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Mixed Histology and Its Implication in Endoscopic Treatment for Early Gastric Cancer

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Endoscopic resection can be curative for selected cases of early gastric cancer. Histological classification is the most important criterion for endoscopic treatment. Histological classifications of gastric cancer include the World Health Organization (WHO), Japanese, Nakamura, and Lauren classification (table 1). Previously, endoscopic therapeutic modality had been recommended only to differentiated type (intestinal, tubular/papillary), and now extended to undifferentiated type (diffuse, poorly cohesive) (table 2).

Mixed carcinoma, first described by Lauren 1965, was referred to tumor which present an equal proportion of diffuse and intestinal-type carcinoma. Based on WHO classification, it is defined as gastric carcinoma, composed of a mixture of morphologically identifiable glandular (tubular/papillary) and poorly cohesive cellular histological components. Mixed carcinomas have been shown to be clonal with heterogeneous phenotype attributed to somatic mutation in CDH1 and restricted to the poorly cohesive component. Histologic heterogeneity in gastric cancer is not uncommon, reported as about 20%. Biologic behavior of mixed carcinoma has been unveiled that higher risk for lymph node metastasis was reported in histological heterogeneity than pure type carcinoma. However, there remains unmet needs for revised or new criteria of endoscopic treatment in mixed carcinoma.

Table 1. Comparison of the WHO, Japanese Gastric Cancer Association (JGCA), and Lauren classification

WHO (2019)	JGCA (2017)	Nakamura (1968)	Lauren (1965)
Papillary adenocarcinoma	Papillary: pap	Differentiated	Intestinal
Tubular, well-differentiated	Tubular 1: tub1		
Tubular, moderately-differentiated	Tubular 2: tub2		
Tubular, poorly-differentiated	Poorly 1 (solid type): por1	Undifferentiated	Indeterminate
Poorly cohesive carcinoma, signet ring cell phenotype	Signet-ring cell: sig	Undifferentiated	Diffuse
Poorly cohesive carcinoma, other cell phenotype	Poorly 2 (non-solid type): por2		
Mixed carcinoma	Description according to the proportion (e.g. Por2>sig>tub2)		Mixed
Mucinous adenocarcinoma	Mucinous adenocarcinoma	Differentiated/Undifferentiated	Intestinal/diffuse
Adenosquamous carcinoma	Adenosquamous carcinoma	Not defined	Not defined
Squamous cell carcinoma	Squamous cell carcinoma		
Undifferentiated carcinoma	Undifferentiated carcinoma		
Carcinoma with lymphoid stroma	Carcinoma with lymphoid stroma		
Hepatoid adenocarcinoma	Hepatoid adenocarcinoma		
Adenocarcinoma with enteroblastic differentiation	Adenocarcinoma with enteroblastic differentiation		
Adenocarcinoma of fundic gland type	Adenocarcinoma of fundic gland type		
Micropapillary adenocarcinoma	type		