

Ablative mucosectomy is the procedure of choice to prevent Barrett's cancer

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OPENING ARGUMENT

Stark strategies face patient and clinician in the presence of a degenerating dysplastic Barrett's mucosa. Surgical removal offers an overaggressive flawed approach reminiscent of the politics of "Total War" (Karl Von Clausewitz 1780–1831: "Vom Kriege"). Decisive action assures eradication but without definitive knowledge of the threat and incurring extensive collateral damage. Surveillance waits for the cancer to develop; then offers a belated radical solution. Selective mucosal ablation is an active directed therapy offering a targeted pre-emptive preventative strike.

I propose that mucosal ablation is currently the procedure of choice to prevent Barrett's cancer.

THE CONTEXT

Cancer in the columnar lined oesophagus develops through a multistep process initiated by chronic gastro-oesophageal reflux progressing through metaplasia, low grade dysplasia to high grade dysplasia which currently remains the best marker of cancer risk.¹ As many as 40% (range 0–73%) of patients with high grade dysplasia may already have a coexistent cancer,^{1,2} and between 5% and 60% of patients will develop cancer during surveillance over 1–7 years.^{3–5} The problems are that dysplasia and early cancer are often symptomatically and endoscopically undetectable. Progression is not inevitable, takes many years, pathological analysis is subjective, and apparent regression has been reported.⁶

THE CHOICES

Surgery

The tenacious orthodoxy of radical surgical removal will ensure that occult cancer is removed. It can be performed with increasing safety and completely prevents cancer. The mortality of oesophagectomy is variable but remains at 11%.⁷ Aggressive preoperative risk analyses of patients with adenocarcinoma have shown the extensive comorbidity accompanying this disease. Patients are usually overweight with significant cardiac and respiratory problems. Careful patient selection can reduce operative mortality from 9.4% to 1.6%.⁸ Surgical resection for high grade dysplasia and occult cancer still has an early morbidity of over 50% and late morbidity of 26%, and the actuarial survival of patients was 79% at five years.⁹ Surgery remains radical prophylaxis only available to some patients, and offering a massive macroscopic morbid solution for a microscopic mucosal problem.

Surveillance

A major predictor of five year survival following surgery is the stage at which disease is detected

(70%—mucosal cancer; 20%—invasive).¹⁰ Surveillance of patients at increased risk of cancer may detect earlier stage disease at a potentially curative stage.¹¹ The major problem is the unresponsiveness to the individual patient, being protocol driven depending on a predetermined biopsy regimen, at predetermined intervals in asymptomatic patients with endoscopically invisible disease, and absence of objective pathology.¹² Thus the disease is allowed to progress escaping mucosal containment to a level where radical surgery is necessary.

Selective mucosal ablation

The potential problem in the columnar lined oesophagus is surface limited to a depth of 0.6 mm.¹³ Resurfacing the oesophagus eradicates the disease and offers the possible prevention of progression. Mucosal ablation with lasers, electro-, and argon plasma coagulators, photodynamic therapy, and endoscopic mucosal resection can remove dysplasia and allow regeneration of neosquamous mucosa following acid reflux control.^{14–16}

Endoscopic mucosal resection of 35 patients with early cancer and high grade dysplasia achieved remission in 97% (12 month follow up).¹⁶ It is very effective when there is a localised visible mucosal abnormality. Multifocal dysplasia carries a greater chance of malignant degeneration,³ and treatment of the whole Barrett's segment is necessary.

Photodynamic therapy with 5 aminolevulinic acid eradicated high grade dysplasia in 10 of 10 patients and 17 of 17 patients with mucosal cancer less than 2 mm in depth (9.9 months of follow up). Deeper lesions were not eradicated.¹⁷ A blinded randomised trial demonstrated complete eradication of low grade dysplasia following photodynamic therapy.¹⁵

Similarly, thermal ablation using the argon plasma coagulator has eradicated low grade dysplasia (nine patients) and high grade dysplasia (nine patients). After 38 months there was no neoplastic progression. Concern has been raised about the histological appearance of buried glands after endoscopic thermal and photodynamic therapy,¹⁸ and cancers have developed in patients after endoscopic therapy.¹⁹

The only randomised partially blinded trial for prevention of cancer in Barrett's oesophagus is still ongoing. Initial reports from this multicentre study, which has recruited 208 patients with high grade dysplasia, are highly encouraging. Patients were randomised (2:1) such that 138 have had photodynamic therapy and omeprazole and 70 have received omeprazole only. At the six month follow up, 80% of patients treated with photodynamic therapy had disease eradication compared with 40% in the control group. The effect

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Summary

- (1) Progression to cancer is unpredictable.
- (2) Surgical removal as prophylaxis has unacceptable morbidity and mortality.
- (3) Surveillance allows cancer to develop from dysplasia.
- (4) Mucosal ablation is directed at the problem and can remove neoplastic mucosa.
- (5) Initial randomised evidence demonstrates that photodynamic therapy can reduce the cancer risk.

was only sustained in the photodynamic therapy group. In patients withdrawn, a strong trend to cancer reduction (9% photodynamic therapy combined with omeprazole versus 18% omeprazole only) is already evident at this very early stage in patients treated with photodynamic therapy.²⁰

CLOSING ARGUMENT

We have a responsibility not to be spectators of the current epidemic rise of oesophageal adenocarcinoma, particularly in overweight middle class White men. Patient comorbidity and operative morbidity make prophylactic surgery an impossible choice for many patients with an unpredictable problem. Surveillance condemns us to be the voyeur, intervening too late. Selective mucosal ablation followed by continued surveillance must now be the preferred choice.

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Debate