings, insertion of hemostatic gauzes and damage to the mucosa. Some authors attribute pain to suture at the pedicle. Many studies have evaluated various analgesic regimens, operative techniques, and surgical instruments to address this important issue[69-76]. A systematic review of the topical drugs used for alleviation of post-hemorrhoidectomy pain included collected data from 24 relevant studies, between 1966 and 2012. The topical preparations used included Botulinum toxin, Calcium Channel Blockers, Glyceryl Trinitrate (GTN), local anesthetics, Metronidazole, Opioids, and Sucralfate. Overall, topical preparations showed encouraging results in reducing pain and analgesic use and improving the wound after hemorrhoidectomy[74]. Currently, the most common methods used to decrease post-hemorrhoidectomy pain include the application of GNT at the site of the wound, or injection of Botulinum toxin into the internal sphincter, or even internal sphincterotomy[74].

Other postoperative complications have been reported after hemorrhoidectomy and include acute retention of urine, postoperative bleeding, sepsis, delayed healing or non-healing of the wound, mucosa prolapse, and anal stricture. The most troublesome complication, fecal incontinence, has been reported to occur in 2%-12% of patients[75-83].

Diathermy hemorrhoidectomy

With diathermy hemorrhoidectomy, coagulation occurs at temperatures higher than 150 ℃. This results in the formation of an eschar that seals the bleeding area. Compared with conventional hemorrhoidectomy (CH), diathermy hemorrhoidectomy has been shown to be associated with less bleeding, shorter operating time and lower postoperative analgesic requirement, but with similar post-operative pain[84].

LigaSure hemorrhoidectomy

The LigaSure vessel sealing system® (Valleylab, Tyco Health Care Group) is a relatively recent method that uses a bipolar electrothermal device for without the need for sutures, *i.e.*, sutureless hemorrhoidectomy. It aims at avoiding painful diathermy burns in the richly innervated anal canal and allowing better tissue adhesions at the wound site, thus decreasing the incidence of postoperative hemorrhage. In a meta-analysis of articles published between January 2000 and September 2009, and RCTs showed superiority of LigaSure hemorrhoidectomy (LH) versus CH regarding operation time, the incidence of postoperative pain and urinary retention, as well as the time required to resume normal physical activity[85-87]. Although Gentile *et al*[88], reported that the additional cost of the disposable device (approximately Eur230) is balanced by a shorter operative time, the possibility of a day-case surgery, and an earlier return to work, They, however, admitted that a limitation of their study can be identified in the small size of the sample and the limited follow-up, and concluded that the benefits of LigaSure as a low-pain and long-term effective technique need to be further evaluated in larger series.

Harmonic scalpel hemorrhoidectomy

The harmonic scalpel® (Johnson and Johnson Medical KK, Ethicon Endo-Surgery, Cincinnati, OH) is an ultrasonically-activated instrument, which vibrates at a rate of 55000 MHz per second. It is known for its ability to coagulate small- and medium-sized vessels by converting electrical energy to a mechanical one. There is less lateral thermal damage, with no passage of electricity to or through the patient, resulting in greater safety for the patient.

There have been several randomized trials to date comparing harmonic scalpel hemorrhoidectomy (HSH) with other various open and closed techniques and the results were inconstant. Some studies showed clear-cut benefit of HSH with respect to operative time, blood loss, postoperative pain, length of hospital stay, and return to normal activity[89-92], whereas others showed no advantages, with even increased cost[89].

Semi-closed hemorrhoidectomy

The technique of Reis Neto involves the pectineal line repair, in which the internal hemorrhoid is forced outwards, becoming fully exposed; and then for the repair of rectal mucosa, in the upper limit of the internal hemorrhoid; three or four full-thickness sutures are made radially, involving the mucosa and submucosa, along the craniocaudal length of the hemorrhoid to be resected. The mucosa and submucosa are cut between the ligations; the external part of the skin plexus is removed until the pectineal line with a V-shaped incision or a racket incision with an external base. This technique is perfect for voluminous and proximally extended internal hemorrhoids, whose full dissection would cause a very high resection of the rectal mucosa[93].

Submucosal hemorrhoidectomy (technique of parks)

This procedure was developed by Parks[94], who published results and details of the technique in 1956. It was designed to reduce postoperative pain and avoid anal and rectal stenosis. It is indicated for second- to fourth-degree hemorrhoids. This technique includes hemorrhoidectomy with preservation of the anal canal mucosa, reducing the surgical wound dimensions and leading to a shorter healing time, as well as lower stenosis index than those with conventional techniques. The surgery starts with the application of Parks retractor and injection of adrenaline solution at the dilution of 1:250000 to reduce bleeding. A Y-shaped incision is then made at the mucocutaneous junction, between the upper mucosa of the anal canal and the anorectal junction, as an inverted racket incision. The vascular pedicle is separated from the mucosa and the sphincter plane, connecting it afterwards. The mucosa is then closed with running suture, leaving a small area open in the perianal region for drainage. The largest series with this technique (1315 patients) was reported by Milito *et al*[95], who reported 82 cases with recurrence (7%), 75 cases of anal skin tag (6.5%), 19 cases of anal stenosis (1.6%), 36 cases of gas incontinence (3.2%). The fact that the mucosa is not included in the ligation leads to reduced postoperative pain. However, the surgical time is longer, the recurrence rate is higher and it involves greater risk of bleeding during the surgery and postoperatively.

Hemorrhoidal artery ligation

Hemorrhoidal artery ligation (HAL) with or without anopexy is a non-excisional procedure aiming at reduction of symptoms of hemorrhoidal disease by reducing the blood flow to the hemorrhoids. Localization of the hemorrhoidal arteries may facilitated by using the Doppler probe; however, this increases the cost of the procedure[96].

A systematic review of 17 studies on 1996 patients with hemorrhoidal disease treated with HAL showed

recurrence of bleeding and prolapse in 6.3% and 7.8% of patients respectively, in 9 studies with a follow-up of less than 1 year, and 9.7% and 10.8% respectively, in the remaining 8 studies with a follow-up of 1 year or more. Out of 17 studies in this systematic review only one study performed also anopexy, which may explain this high rate of recurrence[96]. Excision of skin tags (external piles) may be associated with HAL, with an increase in success rate albeit with a slight increase of complication rate[97,98].

The incidence of reported complications included fever in 3.9% of patients (15/383), thrombosed hemorrhoids in 1.8% (25/1386), anal fissure in 0.8% (14/1695), urinary retention in 0.7% (10/1468), incontinence in 0.4% (3/693), anal fistulas in 0.4% (3/815), and stool retention in 0.1% (1/711). The study stated that bleeding requiring blood transfusion occurred in only three patients[96].

Although this report stated that no studies compared HAL versus sclerotherapy, HAL versus RBL, or HAL performed with versus without Doppler guidance, it concluded that HAL appears to be a potential non-excisional procedure for the treatment of grades Ⅱ and Ⅲ hemorrhoids with minimal postoperative pain and rapid recovery[96].

Giamundo *et al*[66], in 2010, reported that, at their institution, the total cost of HAL is Eur1900 (approximately US$ 2400). This included the cost of one-day hospital admission, as well as the costs of anesthesia, consumables during surgery and operating theatre occupancy.

Farag procedure

There are several methods to ligate hemorrhoidal artery without Doppler guidance like pile suture which is a simple method (introduced by Farag[99] in 1978) in which three interrupted sutures are used to interrupt the blood flow to the prolapsed hemorrhoids. The first suture is passed through the mucosa at the proximal end of the internal hemorrhoids to occlude the superior rectal vessels. The second suture is passed into the distal end of the internal hemorrhoids above the pectinate line to interrupt the connection between the internal and external hemorrhoidal plexuses. A third suture is then introduced between the previous two. However, this technique and its modifications, were not widely accepted because of the initial painful congestion that resulted from interruption of the blood flow to the hemorrhoidal cushions, though it was followed by gradual shrinkage of the prolapsed piles.

Anopexy

Anopexy is a simple technique for the treatment of advanced hemorrhoidal disease. It results in control of bleeding, reduction hemorrhoidal prolapse and fixation of the hemorrhoid cushions to the underlying tissues. This technique is based on two facts, namely: (1) constant anatomical location of the hemorrhoidal vessels such that a stitch placed at the base of the hemorrhoidal cushion significantly reduces the blood flow to the hemorrhoidal plexus; and (2) development of the hemorrhoids upon disintegration of the tissues supporting the anal cushions leading to their downward displacement (sliding anal canal lining theory). This can be corrected by fixation of the hemorrhoidal cushions to the underlying internal sphincter[100].

Several names have been coined to this procedure including "pile suture", "suture ligation", "obliterative suture technique", "ligation and anopexy", and ligation and mucopexy[99-102].

Stapled hemorrhoidopexy

In 1998, Longo[103] proposed the use of a specially designed circular stapler (Ethicon Endo-Surgery, Inc) for treatment of grade Ⅲ and grade Ⅳ hemorrhoids. Stapled hemorrhoidopexy (SH) (also named procedure for prolapse and hemorrhoids) aims at reducing the hemorrhoidal prolapse by excising a complete ring of mucosa above the dentate line and fixing the hemorrhoids to the distal rectal muscular wall leading to repositioning the hemorrhoids into the anal canal. This technique also involves transecting the superior hemorrhoidal arteries, which reduces the venous engorgement by transection of the feeding arteries resulting in reduction of the size of the hemorrhoids. The main advantages of this procedure is the absence of perianal wounds and the reduction of pain as compared to CH, since the stapled mucosa anastomosis in the rectum is performed at least 3 cm above the dentate line, where sensitive receptors are few[104,105].

Burch *et al*[106], in a systematic review and economic evaluation, searched databases up to July 2006 and reviewed 27 RCTs that compared SH with CH technique in patients with prolapsing hemorrhoids for whom surgery is considered a relevant option. They concluded that SH was associated with less postoperative pain albeit with an increased rate of prolapse (residual or in the long-term), and reintervention. The two techniques were similar regarding the rate and type of complications, but the rates of recurrence and reintervention for both techniques are still uncertain.

Jinn *et al*[85], in a systematic review and meta-analysis, concluded that advantages of SH over CH are a shorter operation time, less postoperative pain and urinary retention, and a faster return to normal physical activity. Despite the several short-term benefits of SH, the long-term outcome is relatively poor when compared with CH, mainly regarding residual skin tags and recurrent prolapse[107]. With SH, the persistence of hemorrhoids causes recurrence of symptoms in the long-term up to five times more than after CH. Accordingly, SH is not advisable for patients with symptomatic external hemorrhoids as skin tags and enlarged external hemorrhoids are not removed[104].

Recently, a systematic review, a Cochrane meta-analysis and the practice parameters of the American Society of Colon and Rectal Surgeons[4,108,109] mentioned the rare incidence of devastating complications after SH. Although the most recent systematic review attributed all

major complications to surgical errors, they remain a major life-threatening[110]. In fact, several deaths have been reported[111]. These complications included rectal bleeding (1%-11%), and recto-vaginal fistula (0.2%, 1/449)[112]. Complete rectal obliteration has been reported after SH. It may result from erroneous placement of a purse string, or to firing the stapler outside the purse string in a blind pocket from redundant rectal mucosa[113]. Post-SH complications included also retro-rectal hematoma[114], retro-pneumoperitoneum and pneumo-mediastinum[115] that may result from either filtration of air through the staple line to the extra-peritoneal space or bacterial leakage causing pelvic sepsis and requiring a diverting stoma. Rectal perforation, pelvic sepsis, rectal hematoma leading to intestinal obstruction and other life-threatening complications were also reported after SH[116].

Other minor complications include residual skin tags, thrombosed piles, fecal impaction, proctitis, anal fissure, stricture, local abscess and fistula formation. Severe chronic proctalgia after SH is rarely reported and is either post-defecatory or accompanied by urgency[117,118].

In a systematic review, Giordano *et al*[119] concluded that SH is a safe technique for the treatment of hemorrhoids but carries a significantly higher incidence of recurrences and additional operations compared with CH. This is also confirmed by the reports of Tjandra *et al*[110] and Jayaraman *et al*[112]. In order to decrease the rate of recurrence after SH, a modified technique was introduced by using double stapled hemorrhoidopexy for huge degree of prolapse. However, this technique depends on intra operative assessment to select patients that may get benefit from this modification[120,121].

Regarding the cost of SH, Vito *et al*[122] reported that SH is more expensive than CH because of the cost of the stapler device, which is not offset by other costs such as operation time, shorter hospital stay, and earlier resumption of normal activities. Ho *et al*[123], in a study on total of 119 consecutive patients with prolapsed irreducible hemorrhoids found that with conventional open diathermy technique, patients resumed work later (mean 22.9 d *vs* 17.1 d), but the total costs incurred were less ($921.17 *vs* $1283.09).

Since SH does not remove the source of infection, it is contraindicated in presence of anal abscess or gangrene. Also, since the insertion of a circular anal dilator is essential during SH, anal stenosis is another contraindication to the procedure. Complete rectal prolapse is also considered a contraindication, because it is not adequately treated with SH.

CONCLUSION

Hemorrhoidal disease is one of the most common ano-rectal conditions. Non-operative measures, whether medical treatment or office procedures, can be offered to patients with Grade I and Grade II hemorrhoids. However, when these measures fail, surgical treatment should be considered. For patients with Grade III and Grade IV hemorrhoids, surgical treatment should be offered and tailored to each patient according to the severity of symptoms and the extent of external ano-rectal component, in addition to coexisting ano-rectal diseases. Currently, there are several surgical procedures available to treat prolapsing hemorrhoidal disease, and most of them yield similar success rates. CH, whether open or closed, is considered the gold-standard for surgical treatment of hemorrhoids, albeit with severe post-operative pain, especially with defecation. LH and harmonic scalpel hemorrhoidectomy seem to offer shorter operative time, less post-operative pain and less time off work as compared to CH. SH provides also less post-operative pain, shorter hospital stay and recovery time, and a complication rate generally comparable to that with CH. However, though rare, devastating complications have been reported with SH, so it should be only performed by experienced surgeons. HAL appears to be a potential non-excisional technique for the management of grades II and III hemorrhoids, with the advantages of minimal postoperative pain and quick recovery.

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