# Laparoscopic Mesh-augmented Hiatoplasty With Cardiophrenicopexy Versus Laparoscopic Nissen Fundoplication for the Treatment of Gastroesophageal Reflux Disease

## *A Double-center Randomized Controlled Trial*

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**Objective:** Laparoscopic mesh-augmented hiatoplasty with cardiophrenicopexy (LMAH-C) might represent an alternative treatment of gastroesophageal reflux disease (GERD) and may provide durable reflux control without fundoplication. The expected benefit is the prevention of fundoplication-related side effects. Aim of the present trial was to compare LMAH-C with laparoscopic Nissen fundoplication (LNF) in patients with GERD.

**Methods:** In a double-center randomized controlled trial (RCT) patients with proven GERD were eligible and assigned by central randomization to either LMAH-C (n = 46) or LNF (n = 44). The indigestion subscore of the Gastrointestinal Symptom Rating Scale questionnaire (GSRS) indicating gas-related symptoms as possible side effects of LNF was the primary endpoint. Secondary endpoints comprised pH testing and endoscopy and other symptoms measured by the GSRS, dysphagia, and the Gastrointestinal Quality of Life Index. The follow-up period was 36 months.

**Results:** Indigestion subscore (LMAH-C $2.9 \pm 1.5$ vs LNF $3.7 \pm 1.6$; $P = 0.031$) but not dysphagia ($2.8 \pm 1.9$ vs $2.3 \pm 1.7$; $P = 0.302$) and quality of life ($106.9 \pm 25.5$ vs $105.8 \pm 24.9$; $P = 0.838$) differed between the groups at 36 months postoperatively. Although the reflux subscore improved in both groups, it was worse in LMAH-C patients ($2.5 \pm 1.6$ vs $1.6 \pm 1.0$; $P = 0.004$) corresponding to a treatment failure of 77.3% in LMAH-C patients and of 34.1% in LNF patients ($P < 0.001$).

**Conclusions:** LNF is more effective in the treatment of GERD than LMAH-C. Procedure-related side effects seem to exist but do not affect the quality of life. Laparoscopic fundoplication therefore remains the standard surgical treatment for GERD.

**Keywords:** disease hiatoplasty, gastroesophageal reflux, mesh fundoplication, randomized controlled trial

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The surgical standard treatment for gastroesophageal reflux disease (GERD) is laparoscopic fundoplication.[1,2] However, its efficacy in resolving GERD is accompanied by considerable side effects in up to 60% of the patients who underwent laparoscopic Nissen fundoplication (LNF).[3–5] Sole cardiophrenicopexy was assumed to be an alternative with less side effects. This was, based on the hypothesis that lengthening of the intra-abdominal part of the esophagus improves lower esophageal sphincter (LES) function and, consequentially, resolves gastroesophageal reflux.[6,7] This hypothesis has been supported by experimental findings[8] and meticulous considerations on the physiology of the LES by Stelzner et al. As a consequence of their research, they postulated a stretch closure mechanism of the LES, which improves after isometric distention of the spiral esophageal muscular fibers.[9–11] Initial results of cardiophrenicopexy procedures were promising as reflux control was achieved in up to 90% of patients.[12] However, due to high recurrence rates of up to 60% the technique was abandoned.[13]

Laparoscopic mesh-augmented hiatoplasty with cardiophrenicopexy (LMAH-C) combines the principle of cardiophrenicopexy with hiatal mesh augmentation. The idea behind this combination is to achieve reflux control by cardiophrenicopexy, as explained above, and to prevent recurrence by adhesion-induced anchoring of the cardia to a polypropylene mesh at the dorsal hiatus. The latter idea was based on experimental findings by the authors[14,15] and the experience gained from hiatal hernia surgery, where recurrences can be reduced by mesh augmentation.[16]

In recent analyses of clinical series we obtained evidence that LMAH-C was feasible and safe with few side effects and seemingly effective in controlling gastroesophageal reflux even without fundoplication.[17,18] However, it remains unclear whether LMAH-C is in fact of higher standard regarding side effects caused by antireflux surgery and a comparable therapy for reflux control in comparison to LNF. The aim of the present randomized controlled trial (RCT) was to answer this question.

## METHODS

### Trial Design

A patient- and assessor-blinded, superiority parallel-group trial with balanced randomization (1:1) was performed to compare primarily procedure-related side effects of LMAH versus LNF. As secondary parameters, reflux control and quality of life were analyzed. Patients scheduled for surgical treatment of GERD at the University Hospital of Heidelberg (Germany) and the Kantonsspital of St. Gallen (Switzerland) were screened for trial eligibility. The

trial was approved by the local ethics committees of the participating centers and registered at the German Registry of Clinical Studies (DRKS00004495). All patients provided written informed consent before enrollment.

## Patients

Mandatory inclusion criteria were as follows: typical symptoms (heartburn and/or acid regurgitation) of GERD in combination with endoscopically proven esophagitis of at least grade A according to the Los Angeles classification[19] (n = 64 71.1%) and/or a DeMeester score >14.72 in the pH testing (n = 69; 76.7%), need for continuous standard proton pump inhibitor (PPI) therapy for at least 3 months, over 18 years of age and informed consent. Exclusion criteria were not objectifiable GERD (neither by endoscopy or by pH testing), hiatal hernia type II-IV, American Society of Anesthesiologists (ASA) class IV-V, secondary GERD, previous surgery for GERD, achalasia, Zollinger-Ellison syndrome, or malignant tumor.

## Enrollment, Randomization, and Blinding

Patients were randomly assigned using randomization software (Randomization In Treatment Arms, version 1.31, Evidata, Sereetz, Germany), which generated permuted blocks of varying size with a 1:1 ratio for the experimental and control intervention groups. Patients and assessors were blinded to the procedure. Operating surgeons were not involved in the assessment of the patient outcome. Unblinding was performed at the end of the 36-month follow-up period.

## Interventions

Two surgeons at the University of Heidelberg and 1 surgeon at the Kantonsspital of St. Gallen who each had the experience of more than 50 laparoscopic antireflux procedures performed or supervised the surgeries. The surgical technique of LMAH-C has been previously described in detail elsewhere.[17,18] In brief, after complete mobilization of the esophagogastric junction and posterior hiatoplasty a circular shaped 8 × 8 cm polypropylene mesh (Surgipro™ Mesh, Covidien, Neustadt/Wollerau, Germany/Switzerland) was applied around the esophagus. Mesh fixation toward the diaphragm, including ventral mesh closure, was performed by using the Multifier Endo Hernia™ stapler (Covidien, Neustadt/Wollerau, Germany/Switzerland). A 56-F esophageal tube was used for hiatal calibration. Finally, a cardiophrenicopexy was added with 5 to 7 nonabsorbable sutures posteriorly to the adapted crura and anteriorly to the centrum tendineum of the diaphragm. Special care was paid to ensure that the intra-abdominal length of the esophagus of at least 4 cm was maintained. An LNF, as described in detail elsewhere,[20] was performed on the patients assigned to the fundoplication group. A posterior hiatoplasty with nonabsorbable sutures was added using a 56-F esophageal tube for calibration equally to LMAH-C. The same esophageal tube was also used for the calibration of the width of the fundoplication.

## Outcomes

Primary endpoint was the indigestion syndrome subscore (ISS) of the Gastrointestinal Symptom Rating Scale questionnaire (GSRS)[21] indicating gas-related symptoms like borborygmus, abdominal distention, eructation and increased flatus as possible fundoplication-related side effects.[4] Secondary endpoints comprised other symptoms measured by the GSRS, which was modified with additional questions, defined by the authors, for dysphagia (feeling of pressure or pain behind the sternum) and gas bloating (painful feeling of gastric distention). The GSRS comprises 15 patient-rated symptoms divided into 5 subscores assessing reflux (heartburn, acid regurgitation), abdominal pain (abdominal pain, sucking sensation, and nausea), indigestion (borborygmus, abdominal distension, eructation, and increased flatus), diarrhea (increased stool passage, loose stools, and urgent need for defecation), and constipation syndrome (decreased stool passage, hard stools, and incomplete evacuation) on a Likert scale from 1 (no symptoms) to 7 (continuous and/or severe symptoms during the last 7 days before the visit).[21,22] Furthermore, the quality of life was assessed using the Gastrointestinal Quality of Life Index (GIQLI).[23] The GIQLI comprises 36 questions divided into 5 subcategories (core symptoms, physical items, psychological items, social items, and disease specific items) on a 5-point scale (least desirable option 0 to most desirable option 4), with a maximum score of 144.[24] The ability to belch or to vomit, the presence of pain assessed by the visual analogue scale (VAS)[25] and the use of reflux medication were investigated separately. Self-administered assessment of symptoms and the quality of life were performed preoperatively after cessation of PPI medication for at least 7 days and 3, 12, and 36 months postoperatively.

For objective evaluation of GERD, presence and severity of esophagitis were determined by endoscopy according to the Los Angeles classification[19] preoperatively and at 12-months follow-up. Esophageal pull-through manometry and 24-hour pH testing were performed preoperatively and at the 3-month follow-up visit after cessation of PPI medication for at least 7 days.

Treatment failure was defined according to Lundell et al[26] postulating the presence of at least 1 of the following criteria: reflux subscore ≥3, esophagitis grade ≥B, dysphagia value >2 in combination with acid regurgitation value >1, requirement for daily PPI treatment or need for reoperation due to recurrent GERD.

## Follow-up

Three months postoperatively, 24-hour pH testing was available for 78.3% (36/46) of the LMAH-C patients and for 77.3% (34/44) of the LNF patients. A total of 91.3% (42/46) of LMAH-C patients and 88.6% (39/44) of LNF patients underwent endoscopy 12 months postoperatively. The 3-, 12-, and 36-month follow-up visits for the symptom and quality of life assessment were completed by 95.6% (44/46), 95.6% (44/46), and 89.1% (41/46) of the LMAH-C patients and 95.5% (42/44), 97.7% (43/44), and 93.1% (41/44) of the LNF patients ($P = 0.964$, $P = 0.583$, and $P = 0.499$), respectively. Two 36-month visits took place with delay, 1 at 38 months and the other at 40 months after surgery.

## Statistical Analysis

This trial was designed as an intention-to-treat analysis. A sample size calculation was performed for the primary outcome parameter. A difference in ISS of at least 1.0 was considered relevant. Based on previous studies, a standard deviation of 1.5 was assumed for power calculation.[27,28] Premising 80% power and type 1 error probability of 5%, a sample size of 40 patients within each group was taken.

Continuous parameters were expressed by mean, standard deviation, and range. Ordinal scores were summarized by median and range. Pre- and post-treatment values were compared using paired Wilcoxon tests. Group comparisons of continuous parameters were performed by Mann-Whitney tests. Group comparisons of dichotomized parameters were performed by $\chi^2$ tests. A $P$ value <0.05 was considered statistically significant. Statistical analysis was performed with R environment version 3.0.1 (http://www.r-project.org).

# RESULTS

## Patient Characteristics

Four hundred thirty-one patients were screened for trial eligibility, of which 133 did not meet the inclusion criteria and 208 refused to participate. The remaining 90 patients were

**TABLE 1.** Baseline Characteristics

| | LMAH-C (n = 46) | LNF (n = 44) | *P** |
|---|---|---|---|
| Sex (male/female) | 25/21 | 22/22 | 0.680 |
| Age (years) | 52.9 ± 10.0 | 49.5 ± 15.5 | 0.231 |
| BMI (kg/m$^2$) | 29.9 ± 4.8 | 28.0 ± 3.6 | 0.038 |
| GSRS | 3.5 ± 1.0 | 3.6 ± 0.9 | 0.724 |
| GIQLI | 76.7 ± 22.3 | 72.0 ± 23.6 | 0.343 |
| PPI therapy | 46 (100.0) | 44 (100.0) | 1.0 |
| Esophagitis | 30 (65.2) | 34 (77.3) | 0.304 |
| LA-A | 15 (32.6) | 16 (36.4) | 0.890 |
| LA-B | 7 (15.2) | 12 (27.3) | |
| LA-C | 6 (13.1) | 4 (9.1) | |
| LA-D | 2 (4.3) | 2 (4.5) | |
| DeMeester score | 50.4 ± 61.1 | 42.6 ± 40.9 | 0.516 |
| DeMeester score >14.72 | 35 (76.1) | 34 (77.3) | 0.894 |
| LES pressure (mm Hg) | 9.7 ± 5.8 | 10.1 ± 8.4 | 0.811 |

*Mann-Whitney *U* test for continuous parameters and $\chi^2$ test for binary parameters.
Values denote mean values ± standard deviation or numbers (%) of patients. LA indicates grade of esophagitis according to the Los Angeles classification.[19]

randomized to receive either LMAH-C (n = 46) or LNF (n = 44) (Supplemental Fig. 1, http://links.lww.com/SLA/A851). Baseline data is shown in Table 1.

## Intra- and Postoperative Course

The mean operation time for LMAH-C was 107.2 ± 25.6 minutes compared with 94.2 ± 25.1 minutes for LNF ($P = 0.018$). No intraoperative complication with influence on the postoperative course occurred. Thirty-day morbidity was 4.3% (2/46) in LMAH-C patients and 6.8% (3/44) in LNF patients ($P = 0.609$). During the 36-month follow-up period 9.8% (4/41) of the patients in the LMAH-C group and 12.2% (5/41) of the patients in the LNF group needed to be reoperated ($P = 0.724$). Indications for reoperation were the following for patients who received LMHA-C treatment: recurrent reflux (n = 2), chronic gastric ulcer (n = 1), and mesh migration (n = 1). The migrated mesh became apparent after 17 months and was partially removed combined with a limited gastric wedge resection in the fundus region. The further clinical course was uneventful. The indications for reoperation on the LNF patients were: dysphagia (n = 2), recurrent reflux (n = 1), paraesophageal hernia (n = 1), and gastric leakage (n = 1). In the LMAH-C group, endoscopic treatment was needed in 4.9% (2/41) of the patients, 1 for a gastric ulcer and 1 for a bolus impaction; the respective endoscopic treatment rate in the LNF group was 4.9% (2/41) corresponding to 2 endoscopic balloon dilatations for dysphagia ($P = 1.0$). No mortality occurred.

## Symptomatic Outcome and Quality of Life

In the intention-to-treat analysis ISS was lower for LMAH-C compared with LNF (2.9 ± 1.5 vs LNF 3.7 ± 1.6; $P = 0.031$) at the 36-month follow-up (Fig. 1A). On the other hand, the reflux subscore, although improved in both groups, was higher at the 36-months follow-up in the LMAH-C group (2.5 ± 1.6 vs 1.6 ± 1.0; $P = 0.004$) (Fig. 1B). No significant differences between the groups were found for gas bloating (Fig. 1C), dysphagia (Fig. 1D), pain (Fig. 1E), and other subscores of the GSRS at any time of follow-up (data not shown). A total of 19.5% (8/41) of LMAH-C patients and 29.3% (12/41) of LNF patients were unable to belch ($P = 0.304$). The inability to vomit was reported by 22.0% (9/41) of patients after LMAH-C and 56.1% (23/41) of patients after LNF ($P = 0.002$). Quality of life improved in both groups compared with the preoperative state and did not differ between the groups at any time of follow-up (Fig. 1F).

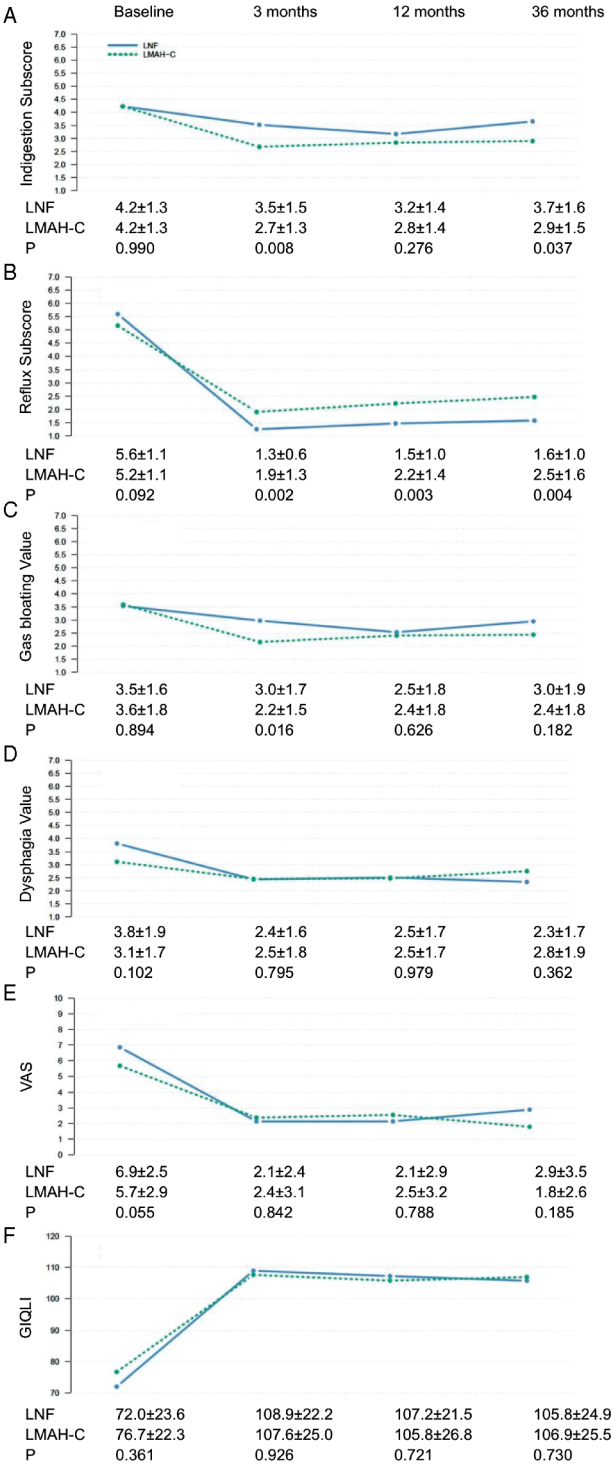


**FIGURE 1.** Development of symptoms and quality of life after LMAH-C and LNF. A, indigestion (GSRS).[21] B, reflux (GSRS).[21] C, gas bloating. D, dysphagia. E, pain (VAS).[25] F, quality of life (GIQLI).[23]

## Objective Outcome

Three months after the operation, the mean DeMeester score was higher in the LMAH-C group than in the LNF group (21.1 ± 19.0 vs 4.6 ± 6.8; $P < 0.001$). Correspondingly, LES pressure was lower

**TABLE 2.** Endoscopic Findings at 12-Month Follow-up

| | LMAH-C (n = 42) | LNF (n = 39) | P* |
|---|---|---|---|
| Esophagitis | 17 (40.5) | 6 (15.4) | 0.024 |
| LA-A | 8 (47.1) | 5 (83.3) | 0.094 |
| LA-B | 2 (11.8) | 1 (16.7) | |
| LA-C | 5 (29.4) | 0 | |
| LA-D | 2 (11.8) | 0 | |

*$\chi^2$-test.
LA indicates grade of esophagitis according to the Los Angeles classification.[19]

in LMAH-C patients compared with LNF patients ($10.2 \pm 3.4$, $15.7 \pm 5.4$; $P < 0.001$). Twelve months after surgery esophagitis was more frequent after LMAH-C (40.5% (17/42) vs 15.4% (6/39); $P = 0.012$) (Table 2).

## Treatment Efficacy

Failure of treatment according to the definition by Lundell occurred in 77.3% (34/44) of the LMAH-C patients compared with 34.1% (14/41) of the LNF patients ($P < 0.001$) (Fig. 2). The signs of reflux recurrence are detailed in Table 3. There was no difference after 36 months between the groups regarding appraisal of the surgical quality. A total of 78.1% (32/41) of the patients in the LMAH-C group and 82.9% (34/41) of the patients in the LNF group reported, that they would have the surgery again ($P = 0.577$).

## DISCUSSION

The primary hypothesis of the present trial was that LMAH-C produces fewer side effects compared with LNF, which in fact could be confirmed by the underlying data and analyses. The ISS in the LMAH-C group was significantly lower compared with LNF. Furthermore, the rate of patients who were unable to belch or to vomit was reduced. However, the quality of life was not better for the patients who received LMAH-C, which was probably due to the disappointing antireflux effect. Therefore, in light of the lesser treatment effect, longer operation time and risk of mesh-related complications LMAH-C is not able to replace laparoscopic fundoplication as the surgical standard procedure for GERD.

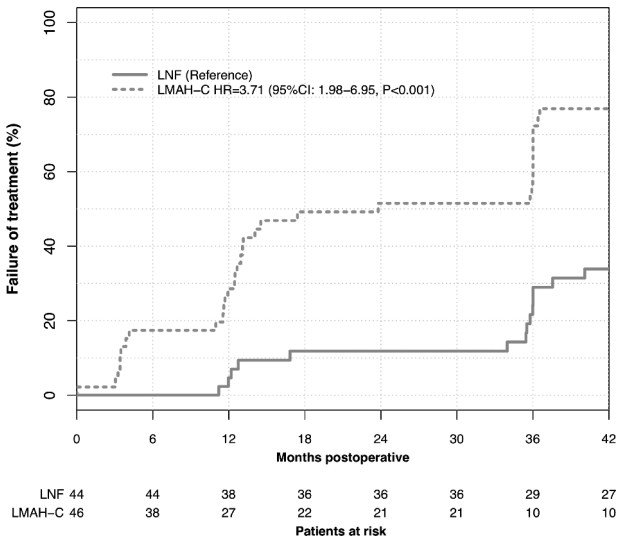


**FIGURE 2.** Failure of treatment after LMAH-C and LNF.

**TABLE 3.** Signs of Treatment Failure According to Lundell et al[26]

| | LMAH-C (n = 44)* | LNF (n = 41) | P† |
|---|---|---|---|
| Esophagitis ≥LA-B | 9 (20.5%) | 1 (2.4%) | 0.010 |
| Reoperation for reflux | 2 (4.5%) | 1 (2.4%) | 0.599 |
| GSRS reflux score ≥3 | 15 (34.1%) | 5 (12.2%) | 0.017 |
| Daily PPI for reflux | 15 (34.1%) | 5 (12.2%) | 0.017 |
| Dysphagia combined with reflux score ≥2 | 7 (15.9%) | 5 (12.2%) | 0.623 |

Values denote numbers (%) of patients.
*Number of patients with completed 36 months symptom and quality of life follow-up, including patients who were lost to this 36-month follow-up, but had presented with a documented recurrence earlier.
†$\chi^2$ test.
LA indicates grade of esophagitis according to the Los Angeles classification.[19]

LMAH-C seems to be far less effective in the treatment of GERD than LNF (Fig. 2). The degree of inferiority is surprising as previous studies, suggested a better outcome of LMAH-C.[17,18] The discrepancy may be best explained by the short follow-up period and a different definition of recurrence in the one study[17] and by the retrospective design of the other study.[18] Nevertheless, LMAH seems to improve reflux control to some extent despite unchanged LES pressure. These findings suggest that lengthening of the intra-abdominal esophagus induces a certain antireflux barrier although not as strong and not as durable as a fundoplication-related valve mechanism with increased LES pressure.

In the present trial, surgical risk was comparable between the groups investigated and matches the published data on laparoscopic fundoplication.[29,30] The main reasons for reoperation after LMAH-C were recurrences and 1 mesh migration. The recurrences reflect the limited antireflux effect of LMAH-C, the mesh migration the risk of mesh-related complications, which is debated extensively to date.[31,32] On the other hand, 4 patients after LNF needed reintervention for dysphagia. However, although the true risk of mesh-related complications might not be as high as feared,[18,33,34] risk-benefit considerations do not justify mesh application for GERD without large hiatal hernia, facing the limited treatment effect of LMAH-C.

There are several limitations of the present trial to be discussed, first of all, the choice of the primary endpoint. The ISS of the GSRS was chosen as the primary endpoint because it was assumed that it best measures gas-related symptoms induced by LNF. Unfortunately, there are no other validated instruments to specifically assess gas bloating. Furthermore, it might be argued, that reflux control would have been a more appropriate primary endpoint, when comparing 2 antireflux procedures. However, a much higher sample size would have been needed to confirm noninferiority of LMAH in terms of reflux control. Therefore, in the first instance, we intended to investigate whether potential advantages of LMAH in terms of side effects indeed exist. For this approach a smaller sample size was needed. This seemed to be the preferred approach also from an ethical point of view. Thus, based on the present findings it seems now, that no further randomization in a consecutive trial with reflux control as primary endpoint is justified. Second, it has to be considered that the findings regarding treatment effect and quality of life in the midterm follow-up exclusively originate from subjective data and from an explorative statistical analysis. Based on the author's experience, it is difficult to convince patients to undergo invasive investigations, especially when they are free of symptoms and surgery took place a long time ago. It was for these reasons that only 1 follow-up pH testing was scheduled at 3 months

postoperatively and then an additional endoscopy at 12 months, which is usually better accepted by the patients, than pH testing. As a consequence, no confirmative statements can be drawn in regard to reflux control. Finally, the 36-month follow-up might be considered too short given the fact that several studies on LNF with a longer follow-up than 10 years already exist. However, since LMAH was already inferior to LNF regarding reflux control after 36 months, a longer follow-up was not essential.

In conclusion, laparoscopic fundoplication still remains the standard surgical treatment for GERD. Compared with LMAH-C, LNF seems to be much more effective and durable in the control of reflux. Procedure-related side effects exist and are more pronounced after LNF. However, the clinical relevance of these side effects can be doubted as they do not seem to affect the patients' quality of life.

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## DISCUSSANTS

### B. Walther (Lund, Sweden):

I want to thank the authors for having the manuscript well in advance and the association for the privilege of the floor. I have 4 questions.

First, the cardiopexy increases the abdominal length of the esophagus about 4 cm. Are there any other steps in your procedure that are proven antireflux techniques?

Second, you screened 431 patients for your study and 90 were included, 133 did not meet inclusion criteria, and 208 refused to participate. How come? What kind of procedure did they have?

Third, 10% (9/90) of your patients were reoperated for different indications but it is not mentioned how they were reoperated. For instance, what procedures were performed for gastric ulcer, for recurrent reflux, and for gastric leakage?

Finally, in Table 1 a significant difference is shown, $P = 0.038$ in body mass index (BMI) for the 2 groups, but is the difference between 29.9 and 28 really a significant difference? If so can the difference in esophagitis frequency and reflux symptoms be well explained by more obese patients in the mesh-augmented group, or. . .?

### Response From B. P. Mueller-Stich (Heidelberg, Germany):

First of all, to achieve an antireflux barrier we only mobilized the esophagus whereby we lengthened its abdominal part. We mobilized the esophagus far up until the mediastinum and took care that we finally had at least 4 cm of intra-abdominal esophagus, which was then anchored by cardiophrenicopexy. We did not perform any kind of fundoplication just to prove the principle that reflux control can be achieved by this procedure with few side effects.

Why did not all of the patients participate in this study? The answer is very simple: We had very stringent selection criteria. Patients presented with reflux symptoms and when we were not able to objectify reflux they were not included. Patients who were eligible for inclusion often already had in mind what kind of procedure they wanted to have. Some wanted to have a fundoplication, others wanted to have a mesh-augmented cardiophrenicopexy without fundoplication. These patients could not be randomized. Our standard procedure, which was offered to all patients that did not want to be randomized within the study, was the laparoscopic fundoplication. Patients who wanted to have a mesh-augmented cardiophrenicopexy without fundoplication had to seek surgical treatment elsewhere.

We had 9 reoperations, 4 in the LMAH-C group and 5 in the LNF group. In the LMAH-C group, we had 2 patients with recurrent reflux, which both received an additional secondary laparoscopic fundoplication. One patient suffered from a chronic ulcer, which we treated with an antrectomy due to fear of the presence of a malignancy; and the fourth patient had a migration of the mesh into the fundus of the stomach. This case was managed by a partial mesh resection and a gastric wedge resection. The further course was uneventful. In the LNF group, we also had 2 patients with recurrent reflux due to a transdiaphragmatic displacement of the fundoplication corresponding to hiatal hernia. In these patients, we added a mesh-augmented hiatoplasty to the fundoplication. Furthermore, we had 2 patients with persisting dysphagia, which we treated with a conversion of the LNF to a laparoscopic Toupet fundoplication. And, finally, 1 patient presented a postoperative gastric leakage due to rupture of a suture at the fundoplication, which could be resutured without further problems.

Concerning the higher BMI in the LMAH-C group, in fact, the difference was significant. However, it remains questionable whether the small difference of 2 BMI points was also clinically relevant. To prove the hypothesis that the difference could be the reason for the worse antireflux effect, postoperative BMI would be needed to correlate it to the postoperative grade of esophagitis. Unfortunately, we did not measure and record the weight postoperatively.

### R. van Hillegersberg (Utrecht, The Netherlands):

Thank you for a very nicely conducted study. I think I may change your conclusion and say that there is no indication for mesh in these kinds of patients and that there is a too high complication rate of mesh. Could you transfer the conclusion more firmly?

### Response From B. P. Mueller-Stich (Heidelberg, Germany):

We stopped to perform mesh-augmented hiatoplasty with cardiophrenicopexy in classical reflux patients without large hiatal hernias based on the findings of the present study. Although mesh-related complications are not that frequent we were convinced that it was no longer possible to justify taking even the smallest of risks for no additional benefit. Would we have found a benefit in favor of the LMAH-C group, this would be a different discussion. And of course, this would be a completely different discussion for patients with large hiatal hernias, which were excluded from the present study.

### T. R. Demeester (Los Angeles, US):

I would like to first of all compliment you on an effort to reduce the side effects of the Nissen fundoplication. We must come to terms with this. The current problem in the treatment of reflux disease is a partial response to PPI therapy in approximately 30% to 40% of patients and the progression of disease while on therapy. This requires that we must apply surgical therapy earlier in the disease. As long as surgical therapy has the side effects, as you pointed out, we will never be able to apply it earlier and surgery will remain at the bottom in the treatment of the disease. Experience has shown the Nissen fundoplication to be a good operation for advanced disease but it does not fit for what is needed today.

Now, the problem that I would like you to explain is that to avoid the side effects of the Nissen fundoplication, why did you pick an old operation designed to protect against reflux caused by challenges of intra-abdominal pressure and leaves challenges of intragastric pressure independent of intra-abdominal pressure uncontrolled? It was predictable that the old operation would fail. The operation you chose to compare with the Nissen in regards to side effects was similar to the Allison procedure and he stood before the American Surgical Association (ASA) in 1973 and in essence said ''gentlemen do not do my operation'' (*Ann Surg.* 1973;178:273–276). So explain how you ended up using a form of this old operation.

My last comment is in regards to your conclusion that we should go back to the Nissen operation. Rather, I would propose that we proceed forward with new ideas, such as LINX and Endo-Stim that prevent effacement of the sphincter from challenges of intragastric pressure that occur independent of intra-abdominal pressure. These kinds of procedures are being developed because there is a need to have an operation that can be used earlier in the disease process without producing side effects. I would appreciate your comment on this thought.

### Response From B. P. Mueller-Stich (Heidelberg, Germany):

I totally agree with you that we have to look for new ideas, but LMAH-C, unfortunately, is not the solution. We decided for a cardiophrenicopexy similar to the Allison procedure since we hypothesized that the very good initial results published by Allison can be preserved by a durable anchoring of the cardia by means of mesh-induced fixation. This is a new concept, which was not available in former times when Allison invented his procedure.

Why did we not do so many different measurements in our patients? The main goal was to successfully finalize the present RCT in a double-center setting. This can usually be best achieved by a design that is as simple as possible. Questions focusing on other antireflux devices like the ones you propose must first be investigated in other RCT.

### G. Zaninotto (London, UK):

Thank you for the nice presentation and the well-conducted study. I have a question for you: Why did you choose to assess the side effects of the procedure as the primary outcome of the study rather than the main effect controlling Nissen complication?

### Response From B. P. Mueller-Stich (Heidelberg, Germany):

To go for side effects as a primary endpoint was again a methodical issue. We had to decide for 1 endpoint to attain a

reasonable sample size of patients to be included in the present trial that was not too big. As you could see, the intervention investigated in the present trial was far away from being a standard treatment and if we had decided for a design with a bigger sample size, we would have had to treat too many patients with an inferior procedure. First, we had to prove that our intervention in fact provided a benefit regarding side effects in a superiority design before we could investigate reflux control as the primary endpoint in a noninferiority design needing a much bigger sample size. However, this was not possible. Consequently, a further trial with reflux control as the primary endpoint would now be unethical to be performed based on the findings of this study.