PRIMEVIEW

OESOPHAGEAL CANCER

nature REVIEWS DISEASE PRIMERS

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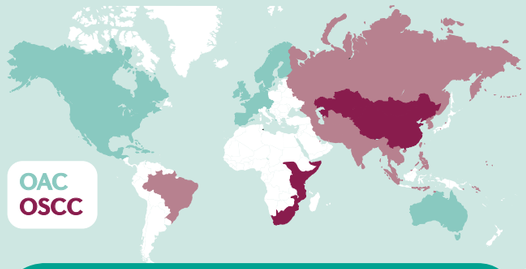
Oesophageal cancer is the sixth most common cause of cancer-related death worldwide. Two biologically distinct entities exist with a common anatomical site: oesophageal squamous cell carcinoma (OSCC) and oesophageal adenocarcinoma (OAC).

EPIDEMIOLOGY

OSCC accounts for 90% of all cases of oesophageal cancer and is especially prevalent in the East, East Africa and South America. By contrast, OAC is most common in industrialized countries in the West. OSCC incidence has been declining in most parts of the world, whereas OAC incidence rates have shown a sharp increase.

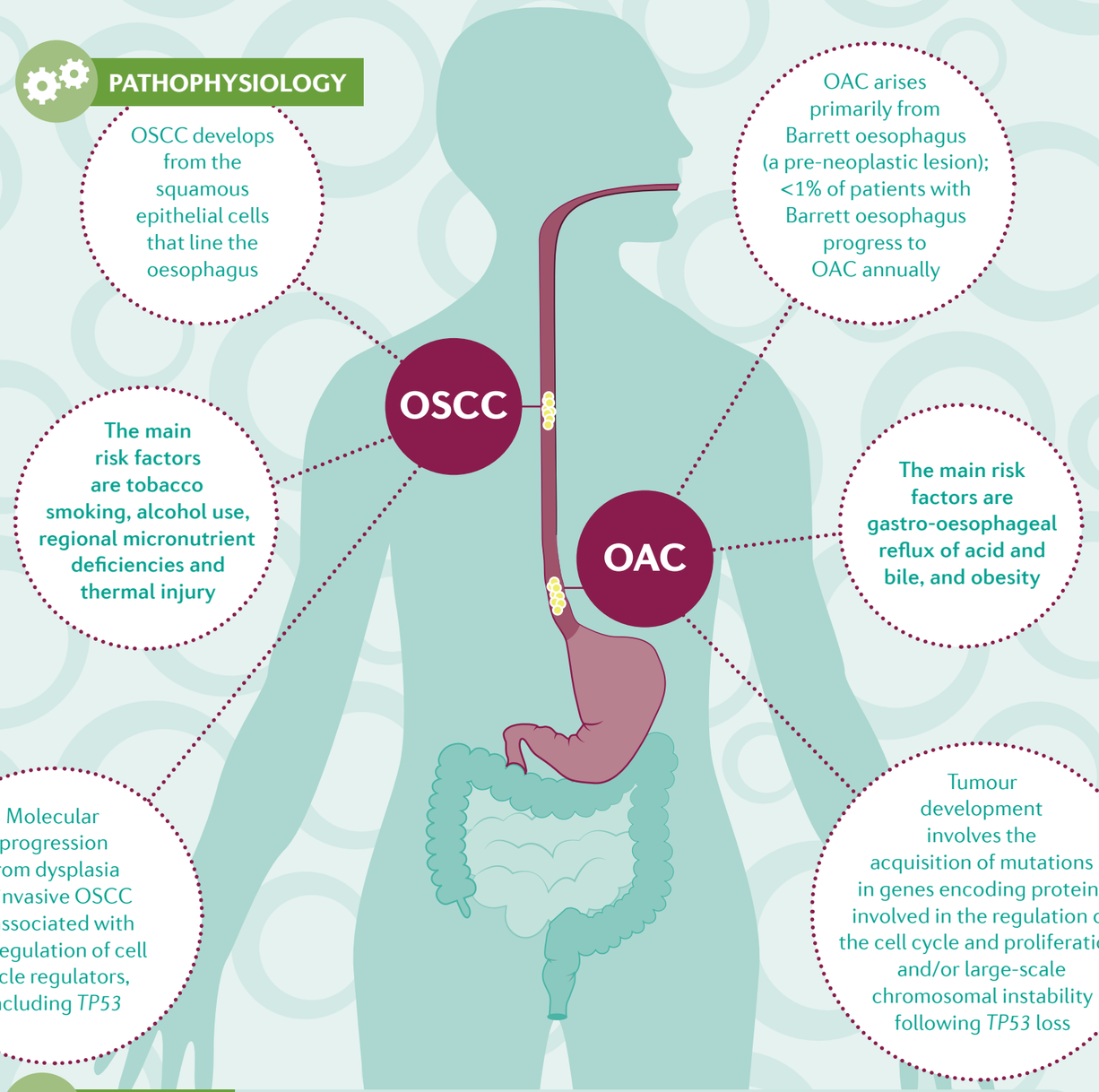


Globally, ~456,000 individuals were diagnosed with oesophageal cancer in 2012

PATHOPHYSIOLOGY

OSCC develops from the squamous epithelial cells that line the oesophagus

OAC arises primarily from Barrett oesophagus (a pre-neoplastic lesion); <1% of patients with Barrett oesophagus progress to OAC annually



The main risk factors are tobacco smoking, alcohol use, regional micronutrient deficiencies and thermal injury

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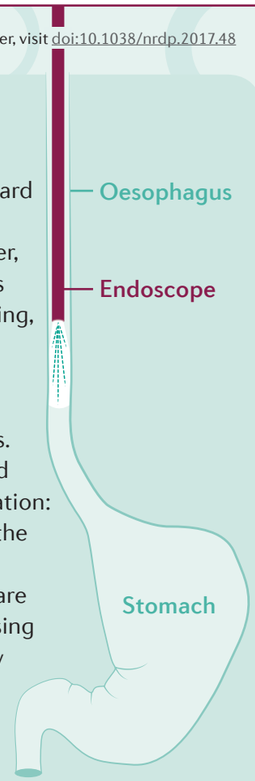
Molecular progression from dysplasia to invasive OSCC is associated with dysregulation of cell cycle regulators, including *TP53*

Tumour development involves the acquisition of mutations in genes encoding proteins involved in the regulation of the cell cycle and proliferation, and/or large-scale chromosomal instability following *TP53* loss

DIAGNOSIS

Endoscopy is the gold-standard technique to detect and diagnose oesophageal cancer, as clinical symptoms (such as difficulty or pain on swallowing, involuntary and progressive weight loss, hoarseness or cough) usually only become apparent at advanced stages. Staging should be performed according the TNM classification: the size and invasiveness of the tumour (T stage) and lymph node involvement (N stage) are preferentially determined using endoscopic ultrasonography and biopsy, whereas CT, PET or a combination should be used to locate distant metastases (M stage).



PREVENTION

Primary prevention is based on avoidance of risk factors. For patients with Barrett oesophagus, secondary prevention could include treatment with proton pump inhibitors or NSAIDs (for example, aspirin), but the effectiveness of these treatments is not yet proven. Routine screening for OAC and OSCC precursor lesions is currently not recommended, except in high-risk areas and for high-risk individuals, although endoscopic treatments result in excellent long-term outcomes.

OUTLOOK

To introduce systemic testing in the population at risk, non-invasive methods to obtain cell samples and biomarkers to assess the risk of progression from Barrett oesophagus to oesophageal cancer are needed. Except for trastuzumab (an anti-HER2 antibody) and ramucirumab (an anti-VEGFR2 antibody), many targeted therapies have not proven successful so far. However, several studies testing targeted therapies and immunotherapies are underway.

MANAGEMENT

Management of patients with oesophageal cancer depends mainly on the TNM stage of the tumour. Very early-stage tumours can be removed by endoscopic ablation or resection. Locally advanced cancers are treated with surgery with or without neoadjuvant chemotherapy or chemoradiotherapy. For patients with metastatic oesophageal cancer, palliative chemotherapy is the only option.

OSCCs are very sensitive to radiotherapy, and neoadjuvant, or even definitive, chemoradiotherapy is the recommended approach

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