Response to neoadjuvant therapy (Core)

There are two commonly used systems to assess tumour regression grade (Table 2). One very common method employed to assess tumour regression is the Mandard classification system (Table 2).[1] This five-tiered system divides tumour regression into five grades based on the proportion of viable tumour tissue present in relation to fibrosis.[1]

There is also a four-tiered system (Becker system) recommended by some authors for having a better reproducibility for pathological assessment (Table 2).[2] This system depends on the proportion of residual cancer cells present by percentage.

The modified Ryan system[3] proposed by the College of American Pathologists (CAP[4]) (Table 3), recognises four grades based on the proportion of residual tumour in a descriptive manner, but this is less commonly adopted in oesophageal cancers.

Although many studies have evaluated and compared these schemes in assessing treatment response in gastrointestinal carcinomas after neoadjuvant therapy, there is no consensus on the optimal way to stratify tumour regression grades. In addition, the inter- and intra-observer variability is high in most schemes. Nevertheless, response to neoadjuvant therapy should be reported, as assessment of histological tumour regression may provide valuable prognostic information and impact on the choice of postoperative therapy.[2] Patients with complete tumour regression have significantly better overall survival compared to patients with residual adenocarcinoma. As there is no current consensus on grading schemes, the three most commonly used systems have been provided by the Carcinoma of the Oesophagus Dataset Authoring Committee.[1,3,5] Subjective elements in interpretation are difficult to avoid. Further comparative studies are needed.

However, regardless of the system used, it is important to assess the tumour regression grade as it is associated with prognosis in patients with oesophageal carcinomas.[5-8]

Table 2: The Mandard and Becker systems for assessing the tumour regression grade (TRG) of carcinoma after neoadjuvant therapy.

Mandard	Becker
TRG 1: Absence of residual cancer, with fibrosis extending through the various layers of the oesophageal wall (complete regression)	**TRG 1a:** No residual carcinoma present
TRG 2: Rare residual cancer cells scattered through the fibrosis	**TRG 1b:** <10% residual carcinoma present
TRG 3: An increase in the number of residual cancer cells, but fibrosis still predominates	**TRG 2:** 10-50% residual carcinoma present
TRG 4: Residual cancer outgrowing fibrosis	**TRG 3:** >50% residual carcinoma present
TRG 5: Absence of regressive changes	

Modified with permission from Lam AK and Kumarasinghe MP (2019). Adenocarcinoma of the oesophagus and oesophagogastric junction not otherwise specified (NOS) In: Odze RD et al (2019). Tumours of the oesophagus. In: *Digestive System Tumours. World Health Organization Classification of Tumours, 5th Edition*, Lokuhetty D, White V, Watanabe R and Cree IA (eds), IARC Press, Lyon, France.[8]

Table 3: Modified Ryan scheme for tumour regression grading system.[3,4]

Description	Tumour Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumour regression (poor or no response)	3

Reproduced with permission from Ryan R et al (2005). Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. *Histopathology* 47(2):141-146.[3]

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