The 8th edition of the AJCC TNM staging system showes slightly improved, but still not perfect prognostication for esophageal carcinomas treated by neoadjuvant therapy followed by surgery

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BACKGROUND AND AIMS

The 8th edition of the UICC/AJCC TNM staging system (TNM8) provides slight, but simplifying changes compared to the preceding 7th edition (TNM7) In addition, the AJCC presents for the first time a specific staging system for esophageal carcinomas treated with neoadjuvant therapy followed by surgery. We compared the prognostic value of this novel staging system of AJCC TNM8 with TNM7.

TNM7			
Stage	pT	pN	pM
IA	1	0	0
IB	2	0	0
IIA	3	0	0
IIB	1, 2	1	0
IIIA	4a	0	0
	3	1	0
	1, 2	2	0
IIIB	3	2	0
IIIC	4a	1,2	0
	4b	Any	0
	Any	3	0
IV	Any	Any	1

yTNM8			
Stage	ypT	ypN	ypM
I	0-2	0	0
II	3	0	0
IIIA	0-2	1	0
IIIB	0-3	2	0
	3	1	0
	4a	0	0
IVA	Any	3	0
	4a	1-2	0
	4b	Any	0
IVB	Any	Any	1

MATERIALS AND METHODS

Patients: Out of 272 patients who consecutively underwent surgery due to esophageal malignancy between 2001 and 2016 in the Department of Visceral Surgery at the Inselspital Bern, we selected all 198 cases with esophageal carcinomas (144 adeno; 54 squamous cell carcinomas) treated with neoadjuvant radiochemotherapy (n= 147) or chemotherapy (n= 51).
Treatment: Preoperative radiation was performed with at least 40Gy. Chemotherapy was 5-FU and Cisplatin/Carboplatin based. For surgery, a transmediastinal esophagectomy with a radical bilateral mediastinal en-bloc lymphadenectomy (TME) was performed in most cases. Mean number of resected lymph nodes was 26. In 180 cases, complete tumor resection was achieved. In 7 cases, no esophagectomy was performed (evidence of distant metastases during surgery), however, these cases were classified as stage IV (TNM7) or IVB (TNM8)

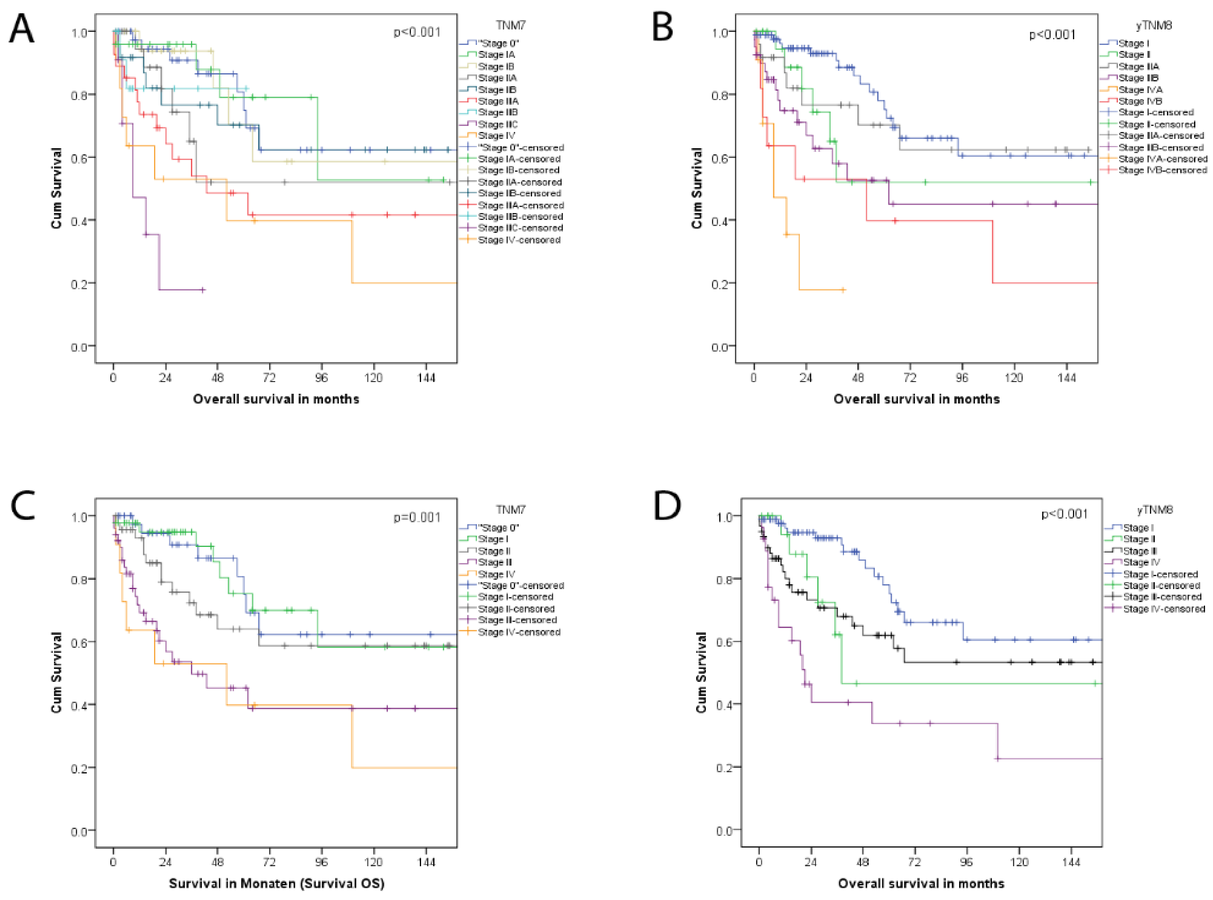
Histology work up The whole macroscopically detectable tumor bed was embedded. HE staining was performed for routine histopathological analysis. In cases without viable tumor in the first sections, additional deeper sections were performed. The ypT, ypN and M categories were recorded from the pathology files, or obtained from the original slides if the information in the original report was unclear
Staging Tumor stage were classified according to TNM7 and TNM8. TNM7 staging was expanded by the additional introduction of a „stage 0“ in cases of ypT0N0M0 tumors which would have been reserved for ypTis tumors in the original staging systems. Cases with lymph node or distant metastases without evidence of residual cancer in the primary tumor site (i.e. ypT0N>0/M>0) were classified according to the lowest T category in the respective

RESULTS

Stage Distribution in TNM7 and TNM8: Complete regression of the primary tumor was observed in 50 cases (25.25%). The cases were included into stage I (ypT0N0M0; n=42), stage IIIA (ypT0N1M0; n=6) stage IVA (ypT0N3M0; n=1) and stage IVB (ypT0N0M1; n=1) in TNM8. Besides the 42 cases with complete regression of the primary tumor and without metastases, 24 cases of TNM7 stage IA and 20 cases of TNM7 stage IB tumors were incorporated into the newly defined yTNM8 stage I group. yTNM8 stage II is equal to TNM7 stage IIA, and yTNM8 stage IIIA is equal to TNM7 stage IIB.
In yTNM8 stage IIIB there are tumors with TNM7 stage IIIA and IIIB now collapsed, meaning a simplification of stages but not literally a stage migration.

		yTNM8						Total
		Stage I	Stage II	Stage IIIA	Stage IIIB	Stage IVA	Stage IVB	
	„Stage 0“	42	0	0	0	0	0	42
	Stage IA	24	0	0	0	0	0	24
	Stage IB	20	0	0	0	0	0	20
	Stage IIA	0	21	0	0	0	0	21
TNM7	Stage IIB	0	0	24	0	0	0	24
	Stage IIIA	0	0	0	27	0	0	27
	Stage IIIB	0	0	0	13	0	0	13
	Stage IIIC	0	0	0	0	11	0	11
	Stage IV	0	0	0	0	0	16	16
Total		86	21	24	40	11	16	198

Survival Analysis Mean survival was 172 months (95%CI 45-300). There was no significant difference between adeno- and squamous cell carcinomas (p=0.71). Higher pT category (p<0.001), pN category (p<0.001), resection status (p=0.003) and in trend presence of distant metastases (p=0.090) were associated with worse overall survival.
Tumor staging in TNM7 showed highly significant prognostic impact (p<0.001). However, stage IIB tumors (pT1/pT2N1) had better prognosis compared to stage IA (ypT1N0), IB (pT2N0) and IIA (pT3N0) tumors. For TNM8, a similar prognostic value was observed when using the novel proposed ypTNM classification (p<0.001), and, likewise stage IIIA tumors (ypT0-2N1) were better than stage II (ypT3N0)



Comparison of TNM7 and yTNM8 Using AIC and SBC as parameters for goodness-of-fit, TNM8 was slightly superior regarding prognostication (TNM7 AIC=1593.239; SBC=1619.088; TNM8 AIC=1589.331; SBC=1605.487: lower values of AIC and SBC indicate superior model fit with the “better” model showing the lowest values for both). A simplified staging with collapsed stages (i.e. stages IIA and IIB collapsed to stage II) did not improve AIC or SBC values. Similar results were seen for adenocarcinomas and squamous cell carcinomas if analyzed separately

CONCLUSION

The 8th edition of the AJCC TNM classification allows for the first time accurate staging esophageal carcinomas treated by neoadjuvant therapy. Prognostication has slightly improved as compared to the preceding TNM7, but still appears not perfect.