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NEW TECHNOLOGY

Novel device to detect enterotomies in real time during laparoscopy: first in human trial during Roux-en-y gastric bypass

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Abstract

Background Undetected bowel perforations occur in 0.3–1% of laparoscopic surgical procedures with an associated mortality rate of 5.3%.

Objective The purpose of the study was to evaluate the clinical feasibility of a novel medical device to accurately detect bowel gas, specifically hydrogen (H_2) and methane (CH_4), from a sample of gas from the abdominal cavity during laparoscopic surgery when a known bowel wall perforation has occurred. Setting: University (Academic) Hospital.

Methods A prospective single arm study was composed of 8 patients undergoing a standard laparoscopic roux-en-y gastric bypass. At seven time points during the operation intra-abdominal gas was pulled from the abdominal cavity and analyzed using the novel device for H_2 and CH_4. The time points included after insufflation (T1), after first jejunotomy (T2), after closure of jejunotomy (T3), after recycle of carbon dioxide gas (T4), after gastrostomy (T5), after jejunotomy (T6), at procedure end (T7).

Results Eight patients were enrolled in the study; in 7 (87.5%) patients data from all 7 time points were obtained. After the first opening of the small bowel (T2) mean hydrogen levels were significantly increased compared to baseline hydrogen levels (T1, T4, T7) ($p < 0.001$). At all time points, there was no significant detection of methane. There were no intra-operative or post-operative complications during the study.

Conclusion Hydrogen gas is released into the intra-abdominal cavity when bowel is opened and can be detected in real time using a novel device during laparoscopic surgery. The presence or absence of hydrogen directly correlates to whether the bowel is open (perforated) or intact. This device could be used in the future to detect unintended bowel perforations during laparoscopic surgery, prior to the conclusion of the operation. This technology could also potentially lead to novel mechanism for detecting postoperative leaks using gas detection technology.

Keywords Laparoscopy · Bowel injury · Bariatric · Bowel perforation · Bowel gas · Injury

Greater than 7.5 million laparoscopic surgeries occur annually in the US and Europe, one of its most feared complications is undetected intraoperative bowel perforation. It is estimated that 0.3–1% of laparoscopic surgical procedures are complicated by iatrogenic bowel perforation [1–3]. In particular, during laparoscopic explorations for small bowel obstruction, intraoperative iatrogenic bowel perforations range from 4.7 to 17.3%. Of these, 1.3–4.8% are unrecognized injuries, diagnosed and treated during the postoperative course [4–6]. Small bowel injuries may also occur during gynecological or urological procedures and occur in 0.4% of hysterectomies for example [7]. Delay in diagnosis and treatment until the postoperative period may result in peritonitis, sepsis, and death. The associated mortality rate for laparoscopic induced bowel injuries ranges from 3.6 to 5.3% [2, 3]. This value, formerly greater than 50%, has decreased with increasing experience, recognition and management of bowel injury; however, morbidity and mortality associated with undetected bowel injury remain a significant challenge [3].

While laparoscopic or minimally invasive surgery has clear and distinct advantages to open laparotomy, there are drawbacks as well. Specifically, the decreased visualization

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inherent in a laparoscopic procedure is a significant contributing factor to bowel perforation risk. These iatrogenic bowel injuries occur at all stages of laparoscopic procedures including the introduction of the Veress needle, trocar placement, intraoperative dissection and cautery [3, 7–9].

Undetected bowel perforations are diagnosed post-operatively and this diagnosis can be delayed due to unclear presentation, false negatives from the CT scan, or misdiagnosis of free air noted on CT [10]. Delay in diagnosis may result in progression to septic shock, multisystem organ failure, and eventually death if the perforation remains undiagnosed. Once recognized, treatment may include a second surgery with possible ostomy formation and/or multiple subsequent surgeries, antibiotic treatment or Interventional Radiology procedures. Independent of the treatment necessary to control perforation, clinical consequences of a bowel injury will often lead to increased duration of hospitalization, admission to the intensive care unit, additional hospitalizations, and development of intra-abdominal abscesses and/or adhesions. However, if the bowel injury is detected intraoperatively, it can typically be repaired at the time of the initial surgery, with little to no additional morbidity.

During laparoscopy, field of vision is necessarily limited by working space and the camera view field. Injuries to the bowel may occur outside of this visual field; therefore any early diagnostic solution cannot rely solely on visual cues. Alternatives, such as the use of smell rather than sight, would allow broad detection of a bowel injury anywhere within the abdominal cavity. Sentire Medical's Perf-Alert is a novel device that will enable the identification of bowel injuries intra-operatively, thus facilitating immediate treatment.

The gastrointestinal tract is known to produce gas composed of carbon dioxide, hydrogen, nitrogen, oxygen, and methane in various quantities depending on diet and specific section of bowel [11–13]. During laparoscopic and robotic surgery, the abdomen is typically insufflated using medical grade carbon dioxide. Provided that the bowel is intact, there should not be any methane or hydrogen present in a given sample of intra-abdominal gas during a laparoscopic surgical operation. However, if the bowel wall has been disrupted, bowel gas containing hydrogen and/or methane will leak from the lumen, disperse within the peritoneal cavity and upon sampling can be detected. This study evaluates the ability of this novel device to detect bowel gas, after intentional opening of the bowel, during a human laparoscopic procedure. Once it is demonstrated that the device can reliably detect bowel gas leak with a known bowel injury, the device can then be evaluated to detect bowel gas leak from unintended and previously undetected bowel injuries.

Early prototypes of the system were evaluated in a series of unpublished in vitro and large animal studies to evaluate the capability of the sensors to detect methane and hydrogen in the small quantities that would be expected to leak from a bowel wall injury during an operation (unpublished data). From these studies, the sensor demonstrated the ability to detect methane and hydrogen within 30 s of sensor analysis. The sensors were able to accurately detect both high (10,000 ppm) and low concentrations (100 ppm) of methane (both in physiologic ranges). These experiments verified that the device was able to detect in near real time, the presence of methane and hydrogen in physiologically relevant concentrations from a simulated carbon dioxide insufflated abdominal cavity.

For laparoscopic surgery, the abdomen is insufflated to a working pressure of 15 mmHg, based on previous publications, the bowel pressure is greater than 20 mmHg, typically at 38–40 mmHg indicating that bowel gas will exit the bowel and enter the peritoneal cavity for evaluation should an injury occur [14].

A porcine model was selected as it is routinely used to evaluate laparoscopic and robotic surgical devices and techniques. A total of two animal studies were completed 5 pigs. The studies evaluated the ability of the sensor to be connected to a trocar and to pull a low flow, low volume sample into the device for gas analysis. The device analyzed between 1 and 3 samples both pre-bowel perforations and post-bowel perforations. Results demonstrated the ability for the sensors to detect bowel gases after perforation, in real time, and indicated when a bowel injury had been sustained.

The aim of this study is to evaluate if the novel device is able to accurately detect changes in gas composition in the abdominal cavity during laparoscopic surgery.

Materials and methods

A prospective, pilot, single arm study was designed to evaluate the clinical feasibility of the device to detect the presence of intestinal gas, specifically methane and hydrogen, from a sample of intra-abdominal gas during a standard laparoscopic roux-en-y gastric bypass surgery.

The prototype consists of a small 10″ × 4″ × 2″ unit containing gas sensors and valves, a small box containing a one-way, ultra-low pressure pump, user controls (buttons) and software algorithms, which control the operation of the device. It is used in conjunction with a single use, disposable kit consisting of sterile tubing and filters used for sample collection and transport. The system's architecture is configured such that sample collection, transport, analysis and feedback occur in a single step such that sample collection and sensor feedback occur in real time. A standard laptop running an analytical software program is connected to the unit to record and log sensor readings taken. The device sensors for methane have a lower detection limit (LDL) of 100 ppm with a sensitivity of 100 ppm, for hydrogen they

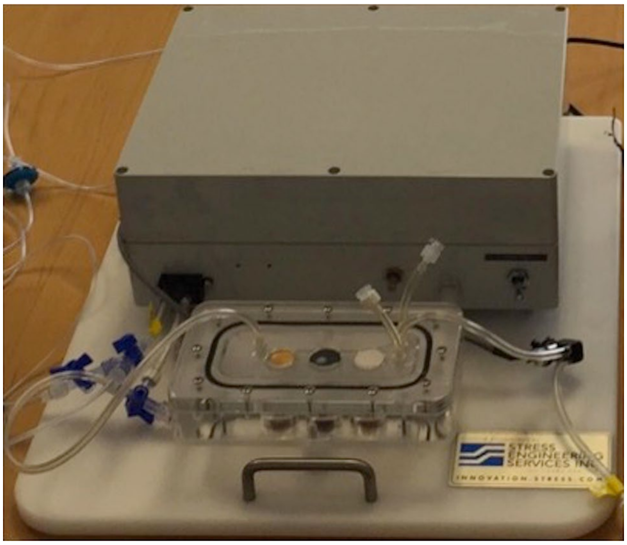

Fig. 1 Perf-Alert device. Contains gas sensors for hydrogen (H_2), methane (CH_4). Connects via sterile luer lock plastic tubing to a standard trocar stop-cock

have an LDL of 20 ppm with a sensitivity of 10 ppm (noise ± 10 ppm), for carbon dioxide LDL 400 ppm with a sensitivity of 200 ppm (noise ± 200 ppm) (Fig. 1).

The study was designed and conducted at Stanford University Hospital with Stanford University approval: IRB 35295, clinicaltrial.gov NCT02679118. Patients were recruited from the Bariatric clinic and the study duration was limited to the intra-operative period. The primary endpoints were as follows: (1) to detect significant change in hydrogen and/or methane levels in the insufflated abdomen following voluntary enterotomy. (2) Determine if is able to detect return to baseline after ex-sufflation and re-insufflation.

All patients were induced and positioned in the standard fashion for the procedure. Separate from the sterile field, the device was set up and prepared. The surgeon gained intra-abdominal access using a Veress needle. After insufflation to working pressure with carbon dioxide (15 mmHg) and port placement, one end of sterile tubing with luer connectors was passed off the field and connected to the device. The sterile end of tubing was connected to the trocar and the following time point samples were obtained according to the following protocol: surgical staff ensured the valve to the device tubing was connected and open between the trocar and the device. The device, using a one-way pump drew and analyzed 1–2 gas samples from the peritoneal cavity at a rate of 150–800 ml/min. Each sample duration was 45 s, with a 45-s purge after each sample. Samples were obtained at the time points listed in Table 1.

A single experienced bariatric surgeon at Stanford University performed the anti-colic laparoscopic roux-en-y gastric bypass. All enterotomies were performed at the standard

Table 1 Gas sample time points during laparoscopic roux-en-y gastric bypass

T1	Following access and initial insufflation to working pressure
T2	Following the initial enterotomy
T3	Following the closure of the small bowel (the jejuno-jejunal anastamosis)
T4	Prior to opening the stomach (after a recycle)
T5	Following opening of the stomach
T6	Following opening of the small bowel
T7	Prior to removal of all trocars (end of case)

Gas samples were collected using Perf-Alert at the listed time points during a standard laparoscopic roux-en-y gastric bypass procedure

time during the case and the surgeons continued to operate during gas sample collection. Approximate size of the jejunal enterotomies was approximately 10–15 mm, in diameter in order to accommodate a standard linear stapler. The size of the gastrotomy was approximately 20 mm in order to accommodate a 25-mm anvil.

All samples were analyzed in real time by the device to detect hydrogen (H_2) and methane (CH_4). Gas composition was analyzed from 30 s after the start of sample collection to 15 s after the end of sample collection. The maximum value for a particular gas –H_2 or CH_4– was identified for analysis. Statistical analysis was completed using excel v14.7.5 with ANOVA/paired *t* test.

Results

A total of 8 patients were enrolled in the study; all patients completed the study. There were no intraoperative complications and no post-operative complications during the study.

Of 8 patients, complete data were obtained from 7 patients (87.5%). In patient 3 (12.5%), data were collected from time points T1–T5, due to personnel time constraints. Therefore, all of patient 3's time points were excluded from analysis. All gas samples were analyzed for H_2 and CH_4 in ppm and maximum values for each time point were identified (Tables 2, 3). For hydrogen, values < 20 ppm are below the lower detection limit for the device, and therefore considered 0.

Baseline hydrogen levels were obtained after initial insufflation (T1), after recycling of the CO_2 (T4) and at the conclusion of the procedure prior to desufflation (T7). The variance between these three time points was not significant ($p = 0.09$), a mean of each patient's hydrogen baseline was compared to hydrogen values at the enterotomy time points. Hydrogen levels showed significant increase after the first enterotomy (jejunum) (T2) compared to baseline levels with an average increase of 44× ($p < 0.001$) (Fig. 2).

Table 2 Maximum hydrogen level at each time point, for each patient

	P1	P2	P3	P4	P5	P6	P7	P8	Mean
T1	11	10	9	28	23	28	13	21	18
T2	25	43	11	49	70	53	38	36	41
T3	10	12	196	25	120	81	24	39	64
T4	7	8	9	22	24	20	13	16	15
T5	337	382	1683	532	372	1056	108	286	595
T6	163	607	NS	51	36	77	33	22	141
T7	9	10	NS	19	20	19	15	17	15

Values that were unable to be obtained are listed as not specified (NS). Values < 20 ppm are considered 0 ppm, per device specifications

Table 3 Maximum methane level at each time point, for each patient

	P1	P2	P3	P4	P5	P6	P7	P8	Avg. all PTs
T1	1	4	1	2	10	2	5	11	4
T2	3	1	0	1	11	0	1	6	3
T3	4	0	2	1	8	2	0	6	3
T4	9	1	1	3	6	1	0	8	4
T5	7	2	12	8	5	7	0	10	6
T6	10	4	NS	5	6	1	4	12	6
T7	9	4	NS	3	8	0	2	9	5

Values that were unable to be obtained are listed as not specified (NS). Values < 100 ppm are considered 0 ppm, per device specifications

After gastrostomy (T5), hydrogen levels were significantly increased compared to baseline levels by an average of 400× ($p < 0.01$) (Fig. 2).

Throughout all time points in all patients, there was no significant detection of methane (Fig. 3).

Discussion

This first in human trial demonstrates that the small intestine, specifically jejunum, and the stomach contain hydrogen gas, which is released into the intra-abdominal cavity during laparoscopy after bowel wall injury, and is detectable in real time using the Perf-Alert device.

Hydrogen previously has been identified in the stomach, small intestine, and colon, whereas methane is predominately located in the colon [11]. This study demonstrated that the stomach and small intestine contain hydrogen at significant values, which were detected after enterotomy. There was no significant measurable detection of methane during the study. Potential explanations include that the amount produced, contained in, and/or released by the stomach and small bowel (jejunum), may not be in sufficient quantities to be detected by the Perf-Alert.

Evaluation of intra-abdominal gas samples during laparoscopic gastric bypass surgery demonstrates that the presence or absence of hydrogen is detectable by the Perf-alert device. Furthermore, presence of hydrogen directly correlates to whether the stomach or small bowel is open (perforated) or closed (intact). Enterotomy time points (T2, T6) and gastrotomy time points (T5) compared to control time points (T1, T4, T7) demonstrate a significant increase in detected levels of hydrogen when bowel is open. The average value for T6 is significantly larger than T2. This is potentially due to some ischemia in the portion of the roux limb which is resected after the circular stapler is passed in the distal roux limb—or gas accumulation in the bowel after it has been transected altering the local bowel gas composition. The average value for T5 is significantly larger than T6 or T2, possibly due to the difference in gas composition between the stomach and the small intestine.

Several key limitations exist in this work. First, the device was used only to evaluate small bowel and gastric perforation during laparoscopic roux-en-y gastric bypass. The bypass procedure was selected as it has multiple intentional enterotomies and a gastrotomy, all of which are standard steps in the surgery. Small bowel enterotomies were of primary interest as the majority of unintended laparoscopic enterotomies are in the small bowel [4]. However, as the large bowel was not involved in the procedure, large bowel enterotomies were not evaluated with the device. The study utilized known perforations—specifically created to create stapled anastomoses. Undetected perforations may be smaller in caliber, which may alter

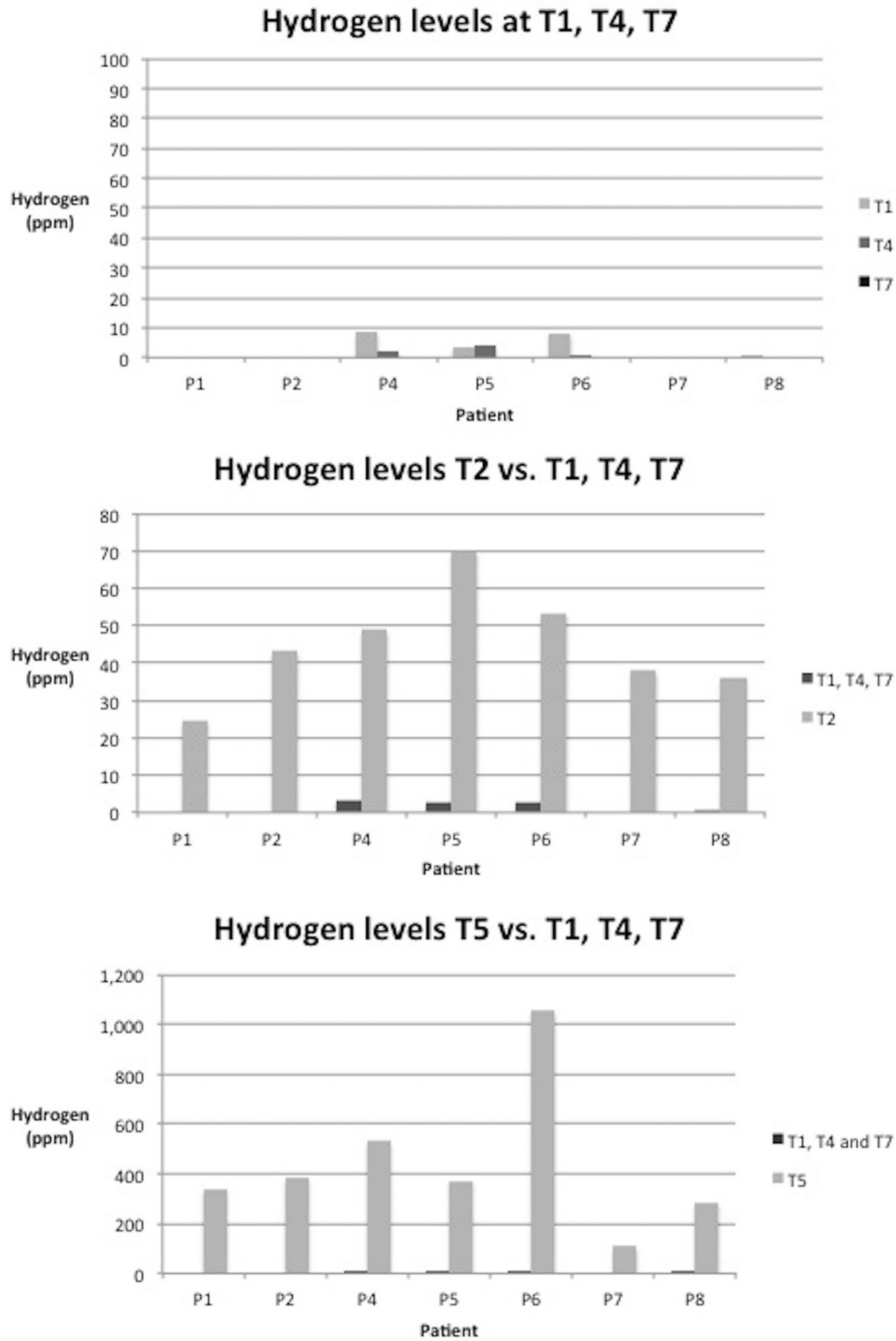

Fig. 2 Hydrogen levels after jejunal enterotomy (T2) and after gastrotomy (T5) were significantly higher than at initial insufflation, recycling of CO_2, or end of procedure (T1, T4, T7) ($p < 0.001$) and ($p < 0.01$) respectively

the amount of hydrogen released in the intra-abdominal cavity and/or may alter the time interval between unintended perforation and detection. While this study demonstrated that the bowel gas can be removed with recycling of intra-abdominal gas and closure of all enterotomies, the duration of detectable bowel gas leakage from a perforation and the persistence over time of detectable gas is not adequately assessed. The bowel gas is sampled from one of the trocars and is a sample from the entire intra-abdominal cavity. For unintended bowel perforations, the device will detect that a perforation is present but will not identify where in the bowel the perforation is located. Finally, since the device detects intra-abdominal gas, perforations that evolve over time, such as thermal injury or partial bowel

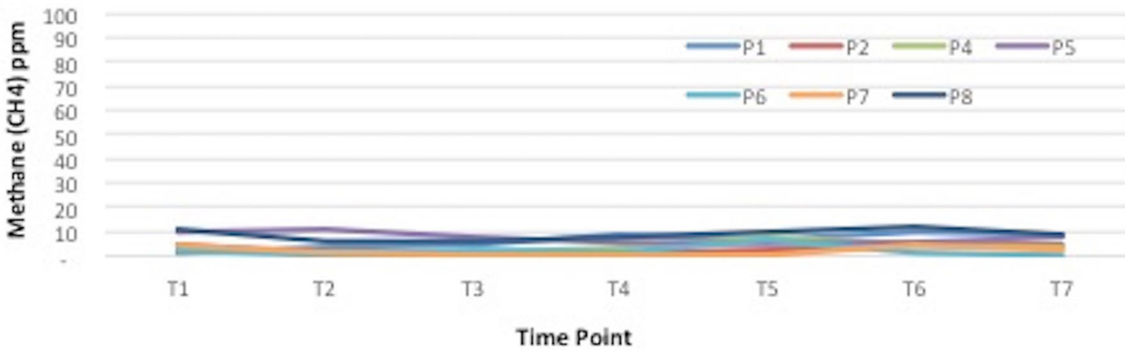

Fig. 3 Measured methane levels throughout the procedure showed no significant methane concentration as all values are less than the lower detection limit for the device of 100 ppm

wall mechanical injury, will not be detected during the index operation.

Further work should examine the bowel gas composition of the colon, determining if it can be detected with hydrogen and/or methane. Additionally, it should determine if small, unintentional perforations could be detected via bowel gas. Lastly it should be evaluated if gas can be detected postoperatively in the setting of anastomotic leaks.

This is an initial study in the work to refine and evaluate a device to detect, intra-operatively in real time, unintended bowel wall perforations during laparoscopic and robotic surgery. Detection prior to conclusion of the surgery would allow for intra-operative repair greatly reducing the morbidity and mortality of unintended bowel perforations in minimally invasive surgery.

Funding The company made the device available at no cost and provided support for its use. No funding was received for this trial.

Compliance with Ethical Standards

Disclosures Dr. Elisabeth Wynne and Dr. Dan Azagury have no conflicts of interest or financial ties to disclose.

References

1. Al-Qurayshi Z, Srivastav S, Slakey DP, Kandil E (2016) Risk of intraoperative injury of nearby structures: national trend, distribution, and burden. J Am Coll Surg 222:624–631
2. van der Voort M, Heijnsdijk EA, Gouma DJ (2004) Bowel injury as a complication of laparoscopy. Br J Surg 91:1253–1258
3. Schwartz MJ, Faiena I, Cinman N, Kucharczyk J, Meriggi JS, Waingankar N, Richstone L, Kavoussi LR (2010) Laparoscopic bowel injury in retroperitoneal surgery: current incidence and outcomes. J Urol 184:589–594
4. Dindo D, Schafer M, Muller MK, Clavien P-A, Hahnloser D (2010) Laparoscopy for small bowel obstruction: the reason for conversion matters. Surg Endosc 24:792–797
5. Wullstein C, Gross E (2003) Laparoscopic compared with conventional treatment of acute adhesive small bowel obstruction. Br J Surg 90:1147–1151
6. Suter M, Zermatten P, Halkic N, Martinet O, Bettschart V (2000) Laparoscopic management of mechanical small bowel obstruction. Surg Endosc 14:478–483
7. Llarena NC, Shah AB, Milad MP (2015) Bowel injury in gynecologic laparoscopy: a systematic review. Obstet Gynecol 125:1407–1417
8. Galleano R, Franceschi A, Ciciliot M, Falchero F, Cuschieri A (2011) Errors in laparoscopic surgery: what surgeons should know. Minerva Chir 66:107–117
9. Deffieux X, Ballester M, Collinet P, Fauconnier A, Pierre F, Obstetricians FNCoGa (2011) Risks associated with laparoscopic entry: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians. Eur J Obstet Gynecol Reprod Biol 158:159–166
10. Singh JP, Steward MJ, Booth TC, Mukhtar H, Murray D (2010) Evolution of imaging for abdominal perforation. Ann R Coll Surg Engl 92:182–188
11. Feldman M, Friedman L, Brandt L (2015) Fordtran's Gastrointestinal and liver disease—pathophysiology, diagnosis, management, 10th edn, Saunders
12. Sharma M, Makharia G (2000) Intestinal gas—its syndromes. JK Science 2:75–80
13. Sahakian AB, Jee SR, Pimentel M (2010) Methane and the gastrointestinal tract. Dig Dis Sci 55:2135–2143
14. Sosna J, Bar-Ziv J, Libson E, Eligulashvili M, Blachar A (2008) CT colonography: positioning order and intracolonic pressure. AJR Am J Roentgenol 191:1100

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