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EDITORIAL

Laparoscopic pancreatoduodenectomy: How far have we come and where are we headed?

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Abstract

Minimally invasive pancreatoduodenectomy is currently a feasible option in selected patients at high volume centers with available expertise. Although the procedure has been described two decades ago, laparoscopic surgeons have been reluctant to perform it since it is technically demanding. Currently there is no standardized training process for minimally invasive pancreatoduodenectomy and this is required to ensure the safety of the procedure. Even the open pancreatoduodenectomy can be a challenging procedure where the outcome depends much upon the patient volume and surgeon's experience. In the minimally invasive setting, all the current evidence comes from retrospective data with inherent selection bias. Although the proposed benefits have been reported in many series, a randomized trial comparing with the open approach is highly unlikely to happen, given the complexity of pancreatic cancer and patient selection for complex surgery. Rather, in a disease for which cure is an utopian statement, perhaps the ultimate aim of minimally invasive pancreatoduodenectomy can be the improvement in the quality of life. Also further studies are needed to assess the immunologic role affecting the oncologic outcomes in patients undergoing minimally invasive pancreatoduodenectomy. The robotic platforms have got easily accepted since they can overcome some of the limitations of the laparoscopic platforms such as limited range of motion, two dimensional visualization and poor ergonomics. The main limitations of robotic procedures are related to the high costs associated with the system and disposable equipment. Currently evidence is lacking regarding the cost effectiveness of the procedure and also the push from the industry is on rise. All these minimally invasive techniques have a long learning curve and prior extensive experience in hepatopancreatobiliary surgery is mandatory for surgeons embarking on these endeavours.

Key words: Laparoscopic pancreatoduodenectomy; Roboticpancreatoduodenectomy; Minimally invasive pancreatoduodenectomy

Core tip: This editorial while discussing the evidence and controversies surrounding minimally invasive pancreatoduodenectomy, aims to update the reader about the highest level of evidence accumulated over the past few years. Pancreatoduodenectomy remains a demanding procedure even in the open approach and only few surgeons in high volume centres have published the outcomes following minimally invasive pancreatoduodenectomy. All these reports are retrospective data with inherent problems related to bias. To settle this issue, any randomized trial is unlikely to happen given the complexity of the cancer and patient selection for surgery in a resectable cancer. All these issues have been addressed in this editorial so that the pros and cons of minimally invasive pancreatoduodenectomy have been well conveyed and the reader takes home a balanced message.

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HISTORY OF LAPAROSCOPIC PANCREATODUODENECTOMY

Ever since the first description of laparoscopic pancreatoduodenectomy (LPD) in 1994 by Gagner and Pomp[1], the procedure has remained a technically challenging one due to many reasons such as difficult access in laparoscopy, daunting task of controlling hemorrhage laparoscopically due to major vascular injury, demanding skills for biliary and pancreatic reconstruction and also the need to maintain oncologic principles. All these aspects require a high level of surgical expertise. While the safety and feasibility of the technique has been established somewhat, only few published series comprise more than 50 patients[2]. This procedure has been proposed to decrease blood loss, shorten hospital stay, expedite recovery and also shorten time to initiate adjuvant treatment. The ultimate aim of performing minimally invasive pancreatoduodenectomy (PD) should be to perform a better PD with lesser complications and with proven oncologic advantages[3]. Till date, majority of the reports which have shown comparable outcomes with laparoscopic approach are retrospective and they are inherently prone to selection and publication bias.

LPD: FEASIBILITY TO REFINEMENT

In an early experience, Palanivelu *et al*[4]reported the safety of this procedure in a series comprising of 42 patients and safe tumour free margins could be obtained in all patients (Table 1). In another series from Mayo clinic[5], 65 patients underwent LPD with comparable median operative time, blood loss and morbidity. They have shown that LPD has the same advantages which are seen with other minimally invasive procedures. In another review by Gumbs *et al*[6] comprising 285 cases of LPD, the rate of conversion to the open approach was 9% with a morbidity and mortality rate of 48% and 2%, respectively. They concluded that laparoscopic pancreatic head resections were feasible with low mortality rates and acceptable morbidity rates. During these early experiences, there was lack of long term follow-up data and also most were small series retrospectively comparing minimally invasive techniques with open techniques. As more and more experience has been gained in these complex procedures, there are reports where even major venous resections have been performed during LPD. In a cohort of 129 patients undergoing LPD, Kendrick *et al*[7] reported 11 major venous resections with a median operative time of 413 min and 500 mL blood loss without any perioperative mortality.

LPD *VS* OPEN PD: IS IT COMPARABLE OBJECTIVELY?

With increasing number of surgeons rapidly gaining experience in complex laparoscopic pancreatic techniques, a number of comparative studies have been recently published. In a retrospective series involving 51 consecutive patients who underwent either an open or LPD, Kuroki *et al*[8] found decreased blood loss in the laparoscopic assisted PD group compared with the open PD group without any significant difference in the postoperative complications. In another series by Asbun *et al*[3], 215 and 53 patients underwent open PD and LPD respectively. There were significant differences favouring LPD with respect to intraoperative blood loss, length of ICU stay and length of hospital stay (12.4 d *vs* 8 d). They also observed that the operative time was significantly longer in LPD group (608 min *vs* 401 min). However no significant differences were observed with respect to pancreatic fistula rate and delayed gastric emptying. Even though the complication rates were similar, the discrepancy in the length of hospital stay could not be explained and this raises the possibility of bias in outcome measurement commonly observed in retrospective studies. With respect to oncologic clearance, there was no difference in resection margin status. Lymph nodal clearance has been shown to be better with the LPD group (23.4 *vs* 16.8) as well as lower lymph node ratio (0.159 *vs* 0.241). In a retrospective series involving 905 patients undergoing PD, long term survival was better in patients with decreased lymph node ratio[9]. The better vision and magnification offered by the laparoscopy might aid in the better nodal clearance and aggressive lymphadenectomy. However further studies are needed to reach firm conclusions. The time to initiation of adjuvant chemotherapy was not affected by the minimally invasive technique and also

Table 1 Retrospective series showing outcomes following Laparoscopic Pancreatoduodenectomy

Ref.	No. of cases	R0 rate (%)	Mean operative time (min)	Mean node retrieval	Mean blood loss (mL)	Pancreatic fistula rate (%)	Overall morbidity (%)	Mortality (%)	Mean length of stay (d)
Asbun *et al*[3]	53	95	541	23	195	16.7	24	5.7	8
Kendrick *et al*[5]	62	89	368	15	240	18	42	1.6	7
Palanivelu *et al*[4]	42	100	370	13	65	7	NR	2	10
Croome *et al*[10]	108	78	379	21	492	11	5.6	1	6

NR: Near.

there were no reports of port site metastases. The main contraindications for minimally invasive PD included either major vascular involvement or patients with previous abdominal surgeries. The minimal blood loss associated with LPD could be explained by the precise dissection that could be possible due to the better clarity and magnification offered by the state of the art minimally invasive technology. In addition, human instinct is such that laparoscopic surgeons tend to be inherently extra careful with bleeding since any bleeding can greatly obscure telescopic vision. The conversion to open procedure was usually due to failure to progress or difficulty to control a hemorrhage[2].

ONCOLOGIC OUTCOMES: ANY BETTER?

In a retrospective series comprising 108 patients undergoing LPD and 214 patients undergoing open PD, Croome *et al*[10] reported the oncologic advantages over the open approaches. There was no significant difference in the incidence of pancreatic fistula in the LPD *vs* open group (11% *vs* 12%). The median time to initiate adjuvant therapy was 48 d in the laparoscopic group and 59 d in the open group. The authors also observed that a significant proportion (12%) of patients in the open PD group had a significant delay in the initiation of adjuvant chemotherapy when compared to the LPD group (5%). Again this observation is surprising given the fact that tumor size and pancreatic fistula rates between both groups were comparable. The overall survival among the two groups was not significantly different. However the progression free survival was in favour of the LPD group. On univariate analysis, significant predictors of survival included tumour size, positive margins, positive nodal status and those patients having delayed initiation of chemotherapy or no chemotherapy at all. Pertinently, with respect to chemotherapy, the recent ESPAC-3 study has shown that overall survival was better determined by the completion of all cycles of chemotherapy rather than the time of initiation as long as it was started within 12 wk[11].

EVOLUTION OF ROBOTIC PD–HAVE THINGS TRULY PROGRESSED FURTHER?

The well known and accepted advantages of robotic systems with improved 3-dimentional imaging, enhanced dexterity, better visualization with magnification and improved ergonomics fare better than the conventional laparoscopic platform in minimal access approaches[12]. There are a lot of interesting observations from the initial experience of using robotics for PD. Giulianotti *et al*[13] reported in 2010 the first series of 50 patients who underwent robotic assisted PD and showed the operative feasibility of this approach. Few investigators have compared robotic assisted PD with open PD. In the retrospective series reported by Chalikonda *et al*[14] comparing robotic assisted PD with open PD, the duration of surgery was significantly longer in the robotic group but the overall blood loss and the duration of hospital stay (9.79 d *vs* 13.26 d) were lower. Similar results were reported by Zhou *et al*[15] on a cohort of 16 patients, though the number was smaller. Based on these data, the robotic approach has been shown to be associated with faster recovery times but longer operative times. With regards to the oncologic outcomes, Zeh *et al*[16] have reported on 50 consecutive patients who underwent robotic assisted PD where the mean lymph node retrieval was 17 and the overall margin negative resection rate was 89%. Another Italian study has reported on 34 patients who underwent robotic PD without any conversion despite three patients requiring vascular reconstruction[17]. There were no reports of bile leaks and this has been attributed to the precision of robotic suturing in this retrospective study. Although the earlier series of robot assisted PD had documented conversion rates of upto 37%, this rate has decreased with increasing experience[18]. The associated decreased blood loss can have an impact in terms of cancer recurrence[19]. In a recent report by Wada *et al*[20], the use of surgical microscope during reconstruction has shown to decrease the incidence of pancreatic fistula. The precise fine movement in multiple axes as offered by the robotic technology along with its magnified 3-D visual has been claimed to reduce the incidence of fistulas following pancreatic reconstruction in robotic PD. In the Italian cohort[17], there were no clinically significant pancreatic fistulas even though the majority had soft pancreas and small ducts. Quite a significant amount of extra time gets utilized in instrument traffic (upto 1 h in the Italian series) and this necessitates the need for further technical improvisation in order to improve the effective utilization of operative room time. In another major series of 132 patients undergoing robotic PD, Zureikat

et al[21] have found the median operative time to be 527 ± 103 min and mortality rate of 1.5%. The conversion rate is equivalent or lower than the conversion rates observed in early series of LPD. They concluded that safety and feasibility metrics including the low incidence of conversion support the robustness of this platform with no extra risks apart from inherent risks of this new technology.

CHALLENGES FACING MINIMALLY INVASIVE PD

The minimally invasive approach has been propagated mainly for the advantage of lesser morbidity and reduced hospital stay thereby decreasing cost of treatment. Due to certain inherent disadvantages with LPD such as prolonged operating times, high cost and technical complexity as well as the low quality of evidences for its advantages, currently it may not be possible to recommend it as the standard of care[3]. While well conducted randomized trials have proven the advantages of laparoscopic resections in colonic cancer, the low prevalence of resectable pancreatic cancer, coupled with the complexity of the procedure and the challenges it faces, is likely to ensure that a adequately powered randomized trial is unlikely to happen in the near future[10]. Further, laparoscopic major venous resections can be endeavoured only with extensive laparoscopic experience in pancreatic resections and this demands a long learning curve in a high volume centre. The excess mean operative cost of robotic PD was up to 6193 Euros which is likely to be questioned in the current era[17]. In addition to various challenges mentioned above, cost is also expected to remain a major challenge for minimally invasive PD.

CONCLUSION

Minimally invasive PD is currently a feasible option in selected patients at high volume centers with available expertise. Although the procedure has been described two decades ago, laparoscopic surgeons have been reluctant to perform it since it is technically demanding. Currently there is no standardized training process for minimally invasive PD and this is needed to ensure the safety of the procedure. Even the open PD can be a challenging procedure where the outcome depends much upon the patient volume and surgeon's experience. Even for the open approach, the learning curve extends till the first 60 cases for improvement in measured outcomes[22]. Standardization and service reconfiguration has been shown to improve outcomes following open PD[23]. In the minimally invasive setting, all the current evidence unfortunately comes from retrospective data with obvious selection bias. Rather, in a disease for which cure is an utopian statement, perhaps the ultimate aim of minimally invasive PD can be the improvement in the quality of life. Further studies are needed to define its role concerning quality of life. The robotic platforms have got easily accepted since they can overcome some of the limitations of the laparoscopic platforms such as limited range of motion, two dimensional visualization and poor ergonomics. The main limitations of robotic procedures are related to the high costs associated with the system and disposable equipment. Currently evidence is lacking regarding the cost effectiveness of the procedure and also the push from the industry is on rise. Clearly, with increasing data in this era of information explosion, the surgical fraternity needs to evolve a consensus about minimally invasive PD.

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Operative considerations for rectovaginal fistulas

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Abstract

To describe the etiology, anatomy and pathophysiology of rectovaginal fistulas (RVFs); and to describe a systematic surgical approach to help achieve optimal outcomes. A current review of the literature was performed to identify the most up-to-date techniques and outcomes for repair of RVFs. RVFs present a difficult problem that is frustrating for patients and surgeons alike. Multiple trips to the operating room are generally needed to resolve the fistula, and the recurrence rate approaches 40% when considering all of the surgical options. At present, surgical options range from collagen plugs and endorectal advancement flaps to sphincter repairs or resection with colo-anal reconstruction. There are general principles that will allow the best chance for resolution of the fistula with the least morbidity to the patient. These principles include: resolving the sepsis, identifying the anatomy, starting with least invasive surgical options, and interposing healthy tissue for complex or recurrent fistulas.

Key words: Rectovaginal fistulas; Anovaginal fistulas

Core tip: There are general principles that will allow the best chance for resolution of a rectovaginal fistula with the least morbidity to the patient. Identifying and addressing the disease process that caused the fistula is critical, including medical management for Crohn's, and resolving inflammation or sepsis with a seton. Then the exact anatomy of the fistula should be defined to determine operative approaches. The operative algorithm should begin with fistula plugs and local advancement flaps, if these fail more invasive options such as diversion, and interposition of healthy tissue should be pursued for complex and recurrent fistulas.

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INTRODUCTION

Rectovaginal fistula (RVF) is an epithelial lined tract between the rectum and vagina, and generally presents with passage of air, stool or even purulent discharge from

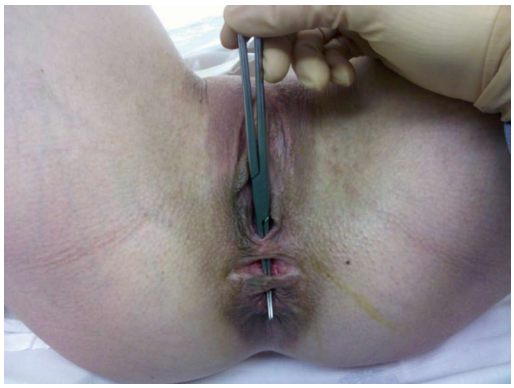

Figure 1 Clamp passing through the rectovaginal fistula. Note that the skin bridge courses across the vaginal introitus.

the vagina (Figure 1). This can result in recurrent urinary tract or vaginal infections, but also creates a serious psychosocial burden for the patient[1]. They are well known to dramatically lower a female's self-esteem and prevent successful intimate relationships. Unfortunately, they are also notoriously difficult to manage, despite the numerous surgical options presently described, and may even require fecal diversion to aid closure. When choosing the optimal method to surgically manage these fistulas, the available literature is limited and there currently are no large prospective trials comparing the numerous surgical options. While the paucity of data is driven in part by the relatively low incidence of RVFs and the complex anatomical differences between individual patients, it remains one of the more challenging conditions that surgeons caring for colorectal disease encounter. In this manuscript we will describe the scope and pathophysiology of RVFs, as well as a systematic approach to treating these patients and determining the most suitable operative approach.

RVF ETIOLOGY

RVFs account for approximately 5% of all perirectal fistulas, most commonly occurring as a result of obstetric trauma (85%) and pelvic surgery (5%-7%); while inflammatory bowel disease, malignancy, and radiation therapy encompass the majority of the remaining etiologies[1]. Although obstetric trauma causes the vast majority of RVFs, they are still relatively uncommon in this population, occurring in only approximately 0.1% of vaginal deliveries in Western countries[2]. In contrast, RVFs are considered almost endemic in sub-Saharan Africa and South Asia secondary to obstetrical trauma, with an estimated incidence of 50000 to 100000 new cases annually[2]. With a prevalence of two million, RVFs in developing nations are related to prolonged labors that cause necrosis of the rectovaginal septum. Overall, the past quarter century has seen the rates of episiotomy and operative vaginal delivery decrease dramatically, and with it the number of RVFs. Yet, vaginal deliveries associated with severe perineal lacerations, shoulder dystocia, operative vaginal delivery and prolonged and obstructed labor still occur and remain the highest risk for causing a RVF[3].

Outside of delivery complications, hysterectomy and rectal surgery are the highest risk procedures for causing RVFs. Use of stapling devices (specifically the double-stapled technique) and placement of perineal or vaginal mesh also have been shown to be associated with an increase in the likelihood of RVF formation[3]. The incidence of RVF after a resection for low rectal cancer is widely variable (0.9% to 10%), likely reflecting the heterogeneity in both the individual tumor and operating surgeon. Another possibility is that an anastomotic leak and the resulting pelvic sepsis may lead to the development of a RVF. To avoid the inciting event (*i.e.*, leak), fecal diversion is commonly utilized following a proctectomy and low-lying anastomosis to "protect" it and minimize the clinical consequence of a leak. Although proximal diversion may play a role in improving outcomes (and is itself used in the management of RVFs), fecal diversion does not completely eliminate the risks of RVF, with up to 11% of patients after a proctocolectomy developing RVFs despite complete enteric diversion[2].

Another setting where RVFs can occur is in the setting of malignancy. Anal cancer, rectal cancer and pelvic cancer can all cause RVFs by various mechanisms. First, the lesion itself can be locally destructive, resulting in direct erosion between the two luminal surfaces. Another potential source of the RVF is from the adjuvant radiation therapy that is commonly used to help treat these pelvic malignancies. In this situation, the radiation is cytotoxic, leading to obliterative endarteritis, chronic inflammation and ischemia, and eventually resulting in a fistula between the two anatomical structures[2]. With regards to inflammatory bowel disease, RVFs are most commonly seen in Crohn's disease and rarely in ulcerative colitis. While still relatively infrequent, women with Crohn's disease have a reported cumulative 10% lifetime risk of developing a RVF. Of these, Crohn's patients who have a significant disease burden in their colon are the most likely to be affected by RVFs[2]. While ulcerative colitis patients, especially following total proctocolectomy and ileal-anal pouch procedures, may still develop a RVF, this should be a "red flag" to providers to re-evaluate the patient for the possibility of a misdiagnosis of Crohn's disease.

CLASSIFYING RVFS

Although several classifications of RVFs exist, most RVF are generally broken down into low *vs* high fistulas and simple *vs* complex fistulas. These basic categorizations are extremely helpful in selecting the optimal surgical procedure for the patient. Low fistulas are generally located through or distal to the sphincter complex, but proximal to the dentate line. Due primarily to their location, they may be approached *via* anal, perineal or

Table 1 Reported outcomes with various rectovaginal fistula repairs

	Published number of cases	Success rate	Complications	Fistula anatomy
Advancement flaps	515[10,11]	68%	Incontinence, Recurrence, Larger Fistula	Low
Transperineal/sphincteroplasty	72[12,13]	64%-100%	Incontinence, Sexual dysfunction, Wound Dehiscence	Low
Gracilis muscle flap	99[14,15]	43%-100%	Sexual dysfunction, Cosmesis, Wound dehiscence	Low + High
Plugs	49	45.9%	Recurrence, Cost	Low
Transabdominal ligation[1]	49[16,17]	95%-100%	Bleeding, Intraperitoneal Rectal injuries	High
Mesh repair	48[10,18]	71%-81%	Recurrence, Larger fistula, Cost	Low + High
Martius flap	104[7,19]	65%-100%	Sexual Function, Cosemsis	Low

[1]For high fistula only.

vaginal routes. Anovaginal fistulas have a rectal opening distal to the dentate line and are generally approached the same as a low fistula. High fistulas are proximal to the sphincteric complex, with a vaginal opening near the cervix, and generally require an abdominal approach for repair.

The other classification (simple *vs* complex) primarily differentiates the RVF on whether it will be amenable to a local repair *vs* a more complicated underlying pathogenesis that will require resection, interposition grafts, and/or diversion. A simple fistula is one that is smaller in size (< approximately 2.5 cm), more distally located along rectovaginal septum, and generally occurred a result of trauma or a cryptograndular infection. Complex fistulas are typically a result of inflammatory bowel disease, radiation or invasive cancer. Fistulas that have failed prior attempts at repair are also included in the category. Complex fistulas are commonly more proximal on the rectovaginal septum and are not amenable to primary repair, though may occur anywhere due to the underlying etiology.

PREOPERATIVE CONSIDERATIONS

To optimize outcomes, it is important to ensure that any associated perineal sepsis has resolved completely before attempting an operative repair. This should be achieved primarily by addressing the underlying cause of the fistula (*e.g.*, medical therapy for Crohn's disease, removal of a foreign body such as a staple, or drainage of an abscess). Once this has been addressed, adjunctive measures such as fecal diversion or a draining seton will help resolve the active inflammation and allow the tissues to soften and be more amenable to operative repair.

SURGICAL OPTIONS

The anatomy of the individual patient and the fistula itself are the foremost factors in determining which procedure to perform. In general, our approach has been to recommend an attempt at less invasive procedures first, and if those fail, to then try more complex and potentially morbid procedures. However, depending on the underlying disease state of the patient, individual co-morbidities and the anatomy of the fistula, a more "complex" repair that includes diversion may be recommended at the initial operation (Table 1).

LOW FISTULAS

Plugs

The plugs currently available are composed of synthetic material or made from porcine small intestine submucosa. Regardless of the composition, the tract is debrided, and the plug is brought through the RVF fistula in an attempt to form a biologic seal. In some cases, surgeons will perform a concomitant endorectal advancement flap with plug placement to improve outcomes. Fistula plugs have shown some benefit in perianal fistulas of cryptoglandular origin; yet, the limited data for RVFs has shown only a 20%-50% closure rate. The length of the tract, which is almost always very short, likely plays a role in the high failure rate of this procedure, as has been seen with anal fistulas having short tracts[4].

Advancement flaps

Advancement flaps may be performed by raising either rectal or vaginal mucosa and using it to cover the fistulous tract. This is performed in conjunction with debridement/excision of the fistula tract and primary closure. Healthy surrounding tissue is mobilized along a wide pedicle to ensure adequate blood supply and brought distally to cover the RVF. Different opinions exist as to the best approach. Those that favor an endorectal flap feel it is easier to mobilize and approximate the rectal mucosa when compared with vaginal mucosa, and that the repair is performed from the high-pressure side. Proponents of the vaginal side feel it is better vascularized, less likely to result in a larger fistula, and an easier recovery. In either instance, the reported success rates of this repair are reported between 60%-90%. In general, this is the procedure of choice for low-lying/simple traumatic RVFs without a history of incontinence[4].

Transperineal

A transperineal repair is accomplished by approaching the fistula tract through the perineum, making an incision at the perineal body and dissecting in the rectovaginal septum above the level of the fistula. The

tract is then excised, and closure is performed in multiple layers on both the sides. The benefit of this approach is that an overlapping sphincteroplasty can be performed simultaneously for those patients that have associated defects or in those patients in which the fistula can be incorporated into the sphincter repair. This is best used in women with preexisting incontinence, or those a history of failed transanal or transvaginal approach[2]. Success rates are reported to be 64.7%-100%; however, this procedure is often more technically challenging, results in higher morbidity rates, and normally is not a first-line procedure[4].

Martius flap

In 1928 Dr. Heinrich Martius, a professor of gynecology in Gottingen, described using the bulbocavernosus muscle and labial fat pad for vaginal wall defects due to its proximity which allows for a single operative field[5]. The Martius flap was first used in cysto- and urethral-vaginal fistulas. Only later was it adapted to its present use in RVFs. In sum, it is ideally suited for RVF repair, providing a local well-vascularized pedicle of adipose/muscular tissue that is mobile and results in low morbidity. It is most suited for complex, recurrent, or recalcitrant RVFs[6]. The Martius flap is best able to treat low and mid-level fistulas up to approximately 5 cm proximal to the vaginal introitus, but in reality is only limited by the reach of the bulbocavernosus pedicle.

There are approximately 104 cases reported in the retrospective literature with a success rate ranging from 65%-100%[4]. Dyspareunia has been reported in as many as 30% of females at six weeks post operatively when they are allowed to resume vaginal intercourse, but it appears to improve with time. The only other more common complication reported in the literature are labial wound issues (< 10%), which largely resolve with local wound care[7].

Gracilis muscle transposition

In this procedure, the gracilis muscle is harvested from the leg, mobilized on a proximal pedicle, and used as an interposition graft between the rectum and vagina. Success rates are reported from 60%-100%, but there is increased morbidity associated with the harvest site and there appears to be a prolonged decrease in sexual function[4]. Dyspareunia is reported in up to 57% of patients undergoing this operation and the decreased sexual desire has been felt to be, in part, related to the relatively large burden of perineal scarring[8]. Furthermore, when the gracilis is harvested for use in other procedures (*e.g.*, plastic surgery free flaps), a short-term decrease in functionality of that leg has been reported for approximately 6 mo in 26% of the patients, and 6% of patients have long-term difficulties[9].

HIGH FISTULAS

Transabdominal ligation

Transabdominal ligation procedures are typically performed when the RVF is high (*i.e.*, vaginal cuff), and may be performed *via* a minimally invasive or open approach. The common bond to these fistulas is often the presence of a prior hysterectomy and an inflammatory condition that resulted in pelvic sepsis that eroded through the vaginal cuff (*e.g.*, Crohn's diverticulitis, anastomotic leak). In this procedure, the offending bowel is resected along with division of the fistula tract. It is often helpful to place a piece of omentum in between the rectum and vagina to avoid recurrence. Some gynecologists prefer to debride and re-close the vaginal cuff, although this is widely variable. Success rates are 95%-100%, and normally this is the preferred treatment for the patient has a high fistula tract[4].

Mesh repair

A mesh repair is essentially the same as transabdominal ligation. However, rather than placing omentum between the rectum and vagina, various biologic meshes have been utilized as an interposition graft between the two structures to prevent re-fistulization. The largest study used porcine small intestine submucosa and showed a success rate of 71%-81% in 48 patients. Other biologic meshes such as acellular porcine dermal graft and acellular human dermal matrix have also been successful in small studies and case reports[4]. Biological mesh placement has also been described following perineal approaches, although this is less well described.

CONCLUSION

RVFs are a disease process that is a significant burden on women that are afflicted, and a difficult problem for surgeons from whom they seek help. The diverse disease pathology has prevented prospective trials, and consensus guidelines on the management of these patients. With a clear understanding of the anatomy, ensuring resolution of the sepsis, and large armentarium of surgical approaches these patients can be treated successfully.

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Irreversible electroporation and the pancreas: What we know and where we are going?

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Abstract

Pancreatic adenocarcinoma continues to have a poor prognosis with 1 and 5 years survival rates of 27% and 6% respectively. The gold standard of treatment is resection, however, only approximately 10% of patients present with resectable disease. Approximately 40% of patients present with disease that is too locally advanced to resect. There is great interest in improving outcomes in this patient population and ablation techniques have been investigated as a potential solution. Unfortunately early investigations into thermal ablation techniques, particularly radiofrequency ablation, resulted in unacceptably high morbidity rates. Irreversible electroporation (IRE) has been introduced and is promising as it does not rely on thermal energy and has shown an ability to leave structural cells such as blood vessels and bile ducts intact during animal studies. IRE also does not suffer from heat sink effect, a concern given the large number of blood vessels surrounding the pancreas. IRE showed significant promise during preclinical animal trials and as such has moved on to clinical testing. There are as of yet only a few studies which look at the applications of IRE within humans in the setting of pancreatic adenocarcinoma. This paper reviews the basic principles, techniques, and current clinical data available on IRE.

Key words: Irreversible pancreatic adenocarcinoma; electroporation; Apoptosis; Percutaneous; Laparotomy; Overall survival

Core tip: Pancreatic adenocarcinoma continues to have a poor prognosis and as such there is considerable interest in pioneering new techniques. Ablation holds promise in this area, however, the earliest studies looked at thermal ablation techniques which resulted in high morbidity rates. Irreversible electroporation, a relatively new technique, produces apoptosis instead of liquefactive necrosis and preclinical data shows it does not destroy scaffolding cells such as bile ducts and blood vessels. These characteristics have made it of interest in the setting of pancreatic adenocarcinoma. The available clinical data as well as the basic principles of this new technique are reviewed here.

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INTRODUCTION

Pancreatic cancer, despite extensive research, remains one of the most aggressive cancers, having a poor prognosis with 1 and 5 years survival rates of 27% and 6% respectively[1]. According to the American Cancer Society and World Health Organization 46420 patients were diagnosed with pancreatic cancer in the United States in 2014 and 338000 in the world in 2012[1,2]. In the United States 39590 of those patients died in 2014, making it the fourth leading cause of death in both women and men with the prevalence increasing by 1.3% per year as well[1].

Only approximately 10% of these patients present with local disease, which is considered surgically resectable, however even in these patients the 5 year survival rate remains low at 24%[1]. Of the remaining 90% of patients approximately 50% present with metastatic disease, leaving about 40% presenting with localized disease, which is considered surgically unresectable, generally secondary to encasement of adjacent vessels such as the portal vein, celiac artery, and superior mesenteric artery[1]. Patients without metastatic disease, but deemed unresectable due to locally advanced disease are now classified as locally advanced pancreatic cancer (LAPC).

While surgical resection, when a viable option, remains the gold standard the majority of patients will receive chemotherapy and/or radiation therapy. The mainstay of chemotherapy in pancreatic adenocarcinoma for close to fifty years was 5-florouracil (5-FU) monotherapy, despite a mean survival of less than 6 mo[3]. In the late 1990s gemcitabine was introduced and demonstrated a survival benefit as compared 5-FU and thus replaced it as first line therapy[3,4]. As gemcitabine became firmly established as the first line chemotherapeutic agent multiple trials looked at combining gemcitabine with a variety of other chemotherapeutic agents, however, only a few demonstrated a survival benefit[3,5]. The combination of gemcitabine with capecitabine showed a trend toward improved survival with *post hoc* analysis of two randomized controlled trials showing statistically significant improvement in overall survival in patients with a good performance status[6-8]. In 2011 a new trial found that FOLFIRINOX (5-FU, leucovorin, irinotecan, and oxaliplatin) demonstrated a significant overall survival benefit in chemotherapy naive patients as compared to gemcitabine alone[9]. Lastly, a study in 2013 revealed a survival benefit when nab-paclitaxel was combined with gemcitabine as compared to gemcitabine alone[10]. Improving chemotherapeutic options for pancreatic adenocarcinoma remains an active area of research with multiple ongoing studies.

Radiation therapy has been used in the setting of pancreatic adenocarcinoma both in the neoadjuvant setting and in an attempt to reduce local recurrence rates after resection. Attempting to prevent local recurrence after resection seemed like a natural role for radiation therapy, however, to date studies have shown a mixed response[11-13]. This controversial area is the focus of the APACT trial which will hopefully provide a clearer answer[14]. The role of radiation therapy in the neoadjuvant setting is also as of yet unclear with a few studies showing some promise[14,15]. This is also an area of active study, with the recent clear definition of borderline resectable disease assisting in making future studies comparable[14,15].

After the introduction of ablation, interest surrounded it as a possible way of improving patient outcomes in this difficult disease process. Initial investigations into ablation as a possible therapy centered on thermal techniques, with radiofrequency ablation (RFA) being the most studied modality. The reported morbidity rates were regrettably unacceptably high in the majority of these published studies[16-19]. Anatomy at least partially accounts for this elevated morbidity as the pancreas is surrounded by multiple delicate structures such as the common bile and pancreatic ducts. Several vessels, including the celiac artery, superior mesenteric artery, portal vein, and splenic vein also surround the pancreas further complicating and restricting efficacy of thermal ablation techniques primarily as a result of heat sink effect[20,21]. When heat sink effect, defined as tissue cooling during ablation by adjacent blood vessels, occurs the temperature surrounding major vessels does not attain high enough levels to manifest cell death. Although microwave ablation (MWA) has been shown to be less susceptible to heat sink affect it remains vulnerable to the phenomenon[22]. The above difficulties associated with the pancreas anatomically also provide a significant obstacle to other thermal ablation techniques including cryoablation, high intensity focal ultrasonography, and MWA which to date have not been as well studied as RFA.

Irreversible electroporation (IRE) provides a unique alternative, allowing tissue ablation without being reliant on thermal effects. It also has the added ability of maintaining the scaffolding of surrounding tissues, making it of great interest in this anatomically complex area.

IRE TECHNIQUE

Reversible electroporation has been used for many years in the basic science setting to implant foreign molecules into cells[23,24]. Reversible electroporation works by applying an electrical field across the membrane causing the membrane to become porous, through a yet incompletely understood process[23,25]. This lets the investigator introduce a desired molecule, such as RNA or DNA, into

the cell[25,26]. IRE uses this theory but applies a higher voltage leading to cell death by apoptosis. Although the exact mechanism by which IRE induces apoptosis is not clear, it appears to be *via* permanent nanopore formation and resultant ion disruption[27].

As previously noted, thermally based techniques struggle with high morbidity when treating pancreatic adenocarcinoma due to the delicate structures in close proximity[28]. IRE on the other hand has been shown, in animal studies, to produce apoptosis of cancer cells while sparing the delicate surrounding scaffolding, including bile ducts and blood vessels[29-31]. This distinctive property makes IRE a desirable modality, particularly given the structurally rich pancreatic region. IRE also provides the benefit of yielding apoptosis, rather than liquefactive necrosis as in thermal techniques, pardoning it from the burdens of heat sink phenomenon[29]. While initially IRE was thought to not induce any thermal effects recent studies have shown that a small area of thermal effect is likely present immediately adjacent to the probe[32].

The unique mechanism of IRE results in a few necessary precautions during its utilization. High voltages created are by IRE and produce significant muscular contractions[33]. It is for this reason the patient must be placed under general anesthesia with full neuromuscular blockade[33]. The blockade is tested with a twitch technique prior to starting. ECG monitoring is also required to monitor for arrhythmias, which are rare and typically transient. The concern of arrhythmia leads some authors to promote the placement and use of arterial lines.

Currently there is one commercially available IRE machine, the NanoKnife (Angio Dynamics, Queensburry, New York). This device supports either unipolar or bipolar probes. The more commonly used unipolar probes require placement in pairs, which is technically challenging as they must be placed in parallel orientation and spaced no further than 1.5-2.0 cm apart. The probes create a relatively small ablation field (approximately 2-3 cm)[34-36] and therefore it is common for multiple probe pairs to be placed, and/or the probes to be repositioned several times during the procedure. Probes can be placed percutaneously, laproscopically, or using an open surgical approach. When placed intraoperatively, intraoperative ultrasound is used[37-39]. When placed percutaneously both ultrasound and CT placement have been described[40,41].

After probe placement the ablation device is set to produce high voltages, usually between 1500-3000 V in pulses of 70-100 microseconds. Typically 90 such pulses are delivered which only takes a few minutes, after which the ablation is complete. Once the intended ablations have been performed the patient will typically undergo imaging, either by intraoperative ultrasound, contrast enhanced ultrasound, or CT to ensure that the lesion has been satisfactorily covered.

After finishing the IRE procedure the patient is observed with the average length of admission varying significantly in the available studies from a same day discharge to admission for two weeks or more[29,37,39-41].

AVAILABLE DATA

A search of the Pubmed database with the terms "IRE AND pancreatic cancer" yielded 34 results, of which 6 studies were found to be case reports, case series, or prospective trials related to IRE and pancreatic cancer without significant patient overlap. Those studies are reviewed here. The remainder represented review articles (n = 16), animal studies (n = 5), or prior publications on a patient set that was reused as discussed below (n = 4). Two studies were excluded as they were case reports only discussing a complication, and therefore not felt to be relevant to this discussion. A single study was eliminated as it was a review of anesthetic requirements during IRE.

Martin and his group have published multiple studies on pancreatic cancer and IRE[37,38,42,43], because of significant patient overlap only two of these studies are included and discussed here. Table 1 provides some of the most pertinent data for the 6 below described studies.

In 2013 Martin *et al*[38] compared a group of fifty-four prospectively gathered IRE patients with pancreatic cancer, retrospectively to a group of eighty-five patients who received only chemotherapy and/or radiation. All of the patients had LAPC disease with none being considered borderline resectable or having metastatic disease. The two groups were matched using propensity scores based on age, size of tumor, performance status, cardiac comorbidities, and pulmonary comorbidities. Of the fifty-four IRE patients fifty-two (96%) patients underwent open surgical ablation and two (4%) underwent laparoscopic ablation. Nineteen patients underwent IRE followed by en bloc resection, after surgical restaging. Forty seven of the fifty-four (87%) IRE patients underwent post procedural chemotherapy while ten (19%) of them underwent post procedural radiation therapy. In a ninety day follow up period thirty two of the fifty-four (59%) IRE patients had adverse events. The average time from diagnosis to treatment was 5.1 mo with a range of 1 to 32 mo. The average length of hospital stay was 7 d. When the IRE and chemoradiation only groups were compared the IRE group had a better overall survival (20.2 mo *vs* 11 mo, P = 0.03), progression-free survival (14 mo *vs* 6 mo, P = 0.01), and distant progression-free survival (15 mo *vs* 9 mo, P = 0.02). However, the survival curves of the two groups appeared to converge back together at twenty months, which was postulated to be secondary to rapid progression of distant metastatic disease by the authors.

Martin *et al*[37] also recently published a series of forty eight patients who had borderline resectable or LAPC disease in which they used IRE in an attempt to obtain a margin free, or R0, resection. Twenty three (48%) of the patients had LAPC while twenty five (52%) had borderline resectable disease. Of note, nineteen of these

Table 1 Comparison of the studies

Ref.	IRE placement technique	No. of patients	Age in years	Sex in male/ female	Time from diagnosis to treatment in months	Survival time in months	Complications	No. of patients with metastasis	No. of patients who received pre IRE chemo and or radiation	No. of patient who received post IRE chemo and or radiation
Martin *et al*[38]	Open 52 (96%) lap 2 (4%)	54	Median 61 range 45-80	23 male/21 female	Median 5.1 range 1-32	Local PFS 14, distant PFS 15, and OS 20	32 (59%)	0 (0%)	49 (90%)	40 (73%)
Martin *et al*[43]	Open 48 (100%)	48	Median 61 range 27-81	26 male/22 female	6 range 4-13	OS 22 and PFS 11	18 (38%)	0 (0%)	33 (69%)	31 (65%)
Paiella *et al*[39]	Open 10 (100%)	10	Median 66	5 male/5 female	Mean 9.2	OS 7.5	2 (20%)	0 (0%)	10 (100%)	3 (30%)
Narayanan *et al*[40]	Perc CT guided 14 (100%)	14	Median 57 range 51-72	7 male/7 female	Mean 16.6 range 2.4-49.5	70% OS at 6 mo	2 (14%)	3 (21%)	14 (100%)	NP
Månsson *et al*[41]	Perc US guided 5 (100%)	5	Median 65 range 46-89	3 male/2 female	NP	40% OS at 6 mo	0 (0%)	0 (0%)	5 (100%)	NP
Bagla *et al*[44]	Perc US with CT confirm	1	78	Male	CT	Alive at 6 mo	None	None	No	No

IRE: Irreversible electroporation; US: Ultrasound; CT: Computed tomography; NP: Nondeterministic polynomial.

patients seem to be included in the previously discussed study by Martin *et al*[38]. Thirty three of the forty eight (69%) had undergone preoperative chemotherapy and thirty one (65%) underwent preoperative radiation therapy[12]. Thirty one of the forty eight (65%) patients underwent R0 resections with the remaining undergoing R1 resections (35%). Adverse events were recorded for 90 d and developed in eighteen of the forty eight (38%) patients. At twenty four months twenty eight patients (58%) had developed recurrence, the majority of which involved the liver or peritoneum.

Paiella *et al*[39] published a prospective study of ten patients who underwent IRE for LAPC utilizing a laparoscopic approach with intraoperative ultrasound (US) guidance. All patients who underwent IRE had previously undergone chemotherapy or chemoradiation therapy. The average length of hospital stay was 9.5 d with 1 patient (10%) developing a postoperative abscess. One other patient (10%) died of septic shock, which was attributed to complications of ulcerative colitis rather than the procedure. The average time of diagnosis to treatment was 9.2 mo. The average overall survival was 7.5 mo following the procedure, with diagnosis to death time averaging 16.8 mo. Three of the ten (30%) patients received post procedural chemotherapy. After treatment, four (40%) patients showed partial response, three (30%) had stable disease burden, and three (30%) demonstrated progressive disease per RECIST criteria.

Narayanan *et al*[40] published a series of fourteen patients who underwent percutaneous IRE in 2012. Eleven (79%) of the patients had disease localized to the pancreas, one (7%) had a sub centimeter lung metastasis, one (7%) had a sub centimeter liver metastasis, and one (7%) had a solitary peritoneal metastasis. All of the procedures were performed using CT guidance and patients were discharged either the same or next day. No grade three toxicities occurred per SIR reporting guidelines. One patient (7%) developed a pneumothorax, while two (14%) others had subclinical complications (small hematoma seen on follow up imaging and subclinical pancreatitis). Two of the fourteen (14%) patients were able to undergo subsequent resection. The median event free survival (EFS) was 6.7 mo, and at 6 mo 70% of the patient cohort remained alive. Additionally the projected overall survival was statistically longer for patients with localized disease as compared to those with metastatic disease (P = 0.02). No difference was seen in the overall survival between the patients who did and did not undergo resection, possibly as a result of the few deaths in the resection group.

Månsson *et al*[41] published a case series of five patients treated with US guided percutaneous IRE ablation. The patients all presented with jaundice and were deemed non-surgical candidates, presumably from LAPC although this was not specified. The patients underwent contrast enhanced US to ensure complete ablation. No grade three or higher complications occurred within the first 30 d. One (20%) patient did develop subclinical pancreatitis. Limited follow up data was presented, but 60% of patients were alive at six months, with two (40%) demonstrating no evidence of recurrence.

In 2012 Bagla *et al*[44] published a case report of a single patient with LAPC who was treated with US guided IRE, followed by a CT to confirm probe placement. This patient underwent two separate ablations two weeks apart due to tumor size. The patient developed liver metastasis at the 3 mo follow up exam, which were subsequently treated with RFA. The patient had no evidence of recurrent disease at the 6 mo follow up

exam and no significant complications were noted.

DISCUSSION

Pancreatic cancer is the fourth leading cause of cancer related death in the US[1]. Despite considerable and meaningful research into surgical techniques and chemoradiation therapy, survival rates remain poor at 27% and 6% at 1 and 5 years respectively[1]. The majority of patients with pancreatic cancer present with unresectable disease, either due to LAPC (approximately 40%) or metastases (approximately 50%)[1]. Only approximately 10% of patients are considered surgically resectable at presentation, and unfortunately even in this group survival at 5 years is only 24%[1].

IRE appears to hold great promise for improving survival in nonresectable patients, most clearly in the LAPC group. Animal studies have shown IRE has the ability to destroy cancer cells while leaving crucial underlying anatomic scaffolding such as blood vessels and bile ducts intact[29]. This is of paramount importance given the location of the pancreas and resultant high morbidity seen when thermal ablation techniques have been employed[19].

Human data is limited, with only 6 relatively small case series published to date. The most promising data comes from the largest series by Martin *et al*[38] which revealed improved overall survival, progression-free survival, and distant progression-free survival when comparing patients who underwent IRE with those who underwent chemotherapy and/or radiation therapy alone. In this study the overall survival showed significant improvement, rising from 11 to 20.2 mo. This improvement of 9 mo is particularly encouraging given the notably poor prognosis of pancreatic cancer and continued difficulty in attaining improved survival with various other novel treatment methodologies such as new chemotherapeutic agents.

With early data demonstrating the possibility of prolonging overall survival of longer than 6 mo it appears that adding IRE may be of great value for patients without hope for cure. In this particular setting quiescing morbidity is the primary objective however, as clearly demonstrated by several authors, on occasion IRE can be used to downstage patients giving them a chance at curative therapy. The use of IRE to provide definitive therapy has also being investigated by Martin *et al*[38] in their attempts to expand the population of patients able to undergo R0 resections. These advances are vastly promising in regards to the treatment of pancreatic adenocarcinoma, yet they also raise several poignant questions.

Currently IRE is being delivered in a range from maximally invasive (open surgical placement) to minimally invasive (percutaneous placement), with laparoscopic placement falling somewhere in between. It appears likely that both the open surgical placement and percutaneous placement techniques are of benefit. Open surgical placement has the best data to support its use thus far and also allows the surgeon to surgically stage the patient and consider proceeding to resection. Percutaneous placement appears to reduce morbidity and potentially hospital stay, although this point would need further clarification given the long average hospital admission seen in the Mansson *et al*[43] paper of 14 d. Reducing morbidity and hospital stay could be of great importance in maintaining quality of life when the disease is likely to remain unresectable and the goal is palliation. Further investigation into patient selection criteria will be essential in order to differentiate those patients best treated by open, from those best treated with percutaneous, placement. In their paper Narayanan *et al*[39] discussed this in brief, pointing out that certain patients, such as those with large varices, would likely not be best treated *via* the percutaneous approach.

Recent studies have demonstrated that stroma plays a larger than previously recognized role in regards to cancer characteristics, indicating this may be a critical area of future investigation[45-48]. Epithelial cancers such as pancreatic cancer are believed to be maximally affected by stromal cells[49]. The stromal activity prevents drug concentration and may at least partially account for the relatively poor response to chemotherapy seen in pancreatic cancer[50,51]. Disruption of the stromal cells and the cancer cells may help improve outcomes, and to some extent explain the encouraging outcomes which have been seen in early IRE studies. This also raises the question as to whether or not IRE's potential to disrupt the stromal effect could produce better outcomes in patients presenting with limited metastatic disease as well. It also highlights the importance of investigating the possible synergistic effects IRE and chemotherapy could obtain.

More data evaluating outcomes in patients with LAPC is also needed in the form of large case cohorts, and more importantly in the form of randomized controlled trials comparing this technique to radiation and chemotherapy alone. During these investigations the delineation of patient selection will be paramount, as there is likely a group of patients that will confer a good survival benefit, while others will likely not benefit from this invasive procedure. The Martin *et al*[37] paper describing the use of IRE to obtain R0 resections is of marked interest, however, again more data is needed in this newly introduced novel realm.

In conclusion IRE remains a new, exciting area of research in pancreatic cancer with multiple promising possible applications that will require investigation in the future.

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ORIGINAL ARTICLE

Retrospective Cohort Study

Single-port laparoscopic cholecystectomy *vs* standard laparoscopic cholecystectomy: A non-randomized, age-matched single center trial

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Abstract

AIM: To compare the safety of single-port laparoscopic cholecystectomies with standard four-port cholecystectomies.

METHODS: Between January 2011 and December 2012 datas were gathered from 100 consecutive patients who received a single-port cholecystectomy. Patient baseline characteristics of all 100 single-port cholecystectomies were collected (body mass index, age, *etc.*) in a database. This group was compared with 100 age-matched patients who underwent a conventional laparoscopic cholecystectomy in the same period. Retrospectively, per- and postoperative data were added. The two groups were compared to each other using independent *t*-tests and χ^2-tests, *P* values below 0.05 were considered significantly different.

RESULTS: No differences were found between both groups regarding baseline characteristics. Operating time was significantly shorter in the total single-port group (42 min *vs* 62 min, $P < 0.05$); in procedures performed by surgeons the same trend was seen (45 min *vs* 59 min, $P < 0.05$). Peroperative complications between both groups were equal (3 in the single-port group *vs* 5 in the multiport group; $P = 0.42$). Although not significant less postoperative complications were seen in the single-port group compared with the multiport group (3 *vs* 9; $P = 0.07$). No statistically significant differences were found between both groups

with regard to length of hospital stay, readmissions and mortality.

CONCLUSION: Single-port laparoscopic cholecystectomy has the potential to be a safe technique with a low complication rate, short in-hospital stay and comparable operating time. Single-port cholecystectomy provides the patient an almost non-visible scar while preserving optimal quality of surgery. Further prospective studies are needed to prove the safety of the single-port technique.

Key words: Single-port; Minimal invasive; Laparoscopy; Safety; Feasibility; Cholecystectomy

Core tip: Single-port cholecystectomies can be performed safe when performed by experienced surgeons. Low complication and conversion rates are seen, similar to standard multiport laparoscopic cholecystectomies. Single-port cholecystectomies can be performed in similar or even shorter operating times compared to the standard procedure. Single-port cholecystectomies can provide the patient an almost non-visible scar while preserving optimal quality of surgery.

van der Linden YTK, Bosscha K, Prins HA, Lips DJ. Single-port laparoscopic cholecystectomy *vs* standard laparoscopic cholecystectomy: A non-randomized, age-matched single center trial. *World J Gastrointest Surg* 2015; 7(8): 145-151 Available from: URL: http://www.wjgnet.com/1948-9366/full/v7/i8/145.htm DOI: http://dx.doi.org/10.4240/wjgs.v7.i8.145

INTRODUCTION

Laparoscopic cholecystectomy is the standard operative procedure for patients with symptomatic cholelithiasis[1]. Introduced in 1985, laparoscopic cholecystectomy, has been an important development in general surgery[2,3]. Its introduction resulted in surgical procedures with reduced blood loss, enhanced recovery and less major wound complications. Single incision laparoscopic surgery techniques were introduced in the 1990s[4]. When performing this particular type of laparoscopic surgery only one incision is made, usually through the umbilicus. In general, smaller and fewer incisions result in less pain, accelerate postoperative recovery and improve cosmetic result[3,5,6].

After its introduction, standard multiport cholecystectomy was for a long time under debate and frequently contradicted, a situation in which nowadays single-port cholecystectomy finds it-self in. Some studies report higher percentages of bile duct injuries, more blood loss and longer operating time when performing single-port cholecystectomy[7,8]. In contrast, although other studies suggest that single site laparoscopic surgery is a safe and adequate procedure, single site surgery for cholecystectomy for uncomplicated cholecystolithiasis is still subject of debate[9-11].

In 2011, single-port laparoscopic (SPL) also known as laparo-endoscopic single site surgery was introduced at the Jeroen Bosch Hospital, 's-Hertogenbosch, The Netherlands. Since its introduction more than 100 patients received a laparoscopic cholecystectomy with only one umbilical incision. The aim of this study is to compare short as well as long term surgical outcome parameters, such as safety and patient-outcome, between SPL cholecystectomy and standard four port laparoscopic cholecystectomy (SLC).

MATERIALS AND METHODS

Patients

Between January 2011 and December 2012 all patients who received a SPL cholecystectomy at the Jeroen Bosch Teaching Hospital ('s-Hertogenbosch, The Netherlands) were included in a prospective database in which relevant patient data and surgical outcome parameters were recorded. Also, all patients who received a SLC in the same study period were identified. After an introduction period (n = 36) of the SPL technique, 100 consecutive patients who were operated upon using the SPL technique were matched by age with a group of 100 patients which received a SLC in the same period.

Preoperative data included: age, gender, body mass index (BMI), indication of surgery, previous abdominal surgery, comorbidity and American Society of Anesthesiologists classification. Peroperative data included: operating time (defined as time from first skin incision to completion of closure), need for extra trocar, conversion to open cholecystectomy, first operator (surgeon or resident supervised by surgeon) and peroperative complications. Peroperative bloodloss of more than 200 mL was registered as a complication. Postoperative data included: duration of stay in hospital (including the day of operation), complications (during hospitalisation), reoperation, readministration to the hospital (within 30 d after discharge) and mortality.

Above normal postoperative pain was defined as pain resulting in prolongation of hospital admission with at least one day, without finding a cause of pain.

Hernia cicatricalis was defined as complaints around the umbilical incision caused by herniation of the abdominal wall. Patients were routinely seen 2-6 wk after surgery at the outpatient department and checked on complaints of the incision. All patients were checked in the medical files if they returned to the hospital with complaints of the umbilical incision.

SPL

SPL cholecystectomy is performed under general anaesthesia. Patients are positioned in a supine position with both legs in holders. The surgeon is positioned

Table 1 Patient characteristics

	SPL	SLC	*P* value
Gender (% female)	80	75	0.397
Age (mean, SD)	45 (15)	46 (15)	0.787
BMI (median, range)	25 (17-40)	28 (19-46)	< 0.001[b]
ASA (%)			0.239
Ⅰ + Ⅱ	98	96	
Ⅲ	1	2	
Indication (%)			0.557
Symptomatic cholelithiasis	80	77	
Cholecystitis	13	18	
Biliary pancreatitis	3	1	
Gallbladder polyp	3	4	
Cyst gallbladder	1	0	

[b]Statistical significant. SPL: Single-port laparoscopic cholecystectomy; SLC: Standard laparoscopic cholecystectomy; BMI: Body mass index; ASA: American Society of Anesthesiologists classification.

between the legs of the patient ("French" position) and the first assistant is at the left side of the patient. Through an umbilical incision a 4-access multiport trocar (TriPort+, Olympus surgical) is introduced. Patients are placed in an anti-Trendelenburg position and left lateral tilt. Additional support holders are preoperative placed. The gallbladder is lifted cranially to the liver using a straight laparoscopic clamp. The procedure is the same as the multiport procedure. Before ligation of the cystic duct and artery a critical view of safety is achieved. Ligation is performed using a 5 mm clip applier. If no critical view of safety can be achieved an extra trocar will be placed or the procedure is converted to an open procedure. Conversion means that the single-port or standard procedure was converted to an open cholecystectomy. Total number of placement of extra trocar(s) was registered.

SLC

The standard four-port technique is performed under general anaesthesia. Patients are positioned in a supine position. The surgeon and assistant are positioned at the left side of the patient. A 10 mm trocar is placed periumbilically by open approach and three 5 mm ports are placed in the upper right abdomen under laparoscopic vision. A critical view of safety is achieved before ligation of the cystic duct and artery. When it is not possible to achieve the critical view of safety, the procedure is converted to an open procedure.

Statistical analysis

Data was collected and statistically analyzed using SPSS (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.).

Continuous variables (means) were analyzed using independent *t*-test. Categorical (ordinal and nominal) variables were analyzed using χ^2-test. *P* values were two tailed. Statistical significance was accepted for *P* values of < 0.05.

RESULTS

In the period January 2011 to December 2012, a total of 795 cholecystectomies were performed of whom 136 patients were treated with the SPL technique. In total 27 of the 795 procedures were converted to an open procedure. All patients' characteristics of the included 100 consecutive patients who underwent a SPL technique and who, matched by age, underwent a four-port technique are noted in Table 1. A significant difference in mean BMI between both groups is observed (25.6 for the SPL group *vs* 28.9 for the SLC group; $P < 0.05$). BMI ranged in the SPL group from 17 to 40 and in the SLC group from 19 to 46.

In the SPL group three operations were performed by residents *vs* 29 in the SLC group. The operating time in the whole SPL group ($n = 100$) was significant shorter compared with the total SLC group ($n = 100$) (mean operating time was 46 min *vs* 62 min, $P < 0.001$). The mean operating time together performed by surgeons was 51 min (SD 24; $n = 168$) whereas the mean operating time for residents for both techniques was 69 min (SD 22; $n = 32$). Operating times in procedures performed by surgeons were significantly shorter in the SPL group, *i.e.*, mean operating time in SPL procedures performed by surgeons ($n = 97$) was 45 min compared to a mean operating time of 59 min in the SLC group ($n = 71$, $P < 0.05$).

A significant correlation ($r = 0.22$; $P = 0.002$) between BMI and operating time was found using the Spearman's rho test ($n = 200$); subgroup analysis showed a significant correlation in the SPL group ($r = 0.21$; $P = 0.037$), but the SLC group did not show a significant correlation ($r = 0.03$; $P = 0.787$). This suggests more influence of BMI on operating times in SPL cholecystectomies. To exclude the effect of the learning curve in analysing the effect of BMI on the operating time, the procedures performed by surgeons were analysed as a subgroup. Regarding all procedures performed by surgeons a significant correlation was found ($r = 0.24$; $P = 0.003$; $n = 168$). Subgroup analysis of procedures performed by surgeons show significant correlation between BMI and operating time in the SPL group ($r = 0.23$; $P = 0.029$; $n = 97$) and no correlation in the SLC group ($r = 0.108$; $P = 0.385$; $n = 71$). No correlation was seen between BMI and placement of extra trocars.

One conversion was observed in the SPL group because of inadequate critical view of safety (*vs* zero in the SLC group, $P = 0.331$). Additional ports were placed in seven patients (one extra trocar in six patients and two extra trocars in one patient) in the SPL group *vs* two patients in the SLC group (both one extra trocar, $P = 0.122$). In this group (extra trocar; $n = 9$) the median BMI was 28 (range 18-31) *vs* 26 (range 17-46) in patients ($n = 191$) without the need of placing an extra trocar ($P = 0.862$). Peroperative complications were seen in three patients in the SPL group (one

Table 2 Operation characteristics

	SPL	SLC	*P* value
Operating time in min (mean, SD)	46 (20)	62 (26)	< 0.001[b]
Peroperative complications (%)	3	5	0.417
Conversions (%)	1	0	0.331
Adding extra ports (%)	7	2	0.122

[b]Statistical significant. SPL: Single-port laparoscopic cholecystectomy; SLC: Standard laparoscopic cholecystectomy.

Table 3 Number of postoperative complications

	SPL	SLC
Bile leakage	1	1
Surgical	0	1
Cardial	0	0
Pulmonairy	2	2
Urogenital	0	0
Pain	0	3
Other	0	2

SPL: Single-port laparoscopic cholecystectomy; SLC: Standard laparoscopic cholecystectomy.

peroperative bleeding, two pneumothoraces) *vs* five patients in the SLC group (all five had a peroperative bleeding; $P = 0.417$). All peroperative characteristics are listed in Table 2.

No patients were admitted to the intensive care and no mortality was seen. A slight difference in postoperative complications in favour of the SPL group in comparison with the SLC group was seen. Three patients of the SPL group suffered from postoperative complications *vs* nine in the SLC group ($P = 0.071$). Postoperative complications are listed in Table 3 (the two complications noted as "other" are biliary colics and neurological dysfunction of one leg; the surgical complication was a superficial wound infection). No significant difference between both groups was found in length of stay in the hospital including the day of operation. Three patients of the SPL group were readmitted *vs* four patients in the SLC group ($P = 0.700$). After a median follow up period of 4 wk (range 1-91 wk) one patient was presented with a hernia cicatricalis in the SPL group *vs* three in the SLC group ($P = 0.312$). For all postoperative data see Table 4.

DISCUSSION

Nowadays, multiport laparoscopic cholecystectomy is worldwide the standard operative procedure for symptomatic cholelithiasis and chronic cholecystitis. This study shows that the single-port procedure (SPL) could be a safe and feasible procedure, performed in a comparable or even shorter operating time. In this age matched control study a similar or even lower percentage of SPL-operated patients suffered from per- and/or postoperative complications compared with data found in literature[12-15].

Table 4 Postoperative characteristics

	SPL	SLC	*P* value
Complications (%)	3	9	0.071
IC admission (%)	0	0	
Length of stay (in days, mean)	1	2	0.239
Readmission (%)	3	4	0.70
Mortality (%)	0	0	

SPL: Single-port laparoscopic cholecystectomy; SLC: Standard laparoscopic cholecystectomy.

This study was not designed for or aimed to identify superiority for either one of the techniques. This study shows SPL to be non-inferior to SLC.

In 92% of the patients a SPL cholecystectomy could be performed safely without placement of extra trocarts or conversions, whereas only eight patients had a conversion ($n = 1$) or additional port placed ($n = 7$). It is noteworthy to mention that patients in the group who received an additional port still had fewer incisions compared with the multiport procedure.

Furthermore, no increase of biliary or other surgical complications in the single-port group compared with the multiport group was observed. In the beginning of the SPL cholecystectomies surgeons placed a transcutaneous suture for retraction of the gallbladder, causing a pneumothorax in some patients. For this reason after around 45 procedures (including the first 36 procedures performed before this analysis) this suture was not used anymore. This explains the two pneumothoraces seen in the SPL group.

In a meta-analysis published by Trastulli *et al*[7] a significant higher procedural failure was found for the SPL technique compared with the SLC technique, ranging from 0% to 67%. It was also mentioned that the SPL technique led to a significantly higher blood loss. This was possibly due to loss of triangulation that makes the use of instruments for suction and diathermy difficult, resulting in less accurate haemostasis. A possible explanation for the findings of Trastulli *et al*[7] could be the fact that in the included studies the SPL procedures were performed during the surgeon's learning curve.

In contrast to the conclusion of the study of Ma *et al*[16] this study shows a shorter operating time in the SPL group and comparable complication rates. Culp *et al*[17] performed a retrospective study and found slightly longer operating times in the SPL group but also a shorter length of stay in the SPL group with comparable complication rates. We did not find a significant shorter length of stay, but we did see shorter operating times in the SPL group. The learning curve could be an explanation of the longer operating times seen in the study of Culp *et al*[17].

No differences were found in postoperative pain, but no validated tests were taken to score postoperative

pain. Single-port laparoscopy is developed to minimize surgical trauma and thereby reduce postoperative pain. Our results suggest less postoperative pain in the SPL group. A study performed by Justo-Janeiro *et al*[18] showed no advantages in postoperative pain for SPL cholecystectomies, however they conclude that more clinical trials are needed. Another shows better postoperative pain scores for a technique comparable to single-port laparoscopy[19]. A study of Sodergren *et al*[20] showed better postoperative pain results and better body image and cosmesis in SPL cholecystectomies.

Despite the fact that the SPL procedure is more challenging to learn for surgeons, no difference in peri-operative complications were found when compared with the multi-port procedure. In literature a learning curve of around 10-15 patients is described for single site laparoscopic cholecystectomy for surgeons with laparoscopic skills. Operating time for SPL procedures became comparable to the SLC operating time when a surgeon performed 10-15 procedures[11]. Another study mentioned a learning curve of 25 patients for surgeons proficient with SLC[21]. In this study the first 36 patients who received a SPL cholecystectomy were excluded, preventing effects of the learning curve.

Last year a Cochrane review concerning fewer than four ports cholecystectomies was published[22]. This review concluded a lack evidence of the benefits of fewer than four ports cholecystectomies. Last years several studies are published regarding the benefits of single-port surgery, to prove its safety and usefulness. One of the benefits of SPL cholecystectomies is better body image[20,23]. As shown by Fransen *et al*[24] the public opinion is in favour for single-port laparoscopy, *i.e.*, when complications risks remain similar, 80% of patients prefers SPL to SLC. Another benefit of the SPL technique is the possible decrease in postoperative pain, however no large clinical trials have proved this advantage yet[20]. Liang *et al*[25] showed some advantages of single-port appendectomies compared to standard laparoscopic appendectomies, like less postoperative complications and returning sooner to oral feeding.

Unfortunately, the study described in this article is limited due to selection bias (higher mean BMI in the SLC group) and bias-by-surgeon. Experienced laparoscopic surgeons performed the majority of the SPL cholecystectomies. Supervised residents performed only three procedures, whereas residents performed 29 SLC procedures. Both sources of bias probably influenced the study outcomes, however the study was designed to investigate safety and feasibility. This reality-based study showed no increase of perioperative complications as result of SPL surgery.

Longer operating time is most frequently mentioned as a disadvantage of performing the single-port technique[16,17,26,27]. A significant shorter operating time was seen in the total SPL group in this study, operating times are is most likely influenced by the experience of the surgeon and possibly the BMI of the patient. Residents performed only three SPL procedures. SLC procedures performed by surgeons showed longer operating times (median operating time for surgeons in the SPL group was 40 min, in the SLC group 51 min). Longer operating times seen in the SLC group could be explained by the higher BMI seen in this group. When analysing all 200 patients included a significant correlation between BMI and operating time is seen (higher BMI results in longer operating time). The same effect is seen in subgroup analysis for the SPL group, however no significant correlation is seen between BMI and operating time in the SLC group. A possible explanation could be that the experience of the surgeon has more influence on the operating time than BMI, more SLC procedures were performed by residents, this could be the cause of no correlation seen between BMI and operating time in the SLC group. However analysis of procedures performed by surgeons show a correlation between operating times and BMI for SPL procedures and not for SLC procedures. This suggests longer operating times in patients with a higher BMI in SPL procedures. Baseline characteristics were significantly different regarding the BMI of the patients comparing the two groups; no conclusions should be made based on this study regarding the effect of BMI on operating times. Nevertheless, in our clinic no limitations regarding BMI are of issue for SPL procedures.

Median follow-up for all patients was four weeks. After cholecystectomy patients regularly are seen only once. Patients suffering from complication or due to other reasons (*i.e.,* malignant disease or trauma) were followed for a longer period. This short follow-up period of four weeks could influence the amount of hernias measured.

Nowadays the single-port technique is not only used for cholecystectomies or other procedures in benign diseases but in malignant resections as well[28-30]. In our hospital more procedures are performed using the single-port technique in the last years, for example hemicolectomies, sigmoidresections and abdomino-perineal resections. In procedures in which the patient will receive a stoma, the single-port device can be placed at the location of the stoma for the best cosmetic result. Surgeons and patients are satisfied with the results. In future these results will be analysed as well.

SPL has the potential to be a safe technique with a low complication rate, short hospital stay and comparable operating time to multiport laparoscopic cholecystectomies. A major advance of SPL cholecystectomy in contrast with other techniques is that it can provide the patient a non-visible scar with preserving optimal quality of surgery. Randomized controlled trials are needed to confirm these advantages of SPL cholecystectomies.

COMMENTS

Background

Single-port procedures are developed to further minimize trauma and provide faster postoperative recovery with a better cosmetic result.

Research frontiers

With this study the safety and feasibility of single-port cholecystectomies is studied. Results of single-port cholecystectomies are compared to standard multiport laparoscopic cholecystectomies, regarding per- and postoperative data.

Innovations and breakthroughs

Previous studies showed single-port laparoscopic (SPL) cholecystectomy to be a safe and feasible technique, but also showed longer operating times and higher conversion rates. The results show faster operating time for the single-port technique with comparable conversions rates and comparable complications. No significant difference was found for the length of stay, but the length of stay was slightly shorter in the single-port group.

Applications

This study shows that SPL cholecystectomies can be performed safe in hands of experienced surgeons. Probably single-port laparoscopy can be performed safe in other laparoscopic procedures as well. Providing patients an almost non-visible scar while preserving high surgical quality.

Terminology

Single-port laparoscopy is a laparoscopic technique in which through one transumbilical incision the laparoscopic instruments are introduced in the intra-abdominal cavity. Using the single-port technique minimalizes surgical trauma and fastens postoperative recovery.

Peer-review

This is a good study.

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SYSTEMATIC REVIEWS

Management and outcome of recurrent gallstone ileus: A systematic review

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Abstract

AIM: To help the surgeon in decision making when treating a patient with recurrent gallstone ileus (RGSI).

METHODS: A systematic review related to RGSI was performed using the databases CINAHL, EMBASE, MEDLINE *via* PubMed from May 1912 to April 2015. All languages were included and the grey literature was also searched. The abstracts were explored for relevance to the topic and full texts obtained as appropriate. A manual search was carried out by scrutinising the reference lists of all the full text articles and further articles were identified and obtained. Total of 903 articles were identified, 656 were excluded after abstract review, 247 full text articles were reviewed and 91 articles selected for final analysis. There were 113 cases of RGSI.

RESULTS: There were 113 cases of RGSI reported in 91 articles. The majority of the recurrences, 62.6%, occurred within 6 wk of the index event. The male to female ratio was 1:7. The mean age was 69.6 years (SD 11.2) with a range of 38-95 years. The small bowel was the commonest site of impaction (92.2%). Treatment data was available for 104 patients. The two main operations performed were: (1) Enterolithotomy without repair of biliary fistula in 70.1% of all patients with a procedural mortality rate of 16.4% (12/73) and (2) a single stage surgery approach involving enterolithotomy with cholecystectomy and repair of the biliary enteric fistula in 16.3% with a procedural mortality of 11.7% (2/17). A subset analysis over last 25 years showed mortality from eneterolithotomy was 4.8% while single stage mortality was 22.2%. Enterolithotomy alone was the commonest operation performed for RGSI with four patients (5.4%) having a further recurrence of gallstone ileus.

CONCLUSION: Enterolithotomy alone or followed by a delayed two-stage treatment approach is the preferred choice offering low mortality and reduced risk of recurrence.

Key words: Recurrent gallstone ileus; Gallstone ileus;

Biliary-enteric fistula; Intestinal obstruction

Core tip: Recurrent gallstone ileus, is an acute but rare surgical condition and there is no clear evidence at present as to the appropriate management of this surgical condition. This review will provide a framework to help decision making for this condition when confronted as an emergency by the general surgeon.

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INTRODUCTION

Gallstone ileus (GSI) is a rare entity first described in 1654 by Bartholini[1,2]. GSI is a result of an inflamed gallbladder becoming adherent to an adjacent part of the enteric system and discharging its stones into the enteric lumen through formation of a biliary-enteric fistula[3-5]. It is estimated that 80% of intraluminal stones will pass spontaneously[6], Gallstones measuring more than 2.5 cm in diameter are a risk factor for impaction and causing bowel obstruction[7]; the latter is referred to as GSI. The mainstay of management is surgical treatment involving enterolithotomy alone or combined with a cholecystectomy and repair of biliary-enteric fistula as a single stage procedure.

Recurrent gallstone ileus (RGSI) is usually a consequence of an untreated biliary-enteric fistula with cholelithiasis[8]. An alternative hypothesis is the presence of a non obstructive biliary calculus more proximal in the small intestine which escaped detection at the first operation despite the need to palpate the entire small bowel looking for a second stone[9]. Predicting the risk of RGSI at the time of first operation is difficult. The literature reports an estimated risk of RGSI of 5%-8%[10-12].

When a patient presents with RGSI the surgeon will not only have to consider how to deal with the emergency obstruction but also how best to manage the cause of the recurrence. There are advocates for enterolithotomy alone without dealing with the biliary-enteric fistula, as low morbidity and mortality are perceived to be associated with this approach. However the advantages of repairing the fistula include preventing recurrence, ascending cholangitis and gallstone related complications[13-15]. These issues are similar to the ones at primary presentation of Gall Stone ileus but increase in significance now as at the primary presentation the risk of recurrence is only 5%-8%.

Although there have been several reviews of GSI, there has been no review focusing on RGSI since 1998[11]. Following a case in our hospital where a patient presented with two recurrences of GSI[16], we performed an up to date systematic review to gain a better understanding of its presentation, management and outcomes. This review will assist clinicians with the management of this rare but important condition.

Aim

To perform a systematic review of the literature from May 1912 to April 2015 to accumulate a body of evidence to help clinicians in the management of patients with RGSI.

MATERIALS AND METHODS

An electronic search was performed using CINAHL, EMBASE, MEDLINE *via* PubMed, from inception of each database to April 2015. A web-based search was also carried out using the Boolean Internet search engine "Google". The search terms used were; "recurrent" or "recurrence" and "intestinal obstruction", "gallstone" or "GSI". The search included articles written in any language.

The abstracts were explored for relevance to the topic and full texts obtained as appropriate. A manual search was carried out by scrutinising the reference lists of all the full text articles and further articles were identified and obtained.

A search of the grey literature was undertaken by searching the Royal College of Surgeon's website and a search of the grey literature database Open Grey http://www.opengrey.eu/. No further articles were identified.

Thirty-six articles of potential relevance in languages other than English were identified. All the articles were translated by native speakers in health related professions. The translations were independently reviewed by the authors before a decision was made about whether the papers were relevant for this review. Of the 36 articles identified, 20 were subsequently included.

Inclusion and exclusion criteria

The definition of a RGSI event was based on a confirmed recurrence of intestinal obstruction by a gallstone demonstrated radiologically or intra-operatively. No article with a case of recurrence of GSI was excluded; papers with incomplete data were included.

Data extraction

Two authors (MS and ZH) independently extracted the data. Data extracted included the names of the authors, date of publication and language. Other data included demographic information about each patient and clinical data such as surgical history, stone characteristics, time interval from the first operation to onset of symptoms, search for second stone at the time of first operation, site of obstruction and its relation to previous enterolithotomy, and details of the surgery performed.

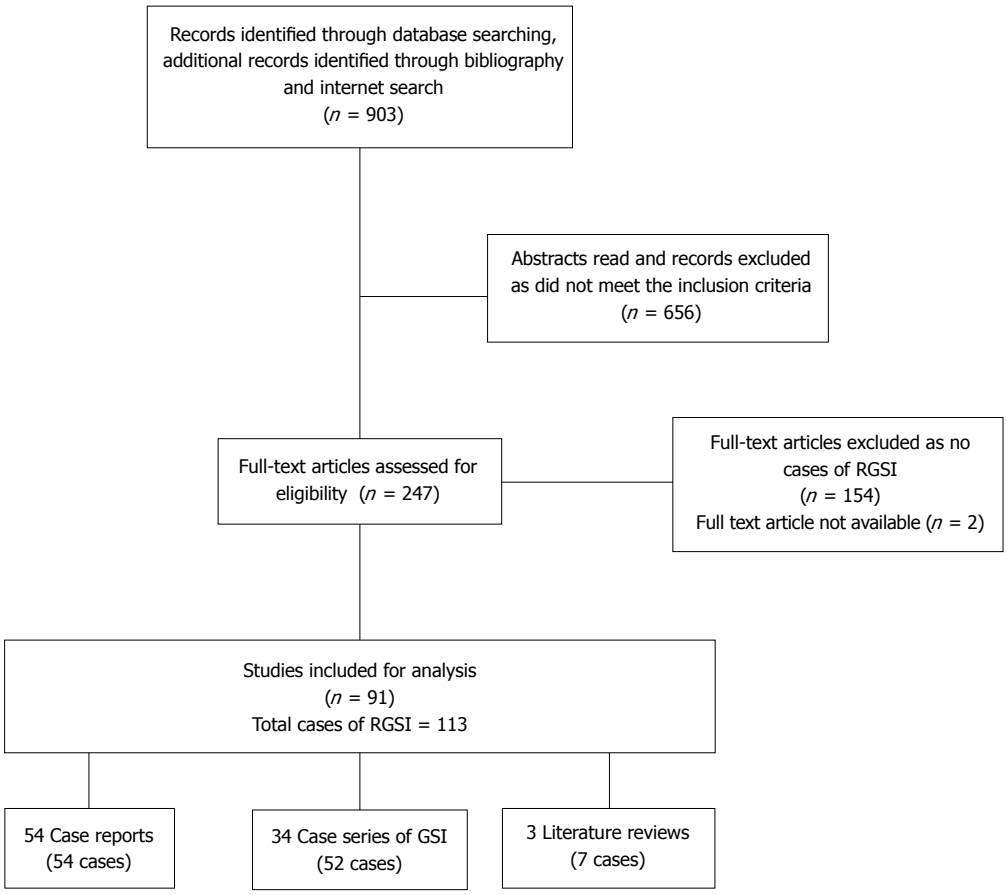

Figure 1 PRISMA flow diagram. RGSI: Recurrent gallstone ileus.

Mortality and morbidity were also noted.

Data analysis

The data analysis was limited to descriptive statistics. No meta–analysis was performed.

RESULTS

The search identified 903 articles from multiple sources as described. Ninety one articles were eventually included (Figure 1). These included 54 individual case reports, 34 case series and 3 review articles[10,17,18]. There were 113 cases of RGSI documented in the 91 articles. Full data were not available on all the categories of interest. Consequently the denominator for each category varies. This is made explicit in the text.

Demographic information

Data on age was available for 89 people. The mean age of these patients was 69.6 years (SD 11.2) with an age range of 38-95 years. The average age in males was 64.5 years (SD 15.1) with an age range of 38-94 years. The average age in females was 70.4 years (SD 10.4) with an age range of 44-95 years.

Data on gender was available for 99 cases. There were 12 males and 87 females (M: F ratio of 1:7). It was not possible to extract the data for age and gender in some case series where data was provided as an aggregate.

The treatment strategies were divided into two broad categories: (1) treatment to relieve intestinal obstruction alone; and (2) treatment to prevent recurrence, *i.e.*, enterolithotomy + cholecystectomy + repair of biliary enteric fistula.

Treatment for primary GSI (n = 106)

We looked at the treatment given for the first episode of GSI that resulted in subsequent recurrence. Data for treatment of this primary gall stone ileus was available for 106 of the 113 patients. The first episode of GSI was treated with enterolithotomy in 92 patients, 86.7%. Five people (4.9%) were treated conservatively and offending stone removed *via* rectum. A single stage surgical approach in two patients (1.9%) still resulted in RGSI. The two patients treated by a single stage procedure by Rodriguez[5] developed recurrence of symptoms two weeks postoperatively. Rodriguez does not mention whether a second stone was missed at the time of the first operation. Other operations included small bowel resection, colostomy, pyloroplasty, gastrostomy accounting for 11.7%.

Cooperman[19] performed transverse colotomy for GSI in a patient who had cholecystostomy three months prior to the first episode of GSI.

Table 1 Surgery for relief of intestinal obstruction alone and mortality (*n* = 87)

Treatment	*n*	%	Mortality	%
Enterolithotomy[1]	73	83.9	12	16.4
Small bowel resection	4	4.5	1	25
Conservative +/manual evacuation	8	9.1	2	25
OGD YAG laser lithotripsy	1	1.1	0	0
Loop colostomy	1	1.1	0	0

[1]Seven patients from this group went on to have an elective cholecystectomy with biliary-enteric fistula repair with no mortality.

Time interval to recurrence (n = 107)

The majority of the recurrences were experienced in the early postoperative period.

In our review, 67 of 107 patients (62.6%) experienced recurrence within six weeks of being treated for GSI. Within six months 91 of the patients out of 107 (85%) had experienced recurrent symptoms. The range varied from 1 d to 3287 d. The median time was 26 d with an interquartile range of 10-90 d.

Of the 16 patients who presented with RGSI after six months, nine had a recurrence of symptoms between six months and a year and seven patients a year or more after the index procedure. We could not elicit data on whether the entire small bowel was palpated for a second gallstone at the primary operation, *i.e.*, whether the reason for RGSI was a missed second gallstone at primary presentation.

Site of recurrent obstruction (n = 103)

The ileum was the commonest site of the stone impaction. Small bowel was the site of obstruction in 92.2% of the patients with RGSI. The recurrent stone was impacted in ileum in 49.5% of the patients. Colon and rectum impaction was seen in 3.8% of the cases respectively.

Size of the stone (n = 56)

The mean size of the obstructing stone was 3.6 cm with a range of 1.5-6 cm. The smallest stone that caused obstruction in the small bowel was 1.5 cm[20] and in the large bowel was 3 cm[21].

The size of the stone appeared to have no correlation with the site of obstruction. The largest impacted stone, measuring 6 cm, was found in the duodenum. The largest stone in the small bowel was 5.5 cm and in the large bowel, 5 cm.

Number of stones (n = 84)

At the time of second laparotomy for RGSI, intestinal obstruction occurred as a consequence of a single stone in 75 cases (89.2%). Two or more stones were found in 9 cases (10.7%), information was not available for 29 cases.

Goldstein[22] published a case in which multiple stones were found at both the laparotomies for GSI.

Table 2 Types of single stage surgery and mortality (*n* = 17)

Treatment	*n*	%	Mortality	%
Enterolithotomy/resection plus cholecystectomy with biliary-enteric fistula repair	14	82.3	2	
Cholecystostomy and repair of biliary enteric fistula	2	11.7	0	11.7
Right hemi-colectomy and cholecystectomy	1	5.8	0	

Shape of the gallstone (n = 36)

The vast majority of the gallstones were faceted in shape. Where the information was found 83.3% of the patients (30 of 36) were faceted in shape. In case of a faceted stone being found at the first surgery the likelihood of finding a second stone is very high and multiple authors have advocated a through search of the residual GI tract to omit recurrence of GSI.

Previous enterolithotomy site and stone impaction (n = 75)

The information comparing the site of obstruction at the first and the second episode was available for 75 patients. In 32 patients (42.5%) the site of impaction was distal to the previous enterolithotomy. In 17 patients (22.6%) the stone impacted at the site of the previous repair, while in 26 patients (34.6%) the site of impaction was proximal to the site of the previous enterolithotomy.

Treatment strategies and mortality in RGSI

Information related to specific treatment for RGSI was available in 104 patients.

In our review the following treatment strategies were adopted.

Surgery on the impacted stone alone[2,3,5,8-10,16-18,20-76]

Enterolithotomy was performed on its own as the main surgical method of relieving the intestinal obstruction in RGSI in 73 patients. When performed on its own it carried a mortality rate of 16.4% (Table 1).

Seven patients treated initially with enterolithotomy alone underwent a staged elective cholecystectomy and repair of the biliary-enteric fistula for the RGSI[9,10,16,17,39,42,51,53,57,61,76,77]. One of these seven patients had a Cholecystostomy with their enterolithotomy[61]. There was no mortality in this group (Table 1).

Other methods to relieve the obstruction were occasionally used. In one patient a stone impacted at the pylorus was dealt with using endoscopic YAG laser lithotripsy accessing the stone by gastroscopylogie[22]. Four patients had small bowel resection with one death, giving a mortality of 25% (Table 1).

Single stage surgery[7,9,77-87]

Only 17 patients had single stage surgery and one of them died giving a mortality rate of 11.7% (Table 2).

Table 3 Morbidity related to recurrent gallstone ileus treatment (n = 36)

Morbidity	Enterolithotomy n = 28	Single stage definitive surgery n = 8
No complications	10	5
Wound related-infection, dehiscence	7	1
Anastomosis related, including leak, fistula, intra-abdominal abscess	2	1
Other medical complications, sepsis, MI, pneumonia, renal failure	9	1

No surgery[18,24,88-91]

Eight patients were treated conservatively with a 25% mortality rate (Table 1). Pybus[88] and Foss[91] each described a person with RGSI not operated on who died and whose RGSI was diagnosed at post-mortem. A conservative approach led to spontaneous passage of the obstructing stone in four cases[18,92]. Rectal impaction of stone necessitated manual evacuation of stone in two patients[89,90].

The mean age of patients in the group who received enterolithotomy alone (data available for 62/73) was 70.5 years (SD 10.5, 47-95 years). The average age of patients in the single stage surgery group (data available for 12/17) was 65 years (SD 13.8, 38-88 years). The youngest patient to have RGSI was 38 years of age, had Crohn's disease, and was treated with right hemi-colectomy and definitive single stage surgery. The oldest patient, 95 years of age, was treated with enterolithotomy and survived.

Morbidity

Data on postoperative morbidity was reported for 36 patients (Table 3). Wound related complication in terms of abscess and wound dehiscence were reported in 8 patients[2,16,24,34,36,40,49,51,64,77,78,83]. Haq[60] reported on a suture line breakdown after a closure of enterolithotomy that was managed conservatively leading to enterocutaneous fistula. McGreevy[38] also reported an enterocutaneous fistula after enterolithotomy for RGSI which was treated with conservative management.

Four case reports also mentioned a recurrent episode of GSI after second enterolithotomy[9,16,73,75].

RGSI treatment in last 25 years

In recent years there has been an improvement in surgical techniques and perioperative care and therefore a subset analysis of treatment outcomes over the last 25 years (1990-2015) was performed.

Thirty published cases of RGSI were found. Twenty one patients (70%) were treated with enterolithotomy with one death (mortality rate 4.8%). This compares with 11 deaths in 52 patients in the previous 77 years for enterolithotomy giving a 21.2% mortality rate (1912 -1989).

Nine patients had single stage surgery (30%) between 1990 and 2015, with two postoperative deaths giving a mortality rate of 22.2%. This compares with no deaths in 8 patients having single stage surgery in the previous 77 years (1912-1989) giving a mortality rate of 0%.

With regard to morbidity in the last 25 years, one patient in the single stage group had an intra-abdominal abscess and five patients in the enterolithotomy group had complications related to wound infection (two), evisceration (one), *C.diff* infection (one) and respiratory failure (one).

DISCUSSION

The literature reports an estimated risk of RGSI of 5%-8%[10-12,74]. However reporting of RGSI is probably underestimated because the figures are based on published case reports or series.

The management of RGSI presents a dilemma for the surgeon. Should one only deal with the presenting obstruction once more, in which case an enterolithotomy will suffice, or should one now also deal with the cause of the recurrence in which case additional cholecystectomy and repair of biliary-enteric fistula will be needed. We sought to review existing literature that would help clinicians choose appropriate treatment strategies when faced with RGSI.

In our review RGSI mainly occurred in patients who had their primary GSI treated with enterolithotomy (86.7%). However two patients who had RGSI had single stage surgery including biliary-enteric fistula repair at the initial episode[5]. The latter suggests that recurrence can be due to pre-existing stones in the bowel that have been missed. Identification of multiple stones at the outset is therefore likely to be helpful. While a pre operative CT scan may help, careful per operative manual searching for additional stones is crucial. The authors have personal experience with a patient who had two episodes of recurrent Gall Stone Ileus having been noted to have visible stones within the gall bladder on the CT scan at the time of initial and second presentation[16].

With regard to per operative searching for additional stones, the shape of the index stone may be a useful indicator. The presence of a faceted or a cylindrical stone at the time of first surgery suggests presence of multiple stones[10]. Most of the articles in our review did not comment on the shape of the stone but of the 36 articles that did, 83.3% of the stones were faceted. This suggests that a search for additional stones may be required more often than not, and that the search will be productive.

Treatment of RGSI is usually surgery, though our review found eight cases that had been dealt with conservatively. The mortality in these latter cases was very high (25%) and therefore should be avoided unless severe co-morbidities prohibit surgical intervention.

The surgical options include enterolithotomy alone with removal of the stone thus relieving the obstruction or an enterolithotomy with a definitive operation involving cholecystectomy and repair of the biliary-enteric fistula in order to prevent future RGSI.

Enterolithotomy alone is seen as technically less demanding than single stage surgery. The increased complexity of the latter procedure theoretically carries a higher operative risk. In addition, elderly patients with multiple medical co-morbidities may present a greater physiological risk and this has to be factored into the management of RGSI.

In our review of RGSI cases comparing the recent 25 years to the preceding 77 years, the operative mortality for single stage surgery was 22.2% (1990-2015) compared to 0% (1912-1989). This is despite advanced in surgical techniques and perioperative care. However these results must be interpreted with caution as this is based on published cases only and relatively small numbers of patients.

Of the cases treated with enterolithotomy the mortality rate for 1912-1989 was 21.2% compared to a rate of 4.8% for 1990-2015. The latter concurs with the mortality rate of 5% reported in 2013 by Halabi *et al*[93] from their analysis of the Project Nationwide inpatient sample (NIS) database of just over 2000 cases.

The mortality rate of the whole cohort over the last 100 years was lower for single stage surgery in comparison to enterolithotomy despite the procedure being technically more demanding (11.7% *vs* 16.4%). If age is used as a surrogate marker for physiological fitness then we can perhaps assume that patients undergoing single stage surgery were not only younger but also fitter. However the number of patients having single stage definitive surgery was small and data on age was not available for all patients therefore caution must be taken in the interpretation of these results.

A two-stage strategy with initial enterolithotomy followed by an elective cholecystectomy and biliary-enteric fistula repair had a better outcome with 0% mortality in the seven patients[10,17,39,51,55,59,83], however this represents less than 10% of the cases and probably represents a selection bias in patients fit enough to consider an elective second surgery. However this option should also be considered in the management of RGSI.

The mortality rates from enterolithotomy alone have reduced in the last 25 years and there is a risk, albeit low, of further recurrence. We recommend it as an appropriate choice for the management of RGSI especially for the non hepato-biliary surgeon who has to deal with an emergency obstruction caused by RGSI.

To deal with the problem of possible recurrence Single stage definitive surgery, despite being more technically demanding, may be worth considering but mortality rates remain high. This approach may be appropriate in younger patients who pose a lower risk. This concurs with recommendation from other authors who have reviewed the outcome of primary GSI.

With improvement of surgical techniques and perioperative care a delayed two-stage treatment approach may provide the best results in selected cases.

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COMMENTS

Background

Gallstones can often migrate to the intestinal tract and cause obstruction, called gallstone ileus (GSI). This migration of gallstones is a consequence of an inflamed gallbladder fistulating into the GI tract. The common operation to treat GSI is an enterolithotomy. Enterolithotomy deals with intestinal obstruction alone but risks have recurrence of gallstone ileus (RGSI). Various estimates put the incidence of gallstone ileus to be 5%-8%. A definitive surgery to prevent recurrence compromises of enterolithotomy and repair of the biliary fistula and cholecystectomy, this is a technically more demanding and prolonged operation with significant risks. The mortality from enterolithotomy has been quoted from 11%-18% in various studies. In acute setting the surgeon is faced with the dilemma of trying to balance between the risks of the operation compared to risk of recurrence of symptoms. This review will consolidate current evidence and help in choosing appropriate treatment in acute settings.

Applications

The review collates evidence towards management of RGSI. This condition is not encountered often in clinical practice and can present management dilemma as treatment options vary. This review will assist clinicians in their decision making process.

Terminology

GSI: Gallstone ileus, intestinal obstruction caused by gallstone passing into the intestinal lumen; RGSI: Recurrent gallstone ileus is recurrence of intestinal obstruction due to a second gallstone. This gallstone could have passed from the gallbladder or due to a missed stone at the initial operation; Enterolithotomy: Removal of gallstone from bowel through an incision to the bowel wall; Single stage surgery: In the article, refers to enterolithotomy combined with removal of gallbladder (cholecystectomy) and repair of the biliary enteric fistula; Two stage surgery: Enterolithotomy followed by cholecystectomy and biliary enteric fistula at a later date.

Peer-review

The review content is innovative and concentrates on a rare but hard-to-deal emergence disease. The authors summarized the characteristics and treatment strategies of RGSI by reviewing case reports of this disease, which are valuable and has guiding significance in clinical practice.

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SYSTEMATIC REVIEWS

Laparoscopic management of intra-abdominal infections: Systematic review of the literature

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Abstract

AIM: To investigate the role of laparoscopy in diagnosis and treatment of intra abdominal infections.

METHODS: A systematic review of the literature was performed including studies where intra abdominal infections were treated laparoscopically.

RESULTS: Early laparoscopic approaches have become the standard surgical technique for treating acute cholecystitis. The laparoscopic appendectomy has been demonstrated to be superior to open surgery in acute appendicitis. In the event of diverticulitis, laparoscopic resections have proven to be safe and effective procedures for experienced laparoscopic surgeons and may be performed without adversely affecting morbidity and mortality rates. However laparoscopic resection has not been accepted by the medical community as the primary treatment of choice. In high-risk patients, laparoscopic approach may be used for exploration or peritoneal lavage and drainage. The successful laparoscopic repair of perforated peptic ulcers for experienced surgeons, is demonstrated to be safe and effective. Regarding small bowel perforations, comparative studies contrasting open and laparoscopic surgeries have not yet been conducted. Successful laparoscopic resections addressing iatrogenic colonic perforation have been reported despite a lack of literature-based evidence supporting such procedures. In post-operative infections, laparoscopic approaches may be useful in preventing diagnostic delay and controlling

the source.

CONCLUSION: Laparoscopy has a good diagnostic accuracy and enables to better identify the causative pathology; laparoscopy may be recommended for the treatment of many intra-abdominal infections.

Key words: Laparoscopy; Post-operative; Treatment; Perforation; Appendicitis; Cholecystitis; Diverticulitis; Infection; Pregnancy

Core tip: Laparoscopic procedures have become widely accepted as a primary means of diagnosing and treating intra-abdominal infections (IAIs). The diagnostic accuracy of laparoscopy enables surgeons to better identify the causative pathology of acute abdominal pain, and related procedures can be employed to effectively treat a variety of IAIs. Depending on the patient's symptoms, pathological severity, and the attending surgeon's personal experience, laparoscopy may be recommended for the treatment of many IAIs.

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INTRODUCTION

Intra-abdominal infections (IAIs) include a variety of pathological conditions, ranging from uncomplicated appendicitis to fecal peritonitis. IAIs are subcategorized in 2 groups: uncomplicated and complicated IAIs[1]. In the event of an uncomplicated case of IAI, the infection involves a single organ and does not spread to the peritoneum. Patients with such infections can be treated with either surgical intervention or antibiotics.

When the infection is effectively resolved by means of surgery, a 24-h regimen of perioperative antibiotics is typically sufficient. In the event of complicated IAI, the infectious process proceeds beyond a single organ, causing either localized or diffuse peritonitis. The treatment of patients with complicated IAIs involves both surgical and antibiotic therapy[1]. Source control action encompasses all measures taken to eliminate the abdominal source of infection and to control ongoing intra-abdominal contamination. Control of the source of infection can be achieved by either operative or non-operative means. The percutaneous drainage of abscesses is an important non-operative interventional procedure. However, surgery remains the undisputed cornerstone of treatment for IAIs. Surgery may be required depending on the underlying pathology and the type and severity of the intra-abdominal infection. Surgical source control may entail resection or suture of diseased or perforated viscera (*e.g.,* diverticular perforation, gastro-duodenal perforation), removal of the infected organ (*e.g.,* appendix, gall bladder), or drainage of abscesses inaccessible by means of percutaneous drainage. Source control typically involves debridement, which is essential for the removal of infected or necrotic tissue.

Laparoscopic procedures have become widely accepted by the medical community as a primary means of diagnosing and treating IAIs.

For patients with complicated IAIs, the laparoscopic approach is an extremely useful technique, particularly for diagnosing uncertain cases[2].

Depending on the anatomical source of infection and the attending surgeon's experience, laparoscopy may be recommended for the treatment of many IAIs. The aim of the present systematic review is to evaluate the role of laparoscopy in the management of the different causes of complicated IAIs.

MATERIALS AND METHODS

Literature search strategy

Electronic searches were performed using MEDLINE, EMBASE (1988-2014), PubMed (January 1980-December 2014), Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and CINAHL from (1966-2014). The search terms were: "appendicitis", "diverticulitis", "perforation", "laparoscopy", "intra-abdominal", "infection", "management" combined with AND/OR. Research included also all the MeSH Terms. No search restrictions were imposed. Progressive filters have been introduced in the research strategy in order to focalize on the highest level of evidence existing articles (*i.e.*, from meta-analysis to case series and case reports). The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. Narrative review articles were also obtained to determine other possible studies. Duplicate published trials with accumulating numbers of patients or increased lengths of follow-up, were considered only in the last or at least in the more complete version (Figure 1).

Selection criteria

Studies which have been judged eligible for this systematic review are those in which patients with IAIs from different causes have been treated with laparoscopic approach. Eligibility for study inclusion into the systematic review and study quality assessment were performed independently by two authors (FeCo, FC). Discrepancies between the two investigators were resolved by discussion.

Level of evidence definition was provided according to Oxford Classification (2011).

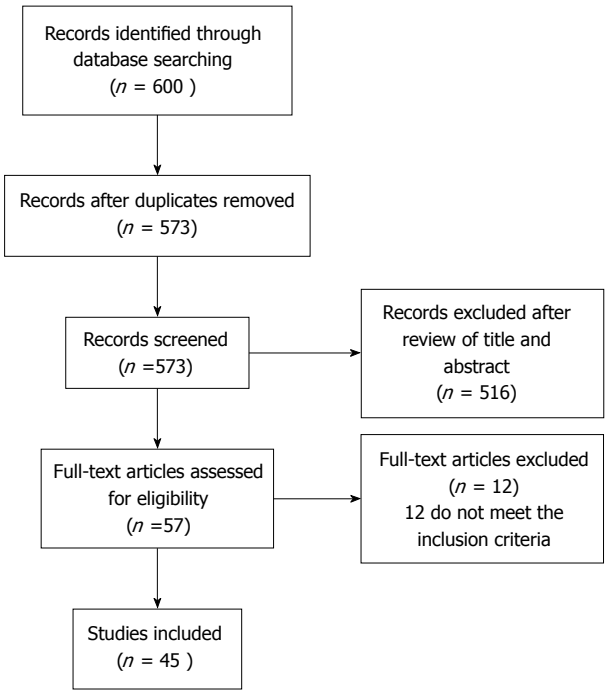

Figure 1 PRISMA flow diagram.

RESULTS

From the research a total of 600 studies were found. Among these papers 45 were selected for the inclusion in the systematic review.

Acute cholecystitis

Laparoscopic cholecystectomy have been widely accepted by the medical community as a safe and effective means of treating acute cholecystitis (AC). About the topic several randomized trials and meta-analysis exist.

The "laparoscopic *vs* open cholecystectomy" debate has been extensively investigated in the past two decades by researchers and clinicians worldwide. In the early 1990s, laparoscopic management techniques for AC were considered highly controversial; however, by today's standards, the laparoscopic cholecystectomy is widely accepted as a safe and effective treatment for AC.

Several randomized trials have demonstrated the safety and efficacy of laparoscopic cholecystectomies in treating AC[3-8].

In 1998, Kiviluoto *et al*[3] published the first randomized trial investigating laparoscopic *vs* open cholecystectomies in the treatment of both acute and gangrenous cholecystitis.

In the Kiviluoto randomized clinical trial, no deaths or bile-duct lesions were reported in both groups, but the post-operative complication rate was significantly higher (P = 0.0048) for the open cholecystectomy (OC) group than it was for the laparoscopic cholecystectomy (LC) group. Seven patients (23%) experienced major complications and six patients (19%) experienced minor complications following OC; by contrast, no patients experienced major complications and only one patient (3%) experienced minor complications following LC. The post-operative hospital stay was significantly shorter for the LC group than it was for the OC group [median 4 (IQR 2-5) d *vs* 6 (IQR 5-8) d; P = 0.0063].

An additional randomized controlled trial was published in 2005 by Johansson *et al*[4]. This study did not report any statistically significant differences between the laparoscopic and open groups in terms of rate of post-operative complications, pain score at time of discharge, or overall sick leave. For eight patients, laparoscopic interventions were converted mid-procedure to OC. The median operating time was 90 min (range 30-155 min) and 80 min (range 50-170 min) for the laparoscopic and open groups, respectively (P = 0.040). The direct medical costs were equivalent for the two groups. Although the median post-operative hospital stay was 2 d in each group, it was significantly shorter for the laparoscopic group (P = 0.011).

Common bile injuries occurring during laparoscopic cholecystectomy for AC remain the most serious complication associated with this procedure. At the beginning of the so-called "laparoscopic era", several studies reported alarmingly high rates of common bile duct injuries, but this rate decreased dramatically as the modern surgeon began to hone and fine-tune laparoscopic techniques[6,9-15].

In 2008, Borzellino *et al*[16] published a detailed meta-analysis compiling the results of laparoscopic cholecystectomy in the treatment of severe AC.

Seven studies with a total of 1408 patients who had undergone laparoscopic cholecystectomy were assessed in the meta-analysis. The risks of conversion (RR = 3.2, 95%CI: 2.5-4.2) and overall post-operative complications (RR = 1.6, 95%CI: 1.2-2.2) were significantly higher for cases of severe AC than they were for the non-severe acute forms. However, no differences were reported in terms of local post-operative complications. The authors concluded that laparoscopic cholecystectomies are less effective in treating severe AC (gangrenous or empyematous cholecystitis) than they are in treating less severe forms. A lower threshold of conversion was recommended in order to reduce the likelihood and intensity of local post-operative complications.

In 2014, Catena *et al*[17] published the results from the ACTIVE trial. 144 consecutive patients were randomly assigned to receive either OC or LC for AC. The two groups were homogeneous. Seven patients (9.7%) required conversion to OC. There were no deaths or bile duct lesions in either group, and the postoperative complication rate was similar (P = NS). The mean postoperative hospital stay was also comparable. Authors concluded that even though LC for acute and gangrenous cholecystitis is technically demanding, in experienced hands it is safe and effective. It does not increase the mortality and the morbidity rate with a low conversion rate and no difference in hospital stay.

The other question widely debated regarding the surgical treatment of AC concerns the timing.

There is strong evidence to support[18-21] that, compared to delayed laparoscopic cholecystectomies, early laparoscopic cholecystectomies for AC reduce both the duration of hospitalization and the risk of readmission due to recurrent AC.

Gurusamy *et al*[18] recently published a meta-analysis of randomized clinical trials contrasting early laparoscopic cholecystectomies (performed within 1 wk of onset of symptoms) with delayed laparoscopic cholecystectomies (performed at least 6 wk after the first onset of symptoms) in the treatment of AC. Five trials involving 451 patients were included in the study. In the resulting meta-analysis, no statistically significant differences were reported between the two groups regarding either bile duct injury or conversion to OC. The early laparoscopic cholecystectomy group featured a shorter overall hospital stay by 4 d.

The last published randomized controlled trial by Gutt *et al*[22] compared the immediate laparoscopic cholecystectomy (within 24 h from the admission) (ILC) and the initial antibiotic treatment, followed by delayed laparoscopic cholecystectomy at days 7 to 45 (DLC) in 618 patients. All patients were treated with moxifloxacin for at least 48 h. The primary endpoint was the occurrence of relevant morbidity within 75 d. Secondary endpoints were: 75-d morbidity, conversion rate, change of antibiotic therapy, mortality, costs and length of hospital stay. The trial showed as morbidity rate was significantly lower in group ILC (304 patients) than in group DLC (314 patients): 11.8% *vs* 34.4%. The conversion rate to open surgery and mortality did not differ significantly between the two groups. The mean length of hospital stay (5.4 d *vs* 10.0 d; $P < 0.001$) and total hospital costs (€2919 *vs* €4262; $P < 0.001$) were significantly lower in group ILC. Authors concluded that laparoscopic cholecystectomy within 24 h since hospital admission has shown to be superior to the conservative approach concerning morbidity and costs. Moreover authors believe that ILC cholecystectomy should become therapy of choice for AC in operable patients.

A recently published meta-analysis demonstrated that The post-operative morbidity rate was half with LC (OR = 0.46). The post-operative wound infection and pneumonia rates were reduced by LC (OR = 0.54 and 0.51 respectively). The post-operative mortality rate was reduced by LC (OR = 0.2). The mean postoperative hospital stay was significantly shortened in the LC group (MD - 4.74 d). There were no significant differences in the bile leakage rate, intraoperative blood loss and operative times [23].

In order to determine if the treatment delay following the initial onset of symptoms was truly correlated with increased conversion rates in patients with AC, a retrospective case study review of patients undergoing emergency cholecystectomies in a single treatment centre in the 4-year period between January 2002 and December 2005 was conducted[24]. Early intervention for AC (preferably within 2 d of initial onset of symptoms) was the most important criterion for a successful laparoscopic cholecystectomy; treatment delays were associated with a higher likelihood of mid-procedure conversion from laparoscopic to open surgery.

In conclusion, in AC cholecystectomy should be attempted laparoscopically at first (Level of Evidence 1).

Acute appendicitis

Acute appendicitis (AA) is the most common intra-abdominal condition requiring emergency surgery. Although antibiotic treatment has proven to be effective in treating select patients with AA[25-27], appendectomies remain the standard treatment of choice[28].

In recent years, the question of which surgical procedure, laparoscopic or open, is the best way of treating AA has been fiercely debated. Randomized trials and meta-analysis investigating the different surgical means of performing appendectomies have been published in the past 20 years.

In 2010, Li *et al*[29] published an extensive meta-analysis of randomized controlled trials (1990-2009) comparing laparoscopic (LA) and open appendectomies (OA) in both adults and children in the 19-year period from. Forty-four randomized controlled trials involving 5292 patients were included in the meta-analysis. Authors found that operating time was 12.35 min longer for LA (95%CI: 7.99-16.72). Hospital stay after LA was 0.6 d shorter (95%CI: -0.85 to 0.36). Patients returned to their normal activity 4.52 d earlier after LA (95%CI: -5.95 to 3.10), and resumed their diet 0.34 d earlier (95%CI: -0.46 to 0.21). Pain after LA on the first postoperative day was significantly less. The overall conversion rate from LA to OA was 9.51%. With regard to the rate of complications, wound infection after LA was definitely reduced (OR = 0.45, 95%CI: 0.34-0.59), while postoperative ileus was not significantly reduced (OR = 0.91, 95%CI: 0.57-1.47). However, intra-abdominal abscess, intraoperative bleeding and urinary tract infection after LA, occurred slightly more frequently (OR = 1.56, 95%CI: 1.01-2.43; OR = 1.56, 95%CI: 0.54-4.48 and OR = 1.76, 95%CI: 0.58-5.29 respectively). Authors concluded that LA provides considerable benefits over OA.

Wei *et al*[30] in 2011 published another meta-analysis analysing 25 RCTs involving 4694 patients (2220 LA and 2474 OA cases). LA showed fewer postoperative complications (OR = 0.74; 95%CI: 0.55-0.98), less pain [length of analgesia: weighted mean difference (WMD), -0.53; 95%CI: -0.91 to -0.15, earlier start of liquid diet (WMD, -0.51; 95%CI: -0.75 to -0.28)], shorter hospital stay (WMD, -0.68; 95%CI: -1.02 to -0.35), and earlier return to work (WMD, -3.09; 95%CI: -5.22 to -0.97) and normal activity (WMD, -4.73; 95%CI: -6.54-12.92). In term of hospital costs the two techniques seemed

comparable. LA demonstrated to need longer operative time (WMD, 10.71; 95%CI: 6.76-14.66). Authors concluded that LA is an effective and safe procedure for AA.

Ohtani *et al*[31] in 2012 published the last meta-analysis reporting results from 39 randomized controlled trials (1990-2012) that compared LA with OA for AA. This meta-analysis included 5896 patients with AA: 2847 had undergone LA, and 3049 had undergone OA. LA was associated with longer operative time (by 13.12 min, 95%CI: 9.72-16.61). As a counterpart, it was associated with earlier resumption of liquid and solid intake, shorter duration of postoperative hospital stay, a reduction in dose numbers of parenteral and oral analgesics, an earlier return to normal activity, work, and normal life, a decreased occurrence of wound infection (OR = 0.44; 95%CI: 0.32-0.60), a better cosmesis and similar hospital charges. Authors concluded that laparoscopic surgery may now be the standard treatment for AA.

From the literature analysis appears that LA has proven to be superior to OA. LA was, however, associated with a slightly increased rate of incidence of intra-abdominal abscesses, intra-operative bleeding, and urinary tract infections. Moreover the use of laparoscopic appendectomy should be used carefully in pregnant women. A systematic review of twenty eight articles (2008) documenting 637 cases of LA in pregnancy were included. The authors concluded that laparoscopic appendectomy in pregnancy is associated with a low rate of intra operative complications in all trimesters. However, LA in pregnancy is associated with a significantly higher rate of fetal loss compared to OA. Rates of preterm delivery appear similar or slightly better following a laparoscopic approach. According to the revised data authors suggested that OA would appear to be the safer option for pregnant women for whom surgical intervention is indicated[32].

A more recent systematic review (2012) with meta-analysis analysing laparoscopic *vs* open appendectomy during pregnancy in eleven studies with a total of 3415 women (599 in laparoscopic and 2816 in open group) showed that fetal loss rate was statistically significantly higher in those women who underwent laparoscopy. The pooled relative risk (RR) was 1.91 (95%CI: 1.31-2.77) with no heterogeneity. The pooled RR for preterm labour was not statistically significant. The mean difference in length of hospital stay was -0.49 (-1.76 to -0.78) d. No significant difference was found for wound infection, birth weight, duration of operation or Apgar score[33]. Authors concluded that laparoscopic appendectomy in pregnant women might be associated with a greater risk of fetal loss.

In conclusion, literature evidences demonstrated that the laparoscopic appendectomy is the treatment of choice in the vast majority of patients (Level of evidence 1).

Diverticulitis

Emergency surgery for colonic diverticular perforations is recommended for patients with large and/or multi-loculated diverticular abscesses inaccessible by means of percutaneous drainage, patients with persistent clinical symptoms following CT-guided percutaneous drainage, and patients presenting with diverticulitis associated with free perforation and purulent or fecal diffuse peritonitis.

When a colectomy is performed to address diverticular disease, a laparoscopic procedure appears to be the most viable approach. Even in the event of complicated diverticular disease, laparoscopic resections have proven to be safe and effective; when performed by experienced surgeons, such procedures do not appear to adversely affect the morbidity and mortality rates. However, in most cases the mainstream medical community does not consider laparoscopic procedures to be the optimal treatment of choice, despite the support of the aforementioned clinical evidence.

Although the intra-operative course for perforated diverticulitis patients undergoing laparoscopic resection may appear challenging, many retrospective studies performed by expert laparoscopic surgery groups have demonstrated at least no significant increase in the duration of surgery or the conversion rate among patients with Hinchey stage Ⅰ, Ⅱ, or Ⅲ disease[34-38].

Furthermore, in situations requiring the use of a Hartmann's procedure, laparoscopic resection with subsequent laparoscopic colostomy reversal has often been implemented successfully[39].

In 2009, the results of the only existing randomized multicentre controlled trial, the Sigma trial, were published[40]. One hundred and four patients were randomized: 52 to receive laparoscopic sigmoid resection (LSR) and 52 to open sigmoid resection (OSR). The two groups were homogeneous for gender, age, Body Mass Index, ASA grade, comorbid conditions, previous abdominal surgery, and indication for surgery. LSR took significantly longer but caused significantly less blood loss The conversion rate was 19.2%. The mortality rate was 1%. There were significantly more major complications in OSR patients (9.6% *vs* 25.0%). Minor complication rates were similar (LSR 36.5% *vs* OSR 38.5%). LSR patients had less pain (Visual Analog Scale 1.6), systemic analgesia requirement, and returned home earlier. The short form-36 questionnaire showed significantly better quality of life for LSR.

In 2013, Mbadiwe *et al*[41] published a vast retrospective trial including a total of 11981 patients. Patients undergoing laparoscopy experienced significantly lower rates of complications with both primary anastomosis (14% *vs* 26%) and colostomy (30% *vs* 37%). The laparoscopic approach was associated with decreased mortality rates for patients undergoing primary anastomosis (0.24% *vs* 0.79%). At the multivariate analysis the laparoscopic approach was associated with lower postoperative morbidity for patients undergoing primary anastomosis. The reduced risk of death for patients undergoing laparoscopic primary anastomosis (*vs*

open approach) didn't achieve a statistical significance. A small number of patients underwent laparoscopic colostomy (n = 237, 2.4%), and they did not have a significantly different risk of death. Authors concluded that the laparoscopic approach is associated with lower complication rates compared with the open approach for the surgical treatment of diverticulitis with colonic resection and primary anastomosis.

Lastly the laparoscopic approach for exploration, peritoneal lavage, and drainage has recently been developed as a treatment option for patients with acute perforated diverticulitis. However only a small number of studies have been published to date[42-44]. Two prospective cohort studies, nine retrospective case series and two case reports reporting 231 patients have been published. The majority of patients (77%) had purulent peritonitis (Hinchey Ⅲ). The laparoscopic peritoneal lavage approach successfully controlled in 95.7% of cases abdominal and systemic sepsis. Mortality was 1.7%, morbidity 10.4%. Four patients (1.7%) received colostomy[42]. In 2010 the Ladies trial protocol has been published about this topic. This is a nationwide multicentre randomised trial on perforated diverticulitis performed in The Netherlands that aims to provide evidence on the merits of laparoscopic lavage and drainage for purulent generalised peritonitis and on them optimal resectional strategy for both purulent and faecal generalised peritonitis (Trial registration: Netherlands Trial Register NTR2037). No results have still been published.

In conclusion, laproscopy in the treatment of acute diverticulitis demonstrated to be a safe and effective procedure (Level of evidence 3).

Iatrogenic colonic perforation

Colonoscopy or foreign bodies induced iatrogenic perforations are slightly rare and serious complications. Resolution of this condition typically requires segmental colonic resection. In this case, a laparoscopic approach may be ideal in order to minimize the effects of such a complication. Especially if exists the possibility to perform a direct suture of a recent and small perforation[44]. No studies exist about the comparison between the open and laparoscopic repair of iatrogenic foreign bodies colonic perforations. Similarly no prospective studies comparing laparoscopic and open approaches have been conducted, but several retrospective studies have demonstrated that laparoscopic resection is often effective in resolving colonic perforation due to colonoscopy and that it may offer certain clinical advantages over the open procedure[45] (Level of evidence 4).

Gastro-duodenal perforations

Gastroduodenal perforations have decreased significantly in recent years due to the widespread use of stress ulcer prophylaxis and other medical therapies for peptic ulcer disease among critically ill patients. Other causes of gastro-duodenal perforation include trauma, neoplasm, foreign body ingestion, or iatrogenic (endoscopic procedures)[46]. No trials exist about the laparoscopic management of post-traumatic, neoplastic, iatrogenic or foreign body due perforations. Literature however reports many studies about the laparoscopic management of perforated peptic ulcer[47].

Although non-operative management is often attempted, in most cases of perforated peptic ulcer the surgery is considered the standard method of source control[48-51].

Several prospective case-control studies have documented the successful laparoscopic repair of perforated gastric and duodenal ulcers. Recently published literature includes a few systematic reviews[52,53], three controlled, randomized trials published in a 10-year period from 1996 to 2009[53-55] compare open and laparoscopic approaches in the treatment of gastroduodenal perforations and one meta-analysis published in 2004[56].

In 2010, Bertleff *et al*[52] published a literature systematic review investigating laparoscopic corrections of perforated peptic ulcers. Data from 56 papers were extracted and systematically analyzed. The overall conversion rate for laparoscopic procedures addressing perforated peptic ulcers was 12.4%. The perforation diameter appeared to be the most significant factor affecting the rate of conversion. The operating time was significantly longer and the incidence of recurrent leakage at the site of repair significantly higher for the laparoscopic groups. However, laparoscopic patients reported significantly less post-operative pain and exhibited reduced morbidity, less mortality, and shorter hospital stays. The authors concluded that there are solid evidence to support the use of laparoscopic procedures as the primary treatment of choice when addressing perforated peptic ulcers. However, patients 70 years or older with a Boey score of 3 and symptoms persisting longer than 24 h were associated with higher morbidity and mortality rates, and as such, they are typically not viable candidates for laparoscopic procedures.

Lau *et al*[53] in 1996 published the first randomized trial where 103 patients were randomly assigned to receive either laparoscopic suture repair or laparoscopic suturless repair or open repair or open sutureless repair of perforated peptic ulcers. Laparoscopic repair of perforated peptic ulcer (either sutureless either not) took significantly longer than open repairs (94.3 ± 40.3 min *vs* 53.7 ± 42.6 min), but the amount of analgesic required after laparoscopic repair was significantly less than in open surgery (median 1 dose *vs* 3 doses). There was no significant difference in the four groups of patients in terms of duration of nasogastric aspiration, duration of intravenous drip, total hospital stay, time to resume normal diet, visual analogue scale score for pain in the first 24 h after surgery, morbidity, reoperation, and mortality rates[53].

In 2002, Siu *et al*[54] published the results from another randomized trial where 130 patients with a

clinical diagnosis of perforated peptic ulcer were randomly assigned to undergo either open or laparoscopic omental patch repair. Nine patients with a surgical diagnosis other than perforated peptic ulcer were excluded; 121 patients entered the final analysis. The two groups were homogeneous in respect to age, sex, site and size of perforations, and American Society of Anesthesiology classification. Nine patients needed conversion to open technique. The laparoscopic repair group patients required significantly less parenteral analgesics and showed a visual analog pain scores in days 1 and 3 after surgery were significantly lower. Laparoscopic repair required significantly less time than open repair. The median postoperative stay was 6 d in the laparoscopic group *vs* 7 d in the open group. The laparoscopic group showed a lower chest infections rate. There were two intra-abdominal collections in the laparoscopic group. One patient in the laparoscopic group and three patients in the open group died after surgery[54].

In 2009, Bertleff *et al*[55] published the results from the last randomized trial where 109 patients with symptoms of perforated peptic ulcer and evidence of air under the diaphragm were scheduled to receive either laparoscopic (52 patients) or open (49 patients) repair. The operating time in the laparoscopy group resulted significantly longer than in the open group (75 min *vs* 50 min). Differences regarding postoperative dosage of opiates and the visual analog scale (VAS) for pain scoring system were in favor of the laparoscopic procedure. The VAS score on postoperative days 1, 3, and 7 was significant lower in the laparoscopic group. Complications were equally distributed. Hospital stay was also comparable (6.5 d in the laparoscopic *vs* 8.0 d in the open group)[55].

The only existing meta-analysis published in 2004 by Lau *et al*[56] in 2004, included 13 studies (658 patients) among which 2 were randomized trials, comparing open and laparoscopic repair in perforated gastro-duodenal peptic ulcers. The overall success rate for laparoscopic repair of perforated peptic ulcer was 84%. Reported rates of conversion to open repair ranged from 0% to 29.1%. Five studies demonstrated a significantly longer operative time for laparoscopic repair, whereas another five trials showed no significant difference. The postoperative assessment of pain score was reported by three studies which showed a lower pain score after laparoscopic repair than after open repair. A significant reduction in the dosage of opiate analgesic required in the laparoscopic group was observed in eight studies. Chest infection was the most common postoperative morbidity. The meta-analyses showed a lower overall chest infection rate after laparoscopic repair (OR = 0.79; 95%CI: 0.38-1.62; P = 0.51). Wound infection was the second most common morbidity after open repair. The meta-analyses showed that laparoscopic repair reduces the wound infection rate (OR = 0.39; 95%CI: 0.16-0.94; P = 0.036). The leakage was more common after laparoscopic repair. The meta-analyses demonstrated a lower leakage rate after open repair (OR = 1.49; 95%CI: 0.53-4.24; P = 0.45). There were no significant difference between open and laparoscopic repair in intra-abdominal collection rate. Prolonged ileus was less common after laparoscopic repair (OR = 0.62; 95%CI: 0.20-1.92; P = 0.41). The reoperation rate after was significantly lower after open repair (OR = 2.52; 95%CI: 1.02-6.20; P = 0.045). The overall mortality rate favored laparoscopic repair (OR = 0.63; 95%CI: 0.34-1.15; P = 0.13)[56].

In conclusion, laparoscopy showed to be safe and effective in treating gastro-duodenal perforations (Level of evidence 1).

Small bowel perforation

Small bowel perforations are more uncommon sources of peritonitis in industrialized nations than they are in less-developed countries. Most small intestinal perforations are a result of undetected intestinal ischemia. Treatment most commonly involves resection of the affected bowel segment. In less-developed countries, small bowel perforations usually accompany enteric fever or intestinal tuberculosis[57].

The laparoscopic management of small bowel perforations has been well documented in retrospective series[58], but studies that systematically compare and contrast this procedure with open surgery especially in intestinal infections are needed (Level of evidence 4).

Post-operative infections

Post-operative peritonitis is a life-threatening manifestation of IAIs that is characterized by high rates of both subsequent complications and mortality.

The inability to effectively control the septic source is one of the most important factors associated with the high mortality rates[59,60].

Delaying a re-laparotomy for more than 24 h in the event of organ failure results in high mortality rates for patients exhibiting post-operative IAIs.

The value of physical tests and laboratory parameters in diagnosing abdominal sepsis is extremely limited. CT scans are believed to yield the most accurate diagnosis. Early (non-delayed) follow-up surgery appears to be the most viable means of treating post-operative infections[59,60].

The laparoscopic control and treatment of post-operative infections have been well documented in recent literature. The diagnostic accuracy of laparoscopy allows for the successful diagnosis of post-operative complications. A few retrospective studies have demonstrated that the laparoscopic approach may prevent delayed diagnoses for post-operative infections and enable experienced surgeons to better control the post-operative source of infection[61,62] (Level of evidence 4).

DISCUSSION

Laparoscopic procedures have become widely accepted by the medical community as a primary means of

diagnosing and treating IAIs.

The diagnostic accuracy of laparoscopy enables surgeons to better identify the causative pathology of acute abdominal disease, and subsequent procedures can be employed to effectively treat a variety of IAIs. Depending on the patients' symptoms and clinical conditions, on pathological severity, and on the attending surgeon's personal experience, laparoscopy may be recommended for the treatment of many IAIs.

COMMENTS

Background

Laparoscopy is gaining interest in the field of emergency surgery with several diagnostic and therapeutic possibilities.

Research frontiers

Laparoscopic procedures are becoming widely accepted as a primary means of diagnosing and treating intra-abdominal infections (IAIs) but good quality evidences are lacking.

Innovations and breakthroughs

This systematic review provides the best level of evidence available on this topic.

Applications

This review provides clearly the status of the art of laparoscopy in intra abdominal infections, suggesting the need of further studies in some specific area.

Peer-review

This is a highly valuable study. It provides the first assessment of laparoscopic therapy for IAIs, and clearly provides a data set for moving the operative management of these infections forward.

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CASE REPORT

Large gangliocytic paraganglioma of the duodenum: A rare entity

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Abstract

Gangliocytic paragangliomas are rare tumors that almost exclusively occur within the second portion of the duodenum. Although these tumors generally have a benign clinical course, they have the potential to recur or metastasize to regional lymph nodes. The case report presented here describes a 57-year-old female patient with melena, progressive asthenia, anemia, and a mass in the second-third portion of the duodenum that was treated by local excision. The patient was diagnosed with a friable bleeding tumor. The histologic analysis showed that the tumor was a 4 cm gangliocytic paraganglioma without a malignant cell pattern. In the absence of local invasion or distant metastasis, endoscopic resection represents a feasible, curative therapy. Although endoscopic polypectomy is currently considered the treatment of choice, it is not recommended if the size of the tumor is > 3 cm and/or there is active or recent bleeding. Patients diagnosed with a gangliocytic paraganglioma should be closely followed-up for possible local recurrence.

Key words: Duodenum; Gangliocytic paraganglioma; Ganglion cells

Core tip: We present the case of a patient with a rare duodenal gangliocytic paraganglioma that was treated by tumorectomy. Although there is currently no consensus for treatment, this report demonstrates that local conservative tumorectomy is a feasible, curative therapy. Patients diagnosed with a gangliocytic paraganglioma should be closely followed-up for possible local recurrence.

Gordillo Hernández A, Dominguez-Adame Lanuza E, Cano Matias A, Perez Huertas R, Gallardo Rodriguez KM, Gallinato Perez P, Oliva Mompean F. Large gangliocytic paraganglioma of the duodenum: A rare entity. *World J Gastrointest Surg* 2015; 7(8): 170-173 Available from: URL: http://www.wjgnet.com/1948-9366/full/v7/i8/170.htm DOI: http://dx.doi.org/10.4240/wjgs.v7.i8.170

INTRODUCTION

Gangliocytic paragangliomas (GPs) are rare neuroendocrine tumors that predominantly arise within the second part of the duodenum. GPs seldom recur or metastasize to regional lymph nodes[1], and are considered epithelial tumors according to the classification of tumors of the digestive tract by the World Health Organization[2]. Diagnosis of GP can be achieved based on histopathology showing epithelioid, spindle and ganglion cells, which are similarly observed for paragangliomas[3]. This report describes the case of a 57-year-old woman with melena, progressive asthenia, anemia, and a mass in the second-third portion of the duodenum that was finally diagnosed as a GP.

CASE REPORT

A 57-year-old female presented with upper abdominal pain associated with melena, asthenia, and anemia. She had a history of gluten intolerance but no fever or weight loss. A physical examination revealed pale conjunctiva and no cervical lymphadenopathy. An abdominal examination revealed tenderness in the upper abdomen with no rebound tenderness, hepatosplenomegaly, or palpable masses. Laboratory analyses showed anemia as the only pathologic finding (hemoglobin level of 9 g/dL), with normal renal and liver function. Ultrasound examination was also normal. A polypoid tumor on the third portion of the duodenum was revealed upon endoscopic examination (Figure 1). The tumor was not amenable to endoscopic resection, however, multiple biopsies were performed showing a cellular pattern of intraepithelial lymphocytes ($CD8^+$) with Marsh grade I. The presence of the polypoid formation in the proximal duodenum was confirmed by a capsule endoscopy.

Resection of the neoplasm using a laparoscopic transduodenal approach and a concomitant intraoperative duodenoscopy were planned. However, technical difficulties prevented clear identification of the lesion, and the procedure was converted to an open surgery. The tumor was then completely resected through a longitudinal duodenotomy.

Histopathologic examination of the tumor indicated a 4 cm GP without a malignant cell pattern. The surgical margin was free of neoplastic infiltration and there were no histologic findings indicative of aggressive behavior, such as mitosis and/or pleomorphism. Immunohistochemical analysis showed that the tumor was positive for synaptophysin and enolase. Additionally, epithelioid cells were immunopositive for chromogranin and cytokeratin, and fusocellular cells were S-100-positive[4] (Figure 2).

The patient had an uneventful postoperative period and was discharged after 4 d. At the 3 mo follow-up, the patient was free of symptoms and the endoscopy was normal.

DISCUSSION

GPs are rare tumors that tend to occur in the 5th decade, and more often affect men (1.8:1)[5]. These tumors typically present with gastrointestinal bleeding, whereas obstructive jaundice is very uncommon. Endoscopic ultrasonography is useful for preoperative differential diagnosis from gastrointestinal stromal tumors, carcinoids, and periampullary adenomas. GPs generally follow a benign course, rarely showing invasive growth patterns or lymph node metastasis.

GPs can be curatively treated by endoscopic resection in the absence of local invasion or distant metastasis. Sathyamurthy *et al*[6] described a case successfully treated with endoscopic retrograde cholangiography with biliary sphincterotomy to relieve jaundice. In their patient, a periampullary nodule was detected that partially obstructed the orifice of the major papilla, which was treated with en bloc endoscopic mucosal resection with an electrocautery snare. Several recent reports indicate that endoscopic polypectomy is the treatment of choice, except in cases where the tumor is > 3 cm and/or there is active or recent bleeding[7-9]. A polypectomy was not performed in the current case due to recent bleeding and the diameter of the neoplasm (4-5 cm).

Evans *et al*[10] reported a case of duodenal GP mimicking an ampullary tumor. In their case, marked secondary obstructive chronic pancreatitis was intraoperatively observed in the remaining pancreas necessitating a pylorus-preserving total pancreatectomy. Two years after surgery, the patient remained alive and well on medical treatment with no evidence of tumor recurrence. Although the recurrence index is quite low after local resection[11], Witkiewicz *et al*[12] concluded that the possibility of recurrence, lymph node involvement, and distant metastasis indicates that more extensive surgical therapy may be warranted. Indeed, surgical treatment is indicated for all GPs that are unresectable by upper gastrointestinal endoscopy and for all malignant forms. However, laparoscopic resection may be adequate for

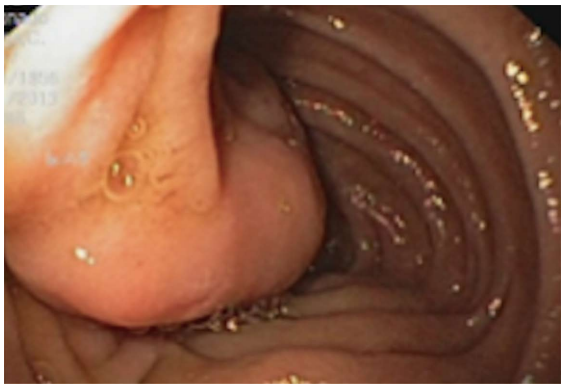

Figure 1 Endoscopic image of the tumor.

benign forms, due to the advantages of the minimally invasive approach, as demonstrated by Parini *et al*[13].

Patients who have undergone successful excision of a large polyp should receive a follow-up endoscopy after 3-6 mo, depending on the histologic findings, to verify that the resection was complete. This process should then be repeated if a residual polyp is detected. If complete resection is not possible after two or three examinations, the patient should then be referred for another surgical therapy.

COMMENTS

Case characteristics

A 57-year-old woman presented with upper abdominal pain associated with melena, asthenia, and anemia.

Clinical diagnosis

A polypoid tumor was observed in the duodenum.

Differential diagnosis

Gastrointestinal stromal tumor; carcinoid; periampullary adenoma.

Laboratory diagnosis

Hemoglobin at 9 g/dL, with normal liver and renal function.

Imaging diagnosis

Computed tomography scans were normal.

Pathological diagnosis

Gangliocytic paraganglioma was diagnosed by microscopic examination and immunohistochemical study.

Treatment

Simple excision of the tumor was performed.

Related reports

Gangliocytic paragangliomas are rare tumors, with very few reports published in the literature.

Term explanation

Gangliocytic paraganglioma is a rare neuroendocrine tumor predominantly arising in the second part of the duodenum, with rare local recurrence or metastasis to regional lymph nodes.

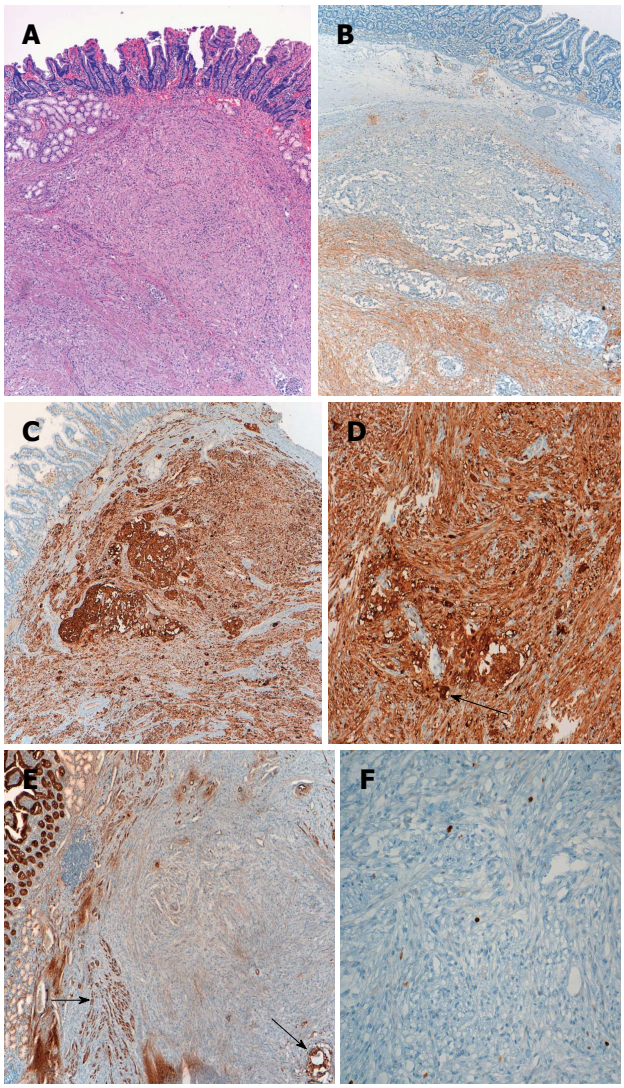

Figure 2 Histologic characteristics of the gangliocytic paraganglioma. A: Submucosal location of the tumor (× 40); B: Immunohistochemistry showing S-100 positivity of the spindle cell component (× 40); C: Immunohistochemistry showing positive staining for neuron-specific enolase in three cellular components (× 40); D: Epithelioid cells showing cytokeratin expression. Black arrow indicates ganglion-like cells (× 40); E, F: Nuclear staining with Ki-67 showing a proliferative index of < 2% (but ranged from 5% to up to 20% in other fields). Black arrows indicate epithelioid (paraganglioma-like) cells (E: × 40; F: × 100).

Experiences and lessons

Complete surgical resection remains the only curative treatment, and long-term careful follow-up is necessary for these patients.

Peer-review

This manuscript is well designed with visual materials and will contribute to the literature. It is a nice case report with good description of symptoms and treatment of this tumor entity.

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CASE REPORT

Congenital peritoneal encapsulation

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Abstract

Peritoneal encapsulation (PE) is a rare congenital malformation, characterized by a thin accessory peritoneal membrane which covers all or part of the small bowel, forming an accessory peritoneal sac. Most cases are asymptomatic and diagnosed incidentally during surgery and/or autopsy. Clinical presentation with intestinal obstruction is extremely rare and we report a case. A 25-year-old male, referred to emergency department with diffuse abdominal pain, crampy, with 8 h evolution, associated with nausea, vomiting and constipation in the last 48 h. The abdominal examination revealed an asymmetric and fixed distension, with hard consistency on palpation of lower abdominal quadrants. The abdominal radiography reveals a small bowel distension and fluid levels. Submitted to laparoscopic surgery that recourse to conversion because there is a total peritoneal encapsulation of the small bowel. After opening the peritoneal sac, we find a rotation of mesentery, at its root, conditioning twisting of small bowel and consequently occlusion. Uneventful postoperative with discharged at the 6th day. The PE is a very rare congenital anomaly characterized by abnormal bowel back into the abdominal cavity in the early stages of development. Your knowledge becomes important because, although rare, it might be diagnosis in patients with intestinal obstruction, in the absence of other etiologic factors.

Key words: Peritoneal encapsulation; Surgery; Intestinal obstruction

Core tip: Peritoneal encapsulation is a rare congenital malformation, characterized by a thin accessory peritoneal membrane which covers all or part of the small bowel, forming an accessory peritoneal sac. Most cases are asymptomatic and diagnosed incidentally during surgery and/or autopsy. Clinical presentation with intestinal obstruction is extremely rare and we report a case.

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INTRODUCTION

Peritoneal encapsulation (PE) is a rare congenital malformation, characterized by an accessory peritoneal membrane covering partially or totally the small bowel. Most cases are asymptomatic and diagnosed incidentally during surgery and/or autopsy[1-4].

PE, abdominal cocoon (AC) and sclerosing encapsulated peritonitis (SEP) are rare entities causing small bowel encapsulation. PE is an embryological malformation, while AC is idiopathic and SEP is predominantly associated with peritoneal dialysis[3]. However, on current literature these entities are predominantly represented by clinical cases.

Clinical presentation with intestinal obstruction is extremely rare[1-4].

CASE REPORT

A 25-year-old male with past history of gastritis, that has no medication or surgical history, referred to Emergency Department presenting diffuse and crampy abdominal pain, within 8 h, associated with nausea, vomiting and constipation for the last 48 h.

At admission, he was hemodynamically stable, apyretic and slightly dehydrated. The abdominal examination reveals a fixed and asymmetrical distension, with superficial and deep pain on palpation, especially in lower quadrants, with hard consistency and signs of peritoneal irritation.

The analytical study hasn't significant changes and the simple abdominal radiograph documented distention of small bowel loops with air-fluid levels. Submitted to laparoscopic surgery that recourse to conversion after establishing pneumoperitoneum.

When abdominal wall was opened, there was a thin membrane covering the small bowel with hypoplasia of the great omental (Figure 1A). The obstruction was caused by the posterior aspect of right edge's sac. The band, which obstructed the small bowel, was traced to the superior mesenteric artery, near its origin, and passed downwards until a few inches proximal to the ileocaecal valve, where it lays just above the sacral promontory (Figure 1B-D). At this point, it trapped the ileum against the sacral promontory causing obstruction. The band was divided to release the obstruction. The band contained a vessel which splits into two branches above the terminal ileum (Figure 1E). One passed downwards and backwards, deep into the pelvis, towards the upper part of the rectum. The other passed across the ileum, to end up in the sigmoid colon. The accessory peritoneal sac was excised.

Histological examination of specimen demonstrated fibrovascular tissue covered by mesothelium of peritoneal origin (Figure 1F).

Postoperative period held without complications and patient has been discharged at the 6th postoperative day.

DISCUSSION

PE is a rare congenital malformation, characterized by an accessory peritoneal membrane covering partially or totally the small bowel. It was first described in 1868 by Cleland. There're less than 20 reports described in literature, the most diagnosed accidentally[1]. However, the actual incidence of PE becomes a challenge due to difficulty in distinguishing between this entity and the AC/SEP.

The boundaries of the peritoneal sac are laterally the ascending and descending colon, superiorly the transverse colon and inferiorly the near surface of parietal peritoneum. The membrane covers entire small bowel, since Treitz angle to ileocolic junction. The great omental, if present, covers the bag but is separated from it in full[1-4].

Embryologically, PE appears to be explained by abnormal return of small bowel to the abdominal cavity during the 12th week of pregnancy. Concomitantly the yolk sac's coat migrates together with intestine, rather than remaining in umbilical pedicle[1].

Most cases are asymptomatic and diagnosed incidentally during surgery and/or autopsy. The case we described exemplifies clinical presentation with intestinal obstruction, which is extremely rare[1-4].

With respect to the physical examination, a patient with intestinal obstruction caused by peritoneal encapsulation presents some clinical signs: asymmetrical and fixed abdominal distension, peristalsis without variation and differences in consistency on abdominal palpation[1,5].

The preoperative diagnosis may be impossible because abdominal radiography is often normal or only reveal distended loops of small bowel, as presented in our case, such as computed tomography scan[1]. During abdominal contrast injection, the AC is characterized as a serpentiniform layout of small bowel, with a set of U-shaped loops, and slowed transit. Abdominal CT scan may reveal a central cluster of small bowel loops, with a dense coat, and signs of obstruction; intestinal wall thickening; ascites and fluid collections[1,3,5]. Differential diagnoses of PE are SEP and AC.

SEP was first described in 1907[6] being an acquired entity, in which the small bowel is covered by a whitish-gray dense collagen membrane. Is usually associated with chronic peritoneal dialysis therapy with beta-blockers, recurrent peritonitis, peritoneum or venous ventricular-peritoneal shunts, sarcoidosis, tuberculosis, Mediterranean fever, protein S deficiency, after liver transplantation, Lupus Erythematosus and fibrogenic foreign material.

The AC was first described by Foo *et al*[7] in 1978. It typically occurs in adolescent females in tropical or subtro

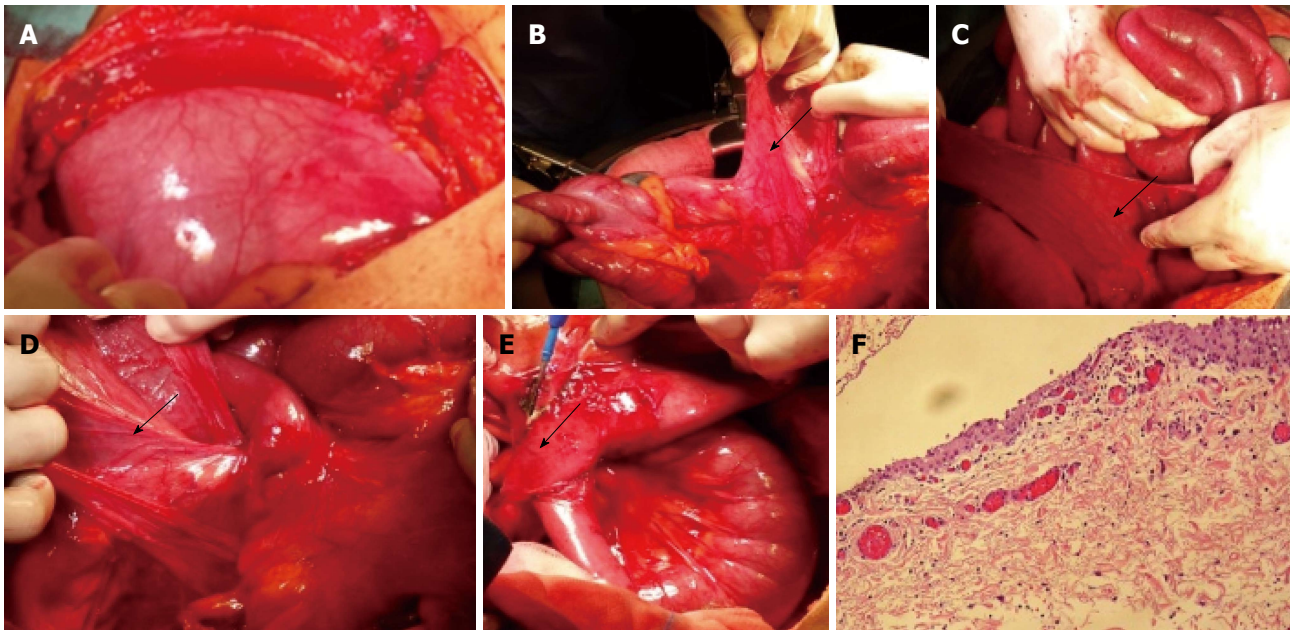

Figure 1 Intraoperative aspect. Total peritoneal encapsulation of small bowel and great omental hypoplasia (A). Opening the peritoneal sac and excision of almost all of anchor points up (B-D). The obstruction was found to be caused by the posterior aspect of the right edge's sac. At this point, it trapped the ileum against sacral promontory causing obstruction. The band was divided to release the obstruction.The band contained a vessel which splits into two branches above the terminal ileum (E). Histological examination of specimen demonstrated fibrovascular tissue covered by mesothelium of peritoneal origin (F).

pical countries. The etiology is unknown, although several theories have been presented, such as the retrograde menstruation with over-viral infection peritonitis and retrograde cell-mediated immune response promoted by gynaecological infection. It is likely that AC may be result of subclinical peritonitis. The small bowel is encapsulated by a fibrocollagenous membrane similar to SEP.

It may be associated with other anomalies such as embryological hypoplasia of great omental, as exemplified by our case, as well as malformations of mesenteric vessels[5].

The therapeutic approach in cases of intestinal obstruction, caused by PE, consists on urgent surgery, with excision of the membrane and lysis of adhesions between loops. Normally, enterectomy is not necessary, except in cases of non-reversible ischemia[3,4].

In our case, there was a twisting of peritoneal membrane, on its emergency root, conditioned by an adherence that, after lysis, provided reversibility on the caliber of small bowel loops, without ischemia. Unlike cases of SEP related to peritoneal dialysis, which earns surgical mortality beyond 60%-80%, the PE has a high survival rate, with low recurrence[5]. Histologically the membrane is composed of fibrovascular tissue covered by mesothelium from peritoneal origin. The postoperative course usually runs uneventfully, with no reported cases of recurrence[2-4].

The PE is an extremely rare congenital anomaly characterized by abnormal bowel back into the abdominal cavity in the early stages of development. Your knowledge becomes important because although rare, it might be diagnosis in patients with intestinal obstruction, in absence of other etiologic factors, such as the authors describe in this clinical case.

COMMENTS

Case characteristics

Peritoneal encapsulation (PE) is a rare congenital malformation, characterized by an accessory peritoneal membrane covering partially or totally the small bowel.

Clinical diagnosis

Most cases are asymptomatic and diagnosed incidentally during surgery and/or autopsy. Asymmetrical and fixed abdominal distension, peristalsis without variation and differences in consistency on abdominal palpation are the main clinical signs.

Differential diagnosis

Differential diagnoses of PE are sclerosing encapsulated peritonitis and abdominal cocoon.

Laboratory diagnosis

The preoperative diagnosis may be impossible because abdominal radiography is often normal or only reveal distended loops of small bowel, as presented in our case, such as computed tomography scan.

Pathological diagnosis

The small bowel is encapsulated by a fibrocollagenous membrane from peritoneal origin.

Treatment

The therapeutic approach in cases of intestinal obstruction, caused by the PE, consists on urgent surgery with excision of the membrane and lysis of adhesions between loops. Normally, enterectomy is not necessary, except in cases of non-reversible ischemia.

Related reports

The postoperative course usually runs uneventfully, with no reported cases of

recurrence.

Peer-review

This paper is reporting an interesting congenital anomaly.

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