Dear colleagues,

I offer you an analysis of an article by Choi YI et al. "Clinical Outcomes and Safety of High-Resolution Manometry Guided Superficial Partial Circular Muscle Myotomy in Per-Oral Endoscopic Myotomy for Jackhammer Esophagus: Two Cases Report" published in World J Clin Cases. [1]. Based on the high-resolution manometry (HRM), the authors diagnosed Jackhammer esophagus (JE). HRM-guided extremely superficial partial circular muscle myotomy was performed while preserving the lower esophageal sphincter (LES). The authors showed that patients' clinical symptoms dramatically improved right after per-oral endoscopic myotomy (POEM), и during a 1-year follow-up period, patients were still in good health and remained symptom free. The authors argue that the POEM method they proposed does not damage the motility of the esophagus, as is often observed after LES dissection.

I have no doubt to the reliability of manometric research, since the manometric criteria for JE fully comply with generally accepted standards: at least 20% of swallows having a distal contractile integral (DCI) value > 8000 mmHg.s.cm. [2]. The following shows the x-ray studies with the signatures from the article.

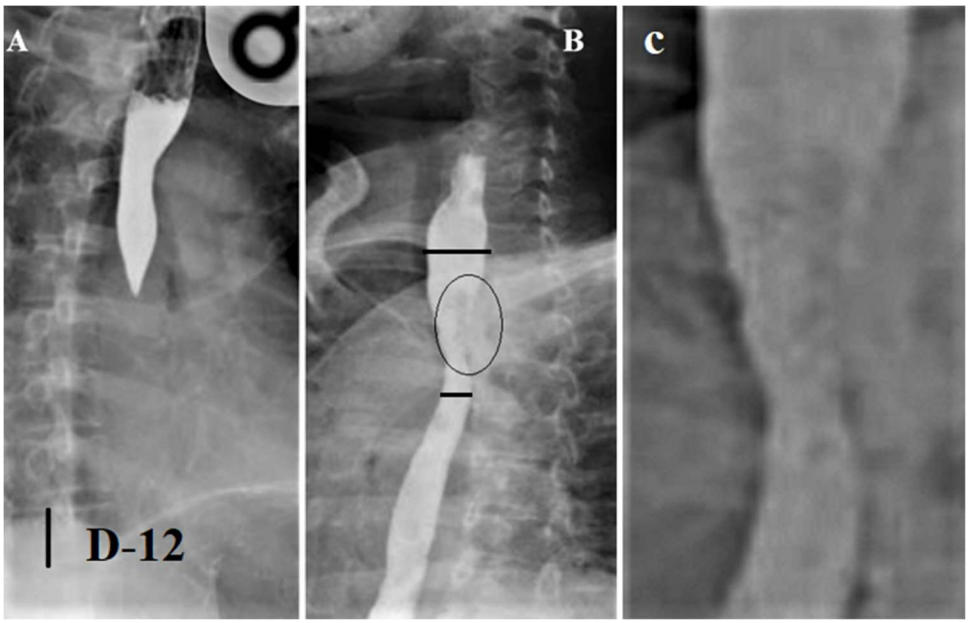

Figure 1. (a) Barium radiography showed spasmodic contraction of the distal esophagus and a narrowing of the esophageal cavity. (b) Post-treatment esophagogram showed improved. (c) Increased dissection site in the upper part of the esophagus.

In figure 1.a, performed in an upright position after taking one swallow of barium, a peristaltic wave was recorded with the contraction of the esophagus in the middle part. This indicates a high tone of the esophagus, since there is normally no peristaltic wave in an upright position. A large gas bubble of the stomach indicates normal patency of the esophagogastric junction (EGJ). The true height of the D-12 is approximately 2.1 cm, which allows to calculate the true parameters on this x-ray.

In Figure 1.b, the upper boundary of the barium column is at the C-6 level. The section of the striated muscle 3.7 cm long on the posterior left wall in the upper part of the esophagus leads to local narrowing of the esophagus and a sharp violation of peristalsis, as evidenced by the absence of peristalsis and the location of the upper border of the barium column above D-4.

First, the peristaltic wave in Figure 1.a. continued to advance to the LES. The fixed moment of its movement does not confirm in any way, a particularly high tone in this place.

Secondly, the absence of peristalsis after POEM in a horizontal position indicates severe damage to the motor function of the esophagus, which contradicts the authors' claim that "post-treatment esophagogram showed improved".

Conclusion: X-ray picture of a 53-year-old woman with odynophagia and regurgitation, which was done before the operation, indicates a high tone of the esophagus and normal evacuation of the bolus into the stomach. The combination

of clinical and radiological symptoms, as well as HRM data indicate an inflammatory process in the esophagus as a result of reflux esophagitis.

The following shows the x-ray studies of the second patient with the signatures from the article.

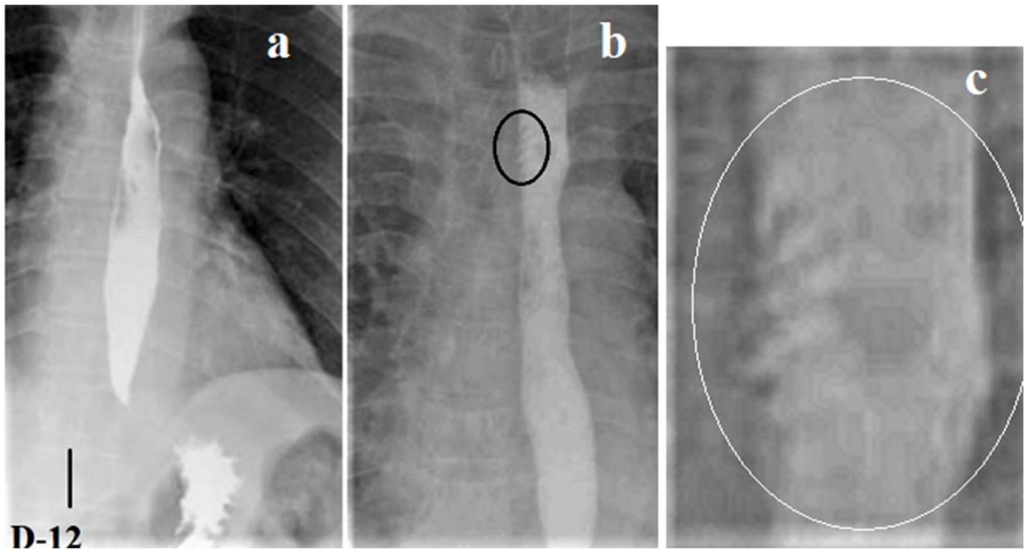

Figure 2. (a) Pre-treatment esophagography showed spasmodic contraction of the distal esophagus. (b) Post-treatment esophagogram showed improved function of passage of esophagus. (c) Increased dissection site in the upper part of the esophagus.

On a radiograph (Figure 2.a), made in a horizontal position, a long peristaltic wave is determined. In the contracted esophagus above the peristaltic wave, longitudinal folds are visible. The walls of the esophagus in the upper part of the peristaltic wave are dense and uneven. The maximum width of the esophagus is 1.8 cm (normal to 1.5 cm). The distance between the distal point of the peristaltic wave and the stomach is due to the contraction of the LES. Its length is 2.2 cm (normal 3.6 ± 0.08 cm) [3].

On a radiograph (Figure 2.b) made in an upright position after dissection of the striated muscle on the right wall of the upper part of the esophagus, the fluid level is between D1-D2. (Norm D-4).

Conclusion. In a 47-year-old man which was referred to the gastrointestinal department for atypical chest pain for 6 months there is a GERD with severe esophagitis.

Article Choi YI et al. does not answer the following questions: 1) What was the diagnosis in patients? 2) Why was the dissection of the muscles in the upper part of the esophagus performed, while HRM showed high-amplitude distal esophageal contractions, 3) How can we explain the disappearance of symptoms? 4) What long-term results can be expected at the site of muscle dissection? 5) How will muscle dissection affect the evacuation of the esophagus in the future? 6) How will POEM affect the development of GERD?

An analysis of this article shows that jackhammer esophagus is not a diagnosis. In both cases, abnormal pressure in the esophagus and LES was due to GERD and esophagitis. The positive effect of manipulation POEM is due to dilation of the esophagus and LES. We have experience dilation the esophagus, LES and the pyloric sphincter with a large tablet, which the patient swallows of it [4]. Dissection of the muscle fibers of the esophagus makes no sense. The long-term results of this procedure are not yet known. The only thing we can agree with the authors of the article that the dissection of the wall of the LES should be avoided, since it is inevitably worsens the already weak antireflux function of the EGJ in patients with GERD.

Discussion

The pathophysiology of JE remains uncertain, even though some observational studies suggested an association with esophagogastric outflow obstruction, gastroesophageal reflux disease, eosinophilic esophagitis and an abnormal cholinergic activity within the esophageal muscle innervation. Regardless of the etiology of JE, the extreme hypercontractility is mainly located in the third contractile segment of the esophagus [2]. Studies [5,6] showed that DCI values

of > 8000 mmHg.s.cm are rarely encountered in control healthy subjects and are usually associated with symptoms, such as dysphagia and chest pain" [2]. This controversial phrase shows uncertainty about the credibility of HRM. First, patients with dysphagia and chest pain complaints cannot be considered control healthy subjects. Secondly, the detection of manometric criteria JE cannot justify any type of treatment without further clarification diagnosis.

Some JE patients have accompanying EGJ outflow obstruction with an elevated IRP. This suggests a possible role of EGJ obstruction in the pathogenesis of JE. Hypercontractility seen in JE may be “fighting contractions”, within the esophageal body, to overcome an obstruction at the LES level. It was shown that JE patients with GEJ outflow obstruction were significantly older compared to the other JE patients [2].

HRM study records the manometric situation that is created at the time of the study. The width of the LES opening is known to be smaller than the width of the esophagus **(Figure 3).**

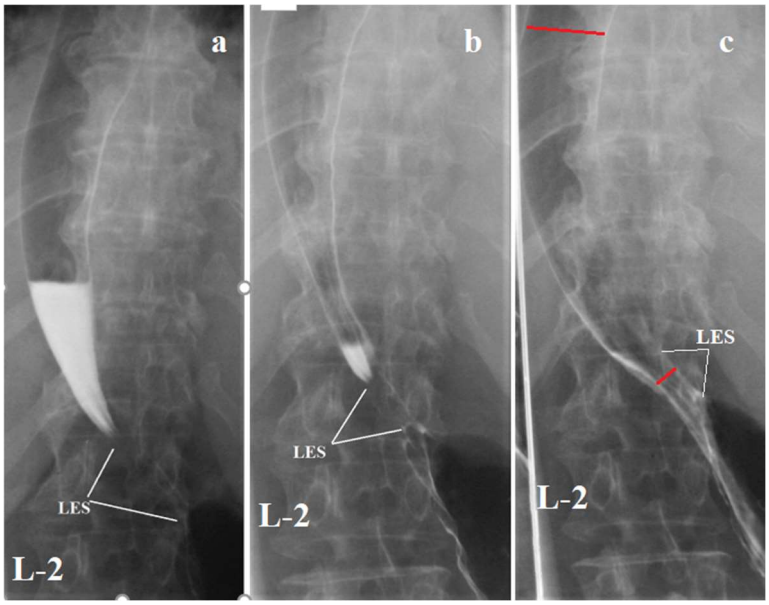

Figure 3. Sequential radiographs of an elderly patient with GERD while swallowing barium in an upright position. The upper boundary of the LES is near the upper edge of L-1. The lower boundary rises from the upper boundary of L-2

(a) to the lower third of L-1 (c). Shortening of the LES, and not the esophagus, occurs due to the disclosure of the abdominal part of the LES. At the same time, the angle of His increases. After emptying the esophagus, the LES opened for burping. Its true width (red color) is 0.4 cm. The width of the esophagus is 2.5 cm (with a norm of 1.5 cm). Evacuation from the esophagus is not impaired. The symptom of "beak" is determined, which is not related to achalasia of the esophagus.

With esophagitis, the muscle fibers in the LES wall swell and fibrous changes appear in it, causing LES rigidity and it poorly stretched. In addition, a manometric catheter with 4.2-mm outer diameter (Medtronic Inc, Shoreview, MN), acting as a foreign body, causes a reflex contraction of LES. Therefore, in some cases, a manometric catheter blocks the lumen of the LES. what manifested during HRM as the EGJ outflow obstruction. This explains the contradictions between HRM and X-ray study. This refers to the cases where the GEJ outflow obstruction in HRM study is diagnosed in patients with normal evacuation of barium from the esophagus to the stomach.

Triggs and Pandolfino believe that like EGJOO, jackhammer esophagus is a very heterogeneous classification. Meeting these criteria, however, is not enough evidence to refer patients for invasive treatments. This pattern can be associated with obstruction at the EGJ and is also seen in the context of gastroesophageal reflux disease (GERD) and EoE. Thus, the diagnosis of an esophagogastric junction outflow obstruction (EGJOO) must be interpreted with caution and a decision regarding intervention should never be made based on this measure alone [7].

From this text it follows that JE is not only not a diagnosis, but also an inaccurate characteristic of the motor function of the esophagus and LES. I am more than sure that patients should be treated in accordance with a medical diagnosis, with understanding the pathophysiology and pathogenesis of the disease. Dissection of the esophageal and LES walls in patients with GERD, which is always accompanied by esophagitis, turns EGJ into an open channel. Unfortunately,

despite the 10-year use of POEM, the literature does not contain the long-term results of this surgery.

The diagnosis, treatments and results.

Before deciding how to treat the patient, it is necessary to make the correct diagnosis. Abdallah and Fass described the case of a 66-year-old woman with dysphagia in whom over the course of the year the disease progressed from partial obstruction of the GEJ to complete obstruction. The authors describe this case as a progression of JE to type II achalasia. The patient underwent Heller myotomy with Dor fundoplication [8]. **Figure 4** shows the radiographs of this patient with the signatures of the authors of the article and my notations (c).

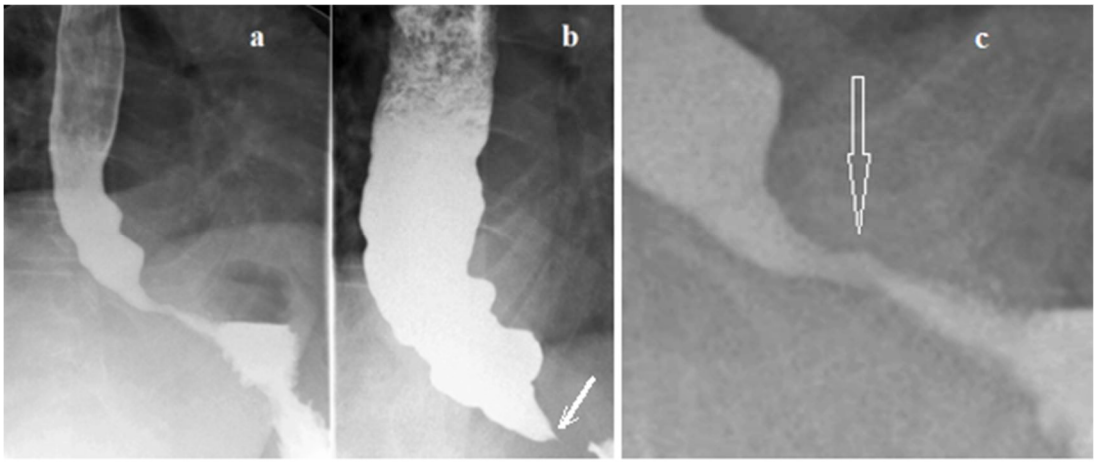

Figure 4. (a) Patient's initial barium swallow which showed a mildly dilated esophagus with tertiary contractions, delayed emptying of the esophagus, and a narrowed gastroesophageal junction. (b) There is a diffuse esophageal dilatation with retained esophageal secretions and barium with only 0–20% change in volume after 5 minutes. There are tertiary peristaltic waves within the distal esophagus, limited emptying of the contrast into the stomach and an air-fluid level. (c) The increase in the LES zone. The arrows indicate the place of stenosis.

In Figure 4.a, local narrowing and deformation in the middle part of the LES is determined. Given the rapid progression of the process, we can assume the

ulcerative nature of stenosis. The authors confuse the functional state (impaired LES patency) with the name of the disease (Esophageal achalasia).

An article by Abdallah and Fass provoked a reaction from Huang and Rezaie. In 2014, they described 3 of 12 cases of JE that are progression of JE to achalasia [9]. They argue that "One common pitfall in measuring the IRP in JE is an upward displacement of the lower esophageal sphincter (LES) due to esophageal shortening caused by vigorous contractions after swallows" [10].

In previous works, we found confirmation of the studies of Chandrasoma and DeMeester, which showed that shortening of the LES occurs during GERD due to the opening of the abdominal part of the LES. The folds of the mucosa at the level of the LES are not related to the folds of the stomach [11]. With GERD during swallowing, the LES is shortened due to the disclosure (weakness) of its abdominal part. But the proximal point of the LES does not move and the length of the esophagus does not change [12,13]. An analysis of the work of Huang et al suggests that they examined patients with GERD. In three cases, upon re-examination, they found a deterioration in evacuation from the esophagus. They confused the functional state with a known diagnosis, including because the manometric catheter blocked the lumen of the LES, and because they mistakenly accept the consensus of the Chicago Classification as a scientific discovery. In no area of knowledge scientists does not resort to consensus to solve scientific problems.

Diagnosis.

In an article by Kristo et al. it was shown that all 37 patients with JE had more than one symptom typical of GERD. In 54.1% (n = 20) was hiatal hernia. Esophagitis was observed in 9 patients (24.3%), diagnosis of Barrett's esophagus in 3 (8.1%). patients. Extensive testing resulted in 16 (43.2%) GERD positive patients and 5 (13.9%) participants were observed to have an acid hypersensitive

esophagus. The authors concluded that true GERD was diagnosed in less than half of this selected cohort [14]. This conclusion was made on the basis ambulatory 24-hour pH impedance monitoring. However, the boundary of the norm of pH-metry was initially determined based on the erroneous selection of supposedly healthy patients. As shown by numerous studies, neither the absence of typical clinical symptoms of GERD, nor the absence of visible signs of inflammation with endoscopy do not exclude reflux disease [12,13]. For example, Chen и Hsu define hypersensitive esophagus as weakly acid-reflux-related nonerosive reflux disease [15]. Any research can be considered scientific only if it relies on the exact boundary of the norm. "On biopsy, the oesophageal epithelium of patients with reflux disease displays histological features including basal cell hyperplasia, elongation of the papillae, increased numbers of inflammatory cells within the mucosa and dilation of the intercellular spaces in the basal parts of the epithelium. These features are present in individuals both with and without macroscopic oesophagitis. Dilated intercellular spaces in particular appear to be a consistent feature in individuals who have GERD and therefore may be particularly useful as an objective, structural marker of the disease" [16]. The concept of functional heartburn is the result of the erroneous selection of "healthy people" to determine the normal range. These are patients with GERD at an early stage of the disease, where there is still a chance to prevent the development of a chronic progressive process.

Based on an analysis of the literature, it can be concluded that most patients in whom HRM detected signs of JE, are GERD patients.

Treatment

The recommendations of the authors and the long-term results of treatment of JE are so different that it seems that we are talking about a heterogeneous group of patients. The long-term follow-up data by Kahn et al suggest that JE,

irrespective of LES involvement, may improve without treatment. They conclude, further study is needed to clarify which patients merit therapeutic intervention [17].

Jia et al showed that dysphagia (8/8) was the dominant indication for the manometric study, whereas the clinical background setting was gastroesophageal reflux disease (4/8) and hiatal hernia (1/8). Treatments included smooth muscle relaxation, antireflux regimens, and pneumatic dilation of the LES [18].

Funaki et al described a markedly effective steroid treatment of three patients with allergy-related JE [19]. However, only two of them were diagnosed with eosinophilic esophagitis (EoE). Esophageal eosinophilia was initially considered solely a manifestation of GERD. Eosinophilic esophagitis is currently defined as a chronic, immune-mediated or antigenmediated esophageal disease characterized by symptoms related to esophageal dysfunction and eosinophil-predominant inflammation, in which esophageal mucosal eosinophilia of at least 15 eosinophils per high-power field is present. Other causes of these findings, particularly GERD, must be ruled out. However, GERD may be difficult to rule out, because neither the response to proton-pump inhibitors nor the duration of exposure to esophageal acid, measured by means of ambulatory pH monitoring, definitively distinguishes GERD from eosinophilic esophagitis [20]. The presence of at least 15 eosinophils per high-power field is the only dubious symptom distinguishing EoE from GERD. It is known that the inflammatory process in any organ acquires microscopic features in the presence of allergies. For example, eosinophilia is observed in uncomplicated forms of appendicitis, but it is not the cause of inflammation [21]. An allergy predisposes to GERD because histamine, which is an allergy mediator, increases the secretion of hydrochloric acid, which can be a cause of poor response to PPI treatment. Eosinophilic esophagitis is an allergic reaction to primary damage to the esophagus by a reflux agent (hydrochloric acid, pepsin and bile acids).

Therefore, esophageal distension, which is recommended for EoE, alleviates the symptom of dysphagia, but does not cure the patient from GERD.

The treatment of patients in whom HRM has detected JE should be based on the pathological physiology of the disease. As a rule, this is an exacerbation of the reflux-esophagitis.

1. Antireflux therapy, which includes:

a) dilation of the esophagus, LES and pyloric sphincter to eliminate their rigidity (we offer the patient to swallow a large tablet [4]),

c) frequent meals in small portions except for meat and fatty foods.

c) sleep with an empty stomach

2. PPI and antacids

3. Anti-inflammatory treatment

a) antihistamines

c) corticoids

(contraindications antispasmodics and relaxants)

Chandan et al performed in a systematic review and meta-analysis to evaluate efficacy of the POEM in patients with diffuse esophageal spasm, jackhammer esophagus, and type 3 achalasia. They found that the pooled rate of clinical success for POEM was 89.6% [22]. The above cases of surgical treatment of JE reflect the current state of surgical treatment of undiagnosed pathologies of the esophagus and GEJ. Dissection of the circular muscles of the esophagus and LES has no scientific justification. Articles in which relief of the symptoms of dysphagia is observed after POEM, as a rule, do not describe the onset of symptoms of GERD, which in a significant number of cases require surgery of fundoplication. These articles raise the following questions:

1. Why in most patients who underwent POEM surgery, other diagnostic methods were not performed for establish a pathophysiological diagnosis, as recommended by the authors of voluminous studies [2].

2. Why do they produce POEM without fully testing the conservative methods of treatment and balloon dilation of the esophagus and LES, which in many patients provide success?

3. Why do not publish long-term POEM results?

4.Why is surgical treatment better than drug therapy if it is known that JE may improve without treatment [17]? Why is POEM better than balloon dilatation? Why is POEM better than anti-inflammatory treatment?

5. Why do articles, advertising POEM, with low scientific credibility disproportionately lot published in the open access?

6. Why are there no critical articles on such a serious and not entirely understandable problem?

An analysis of an article by Choi et al. Showed that, in favor of manufacturers of medical equipment, instead of a scientific approach to the very common medical problems of Western Civilization, a wide road for experimentation is open.

Sincerely,

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