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EDITORIAL PERSPECTIVE

What is the Best Anti-Reflux Operation? All Fundoplications are Not Created Equal

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This month's issue of the World Journal of Surgery presents a meta-analysis and systemic review of laparoscopic anterior versus posterior fundoplication for gastro-esophageal reflux disease [1]. The authors' aim was to answer the above (very important) question, which is asked of an upper gastrointestinal surgeon countless times by his/her patients. However, although the authors have prepared a comprehensive and thorough review, their study design has not answered this question. By not addressing the anatomical differences between varying degrees of fundoplication, misleading outcomes might have been generated that will not influence current surgical practice.

Why is the design of this study problematic? Similar to a meta-analysis published in Annals of Surgery in 2011 [2] by a group from the Netherlands, the authors of the current study have grouped together 90°, 120°, and 180° wraps into an 'anterior' group, and 270° and 360° wraps into a 'posterior' group. The decision to combine these quite different operations into only two groups might have falsely minimized the side effects reported in the posterior group, and falsely decreased the apparent efficacy in the anterior group, thereby leading to the conclusion that laparoscopic posterior fundoplication is the best anti-reflux operation, which may not be true.

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A brief review of the history of laparoscopic fundoplication illustrates the differences between wraps. Initial reports describing the technique of a laparoscopic 360° (Nissen) fundoplication emerged in 1991 [3, 4]. The principles of this operation closely followed the open technique for Nissen fundoplication, which at that time included division of the short gastric vessels, posterior closure of the diaphragmatic hiatus, and creation of a 1–2 cm 360° fundoplication, calibrated by at least a 52 Fr intra-esophageal bougie. Results were very good, with excellent reflux control. However, adverse effects including dysphagia, inability to belch, gas bloat, and excessive flatulence were not uncommon, and a flood of research ensued (which continues today) to achieve an effective anti-reflux barrier with less side effects.

The posterior 270° wrap was the first partial fundoplication to emerge in the laparoscopic era, with Cuschieri et al. describing their experience with the laparoscopic Toupet (270°) fundoplication in 1993 [5]. The 270° wrap is a 'semi-fundoplication' with intra-abdominal fixation of the fundus to the diaphragm, and placement of the fundus behind the esophagus. In 2010, it was compared to the Nissen 360° fundoplication in a well-constructed meta-analysis (compiling data from seven randomized controlled trials) [6]. The total 360° wrap was found to have a significantly higher prevalence of adverse effects, with equal reflux control to the 270° wrap. It was clear from this meta-analysis that the laparoscopic 270° wrap is *not* equivalent to the 360° wrap, and the author's decision (in the current meta-analysis) to group both of these wraps together is questionable.

Reports of a laparoscopic anterior partial fundoplication began to emerge in the early 1990s, but not as an anti-reflux procedure. As described by Dor in 1962, an anterior 180° fundoplication was designed to reduce reflux in

patients undergoing a laparoscopic Heller's cardiomyotomy for achalasia. Our group in Adelaide, Australia modified this approach for laparoscopic use. Critically, this procedure constructed a fundoplication that fully covered the anterior and right esophagus, and anchored the fundus and right esophagus to the right hiatal rim. A prospective randomized trial of laparoscopic anterior 180° versus 360° fundoplication in 107 patients with proven gastro-esophageal reflux was reported [7]. This showed no differences in clinical outcomes (albeit with short follow-up times), but with the 360° fundoplication generating significantly higher lower esophageal sphincter pressures than the 180° wrap. In 2013, a meta-analysis was published in the Annals of Surgery, combining data from five randomized controlled trials comparing the anterior 180° wrap to the 360° wrap [8]. At one and 5 years follow-up, reflux control was similar for the two wraps, but dysphagia and gas bloat were less after the 180° wrap, demonstrating the efficacy of the anterior 180° approach.

Watson et al. described a 120° anterior partial wrap in 1991 [9], and claimed this to be a "more physiological approach". He then published a small series of laparoscopic cases in 1995 [10]. The 120° wrap entailed closure of the hiatal defect, 'esophagopexy' to the right diaphragmatic pillar, re-creation of the angle of His, and a 120° anterolateral fundoplication, which left the right anterolateral esophagus uncovered. With this approach, the fundus was not anchored to the right hiatal pillar. Only one group has evaluated the 120° wrap in a randomized manner [11]. The second randomized trial (Khan et al.) in the meta-analysis described in this issue of the journal did not compare a 120° versus 270° wrap as reported, but compared a 180° versus 270° wrap [12]. In the only trial, Hagedorn et al. demonstrated that the 120° wrap was inferior to the 270° wrap when evaluated with objective postoperative pH and manometric studies [11]. The 120° wrap has largely been abandoned, at least in the literature.

Following on from our experience with the 180° wrap, a 90° wrap was conceived in Adelaide using a porcine model in 1999 [13]. This was then evaluated in a multicenter, prospective, double blind, randomized controlled trial between 2000 and 2003 [14]. This procedure was modeled after Allison's "anatomical" repair of hiatus hernia, where a transthoracic approach was used to reduce the hiatus hernia, close the esophageal hiatus, and accentuate the angle of His. This procedure was more similar to the 120° wrap than the 180° wrap, as the right anterolateral esophagus was not covered by the fundoplication and the fundus was not sutured to the right hiatal pillar. Initial results were promising, with good acid control and obvious reduction in dysphagia and bloating. Unfortunately, long-term results (5 years or more) found the 90° wrap to be less effective than a 360° fundoplication, and the procedure is now rarely performed in our centers for the treatment of severe gastro-esophageal reflux disease [15, 16].

It is clear that the 90° and 120° wraps for the treatment of gastro-esophageal reflux have not withstood the test of time, unlike the 180° anterior wrap which provides effective reflux control and very good overall outcomes. Hence, it is not inappropriate to group 90°, 120°, and 180° anterior wraps into a single anterior fundoplication group for meta-analysis, as this combines procedures which vary in efficacy, and biases the meta-analysis toward poorer reflux control in the anterior group. Similarly, combining the posterior 270° partial and Nissen 360° fundoplications into a single group might also bias that group toward less side effects, thereby yielding a biased study design with misleading results.

Probably, the more interesting question is how does a 180° fundoplication compare to a 270° fundoplication? We attempted to answer this question with a randomized controlled trial published this year [17]. Unfortunately, we were hampered with recruitment issues and our study was underpowered. However, at 12 months, mean heartburn scores were higher in the 180° wrap patients, and less patients could belch in the 270° fundoplication group. Khan et al. found similar results with a trade-off between recurrent reflux versus side effects, but their trial suffered from poor follow-up (58 %) at 12 months [10]. It is certainly conceivable that there is some trade-off between reflux symptoms versus side effects, but the overall outcomes for both procedures appear to be good, with high rates of patient satisfaction.

How do we then determine the best anti-reflux operation? There is no doubt that for reflux control the Nissen 360° wrap has withstood the test of time. It is a reliable, effective anti-reflux barrier, but it carries with it a higher risk of side effects—dysphagia, gas bloat, and increased flatulence. Our preference is to offer the 360° wrap mainly to patients who are young, male, and without significant motility problems, with the knowledge that adverse effects will be better tolerated in these individuals, and then subside over time. A 360° wrap is also preferentially used in patients with Barrett's esophagus with low-grade dysplasia, and in those with a peptic stricture from severe reflux. In all other patients, our institutional preference is for a partial fundoplication, as this has a much lower incidence of short-term side effects, and does not compromize reflux control. In our institutions, this tends to be an anterior 180° wrap, perhaps due to convention, but there is no doubt that in an overall experience with more than 2,200 patients, satisfaction levels remain equal to patients undergoing 360° fundoplication [18].

The search for the perfect anti-reflux operation continues, and well-constructed trials and meta-analyses, such as Memon et al's [1] systematic review, are an essential part

of this process. However, careful study design prior to study implementation is important, and a better choice of comparators in the current paper might have been more informative. We thank the journal editor's for giving us the opportunity to comment on the (short) history of laparoscopic anti-reflux surgery.

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