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Dataset for the reporting of carcinoma of the oesophagus in resection specimens: recommendations from the International Collaboration on Cancer Reporting

Alfred K. Lam, MBBS MD PhD FRCPA, Michael J. Bourke, MBBS FRACP, Renyin Chen, MD, Roberto Fiocca, MD PhD, Fumiyoshi Fujishima, MD PhD, Satoshi Fujii, MD PhD, Marnix Jansen, MD PhD MSc, Priyanthi Kumarasinghe, MBBS MD FRCPA, Rupert Langer, MD, Simon Law, MBBChir MS PhD FRCSEd FCSHK FHKAM, Sybren L. Meijer, MD PhD, Cian Muldoon, MB BCh BAO FRCPath, Marco Novelli, MBChB MSc PhD FRCPath, Chanjuan Shi, MD PhD, Laura Tang, MD PhD, Iris D. Nagtegaal, MD PhD

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Alfred K. Lam MBBS MD PhD FRCPA^{a,b,c}, Michael J. Bourke MBBS FRACP^{d,e}, Renyin Chen MD^f, Roberto Fiocca MD PhD^g, Fumiyoshi Fujishima MD PhD^h, Satoshi Fujii MD PhD^{i,j}, Marnix Jansen MD PhD MSc^k, Priyanthi Kumarasinghe MBBS MD FRCPA^l, Rupert Langer MD^m, Simon Law MBBChir MS PhD FRCSEd FCSHK FHKAMⁿ, Sybren L. Meijer MD PhD^o, Cian Muldoon MB BCh BAO FRCPath^p, Marco Novelli MBChB MSc PhD FRCPath^q, Chanjuan Shi MD PhD^r, Laura Tang MD PhD^s, Iris D. Nagtegaal MD PhD^t

- a. Pathology, School of Medicine, Gold Coast campus, Griffith University, Gold Coast, Queensland, 4222 Australia. Email: A.Lam@griffith.edu.au
- b. Pathology Queensland, Gold Coast University Hospital, Southport, Queensland, 4222 Australia
- c. Faculty of Medicine, The University of Queensland, Herston, Queensland, 4006 Australia
- d. Westmead Hospital, Department of Gastroenterology and Hepatology, Sydney, New South Wales, 2145 Australia. Email: michael@citywestgastro.com.au
- e. University of Sydney, Westmead Clinical School, Sydney, New South Wales, 2145 Australia
- f. Department of Pathology, The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe East Road, Zhengzhou, 450052, Henan Province, People's Republic of China. Email: chenrenyin@zzu.edu.cn
- g. Department of Pathology, University of Genova, 16132 Genova, Italy. Email: fiocca@unige.it
- h. Department of Pathology, Tohoku University Hospital, Aoba-ku, Sendai 980-8574, Japan. Email: ffujishima@patholo2.med.tohoku.ac.jp
- i. Department of Molecular Pathology, Yokohama City University Graduate School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan. Email: sfujii@yokohama-cu.ac.jp
- j. Department of Pathology and Clinical Laboratories, National Cancer Centre Hospital East, Kashiwa, 6-5-1 Japan

- k. University College London (UCL) Cancer Institute, London, United Kingdom; University College London Hospitals NHS Trust, London, WC1E 6DD, United Kingdom. Email: m.jansen@ucl.ac.uk
- l. PathWest Laboratory Medicine, PathWest QEII Medical Centre, Perth 6009, Western Australia, Australia. Email: priyanthi.kumarasinghe@health.wa.gov.au
- m. Institute of Pathology, University of Bern, 3012 Bern, Switzerland. Email: rupert.langer@kepleruniklinikum.at
- n. Queen Mary Hospital, The University of Hong Kong, Hong Kong, China. Email: slaw@hku.hk
- o. Department of Pathology, Amsterdam UMC, University of Amsterdam, 1105 AZ Amsterdam, The Netherlands. Email: s.l.meijer@amsterdamumc.nl
- p. Histopathology Department, St James's Hospital, Dublin D08 NHY1, Ireland. Email: cmuldoon@stjames.ie
- q. Research Department of Pathology, University College London Medical School, London, WC1E 6DD, United Kingdom. Email: m.novelli@ucl.ac.uk
- r. Department of Pathology, Duke University School of Medicine, Durham, NC 27708, United States. Email: Chanjuan.shi@duke.edu
- s. Department of Pharmacy, Memorial Sloan Kettering Cancer Centre, New York City, NY, 10065, United States. Email: tangl@mskcc.org
- t. Department of Pathology, Radboud University Medical Centre, 6500, Nijmegen, The Netherlands. Email: Iris.Nagtegaal@radboudumc.nl

Short running title: ICCR oesophageal carcinoma dataset

Corresponding author:

Professor Alfred K. Lam

Pathology, School of Medicine

Gold Coast campus, Griffith University

Gold Coast, QLD 4222

Australia

Tel: +61 7 5678 0718

Fax: +61 7 5687 6797

E-mail: A.Lam@griffith.edu.au

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Abstract

Background and objectives: A standardised dataset for oesophageal carcinoma pathology reporting was developed based on the approach of the International Collaboration on Cancer Reporting (ICCR) for the purpose of improving cancer patient outcomes and international benchmarking in cancer management.

Materials and Methods: The ICCR convened a multidisciplinary international expert panel to identify the best evidence-based clinical and pathological parameters for inclusion in the dataset for oesophageal carcinoma. The dataset incorporated the current edition of the World Health Organization Classification of Tumours of the Digestive System, and Tumour-Node-Metastasis (TNM) staging systems.

Results: The scope of the dataset encompassed resection specimens of the oesophagus and oesophagogastric junction with tumour epicentre ≤ 20 millimetres into the proximal stomach. Core reporting elements included information on neoadjuvant therapy, operative procedure used, tumour focality, tumour site, tumour dimensions, distance of tumour to resection margins, histological tumour type, presence and type of dysplasia, tumour grade, extent of invasion in the oesophagus, lymphovascular invasion, response to neoadjuvant therapy, status of resection margin, ancillary studies, lymph node status, distant metastases and pathological staging. Additional non-core elements considered useful to report included clinical information, specimen dimensions, macroscopic appearance of tumour, and coexistent pathology.

Conclusions: This is the first international peer-reviewed structured reporting dataset for surgically resected specimens of the oesophagus. The ICCR carcinoma of the oesophagus dataset is recommended for routine use globally and is a valuable tool to support standardised reporting, to benefit patient care by providing diagnostic and prognostic best-practice parameters.

Keywords: oesophagus, carcinoma, pathology, dataset, structured report, International Collaboration on Cancer Reporting.

1. Introduction

Oesophageal carcinoma is a common malignancy of high mortality and morbidity [1]. Although the overall global incidence has decreased in the last decade [2], oesophageal cancer ranked ninth in incidence (4.2% of all new cancers) and fifth in mortality (6.8% of all cancer deaths) amongst all cancers in 2020 [1]. The incidence and histological types of oesophageal carcinoma vary globally with high incidence areas include Asia, Africa, and Central/South America having squamous cell carcinoma and low incidence areas, mainly Western populations having adenocarcinoma [2]. The recently updated clinicopathological and genomic complexity of oesophageal tumours as well as unique epidemiological features are reflected in the current editions of the Union for International Cancer Control (UICC) [3] and American Joint Committee on Cancer (AJCC) [4] TNM Staging Manuals and the World Health Organization (WHO) Classification of Tumours of the Digestive System, 5th edition, published in 2019 [5, 6].

Many patients with oesophageal carcinoma are treated with neoadjuvant therapy and surgical excision as the mainstay of treatment [7, 8]. The pathological assessment of surgical excision specimens for extent of disease as well as response to neoadjuvant therapy are important for determining the diagnosis, prognosis, and a personalised management plan for patients with oesophageal carcinoma. Thus, a globally unified approach, which includes recent advancements in the field, is important for optimal patient care.

A structured standardised approach to cancer reporting leads to improvements in the quality and completeness of pathology cancer reports, and is advocated by fellows of Pathology Colleges of the United Kingdom, United States and Australasia, along with many other centres around the world who are engaged in the development of national or local best-practice standards. However, while each of these local standards often are based on the same cohort of evidence, they may utilise different terminology and methodologies.

The International Collaboration on Cancer Reporting (ICCR) is a not-for-profit organisation founded in 2011, with the goal of standardising pathology reporting internationally to improve cancer patient outcomes worldwide and to advance international benchmarking in cancer management. The ICCR datasets are made freely available for use by organisations and individuals globally. It is anticipated that, in time, this will enable the alignment and normalisation of pathology cancer data around the world. In this report, we present the process of development of the ICCR carcinoma of the oesophagus dataset, as well as outline the scope and the major features important for structured reporting of this cancer.

2. Materials and Methods

The previously published ICCR framework for the development of cancer datasets (Guidelines for the Development of ICCR Datasets, <http://www.iccr-cancer.org/datasets/dataset-development>) that have been described in detail in previous publications were followed. In brief, the process was initiated by the ICCR Dataset Steering Committee (DSC) who selected Professor Iris Nagtegaal as Series Champion to lead the development process for all the gastrointestinal cancer datasets and Professor Alfred Lam as Chair of the carcinoma of the oesophagus Dataset Authoring Committee (DAC). Under the leadership of Professor Lam, an internationally recognised panel of anatomical pathologists and clinicians with specialist expertise in oesophageal carcinoma was established to work on the dataset. The geographically diverse panel also included project managers to coordinate meetings and editing of the dataset. The ICCR DSC also ensured there was harmony of terminology and approach across the different gastrointestinal tract cancer datasets.

A preliminary dataset was drafted by the project managers and Chair following a review of existing datasets from the College of American Pathologists (CAP), Royal College of Pathologists (RCPATH), United Kingdom, and Royal College of Pathologists of Australasia (RCPA). The expert panel met via several web/teleconferences, in addition to accompanying email correspondence, to discuss proposed elements for inclusion in the dataset. The resulting draft carcinoma of the oesophagus dataset was then submitted to an eight-week period of open international consultation. The dataset was further refined following consideration of feedback received during the open consultation. The dataset was then published on the open access ICCR website (<http://www.iccr-cancer.org/datasets>).

3. Results

3.1 Scope

The dataset has been developed for the pathology reporting of resection specimens of carcinomas of the oesophagus. Carcinomas involving the oesophagogastric junction (OGJ) with tumour epicentre ≤ 20 millimetres (mm) into the proximal stomach were included. A separate dataset is available for endoscopic resections of the oesophagus (<http://www.iccr-cancer.org/datasets/published-datasets/digestive-tract>). Neuroendocrine carcinomas (NECs) and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs) of the oesophagus are

included. Neuroendocrine tumours (NETs), non-epithelial malignancies such as melanoma and secondary tumours are excluded from this dataset.

3.2 Core elements

Core elements are those which are essential for the clinical management, pathological staging, or prognosis of patients with oesophageal carcinoma. These elements had evidentiary support at Level III-2 or above, based on prognostic factors outlined in the National Health and Medical Research Council levels of evidence [9]. In rare circumstances, an exception was made where level III-2 evidence was not available, but there was unanimous agreement by the expert panel. A summary of the core elements is outlined in Table 1, and each is described in further detail as follows:

3.2.1 Neoadjuvant therapy

The main treatment option for curative intent for advanced stages oesophageal carcinoma are neoadjuvant chemoradiation with surgery or definitive chemoradiation [10]. Response to neoadjuvant therapy, including regression grade and lymph node downstaging, has a marked impact on cancer recurrence and survival of patients with oesophageal adenocarcinoma and squamous cell carcinoma[11-16].

The use of neoadjuvant therapy may shrink the cancer or result in complete or near-complete response, with fibrosis detected macroscopically (Figure 1A) [17]. As a result, identification of the lesion macroscopically can be difficult. Furthermore, prognostic TNM stage groups differ for oesophageal carcinoma with or without receiving neoadjuvant therapy [4, 5]. Therefore, it is essential for pathologists to have the relevant clinical information as to whether the patient with oesophageal carcinoma has been treated with neoadjuvant therapy, to ensure proper specimen handling and prognostic stage grouping of the cancer.

3.2.2 Operative procedure

Reporting on the type of resection is a core element, as processing is dictated by the type of specimen. ‘Oesophagectomy’ includes the oesophagus and a tiny strip of stomach and is also referred to as ‘oesophagogastrectomy’ which is removal of the oesophagus and the proximal portion of stomach. There is a general lack of uniformity as to the definition of the term lymphadenectomy in the context of oesophageal cancer surgery. For the purposes of the dataset, the definitions standardised by the International Society of Diseases of the

Oesophagus and reviewed in Jamieson et al (2009) were used [18]. Ideally, lymph nodes should be submitted in groups and labelled separately by surgeons for the purpose of unambiguous identification.

A two-field lymphadenectomy refers to dissection of the mediastinum as well as the upper abdominal lymph nodes around the coeliac trifurcation. Three-field lymphadenectomy refers to the addition of bilateral cervical lymphadenectomy. Three-field lymphadenectomy is optimal for an upper or middle thoracic oesophageal cancer with metastasis in the lymph node(s) based on improved long-term survival data [19]. Therefore, the extent of lymphadenectomy should be recorded [18, 19].

3.2.3 Tumour focality

Multifocal oesophageal squamous cell carcinoma can occur and may be related to the field effect of exposure to a carcinogenic factor such as smoking or the spread of tumour in the rich lymphatic plexus of the oesophagus [20]. Multifocal oesophageal carcinomas should be documented (Figure 2). If there are synchronous primary lesions (i.e., two or more individual tumours), separate datasets should be used for each lesion.

3.2.4 Tumour site

The location of the tumour is important for staging of oesophageal cancer [4]. The location of a cancer is based on endoscopic examination and landmarks (Figures 3 and 4). A description of the tumour site is ideally provided by the surgeon and should be documented by the pathologist. In addition, specific observations should be recorded by the pathologist which may help establish the exact site of origin of the tumour.

In the absence of clinical information, the location of the tumour could be estimated from the relationship of the tumour to the OGJ by the pathologist. The epicentre/midpoint of the tumour should be considered as the point of measurement for the pathological examination. The exact distance of tumour from epicentre/midpoint to the OGJ is a non-core element because it is only for clinical correlation purposes. The AJCC and CAP define the OGJ as the junction of the tubular oesophagus and the stomach, irrespective of the type of epithelial lining of the oesophagus, and this definition is recommended by the DAC [4, 21].

Some proximal stomach tumours which appear to be of gastric origin, under the AJCC 8th Edition Classification, may be classified as tumours of the oesophagus and OGJ somewhat artificially and thus reported using the oesophageal dataset [4]. When reporting such tumours, it should be noted that the tumour may have arisen within the stomach. A

tumour arising from the oesophagus with a tumour epicentre beyond the 20 mm mark, is staged as a gastric tumour.

3.2.5 Tumour dimensions

Where possible, the pathologist should record the maximum longitudinal dimension of the tumour mass and the distance of the tumour midpoint from the OGJ in the oesophagus and in the stomach. If no tumour is macroscopically visible, or for small tumours where the macroscopic dimensions may not be accurate then the microscopic dimensions should be documented. If the specimen is fragmented, measurements of the reconstructed tumour should be estimated, where possible. Otherwise, the clinical and/or radiological measurements should be used.

3.2.6 Macroscopic distance of tumour to the margin

A clear proximal resection margin may be difficult to obtain in oesophageal squamous cell carcinoma located in the upper portion. A positive resection margin is an important prognostic factor affecting survival rates [22]. The distance of the tumour from the closest resection margin, whether it is the distal, proximal, or circumferential margin, should be recorded. For tumours close to the resection margin, an accurate macroscopic assessment may not be possible, and the microscopic measurement is used.

3.2.7 Histological tumour type

It is important to refer to the current updates on the 2019 WHO Classification for the histology typing of oesophageal malignant neoplasms [5, 6]. The two major groups of malignant oesophageal tumours are adenocarcinoma and squamous cell carcinoma. Pathological staging is different for each of these two major groups [4]. The other histological variants of malignant oesophageal tumours basically follow the stage grouping of either that of squamous carcinoma or adenocarcinoma.

Adenoid cystic carcinoma, undifferentiated carcinoma or mixed neuroendocrine-non-neuroendocrine carcinomas (the neuroendocrine component is nearly always neuroendocrine carcinoma) with an adenocarcinoma component use the adenocarcinoma stage grouping [23].

There is no definite evidence indicating whether the staging of adenosquamous carcinoma or mucoepidermoid carcinoma should follow that of squamous cell carcinoma or adenocarcinoma staging groups [6].

3.2.8 Dysplasia

There are two types of dysplasia, squamous dysplasia and columnar/glandular (either Barrett or non-Barrett) dysplasia. In the current WHO Classification, both squamous and Barrett dysplasia are classified using a two-tiered system, high and low grade [5, 6].

Columnar dysplasia is mainly Barrett dysplasia. The presence of Barrett dysplasia supports oesophageal origin of an adenocarcinoma in cancer from the OGJ. The term Barrett dysplasia in the WHO Classification is adopted because of the aetiological link with Barrett oesophagus. However, rare cases of oesophageal adenocarcinoma may not arise from Barrett dysplasia. For instance, some rare adenocarcinomas of the mid oesophagus have no relationship with Barrett dysplasia [6]. Oesophageal columnar neoplasia is broadly divided into gastric, intestinal and mixed (hybrid) types, based on morphological and immunohistochemical feature [6]. The clinical significance of this division is yet to be determined and is not needed for routine clinical care.

Squamous dysplasia may present adjacent to squamous carcinoma in the cervical or upper thoracic oesophagus. Due to the anatomical limit of resection, dysplasia may extend to the proximal resection margin.

3.2.9 Histological tumour grade

Histological tumour grade (differentiation) is applicable to squamous cell carcinoma and adenocarcinoma only. The grade of the oesophageal carcinoma contributes to pathological staging or pathological prognostic grouping [4]. The 5th Edition of the WHO Classification has defined the morphological criteria for grading of adenocarcinoma and squamous cell carcinoma [6]. In adenocarcinoma, grade 1 is defined as adenocarcinoma with >95% of the carcinoma with well-formed glands; grade 2 with 50% to 95% with well-formed glands; and grade 3 is <50% with glandular formation [23]. In squamous cell carcinoma, grade 1 to grade 3 depends on the amount of keratin pearls, cytological atypia, mitotic activity and proportion of basaloid cells [24].

The three-tiered grading system is preferred to the two-tiered system as each grade may have an impact on early staged oesophageal cancers not treated by pre-operative adjuvant therapy based on AJCC stage grouping. It is acknowledged that after neoadjuvant therapy, it may be difficult to grade the carcinoma. However, this does not impact pathological staging.

3.2.10 Extent of invasion

Extent of invasion in the oesophagus is important for pathological staging of the carcinoma. It is divided into T1 to T4 depending on the level of involvement in the wall of oesophagus [5].

3.2.11 Lymphovascular invasion

Lymphovascular invasion is a known poor prognostic factor in oesophageal carcinomas and is designated a core element [6] (Figure 5). Identifying invasion into the extramural veins is important. The value of subdividing lymphovascular invasion into large vessel (venous) and small vessels (lymphatic, capillary and venular) has not been investigated. However, recording of this type of data will be useful to aid further investigation.

3.2.12 Response to neoadjuvant therapy

Neoadjuvant therapy changes the morphology of oesophageal carcinoma (Figure 1B). There are two commonly used systems to assess tumour regression grade. One very common method employed to assess tumour regression is the Mandard Classification System [25]. This five-tiered system divides tumour regression into five grades based on the proportion of viable tumour tissue present in relation to fibrosis [25].

There is also a four-tiered system (Becker system) recommended by some authors for having a better reproducibility for pathological assessment [13, 26, 27]. This system depends on the proportion of residual cancer cells present by percentage.

The modified Ryan system [28] proposed by the CAP [21], 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 [27]. 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 DAC [12, 25,

28]. Subjective elements in interpretation are difficult to avoid. Further comparative studies are needed.

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 [6, 12, 16, 29].

3.2.13 Margin status

The proximal resection margin is important in oesophageal squamous cell carcinoma due to the anatomical limit for resection and may be difficult to achieve a negative margin in patients with cancer in the upper oesophagus (Figure 6A). In addition, in many studies, the circumferential margin is associated with a poorer outcome for patients with oesophageal carcinomas [30, 31] (Figure 6B). There is controversy in defining when to call a circumferential margin positive, with some labelling margins of <1 mm positive and others defining it as the presence of tumour cells at the resection margin. No consensus has been reached. When patients with a positive circumferential margin via either definition were compared with those with a margin clearance of >1 mm, overall survival was significantly prolonged in the latter [32].

For multifocal tumours, the presence of positive margin in any tumour should be indicated as 'positive', and the closest margin can be measured from any tumour in the specimen.

3.2.14 Lymph node status

The number of lymph nodes infiltrated by carcinoma is a core element. More important is the minimum number of lymph nodes sampled for accurate assessment.

Lymph node harvest during oesophagectomy and high negative node counts after neoadjuvant therapy and oesophagectomy are associated with better survival in patients with oesophageal carcinoma [33]. There are no definite guidelines for the number of lymph nodes required, but in general, seven or more negative lymph nodes is the first cut-off value to have survival advantages in patients with oesophageal squamous cell carcinoma. The UICC[3]/AJCC[4] Classification System N3, is seven or more lymph nodes. According to UICC[3]/AJCC[4] 8th Editions, although it is suggested that at least 16 regional lymph nodes be removed and assessed pathologically, removal and evaluation of greater than or equal to 30 lymph nodes is desirable due to the prognostic value of increased nodal yield on overall survival [16, 34, 35].

The presence or absence of regressive changes observed in lymph node metastases after neoadjuvant therapy could be recorded, as there is some evidence that this has prognostic impact [36, 37].

Like the situation in squamous cell carcinomas in the head and neck region, extranodal extension in oesophageal squamous carcinoma was shown to have prognostic impact for patients [38]. Nevertheless, more studies are needed to validate the use of extranodal extension as a prognostic marker, and it is therefore a non-core element.

3.2.15 Ancillary studies

For oesophageal neuroendocrine carcinomas including mixed neuroendocrine-non-neuroendocrine carcinomas (MiNECs), the reporting of neuroendocrine marker expression and Ki-67 proliferation index are core elements. These elements are non-core for other types of oesophageal carcinomas.

Neuroendocrine neoplasms are classified into NETs, NECs and MiNENs. NETs are graded 1-3 using the mitotic count and Ki-67 proliferation index but pure NETs are not considered within the scope of this dataset [6]. Most NECs show marked cytological atypia, brisk mitotic activity, and are subclassified into small cell and large cell subtypes. MiNENs are usually composed of a poorly differentiated NEC component and an adenocarcinoma component. If a pure or mixed NEC is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation, usually applying synaptophysin and chromogranin A as a minimum [6].

Other ancillary tests are non-core elements which include human epidermal growth factor receptor 2 (HER2), programmed death-ligand 1 (PD-L1), microsatellite instability markers, etc. HER2 is important for planning targeted therapy for metastatic or unresectable OGJ adenocarcinoma. It should be tested by immunohistochemistry and could be confirmed by in situ hybridisation [6]. PD-L1 or microsatellite instability markers as detected by immunohistochemistry are helpful in predicting response to immunotherapy. They may be considered if immunotherapy is to be used for treatment of advanced oesophageal carcinoma.

3.2.16 Histologically confirmed distant metastases

The presence of distant metastases is one of the most important parameters for staging of patients with oesophageal carcinomas [3, 4]. Biopsy of the distant site to confirm metastases could be received during operation of the primary tumour. It is worth finding out whether there is also biopsy proven distant metastases before the operation.

3.2.17 Pathological staging

Pathological staging, according to the agreed criteria of the UICC [3] and AJCC [4] 8th Editions, is the most important factor to predict the survival of patients and planning treatment for patients with oesophageal carcinomas.

It is worth noting that although the pathological criteria of T (tumour), N (node), M (metastasis) remain the same, the stage grouping is different from squamous cell carcinoma and adenocarcinoma [4]. The differentiation (grades) of the carcinomas and location of the carcinoma are important criteria for the prognostic stage grouping in patients with oesophageal carcinoma.

In the AJCC 8th Edition Staging Manual, there is only one staging grouping for both squamous cell carcinoma and adenocarcinoma after receiving neoadjuvant therapy [4]. The stage grouping is different from that without therapy. In patients who had oesophagectomy after receiving neoadjuvant therapy, the grade of carcinoma is not a criterion for the stage grouping [4, 23, 24].

3.3 Non-core elements

Non-core elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management. A summary of the non-core elements is outlined in Table 1 and each is briefly described as follows:

3.3.1 Clinical information

Clinical information can be provided by the clinician on the endoscopy report or the pathology request form. Endoscopic location or information regarding the location of the tumour from the clinician, are an important guide as the specimen received may have retraction artefact after formalin fixation. Information on clinical stage, such as the presence of distant metastases and involvement of adjacent structures, is essential information for pathologists. In addition, multiple tumours may occur in the oesophagus, and especially in patients with a previous history of cancer e.g., carcinoma of hypopharynx.

3.3.2 Specimen dimensions

Recording of the specimen dimensions is recommended for each specimen. The dimensions of the specimen are normally measured to provide reference to the location of the tumour. It is noted that the oesophagus is approximately 250 mm in length. If a specimen is received piecemeal and submitted in the one container, then a reconstructed measurement of size is recommended.

3.3.3 Macroscopic appearance

There is no evidence that macroscopic appearance has prognostic value in oesophageal cancer. However, the macroscopic appearance of the lesion, such as having an ulcerative appearance, could indicate the potential for a more advanced lesion.

The WHO descriptions for oesophageal squamous cell carcinoma are recommended [6]. The macroscopic description for oesophageal adenocarcinoma is stricturing, polypoid, fungating, ulcerative, or diffuse infiltrating lesions whereas in squamous cell carcinoma, tumours are described as early versus advanced [6]. Advanced squamous cell carcinoma is defined as protruding, ulcerative and localised, ulcerative and infiltrative as well as diffusely infiltrative [6]. There is no WHO recommendation on the macroscopic description for other tumour types. Nevertheless, there is no clinical significance attributed to these macroscopic features. In this dataset, we have unified the macroscopic descriptions to account for the effect of neoadjuvant therapies. It is worth noting that in specimens obtained post neoadjuvant therapy, there may be no macroscopically detectable lesion, or just a small scar seen.

3.3.4 Barrett mucosa

The presence of Barrett mucosa points to the aetiology of the adenocarcinoma and helps to differentiate the origin of the lesion i.e., oesophageal versus gastric. The definition of Barrett mucosa varies between countries. In many regions, the presence of goblet cells is required for the diagnosis of Barrett mucosa. Nevertheless, it is a non-core element on macroscopic examination as Barrett mucosa may be obscured by the cancer.

3.3.5 Perineural invasion

The existence of perineural infiltration after neoadjuvant treatment is closely associated with poor prognosis and could be utilised along with the TNM staging system for better discrimination between patients with oesophageal squamous cell carcinoma or

adenocarcinoma [39]. However, as more studies are needed to validate the impact of perineural invasion, it is designated as a non-core parameter.

3.3.6 Coexistent pathology

Common coexisting pathologies other than Barrett oesophagus may include scar tissue, leiomyoma, squamous papilloma, etc. It is worth documented these as they may contribute to the co-morbidities of the patient.

4. Discussion

The ICCR carcinoma of the oesophagus dataset incorporates the information provided by the most recent updates from the WHO Classification [6], TNM staging[3, 4] and current management of oesophageal carcinoma. The core and non-core elements of this dataset were selected and reviewed by our global group of pathologists and clinicians involved in the management of patients with oesophageal cancers. The resulting dataset caters for oesophageal cancer histology types common in different localities in different populations. We hope that this dataset will be adopted by pathologists worldwide in routine practice to harmonise the pathological reporting of oesophageal carcinoma. This will provide optimal pathological data for current and personalised management of patients with oesophageal carcinoma in a more rational manner. The dataset promotes international best practice in oesophageal cancer reporting by incorporating comprehensive quality and evidence-based data from the literature. In addition, the uniform pathological reporting of the cancer will provide internationally comparable data to facilitate translational research and clinical trials in scientific, medical and health disciplines. It also facilitates comparison of data of oesophageal carcinomas in multiple centres both nationally and internationally.

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Figure Legends

Figure 1. Effect of neoadjuvant therapy

A. On macroscopic examination of resected section after neoadjuvant therapy, the oesophageal tumour may be sunken to haemorrhagic scar like tissue (arrows) and difficult to be identified.

B. On microscopic examination after neoadjuvant therapy, the relative portion of the carcinoma decreases. Fibrosis, foreign body giant cells (arrows) and inflammatory cells are present in the tumour stroma.

Figure 2. Double tumours in the oesophagus

A. The upper tumour is a stenosing tumour and the lower tumour is an ulcerative tumour (arrows).

B. An ulcerative tumour in the lower portion of the oesophagus plus another tumour in the oesophagogastric junction (arrows).

Figure 3. Anatomic subdivisions of the oesophagus as follows:

- The cervical oesophagus begins at the hypopharynx and extends to the thoracic inlet (at the level of the sternal notch); 15 centimetres (cm) to <20 cm from the incisors.
- Upper thoracic oesophagus extends from the thoracic inlet to the lower border of the azygos vein; 20 cm to <25 cm from the incisors.
- Middle thoracic oesophagus extends from the lower border of the azygos vein to the lower border of the inferior pulmonary vein; 25 cm to <30 cm from the incisors.
- Lower thoracic (distal) oesophagus extends from the lower border of the inferior pulmonary vein to the stomach, including the abdominal oesophagus; 30-40 cm from the incisors.
- Upper oesophagus is equal to cervical oesophagus and upper thoracic oesophagus.
- Middle oesophagus is equal to middle thoracic oesophagus.
- Lower oesophagus is equal to lower thoracic oesophagus or distal oesophagus.

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Figure 4.

A. Oesophagogastric junction (OGJ) tumours with their epicentre located >20 mm into the proximal stomach are staged as stomach cancers.

B. Cancers in proximal stomach not involving the OGJ are staged as stomach cancers.

C. Tumours involving the OGJ with their epicentre <20 mm into the proximal stomach are staged as oesophageal cancer. Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the American Joint Committee on Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing.

Figure 5. Oesophageal carcinoma with involvement of nerve (blue arrow) and invading into a vessel (black arrow).

Figure 6. Margins in resected specimen.

A. Proximal margin status: The extent of the carcinoma may be more than the macroscopic appearance of the tumour (T). There is a satellite growth (S) near the proximal margin and with narrow macroscopic margin (arrow). The exact margin requires microscopic confirmation.

B. Adventitia margin status: Oesophageal carcinoma with superficial involvement into adventitia (T3). The measurement of the tumour from the inked adventitial (circumferential) margin is shown.

Table 1. Core and non-core elements for the pathology reporting of carcinoma of the oesophagus.

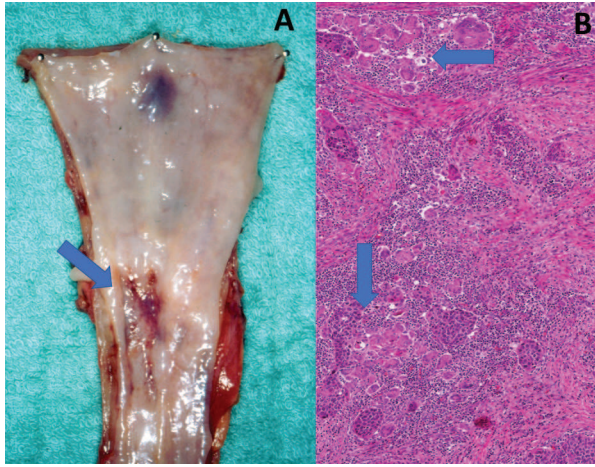
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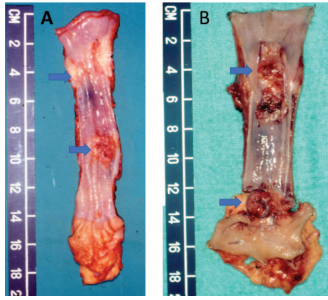
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Table 1: Core and non-core elements for the pathology reporting of carcinoma of the oesophagus.

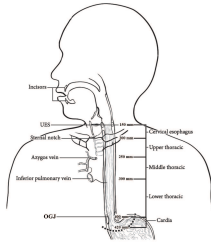
CORE	NON-CORE
Neoadjuvant therapy	Clinical information
Operative procedure	Specimen dimensions
Tumour focality	Macroscopic appearance
Tumour site	Tumour site <ul style="list-style-type: none"> Distance from epicentre/midpoint of tumour to oesophagogastric junction
Tumour dimensions <ul style="list-style-type: none"> Maximum tumour dimension 	Tumour dimensions <ul style="list-style-type: none"> Additional dimensions
Macroscopic distance of tumour to the margin	Barrett mucosa
Histological tumour type <ul style="list-style-type: none"> World Health Organization Classification 	Perineural invasion
Dysplasia	Lymph node status <ul style="list-style-type: none"> Extranodal extension
Histological tumour grade	Coexistent pathology
Extent of invasion	Ancillary studies <ul style="list-style-type: none"> HER2 testing performed PD-L1 Microsatellite instability Other
Lymphovascular invasion	
Response to neoadjuvant therapy	
Margin status	
Lymph node status	
Ancillary studies <i>For neuroendocrine neoplasms only</i> <ul style="list-style-type: none"> Neuroendocrine markers Ki-67 proliferation index 	
Histologically confirmed distant metastases	
Pathological staging	



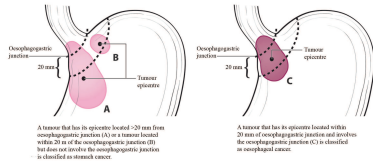
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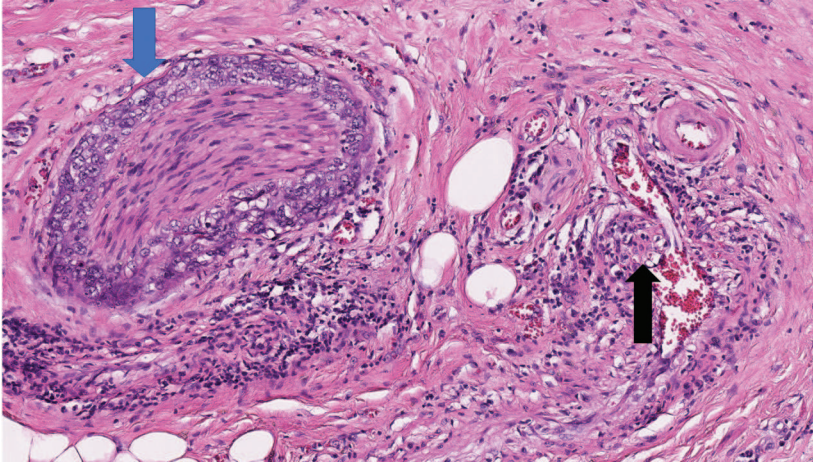
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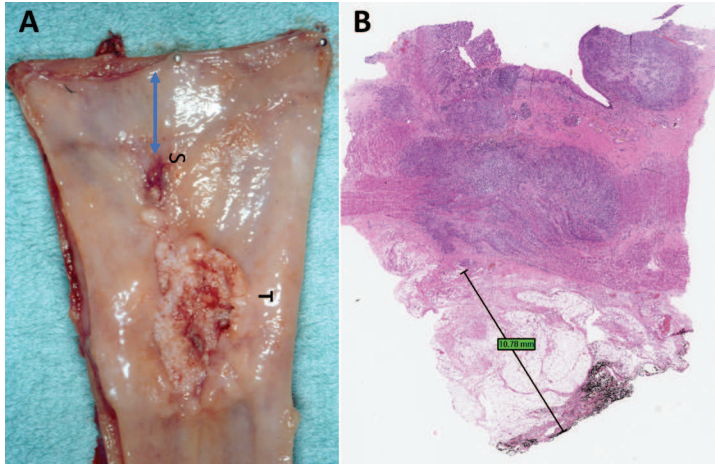
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