FINAL ID: S31

SESSION SYMPOSIUM NAME:

TITLE: Lateral Pelvic Lymph Node Positivity (LPLNP) score: predictive clinico-radiological model of lateral pelvic lymph nodes involvement in rectal cancer patients

ABSTRACT BODY:

Purpose/Background: Japanese guidelines recommend prophylactic lateral pelvic lymph node dissection (LPLND) for all advanced low rectal cancer. Recently, LPLN short axis >6-8 mm on MRI was proposed to plan selective LPLND. But tumor invasiveness or MRI LPLN size only can't accurately predict LPLN metastases (LPLN+). Thus, a more precise clinico-radiologal tool is needed to evaluate the risk of LPLN+ and plan highly “selective” LPLND.

Methods/Interventions: This was a retrospective-prospective single center study of patients with curative resection and LPLND for stage II–III low rectal adenocarcinoma. In retrospective patients, MRI T-stage, extramural vascular invasion (mrEMVI), mesorectal fascia involvement, mucinous tumour, suspicious LPLNs (mrLPLN+) having short-axis ≥6 mm and/or irregular borders, heterogeneous signal, or round shape were evaluated. Some patients underwent long-course chemoradiotherapy. Open, laparoscopic or robotic anterior, low anterior, intersphincteric, or abdominoperineal resections were performed. Selective bilateral LPLND was done if suspicious LPLNs were found on pretreatment MRI. Some patients had prophylactic bilateral LPLND (no suspicious LPLN). Clinical and MRI factors associated with LPLN+ were identified, and a logistic regression and ROC-analyses used to build up LPLNP score. It was further tested on a prospective cohort.

Results/Outcomes: 1091 patients underwent curative rectal resection in 2009-2019. Among them, 120 had LPLND: 91 selective and 29 prophylactic. The incidence of LPLN+ was 29.2% (35 patients). LPLN+ were found in 4 out of 25 patients (16%) with no visible LPLNs on MRI and in 1 out of 7 patients with LPLNs <6 mm. Compared to pathology, MRI had high sensitivity (88.6%), but low specificity (12.9%) in determining LPLN+. After stepwise reduction, the following parameters were included in the model: tumor distance from the anal verge, mrEMVI status, LPLN short-axis diameter on pretreatment MRI, mr-T stage, and histological differentiation on pretreatment biopsy. Finally, to make LPLNP score, each factor was assigned a numeric value (Figure 1). In ROC-analysis, a cut-off score of 0.23 with highest sensitivity and specificity (82.9% and 69.4%) was selected. When tested on 66 prospectively selected low rectal cancer patients, 40 had LPLND score >0.23 and thus underwent selective LPLND. Among them, LPLN+ were confirmed in 55%. LPLND score negative predictive value was 96%, sensitivity – 96%, specificity – 58%.

Conclusions/Discussion: This is the largest reported cohort of western rectal cancer patients with LPLND. MRI alone has low specificity in determining LPLN+: metastases were found not only in enlarged LPLNs, but in LPLN <6 mm or no visible LPLNs. When LPLND is done based on only clinical or MRI factors, the incidence of LPLN+ was 29%. When a complex clinico-radiological tool was applied, the incidence of LPLN+ increased up to 55%.

(no table selected)

Clinico-radiologic LPLNP score

		Variable	Numeric value
k1	cm from anal verge	0-6.0 6.1-12.0 >12.1	1 2 3
k2	mrEMVI	positive negative	1 0
k3	LPLN short-axis on MRI (mm)	no visible 0.1-6.0 6.1-10.0 10.1-20.0 >20.0	0 1 2 3 4
k4	mrT-stage	mrT1 mrT2 mrT3 mrT4	1 2 3 4
k5	tumor differentiation at pretreatment biopsy	G1 G2 G3 mucinous signet cell	0 1 2 3 4

Logistic regression equation

$$D = \frac{1}{1 + e^{-z}}$$

D = probability of event of interest
z = standard regression equation
e = Euler's number (2.71828)

Standard regression equation (z)

$$z = a1 \times k1 + a2 \times k2 + a3 \times k3 + a4 \times k4 + a5 \times k5 + a0$$

a1, a2, a3, a4, a5 = logistic regression coefficients
a0 = intercept
k1, k2, k3, k4, k5 = numeric values (from table above)

Online calculator can be found at https://siterscs.com/LPLNDscore

Example 1

- 4 cm from the anal verge (k1 = 1)
- mrEMVI positive (k2 = 1)
- no visible LPLN on pretreatment MRI (k3 = 0)
- mrT4 (k4 = 4)
- G2 tumor at bipsy (k5 = 1)

D = 0.26 (>0.23 cut-off)
LPLND is indicated even in the absence of visible LPLN

Example 2

- 12 cm from the anal verge (k1 = 3)
- mrEMVI negative (k2 = 0)
- Short-axis of LPLN 12 mm on pretreatment MRI (k3 = 3)
- mrT4 (k4 = 4)
- G3 tumor at bipsy (k5 = 2)

D = 0.046 (<0.23 cut-off)
LPLND is not indicated even the short-axis LPLN is greater than 8 mm

IMAGE CAPTION:

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S30A
RACS Killingback Award Winner

Immune Profile of Rectal Tumours in the Setting of Neo-adjuvant Immune Checkpoint Blockade (PD-L1) as Part of the AveRec Phase II Clinical Trial.

Purpose/Background: The treatment break between neoadjuvant chemoradiotherapy and surgery in rectal cancer can be utilised to investigate novel treatments. To investigate the role of PD-L1 blockade (velumab) as a neoadjuvant agent in rectal cancer we conducted a phase II clinical trial (Ave-Rec). The translational component of this study was to investigate the impact of PD-L1 therapy on the immune landscape of rectal cancer patients. Of particular interest were tissue resident memory cells (T_{RM}), a relatively newly described lymphocyte lineage that do not recirculate in the lymphatics. T_{RM} cells have been implicated in local responses to cancer and $CD8^+$ T_{RM} cells express high levels of PD-1, making them attractive targets for immune checkpoint blockade (ICB). Multiplex immunohistochemistry (mIHC) combined with multispectral imaging is a rapidly evolving technology that has extended the information gained from traditional immunohistochemistry by enabling the detection of multiple biomarkers on a single slide. This digital pathology technique can be utilised to gain substantial information about immune cell subsets. The aim of this study was to investigate the role of neo-adjuvant ICB on the immune landscape in rectal cancer utilising mIHC.

Methods: A phase II multicentre trial was conducted. Patients received long course chemoradiotherapy (LCCRT) consisting of 50.4 Gy of radiotherapy in conjunction with 5FU/Capecitabine followed by 4 cycles of Avelumab (10mg/kg). Research biopsies were obtained for patients at three time points (screening, post LCCRT and post avelumab). An additional cohort of patients who received only LCCRT were used as a control. OPAL POLARIS mICH was completed for 3 panels (T_{RM}, T-cell and pan immune) to assess the following cell populations; T_{RM}, $CD8^+$ $T_{RM,}$ T-Cell, $CD8^+$ T-cell, $CD4^+$ T-cell, B -cell, macrophage, T_{REG}, as well as PD-1 and PD-L1 expression. Additionally, tertiary lymphoid like structures were identified and characterised.

Results: There was an increase in the number of $CD8^+$ T_{RM} cells present post treatment with when compared with pre-treatment biopsies ($p=<0.05$) and with biopsies obtained following treatment with LCCRT ($p=<0.05$). In addition, there was an increase in the number of B cells ($p=<0.01$) and PD-L1 expressing macrophages ($p=<0.05$) in patients receiving immunotherapy compared to the control cohort. Overall PD-L1 expression was significantly increased within tertiary lymphoid like structures of patients receiving Avelumab ($p=<0.05$).

Conclusion: To our knowledge this is the first description of $CD8^+$ T_{RM} cells pre and post PD-L1 therapy in rectal cancer. $CD8^+$ T_{RM} cell numbers appear to increase in response to treatment with Avelumab but not LCCRT. In addition, PD-L1 therapy appears to have a dramatic influence on the expression of PD-L1 within tertiary lymphoid structures.

Disclosures:
Funding from this trial was obtained from Merck.

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FINAL ID: S32

SESSION SYMPOSIUM NAME:

TITLE: “Watch-and-Wait” or “Lost to follow-up”: Real-world Adherence to Surveillance for Non-operative Management of Rectal Cancer

ABSTRACT BODY:

Purpose/Background: Due to shortcomings in existing restaging techniques and subsequent local regrowth in up to 30% of patients undergoing active non-operative management of rectal cancer, current guidelines recommend intensive surveillance as part of any “watch-and-wait” paradigm. These regimens impose significant burden on patients despite the relative paucity of data regarding optimal frequency of examinations. The aim of this study is to evaluate patient compliance with recommended active surveillance and identify differences in oncologic outcomes associated with poor compliance.

Methods/Interventions: All patients with adenocarcinoma of the rectum received total neoadjuvant therapy with short-course radiation followed by consolidation chemotherapy (SC-TNT). Patients who opted for NOM after complete clinical response (cCR) were identified in an institutional, prospectively-maintained rectal cancer registry. Minimum recommended surveillance was defined as intraluminal exam every 4 months, pelvic MRI every 6 months, and annual CT chest/abdomen/pelvis. Compliance was quantified as the percentage of recommended examinations completed out of 6 total (3 imaging + 3 intraluminal) by each patient annually or until local recurrence was identified. Patients were grouped into compliance tertiles for analysis.

Results/Outcomes: Out of 255 patients who received SC-TNT from June 2016 to October 2021, 107 were found to have a cCR and met criteria for inclusion. 65 of these 107 patients were eligible for a second year of surveillance based on cCR date. Compliance results can be found in Table 1. 54 patients (50.5%) were fully compliant with the minimum number of recommended surveillance exams during the first year of NOM, and 22 patients (34%) during the second year. Average compliance with imaging and intraluminal exams was 86% and 82%, respectively, in year 1. In year 2, average compliance was 74% and 65%, respectively. Local recurrence was identified in 31 patients (29%), all but 1 of whom proceeded to surgery for definitive resection. Only one patient developed distant metastases (as well as local recurrence) during NOM and ultimately expired from complications.

Conclusions/Discussion: Half of our patients were fully compliant with the minimum number of recommended surveillance exams during the first year of NOM, and only 1/3 of patients during the second year. Real-world compliance may not reflect compliance in published clinical trials. While we regularly provide patient education and encouragement, compliance is ultimately patient-driven and requires commitment to rigorous surveillance. Conclusions regarding oncologic outcomes are significantly limited by patients with poor compliance or who were lost to follow-up.

(no table selected)

	YEAR 1			YEAR 2		
% compliance	# of patients (% of cohort)	# w/ local recurrence	# w/ development of distant metastasis	# of patients (% of cohort)	# w/ local recurrence	# w/ development of distant metastasis
Lost to follow-up (0%)	1 (1%)	0*	0*	6 (9%)	0*	0*
1-34%	7 (6.5%)	0	0	7 (11%)	0	0
35-67%	14 (13%)	0	0	18 (28%)	0	0
68-99%	31 (29%)	4	1	12 (18%)	1	0
Fully compliant (100%)	54 (50.5%)	24	0	22 (34%)	2	0

Table 1. Number of patients by average percent compliance with imaging and intraluminal exams (* = limited by lack of follow-up)

IMAGE CAPTION:

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