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REVIEW

Laparoscopic appendectomy for acute appendicitis: How to discourage surgeons using inadequate therapy

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Abstract

Acute appendicitis (AA) develops in a progressive and irreversible manner, even if the clinical course of AA can be temporarily modified by intentional medications. Reliable and real-time diagnosis of AA can be made based on findings of the white blood cell count and enhanced computed tomography. Emergent laparoscopic appendectomy (LA) is considered as the first therapeutic choice for AA. Interval/delayed appendectomy at 6-12 wk after disease onset is considered as unsafe with a high recurrent rate during the waiting time. However, this technique may have some advantages for avoiding unnecessary extended resection in patients with an appendiceal mass. Non-operative management of AA may be tolerated only in children. Postoperative complications increase according to the patient's factors, and temporal avoidance of emergent general anesthesia may be beneficial for high-risk patients. The surgeon's skill and cooperation of the hospital are important for successful LA. Delaying appendectomy for less than 24 h from diagnosis is safe. Additionally, a semi-elective manner (*i.e.*, LA within 24 h after onset of symptoms) may be paradoxically acceptable, according to the factors of the patient, physician, and institution. Prompt LA is mandatory for AA. Fortunately, the Japanese government uses a universal health insurance system, which covers LA.

Key words: Laparoscopic appendectomy; Acute appendicitis; Interval appendectomy; Surgery; Delayed appendectomy

Core tip: Acute appendicitis develops in a progressive and irreversible manner, and emergent laparoscopic appendectomy (LA) is mandatory. The Japanese government uses a universal health insurance system. Any physician and institution can routinely perform expensive emergent LA in Japan, in accordance with medical ethics. Unsafe, but cost-effective, treatments such as interval/delayed appendectomy and conservative management only are unsuitable in Japan. Time-honored practices, (*i.e.*, emergent LA) should be respected in Japan.

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INTRODUCTION

Acute appendicitis (AA) is a clinical diagnosis[1,2]. The first appendectomy was performed in New York in 1886[1], and thereafter, appendectomy was considered the most common emergency surgery[2-4]. Prompt appendectomy has long been the standard of care for AA because of the risk of progression to advanced pathophysiology[3].

Currently, laparoscopic appendectomy (LA) is available as the first therapeutic choice for AA[1,3]. However, surgeons on call when a patient is admitted is an important factor for determining whether a patient can receive an advantageous LA or conventional open surgery[5]. Additionally, a poor clinical course in a hospital with an unfavorable combination for emergent laparoscopic surgery is a critical matter[3,6]. In brief, factors of hospitals and physicians affect the severity of AA[3,5-7].

A 24-h surgical shift in a quadratic/tertiary care hospital is stressful for surgeons[8]. Emergent surgeries during overtime service and off-days result in higher rates of morbidity and mortality[9,10]. However, AA indicates a surgical emergency.

AA may be managed in an elective manner once antibiotic therapy is initiated[2,11-14]. Initial non-operative management followed by interval and/or delayed appendectomy for AA has been challenged, especially in pediatric patients[3]. However, the necessity and validity of an interval/delayed appendectomy is still controversial in adult patients[2,3,11-18], though some researchers believed that interval/delayed appendectomy has some advantages only for treatment of appendiceal mass[12,14].

We review major controversy in management of AA based on previous studies, and discuss what practice is the best option for patients with AA.

PATHOPHYSIOLOGY

The exact mechanism of AA is still unclear, but is believed to be multifactorial. Inadequate dietary fiber, familial factors, and luminal obstruction from fecalith impaction or lymphoid hyperplasia, and other processes, such as parasitic infestation, may be involved[19-22]. Luminal obstruction by external (*i.e.*, lymphoid hyperplasia) or internal (*i.e.*, inspissated fecal material and appendicoliths) compression plays a major pathophysiological role[3]. This subsequently leads to increased mucus production, bacterial overgrowth, viral infection, and stasis, which increase appendiceal wall tension[3,19-24]. Consequently, blood and lymph flow is diminished, and necrosis and perforation follow[3]. Because these events occur over time, only an early surgical approach might prevent progression of disease[3,4]. The immunological orchestra around the ileocecal portion is well developed and complicated, and the appendix has its own immunological features[25-28]. Many major immunological and cellular function-associated gene sets involved in the protective effect of AA followed by appendectomy in experimental colitis have been identified[25].

Once disease is triggered, AA develops in a progressive and irreversible manner[3,4,29]. Even a histologically normal appendix clearly shows evidence of inflammatory responses against AA, as shown by cytokine production/expression[29].

An appendiceal mass (tumor formation after perforating AA) is the end result of a walled-off appendiceal perforation[2,16]. Pathologically, this mass may range from phlegmon to abscess[16]. A pus-containing mass is an inflammatory tumor consisting of an inflamed appendix, its adjacent viscera, and the greater omentum[16].

In AA, tumor necrosis factor-α is at the top of the pathway[29,30], and interferon-γ and interleukin-6 play an important role[30,31]. Fas-mediated induction of apoptosis is a major factor in selection of lymphocytes and downregulation of immunological processes, and endothelial Fas-ligand expression is elevated in AA[26]. AA develops in a progressive and irreversible pathway[2,16], even if the clinical course of AA can be temporarily modified by intentional medications[32].

DIAGNOSTIC VALUE

Physical findings of AA are well established[33]. Many researchers, such as Charles McBurney, Niels Thorkild Rovsing, Jacob Moritz Blumberg, Otto Lanz, Frederic

Treves, and others were involved in the initial study of AA[1,34]. Most patients present early in the disease process[2], although, in 2%-6% of patients, diagnosis is made when an appendiceal mass is discovered on preoperative imaging[16,35]. Young female patients have the highest risk of being falsely diagnosed with AA and thus have unnecessary surgery[36].

Computed tomography (CT) is more reliable for diagnosis than an ultrasound examination[37,38], and enhanced CT should be routinely performed for suspected appendicitis[39]. Enhanced CT scans have become the main diagnostic tool for patients with AA and have a high sensitivity and specificity[39]. Briefly, enhanced CT is a powerful tool for a strict diagnosis and assessment of the degree of inflammation[15,36,37,39-42], and enhanced CT is superior to a physician's clinical examination[36,37,39,40]. A helical CT image study should be performed with contrast enhancement, even with lower doses[37,43]. Routine CT for suspected appendicitis improves patients' care, shortens the duration to surgery, and reduces the use of hospital resources and overall admission costs[39].

Laboratory data show that serum levels of the white blood cell (WBC), C-reactive protein (CRP), and interleukin-6 are related to AA[44-46]. The most reliable marker is neither the neutrophil count nor CRP, but the WBC count[1,44].

The WBC count and CT findings equally provide surgeons with complementary information in discerning the necessity for an urgent operation[36,44,47]. With development of WBC measurement and enhanced CT imaging, the rate of negative appendectomy has decreased to as low as < 5%[1,36,40,48].

HISTORY OF LA

LA was reported in 1983[49]. Thereafter, some advantages of LA, such as less pain, fine cosmetics, shorter hospital stay, faster recovery, less wound infection, and lower cost, compared with conventional open surgery were shown from the 1990s[50-63]. Postoperative complications are also lower in LA than in conventional open surgery[56,64-66]. Therefore, LA has spread to become the standard surgery worldwide[1,15,50,62,65-67]. Although the operative time, including buried sutures, may be longer in LA[50-52,55], there are no significant differences in the rate of severe morbidity/mortality between open and laparoscopic appendectomies[68]. Currently, natural orifice transluminal endoscopic surgery is also considered as safe and feasible[69,70].

DURATION TO SURGERY

Many physicians have an interest in the duration from onset of symptoms to surgery. In adult patients with AA, the risk of developing advanced pathophysiology and postoperative complications increases with time[3,4]. However, there is the minority opinion that the duration from surgical admission to induction of anesthesia is not predictive in regression models for overall morbidity or serious morbidity/mortality[71].

Interval/delayed appendectomy is considered as unsafe[3], although the term of "interval appendectomy" can be used only in case of appendiceal mass and performed after 6-12 wk of the beginning of disease[1,12,14]. Any delays in seeking medical help results in difficulty in controlling AA, and prompt appendectomy is mandatory[3,4]. Interval/delayed appendectomy may not increase the risk of perforation and moderate/severe complications[1,71,72], but is significantly associated with an increased risk of surgical site infection (SSI) in patients with nonperforated appendicitis and prolongation of the hospital stay[71,73]. Prompt surgical intervention is warranted to avoid additional morbidity in this population[73].

Transferred patients are less likely to be ruptured, primarily because they present earlier[72]. Morbidity is not increased in patients who have appendectomy that is delayed for up to 24 h[1]. Delaying an appendectomy for longer than 6 hours, but less than 24 h, from diagnosis is safe and does not lead to worse outcomes[74]. This can help limit disruption to the schedules of the surgeon and the operating room[74]. Paradoxically, AA that is approached in a semi-elective manner (*i.e.*, LA within 24 h after symptom onset) may be acceptable, according to the factors of physicians and hospitals[1,3,5-7,74].

A physician's delay in avoiding negative appendectomy does not affect the stage of disease[7]. A surgeon's decision to observe patients in hospital to clarify the diagnosis is justified[7], as it does not adversely affect the outcome[7].

SURGICAL PROCEDURES

Actual procedures of LA are shown in detail in Figures 1-3. Gastric and bladder catheters are placed only during surgeries for decompression to avoid unexpected injuries[1].

Stump appendicitis is a critical result of an incomplete surgery[75], and management of the base of the appendix during LA is important. Surgeons need to decide the best management of the base of the appendix; choices include a clip, ligate, or staple. A flexible endostaple has some advantages in application of LA for day surgery and extended resection to the cecum[76-79]. However, an endostaple (Tri-staple camel 45 mm and iDrive; Medtronic, Minneapolis, MN, United States) may be excessive in quality and have a higher cost than a ligation tool (Endoloop; Ethicon, Cincinnati, OH, United States) or clip closure[80]. If there is any concern about the stump, a couple of interrupted seromuscular sutures can be added, although the suture technique is technically demanding[80].

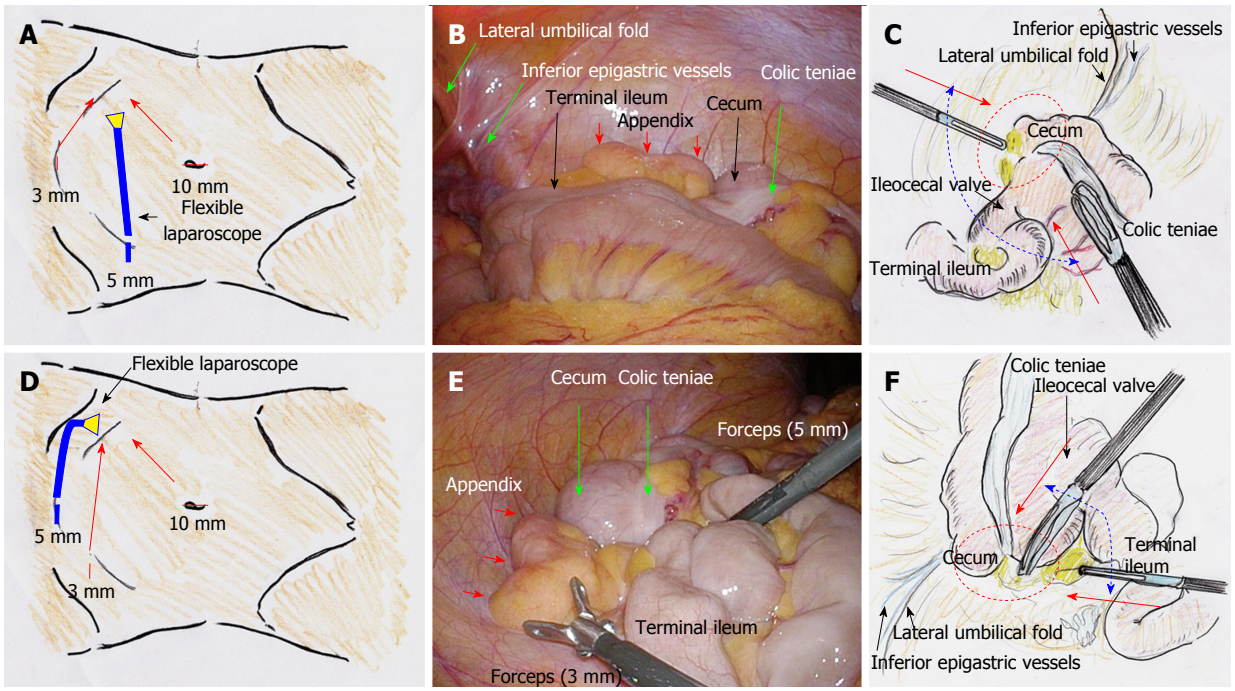

Figure 1 Port placement and laparoscopic view. A-C: If the left lateral port is set for laparoscope, a wider angle of working forceps can be made. However, a stab scar of 5 mm remains visible; D-F: Port placements for LA using an endostaple with the best cosmesis are shown. LA: Laparoscopic appendectomy.

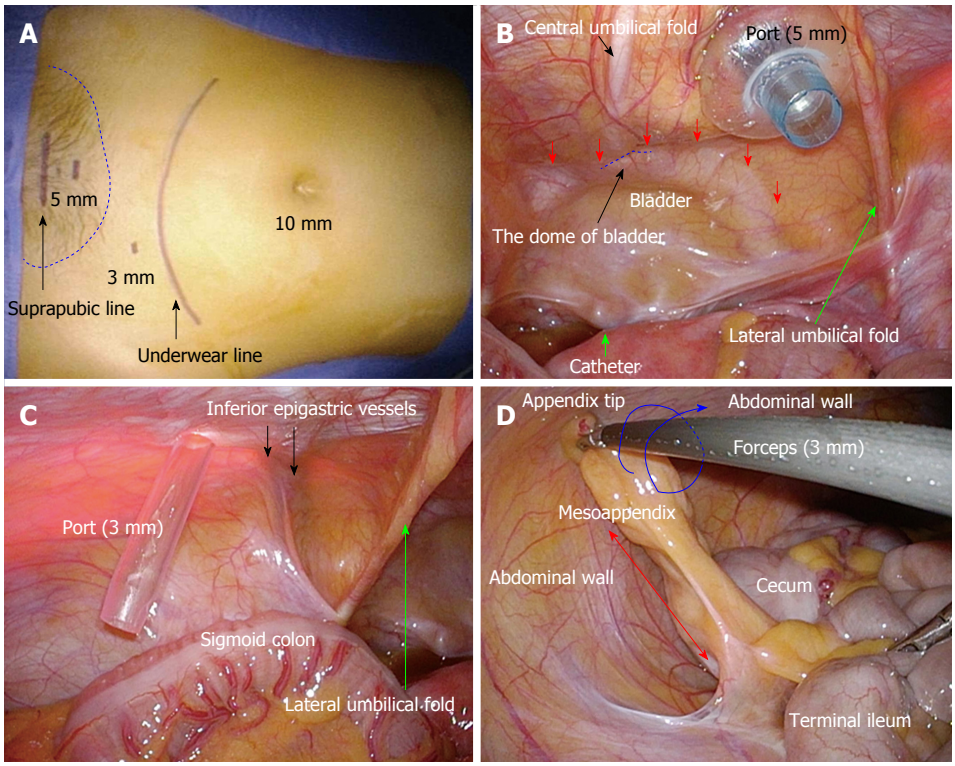

Figure 2 Major techniques during laparoscopic appendectomy. A: A suprapubic port (5 mm) for a flexible laparoscope is placed within the area of pubic hair (dotted blue line) to hide the postoperative stab scar. A left lateral port (3 mm) is placed as low as possible, to enable an adequate angle for the working forceps and to hide the postoperative stab scar by underwear; B: The bladder wall (red arrows), the dome of the bladder (dotted blue line), and the central umbilical fold should be recognized. Although the suprapubic peritoneum easily extends during port insertion, a suprapubic port should be placed without bladder injury; C: Any injury of the left inferior epigastric vessels should be avoided; D: Countertraction of the mesoappendix (red arrow) should be made without obstruction of the abdominal wall. Gripping and rotating forces of 3-mm forceps are sufficient. The appendix can be shortened in a rolled-in fashion (blue arrow) to avoid any disturbance by the abdominal wall.

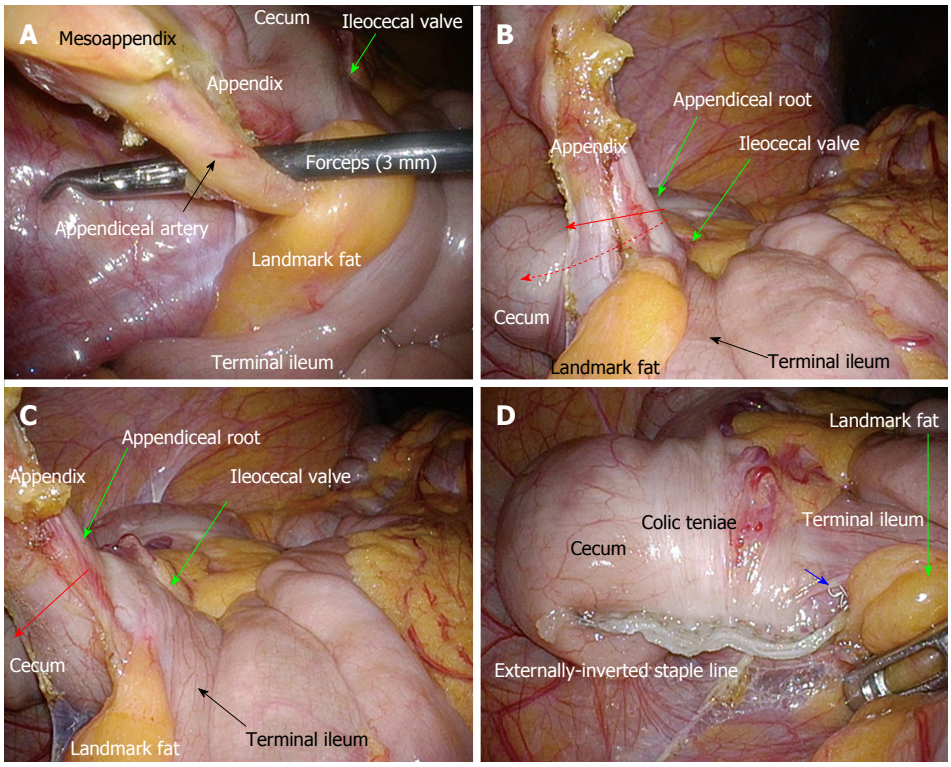

Figure 3 Key techniques during laparoscopic appendectomy. A: Appendiceal vessels should be clearly dissected and be sealed without a clip for subsequent use of an endostaple; B: Total resection of the appendiceal root should be made (red solid arrow). A flexible endostaple has an advantage in extended resection to the cecum (red dotted arrow); C: The ileocecal valve should be recognized before an endostaple is placed (red arrow). Any involvement of this valve should be avoided; D: The externally-inverted staple line should be carefully checked. If there is any concern about a stump, a couple of interrupted seromuscular sutures can be added. Unrelated and spilled staples (blue arrow) should be removed.

PERITONEAL LAVAGE IN PERFORATING AA

Surgeons should be aware of a potentially higher incidence of intraabdominal abscess formation following LA[68,81,82]. Use of endobags (Rüsch MemoBag; Teleflex, Wayne, PA, United States), inversion of the appendiceal stump, and carefully conducted local irrigation of the abdomen in the supine position may reduce the incidence of abscess formation[81]. Peritoneal lavage during surgery is an effective, safe, and simple treatment for generalized peritonitis[83]. Irrigation of the abdominal cavity with more than 10 L of saline should be performed[84,85], and a cut-off level of saline volume to prevent intraabdominal abscess formation after surgery is 12 L[83]. Do not hesitate to place a drain. A drain pathway through the abdominal wall is adequately made at the right abdomen, to prevent a drain dislocation.

COSMESIS

Primary closure is currently accepted, even in complicated appendicitis with a dirty abdominal wound[86-88]. However, delayed closure, which can occur several days after surgery, can lead to a decrease in SSI, a shorter hospital stay, and lower cost[89,90]. LA has an advantage of a lower rate of SSI, even in complicated appendicitis[82,91-93].

STABILITY OF RESIDENTS ON LA

Video game playing, such as Nintendo Wii (Nintendo Co., Ltd., Kyoto, Japan) and Playstation 2 (Sony Interactive Entertainment Inc., Tokyo, Japan)[94-101], and laparoscopic performance skill are well associated. Therefore, the younger generation may be suitable for performing laparoscopic surgery[94-101]. LA performed by residents under the guidance of a staff surgeon is safe and feasible[102,103]. Operative time and postoperative complications can be reduced with increasing experience of a resident[104]. Incidental appendectomy during conventional open surgery is also important to educate young surgeons[105].

INTERVAL/DELAYED APPENDECTOMY AND RECURRENCE DURING THE WAITING TIME

Some physicians consider that management of AA remains controversial[2,42]. An appendiceal mass is a misery form of perforated AA[2,16]. Initial conservative management of an appendiceal mass was first

advocated in 1901 as a solution[106]. Interval/delayed appendectomy is performed electively after initial non-operative management[2,11-14], but has been questioned by a growing amount of evidence[2,11-18,107,108].

The recurrence rate of AA during the waiting time for interval/delayed appendectomy is 6%-37%[13-15,109-114], and the complication rate of surgery for recurrent AA is also not low (3%-23%)[11,107,109,115-117]. Advocates of interval/delayed appendectomy believe that the recurrence of AA is low, even though the actual rate is high, during the waiting period[3,13-15,109-114]. Interval/delayed appendectomy is routinely performed at 6-12 wk, mainly because of fear of recurrent appendicitis or because of concerns about the presence of malignancy[12,14,118,119].

Especially in a phlegmon or appendiceal mass, interval/delayed appendectomy may have some advantages. These advantages include providing a definite diagnosis, to rule out any underlying masquerading malignancy and to avoid an unnecessary extended resection[12,14,108,118-121].

POSTOPERATIVE COMPLICATIONS

This review shows that the severity of pathophysiology and the complication rate in adult patients with AA are time-dependent[3], and thus suggests that delaying appendectomy is unsafe[3,4].

Mortality due to AA is difficult to observe[3,76], and the mortality rate after appendectomy is nearly zero[76]. However, the rates of morbidity and mortality are clearly increased in older patients, male patients, and patients with steroid use, baseline disease, active pneumonitis, and a bleeding tendency[3,56,122]. Perioperative injection of antibiotics should be considered to reduce complications, including SSI[1,123,124]. Postoperative complications are also lower in LA than in conventional open surgery[56,64,65].

CONSERVATIVE TREATMENT ALONE

Notably, non-operative management has a cost advantage over routine interval/delayed appendectomy after initial successful conservative management[2]. Patients who recover from conservative treatment of an appendiceal mass should undergo colonoscopy or barium enema to detect any underlying diseases and to rule out coexistent colorectal cancer[12,14,108,118-121].

Laparoscopic surgery by experienced surgeons is a safe and feasible first-line treatment for appendiceal abscess[32,67]. Additionally, laparoscopic surgery is associated with fewer readmissions and fewer additional interventions than conservative treatment with a comparable hospital stay[67]. However, non-operative management is well tolerated and efficacious in select populations, especially in children[125-127]. Some patients who initially receive conservative treatments do not require surgical intervention[13,17,107,120,128], and AA should no longer be regarded as an indication for interval/delayed appendectomy[13,17,107,120,128,129]. Routine interval/delayed appendectomy benefits less than 20% of patients[14]. The majority of recurrence occurs in the first 6 mo[14,109-112], but the rate decreases to approximately 2% at 1 year[107,112,118]. Importantly, AA develops in a progressive and irreversible pathway[2,16], even if the clinical course of AA can be temporarily modified by intentional antibiotics[32]. The length of hospital stay and postoperative complications increase with advanced pathology during antibiotic treatment[3].

A gradual, adapted antibiotherapy in non-operative management of an appendiceal abscess and mass is effective[130]. There is no relevant predictive factor of failure of first-line antibiotics[130]. Monotherapy with a second-generation, broad-spectrum cephalosporin, such as cefotetan, administered twice a day, is an economical and effective adjunctive regimen[38]. A third-generation cephalosporin can be used[15], but is not recommended yet[131].

SPECIFIC SITUATIONS

Some situations of patients are especially listed in surgical indications, such as older people, pregnancy, and negative appendectomy[1,48,129]. Although LA in pregnant women has been already reported, fetal loss and negative appendectomy should be avoided in this population[132,133]. The available low-grade evidence suggests that LA in pregnant women is associated with a greater risk of fetal loss[132,134]. Appendectomy and early appendicitis are associated with increased pregnancy rates[135]. Young women with early appendicitis have better pregnancy rates than those with advanced appendicitis. Early referral for laparoscopy and appendectomy is advocated[135]. Appendiceal tumors may be incidentally detected[136,137].

REASONABLE COST

The cost effectiveness of LA has been reported[57]. Non-operative management without LA is the least costly[138]. Non-operative management has a cost advantage over routine interval appendectomy after initial successful conservative management[2].

Despite liberal use of disposable equipment, LA can still be performed within the confines of the national tariffs[139]. There is considerable variation in the cost of this procedure, and it may be possible to reduce costs by more stringent use of disposable equipment and standardizing recovery protocols[139].

DISCUSSION

Clinically, many surgeons believe that LA is an appropriate treatment[76]. However, LA requires general anesthesia, although LA under combined spinal-epidural or local anesthesia is currently being attempted[140,141]. LA in a semi-elective manner (within 24 h after onset of symptoms) may be beneficial for avoiding

uncomfortable situations for anesthetic induction, such as a full stomach and dehydration[142,143]. However, even in a high-volume center, unfavorable combinations, such as low activity of the operation room during night time, affects the clinical course of AA[6]. Overall, LA in a semi-elective manner may be acceptable.

Each country has its own health insurance system. The Japanese government uses a universal health insurance system. Therefore, expensive imaging studies and emergent surgery can easily be performed in Japan. However, expensive studies and therapeutic options may be uncertain in the United States and Europe[144,145]. Novel procedures in Japan are not authorized until they are included in the health insurance system's listing by the governmental council[146]. Paradoxically, if a surgery is once listed in Japanese health insurance system, any physician and institution can routinely perform it, even an expensive emergent surgery, in accordance with medical ethics. We have to consider how to dismantle interval/delayed appendectomy and antibiotics alone, in Japan.

Diagnostic methodology and subsequent management pathway have been already established[147]. The LA under the hands or directions of experienced surgeons is safe and has a lot of beneficial advantages[148,149]. High-volume centers should routinely perform emergent laparoscopic surgery including LA[148]. Physicians and surgeons have a large interesting frontier.

CONCLUSION

AA is pathophysiologically progressive. As time passes, AA is difficult to control. Prompt LA in a quadratic/tertiary care hospital is mandatory for AA, and this time-honored practice should be respected. Interval/delayed appendectomy and conservative management are unsuitable in Japan. The question can be asked: "Where should emergency physicians or general surgeons head in the next decade?". We consider that it is important to focus on stabilizing prompt LA for AA around the world.

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