



Barrett's oesophagus, cancer and antireflux surgery

With the incidence of gastro-oesophageal reflux and oesophageal adenocarcinoma continuing to increase across the Western world, understanding Barrett's oesophagus, the disease stage that links reflux to cancer, is critical to improving outcomes for oesophageal adenocarcinoma. Dr Grigg aids our understanding of this field by providing a unique historical perspective and first-hand insight into the early days of surgery for gastro-oesophageal reflux, Barrett's oesophagus and their impact on the development of oesophageal cancer.¹ In doing this, he reminds us that some of the lessons our surgical forebears understood years ago are still relevant to modern practice.

We are reminded that Philip Allison made major contributions to the development of a rational approach to surgery for gastro-oesophageal reflux, and that antireflux surgery and Nissen fundoplication should not be considered to be synonymous. It is true that Allison's operation, essentially an anatomical repair via a left thoracotomy with reduction of hiatus hernia, narrowing of the hiatal ring and accentuation of the angle of His, did actually work, and a clinical success rate of 91% was reported at short-term follow-up.² However, this operation was abandoned after 20-year follow-up reported by Allison suggested a success rate of only 66%.³ Most surgeons considered these outcomes to be unacceptable, even though excellent long-term outcomes with success rates of up to 90% were reported by others.⁴

Concurrently, the apparent success of the Nissen fundoplication shifted the focus of surgeons towards wrapping the stomach around the lower oesophagus, a procedure offering more effective reflux control. As most surgeons focused on the outcome of recurrent reflux when discussing success versus failure, it was generally believed that the Nissen fundoplication was better, and this rapidly became the 'gold standard' for surgery for gastro-oesophageal reflux. However, it was also clear that following Nissen's fundoplication good reflux control was traded off against an increased risk of significant side effects, including dysphagia, flatulence and difficulty belching.⁵ Awareness of these side effects, which were troublesome in many individuals, discouraged referral for surgery once better medical therapy (proton pump inhibitors) became available.

The intense focus on achieving good reflux control using the Nissen fundoplication procedure also led surgeons to overlook the reality that Allison's procedure had shown that restoration of normal hiatal anatomy did actually stop gastro-oesophageal reflux in most patients, and often without the side effects associated with Nissen's operation.²⁻⁴ In their enthusiasm for the Nissen procedure, surgeons have also failed to consider the scarcity of long-term outcome studies following Nissen fundoplication. Only the study published by Luostarinen *et al.* reports late follow-up, with a

success rate of 76% reported at 20-year follow-up in a small cohort of 25 patients.⁶

Arguably, thinking has now come full circle, with a renewed focus on minimizing side effects following surgery for gastro-oesophageal reflux, and a trend towards partial fundoplications in an attempt to minimize side effects but still correct reflux. To minimize side effects, some of the procedures now performed aim to reconstruct hiatal anatomy and create a minimal partial fundoplication,⁷ a procedure that is remarkably similar to Allison's original description, but performed now laparoscopically, rather than via a left thoracotomy.

When laparoscopic fundoplication was introduced, outcomes were subjected to more scrutiny than in the open surgery era, and prospective audit was initiated by many high-volume units.^{8,9} This led to the early detection of problems such as a high hiatus hernia recurrence rates in patients who underwent fundoplication without hiatal repair. Subsequent advocacy for routine hiatal repair lead most surgeons to incorporate hiatal repair as standard for laparoscopic antireflux surgery.¹⁰ The higher level of scrutiny of outcomes also highlighted areas that were subsequently evaluated in a series of randomized controlled trials, and a much sounder evidence base now underpins surgical decision making in the laparoscopic era. For example, these trials have shown that antireflux surgery achieves better control of reflux than proton pump inhibitor medication,¹¹ that outcomes are better following laparoscopic surgery compared to open surgery¹² and that partial fundoplications outperform the Nissen procedure with less side effects and good reflux control.¹³

Dr Grigg also highlights the rapid increase in the incidence of oesophageal adenocarcinoma, with a concurrent shift from squamous to adenocarcinoma, and suggests that this has been driven by the preference for treating reflux and Barrett's oesophagus with medication rather than surgery. Although few would argue against the belief that gastro-oesophageal reflux is a risk factor for Barrett's oesophagus and oesophageal adenocarcinoma, the rapid increase in the prevalence of this problem is only partly explained by gastro-oesophageal reflux, and there is not much evidence to support the hypothesis that antireflux surgery prevents cancer. Much research is now underway investigating the aetiology of oesophageal adenocarcinoma, and the cause(s) are multifactorial. Any explanation for the development of this problem should explain why men and women are equally likely to develop gastro-oesophageal reflux, yet the male : female ratio for Barrett's oesophagus is 2:1, but for oesophageal adenocarcinoma it exceeds 8:1.¹⁴ Population studies suggest that the obesity epidemic is also contributing to the development of oesophageal adenocarcinoma, with obesity interacting synergistically with reflux to amplify the cancer risk.¹⁵ Other factors also contribute to this problem.

Although surgeons intuitively would like to believe that they can prevent oesophageal adenocarcinoma in higher risk individuals by constructing a fundoplication, this proposition is not supported by high-quality evidence. Case series evidence is conflicting, with progression from Barrett's oesophagus to cancer seen infrequently after fundoplication in some series,¹⁶ but not in others.¹⁷ Furthermore, fundoplication is not risk free. It is associated with morbidity and side effects, and even a low (0.1%) mortality risk.⁸ The risk of cancer progression in Barrett's oesophagus is also low, approximately 0.2–0.5% per year, so the risks versus benefits of surgery need to be weighed carefully, and fundoplication is unlikely to be a valid cancer prevention strategy.

For now, the current management of gastro-oesophageal reflux and Barrett's oesophagus should continue to focus on treating troublesome reflux symptoms without creating adverse outcomes. Further work is required to understand what is driving the rapid increase in oesophageal adenocarcinoma, as ultimately the solution to this problem will be driven by a population prevention strategy rather than surgical control of gastro-oesophageal reflux.

References

1. Grigg L. Re: Current Australian practice in the diagnosis and management of Barrett's oesophagus. *ANZ J. Surg.* 2014; **84**: 596–7.
2. Allison PR. Reflux esophagitis, sliding hiatal hernia and the anatomy of repair. *Surg. Gynecol. Obstet.* 1951; **92**: 419–31.
3. Allison PR. Hiatus hernia: a 20-year retrospective survey. *Ann. Surg.* 1973; **178**: 273–6.
4. Pearson JB, Gray JG. Oesophageal hiatus hernia: long-term results of the conventional thoracic operation. *Br. J. Surg.* 1967; **54**: 530–3.
5. Watson DI, Jamieson GG. Antireflux surgery in the laparoscopic era. *Br. J. Surg.* 1998; **85**: 1173–84.
6. Luostarinen M, Isolauri J, Laitinen J *et al.* Fate of Nissen fundoplication after 20 years. A clinical, endoscopic, and functional analysis. *Gut* 1993; **34**: 1015–20.
7. Watson DI, Jamieson GG, Lally C *et al.* Multicentre prospective double blind randomized trial of laparoscopic Nissen versus anterior 90 degree partial fundoplication. *Arch. Surg.* 2004; **139**: 1160–7.
8. Engström C, Cai W, Irvine T *et al.* Twenty years of experience with laparoscopic antireflux surgery. *Br. J. Surg.* 2012; **99**: 1415–21.
9. Morgenthal CB, Shane MD, Stival A *et al.* The durability of laparoscopic Nissen fundoplication: 11-year outcomes. *J. Gastrointest. Surg.* 2007; **11**: 693–700.
10. Watson DI, Jamieson GG, Devitt PG, Mitchell PC, Game PA. Para-oesophageal hiatus hernia: an important complication of laparoscopic Nissen fundoplication. *Br. J. Surg.* 1995; **82**: 521–3.
11. Grant AM, Boachie C, Cotton SC *et al.* Clinical and economic evaluation of laparoscopic surgery compared with medical management for gastro-oesophageal reflux disease: 5-year follow-up of multicentre randomised trial (the REFLUX trial). *Health Technol. Assess.* 2013; **17**: 1–167.
12. Salminen P, Hurme S, Ovaska J. Fifteen-year outcome of laparoscopic and open Nissen fundoplication: a randomized clinical trial. *Ann. Thorac. Surg.* 2012; **93**: 228–33.
13. Broeders JA, Roks DJ, Ali UA *et al.* Laparoscopic anterior 180° versus Nissen fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann. Surg.* 2013; **257**: 850–9.
14. Zingg U, Gotley DC, Smithers BM *et al.* Factors associated with post-operative pulmonary morbidity after esophagectomy for cancer. *Ann. Surg. Oncol.* 2011; **18**: 1460–8.
15. Whiteman DC, Sadeghi S, Pandeya N *et al.* Combined effects of obesity, acid reflux and smoking on the risk of adenocarcinomas of the oesophagus. *Gut* 2008; **57**: 173–80.
16. Zehetner J, DeMeester SR, Ayazi S *et al.* Long-term follow-up after anti-reflux surgery in patients with Barrett's esophagus. *J. Gastrointest. Surg.* 2010; **14**: 1483–91.
17. Yau P, Watson DI, Devitt PG, Game PA, Jamieson GG. Laparoscopic antireflux surgery in the treatment of gastroesophageal reflux in patients with Barrett esophagus. *Arch. Surg.* 2000; **135**: 801–5.

David I. Watson, MD, FRACS
*Flinders University Department of Surgery, Flinders Medical
 Centre, Adelaide, South Australia, Australia*

doi: 10.1111/ans.12644