

Appendix 1: supplementary materials

A1: staging methods

Clinical stage measures the extent of the cancer based mainly on imaging findings prior to commencing neoadjuvant therapy using TNM classification and pathological stage is the stage based on histopathological examination of the resected specimen (28).

The TNM components of the clinical and post neoadjuvant stage were obtained from the data set in the gastro-oesophageal surgical registry at Alfred Health based on histopathological and radiological reports. The eighth edition of the American Joint Committee on Cancer (AJCC) staging of epithelial cancers of the oesophagus and gastroesophageal junction was then used to assign clinical (cTNM) and post-neoadjuvant (ypTNM) stage groups which included A and B staging. This was then simplified to an aggregated staging format from lowest to highest: stages I or II, stage III, and stage IV but adding an additional lowest category of complete pathological response (CR). Although surgery would not be indicated for Stage IV in the AJCCv8, at the time some patients underwent surgery, they would have qualified based on the AJCCv7. This retrospective cohort study involved reclassifying patients based on AJCCv8.

Downstaging was defined as moving down a category between clinical diagnosis stage and post-neoadjuvant stage, i.e., attaining a partial or complete response. Progressive disease was defined as moving up a stage category.

A2: neoadjuvant therapy regimens

The purpose of this analysis was not to assess the specifics

of the type of neoadjuvant chemotherapy or neoadjuvant chemoradiotherapy but to look in broad terms of the effect of either regimen on the post-neoadjuvant stage to evaluate prognostic outcomes. The majority of patients (85%) who received a neoadjuvant chemotherapy were in the form of a perioperative regimen of ECF/ECX of the MAGIC protocol. Please refer to *Table 1* for a breakdown of neoadjuvant chemotherapies. On the other hand neoadjuvant chemoradiotherapy was administered in the form of the CROSS protocol which included: 41.4 Gy/23#: 1.8Gy #5 days a week, neoadjuvant concurrent chemotherapy (NACT – Carboplatin AUC 2 and Paclitaxel (50 mg/m² of BSA on days 1, 8, 15, 22 and 29) with surgery 4–6 weeks after completion.

A3: positron emission tomography (PET) usage

Data on whether a PET scan was performed for a patient was not collected. However, in the time period in which neoadjuvant chemoradiotherapy was utilized, more accurate imaging modalities (such as PET scans) were more generally available which may have led to a bias in this cohort of patients.

References

28. Rice TW, Gress DM, Patil DT, et al. Cancer of the esophagus and esophagogastric junction-Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin* 2017;67:304-17.

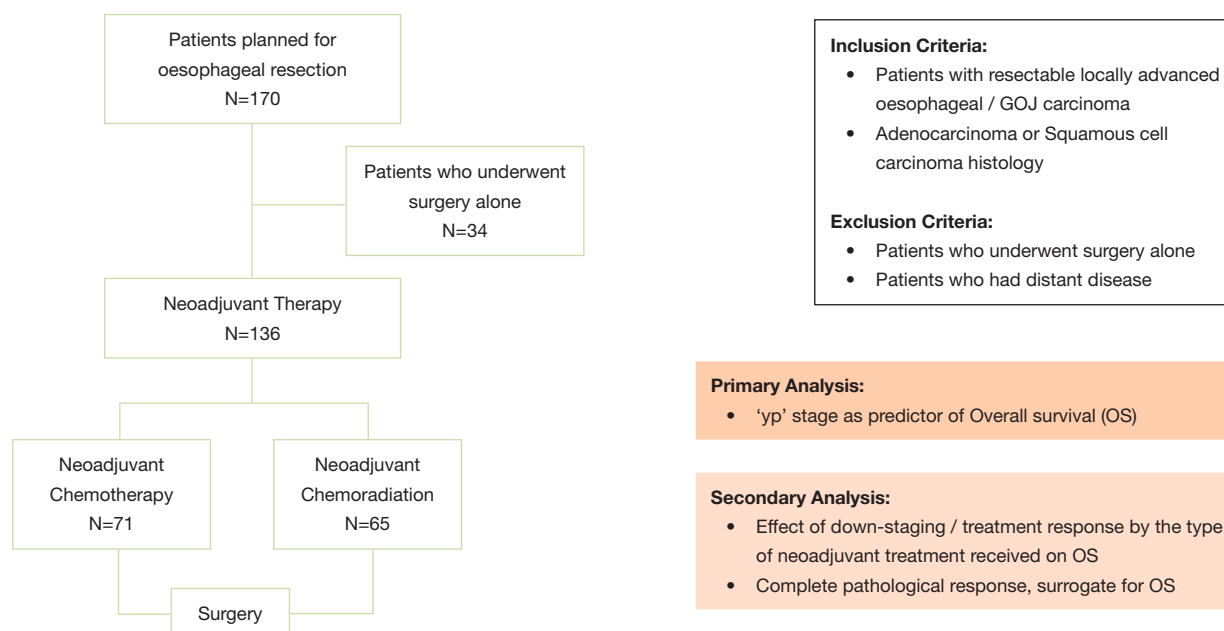


Figure S1 Study design for retrospective observational cohort study. GOJ, gastro-oesophageal junction.

Table S1 Clinical and yp stage by neoadjuvant treatment, adenocarcinoma only

Type of neoadjuvant therapy	yp stage, n [row %]			
	CR	I/II	III	IV
Chemotherapy				
I/II	1 [11]*	3 [33]	1 [11]**	4 [44]**
III	4 [8.2]*	16 [33]*	18 [37]	11 [22]**
IV	1 [13]*	2 [25]*	4 [50]*	1 [13]
Chemoradiation				
I/II	3 [43]*	3 [43]	0**	1 [14]**
III	4 [13]*	13 [41]*	11 [34]	4 [13]**
IV	1 [25]*	1 [25]*	2 [50]*	0

** , indicate progressive disease; * indicate downstaging (partial response and complete response). n, number of patients; (row %), percentage in row that achieved the "yp" stage category. CR, complete response.

Table S2 Pattern of relapse based on neoadjuvant therapy received

	Local recurrences	Distant recurrences	Both local and distant recurrences	No recurrence at last review	Unknown/additional malignancy
Neoadjuvant chemoradiotherapy (n=65)	1 (2%)	15 (23%)	3 (5%)	42 (65%)	4 (6%)
Neoadjuvant chemotherapy (n=71)	10 (14%)	27 (38%)	3 (4%)	29 (41%)	2 (3%)

n = number of patients, (%) = percentage of patients in cohort.

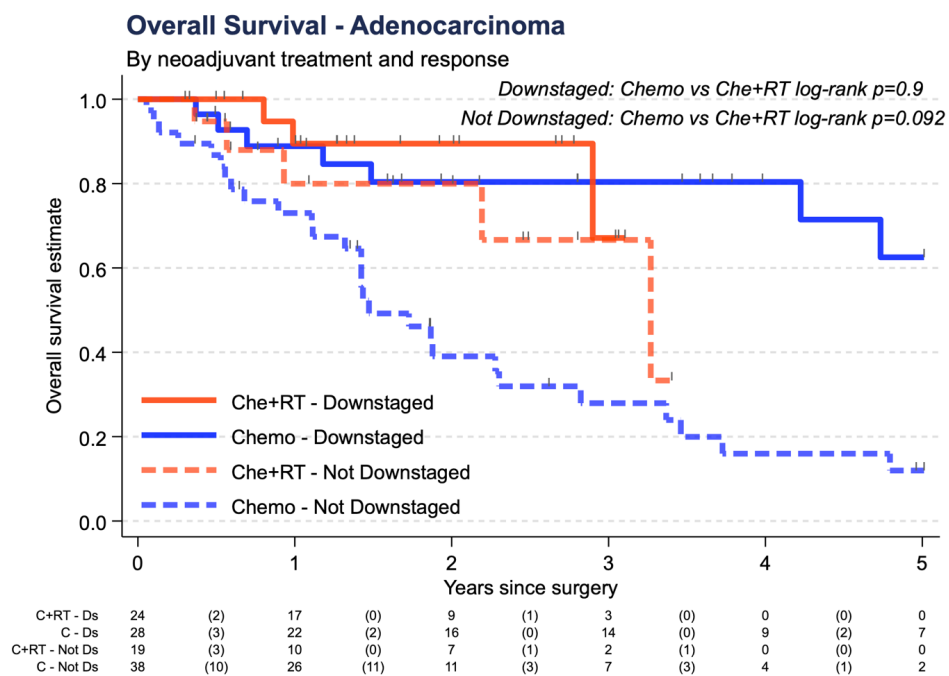


Figure S2 Adenocarcinoma only overall survival Kaplan-Meier curves, by neoadjuvant treatment and if downstaged between clinical and pathological stage. Che + RT, chemotherapy + radiation therapy; Ds, downstaged.