Stents for oesophageal cancer in resource-poor settings

In many resource-poor settings, treatment options for advanced oesophageal carcinoma are limited. In this issue of *The Lancet Oncology*, White and colleagues report a prospective analysis of stent placement to treat advanced oesophageal cancer at a hospital in Kenya where chemotherapy and radiotherapy are unavailable. On face value, one could equate this to attempting to launch a haute-cuisine restaurant in London where the only dish you have to serve is chicken and you only have a one-plate stove. To adapt you must cook your entrées with flair and creativity. Indeed, in the face of enormous challenges, the authors have produced a very respectable series of results for a formidable disease. The question posed is whether any of this experience can be translated to practices in other parts of the world.

The success of the treatment approach in this study is evident. Most patients presented with advanced oesophageal cancer and were severely symptomatic with dysphagia; most were treated as outpatients with little time-consuming or expensive investigation. After placement of the stent, patients had immediate improvement in quality of life and were discharged expediently. Reported survival was better than in many published studies of the use of stents in obstructing carcinoma. Furthermore, the results are comparable to many studies of similarly staged diseases treated with more aggressive methods. The cost to both patients and treating facilities was enticingly small. These results would seem to make stent placement an attractive strategy for institutions that are constrained by cost or limited infrastructure.

However, although eminently successful in the study setting, the approach may be difficult to deploy elsewhere. The self-expanding metal stents (SEMS) were provided free or at subsidised cost by the manufacturers. From our own experience in South Africa—a country of limited health-care resources—the initial cost of SEMS has prohibited their general use for patients under the national health programme. Motivation for use is problematic because of poor survival, often less than 90 days, and substantial morbidity for stenting of oesophageal malignancy in local previous studies. Treatment with stents alone may be associated with poor outcomes because, as the authors point out, it is more common in patients viewed as not being candidates for radiotherapy or other forms of treatment. Furthermore, this view is also based on results from past studies with poor equipment and few dedicated staff. If survival in the range of 250 days as reported by White and colleagues could be replicated, this strategy may be more justifiable. Another limitation is the availability of suitable endoscopy equipment and expertise to place stents. The advisability of placing stents where histology is not confirmed is also questionable; although recognising the costs and time this procedure might add, it could be problematic in areas where squamous carcinoma is not endemic.

White and colleagues’ study challenges some basic tenants of standard oncology care for oesophageal cancer in countries with more developed economies than Kenya’s. Although approaches vary, most early-stage disease is considered for surgery, with or without adjuvant or neoadjuvant chemotherapy. Most advanced-stage disease is given palliative care with chemotherapy or radiotherapy. SEMS are generally also thought to be palliative as they have no ablative effect on the tumour. In many settings, stents are used only when other treatments have failed for patients with poor prognosis. The researchers argue that the results are comparable to series in which chemotherapy or radiotherapy was used to treat similar stage disease. Although, raw survival figures support this assertion, in the absence of extensive clinical staging we would be remiss to accept such a
generalisation. However, many treatment strategies that we have previously thought of as superior are highly biased towards patients with good performance status and thus are inherently associated with improved survival. SEMS should, therefore, be compared with other established treatments in controlled trials.

In summary, the use of stents alone for advanced oesophageal cancer seems a rational approach in settings where treatment options are severely limited and the infrastructure for placement is available. The use of SEMS as a primary treatment instead of other established forms of treatment may deserve further comparative trials. Finally, the authors deserve recognition for the initiative and lateral thought that went into developing this very successful treatment programme. Their motivation and ingenuity for treatment of a difficult disease with limited resources available is noteworthy.

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Targeting the future in head and neck cancer

In this issue of The Lancet Oncology, Cohen and colleagues report results from their investigation of simultaneous erlotinib and bevacizumab therapy for recurrent or metastatic squamous-cell head and neck cancer. This is the first study of concurrent use of multiple molecularly-targeted agents and is an important step toward better management and assessment of the disease. The results are most relevant for leading the way for further investigation.

For patients with head and neck cancer, tumour hypoxia is a potent predictor of adverse outcomes. Hypoxia stimulates angiogenesis through upregulation of the hypoxia-inducible factor 1 alpha (HIF1α)–vascular endothelial growth factor receptor (VEGFR) pathway. Head and neck cancer that is both hypoxic and highly angiogenic has a poor prognosis even after chemoradiation, and patients with substantial overexpression of VEGF have a two-times increased risk of dying. Epidermal growth factor receptor (EGFR) signalling also stimulates angiogenesis but via mechanisms independent of hypoxia and HIF1α. Inhibition of one pathway (eg, EGFR) probably upregulates signalling of alternative pathways (eg, VEGF). These redundant signalling pathways confirm our understanding of cancer as an ultimate survival machine, capable of adapting to the attacks that we collectively term “treatment”. Cohen’s idea to simultaneously block both VEGFR and EGFR pathways is an innovative approach that draws on the proven concept of combining multiple drugs to overcome resistance.

Cohen and colleagues use response evaluation criteria in solid tumours (RECIST) to determine efficacy, although these criteria are inadequate to assess the effects of molecularly-targeted therapies—especially in