Peer Review File

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Reviewer A

Thank you for the opportunity to review your high-quality paper. I find it very informative, innovative and methodically sound. More paper should be of this quality. The only limitation is the restricted number of patients, submitted as a case series report it is fair enough. My only suggestion would be to present your data, such as age, as median (range), since with n=5 patients data normal distribution cannot be reliably tested and a mean value is. It representative. Otherwise, I suggest the paper should be accepted in its current form.

Comment 1: Present your data, such as age, as median (range).
Reply 1: Thank you for this advice. I have corrected from mean to median.
Changes in the text: Line 130-137.

Reviewer B

This is a well-written, relatively small case series regarding the mechanism of resolution of gastro-esophageal reflux following anti-reflux surgery with well visualized videos and figures. This is also a valuable addition to the literature elucidating the complex physiologic mechanism of proper esophageal contractility.
I do have some concerns regarding the manuscript:

Comment 1: Methods: Was an Institutional Review Board (IRB) approve the study protocol? It should be stated in the methods.
Reply 1: Thank you for this advice. I added an appropriate statement in methods.
Changes in the text: Line 117-129.

Comment 2: *How were patients diagnosed with reflux? did the patients undergo any objective study such as EGD/Bravo or pH-manometry? how was resolution of reflux assessed.*
Did patients answer any subjective validated questionnaire regarding reflux?
Reply 2: Thank you for addressing these points. I completely share your objections. With the intention of keeping this paper of a cases series short, I took the liberty of referring to the publication: "Clinical outcomes of a 10-year retrospective, uncontrolled clinical study on 1351 patients with hiatal hernia operated on exclusively with DeltaMesh-enhanced hiatus reconstruction without fundoplication" with regard to these methodological details". (Ref.9).
In fact, the results of this clinical study raised the crucial question of why surgical repositioning of the esophagus alone leads to restoration of esophageal function. Unfortunately the paper is still in the review process of LS Journal.
However, I include the methodology of this paper here, as all 5 patients studied

were from this patient collective. The whole study ref. 9 should be available for you by the LS Editorial.

"METHODS

Study design

This study was retrospectively conducted over a 10-year period, from January 2007 to December 2016. All consecutively enrolled patients with symptomatic hiatal hernias from Germany and other EU countries who met the inclusion criteria underwent surgery according to LOEHDE using DeltaMesh in all cases. Surgeries were performed in two hospitals in Berlin, Germany: the Parksanatorium Dahlem, D-14199 (2007-2013, presently closed) and the DRK-Klinikum Westend, D-14050 (2014-2017). The continuous follow-up of the patients ended in December 2019. This study had no control group and was not randomised, as all patients were specifically operated on with LOEHDE only without fundoplication or other techniques. This study had no control group and was not randomised, as all patients specifically wanted to be operated on with LOEHDE only without fundoplication or other techniques. This was respected and, for ethical reasons, patients were not persuaded to undergo fundoplication instead.

Inclusion criteria

All types of hiatal hernias (types I–IV) were included. The definition of "symptomatic" was based on the following four symptom categories: A. Fluid reflux such as heartburn, bending forward reflux, nocturnal cough, and a need for diet; B. Aerosol reflux such as hoarseness, throat clearing, globus sensation, sinus swelling, and posterior laryngitis; C. Core symptoms such as chest pain, feeling of incarceration, cardiac sensations, back pain, and dyspnoea; D. Functional disorders such as belching, fast eating, aerophagia, dysphagia, and bloating.

The inclusion criteria for the entire study period were as follows: 1. age ≥ 15 years (mandatory); 2. increasing symptoms in categories A, B, C, and D with significant impairment of daily life (mandatory); 3. endoscopic findings of an incompetent cardia or hiatal hernia, irrespective of size (mandatory) 4. oesophagitis with a Savary–Miller grade ≥ 2 or Los Angeles classification grade ≥ B (12,13); 5. histopathological findings of oesophagitis or Barrett's metaplasia or dysplasia; 6. ineffectiveness of proton pump inhibitors (PPIs) or adverse effects; and 7. pathological findings of pH measurement, manometry, X-ray contrast swallow evaluation, computed tomography (CT), or magnetic resonance imaging (MRI) (14). Patient's physical status was classified by the physical status classification system of the American Society of Anesthesiologists (ASA) (15).

The exclusion criteria were age < 15 years, suspected achalasia or malignancy, comorbidities that did not justify surgical treatment, and a doubt about diagnosis.

Data collection

Basic data were collected from the patient records. Outcome data were collected at 4 observation points:

1. T0Med- = preoperative status, if PPIs were not administered; 2. T0Med+ = preoperative status, if PPIs were administered; 3. T1 = postoperative status, 1 year postoperatively without PPIs; 4. T5 = postoperative status, 5 years postoperatively

*without PPIs. Data were collected by questionnaires through direct contact with the patients, by post, mail, or telephone. Forty-three standardised and open questions were asked preoperatively at T0Med- and T0Med+, and 24 and 22 questions were asked postoperatively at T1 and T5, respectively. The questionnaires contained questions on symptoms, medical history, nutrition, quality of life, medication, examinations performed, postoperative problems, and therapy evaluation. [**Supplement 1-3**].*

Patient-reported outcome

*The **symptom score** records 12 frequently occurring symptoms of the A-D classified complaints. It was recorded at all four observation points on a scale of 0–4, reflecting "well-being" at a high score: 0 = complaints all the time (daily); 1 = often (2–3×/week); 2 = on and off (1×/week); 3 = rarely (1×/month); and 4 = never (does not occur). These time intervals were chosen to help patients describe the frequency of their complaints in a structured and comparable way. The symptom score has not yet been validated. [**Supplementary Materials 1–3**].*

*The **Visick score** I-IV was recorded at all four observation points on a scale of I–IV, reflecting "well-being" at a low score: I = no complaints; II = mild complaints and doctor visits are rare; III = moderate complaints and doctor visits are often; IV = no improvement (16). The Visick score was chosen to help patients express the intensity of their complaints in a simple and comparable way. (16).*

*[**Supplementary Materials 1–3**].*

***Patient ratings** as an overall assessment of PPI drug treatment compared to surgical therapy were collected at T1 and T5 on a scale of 1–5, reflecting "well-being" at a low score: 1 = excellent; 2 = good; 3 = satisfying; 4 = sufficient; and 5 = poor. The patients' ratings were based on the German school grading system to help patients classify their rating in a familiar and comparable system. [**Supplementary Materials 2–3**].*

Clinical observation

The clinical observation reflects the subjective experiences of the two surgeons from their daily clinical routine with the patients and follow-up by telephone 1-4 weeks postoperatively. This observation is not objectified.

DeltaMesh

*The DeltaMesh is a V-shaped, 30×40×11 mm, 3-dimensional polyvinylidene fluoride mesh designed to target the specific anatomy of the hiatus. The two wings and the vertical lengthwise rising central fold form two compartments that adapt the principle of a 3-dimensional T-profile (**Figure 1**). This allows for tight intermuscular bi-angular embedding of the crura. The DeltaMesh is designed for the retroperitoneal position, and the contact is almost exclusively limited to the crura. The wide wings unfold retrocrurally in the area of maximum tensile forces and form a stable retrocrural shield that protects the delicate musculature from the tension of the hiatal sutures. The centrefold rises intercrurally in a precisely concentric position to support edge-to-edge fusion of the crura and longitudinal stability. The DeltaMesh does not require additional fixation but is integrated into regular hiatus sutures (**Figure 2**). (DynaMesh®-DELTA by FEG Textiltechnik*

Forschungs- und Entwicklungsgesellschaft mbH, Aachen, Germany, and approved in Germany by TÜV Süd, referring to the guidelines of the European Union 93/42/EWG and 2007/47/EG, certificate number: G1 107055 0001 Rev.02. The DeltaMesh has not yet been approved by the US Food and Drug Administration in the USA).

LOEHDE

The procedure involved a 5-trocar technique (2×10 mm; 3×5 mm) with the patient in the reverse Trendelenburg position and insertion of a 30 Ch. gastric tube. First, an incision was made in the minor omentum and ventral peritoneal lining of the hiatus. Then, the oesophagus and the right Vagal nerve branch were exposed and jointly secured by a loop of easy flow drainage pulled up in the 2 o'clock position. The herniated organs were predominantly repositioned without resection of the hernia sac. The shortened dorsal mesooesophagus was released into the mediastinum over approximately 5 cm to allow for the necessary oesophagus ascent, and the posterior sides of both crura were exposed to ensure free spreading of the DeltaMesh wings retrocrurally.

As the next step, the loop was pulled down towards the 7 o'clock position to dissect the left hiatal circumference while preserving the left Vagal nerve branch. Finally, the ventral embedment site was prepared, and the oesophagus was relocated to its correct position. Hernia size was estimated as the distance between the dorsal oesophageal wall and posterior confluence of the crura after complete repositioning.

*The loop was again pulled up towards the 2 o'clock position, and the hiatus was closed in a reverse closure procedure. For this, the crucial first suture (Ethicon® PROLENE™ 0 CT-2 Plus) was placed directly below the oesophagus, taking 8–10 mm of the left crus but sparing the vaso-nervous diaphragmatic branch. Threading of the suture along the DeltaMesh base was performed extracorporeally. The DeltaMesh was inserted with the base up and the tip down directly below the oesophagus, and the right crus correspondingly grasped in a horizontal line. The hiatus was closed with an immediate tight locking suture using an extracorporeal knot technique under tension. This first suture neutralised all tensile forces in the hiatus. Adequate longitudinal expansion of the DeltaMesh and complete hiatus closure were ensured by one or two downward sutures that capture only the crura and centrefold. Thus, the oesophagus was re-embedded in a tight and stable manner without constriction, allowing a smooth run of the controlling 30 Ch gastric tube. The DeltaMesh was positioned in the centreline of the hiatus, with the wings spread retrocrurally, sealed off from adjacent abdominal organs. The abdominal and thoracic compartments were then separated. Additional fixation or anti-reflux procedures were not required (**Figure 3**).*

In cases of recurrence after the Nissen/Toupet procedure or other procedures, fundoplication was reset as far as possible occasionally with fundus resection if necessary, followed by LOEHDE. In cases of recurrence after LOEHDE, the procedure was repeated with an additional small DeltaMesh, leaving the first one in place. Fundoplication or other procedures were not performed in any case.

Recurrence

Recurrence was primarily defined as patients complaining of persistent symptoms, requiring PPIs and dietary changes for relief, and ruling out of other causes. Clinical suspicion was always confirmed by endoscopy, and in cases of doubt, by pH measurement or other methods. Each patient was offered a re-do surgery.

Statistics

Data from questionnaires were transferred to Excel and consecutively analysed using SPSS® (IBM SPSS Statistics, RRID: SCR_019096 version, Armonk, NY) and R version 3.5.0. (R Project for Statistical Computing, RRID: SCR_001905, R Core Team 2018, R Foundation for Statistical Computing, Vienna, Austria, URL: http://www.R-project.org. Regression models were fitted using the ordinal Christensen RHB (2019), Ordinal-Regression Models for Ordinal Data, R package version 2019.12-10. https://CRAN.R-project.org/package, and brms packages (18).

Data are presented as standard descriptive statistics including frequencies, proportions, means, medians, and quartiles. The Visick score, symptom score, and patient ratings were analysed using hierarchical ordered logistic regression models. Separate models were constructed for each score type. Fixed effects (indicator variables) for measurement occasions were included in all models, and a therapy indicator was included in the model for patient rating. Treatment-time interaction was initially tested and omitted from the final model based on a likelihood ratio test of the interaction term. All models included random intercepts grouped by patients.

To test the overall time effect on symptoms, a model including all symptom types was used, with random effects grouped by symptom type. Random effects for individuals and symptom types were assumed to be independent. Likelihood ratio tests were employed to test for fixed effects. Food intolerance was coded as a dichotomous variable and modeled using a mixed-effects logistic regression model with fixed effects for measurement occasions and random intercepts grouped by individuals and food types, respectively. The likelihood ratio test was used to test the overall differences across measurement occasions (T0Med+, T1, and T5).

Significance is indicated as P<0,0001 or P<0,001 as indicated. Incomplete and missing data are marked as not available in the graphical presentations in figures and supplemental appendix."

Changes in the text: None

Comment 3: Did any of the patients have previous anti-reflux, gastric, esophageal or bariatric operations? What was the BMI of the patients? any of them morbid obese?

Reply 3: Thank you! I implemented your thoughts in "Results".

Changes in the text: 130-138

Comment 4**:** *line 84: what is "oesophageal hiatal DeltaMesh enhancement"?*

Reply 4: The laparoscopic oesophagohiatal DeltaMesh enhancement (LOEHDE) is a newly developed surgical procedure for hiatal hernia surgery, which focuses exclusively on the stable anatomical reconstruction of the oesophagus and the

hiatal unit. Fundoplication or other anti-reflux procedures were strictly omitted in all patients. A newly developed 3-dimensional DeltaMesh was used to enhance crural fusion for long-term hiatal stabilisation. Details are described in the methodology of the ref. 9 attached above in chapter "DeltaMesh" and "LOEHDE". Therefore, I have referred to this paper in the text here.
But I added some more details in the text here. Thank you.
Changes in the text: Line 100-108

Comment 5: Please add explanation or proper citation of operative technique. How long were the patients followed? 3-months post-op?
Reply 5**:** I would like to refer again to the methodology of the clinical study ref. 9 attached above. Patients were followed 5 years by questionnaires.
Changes in the text: None

Comment 6**:** What were the mean heart measurements? Wall thickness, septum size, ventricular volume etc. Any of the patients previously diagnosed heart disease? CHF in particular. If so, was echocardiogram obtained and what was LVEF?
Reply 6: I cannot satisfy your objections. Specific cardiac examinations were not done other than routine preoperative examinations including ECG because there appeared no clinical need. Patients were Patients were ASA1 and ASA2.
Changes in the text: Line 97-99, 132-133

Comment 7: Results: line 101: only 5 patients, data should be there... Minimal demographics, anthropometrics, clinical and surgical data should be presented.
Reply 7: Thank you for these objections! I corrected and extended the text.
Changes in the text: Line 130-137

Comment 8: Discussion: References number 9 by Löhde et al., is repeatedly cited, yet it is not accessible.
Reply 8: I agree with you completely. The two publication are very closely linked: The paper ref. 9 reports on the clinical 10 years results of sole hiatal reconstruction without fundoplication while this paper tries to find an explanation why surgical correction of the esophageal position alone can be so successful. Therefore, of course, parts of the methodology and discussion overlap. Thus, it would be excellent if publication ref. 9 would be available to you. I hope the editors might provide you with the article. But as far as I know, it not yet accepted.
Changes in the text: None

Comment 9: Outcomes of the study should be presented in an objective manner and not conclusive, especially with a small series and a short period of follow up. GERD may have a delayed presentation, even 10 years following anti-reflux surgery, including RYGB; discuss Holmberg D, Santoni G, Xie S, Lagergren J. Gastric bypass surgery in the treatment of gastro-oesophageal reflux symptoms.

Aliment Pharmacol Ther. 2019;50:159–66.

Reply 9: Thank you again for your objections! I would like to go into a little more detail on this part of the clinical significance. With reference to the ref. 9 and our clinical experience of meanwhile >2000 anti-reflux operations without fundoplication since 2005 our finding is:

GERD and associated complaints are actually always(!) a consequence of a displacement of the esophagus in the oesophagohiatal unit and its sliding out of the pressure zone of the heart. This is the case for severely overweight patients as well as for normal or underweight ones, young and older etc.. Repositioning the esophagus back to its correct anatomical position predictably results in return of reflux control function. It must be noted that simply closing the hiatus is not sufficient for reconstruction, and especially in obese patients the anatomical setting may be more difficult.

This also applies to patients who develop reflux symptoms again after Nissen, Toupet, Dor, Re-Nissen, or other variations even if the diagnostics by means of endoscopy, MRI etc. show seemingly regular conditions. However, hiatal instability and esophageal malposition are regularly identified at re-laparoscopy in patients with a reliably described recurrency of reflux symptoms.

It should be noted that this special positional relationship between the heart, diaphragm and the esophagus cannot actually be detected in standard endoscopy without endosonography. Endoscopy only considers the axial displacement of the stomach and cannot assess the crucial displacement of the oesophagus in the sagittal plane and its ascending angle.

Similarly young patients often present in with reflux and esophagitis but without endoscopic evidence of hiatal hernia. Intraoperatively, we see in these patients that the esophagus has not or only marginally reached the pressure zone of the heart during growth. The result is GERD without an endoscopically detected hiatal hernia. Even a normal MRI can not detect this situation. After appropriate anatomic reconstruction, these patients are also cured immediately. In any case, the decisive key to reflux control lies in the anatomy of the oesophagohiatal unit and its angles in all patients regardless of weight, age, prior surgery etc..

The crural anatomy in the hiatus is very vulnerable but at the same time exposed to significant axial and bilateral force vectors. Therefore, the stability of the esophageal unit determines how long patients remain symptom-free just like in an on and off mode. For this purpose, we have developed the new three-dimensional DeltaMesh, which is specially adapted to the requirements of the hiatus (9).

The approach of an RYGB for reflux reduction is completely different: 1. RYGB means complete Vagotomy with a corresponding decrease in gastric acid production and gastric emptying. 2. The outflowing gastric acids are quickly neutralized by the alkaline bile acid and the alkaline environment in the duodenum before possible acid reflux can occur. 3. The ascending path via the Roux loop into the esophagus is long, which further hinders the development of reflux into the oesophagus. This therapeutic approach is very invasive. Reflux

control can be successfully performed at any time even in obese patients by esophageal reconstruction and hiatus stabilization.
Changes in the text: None

Reviewer C

This hypothesis is innovative, insightful, and provides possible answers to the pathogenesis of reflux. It has the potential to impact the technique of antireflux surgery. More prospective dedicated clinical studies are needed to establish this concept of CODIS.
I would like to congratulate the author for this insightful manuscript. This is a well written and persuasive new concept that should be studied further in dedicated clinical trials.
I have the following questions

Comment 1: LINE 79. Do you have any further characterization of these sliding hiatal hernia (the difference between the GEJ and the diaphragmatic Pinch)?
Reply 1: Thank you for your encouraging words! No, I did not characterise the hiatal hernia in these patients other than that they were axial hernias with endoscopically diagnosed protrusion into the thorax. The patients are part of the clinical study ref. 9, which is still in the review process of LS Journal. With regard to this methodological aspect, I may refer you to the methodology of ref. 9, which I may enclose here:

..."METHODS

Study design

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All types of hiatal hernias (types I–IV) were included. The definition of "symptomatic" was based on the following four symptom categories: A. Fluid reflux such as heartburn, bending forward reflux, nocturnal cough, and a need for diet; B. Aerosol reflux such as hoarseness, throat clearing, globus sensation, sinus swelling, and posterior laryngitis; C. Core symptoms such as chest pain, feeling of

incarceration, cardiac sensations, back pain, and dyspnoea; D. Functional disorders such as belching, fast eating, aerophagia, dysphagia, and bloating.

The inclusion criteria for the entire study period were as follows: 1. age ≥ 15 years (mandatory); 2. increasing symptoms in categories A, B, C, and D with significant impairment of daily life (mandatory); 3. endoscopic findings of an incompetent cardia or hiatal hernia, irrespective of size (mandatory) 4. oesophagitis with a Savary–Miller grade ≥ 2 or Los Angeles classification grade ≥ B (12,13); 5. histopathological findings of oesophagitis or Barrett's metaplasia or dysplasia; 6. ineffectiveness of proton pump inhibitors (PPIs) or adverse effects; and 7. pathological findings of pH measurement, manometry, X-ray contrast swallow evaluation, computed tomography (CT), or magnetic resonance imaging (MRI) (14). Patient's physical status was classified by the physical status classification system of the American Society of Anesthesiologists (ASA) (15).

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*The **symptom score** records 12 frequently occurring symptoms of the A-D classified complaints. It was recorded at all four observation points on a scale of 0–4, reflecting "well-being" at a high score: 0 = complaints all the time (daily); 1 = often (2–3×/week); 2 = on and off (1×/week); 3 = rarely (1×/month); and 4 = never (does not occur). These time intervals were chosen to help patients describe the frequency of their complaints in a structured and comparable way. The symptom score has not yet been validated. [**Supplementary Materials 1–3**].*

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*"well-being" at a low score: 1 = excellent; 2 = good; 3 = satisfying; 4 = sufficient; and 5 = poor. The patients' ratings were based on the German school grading system to help patients classify their rating in a familiar and comparable system. [**Supplementary Materials 2–3**].*

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The clinical observation reflects the subjective experiences of the two surgeons from their daily clinical routine with the patients and follow-up by telephone 1-4 weeks postoperatively. This observation is not objectified.

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*The DeltaMesh is a V-shaped, 30×40×11 mm, 3-dimensional polyvinylidene fluoride mesh designed to target the specific anatomy of the hiatus. The two wings and the vertical lengthwise rising central fold form two compartments that adapt the principle of a 3-dimensional T-profile (**Figure 1**). This allows for tight intermuscular bi-angular embedding of the crura. The DeltaMesh is designed for the retroperitoneal position, and the contact is almost exclusively limited to the crura. The wide wings unfold retrocrurally in the area of maximum tensile forces and form a stable retrocrural shield that protects the delicate musculature from the tension of the hiatal sutures. The centrefold rises intercrurally in a precisely concentric position to support edge-to-edge fusion of the crura and longitudinal stability. The DeltaMesh does not require additional fixation but is integrated into regular hiatus sutures (**Figure 2**). (DynaMesh®-DELTA by FEG Textiltechnik Forschungs- und Entwicklungsgesellschaft mbH, Aachen, Germany, and approved in Germany by TÜV Süd, referring to the guidelines of the European Union 93/42/EWG and 2007/47/EG, certificate number: G1 107055 0001 Rev.02. The DeltaMesh has not yet been approved by the US Food and Drug Administration in the USA).*

LOEHDE

The procedure involved a 5-trocar technique (2×10 mm; 3×5 mm) with the patient in the reverse Trendelenburg position and insertion of a 30 Ch. gastric tube. First, an incision was made in the minor omentum and ventral peritoneal lining of the hiatus. Then, the oesophagus and the right Vagal nerve branch were exposed and jointly secured by a loop of easy flow drainage pulled up in the 2 o'clock position. The herniated organs were predominantly repositioned without resection of the hernia sac. The shortened dorsal mesooesophagus was released into the mediastinum over approximately 5 cm to allow for the necessary oesophagus ascent, and the posterior sides of both crura were exposed to ensure free spreading of the DeltaMesh wings retrocrurally.

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*closed in a reverse closure procedure. For this, the crucial first suture (Ethicon® PROLENE™ 0 CT-2 Plus) was placed directly below the oesophagus, taking 8–10 mm of the left crus but sparing the vaso-nervous diaphragmatic branch. Threading of the suture along the DeltaMesh base was performed extracorporeally. The DeltaMesh was inserted with the base up and the tip down directly below the oesophagus, and the right crus correspondingly grasped in a horizontal line. The hiatus was closed with an immediate tight locking suture using an extracorporeal knot technique under tension. This first suture neutralised all tensile forces in the hiatus. Adequate longitudinal expansion of the DeltaMesh and complete hiatus closure were ensured by one or two downward sutures that capture only the crura and centrefold. Thus, the oesophagus was re-embedded in a tight and stable manner without constriction, allowing a smooth run of the controlling 30 Ch gastric tube. The DeltaMesh was positioned in the centreline of the hiatus, with the wings spread retrocrurally, sealed off from adjacent abdominal organs. The abdominal and thoracic compartments were then separated. Additional fixation or anti-reflux procedures were not required (**Figure 3**).*

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Recurrence

Recurrence was primarily defined as patients complaining of persistent symptoms, requiring PPIs and dietary changes for relief, and ruling out of other causes. Clinical suspicion was always confirmed by endoscopy, and in cases of doubt, by pH measurement or other methods. Each patient was offered a re-do surgery.

Statistics

Data from questionnaires were transferred to Excel and consecutively analysed using SPSS® (IBM SPSS Statistics, RRID: SCR_019096 version, Armonk, NY) and R version 3.5.0. (R Project for Statistical Computing, RRID: SCR_001905, R Core Team 2018, R Foundation for Statistical Computing, Vienna, Austria, URL: http://www.R-project.org. Regression models were fitted using the ordinal Christensen RHB (2019), Ordinal-Regression Models for Ordinal Data, R package version 2019.12-10. https://CRAN.R-project.org/package, and brms packages (18).

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To test the overall time effect on symptoms, a model including all symptom types

was used, with random effects grouped by symptom type. Random effects for individuals and symptom types were assumed to be independent. Likelihood ratio tests were employed to test for fixed effects. Food intolerance was coded as a dichotomous variable and modelled using a mixed-effects logistic regression model with fixed effects for measurement occasions and random intercepts grouped by individuals and food types, respectively. The likelihood ratio test was used to test the overall differences across measurement occasions (T0Med+, T1, and T5).
Significance is indicated as P<0,0001 or P<0,001 as indicated. Incomplete and missing data are marked as not available in the graphical presentations in figures and supplemental appendix."
Changes in the text: 130-137

Comment 2: The size of a hiatal hernia surely affects the part of the esophagus /stomach compressed between the heart and the spine?
Reply 2: Yes and no. The oesophago-cardiac junction can be divided into two parts: In the proximal initial part, the oesophagus is firmly embedded between the heart, spine and aorta. This firm embedding does not seem to be affected even by hiatus destruction and herniation of the stomach into the thorax. It seems to be a kind of firmly anchored fixed point.
In the following, the oesophagus concavely rises freely and elastically along the heart to the next fixed point, the hiatus. This part appears to be most crucial for the reflux control function, as here the cardiac pump develops its greatest rollout effect on the oesophagus. When this part shifts according to the yielding situation in the hiatus, the ascending angle is flattened and symptoms slowly develop more and more. This shift can certainly occur or be exacerbated significantly by the prolapsing stomach.
But this dislocation of the oesophagus can also occur if the stomach does not prolapse into the thorax at all. We often see this in young patients who do not have a real hiatal hernia endoscopically but show clear GERD symptoms and oesophagitis. Intraoperatively, the crucial oesophageal displacement is always present and can be easily corrected. Then the patients are symptom-free.
This may also explain the different symptoms of paraoesophageal hernias. If the stomach slides strictly "paraoesophageal" without pushing the oesophagus too far out of the cardiac pressure zone, the patients will have no or minor reflux problems. However, if the cardio-oesophageal connection is impaired, reflux problems will arise significantly. Most often, of course, we find mixed forms. But it always seems to be the same problem, only in different forms and manifestations.
Changes in the text: None

Comment 3: LINE 84 You mentioned that patients had full reflux control. Do you have pre and postoperative GERD questionnaires to justify this statement?
Reply 3: Yes, data were collected at 4 observation points: 1. Pre-op without PPI, 2. Pre-op with PPI, 3. Postop 1 year, 4. Post-op 5 years. Please see the attached

methodology of ref. "9" above The whole study and the questionnaires should be available by the LS Editorial.
Changes in the text: None

Comment 4: *Also, the reason to obtain the postoperative MRI was symptoms such as dysphagia?*
Reply 4: In these special cases the problem was an unclear feeling of pressure and pain in the thorax and the need to exclude possible associations to the operation. However, dysphagia is common to some extent in the postoperative period for about 1-3 weeks, which is not really surprising. Rarely it lasts longer, but it does happen.
Reasons for dysphagia are not always easy to assess. It may be the result of a still a remaining swelling in the distal oesophagus or even early scarring. In our experience, X-ray swallowing should always be done with liquid and e.g. chewed bread, as this helps to objectify the cause of the dysphagia. In the meantime, we advise the diagnostic laparoscopy early in objectified dysphagia, as the cause is usually a kind of tissue impingement in the hiatus that cannot be detected by endoscopy or MRI. Re-operation clarifies the situation immediately and the problem can be solved.
Changes in the text: None

Comment 5: LINE 85 Reference 9 is unpublished data and should not be referred to as evidence
Reply 5: Indeed, ref. 9 is very important for this article. It is still in the review process of the LS Journal. Attached I send you the abstract of ref. 9 for your information. But you might ask the LS editor for the full PDF of the paper.
Abstract
Background: *Fundoplication as the "gold standard" of anti-reflux surgery is supposed to strengthen the lower oesophageal sphincter, although there are conceptual inconsistencies and its actual existence has not yet been proven beyond doubt. New pathophysiological findings show the fundamental role of the hiatal architecture and the heart in reflux control. Based on this, the new technique of laparoscopic oesophagohiatal DeltaMesh enhancement was developed, which focuses exclusively on the correct anatomical reconstruction of the oesophagohiatal unit and repositioning of the oesophagus in the system. Fundoplication or other anti-reflux procedures were strictly omitted in every patient. A new 3-dimensional DeltaMesh, specially developed for this procedure, was used in all patients for long-term stabilisation of the reconstructed hiatus.*
Method: *In a 10-year retrospective clinical study from January 2007 to December 2016, all consecutively admitted patients with symptomatic hiatal hernia who met the inclusion criteria underwent the laparoscopic oesophagohiatal DeltaMesh enhancement. The follow-up was recorded by standardised questionnaires given preoperatively on admission (T0; 43 questions), postoperatively at 1 year (T1; 24 questions) and 5 years (T5; 22 questions). There was no randomisation and no*

control group, as all patients explicitly wanted the new surgical procedure and refused any other form of surgery, especially fundoplication.
Results: *A total of 1351 patients were included and operated on. The follow-up rate was 96% at T0 (1297/1351), 68.6% at T1 (927/1351), and 14.8% at T5 (200/1351). The Visick score, symptom score, and patient rating significantly improved postoperatively at T1 and T5 (P<0.0001) compared with the situation under medical treatment at T0 in all symptom categories: A (reflux, heartburn); B (hoarseness, coughing); C (palpitation, dyspnoea); and D (belching, nausea). Recurrence was observed in 91 of the 1351 (6.7%) patients. DeltaMesh penetration was observed in the oesophagus (n=2) and stomach (n=3). Mortality (n=1) was 0.07%.*
Conclusion: *Anatomical reconstruction of the oesophagohiatal unit alone significantly restored oesophageal function and cured patients without fundoplication, supporting new insights into a complex heart-mediated anti-reflux system. The new laparoscopic oesophagohiatal DeltaMesh enhancement procedure proved to be a safe, efficient, and standardisable surgical approach for the treatment of symptomatic hiatal hernia.*
Changes in the text: None

Comment 6: LINE 100. How did you measure the esophageal hiatus? Did you compare it to postoperative measurement?
Reply 6: The defect in the hiatus was measured intraoperatively. No measurements were taken postoperatively because MRI findings are not reliable. I added your objection to "Results".
Changes in the text: Line 135-137

Comment 7: LINE 162. Do you have the pre and postoperative manometry data to evaluate the peristalsis of these patients? it could be intact/vigorous as these are young patients.
Reply 7: Thank you! This is a sore point. Unfortunalely we do not perform manometric examinations by ourselves. The manometry data brought in by the patients are usually so inconclusive and contradictory that they were of little significance to us. We can neither justify nor reject any indication for surgery on the basis of manometry findings. We only use it if there is a preoperative suspicion of achalasia or another special question. The careful anamnesis in combination with endoscopic and histological findings is decisive for answering the crucial question: Is the closure intact or not. Please note the indication criteria from ref. 9 above. I added your objections to the text.
Changes in the text: Line 328-334

Comment 8: LINE 198. The statement that EGJ is open contradicts the manometry findings which showed synchronized opening when the swallow is initiated
Reply 8: I wanted to emphasize that there is no firm static closure in the GEJ, no

valve etc., which would be biologically and technically impossible. Data suggest that it is a functional protection system through constant antegrade flow in a thus "basically" open system. This would explain many inconsistencies of the common LES hypothesis.
But I suggest that the oesophageal musculature certainly also plays an important role in the system. However, not as the main actor, but the pressure transmission from the heart to the oesophageal lumen may be influenced by relaxation, contraction, and changing tone. It would certainly be very interesting to carry out manometric measurements just against the background of this new hypothesis and try to develop an overall concept.
Changes in the text: Line 328-334

Comment 9: LINE 215. Reference 9 is unpublished data and should not be referred to as evidence.
Reply 9: I agree with you completely. I hope both works will appear together. If not I will change.
Changes in the text: None yet

Comment 10: LINE 269. “Conclusive” physiological hypothesis is not the best description. It should be plausible.
Reply 10: Thank you. Done.
Changes in the text: Line 337

Comment 11: LINE 279. While hiatal hernia repair and hiatoplasty without fundoplication can control reflux, there are numerous prospective studies showing the benefits of fundoplication. b I urge the author to read about Hill’s repair as it will reinforce the hypothesis in this manuscript.
Reply 11: Thank you very much! This points to a central question, which has to be answered: how can other surgical procedures such as Hill, Nissen, Toupet etc. also achieve good results?

I personally think that all surgical procedures in which the oesophagus is correctly ventralised and the hiatus is firmly reconstructed will lead to success. However, the aim of common operations is about the reconstruction of a valve etc.. Therefore, in my opinion, a number of individual surgical steps are not necessary in these operations. So in Hill's operation, the stable dorsal hiatoplasty definitely is the decisive measure. However, the fixation at the preaortic fascia should superfluous because the oesophagus is already repositioned. I have attached my thoughts on fundoplication from ref. 9:
"...Undoubtedly, fundoplication as the common "gold standard" in reflux surgery can restore reflux control. The success of the fundoplication procedure has generally been attributed to gastric wrapping for the external support of the hypothetical LES than to hiatal reconstruction. Surprisingly, however, the data do not show major differences in outcomes between 90°, 180°, 270°, and 360°

fundoplication, which would undoubtedly be expected with such fundamentally different surgical procedures (29-31).
In view of the identified crucial importance of oesophageal ventralisation in the hiatus, the success of different forms of fundoplication could be explained by the fact that the dorsal pull-through of the gastric cushion eventually pushes the oesophagus into its required elevated position in the hiatus, despite possibly inadequate hiatoplasty. In this respect, a 90° or 360° wrapping should indeed be of secondary importance as demonstrated, rather than the actual volume of the gastric cushion, which in principle might give some more advantage in Nissen and Toupet procedures.
Considering these two parts of the fundoplication procedure, gastric wrapping thus seems to be able to compensate for an inadequate hiatus reconstruction, but appears superfluous in the case of a pathophysiologically regular rearrangement of the oesophagus. Accordingly, the complete release of the cuff had no negative effect on any of the 48 operated fundoplication recurrences when followed by stable oesophageal repositioning according to LOEHDE and hiatal instability proved to be the most important factor and main cause of recurrency."
Changes in the text: None

Comment 12: LINE 280. Reference 9 is unpublished data and should not be referred to as evidence.
Reply 12: I agree.
Changes in the text: None yet