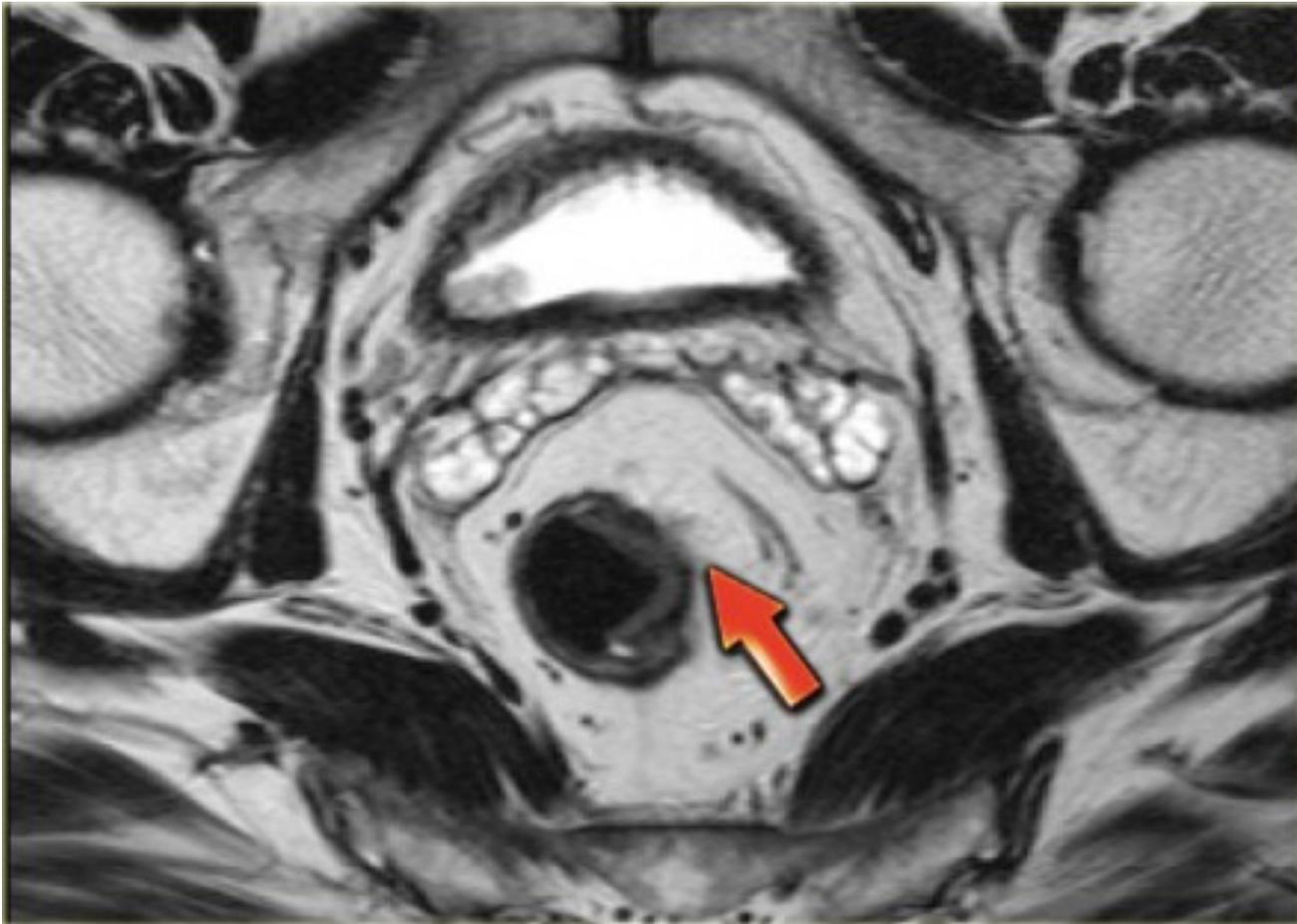


The relationship between the degree of T3 mesorectal invasion in rectal cancer and the complete pathological response rate after neoadjuvant long-course chemoradiotherapy

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Background



Picture from tinyurl.com/qchxlc2



Background

- **Typical Rectal cancer treatment:**

Diagnosis: MRI or ultrasound

Therapy (Short course radiotherapy - 5 days
or long course chemoradiation therapy - 5 wks)

Interval (SCRT - 12 days, LCCRT - 8 weeks)

(Restaging MRI)

Surgery (complete pathological response (pCR)?)

Adjuvant chemotherapy

pCR outcomes result in better overall survival (93% 5 year survival rate),
lower local recurrence rates, adjuvant therapy can be omitted

Aim

- To document the pCR rate and outcomes in patients receiving preoperative long-course chemoradiotherapy stratified for the extent of T3 mesorectal invasion measured on preoperative MRI



Methods

- A retrospective study of prospectively collected data of rectal cancer patients from the Cabrini Monash University colorectal neoplasia database.
Cabrini and Alfred Hospital patients between Jan. 2010 and June 2014
(Selection criteria: T3 rectal cancer, MRI diagnosis, LCCRT, surgery)
- Additional data from patient histories and MRI films from regional imaging centres
- Degree of mesorectal invasion in patient MRI films all re-assessed by same Radiologist blind to patient outcome (according to Mercury protocol)
- Patients followed-up for at least 12 months to June 2015



Overview of patient cohort

- 118 patients met the selection criteria
- 66.9% male
- Mean age 61.5 years (no significant difference between male/female)
- Median follow-up time was 36.9 months (range 0.2-65)
- Down-staging seen in 61.9%
- 26 patients achieved pCR (22.03%)



Comparing pCR to No pCR outcomes

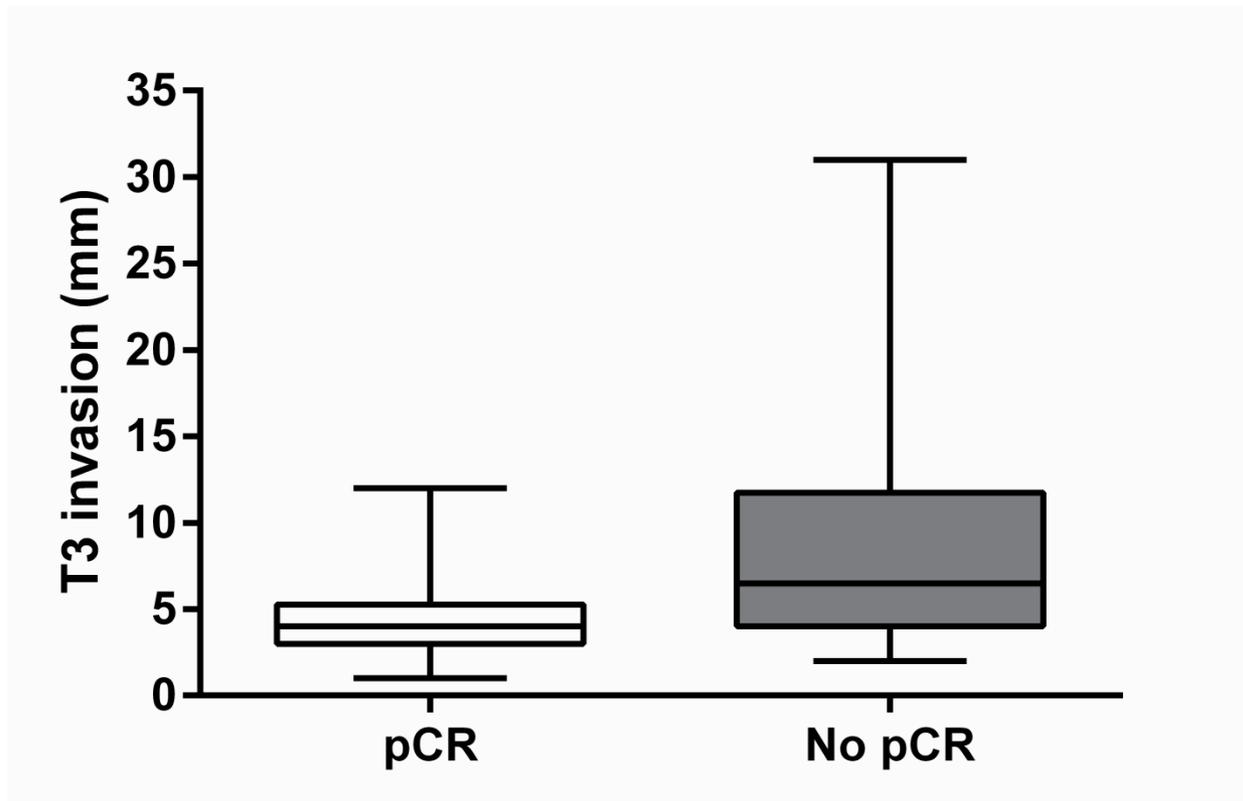
	pCR	No pCR	p
Days between LCCRT and surgery- Mean (SEM)	56.6 (± 2.7)	57.0 (± 1.6)	0.89 [†]
Mean (SEM) distance from anal verge in cm	7.2 (± 0.6)	7.1 (± 0.3)	0.86 [†]
Median T3 invasion in mm (range)	4 (1-12)	7 (2-31)	<0.001*

([†] unpaired two-tailed t-test, *Kruskal-Wallis equality of populations test)

No significant difference between pCR and 'No pCR' groups in chemotherapy type, radiation dose, procedure type, rectal cancer site (upper, middle, lower), preoperative nodal status



Less T3 invasion in pCR than No pCR patients



pCR mean (SEM) 4.4 ± 0.5 , No pCR 8.7 ± 0.6
(Unpaired two-tailed t-test $p < 0.001$)



Linear relationship between invasion and pCR

- Less T3 invasion was associated with a higher likelihood of pCR (Odds Ratio 0.74, 95% CI 0.62-0.90, $p < 0.002$, logistic regression)
- The chance of achieving a pCR outcome was decreased by ~35% for every mm of invasion (depth of invasion as predictor value and pCR as outcome variable)
- Not associated with pCR outcome:
 - Preoperative nodal status
 - Interval between LCCRT completion and surgery
 - Distance of tumour from anal verge
 - Surgical procedure type

Disease-free survival in patients

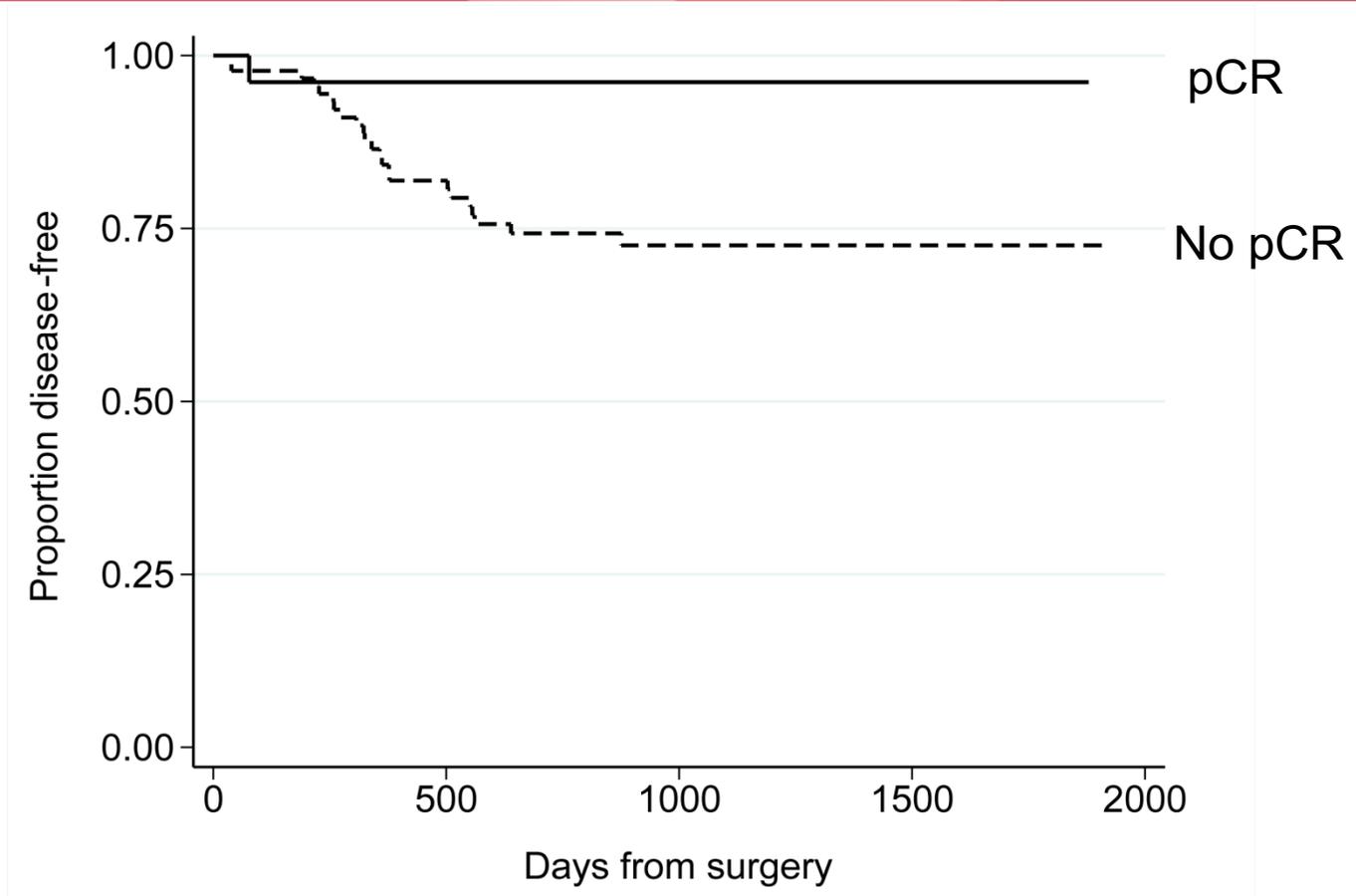
	pCR	No pCR	p
Local recurrence	0%	1.1%	0.78‡
Distant metastasis	3.8%	23.9%	0.02**

‡ Fisher's exact test, **Log-rank test

- Significantly higher rate of metastasis in 'No pCR' patients (p=0.02)
- pCR associated with lower risk of cancer progression (p=0.046, Cox regression univariate)
- No association: age, gender, depth of invasion, distance of tumour from anal verge, interval between LCCRT completion and surgery



Disease-free survival in patients



Significantly higher rate of disease free survival for pCR patients ($p=0.018$)

Overall survival in patients

- 'No pCR' patients had a significant higher rate of death following surgery (14.1% vs. 0%, $p=0.032$ Fisher's Exact test)
- Depth of T3 invasion was associated with increased risk of post-op death
Hazard Ratio increased by 1.07 (95% CI 1.00-1.15) for each 1 mm of invasion
- No association: age, gender, distance of tumour from anal verge, interval between LCCRT completion and surgery. No deaths in pCR group so no HR.



Conclusions

- pCR rate is related to degree of T3 mesorectal invasion
- Likelihood of pCR is reduced by 35% for every mm of T3 invasion
- A pCR outcome is associated with a lower risk of cancer progression
- Every mm of T3 invasion increases chances of post-operative death
- No association of a pCR outcome with nodal status, age, gender, surgical procedure, tumour type, distance from anal verge
- Limitations of this study: Not a randomised clinical trial, data from two centres however all data except T3 invasion was prospectively collected



Complete Pathological Response After Neoadjuvant Long-Course Chemoradiotherapy for Rectal Cancer and Its Relationship to the Degree of T3 Mesorectal Invasion

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DCR podcast discussion on the article coming soon!



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