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World Journal of Gastrointestinal Surgery
Baishideng Publishing Group Inc
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
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Baishideng Publishing Group Inc
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Telephone: +1-925-2238242
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MINIREVIEWS

Dolichocolon revisited: An inborn anatomic variant with redundancies causing constipation and volvulus

Dennis Raahave

Dennis Raahave, Department of Surgery, Copenhagen University North Sealand Hospital, Hilleroed 3400, Denmark

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Correspondence to: Dennis Raahave, MD, PhD, DMSci, Consultant Surgeon, Senior Researcher, Department of Surgery, Copenhagen University North Sealand Hospital, Dyrehavevej 29, Hilleroed 3400, Denmark. dr.dr@dadlnet.dk
Telephone: +45-40-258626

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Abstract

The objective of this review is to examine whether a redundant colon gives rise to symptoms like constipation and volvulus. In 1820, Monterossi made drawings of colons with displacements and elongation of the colon found during autopsy. In 1912, Kienböeck first visualized a redundant colon using bismuth, and Lardennois and Auborg named the anatomic variant dolichocolon in 1914. The criteria were later: A sigmoid loop rising over the line between the iliac crests, a transverse colon below the same line and extra loops at the flexures. The incidence of dolichocolon is 1.9%-28.5%. Dolichocolon seems to be congenital, as fetuses, newborns, and infants exhibit colonic redundancies. Studies have identified a triade of constipation, abdominal pain, and distension. Colon transit time was recently shown to increase significantly with increased number of redundancies, which increases abdominal pain, bloating and infrequent defecation. The diagnosis of dolichocolon is established by barium enema or CT-colonography. Treatment is conservative, or surgical in case of volvulus or refractory constipation.

Key words: Dolichocolon; Colon elongatum; Functional gastrointestinal disorders; Constipation; Volvulus

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Core tip: Dolichocolon is an inborn anatomic variant, where redundancies may be located in the right, middle and left part of the colon and at the flexures. This review investigated the literature on dolichocolon. The prevalence is not known. The incidence is 1.9%-28.5% in patient series. The dominating symptoms of dolichocolon are constipation, abdominal pain and volvulus. Colon transit time is prolonged and increases significantly with increased number of redundancies, which increases abdominal pain, bloating and infrequent defecation. The diagnosis is established by a barium enema or CT-colonography. Treatment is conservative, or surgical in case of volvulus or refractory constipation.

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INTRODUCTION

The redundant colon represents an unusually lengthened large bowel folded up upon itself, forming extra loops, tortuosities and kinks. The redundancy may involve the entire colon or it may be limited to certain areas as the hepatic flexure, transverse colon, splenic flexure, but the distal colon especially the region of the sigmoid is the most commonly affected. There has long been a debate about whether a redundant colon gives rise to symptoms like constipation and volvulus. The objective of this review is to critically examine this issue.

Embryological development of the colon

The development of the midgut in the embryo is characterized by a rapid elongation of the gut and its mesentery, resulting in formation of the primary intestinal loop. The cephalic limb of the loop develops into the distal part of the duodenum, the jejunum, and part of the ileum. The caudal limb becomes the lower portion of the ileum, the caecum, the appendix, the ascending colon and the proximal two-thirds of the transverse colon. In adults, the junction of the cranial and caudal limb can only be recognized if a portion of the vitelline duct persists as a Meckel's diverticulum[1]. Coinciding with the growth in length, the primitive intestinal loop rotates around an axis formed by the superior mesenteric artery. Subsequently, elongation of the small intestinal loop continues, forming coiled loops. Similarly, the large intestine grows considerably in length, but fails to participate in the coiling phenomenon. At the end of the third month, the intestinal loops return to the abdominal cavity from the extra-embryonic coelom. The caecal bud is temporarily located in the right upper quadrant below the liver before it descends into the right iliac fossa, thereby forming the ascending colon and hepatic flexure. The distal end of the caecal swelling forms a narrow diverticulum, the appendix. As the intestine returns to the abdominal cavity, their mesenteries are pressed against the posterior abdominal wall where they fuse with the parietal peritoneum, fixing the right and left colon. The colon is now as it is in the adult.

ANCIENT ANATOMIC OBSERVATIONS OF THE COLON

In 1820, Monterossi[2] noted from autopsies an increased length of the colon, which was depicted in handmade drawings showing sigmoid loops and duplication of the right and left colonic flexure (Figure 1). Treves[3] dissected the bodies of patients who died from reasons other than abdominal diseases. He was convinced that the length of the bowel was independent of age, height, and weight. In the full-term fetus, he found that the length of the intestine, and especially the colon, was significantly constant. Shober[4] reported 18 cases selected from different investigators between 1826 and 1896 in which the sigmoid flexure was found on the right side of the pelvis. Various other abnormalities were reported, including a caecum in the right hypochondriac region with extensive mesentery. It seems that the colon was likely to vary in length and in mode of disposition more than any other part of the intestinal canal[5]. This was further demonstrated by Black[6] in a series of drawings from textbooks and journal papers between 1836 and 1911, showing a multitude of displacement and elongation of the left colon. The hepatic and splenic flexures were permanently in place.

Bryant[7] measured the intestines after removed from the body. His data showed that Treves[3] was incorrect in stating that all children start life with practically the same length of intestine. He found great variations in the small intestine and colon before the fifth month of fetal life. At the age of 10 years, the child has a length of colon considered normal for the adult. He also found that the colon varied in length from 1.25 to 2.00 m, with an average length of 1.52 m. Furthermore, he reported that the length of the colon increased about 20 cm between 20 and 80 years of age.

NEWER OBSERVATIONS OF COLON LENGTH

Phillips *et al*[8] reported colon length from several studies of cadavers, using laparotomy, barium enema or CT-colonography, between 1955 and 2015. The mean length of the colon varied between 109.0 cm and 169.0 cm. A redundant colon with loops was not mentioned. In their own study, they found a significant proportion of colons had mobility of the ascending and descending segments, with the length of the latter being highly variable. This may indicate loose redundancies.

RADIOLOGY OF DOLICHOCOLON

By combining a bismuth meal and a bismuth clysma, Kienböck[9] was the first to visualize a redundant colon. An extremely long mobile descending colon and sigmoid ran from the left flexure through the abdomen up under the liver and then distally superimposed to the ascending colon and caecum, before joining the rectum. A few years later, Lardennois and Aubourg[10] using the same technique demonstrated various redundancies in all parts of the colon, in both adults and children. These investigators named the anatomic variant dolichocolon (dolicho-, Greek: long). During the following years, many case-series with all positions of colonic redundancies were published, using this new X-ray technique[11-14]. The colon length or that of the redundancies was not measured. Years later, the redundant colon was characterized by the following criteria: a sigmoid loop rising over the line between the iliac crests, a transverse colon below the same line and extra loops at the hepatic and splenic flexure. A fully developed dolichocolon occurs when all redundancies

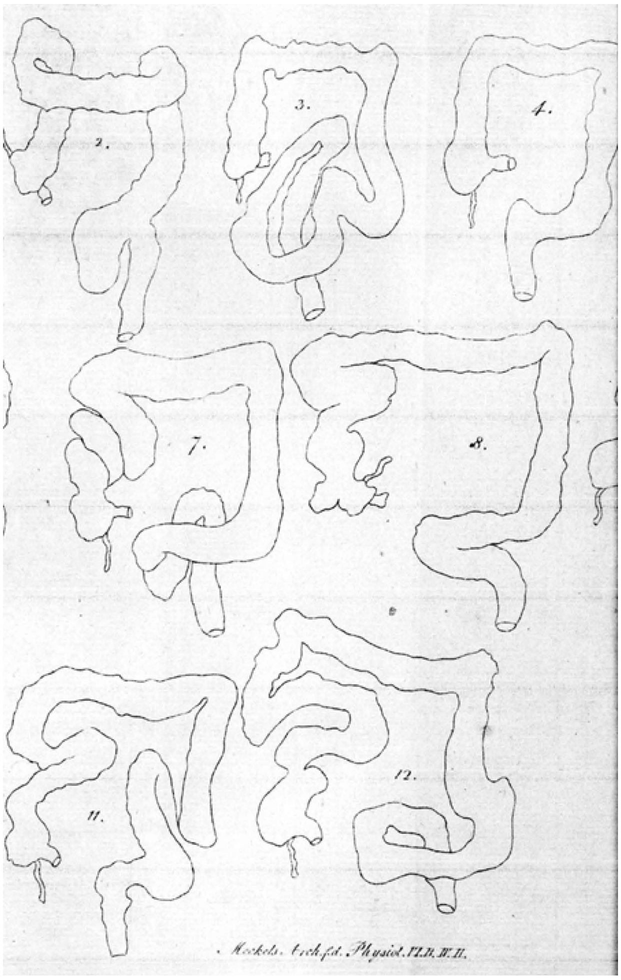

Figure 1 Handmade drawings of dolichocolon forming tortuosities, loops and kinks. From Monterossi[2], 1820.

are present simultaneously[15-17] (Figures 2 and 3).

A long colon may result in an incomplete colonoscopy, as demonstrated in a study in which the colorectal length was 45 cm longer than the length in a group who underwent complete colonoscopy[18].

ETIOLOGY OF DOLICHOCOLON

Redundancy of the colon is a far from seldom variant. In 1934, Kantor[19] reported 258 cases from 1614 patients who underwent roentgenography, an incidence of 16.0%. However, Moeller[13] found redundant colon in 18 out of 744 cases, an incidence of 2.4%. A high incidence of 28.5% was found among 562 cases reported by Larimore[12], and in 116 newborn infants, he found redundancy with the same frequency and variation as in adults. In cadavers, Bryant[7] reported an incidence of 14% among 242 subjects. Thus, redundancy seems to occur at any age, in either sex, and without special preference to any habitus[20].

For the next half century, the interest in redundant colon seemed to wane. The prevalence of dolichocolon in a population is not known, because healthy people have not been investigated for that purpose. The closest to such an evaluation is a study by Brumer[21] in which 53 patients had a barium enema for reasons other than constipation; one patient (1.9%) had a redundant colon. In 2009, Raahave *et al*[17] published a study of 236 patients with constipation disorders, finding high frequencies of colonic redundancies.

The question for many authors has been whether dolichocolon is a congenital anatomic variant, an abnormal growth, or pathological stretching. Treves[3] and Bryant[7] assumed that colon growth is associated with activity and function depending on the diet. Very recently, the large bowel was shown in mice to undergo substantial changes in length, as it fills with fecal matter, and that the stretching of longitudinal muscles results in slow colonic transit[22]. However, using barium enema, several authors have shown that fetuses, newborns, and infants exhibit colonic redundancies[10,12,23]. Recently, colonic elongation has been shown in children by nuclear transit scintigraphy[24]. A familiar occurrence of dolichocolon has also been observed[25]. In general, there are great variations in the frequency and positions of redundancies. Most investigators have found them to occur in the middle and left side of the colon[11,12,17,23].

Thus, dolichocolon is mainly congenital, but function and fecal transport may also promote some changes.

SYMPTOMS FROM THE REDUNDANT COLON

The dominating symptom of dolichocolon is constipation[4,6,9,13,14,19,23,25,26], and patients have died from it[5]. In 1962, Brumer[21] examined 106 patients with chronic constipation using barium enema and found 32 (30.2%) had a redundant colon. Among 53 controls, only one (1.9%) had a colon with redundancies. He concluded that a causal connection must exist between this anomaly and constipation. The most common related cause of constipation after anorectal myectomy was later found to be a redundant colon[27]. When evaluating patients with slow transit constipation, the cause was always associated with dolichocolon[28]. Recently, a high proportion of patients with constipation disorders was shown to have redundant colon[17].

Pain sometimes cramp-like, often occurs in the lower abdomen[4,11,13,17,19,23,25], where a tender mass may sometimes be felt[6,17,19]. Constipation and pain are often followed with distension, and many cases demonstrate how much these patients have suffered.

Non-specific symptoms have also been linked to redundant colon, such as general weakness, headache, and mild fever attacks suggested to be caused by a toxic condition because of fecal stasis[4,10,23,29]. In the beginning of the 20th century, a theory of autointoxication was formulated[30], but then discredited among little proof of bacterial toxin production. However, immune activation is detected in constipated patients based on levels of $CD3^+$, $CD4^+$, $CD8^+$, and $CD25^+$ T-cells and by spontaneous proliferation of lymphocytes. T-cell activation, elevated

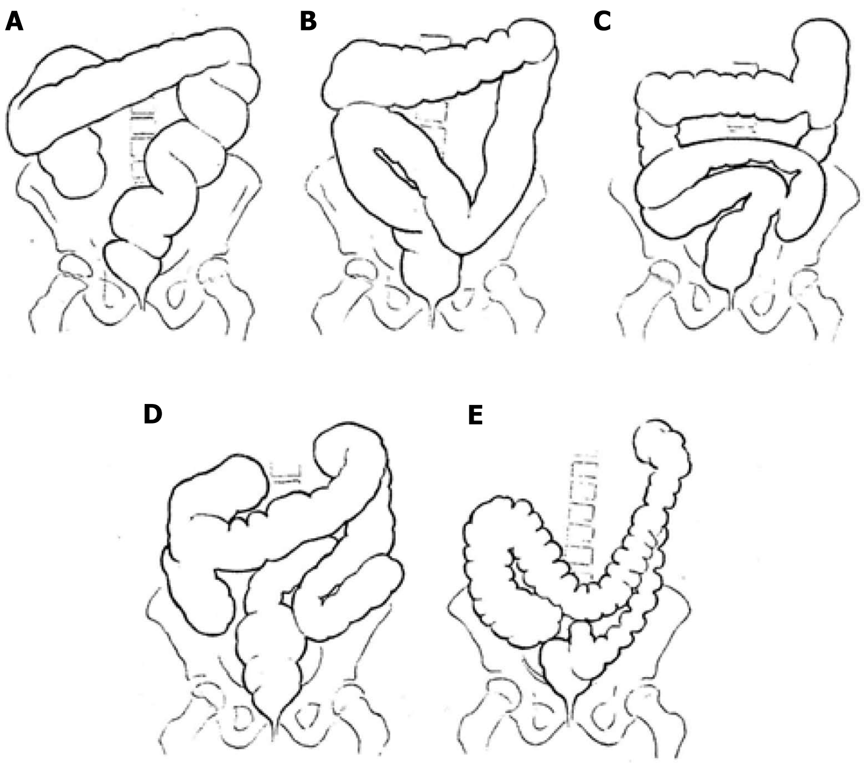

Figure 2 Different types of dolichocolon. A-C: Redundancies in the sigmoid; D: Generalized redundancies; E: Low transverse colon. From Caffey[16], 1961.

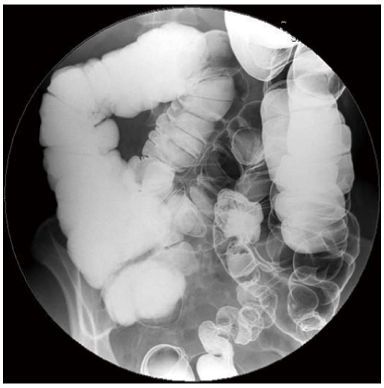

Figure 3 Barium enema showing a fully developed dolichocolon: A sigmoid loop rising over the line between the iliac crests, a transverse colon below the same line and extra loops at the flexures.

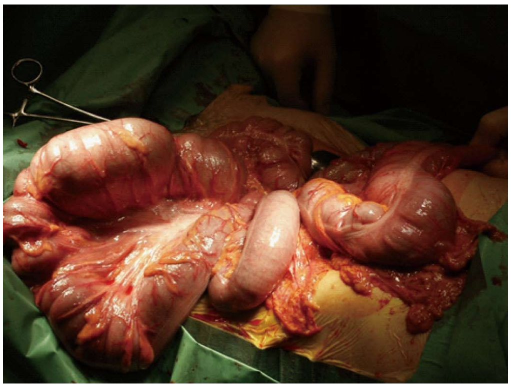

Figure 4 Dolichocolon with loose mesenteries allowing the colon to be drawn out of the abdomen: The transverse colon is localized at the right, and the sigmoid loop at the left.

levels of antibacterial antibodies, and a tendency towards elevated concentrations of IgG, IgM, and circulating immune complexes, provide evidence of the stimulation of systemic cellular and humoral immunity in chronic constipation[31].

An elongated colon is often associated with a failure of agglutination of the mesentery with the parietal peritoneum. Consequently, the elongated colon is not fixed to the dorsal wall and can swing free on a long mesentery (Figure 4), and loose redundant loops have a potential risk of volvulus.

FUNCTION OF A REDUNDANT COLON

Information to the function of a redundant colon is scarce. Atony and a weak muscular tone may be limited to the site of the redundancy[14] or dysfunction may be the result of derangement of the autonomous intestinal nervous system[32]. Kantor[19] suggested that constipation varies directly with colon length, and Metcalf *et al*[33] later stated that transit is largely proportional to the length and volume of a colon segment. In an overview, Müller-Lissner *et al*[34] stated that, although a long colon could prolong stool residence time, no studies have correlated colonic transit time with colon length. Subsequently, Raahave *et al*[17] demonstrated that the mean colon transit time was 36.26 h in patients without redundancies, 43.80 h in those with one redundancy, 41.65 h in those with two redundancies, and 52.27 h in those with three to four redundancies. The mean colon transit time of 44 controls was 24.75 h. The difference in colon transit time between the four levels of redundancies was significant. Abdominal pain, bloating, and infrequent defecation increased significantly with an increased number of redundancies. A separate analysis found a significant positive correlation between colon transit time and fecal load and a redundant sigmoid colon.

In studies of patients undergoing subtotal colectomy for slow transit constipation, the majority of colon specimens were significantly redundant[35-38]. Colon transit time is meant to be a measure of the speed of fecal propulsion through the colon, and an even distribution of radiopaque markers suggests the same function of all parts of the colon, including redundancies. Possible reasons for dysmotility are disorders of the enteric nervous system, neuroendocrine system or brain-gut axis, including lack of interstitial cells of Cajal[39].

DIAGNOSIS OF DOLICHOCOLON

A redundant colon should be suspected in patients with constipation, abdominal pain, distension and seldom defecation, especially when symptoms have been present from childhood. However, these symptoms may also come from pure functional colonic disorders, which is why many patients with dolichocolon have not received a diagnosis. A colon transit study and a barium enema or CT-colonography is needed to confirm the diagnosis. This is essential in guiding therapy.

TREATMENT OF CONSTIPATION

From the very beginning, chronic constipation was suggested to be treated with enemas, mineral oil, other laxatives, abdominal massage, a supporting corset, and eventually sedatives[4,10,11]. Murray[40] focused on diet and advocated cereals containing husk, as well as the use of salads, raw fruits and vegetables, that grow above the ground. Large quantities of water must be taken, and moderate use of weak tea and coffee is allowed, but no alcoholic beverages. The colonic content was lubricated with oil and a tincture of belladonna given three times a day to increase the intestinal tone. In addition, abdominal electrotherapy was used over the abdomen, just as an afternoon siesta took place since the patients tire very easily. Short walks were advised as exercise. A mild sedative was eventually added[14]. The intervention was discontinued, when the function of the colon was restored, except the retention enema with oil and high residue diet may be more or less a permanent part of the regimen. The majority of patients with a redundant colon who are given this treatment will then return to a state of approximate well-being. In the subsequent years, most authors agreed with these principles[23,29,32,41]. A gap of interest in redundant colon then followed for nearly half a century. In general, redundancy of the colon was regarded as an unimportant observation.

Redundant colon is not mentioned in a European Perspective of Diagnosis and Treatment of Chronic Constipation[42] or in the current American Gastroenterological Association Medical Position Statement on Constipation[43]. This is a surprise, considering existing knowledge. Patients with constipation disorders and a redundant colon have had improvements in their quality of life by a fiber-rich diet supplemented with husk, sufficient water intake, a prokinetic drug, and physical activity[39]. Apart from the prokinetic drug, current treatment resembles the regimen of a hundred years ago.

SURGERY FOR DOLICHOCOLON

Immediate surgery was advocated when a sigmoid loop is twisted (volvulus)[11,20,23,29,41]. In this context, it is notable that sigmoid volvulus accounts for a disproportionally high number of cases of intestinal obstruction in developing countries such as Africa (20%-45%) compared to developed countries (1%-7%). In addition, sigmoid volvulus occurs in much younger patients[44]. Today, it will first be tried to straighten out the twisted loop by an endoscopic maneuver. If this fails, acute surgery is necessary.

Most authors advise against surgery for dolichocolon[11,19,23,32,41]. Lane[30] introduced colectomy for chronic constipation with a death rate of 20.5%, but without giving any information with regard to colon anatomy among 39 patients. Subtotal colectomy for a redundant colon was mentioned as a possibility in 1914[10]. However, resection of colonic segments was performed with satisfactory results in five cases[45] and without improvement in three cases[13]. In 1960, Davis[46] presented the results of 14 children operated on for symptomatic dolichocolon resistant to conservative treatment. No failures occurred, and the results were excellent in eight patients, good in three, and fair in three. Hollender[25] reported good functional results after various colonic resections in 11 patients with dolichocolon. In other studies of patients who underwent subtotal colectomy for slow transit constipation, the majority of colon specimens were significantly redundant[35-37].

In 15 patients, the cause of constipation was slow colonic transit, which was associated with dolichocolon[28]. After hemicolectomy or colectomy, the patients received daily evacuations and experienced less pain. Recently 31 patients with slow transit constipation and a dolichocolon underwent colectomy[38]. At follow-up, most patients reported daily defecation and no uncontrolled diarrhea. Abdominal pain was very seldom and patient satisfaction high.

FUTURE PERSPECTIVES

The prevalence of dolichocolon is not known, because population based investigations have not been made. However, in projects with colonoscopic screening for cancer it may be possible to estimate the number and localization of colonic redundancies. Colorectal length may be determined by magnetic resonance imaging or by tracking the progression of an electromagnetic capsule[47]. It will hopefully then be possible to determine the prevalence of dolichocolon and a causal relationship to constipation and volvulus.

CONCLUSION

Dolichocolon is an anatomic variant with redundancies of the colonic segments and flexures. The diagnosis is established by barium enema or CT-colonography. Accumulating data from 200 years shows dolichocolon is congenital and causes constipation. Treatment is conservative, and only patients refractive to this therapy may undergo a subtotal colectomy. A redundant loop may cause volvulus, requiring an endoscopic maneuver or surgery. Future research has to show the prevalence of dolichocolon in a population and to determine whether it always gives rise to constipation.

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REFERENCES

1 **Langman J**. Medical embryology. 3rd ed. Baltimore: The Williams & Wilkins Company, 1975
2 **Monterossi P**. Über widernatürlische Biegungen des Dickdarms als Uhrfache des Todes neugeborener Kinder. *Deutsch Arch Physiol* 1820; **6**: 556-571
3 **Treves F**. Lectures on the Anatomy of the Intestinal Canal and Peritoneum in Man. *Br Med J* 1885; **1**: 415-419 [PMID: 20751176 DOI: 10.1136/bmj.1.1261.415]
4 **Shober JB.** Anomalous positions of the colon. *Am J Med Sci* 1898; **116**: 405-419 [DOI: 10.1097/00000441-189810000-00003]
5 **Buchanan A**. Fatal cases of the obstruction and enormous distension of the belly. *London Med Gazette* 1839; **2**: 639-644
6 **Black CE**. XI. Displacements of the Colon. *Ann Surg* 1912; **56**: 888-899 [PMID: 17862941 DOI: 10.1097/00000658-191212000-00011]
7 **Bryant J**. Observations upon the growth and length of the human intestine. *Am J Med Sci* 1924; **167**: 499-520 [DOI: 10.1097/00000441-192404000-00003]
8 **Phillips M**, Patel A, Meredith P, Will O, Brassett C. Segmental colonic length and mobility. *Ann R Coll Surg Engl* 2015; **97**: 439-444 [PMID: 26274737 DOI: 10.1308/003588415X14181254790527]
9 **Kienböck R**. Ueber das Sigma elongatum mobile (Röntgenbefund). *Muench Med Wochen* 1913; **60**: 68-70
10 **Lardennois G,** Aubourg P. Allongements segmentaires du gros intestin les dolichocolies. *Jour Radiol Electrol* 1914; **1**: 65-74
11 **White FW**. The redundant colon. *Med Clin N Am* 1924; **8**: 1611-1633
12 **Larimore JW**. The human large intestine in the newborn and in the adult. *Ann Clin Med* 1926; **5**: 439-463
13 **Moeller PF**. The redundant colon. *Acta Radiol* 1926; **6**: 432-457 [DOI: 10.1177/028418512600600137]
14 **Gauss H**. Redundant colon. *Arch Surg* 1927; **15**: 560-579 [DOI: 10.1001/archsurg.1927.01130220063005]
15 **Kantor JL**. Anomalies of the colon: Their roentgen diagnosis and clinical significance. *Radiology* 1934; **23**: 651-662 [DOI: 10.1148/23.6.651]
16 **Caffey J**. Pediatric X-ray diagnosis. 4th ed. Chicago: Year Book Medical Publishers, 1961
17 **Raahave D**, Christensen E, Loud FB, Knudsen LL. Correlation of bowel symptoms with colonic transit, length, and faecal load in functional faecal retention. *Dan Med Bull* 2009; **56**: 83-88 [PMID: 19486620]
18 **Hanson ME**, Pickhardt PJ, Kim DH, Pfau PR. Anatomic factors predictive of incomplete colonoscopy based on findings at CT colonography. *AJR Am J Roentgenol* 2007; **189**: 774-779 [PMID: 17885044 DOI: 10.2214/AJR.07.2048]
19 **Kantor JL**. Common anomalies of the duodenum and colon: Their practical significance. *JAMA* 1931; **97**: 1785-1790 [DOI: 10.1001.jama.1931.02730240035008]
20 **Galambos A**, Galambos WM. Redundancy of the colon. *Am J Dig Dis* 1946; **13**: 87-101 [PMID: 21022340 DOI: 10.1007/BF03002757]
21 **Brumer P,** Seppälä P, Wegelius U. Redundant colon as a cause of constipation. *Gut* 1962; 3: 140-141 [DOI: 10.1136/gut.3.2.140]
22 **Heredia DJ**, Dickson EJ, Bayguinov PO, Hennig GW, Smith TK. Colonic elongation inhibits pellet propulsion and migrating motor complexes in the murine large bowel. *J Physiol* 2010; **588**: 2919-2934 [PMID: 20547675 DOI: 10.1113/jphysiol.2010.191445]
23 **Friedenwald J,** Feldman M. Clinical observations on the redundant colon (dolichocolon). *South Med J* 1934; **27**: 147-154 [DOI: 10.1097/00007611-193402000-00010]
24 **Yik YI**, Cook DJ, Veysey DM, Tudball CF, Cain TM, Southwell BR, Hutson JM. How common is colonic elongation in children with slow-transit constipation or anorectal retention? *J Pediatr Surg* 2012; **47**: 1414-1420 [PMID: 22813806 DOI: 10.1016/j.jpedsurg.2012.01.007]
25 **Hollender LF**, Muller AM, Viville C, Santizo G. [Dolichocolon in adults: surgical indications]. *Acta Gastroenterol Belg* 1965; **28**: 550-567 [PMID: 5844749]
26 **Kantor JL.** A clinical study of common anatomical abnormalities of the colon. I. The redundant colon. *Am J Roentgenol Soc* 1924; **12:** 414-430
27 **Tomita R**, Howard ER. Clinical studies on anorectal myectomy for chronically constipated patients with outlet obstruction in childhood. *Hepatogastroenterology* 2008; **55**: 1600-1605 [PMID: 19102350]
28 **Ripetti V**, Caputo D, Greco S, Alloni R, Coppola R. Is total colectomy the right choice in intractable slow-transit constipation? *Surgery* 2006; **140**: 435-440 [PMID: 16934606 DOI: 10.1016/j.surg.2006.02.000]
29 **White FW**. Studies of the redundant colon. *N Engl J Med* 1928; **198:** 783-787 [DOI: 10.1056/NEJM192805311981501]
30 **Lane WA**. Remarks on the results of the operative treatment of chronic constipation. *Br Med J* 1908; **1**: 126-130 [PMID: 20763645 DOI: 10.1136/bmj.1.2455.126]
31 **Khalif IL**, Quigley EM, Konovitch EA, Maximova ID. Alterations in the colonic flora and intestinal permeability and evidence of immune activation in chronic constipation. *Dig Liver Dis* 2005; **37**: 838-849 [PMID: 16169298 DOI: 10.1016/j.dld.2005.06.008]
32 **LaRochelle FD,** Smith EE. The dolichocolon. *Radiology* 1932; **18**: 1111-1114 [DOI: 10.1148/18.6.1111]
33 **Metcalf AM,** Phillips SF, Zinsmeister AR, MacCarty RL, Beart RW, Wolf BG. Simplified assessment of segmental colonic transit. *Gastroenterology* 1987; **92**: 40-47 [DOI: 10.1016/0016-5085(87)90837-7]
34 **Müller-Lissner SA**, Kamm MA, Scarpignato C, Wald A. Myths and misconceptions about chronic constipation. *Am J Gastroenterol* 2005; **100**: 232-242 [PMID: 15654804 DOI: 10.1111/j.1572-0241.2005.40885.x]
35 **Lux N,** Athanasiadis S, Fischbach N, Meyer B. Funktionelle Ergebnisse nach subtotaler und partieller colektomie bei der therapiresistenten chronischen obstipation. *Chirurg* 1992; **68**: 739-747
36 **Webster C,** Dayton M. Results after colectomy for colonic inertia: a sixteen-year experience. *Amer J Surg* 2001; **182**: 639-644 [DOI:

10.1016/S0002-9610(01)00820-0]
37 **Lundin E**, Karlbom U, Påhlman L, Graf W. Outcome of segmental colonic resection for slow-transit constipation. *Br J Surg* 2002; **89**: 1270-1274 [PMID: 12296895 DOI: 10.1046/j.1365-2168.2002.02213.x]
38 **Raahave D**, Loud FB, Christensen E, Knudsen LL. Colectomy for refractory constipation. *Scand J Gastroenterol* 2010; **45**: 592-602 [PMID: 20408774 DOI: 10.3109/00365521003587796]
39 **Raahave D**. Faecal retention: a common cause in functional bowel disorders, appendicitis and haemorrhoids--with medical and surgical therapy. *Dan Med J* 2015; **62**: pii B5031 [PMID: 25748875]
40 **Murray RS**. Redundant colon. *J Tenn Med Ass* 1925; **18**: 37-43
41 **Kantor JL**. The common affections of the colon, their origin and their management. *Bull NY Acad Med* 1928; **4**: 757-788
42 **Tack J**, Müller-Lissner S, Stanghellini V, Boeckxstaens G, Kamm MA, Simren M, Galmiche JP, Fried M. Diagnosis and treatment of chronic constipation--a European perspective. *Neurogastroenterol Motil* 2011; **23**: 697-710 [PMID: 21605282 DOI: 10.111/j.1365-2982.2011.01709.x]
43 **American Gastroenterological Association**, Bharucha AE, Dorn SD, Lembo A, Pressman A. American Gastroenterological Association medical position statement on constipation. *Gastroenterology* 2013; **144**: 211-217 [PMID: 23261064 DOI: 10.1053/j.gastro.2012.10.029]
44 **Madiba TE**, Haffajee MR. Sigmoid colon morphology in the population groups of Durban, South Africa, with special reference to sigmoid volvulus. *Clin Anat* 2011; **24**: 441-453 [PMID: 21480385 DOI: 10.1002/ca.21100]
45 **Slesinger EG.** Elongation of the pelvic colon and its surgical treatment. *Lancet* 1926; **2**: 274-275
46 **Davis DA.** A new concept in the treatment of symptomatic redundant colon or dolichocolon. *West J Surg Gynecol* 1960; **68**: 101-106
47 **Mark EB**, Poulsen JL, Haase AM, Frøkjaer JB, Schlageter V, Scott SM, Krogh K, Drewes AM. Assessment of colorectal length using the electromagnetic capsule tracking system: a comparative validation study in healthy subjects. *Colorectal Dis* 2017; **19**: O350-O357 [PMID: 28688203 DOI: 10.1111/codi.13810]

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ORIGINAL ARTICLE

Clinical Trials Study

Transcutaneous electroacupuncture alleviates postoperative ileus after gastrectomy: A randomized clinical trial

Kai-Bo Chen, Yi-Qiao Lu, Jian-De Chen, Di-Ke Shi, Zhi-Hui Huang, Yi-Xiong Zheng, Xiao-Li Jin, Zhe-Fang Wang, Wei-Dong Zhang, Yi Huang, Zhi-Wei Wu, Guo-Ping Zhang, Hang Zhang, Ying-Hao Jiang, Li Chen

Kai-Bo Chen, Di-Ke Shi, Xiao-Li Jin, Yi-Huang, Zhi-Wei Wu, Yi-Xiong Zheng, Department of General Surgery, Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310000, Zhejiang Province, China

Yi-Qiao Lu, Department of Obstetrics and Gynecology, Women's Hospital, Zhejiang University School of Medicine, Hangzhou 310006, Zhejiang Province, China

Jian-De Chen, Division of Gastroenterology and Hepatology, Johns Hopkins University School of Medicine, Baltimore, MD 21224, United States

Zhi-Hui Huang, Department of Gastroenterology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, Zhejiang Province, China

Zhe-Fang Wang, Department of General, Visceral and Cancer Surgery, University of Cologne, Cologne 50937, Germany

Wei-Dong Zhang, Department of Thyroid Surgery, Ningbo No. 2 Hospital, Ningbo 315000, Zhejiang Province, China

Guo-Ping Zhang, Department of Chinese Medicine Rehabilitation, Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310000, Zhejiang Province, China

Ying-Hao Jiang, Department of General Surgery, First People's Hospital of Wenling, Taizhou 317500, Zhejiang Province, China

Author contributions: Chen KB, Lu YQ, Chen JD, Chen L, Shi DK and Huang ZH designed and established the study process; Chen KB, Lu YQ, Chen L and Shi DK performed the study, collected and analyzed the data and wrote and revised the manuscript; Wang ZF, Huang Y, Wu ZW and Jiang YH contributed to patient recruitment and performing the study; Zheng YX assisted with protocol development and patient management; Zhang GP assisted with acupuncture techniques; Chen KB and Lu YQ contributed equally to this research.

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Correspondence to: Li Chen, MD, Professor, Department of General Surgery, Second Affiliated Hospital of Zhejiang University School of Medicine, 88 Jie-fang Road, Hangzhou 310000, Zhejiang Province, China. li-chen@zju.edu.cn
Telephone: +86-571-87783777

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Abstract

AIM
To investigate the efficacy and safety of transcutaneous

electroacupuncture (TEA) to alleviate postoperative ileus (POI) after gastrectomy.

METHODS

From April 2014 to February 2017, 63 gastric cancer patients were recruited from the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China. After gastrectomy, the patients were randomly allocated to the TEA (n = 33) or control (n = 30) group. The patients in the TEA group received 1 h TEA on Neiguan (ST36) and Zusanli (PC6) twice daily in the morning and afternoon until they passed flatus. The main outcomes were hours to the first flatus or bowel movement, time to nasogastric tube removal, time to liquid and semi-liquid diet, and hospital stay. The secondary outcomes included postoperative symptom assessment and complications.

RESULTS

Time to first flatus in the TEA group was significantly shorter than in the control group (73.19 ± 15.61 *vs* 82.82 ± 20.25 h, P = 0.038), especially for open gastrectomy (76.53 ± 14.29 *vs* 87.23 ± 20.75 h, P = 0.048). Bowel sounds on day 2 in the TEA group were significantly greater than in the control group (2.30 ± 2.61/min *vs* 1.05 ± 1.26/min, P = 0.017). Time to nasogastric tube removal in the TEA group was earlier than in the control group (4.22 ± 1.01 *vs* 4.97 ± 1.67 d, P = 0.049), as well as the time to liquid diet (5.0 ± 1.34 *vs* 5.83 ± 2.10 d, P = 0.039). Hospital stay in the TEA group was significantly shorter than in the control group (8.06 ± 1.75 *vs* 9.40 ± 3.09 d, P = 0.041). No significant differences in postoperative symptom assessment and complications were found between the groups. There were no severe adverse events related to TEA.

CONCLUSION

TEA accelerated bowel movements and alleviated POI after open gastrectomy and shortened hospital stay.

Key words: Transcutaneous electroacupuncture; Gastrectomy; Postoperative ileus

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Core tip: Transcutaneous electroacupuncture (TEA) is a non-invasive and portable device. We applied TEA on postoperative gastric cancer patients to promote the bowel motility recovery. As far as we are concerned, it was the first attempt to investigate the efficacy and safety of TEA to alleviate postoperative ileus after gastrectomy.

Chen KB, Lu YQ, Chen JD, Shi DK, Huang ZH, Zheng YX, Jin XL, Wang ZF, Zhang WD, Huang Y, Wu ZW, Zhang GP, Zhang H, Jiang YH, Chen L. Transcutaneous electroacupuncture alleviates postoperative ileus after gastrectomy: A randomized clinical trial. *World J Gastrointest Surg* 2018; 10(2): 13-20 Available from: URL: http://www.wjgnet.com/1948-9366/full/v10/i2/13.htm DOI: http://dx.doi.org/10.4240/wjgs.v10.i2.13

INTRODUCTION

Gastric cancer is one of the most common malignancy burdens in China, especially in economically less developed regions. The standard surgery is total or subtotal gastrectomy with D2 lymph node dissection for gastric cancer with radical-cure intention. However, postoperative ileus (POI) is not rare and causes symptoms such as abdominal pain, distention, nausea and vomiting due to the accumulation of gas and secretions[1]. This probably affects patient recovery, prolongs hospital stay, and increases cost. The treatment for POI includes fasting, nasogastric depression, maintenance of fluid and electrolyte balance, parenteral nutrition, and exercise[2]. There is no clinical evidence for the use of prokinetic agents in POI and they may have severe adverse effects[3].

Modern electroacupuncture (EA) was developed from traditional Chinese medicine, which has been shown to accelerate gastric emptying and colonic motility[4,5]. A clinical study showed that electroacupuncture reduced the duration of POI after laparoscopic surgery for colorectal cancer[6]. A study in dogs indicated that transcutaneous EA (TEA) on Neiguan (ST36) is as effective as EA in improving rectal distention-induced intestinal dysmotility[7]. It is non-invasive and more portable.

Therefore, we applied the novel technique of TEA in gastric cancer patients to promote postoperative recovery of bowel motility. To the best of our knowledge, this was the first attempt to investigate the efficacy and safety of TEA to alleviate POI after gastrectomy.

MATERIALS AND METHODS

Patients

From April 2014 to February 2017, 63 patients were recruited from the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China. All the patients underwent total or partial gastrectomy. Inclusion criteria were as follows: (1) Gastric cancer patients without distal metastases; (2) age 18-85 years; (3) no severe history of cardiovascular, hepatic, hematological and renal diseases; (4) Eastern Cooperative Oncology Group (ECOG) performance status score ≤ 2; and (5) written informed consent was obtained before the study. Exclusion criteria were as follows: (1) Bile leakage or acute peritonitis; (2) cardiac pacemaker; (3) medication, such as metoclopramide, that affects bowel function; (4) history of chronic constipation; (5) history of abdominal surgery; (6) palliative gastrectomy; and (7) postoperative enema.

Procedures and TEA

This study was designed collaboratively by doctors from

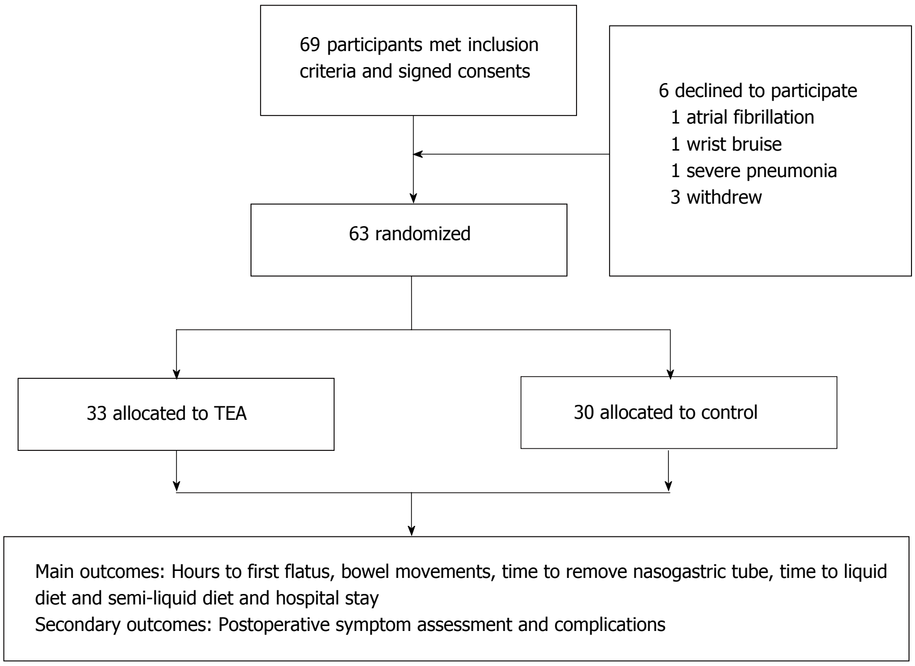

Figure 1 Flow chart of study participants. TEA: Transcutaneous electroacupuncture.

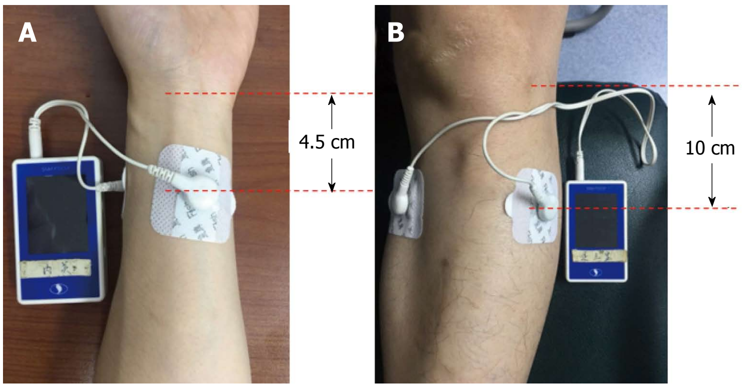

Figure 2 Transcutaneous electroacupuncture sites used in this study. A: Neiguan (ST36): Two electrodes were oppositely attached on the skin approximately 4.5 cm below the wrist wrinkle; B: Zusanli (PC6): Two electrodes were oppositely attached on the skin 10 cm below the lateral patella pit.

the Second Affiliated Hospital of Zhejiang University and Division of Gastroenterology and Hepatology, Department of Medicine, Johns Hopkins University, United States. TEA was developed by Professor Jian-De Chen in the Clinical Gastrointestinal Motility Laboratory, Johns Hopkins University School of Medicine, and gained safety certification in Zhejiang Province. The doctors who participated in the study were all trained in the TEA technique in Pace Translational Medical Research Center, Ningbo, China.

Sixty-nine patients were initially recruited but six declined to participate because of atrial fibrillation (n = 1), wrist bruise (n = 1), severe pneumonia (n = 1) and withdrawal without any reasons (n = 3). The remaining 63 patients were randomly allocated by computer algorithm to the TEA (n = 33) or control (n = 30) group (Figure 1). The TEA group started treatment on on day 1 after surgery, until passing flatus or on day 5. They had 1 h TEA on ST36 and Zusanli (PC6) twice daily in the morning (09:00-10:00) and afternoon (14:00-15:00). The EA sites of ST36 and PC6 were consistent with other studies (Figure 2). The parameters for ST36 were 2 s on, 3 s off, 25 Hz, 0.5 ms, 2-6 mA; while for PC6 it was 0.1 s on, 0.4 s off, 100 Hz, 0.25 ms, 2-6 mA. The electric current was gradually increased just below the patient's pain threshold, and could be minimally adjusted during the procedure. The patients were allowed to sit even walk during the treatment as long as the TEA was continuously functioning well. The control group received no treatment and without any TEA being binded. The main outcomes were hours to the first flatus or bowel movement, time to nasogastric tube removal, time to liquid and semi-liquid diet, and hospital stay. And the secondary outcomes included postoperative symptom assessment based on each patient's subjective scale (0-10, including pain, tiredness, nausea, shortness of

Table 1 Baseline patient characteristic

	TEA (n = 33)	Control (n = 30)	P value
Age (yr)	63.0 ± 9.70	59.0 ± 8.30	0.103
Sex (M/F)	22/11	24/6	0.183
Chronic gastritis	8/25	9/21	0.409
Diabetes	1/32	0/30	0.524
Hypertension	10/23	9/21	0.599
BMI	22.32 ± 3.23	21.85 ± 3.21	0.561
ECOG score (1/2)	27/6	24/6	0.553
Preoperative activity level	1.18 ± 0.392	1.17 ± 0.46	0.888
Preoperative albumin (g/L)	40.70 ± 3.38	40.08 ± 5.09	0.564
Preoperative chemotherapy (Y/N)	2/31	2/28	0.657
Surgery (Open/laparoscopic)	10/23	7/23	0.369
Surgery (Billroth-I/II/Rou-en-Y)	10/11/12	11/13/6	> 0.05
Surgery time (min)	210.79 ± 53.40	213.36 ± 69.12	0.868
pT staging (T0/1/2/3/4)	1/7/14/8/3	0/8/7/10/5	-
pN staging (N0/1/2/3a/3b)	1/7/14/8/3	11/5/4/10/0	-
Nasal enteral nutrition (Y/N)	11/22	9/21	0.496
PCIA/PCEA	32/1	29/1	0.833

TEA: Transcutaneous electroacupuncture; BMI: Body mass index.

breath, and wellbeing according to Edmonton Symptom Assessment System), and postoperative complications and hospital stay. Prolonged POI was defined as not passing flatus at > 5 d after surgery.

Statistical analysis

Statistical analysis was performed using SPSS version 24.0, using Student's t test and χ^2 test, and variables were expressed as mean ± SD. P < 0.05 was considered as statistically significant.

RESULTS

A total of 63 patients (46 male, 17 female, age range: 37-75 years) were recruited and randomized to the TEA group (n = 33) and control group (n = 30). In the TEA group, 23 patients underwent open gastrectomy and 10 underwent laparoscopic gastrectomy. In the control group, 23 patients underwent open gastrectomy and 7 patients underwent laparoscopic gastrectomy. The baseline characteristics did not differ significantly between the groups (Table 1). The operating time in the TEA group was 210.79 ± 53.40 min compared with 213.36 ± 69.12 min in the control group (P = 0.868).

Time to first flatus in the TEA group was significantly shorter than in the control group (73.19 ± 15.61 *vs* 82.82 ± 20.25 h, P = 0.038), especially for open gastrectomy (76.53 ± 14.29 *vs* 87.23 ± 20.75 h, P = 0.048). Bowel sounds on day 2 in the TEA group were significantly greater than in the control group (2.30 ± 2.61/min *vs* 1.05 ± 1.26/min, P = 0.017). For open gastrectomy, bowel sounds on day 2 and day 3 in the TEA group were significantly greater than in the control group (P = 0.006, 0.028, respectively) (Table 2). Time to nasogastric tube removal was earlier in the TEA than control group (4.22 ± 1.01 *vs* 4.97 ± 1.67 d, P = 0.049). Time to starting liquid diet was shorter in the TEA than control group (5.00 ± 1.34 *vs* 5.83 ± 2.10 d, P = 0.039). Hospital stay was significantly shorter in the TEA than in the control group (8.06 ± 1.75 *vs* 9.40 ± 3.09 d, P = 0.041) (Table 2). Then, we excluded patients with complications of pneumonia, chyle leakage and pancreatic leakage, the hospital stay in the TEA group was still significantly shorter compared to the control group (7.73 ± 1.14 *vs* 8.59 ± 1.67 d, P = 0.026) (Table 2).

There was no significant difference in symptoms between the two groups including pain, tiredness, nausea, shortness of breath and wellbeing (Table 3).

There was no significant difference in postoperative complications between the two groups (P = 0.270) (Table 4). There was no prolonged ileus in TEA group, while there were three such cases in the control group. An adverse event of bruising on the wrist due to TEA was reported and the patient withdrew from the study. However, there was no severe adverse event.

DISCUSSION

In this prospective and randomized clinical study, we confirmed the role of TEA in the treatment of post-gastrectomy bowel motility recovery for the first time. TEA in gastric cancer patients significantly increased postoperative bowel movement; shortened time to first flatus, nasogastric tube removal, liquid diet and hospital stay, and it was safe.

POI is caused by impaired motility of the whole gastrointestinal tract due to abdominal or extra-abdominal surgery, which is the main reason for symptoms of discomfort and prolonged hospital stay. POI costs $1.5 billion annually in the United States[8]. Pathophysiologically, it is explained by release of inhibitory neural reflexes and inflammatory mediators from the site of injury[1]. However, the complex pathogenesis remains incompletely understood. Treatment for POI includes fasting, nasogastric depression, maintenance of fluid and electrolyte balance, and ambulation. Recent evidence supports that early oral or

Table 2 Main outcomes

	TEA (*n* = 33)	Control (*n* = 30)	*P* value
Time to first flatus (h)			
Total	73.19 ± 15.61	82.82 ± 20.25	0.038[b]
Open	76.53 ± 14.29	87.23 ± 20.75	0.048[b]
Laparoscopic	65.52 ± 16.53	68.31 ± 9.08	0.692
Bowel sound on day 1 (/min)	0.96 ± 1.80	0.63 ± 1.63	0.461
Bowel sound on day 2 (/min)	2.30 ± 2.61	1.05 ± 1.26	0.017[b]
Bowel sound on day 3 (/min)	4.30 ± 3.11	2.85 ± 2.19	0.068
Bowel sound on day 1 (open) (/min)	0.70 ± 1.29	0.70 ± 1.83	1.000
Bowel sound on day 2 (open) (/min)	2.52 ± 2.56	0.80 ± 1.0	0.006[b]
Bowel sound on day 3 (open) (/min)	4.74 ± 3.10	2.77 ± 2.23	0.028[b]
Walk independently (h)	27.10 ± 15.24	36.73 ± 25.91	0.074
Walking duration per day (min)	10.36 ± 6.65	9.13 ± 6.16	0.452
Remove nasogastric tube (POD)	4.22 ± 1.01	4.97 ± 1.67	0.049[b]
Liquid diet (POD)	5.00 ± 1.34	5.83 ± 2.10	0.039[b]
Semiliquid diet (POD)	6.68 ± 1.78	7.60 ± 2.33	0.087
Hospital stay (POD)	8.06 ± 1.75	9.40 ± 3.09	0.041[b]
Modified liquid diet (POD)	4.73 ± 0.94 (30)	5.30 ± 1.23 (27)	0.057
Modified semiliquid diet (POD)	6.30 ± 1.12 (30)	7.11 ± 1.74 (27)	0.039[b]
Modified hospital stay (POD)	7.73 ± 1.14 (30)	8.59 ± 1.67 (27)	0.026[b]

[b]*P*: Significant difference. TEA: Transcutaneous electroacupuncture; POD: Postoperative day.

Table 3 Secondary outcomes according to Edmonton Symptom Assessment System

	TEA (*n* = 33)	Control (*n* = 30)	*P* value
Pain on day 1	3.79 ± 1.35	3.38 ± 1.50	0.266
Pain on day 2	2.79 ± 1.10	2.55 ± 1.08	0.391
Pain on day 3	2.39 ± 1.20	2.14 ± 0.90	0.416
Tiredness on day 1	5.29 ± 2.13	5.42 ± 2.21	0.815
Tiredness on day 2	4.17 ± 2.01	4.53 ± 1.96	0.467
Tiredness on day 3	3.41 ± 2.58	4.33 ± 1.77	0.162
Nausea on day 1	0.88 ± 1.77	0.55 ± 0.90	0.352
Nausea on day 2	0.49 ± 1.50	0.38 ± 0.72	0.730
Nausea on day 3	0.43 ± 1.72	0.32 ± 0.61	0.764
SOB on day 1	0.73 ± 1.66	0.30 ± 0.97	0.213
SOB on day 2	0.52 ± 1.60	0.35 ± 1.33	0.657
SOB on day 3	0.55 ± 1.74	0.19 ± 0.96	0.391
Wellbeing on day 1	5.97 ± 1.54	5.68 ± 1.75	0.494
Wellbeing on day 2	6.88 ± 1.24	6.62 ± 1.57	0.469
Wellbeing on day 3	7.41 ± 1.69	6.83 ± 1.64	0.225

TEA: Transcutaneous electroacupuncture; SOB: Shortness of breath.

parenteral nutrition could be an option[2], but for gastric cancer patients, oral nutrition may increase anastomotic leakage rate in the early stage, and parenteral nutrition cannot be tolerated postoperatively. The use of prokinetic agents for treatment of POI is still controversial[3]. In short, there is currently no effective way to accelerate bowel motility recovery.

Acupuncture has been widely used for treatment of gastrointestinal diseases for thousands of years in China, and several studies have demonstrated that it helps gastric and colon cancer patients recover from POI[9,10]. A modern method of EA, which is modified from the traditional acupuncture, also controls postoperative pain and improves gastrointestinal motility after surgery. A randomized controlled trial indicated that EA reduced duration of POI after laparoscopic surgery for colorectal cancer[6]. Animal experiments found that EA at ST36 accelerated colonic motility and transit in freely moving rats[11], and improved restraint-stress-induced delay of gastric emptying *via* central glutamatergic pathways in conscious rats[12]. Jun-fan Fang *et al*[13] revealed that EA affected the patients by activating the vagus nerve instead of regulating local inflammation. EA also has a therapeutic effect on diabetic gastroparesis[14].

TEA is a new method of electrical stimulation *via* cutaneous electrodes placed at acupoints without needles. It is a non-invasive method that can be easily accepted by patients and even self-administrated at home. Chen *et al*[4,15,16] has proved that electroacupuncture improves impaired gastric, small intestinal[17] and colonic[18] motility, ameliorates gastric dysrhythmia[19], and accelerates gastric emptying[5,20], and it is used to treat gastroesophageal reflux, functional dyspepsia and irritable bowel syndrome[4]. TEA is effective in

Table 4 Postoperative complications

	TEA (n = 33)	Control (n = 30)	P value
Prolonged postoperative ileus	0	3	0.102
Wound infection	1	1	0.730
Pneumonia	1	1	0.730
Chyle leakage	2	1	0.182
Ventricular premature beat	1	0	0.524
Liver impairment	1	0	0.524
Pancreatic leakage	0	1	0.476
Total	6	7	0.270

TEA: Transcutaneous electroacupuncture.

treatment of functional dyspepsia[21] and chemotherapy-induced nausea and vomiting[22]. Experiments in dogs have shown that EA and TEA at ST36 both improve the rectal distention-induced impairment of intestinal contraction, transit and slow waves mediated *via* the vagal mechanism[7], and needleless TEA is as effective as EA in ameliorating intestinal hypomotility[7]. Huang *et al*[23] investigated the effects of TEA on healthy volunteers, and found that TEA improved impaired gastric accommodation and slow waves induced by cold drinks.

Acupuncture seems promising for treating POI after gastrectomy[9,24] and control of emesis during chemotherapy[25]. To the best of our knowledge, this was the first attempt to investigate the effectiveness of TEA to alleviate POI after gastrectomy. We found that TEA shortened the time to first flatus, along with more bowel sounds on days 2 and 3 in subgroup analysis of patients with open gastrectomy. There may be an approximate correlation between quantity or quality of bowel sounds and bowel function, but it has not been established as a definitive association. Some studies have inserted a Sitz marker capsule into the distal anastomosis to evaluate bowel movements[9,26]. As we noted, bowel sounds became more frequent and louder during the recovery period and increased to more than 2-4/min on days 2 and 3, which could be a good predication of normal bowel function transition.

In contrast, postoperative pain results in stress and affects the mobilization of patients after surgery. Early mobility or activity is recognized as a critical step in enhanced recovery after surgery (ERAS)[27]. The anesthetists would like to perform patient-controlled epidural analgesia (PCEA) or patient-controlled intravenous analgesia (PCIA) after surgery in our center, and we routinely give patients analgesics to relieve abdominal pain. As a consequence, the postoperative pain score was < 4 on day 1, and there was no significant difference between the two groups; it gradually decreased to < 3 on days 2 and 3. Several studies have proved that acupuncture or EA reduces pain in patients undergoing thoracic[28], abdominal[6], inguinal hernia surgery[29], breast cancer[30], or kidney[31] surgery. The postoperative patients in our study had less pain because of PCEA or PCIA, most of the patients tolerated pain well, they could even sit up and stand on the morning of day 1 after operation, thus the pain-control availability of TEA was not validated.

Epidural anesthesia might diminish the positive effects of acupuncture by blocking the afferent and efferent neural pathways[32]. Administration of local anesthetic through a thoracic epidural catheter may decrease POI by reducing sympathetic neural input[1]. Based on these reasons, Simon *et al*[6] excluded patients who received epidural anesthesia or analgesia, and revealed that EA significantly reduced the duration of POI and postoperative analgesic requirement after laparoscopic surgery for colorectal cancer. Several laboratory and clinical studies have also proved that parasympathetic nerve activity was involved in the process of EA or TEA. Nevertheless, as mentioned before, PCEA or PCIA was routinely used in our center for pain control, which might have affected the outcomes, although there was no significant difference between the two groups.

This study had several limitations. First, the number of patients may have been inadequate to make the results convincing. Second, we did not apply ERAS to the postoperative recovery, which had been proved effective to reduce POI[27]. Third, the mechanisms underlying perioperative gastrointestinal waves or vagal tone associated with TEA should be confirmed in the future. Fourth, it was not a double-blind research, thus we could not exclude the placebo effect.

In conclusion, TEA accelerated bowel movements and alleviated POI and decreased hospital stay after open gastrectomy. It is a safe and convenient treatment for recovery from POI.

ARTICLE HIGHLIGHTS

Research background

Postoperative ileus (POI) after gastrectomy is not rare and causes various symptoms, which probably affects patient recovery, prolongs hospital stay, and increases cost. However, there is no effective way to alleviate POI until now.

Research motivation

Transcutaneous electroacupuncture (TEA) is a new-developed, non-invasive and portable device. It has been validated to improve intestinal dysmotility in dog experiment. But it remains unknown whether it is useful to alleviate POI for post-gastrectomy patients clinically.

Research objectives

The aim of this article was investigating the efficacy and safety of TEA to alleviate POI after gastrectomy.

Research methods

From April 2014 to February 2017, 63 gastric cancer patients were recruited from the Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China. After gastrectomy, the patients were randomly allocated to the TEA (n = 33) or control (n = 30) group. The patients in the TEA group received 1 h

TEA on Neiguan (ST36) and Zusanli (PC6) twice daily in the morning and afternoon until they passed flatus. The main outcomes were hours to the first flatus or bowel movement, time to nasogastric tube removal, time to liquid and semi-liquid diet, and hospital stay. The secondary outcomes included postoperative symptom assessment and complications.

Research results

Time to first flatus in the TEA group was significantly shorter than in the control group (73.19 ± 15.61 *vs* 82.82 ± 20.25 h, P = 0.038), especially for open gastrectomy (76.53 ± 14.29 *vs* 87.23 ± 20.75 h, P = 0.048). Bowel sounds on day 2 in the TEA group were significantly greater than in the control group (2.30 ± 2.61/min *vs* 1.05 ± 1.26/min, P = 0.017). Time to nasogastric tube removal in the TEA group was earlier than in the control group (4.22 ± 1.01 *vs* 4.97 ± 1.67 d, P = 0.049), as well as the time to liquid diet (5.0 ± 1.34 *vs* 5.83 ± 2.10 d, P = 0.039). Hospital stay in the TEA group was significantly shorter than in the control group (8.06 ± 1.75 *vs* 9.40 ± 3.09 d, P = 0.041). No significant differences in postoperative symptom assessment and complications were found between the groups. There were no severe adverse events related to TEA.

Research conclusions

In this prospective and randomized clinical study, we confirmed the role of TEA in the treatment of post-gastrectomy bowel motility recovery for the first time. TEA in gastric cancer patients significantly increased postoperative bowel movement; shortened time to first flatus, nasogastric tube removal, liquid diet and hospital stay, and it was safe.

Research perspectives

The authors proved that TEA was effective and safe to recovery post-gastrectomy patients from POI. So it will probably provide clinical surgeons with a novel non-invasive device to accelerate bowel function recovery and reduce hospital stay, which satisfies the concept of enhanced recovery after surgery (ERAS). Besides, TEA could be considered to be applied on other abdominal surgeries as well.

REFERENCES

1 **Mattei P**, Rombeau JL. Review of the pathophysiology and management of postoperative ileus. *World J Surg* 2006; **30**: 1382-1391 [PMID: 16850151 DOI: 10.1007/s00268-005-0613-9]

2 **Holte K**, Kehlet H. Postoperative ileus: a preventable event. *Br J Surg* 2000; **87**: 1480-1493 [PMID: 11091234 DOI: 10.1046/j.1365-2168.2000.01595.x]

3 **Traut U**, Brügger L, Kunz R, Pauli-Magnus C, Haug K, Bucher HC, Koller MT. Systemic prokinetic pharmacologic treatment for postoperative adynamic ileus following abdominal surgery in adults. *Cochrane Database Syst Rev* 2008: CD004930 [PMID: 18254064 DOI: 10.1002/14651858.CD004930.pub3]

4 **Yin J**, Chen JD. Gastrointestinal motility disorders and acupuncture. *Auton Neurosci* 2010; **157**: 31-37 [PMID: 20363196 DOI: 10.1016/j.autneu.2010.03.007]

5 **Xu S**, Hou X, Zha H, Gao Z, Zhang Y, Chen JD. Electroacupuncture accelerates solid gastric emptying and improves dyspeptic symptoms in patients with functional dyspepsia. *Dig Dis Sci* 2006; **51**: 2154-2159 [PMID: 17082991 DOI: 10.1007/s10620-006-9412-x]

6 **Ng SS**, Leung WW, Mak TW, Hon SS, Li JC, Wong CY, Tsoi KK, Lee JF. Electroacupuncture reduces duration of postoperative ileus after laparoscopic surgery for colorectal cancer. *Gastroenterology* 2013; **144**: 307-313.e1 [PMID: 23142625 DOI: 10.1053/j.gastro.2012.10.050]

7 **Song J**, Yin J, Chen J. Needleless transcutaneous electroacupuncture improves rectal distension-induced impairment in intestinal motility and slow waves via vagal mechanisms in dogs. *Int J Clin Exp Med* 2015; **8**: 4635-4646 [PMID: 26064396]

8 **Vather R**, Bissett I. Management of prolonged post-operative ileus: evidence-based recommendations. *ANZ J Surg* 2013; **83**: 319-324 [PMID: 23418987 DOI: 10.1111/ans.12102]

9 **Jung SY**, Chae HD, Kang UR, Kwak MA, Kim IH. Effect of Acupuncture on Postoperative Ileus after Distal Gastrectomy for Gastric Cancer. *J Gastric Cancer* 2017; **17**: 11-20 [PMID: 28337359 DOI: 10.5230/jgc.2017.17.e2]

10 **Kim KH**, Kim DH, Kim HY, Son GM. Acupuncture for recovery after surgery in patients undergoing colorectal cancer resection: a systematic review and meta-analysis. *Acupunct Med* 2016; **34**: 248-256 [PMID: 26921418 DOI: 10.1136/acupmed-2015-010941]

11 **Iwa M**, Matsushima M, Nakade Y, Pappas TN, Fujimiya M, Takahashi T. Electroacupuncture at ST-36 accelerates colonic motility and transit in freely moving conscious rats. *Am J Physiol Gastrointest Liver Physiol* 2006; **290**: G285-G292 [PMID: 16254048 DOI: 10.1152/ajpgi.00068.2005]

12 **Iwa M**, Nakade Y, Pappas TN, Takahashi T. Electroacupuncture improves restraint stress-induced delay of gastric emptying via central glutaminergic pathways in conscious rats. *Neurosci Lett* 2006; **399**: 6-10 [PMID: 16406343 DOI: 10.1016/j.neulet.2005.11.069]

13 **Fang JF**, Fang JQ, Shao XM, Du JY, Liang Y, Wang W, Liu Z. Electroacupuncture treatment partly promotes the recovery time of postoperative ileus by activating the vagus nerve but not regulating local inflammation. *Sci Rep* 2017; **7**: 39801 [PMID: 28051128 DOI: 10.1038/srep39801]

14 **Sarosiek I**, Song G, Sun Y, Sandoval H, Sands S, Chen J, McCallum RW. Central and Peripheral Effects of Transcutaneous Acupuncture Treatment for Nausea in Patients with Diabetic Gastroparesis. *J Neurogastroenterol Motil* 2017; **23**: 245-253 [PMID: 28163260 DOI: 10.5056/jnm16097]

15 **Li H**, Yin J, Zhang Z, Winston JH, Shi XZ, Chen JD. Auricular vagal nerve stimulation ameliorates burn-induced gastric dysmotility via sympathetic-COX-2 pathways in rats. *Neurogastroenterol Motil* 2016; **28**: 36-42 [PMID: 26486522 DOI: 10.1111/nmo.12693]

16 **Chen J**, Song GQ, Yin J, Koothan T, Chen JD. Electroacupuncture improves impaired gastric motility and slow waves induced by rectal distension in dogs. *Am J Physiol Gastrointest Liver Physiol* 2008; **295**: G614-G620 [PMID: 18653722 DOI: 10.1152/ajpgi.90322.2008]

17 **Sun Y**, Song G, Yin J, Chen J, Chen JH, Song J, Chen JD. Effects and mechanisms of electroacupuncture on glucagon-induced small intestinal hypomotility in dogs. *Neurogastroenterol Motil* 2010; **22**: 1217-1223, e318 [PMID: 20723072 DOI: 10.1111/j.1365-2982.2010.01565.x]

18 **Jin H**, Liu J, Foreman RD, Chen JD, Yin J. Electrical neuromodulation at acupoint ST36 normalizes impaired colonic motility induced by rectal distension in dogs. *Am J Physiol Gastrointest Liver Physiol* 2015; **309**: G368-G376 [PMID: 26113299 DOI: 10.1152/ajpgi.00467.2014]

19 **Yin J**, Chen J, Chen JD. Ameliorating effects and mechanisms of electroacupuncture on gastric dysrhythmia, delayed emptying, and impaired accommodation in diabetic rats. *Am J Physiol Gastrointest Liver Physiol* 2010; **298**: G563-G570 [PMID: 20093561 DOI: 10.1152/ajpgi.00252.2009]

20 **Ouyang H**, Yin J, Wang Z, Pasricha PJ, Chen JD. Electroacupuncture accelerates gastric emptying in association with changes in vagal

activity. *Am J Physiol Gastrointest Liver Physiol* 2002; **282**: G390-G396 [PMID: 11804862 DOI: 10.1152/ajpgi.00272.2001]
21 **Liu S**, Peng S, Hou X, Ke M, Chen JD. Transcutaneous electroacupuncture improves dyspeptic symptoms and increases high frequency heart rate variability in patients with functional dyspepsia. *Neurogastroenterol Motil* 2008; **20**: 1204-1211 [PMID: 18694444 DOI: 10.1111/j.1365-2982.2008.01164.x]
22 **Zhang X**, Jin HF, Fan YH, Lu B, Meng LN, Chen JD. Effects and mechanisms of transcutaneous electroacupuncture on chemotherapy-induced nausea and vomiting. *Evid Based Complement Alternat Med* 2014; **2014**: 860631 [PMID: 25254060 DOI: 10.1155/2014/860631]
23 **Huang Z**, Zhang N, Xu F, Yin J, Dai N, Chen JD. Ameliorating effect of transcutaneous electroacupuncture on impaired gastric accommodation induced by cold meal in healthy subjects. *J Gastroenterol Hepatol* 2016; **31**: 561-566 [PMID: 26399958 DOI: 10.1111/jgh.13168]
24 **Hsiung WT**, Chang YC, Yeh ML, Chang YH. Acupressure improves the postoperative comfort of gastric cancer patients: A randomised controlled trial. *Complement Ther Med* 2015; **23**: 339-346 [PMID: 26051568 DOI: 10.1016/j.ctim.2015.03.010]
25 **Shin YH**, Kim TI, Shin MS, Juon HS. Effect of acupressure on nausea and vomiting during chemotherapy cycle for Korean postoperative stomach cancer patients. *Cancer Nurs* 2004; **27**: 267-274 [PMID: 15292721 DOI: 10.1097/00002820-200407000-00002]
26 **Chae HD**, Kwak MA, Kim IH. Effect of Acupuncture on Reducing Duration of Postoperative Ileus After Gastrectomy in Patients with Gastric Cancer: A Pilot Study Using Sitz Marker. *J Altern Complement Med* 2016; **22**: 465-472 [PMID: 27219115 DOI: 10.1089/acm.2015.0161]
27 **Feng F**, Ji G, Li JP, Li XH, Shi H, Zhao ZW, Wu GS, Liu XN, Zhao QC. Fast-track surgery could improve postoperative recovery in radical total gastrectomy patients. *World J Gastroenterol* 2013; **19**: 3642-3648 [PMID: 23801867 DOI: 10.3748/wjg.v19.i23.3642]
28 **Chen T**, Wang K, Xu J, Ma W, Zhou J. Electroacupuncture Reduces Postoperative Pain and Analgesic Consumption in Patients Undergoing Thoracic Surgery: A Randomized Study. *Evid Based Complement Alternat Med* 2016; **2016**: 2126416 [PMID: 27073400 DOI: 10.1155/2016/2126416]
29 **Dalamagka M**, Mavrommatis C, Grosomanidis V, Karakoulas K, Vasilakos D. Postoperative analgesia after low-frequency electroacupuncture as adjunctive treatment in inguinal hernia surgery with abdominal wall mesh reconstruction. *Acupunct Med* 2015; **33**: 360-367 [PMID: 26040491 DOI: 10.1136/acupmed-2014-010689]
30 **Giron PS**, Haddad CA, Lopes de Almeida Rizzi SK, Nazário AC, Facina G. Effectiveness of acupuncture in rehabilitation of physical and functional disorders of women undergoing breast cancer surgery. *Support Care Cancer* 2016; **24**: 2491-2496 [PMID: 26670916 DOI: 10.1007/s00520-015-3054-5]
31 **Tabassi KT**, Amini P, Mohammadi S, Razavizadeh RT, Golchian A. The effect of acupuncture on pain score after open kidney surgery. *J Complement Integr Med* 2015; **12**: 241-244 [PMID: 25924232 DOI: 10.1515/jcim-2014-0071]
32 **Meng ZQ**, Garcia MK, Chiang JS, Peng HT, Shi YQ, Fu J, Liu LM, Liao ZX, Zhang Y, Bei WY, Thornton B, Palmer JL, McQuade J, Cohen L. Electro-acupuncture to prevent prolonged postoperative ileus: a randomized clinical trial. *World J Gastroenterol* 2010; **16**: 104-111 [PMID: 20039456 DOI: 10.3748/wjg.v16.i1.104]

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ORIGINAL ARTICLE

Observational Study

Perioperative liver and spleen elastography in patients without chronic liver disease

Sam Eriksson, Hanna Borsiin, Carl-Fredrik Öberg, Hannes Brange, Zoran Mijovic, Christian Sturesson

Sam Eriksson, Hanna Borsiin, Carl-Fredrik Öberg, Hannes Brange, Christian Sturesson, Department of Surgery, Lund University, Skåne University Hospital, Lund S-221 85, Sweden

Zoran Mijovic, Department of Radiology, Lund University, Skåne University Hospital, Lund S-221 85, Sweden

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Correspondence to: Christian Sturesson, MD, PhD, Associate Professor, Surgeon, Department of Surgery, Lund University, Skåne University Hospital, Lund S-221 85, Sweden. christian.sturesson@med.lu.se
Telephone: +46-46-172347
Fax: +46-46-172335

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Abstract

AIM

To investigate changes in hepatic and splenic stiffness in patients without chronic liver disease during liver resection for hepatic tumors.

METHODS

Patients scheduled for liver resection for hepatic tumors were considered for enrollment. Tissue stiffness measurements on liver and spleen were conducted before and two days after liver resection using point shear-wave elastography. Histological analysis of the resected liver specimen was conducted in all patients and patients with marked liver fibrosis were excluded from further study analysis. Patients were divided into groups depending on size of resection and whether they had received preoperative chemotherapy or not. The relation between tissue stiffness and postoperative biochemistry was investigated.

RESULTS

Results are presented as median (interquartile range). 35 patients were included. The liver stiffness increased in patients undergoing a major resection from 1.41 (1.24-1.63) m/s to 2.20 (1.72-2.44) m/s (P = 0.001). No change in liver stiffness in patients undergoing a minor resection was found [1.31 (1.15-1.52) m/s *vs* 1.37

(1.12-1.77) m/s, P = 0.438]. A major resection resulted in a 16% (7%-33%) increase in spleen stiffness, more (P = 0.047) than after a minor resection [2 (-1-13) %]. Patients who underwent preoperative chemotherapy (n = 20) did not differ from others in preoperative right liver lobe [1.31 (1.16-1.50) *vs* 1.38 (1.12-1.56) m/s, P = 0.569] or spleen [2.79 (2.33-3.11) *vs* 2.71 (2.37-2.86) m/s, P = 0.515] stiffness. Remnant liver stiffness on the second postoperative day did not show strong correlations with maximum postoperative increase in bilirubin (R^2 = 0.154, Pearson's r = 0.392, P = 0.032) and international normalized ratio (R^2 = 0.285, Pearson's r = 0.534, P = 0.003).

CONCLUSION

Liver and spleen stiffness increase after a major liver resection for hepatic tumors in patients without chronic liver disease.

Key words: Chemotherapy; Adjuvant; Colorectal neoplasms; Elasticity imaging techniques; Hepatectomy; Liver neoplasms

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Core tip: Point shear-wave elastography is an ultrasound-based technique which lets the user measure tissue stiffness. The technique has previously mostly been used to study patients with chronic liver disease and cirrhosis. In the current study we investigate changes in liver and spleen stiffness in patients without chronic liver disease undergoing chemotherapy and liver resection for liver tumors. A major liver resection resulted in a 42% increase in liver stiffness. Also, spleen stiffness increased more in a major than a minor resection. However, there was no difference in tissue stiffness between patients who received preoperative chemotherapy or not.

Eriksson S, Borsiin H, Öberg CF, Brange H, Mijovic Z, Sturesson C. Perioperative liver and spleen elastography in patients without chronic liver disease. *World J Gastrointest Surg* 2018; 10(2): 21-27 Available from: URL: http://www.wjgnet.com/1948-9366/full/v10/i2/21.htm DOI: http://dx.doi.org/10.4240/wjgs.v10.i2.21

INTRODUCTION

Liver elastography implies reporting metrics related to the mechanical stiffness of the liver, using either ultrasound or magnetic resonance techniques[1]. Ultrasound-based techniques include virtual touch tissue quantification (VTTQ) (Siemens, Erlangen, Germany) which is a software based on point shear-wave elastography (SWE) technology, used to measure tissue elasticity[2-4]. Using standard ultrasound equipment, an acoustic pulse is applied to a region of interest within the tissue under investigation[5]. The pulse will cause small displacements of the tissue and generate shear waves perpendicular to the original pulse. The shear wave propagation velocity will differ depending on the elastic properties, *i.e.,* stiffness, of the tissue[6]. High shear wave velocity denotes a stiffer tissue. In relation to surgical resection of liver tumors, a high preoperative liver stiffness has been shown to increase the risk of postoperative liver failure after resection of hepatocellular carcinoma in patients with chronic liver disease[7].

Changes in perioperative liver stiffness in patients without chronic liver disease undergoing liver resection for tumors have not been previously investigated. Surgical resection offers a potential cure for both primary liver tumors and liver metastasis[8,9]. The risk of postoperative liver failure is the most important factor for postoperative mortality limiting the size of the resection[10]. An otherwise healthy liver can withstand a larger resection than a liver with parenchymal damage, which requires a larger liver remnant to ensure a sufficient postoperative liver function. Parenchymal damage can be due to chronic liver disease because of hepatitis or alcohol abuse but also occurs in non-alcoholic fatty liver disease or because of chemotherapy[11-13]. Chemotherapy associated parenchymal damage include steatosis, steatohepatitis and sinusoidal obstruction syndrome which all have been suggested to increase postoperative morbidity or mortality[12,14,15].

The current study aimed to investigate changes in hepatic and splenic stiffness during liver resection for hepatic tumors in patients without chronic liver disease, effects of preoperative chemotherapy on tissue stiffness and its relation to early postoperative biochemistry with the aim to detect postoperative liver failure.

MATERIALS AND METHODS

Patient selection

The study protocol was approved by the Regional Ethical Review Board. Patients scheduled for liver resection for hepatic tumors at a single center were considered for enrollment. Patients were given both written and oral information about the study and gave their written consent prior to enrollment. Patients' clinical data were recorded from patient medical records. Patients with marked liver fibrosis were excluded from study analysis.

To study the effect of liver resection on liver stiffness patients were divided into two groups depending on whether they underwent a major resection (hemihepatectomy or extended hemihepatectomy) or a minor resection. Liver resection was performed as previously described[16]. If necessary, the blood flow of the portal vein and hepatic artery was temporarily occluded (Pringle's maneuver). Preoperative chemotherapy was defined as receiving chemotherapy within 3 mo prior to surgery[17].

Liver stiffness measurements

Measurements of liver and spleen stiffness were made

Table 1 Patient characteristics

	No resection	Minor resection	Major resection
No. of patients	4	16	15
Gender (male:female)	1:3	8:8	8:7
Age (yr)	69 (56-76)	75 (66-79)	66 (50-74)
BMI (kg/m²)	23.5 (21.4-28.6)	24.7 (21.8-26.8)	26.8 (25.2-28.7)
Weight (kg)	64 (53-86)	72 (63-83)	78 (70-90)
ASA physical status (1/2:3/4)	3:1	10:6	10:5
Preoperative bilirubin (μmol/L)	5 (4-7)	6 (5-10)	7 (6-11)
Preoperative INR	1.0 (0.9-1.0)	1.0 (0.9-1.1)	1.0 (1.0-1.1)
Diagnosis			
Colorectal metastases	3	13	11
Other malignant tumors	0	2	3
Benign tumors	1	1	1
Number of hepatic tumors	5 (1-7)	1 (1-2)	2 (2-6)
Largest hepatic tumor (mm)	42 (17-57)	30 (10-45)	30 (23-51)
Preoperative chemotherapy	2	6	12
Oxaliplatin-based therapy	2	4	9
Liver lobe operated (right lobe:left lobe:both lobes)	-	7:4:5	7:0:8
Operating time (h)	2.5 (2-3)	3 (3-5.5)	6 (4.5-7)
Operative bleeding (mL)	125 (100-150)	275 (150-500)	650 (400-1100)
Length of hospital stay (d)	3 (2-6)	6 (3-9)	6 (5-7)
Liver parenchyma damage			
Steatosis	-	0	1
Steatohepatitis	-	0	0
SOS	-	0	0

Data are presented as number or median (interquartile range). BMI: Body mass index; ASA: American Society of Anesthesiologists; INR: International normalized ratio; SOS: Sinusoidal obstruction syndrome.

using a Siemens ACUSON S2000 ultrasound system (Siemens Medical Solutions Inc., Mountain View, CA, United States) accompanied by the VTTQ software package. A 4C1 transducer (Siemens Medical Solutions Inc., Mountain View, CA, United States) was used. Patients were fasting 4 h before examination. To decrease movement artefacts patients were asked to hold their breath during the seconds of measurement. Measurements were conducted before and after liver resection.

Preoperative measurements were conducted in both the right and the left liver lobe as well as in the spleen. A region of interest within the respective parenchyma was chosen at a depth of 3-6 cm from the transducer[3]. The regions were chosen so that major blood vessels and bile ducts were avoided. For measurements in the right liver lobe intercostal transducer placement was used. Each region was measured 10 times and a median of the 10 measurements was calculated. Comparison between the pre- and postoperative measurements were made on the spleen and the remnant liver lobe, *e.g.*, on the right liver lobe if the patient was undergoing a left hemihepatectomy. Tissue stiffness data was presented as the shear wave velocity (m/s).

Histological analyses

Histological analysis of the resected liver specimen was conducted in all patients. The pathologist was blinded to stiffness results. Steatosis was graded (0-3), steatohepatitis (0-8) and fibrosis (0-4), according to the non-alcoholic fatty liver disease activity score, NAS[18]. A steatosis grade ⩾ 2 was defined as steatosis. A NAS ⩾ 5 was defined as steatohepatitis and fibrosis > 2 was defined as marked fibrosis. Sinusoidal obstruction syndrome was defined as a sinusoidal dilatation grade ⩾ 2 according to Rubbia-Brandt *et al*[11].

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 23 (IBM, Armonk, NY, United States). The statistical methods were reviewed by a biomedical statistician. To compare continuous data the Mann-Whitney *U*-test or the Wilcoxon test for paired samples was used. Categorical data was compared with a χ^2 test. Correlations were made using linear regression analysis and by calculating a Pearson's correlation coefficient, *r*. A *P*-value < 0.05 was considered statistically significant. All results are presented as median (interquartile range) if not stated otherwise.

RESULTS

Patient enrollment and preoperative measurements

About 47 patients were enrolled in the study. Nine patients failed to complete the study protocol and were excluded from the study; 6 patients declined to participate after enrollment, mostly due to postoperative pain and 3 patients were transferred to a different hospital before the second measurement. In addition, 3 patients were excluded from study analysis because of marked fibrosis on histological analysis of the liver specimen, leaving 35 patients included for study analysis.

Table 2 Liver and spleen stiffness measurements for the minor and major resection groups

	Minor resection	Major resection	*P* value
No. of patients	16	15	-
Future liver remnant (m/s)	1.31 (1.15-1.52)	1.41 (1.24-1.63)	0.318
Right liver lobe preoperative (m/s)	1.29 (1.12-1.49)	1.38 (1.14-1.57)	0.423
Left liver lobe preoperative (m/s)	1.35 (1.06-1.71)	1.41 (1.29-1.63)	0.667
Spleen preoperative (m/s)	2.76 (2.36-2.91)	2.69 (2.33-3.11)	0.984
Liver remnant postoperative (m/s)	1.37 (1.12-1.77)	2.20 (1.72-2.44)	< 0.001
Spleen postoperative (m/s)	2.83 (2.44-3.18)	2.90 (2.63-3.50)	0.216
Relative difference in liver remnant (%)	4 (-16-24)	42 (33-71)	0.001
Relative difference in the spleen (%)	2 (-1-13)	16 (7-33)	0.047

Data are presented as median (interquartile range).

Postoperative liver measurements were made typical on postoperative day 2 (postoperative day 1-3). Patient characteristics are presented in Table 1. Median preoperative shear wave velocity in all patients in the right liver lobe was 1.33 (1.15-1.50) m/s and in the left liver lobe 1.41 (1.20-1.66) m/s. The shear wave velocity in the left lobe was higher than in the right, P = 0.026. Median preoperative shear wave velocity of the spleen was 2.76 (2.37-3.02) m/s.

Four patients did not undergo resection because of intraoperatively discovered unexpected excessive liver tumor disease precluding resection (n = 2) and two patients without intraoperatively detectable tumor disease. No difference in pre- and postoperative liver or spleen stiffness was found for these patients (results not shown).

Tissue stiffness in minor vs major resection

Liver and spleen stiffness measurements for the minor and major resection groups are presented in Table 2. There were no differences between groups regarding gender ratio, body mass index, American Society of Anesthesiologists (ASA) physical status classification or diagnosis. However, patients who underwent a minor resection were older than patients undergoing a major resection [75 (66-79) *vs* 66 (50-74) years, P = 0.033] and did not undergo preoperative chemotherapy as frequent as the patients who underwent a major resection (6 *vs* 12 patients, P = 0.017).

The stiffness of the liver remnant increased in patients undergoing a major resection (P = 0.001) as compared to preoperative measurements. There was no difference for patients undergoing a minor resection (P = 0.438).

Chemotherapy

Patients who underwent preoperative chemotherapy (n = 20) did not differ from others in preoperative right liver lobe [1.31 (1.16-1.50) *vs* 1.38 (1.12-1.56) m/s, P = 0.569] or spleen [2.79 (2.33-3.11) *vs* 2.71 (2.37-2.86) m/s, P = 0.515] stiffness.

There was no difference between patients preoperatively treated with oxaliplatin (n = 15) compared to others in preoperative right liver [1.31 (1.16-1.50) *vs* 1.38 (1.14-1.61) m/s P = 0.670] or spleen [2.76 (2.34-2.97) *vs* 2.76 (2.37-3.07) m/s, P = 0.892] stiffness.

Correlation between tissue stiffness and postoperative bilirubin and international normalized ratio

The correlation between shear wave velocity in the liver remnant and maximum postoperative increase of bilirubin and international normalized ratio (INR) are presented in Figure 1 respectively.

DISCUSSION

The current study presents data on changes in liver and spleen stiffness after liver resection for hepatic tumors in patients without chronic liver disease. In patients who underwent a major resection, the stiffness of the liver remnant increased by 42% as measured with point SWE. No change in liver stiffness was found in patients who underwent a minor resection. The spleen stiffness increased by 16% after a major resection, more than after a minor resection (Table 2).

Liver elastography is most frequently used to non-invasively quantify the degree of liver fibrosis in patients with chronic liver disease[2]. As patients with liver fibrosis were excluded in the present study, the reasons for increase in liver stiffness found must be unrelated to histological fibrosis. The increase in tissue stiffness may be explained by a postoperative increase in portal pressure which causes a congestion in the smaller liver remnant[19]. In comparison, an elevated liver stiffness has been shown in patients with acute decompensated heart failure[20] and also in patients with extrahepatic biliary obstruction[21]. No comparative measurements of portal pressure were conducted in the current study. In animal models, increase in hepatic perfusion in small-for-size liver grafts has shown to be of importance in both liver regeneration and liver damage[22]. However, the significance of liver stiffness on liver regeneration is yet to be investigated. A postoperative increase in liver stiffness has previously been demonstrated after liver resection for living donor transplantation[19].

Mean shear wave velocity in healthy livers range about 0.8-1.7 m/s[5]. The present preoperative measurements are in alignment with these values. In addition, there

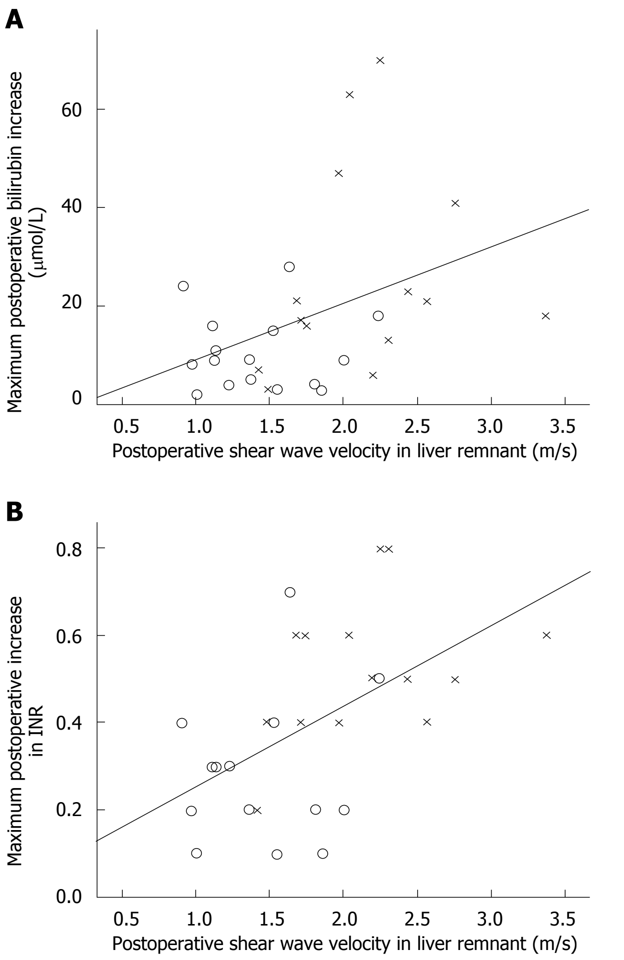

Figure 1 Correlation between maximum postoperative bilirubin increase (A), international normalized ratio (B) and stiffness in liver remnant for patients who underwent minor (O) and major (X) resection. A: $R^2 = 0.154$, Pearson's $r = 0.392$, $P = 0.032$; B: $R^2 = 0.285$, Pearson's $r = 0.534$, $P = 0.003$. INR: International normalized ratio.

was a significant difference between measurements in the right and left liver lobes. This has been observed previously[23], and may be due to the smaller volume of the left lobe or its close position to the heart, causing movement artefacts. The same authors have suggested that more reliable measurements are obtained at a greater depth than superficial measurements. For that reason measurements in the current study was conducted at a depth of 3-6 cm from the transducer[23].

Point SWE measurements allow fast and non-invasive measurements of tissue stiffness. Compared to transient elastography with Fibroscan®, another ultrasound-based tissue stiffness diagnostic technique, point SWE can be made using standard ultrasound equipment, without the need for an extra examination and a region of interest within the tissue can easily be defined by the operator using a real-time conventional B-mode image[5,24].

Measurements were done on the second postoperative day as earlier measurements were found difficult to make due to postoperative pain.

No differences in liver or spleen stiffness were found in patients undergoing preoperative chemotherapy. Chemotherapy-induced liver parenchyma damage could worsen outcome after a liver resection[12,14,15] and perioperative identification of parenchymal damage would be desirable. Oxaliplatin, often included in preoperative treatment of colorectal liver metastasis, has previously been shown to induce splenic enlargement[25], proposed as a result of induced sinusoidal obstruction syndrome[26]. In the present study, no differences were found in preoperative splenic or liver stiffness in patients who received oxaliplatin. However, only one patient showed histological signs of steatosis and none presented with sinusoidal obstruction syndrome or steatohepatitis, which is a considerably lower frequency than previously reported[11-13]. One limitation of the current study is the relative small number of patients included, which may explain the differences.

Postoperative liver failure has high morbidity and mortality rates and early detection is of great interest to rapidly initiate treatment measures[27]. There is currently no good method for its early diagnosis and signs of liver failure are first detected several days after surgery when patients develop high bilirubin and INR values[28]. The present measurements on the second postoperative day showed weak but significant correlations with maximum postoperative increase in bilirubin and INR, as shown in Figure 1. A study on living liver donors have presented similar results on maximum bilirubin[19]. In a small report on 3 patients with acute liver failure due to intoxication, liver stiffness was suggested to be higher than healthy controls but similar to patients with liver cirrhosis[29]. Point SWE measurements may play a role in the early detection of liver failure, however further study is needed on the dynamics of normal and pathological liver stiffness after liver resection.

In conclusion, liver and spleen stiffness changes after liver resection for hepatic tumors using point SWE measurements have been presented. The size of resection matters to the dynamics of liver stiffness. The potential of point SWE in the detection of chemotherapy induced liver damage and postoperative liver failure needs further investigation.

ARTICLE HIGHLIGHTS

Research background

Surgical resection offers a potential cure for both primary liver tumors and liver metastases. The risk of postoperative liver failure is the most important factor for postoperative mortality and limits the size of the resection. An otherwise healthy liver can withstand a larger resection than a liver with parenchymal damage, which requires a larger liver remnant to ensure sufficient postoperative liver function. Liver elastography implies reporting metrics related to the mechanical stiffness of the liver. Liver elastography is most frequently used to non-invasively quantify the degree of liver fibrosis in patients with chronic liver disease. Changes in perioperative liver stiffness in patients without chronic liver disease undergoing liver resection for tumors have not been investigated.

Research motivation

Postoperative liver failure has high morbidity and mortality rates and early detection is of great interest to rapidly initiate treatment measures. There is currently no good method for its early diagnosis and signs of liver failure are first detected several days after surgery when patients develop high bilirubin and international normalized ratio values.

Research objectives

The current study aimed to investigate the changes in hepatic and splenic stiffness during liver resection for hepatic tumors in patients without chronic liver disease; and to investigate effects of preoperative chemotherapy on tissue stiffness and its relation to early postoperative biochemistry with the aim to detect postoperative liver failure.

Research methods

Tissue stiffness measurements on liver and spleen were conducted before and two days after liver resection for hepatic tumors using point shear-wave elastography (SWE). Patients were divided into groups depending on size of resection and whether they had received preoperative chemotherapy or not.

Research results

The stiffness of the liver remnant increased by 42% as measured with point SWE in patients who underwent a major resection. In patients who underwent a minor resection, no change in liver stiffness was found. The spleen stiffness increased by 16% after a major resection, more than after a minor resection. In patients undergoing preoperative chemotherapy, no differences in liver or spleen stiffness were found. Remnant liver stiffness on the second postoperative day did not show strong correlations with maximum postoperative increase in bilirubin and international normalized ratio.

Research conclusions

Liver and spleen stiffness increase after a major liver resection for hepatic tumors in patients without chronic liver disease. The potential of point SWE in the detection of chemotherapy induced liver damage and postoperative liver failure needs further investigation.

Research perspectives

Point SWE measurements may play a role in the early detection of liver failure; however, further study is needed on the dynamics of normal and pathological liver stiffness after liver resection.

REFERENCES

1 **Tang A**, Cloutier G, Szeverenyi NM, Sirlin CB. Ultrasound Elastography and MR Elastography for Assessing Liver Fibrosis: Part 1, Principles and Techniques. *AJR Am J Roentgenol* 2015; **205**: 22-32 [PMID: 25905647 DOI: 10.2214/AJR.15.14552]

2 **Toshima T**, Shirabe K, Takeishi K, Motomura T, Mano Y, Uchiyama H, Yoshizumi T, Soejima Y, Taketomi A, Maehara Y. New method for assessing liver fibrosis based on acoustic radiation force impulse: a special reference to the difference between right and left liver. *J Gastroenterol* 2011; **46**: 705-711 [PMID: 21264479 DOI: 10.1007/s00535-010-0365-7]

3 **Karlas T**, Pfrepper C, Wiegand J, Wittekind C, Neuschulz M, Mössner J, Berg T, Tröltzsch M, Keim V. Acoustic radiation force impulse imaging (ARFI) for non-invasive detection of liver fibrosis: examination standards and evaluation of interlobe differences in healthy subjects and chronic liver disease. *Scand J Gastroenterol* 2011; **46**: 1458-1467 [PMID: 21916815 DOI: 10.3109/00365521.2011.610004]

4 **Friedrich-Rust M**, Wunder K, Kriener S, Sotoudeh F, Richter S, Bojunga J, Herrmann E, Poynard T, Dietrich CF, Vermehren J, Zeuzem S, Sarrazin C. Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. *Radiology* 2009; **252**: 595-604 [PMID: 19703889 DOI: 10.1148/radiol.2523081928]

5 **D'Onofrio M**, Crosara S, De Robertis R, Canestrini S, Demozzi E, Gallotti A, Pozzi Mucelli R. Acoustic radiation force impulse of the liver. *World J Gastroenterol* 2013; **19**: 4841-4849 [PMID: 23946588 DOI: 10.3748/wjg.v19.i30.4841]

6 **Nightingale K**, Soo MS, Nightingale R, Trahey G. Acoustic radiation force impulse imaging: in vivo demonstration of clinical feasibility. *Ultrasound Med Biol* 2002; **28**: 227-235 [PMID: 11937286 DOI: 10.1016/S0301-5629(01)00499-9]

7 **Cescon M**, Colecchia A, Cucchetti A, Peri E, Montrone L, Ercolani G, Festi D, Pinna AD. Value of transient elastography measured with FibroScan in predicting the outcome of hepatic resection for hepatocellular carcinoma. *Ann Surg* 2012; **256**: 706-712; discussion 712-713 [PMID: 23095613 DOI: 10.1097/SLA.0b013e3182724ce8]

8 **Adams RB**, Aloia TA, Loyer E, Pawlik TM, Taouli B, Vauthey JN; Americas Hepato-Pancreato-Biliary Association; Society of Surgical Oncology; Society for Surgery of the Alimentary Tract. Selection for hepatic resection of colorectal liver metastases: expert consensus statement. *HPB* (Oxford) 2013; **15**: 91-103 [PMID: 23297719 DOI: 10.1111/j.1477-2574.2012.00557.x]

9 **Poon RT**, Fan ST, Lo CM, Liu CL, Wong J. Long-term survival and pattern of recurrence after resection of small hepatocellular carcinoma in patients with preserved liver function: implications for a strategy of salvage transplantation. *Ann Surg* 2002; **235**: 373-382 [PMID: 11882759 DOI: 10.1097/00000658-200203000-00009]

10 **Rahbari NN**, Garden OJ, Padbury R, Brooke-Smith M, Crawford M, Adam R, Koch M, Makuuchi M, Dematteo RP, Christophi C, Banting S, Usatoff V, Nagino M, Maddern G, Hugh TJ, Vauthey JN, Greig P, Rees M, Yokoyama Y, Fan ST, Nimura Y, Figueras J, Capussotti L, Büchler MW, Weitz J. Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). *Surgery* 2011; **149**: 713-724 [PMID: 21236455 DOI: 10.1016/j.surg.2010.10.001]

11 **Rubbia-Brandt L**, Audard V, Sartoretti P, Roth AD, Brezault C, Le Charpentier M, Dousset B, Morel P, Soubrane O, Chaussade S, Mentha G, Terris B. Severe hepatic sinusoidal obstruction associated with oxaliplatin-based chemotherapy in patients with metastatic colorectal cancer. *Ann Oncol* 2004; **15**: 460-466 [PMID: 14998849 DOI: 10.1093/annonc/mdh095]

12 **Vauthey JN**, Pawlik TM, Ribero D, Wu TT, Zorzi D, Hoff PM, Xiong HQ, Eng C, Lauwers GY, Mino-Kenudson M, Risio M, Muratore A, Capussotti L, Curley SA, Abdalla EK. Chemotherapy regimen predicts steatohepatitis and an increase in 90-day mortality after surgery for hepatic colorectal metastases. *J Clin Oncol* 2006; **24**: 2065-2072 [PMID: 16648507 DOI: 10.1200/jco.2005.05.3074]

13 **Peppercorn PD**, Reznek RH, Wilson P, Slevin ML, Gupta RK. Demonstration of hepatic steatosis by computerized tomography in patients receiving 5-fluorouracil-based therapy for advanced colorectal cancer. *Br J Cancer* 1998; **77**: 2008-2011 [PMID: 9667683 DOI: 10.1038/bjc.1998.333]

14 **Tamandl D**, Klinger M, Eipeldauer S, Herberger B, Kaczirek K,

Gruenberger B, Gruenberger T. Sinusoidal obstruction syndrome impairs long-term outcome of colorectal liver metastases treated with resection after neoadjuvant chemotherapy. *Ann Surg Oncol* 2011; **18**: 421-430 [PMID: 20844968 DOI: 10.1245/s10434-010-1317-4]

15 **Gomez D**, Malik HZ, Bonney GK, Wong V, Toogood GJ, Lodge JP, Prasad KR. Steatosis predicts postoperative morbidity following hepatic resection for colorectal metastasis. *Br J Surg* 2007; **94**: 1395-1402 [PMID: 17607707 DOI: 10.1002/bjs.5820]

16 **Blind PJ**, Andersson B, Tingstedt B, Bergenfeldt M, Andersson R, Lindell G, Sturesson C. Fast-track program for liver resection--factors prolonging length of stay. *Hepatogastroenterology* 2014; **61**: 2340-2344 [PMID: 25699379]

17 **Sturesson C**, Nilsson J, Eriksson S, Spelt L, Andersson R. Limiting factors for liver regeneration after a major hepatic resection for colorectal cancer metastases. *HPB* (Oxford) 2013; **15**: 646-652 [PMID: 23458360 DOI: 10.1111/hpb.12040]

18 **Kleiner DE**, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, Ferrell LD, Liu YC, Torbenson MS, Unalp-Arida A, Yeh M, McCullough AJ, Sanyal AJ; Nonalcoholic Steatohepatitis Clinical Research Network. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology* 2005; **41**: 1313-1321 [PMID: 15915461 DOI: 10.1002/hep.20701]

19 **Ninomiya M**, Shirabe K, Ijichi H, Toshima T, Harada N, Uchiyama H, Taketomi A, Yoshizumi T, Maehara Y. Temporal changes in the stiffness of the remnant liver and spleen after donor hepatectomy as assessed by acoustic radiation force impulse: A preliminary study. *Hepatol Res* 2011; **41**: 579-586 [PMID: 21561532 DOI: 10.1111/j.1872-034X.2011.00809.x]

20 **Colli A**, Pozzoni P, Berzuini A, Gerosa A, Canovi C, Molteni EE, Barbarini M, Bonino F, Prati D. Decompensated chronic heart failure: increased liver stiffness measured by means of transient elastography. *Radiology* 2010; **257**: 872-878 [PMID: 20935077 DOI: 10.1148/radiol.10100013]

21 **Millonig G**, Reimann FM, Friedrich S, Fonouni H, Mehrabi A, Büchler MW, Seitz HK, Mueller S. Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. *Hepatology* 2008; **48**: 1718-1723 [PMID: 18836992 DOI: 10.1002/hep.22577]

22 **Fondevila C**, Hessheimer AJ, Taurá P, Sánchez O, Calatayud D, de Riva N, Muñoz J, Fuster J, Rimola A, García-Valdecasas JC. Portal hyperperfusion: mechanism of injury and stimulus for regeneration in porcine small-for-size transplantation. *Liver Transpl* 2010; **16**: 364-374 [PMID: 20209596 DOI: 10.1002/lt.21989]

23 **D'Onofrio M**, Gallotti A, Mucelli RP. Tissue quantification with acoustic radiation force impulse imaging: Measurement repeatability and normal values in the healthy liver. *AJR Am J Roentgenol* 2010; **195**: 132-136 [PMID: 20566806 DOI: 10.2214/AJR.09.3923]

24 **Crespo G**, Fernández-Varo G, Mariño Z, Casals G, Miquel R, Martínez SM, Gilabert R, Forns X, Jiménez W, Navasa M. ARFI, FibroScan, ELF, and their combinations in the assessment of liver fibrosis: a prospective study. *J Hepatol* 2012; **57**: 281-287 [PMID: 22521355 DOI: 10.1016/j.jhep.2012.03.016]

25 **Jung EJ**, Ryu CG, Kim G, Kim SR, Park HS, Kim YJ, Hwang DY. Splenomegaly during oxaliplatin-based chemotherapy for colorectal carcinoma. *Anticancer Res* 2012; **32**: 3357-3362 [PMID: 22843915]

26 **Park S**, Kim HY, Kim H, Park JH, Kim JH, Kim KH, Kim W, Choi IS, Jung YJ, Kim JS. Changes in Noninvasive Liver Fibrosis Indices and Spleen Size During Chemotherapy: Potential Markers for Oxaliplatin-Induced Sinusoidal Obstruction Syndrome. *Medicine* (Baltimore) 2016; **95**: e2454 [PMID: 26765438 DOI: 10.1097/md.0000000000002454]

27 **Jin S**, Fu Q, Wuyun G, Wuyun T. Management of post-hepatectomy complications. *World J Gastroenterol* 2013; **19**: 7983-7991 [PMID: 24307791 DOI: 10.3748/wjg.v19.i44.7983]

28 **Balzan S**, Belghiti J, Farges O, Ogata S, Sauvanet A, Delefosse D, Durand F. The "50-50 criteria" on postoperative day 5: an accurate predictor of liver failure and death after hepatectomy. *Ann Surg* 2005; **242**: 824-828; discussion 828-829 [PMID: 16327492]

29 **Karlas TF**, Pfrepper C, Rosendahl J, Benckert C, Wittekind C, Jonas S, Moessner J, Tröltzsch M, Tillmann HL, Berg T, Keim V, Wiegand J. Acoustic radiation force impulse (ARFI) elastography in acute liver failure: necrosis mimics cirrhosis. *Z Gastroenterol* 2011; **49**: 443-448 [PMID: 21476180 DOI: 10.1055/s-0029-1245690]

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