

Can Imaging Response following Neoadjuvant Chemotherapy in Upper Tract Urothelial Cancer be a Surrogate for Pathologic Response?

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Introduction

- Pathological response following neoadjuvant chemotherapy (NAC) has been shown to be an excellent surrogate for survival in bladder cancer.
- Preoperative endoscopic and pathologic assessment of response is difficult in upper tract urothelial cancer (UTUC).
- The aim of this study was to see whether imaging response following NAC predicted the final pathologic stage and outcomes following radical nephroureterectomy (NU).

Methods

- Of the 685 NUs, cytology and/ biopsy proven, $\geq cT2$ any NM0 high grade UTUC patients who underwent NAC with cisplatin based chemotherapy from Jan 1997 – Jul 2017 were analyzed.
- CT/MR urography was available both before and after NAC. Radiological response rate (RRR) was estimated using the RECIST criteria and pathologic response was defined as $< pT2$.
- We assessed the association between response on radiology and final pathology using Fisher's exact test. Multivariable Cox proportional hazard regression model was used to assess association between RRR and overall survival.

Results

- 62 (9.1%) underwent cisplatin based NAC prior to surgery.
- 16% of patients had complete response on imaging, 52% had partial response, 27% had stable disease, and the remaining 5% progressed. Thirty-six patients (58%; 95% CI 45%, 70%) responded to NAC on pathology.
- The median radiological response rate was 0.44 (0.22, 0.80). The mean RRR stage for responders was 0.64 and 0.21 for the non-responders ($p < 0.0001$), Figure 1.
- Radiological response was significantly associated with pathological response on both univariate (OR 8.45; 95% CI 2.49, 28.74; $p = 0.001$) and multivariable (9.14; 95% CI 2.57, 32.56; $p = 0.001$) analyses, Table 1.
- Pathological response was associated with significant better overall survival (HR 0.20; 95% CI 0.06, 0.64; $p = 0.007$), Figure 2.
- On multivariable analysis, radiological response was associated with non-significant better overall survival (HR 0.48; 95% CI 0.17, 1.31; $p = 0.2$).

Figure 1 Mean RRR for responders vs. non-responders

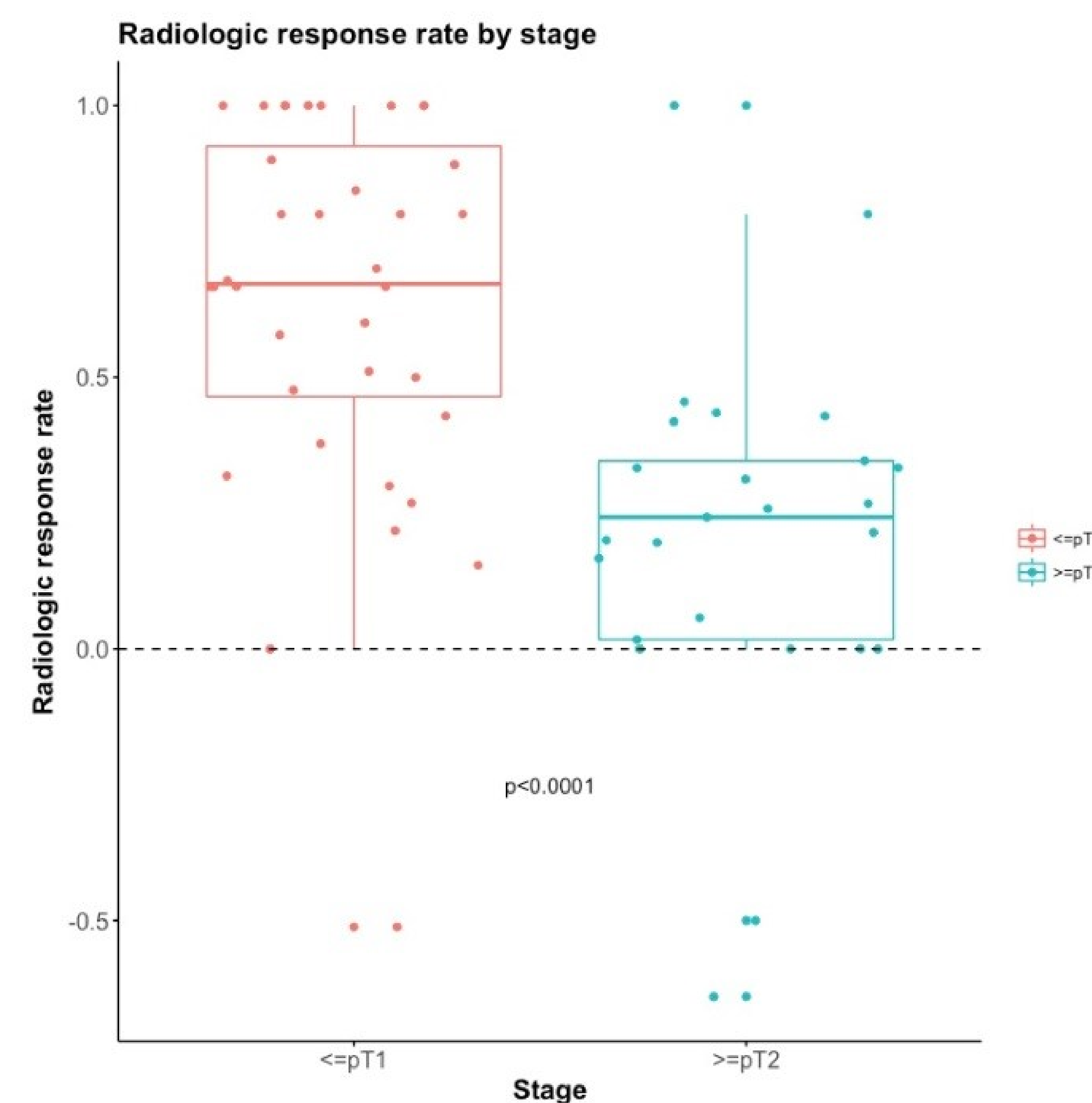
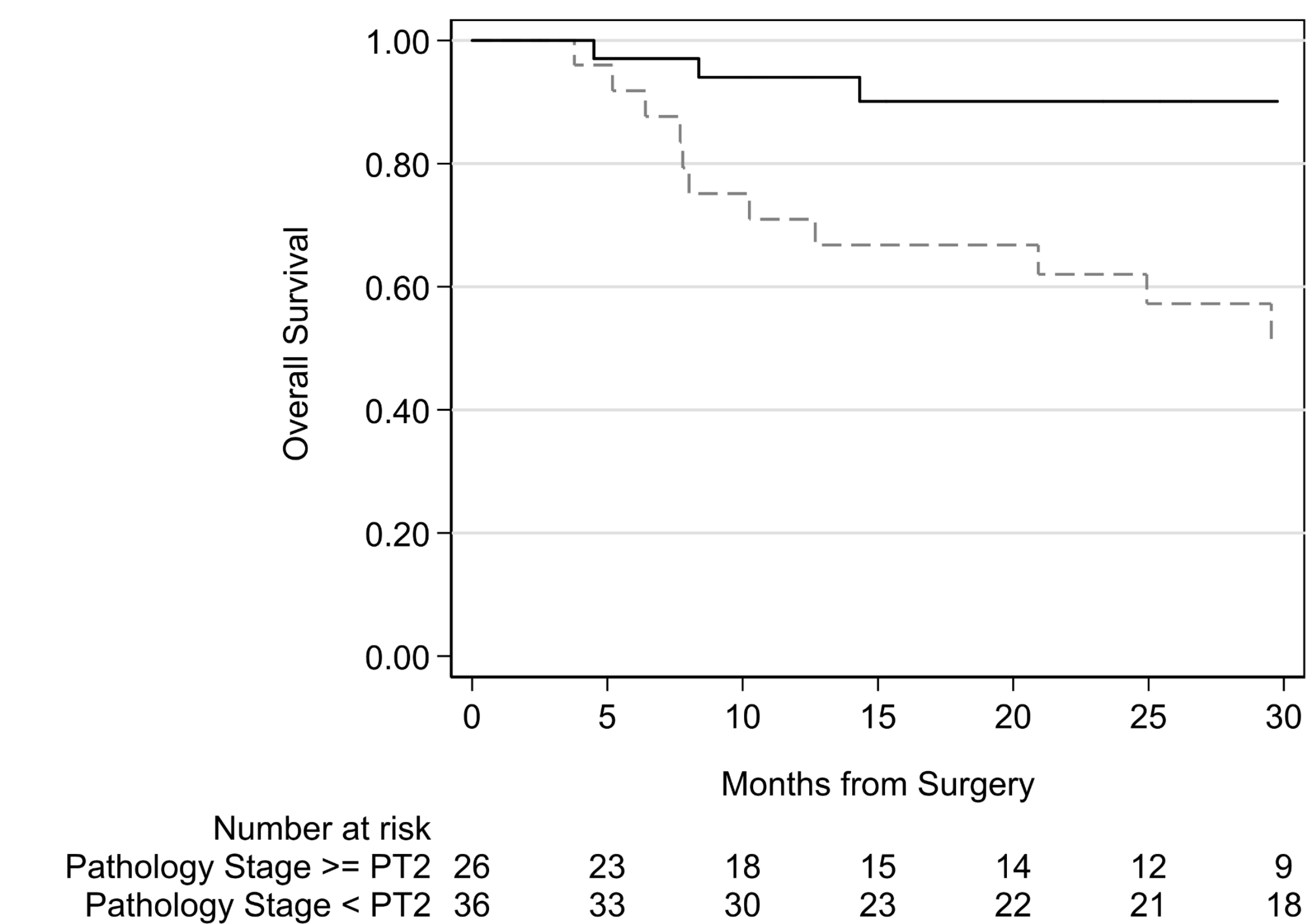


Table 1 Patients based on response on radiology scans and pathology (Fisher's exact $p = 0.0004$)

Response to Chemotherapy		Pathological response	
		Yes	No
Radiological response	Yes	31	11
	No	5	15

Figure 2 Kaplan-Meier estimated overall survival probability for patients with response on pathology (solid black line) and no response on pathology (dashed grey line)



Conclusions

- Radiological response rates following NAC in UTUC is significantly associated with pathologic response and non-significantly associated with better overall survival following NU.
- Unlike bladder cancer, there is lack of level I evidence recommending NAC in UTUC. Moreover, toxicity and overtreatment are major concerns.
- Therefore, RRR could be used as a preoperative tool to predict prognosis and identify the "chemo-resistant" cohort who could then be counseled for alternate treatment modalities.