

# Is Radical Resection Necessary for ypT2 Rectal Cancer? Local Recurrence after Local Excision

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## Research Article

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# Abstract

## Purpose:

Downstaging following neoadjuvant therapy has prompted interest in organ preservation for rectal cancer. Questions remain regarding the adequacy of care when residual disease is confined to the rectal wall (ypT2). Some advocate radical resection (RR) in all such cases. We hypothesize that if cancer is confined to the muscular wall after neoadjuvant therapy, full-thickness local excision (FTLE) may serve as definitive treatment.

## Methods:

From a prospectively maintained database of rectal cancer, we identified all pathological T2 patients who received neoadjuvant therapy (ypT2). Patients were stratified by surgical approach: FTLE or RR. Clinical, perioperative, and oncologic outcomes were analyzed and compared between groups.

## Results:

Between 04/2000–07/2024, 216 patients with ypT2 rectal cancer were identified, 180 underwent RR and 36 underwent FTLE. Perioperative demographics, characteristics and outcomes were similar in both groups with differences in age, EBL and diverting stomas. Median follow-up was 75.9 months (range 0.4–289). Local recurrence was 2.8% in the FTLE group and 5% in the RR group ( $p=.999$ ). 5-year disease-free survival (DFS) rate was 82.7% for FTLE and 73.7% for RR patients ( $p=.494$ ). FTLE was associated with significantly lower CD grade  $\geq$  II complications ( $p < 0.001$ ).

## Conclusion:

FTLE with clear margins after neoadjuvant therapy appears to be a safe and effective definitive treatment for selected patients with ypT2 rectal cancer, potentially sparing RR. While additional experience and randomized trials will help better define the exact role of organ preservation with FTLE after downstage rectal cancer confined to the rectal wall, these findings support as expansion of this approach.

## Introduction

The management of rectal cancer has traditionally posed significant surgical challenges. A confined pelvic space, involvement of autonomic nerves, and proximity to the anal sphincter contribute to increased risks of local recurrence (LR) and functional complications when attempting adequate oncologic resection while also preserving sphincter function.[1], [2]

After a century of treatment dominated by abdominoperineal resection (APR), a multitude of interrelated developments offer new options for rectal cancer patients. Total mesorectal excision (TME) demonstrated improved outcomes with proper surgical technique, making it the most influential contribution and current surgical standard.[3], [4] However, major pelvic surgery is associated with a high morbidity profile.[5] Local excision has long been of interest, as it avoids major abdominal surgery and colostomy, offering better functional outcomes and reduced morbidity and mortality.[6], [7] Local excision is advocated as definitive surgical therapy for early T1 rectal cancers.[8] Currently, for rectal cancer beyond low-risk T1, local excision alone is only indicated in patients who are unsuitable for radical surgery.[9]

To expand sphincter preservation and decrease LR rates, radiation and chemotherapy have been employed.[10], [11] One benefit of neoadjuvant treatment in rectal cancer is the significant downstaging that occurs. Complete sterilization of the rectum, a complete pathologic response, can be achieved. This led to an interest in less radical surgery or observation without surgery.<sup>12,13</sup>

The optimal treatment strategy for downstaged tumors confined to the rectal wall without radiographic LN involvement after neoadjuvant therapy remains a subject of ongoing debate.

A Full-Thickness Local Excision (FTLE) is often performed to evaluate a scar with a question of residual cancer after neoadjuvant chemoradiotherapy.[12] This can be considered as an excisional biopsy or a therapeutic excision. Uncertainty exists regarding what should be done if residual cancer is found. Some advocate radical surgery for a ypT2 cancer, reasoning that persistent cancer cells are indicative of an unfavorable tumor biology, with potential lymph node (LN) involvement or distant metastasis.[13], [14] As part of a long-standing rectal cancer management program, our unit was the first to perform FTLE after preoperative radiation therapy and have considered FTLE as a definitive approach for ypT2 cancer.[15] The purpose of the study is to address the question of oncologic outcomes. We analyzed our long-term outcomes with FTLE as definitive therapy of ypT2 rectal cancer, to determine if local excision of ypT2 rectal cancer constituted adequate oncological treatment with a reasonable safety profile.

## Methods

From a prospectively maintained database of rectal cancer operations between April 2000 and July 2024 (IRB: E-22-5257) in a high-volume tertiary referral center, we identified all sequential pathological T2 patients who received neoadjuvant therapy (ypT2) for primary rectal adenocarcinoma, metastatic and recurrent cases were excluded.

Preoperative evaluation included a complete history and physical examination with clinical staging using digital rectal examination (DRE) and flexible sigmoidoscopy, and radiological staging using MRI, CT, and/or transrectal ultrasound interpreted by radiologists according to standard oncologic imaging protocols. The same modalities were used for re-staging after completion of neoadjuvant therapy. Tumor characteristics were recorded on presentation, and final post-radiation assessment was performed at 8–

10 weeks after completion of therapy. All patients diagnosed with rectal cancer in the distal half of the rectum)  $\leq 6$  cm from the anorectal ring), and T3 and node positive cancers at all levels were recommended to undergo chemo-radiation neoadjuvant therapy. The radiotherapy target dose was 5040–5580 cGy. Variances occurred as some patients were first evaluated after completion of radiotherapy elsewhere. All decisions regarding surgical approach were based on the rectal cancer following completion of neoadjuvant therapy. Patients with induction chemotherapy or total neoadjuvant therapy (TNT) were excluded, as well as “Watch & Wait” patients, as they had no pathologic specimen.

Inclusion criteria were based only on the final pathologic stage of the cancer (ypT2), regardless of initial or post treatment staging.

## Surgical selection criteria:

In considering cancer patients for FTLE, the following criteria were used:

- Elective-staged-patients: Post-neoadjuvant tumors staged at  $\leq$  T2 and size  $\leq 4$  cm for which FTLE is considered a reasonable alternative due to clinical response, patient refusal of radical surgery, or comorbid disease considerations making the patient an above average risk for radical surgery. If T3 cancer or positive LNs were found in the specimen, the patient proceeds to radical surgery at 6–12-week interval.
- Medically-compromised-patients: Post-neoadjuvant tumors preoperatively staged  $\geq$  T3 for which radical surgery is traditionally indicated but is not an option because the patient is unsuitable for radical surgery due to comorbid conditions. Local excision represents definitive therapy regardless of pathology.

For this study, all patients with pathologic residual cancer in the rectal wall (ypT2) after resection were identified. For analysis, as per study design patients were divided into two groups: FTLE and RR – proctectomy with total or partial mesorectal excision. FTLE was performed using endoluminal surgery with Transanal Endoscopic Microsurgery (TEM) or Single Port robotic Transanal Minimally Invasive Surgery (SP rTAMIS). Resection was carried out in a full-thickness fashion of the rectal wall with a portion or all of the mesorectum excised en-bloc. For RR partial-TME or TME technique was employed, depending on level of the cancer in the rectum. These groups were subsequently analyzed and compared in terms of initial preoperative data, tumor characteristics, neoadjuvant therapy, LR, 5-year overall survival (OS), disease-specific survival, morbidity using the Clavien-Dindo (CD) classification, and mortality.[16]

In follow up, disease status was designated to the following 4 categories: NED – no evidence of disease, DOC – dead of other cause, AWD- alive with disease and DOD- dead of disease.

## Statistical Analysis:

Descriptive statistics summarized baseline, initial clinical assessment (ICA), post-radiation, postoperative, and follow-up data. Comparisons between surgical groups used t-tests, Wilcoxon rank-

sum tests, and chi-square or Fisher's exact tests, as appropriate. Missing ICA data were imputed using the `rflmpute` function in R. Group balance was achieved via entropy balancing on selected ICA variables, with covariate balance assessed using standardized mean differences (SMD); all variables reached an  $SMD < 0.001$  post-weighting. Fine and Gray competing risk models evaluated LR, disease-free survival (DFS), and cancer-specific mortality, while Cox regression assessed all-cause mortality. Sensitivity analyses included unadjusted, entropy-weighted, and double robust models with additional ICA covariates. Kaplan-Meier curves were generated for all outcomes, and five-year survival was compared using log-rank tests. Analyses were conducted in R and Stata 18.0.

## Results

We identified 216 consecutive patients who received neoadjuvant therapy and had residual pathologic T2 cancer (ypT2). Patients were stratified based on the surgical approach: FTLE (N = 36) versus RR (N = 180).

The overall group average age (years/range) was 59.6 (26–91), FTLE average age was 69.3 (40–91), and RR average age was 57.7 (26–89) ( $p < 0.001$ ). 32% (N = 68) of patients were female, with similar distributions in both groups: 31% in the FTLE group and 32% in the RR group ( $p = 0.896$ ).

Overall mean BMI was 26.8 (17.2–47.5), FTLE mean BMI was 27.7 (17.2–45.9) and RR mean BMI was 26.6 (17.6–38.2) ( $p = 0.252$ ).

Demographics and tumor characteristics during initial clinical assessment are described in Table 1.

Table 1  
– Demographics and Initial Clinical Assessment

| <b>Age (mean/sd)</b>                        | <b>Full Thickness Local Excision (n = 36)</b> | <b>Radical Resection (n = 180)</b> | <b>p</b>           |
|---------------------------------------------|-----------------------------------------------|------------------------------------|--------------------|
|                                             | <b>69.3 (12.1)</b>                            | <b>57.7 (12.4)</b>                 | <b>&lt; 0.0001</b> |
| Sex (Female, n%)                            | 11 (30.6%)                                    | 57 (31.7%)                         | 0.896              |
| BMI (mean/sd)                               | 27.7 (5.6)                                    | 26.6 (5.0)                         | 0.252              |
| ASA (n%)                                    |                                               |                                    | < 0.0001           |
| 1                                           | 0 (0)                                         | 15 (8.3%)                          |                    |
| 2                                           | 5 (13.9%)                                     | 85 (47.2%)                         |                    |
| 3                                           | 19 (52.8%)                                    | 78 (43.3%)                         |                    |
| 4                                           | 12 (33.3%)                                    | 2 (1.1%)                           |                    |
| Initial Clinical Assessment                 |                                               |                                    |                    |
| Anorectal Ring (median/range, cm)           | 2.5 (-0.2-8)                                  | 2 (-0.3-16)                        | 0.323              |
| Size (median/range, cm)                     | 3.5 (1.5-6)                                   | 5 (2–16)                           | < 0.0001           |
| ICA Clinical T Stage                        |                                               |                                    | < 0.0001           |
| 0 or 1                                      | 8.3%                                          | 1.7%                               |                    |
| 2                                           | 47.2%                                         | 13.3%                              |                    |
| 3 or 4                                      | 44.4%                                         | 85.0%                              |                    |
| Positive Lymph Nodes (yes, n%)              | 16.7%                                         | 43.9%                              | 0.002              |
| Fixity (n%)                                 |                                               |                                    | 0.002              |
| Mobile                                      | 69.4%                                         | 41.7%                              |                    |
| Tethered                                    | 27.8%                                         | 32.2%                              |                    |
| Fixed                                       | 2.8%                                          | 26.1%                              |                    |
| ICA – Initial Clinical Assessment           |                                               |                                    |                    |
| BMI – Body Mass Index                       |                                               |                                    |                    |
| ASA – American Society of Anesthesiologists |                                               |                                    |                    |

| Age (mean/sd)                               | Full Thickness Local Excision (n = 36) | Radical Resection (n = 180) | p        |
|---------------------------------------------|----------------------------------------|-----------------------------|----------|
|                                             | 69.3 (12.1)                            | 57.7 (12.4)                 | < 0.0001 |
| Ulceration (n%)                             |                                        |                             | < 0.0001 |
| None                                        | 36.1%                                  | 10.6%                       |          |
| Superficial/Minimal                         | 27.8%                                  | 18.9%                       |          |
| Moderate/Moderate Deep                      | 30.5%                                  | 37.2%                       |          |
| Deep                                        | 5.6%                                   | 33.3%                       |          |
| Position (n%)                               |                                        |                             | 0.005    |
| Anterior                                    | 27.8%                                  | 31.1%                       |          |
| Circumferential                             | 0                                      | 25.0%                       |          |
| Left Lateral                                | 27.8%                                  | 15.0%                       |          |
| Posterior                                   | 19.4%                                  | 15.6%                       |          |
| Right Lateral                               | 25.0%                                  | 13.3%                       |          |
| ICA – Initial Clinical Assessment           |                                        |                             |          |
| BMI – Body Mass Index                       |                                        |                             |          |
| ASA – American Society of Anesthesiologists |                                        |                             |          |

17% of the FTLE cohort presented with positive LNs, compared to 44% in the RR cohort ( $p < 0.05$ ).

For neoadjuvant radiotherapy treatment, the FTLE group received a median dose of 5300 cGy (range: 3960–5940), and the RR group received a median dose of 5400 cGy (range: 2500–8300) ( $p = 0.233$ ).

Neoadjuvant chemotherapy was Xeloda, in 51.7% in the FTLE group and 48.5% of the RR group. Five-Fluorouracil continuous venous infusion (5 FU CVI) was given to 48.3% of the FTLE patients and 46% of the RR patients. Five-point five percent of the RR group was treated with other regimens ( $p = 0.999$ ).

Post radiation tumor assessments are described in Table 2. After neoadjuvant therapy, none of the FTLE patients had positive LNs on re-staging compared to 17% ( $N = 6$ ) previously. 14% ( $N = 26$ ) of the RR patients demonstrated positive LNs during re-staging compared to 44% ( $N = 79$ ) prior to treatment.

Table 2  
– Post Radiation Assessment

|                                        | <b>Full Thickness Local Excision (n = 36)</b> | <b>Radical Resection (n = 180)</b> | <b>p</b> |
|----------------------------------------|-----------------------------------------------|------------------------------------|----------|
| <b>Post Radiation Assessment</b>       |                                               |                                    |          |
| Anorectal Ring (median/range, cm)      | 3 (-0.2-12)                                   | 1.5 (-0.2-15)                      | 0.192    |
| Size (median/range, cm)                | 2 (0.5-4)                                     | 3 (0–10)                           | < 0.0001 |
| Post Radiation Size Reduction (%)      | 42.9                                          | 40                                 | 0.391    |
| PRA Clinical T Stage                   |                                               |                                    | < 0.0001 |
| 0 or 1                                 | 15.6%                                         | 5.7%                               |          |
| 2                                      | 78.2%                                         | 36.7%                              |          |
| 3 or 4                                 | 6.2%                                          | 57.6%                              |          |
| Positive Lymph Nodes (yes, n%)         | 0%                                            | 14.4%                              | 0.01     |
| Fixity (n%)                            |                                               |                                    | 0.192    |
| Mobile                                 | 87.5%                                         | 73.3%                              |          |
| Tethered                               | 12.5%                                         | 22.9%                              |          |
| Fixed                                  | 0                                             | 3.8%                               |          |
| Ulceration (n%)                        |                                               |                                    | 0.135    |
| None                                   | 18.7%                                         | 18.0%                              |          |
| Superficial/Minimal                    | 56.3%                                         | 31.1%                              |          |
| Moderate/Moderate Deep                 | 25%                                           | 42.2%                              |          |
| Deep                                   | 0                                             | 8.7%                               |          |
| Position (n%)                          |                                               |                                    | 0.032    |
| Anterior                               | 27.3%                                         | 34.5%                              |          |
| Circumferential                        | 0                                             | 11.8%                              |          |
| Left Lateral                           | 24.2%                                         | 19.0%                              |          |
| <b>PRA – Post Radiation Assessment</b> |                                               |                                    |          |

|                                  | Full Thickness Local Excision (n = 36) | Radical Resection (n = 180) | p |
|----------------------------------|----------------------------------------|-----------------------------|---|
| <b>Post Radiation Assessment</b> |                                        |                             |   |
| Posterior                        | 15.2%                                  | 20.3%                       |   |
| Right Lateral                    | 33.3%                                  | 14.4%                       |   |
| PRA – Post Radiation Assessment  |                                        |                             |   |

Intraoperatively, EBL was 45 cc (0-500) (median, range) in the FTLE group and 200 (0-2200) in the RR group ( $p < 0.001$ ).

Blood transfusions occurred in 2% of the RR group compared to 0% in the FTLE group.

All study participants had clear proximal, distal and deep margins on the specimen.

By inclusion criteria, no patients in the FTLE group had radiologically suspicious LN (0%) vs. 14% in the RR group at restaging. Positive pathological LN were identified in 24.1% of RR specimens.

Twenty-three percent of total patients with ypT2 cancer developed 30-day post-operative morbidity, with 14% the FTLE group and 25% in the RR group ( $p = 0.149$ ) (Table 3). Wound separation rate after FTLE was 14% and represented all complications in this group.

Table 3  
– Procedure and 30 Day Postoperative Morbidity

|                                      | <b>Full Thickness Local Excision (n = 36)</b> | <b>Radical Resection (n = 180)</b> | <b>p</b> |
|--------------------------------------|-----------------------------------------------|------------------------------------|----------|
| <b>Peri-operative</b>                |                                               |                                    |          |
| SPS*(n%)                             | N/A                                           | 156 (86.6%)                        |          |
| APR**/Pelvic exenteration (n%)       | N/A                                           | 24 (13.3%)                         |          |
| Diverting stoma (n%)                 | N/A                                           | 179 (98.4%)                        |          |
| Reversal of Stoma for SPS (n%)       | N/A                                           | 142 (91.6%)                        |          |
| Permanent Stoma (n%)                 | N/A                                           | 37 (20.5%)                         |          |
| EBLcc (median/range)                 | 45 (0-500)                                    | 200 (0-2200)                       | < .0001  |
| Transfusion (yes, n%)                | 0 (0)                                         | 3 (1.7%)                           | 0.999    |
| <b>Morbidity</b>                     |                                               |                                    |          |
| 30 day Morbidity (yes, n%)           | 5 (13.9%)                                     | 45 (25.0%)                         | 0.149    |
| Clavien-Dindo I (n%)                 | 0 (0)                                         | 13 (28.9%)                         | 0.13     |
| Clavien-Dindo II (n%)                | 5 (100%)                                      | 24 (53.3%)                         | 0.07     |
| Clavien-Dindo III/IV (n%)            | 0 (0)                                         | 8 (17.8%)                          | 0.3      |
| 30 day Reoperation (yes, n%)         | 0 (0)                                         | 5 (2.8%)                           | 0.593    |
| <b>*Sphincter Preserving Surgery</b> |                                               |                                    |          |
| <b>**Abdominoperineal resection</b>  |                                               |                                    |          |

All FTLE morbidity events were 30-day CD Grade II, compared with 53% in the RR group ( $p = 0.07$ ). There were no Grade III/IV complications in the FTLE cohort, whereas the RR cohort had 18% ( $p = 0.3$ ). In the RR group, 2.8% of patients required re-operation within 30 days in contrast to none in the FTLE group ( $p = 0.593$ ). After adjustment for baseline characteristics using entropy-weighted logistic regression, FTLE was associated with significantly lower odds of CD grade  $\geq$  II complications compared with RR (OR 0.09, 95% CI 0.02–0.30;  $p < 0.001$ ).

86% of the RR patients had sphincter-preserving surgery (SPS), either a low anterior resection or a transanal TME (TATA), with a diverting ostomy. The remaining patients underwent an APR or pelvic exenteration (Table 3). Among those who had SPS, 8.4% did not undergo ostomy reversal, resulting in a

permanent ostomy. Overall, 20% of patients in the RR group had a permanent ostomy. In contrast, none of the patients in the FTLE group required diversion ( $p < 0.001$ ).

## Oncological outcomes

There were no differences in follow-up duration, LR, or DFS between the FTLE and RR groups (Table 4). The FTLE group had a mean follow-up of (months/range) 77.9 (0.4–233). LR was 2.8% in the FTLE group and 5% in the RR group ( $p = 0.53$ ). There were no mesorectal nodal recurrence or lateral pelvic LN recurrences in the FTLE group. LR in the RR was as follows: extramurally (45%), on the pelvic side wall (33%), in the vaginal wall (11%), and at the anastomosis (11%). The mean time for LR among RR patients was 34 months (5–57).

Table 4  
– Oncologic Outcomes

| Follow-up, months<br>(range) | Overall<br>(n = 216)  | Full Thickness Local<br>Excision (n = 36) | Radical<br>Resection<br>(n = 180) | p          |
|------------------------------|-----------------------|-------------------------------------------|-----------------------------------|------------|
|                              | <b>75.9 (0.4–289)</b> | <b>77.9 (0.4–233)</b>                     | <b>75.5 (0.7–289)</b>             | <b>0.4</b> |
| Local Recurrence (%)         | 4.6                   | 2.8                                       | 5                                 | 0.53       |
| 5-year DFS (%)               | 75.4                  | 82.7                                      | 73.7                              | 0.49       |
| Overall Survival (%)         | 80.6                  | 72.6                                      | 82.7                              | 0.06       |
| NED (n%)                     | 69.4                  | 47.2                                      | 75.6                              | < .0001    |
| AWD (n%)                     | 7.8                   | 5.6                                       | 8.5                               | 0.74       |
| DOD (n%)                     | 5.5                   | 5.6                                       | 5.7                               | 1          |
| DFS – Disease Free Survival  |                       |                                           |                                   |            |
| NED – No Evidence of Disease |                       |                                           |                                   |            |
| AWD – Alive with Disease     |                       |                                           |                                   |            |
| DOD – Died of Disease        |                       |                                           |                                   |            |

The only LR in the FTLE group was a mucosal LR diagnosed 9 months post FTLE and was salvaged with a radical resection (transanal-transabdominal proctosigmoidectomy, TATA). Salvage procedures for the RR group included a single APR for an isolated vaginal wall recurrence and a single robotic right lateral pelvic LN dissection for a solitary pelvic side wall recurrence. Patients not amenable to surgical salvage were referred to oncology for further management.

The overall 5-year DFS was 75.4% and 5-year OS was 80.6%. For FTLE 5-year DFS was 82.7% and for RR 5-year DFS was 73.7% ( $p = 0.494$ ). There were no perioperative mortalities in either group.

In the FTLE cohort, 47.2% of patients were alive with no evidence of disease (NED), 5.6% were alive with disease (AWD), 5.6% had died of disease (DOD), and 41.6% had died of other causes (DOC). The 5-year DFS was 82.7% ( $p = 0.494$ ).

In the RR group, 75.6% of patients were alive with no evidence of disease (NED), 8.5% were alive with disease (AWD), 5.7% had died of disease (DOD), and 10.2% had died of other or unknown causes (DOC). Five-year DFS was 73.7% ( $p = 0.494$ ).

Both groups had similar rates of DOD (5.6% vs 5.7%). The FTLE group demonstrated higher DOC rates (41.6% vs 10.2%,  $p < 0.0001$ ), and the RR group demonstrated higher NED rates (75.6% vs 47.2%,  $p < 0.0015$ ).

In evaluating oncologic outcomes using entropy-balanced competing risk analysis, a technique to control for baseline imbalance, there was no significant difference in LR (SHR 0.23 (95% CI 0.03, 2.1),  $p = 0.195$ , Fig. 1), DFS (SHR 1.7 (95% CI 0.4, 8.1),  $p = 0.485$ , Fig. 2), cancer-related mortality (SHR 0.66 (0.1, 5.3),  $p = 0.699$ ). There was a significant difference in overall all-cause mortality (HR 3.02 (1.5, 6.2),  $p = 0.003$ , Fig. 3). The results were similar in the weighted double robust results.

## Discussion

In this study of patients with ypT2 rectal cancer, treated with full-thickness local excision and a mean follow up of over 6 years, we found a very low rate of LR, absence of mesorectal LR in the FTLE group and low wound complication rates. There was no significant difference in the risk of LR and DFS between the groups who underwent full-thickness local excision or radical resection. The similar rates of LR in both groups (2.8%, for FTLE vs. 5% for RR) aligns, but more importantly expands on findings from other multicenter studies that had shorter follow up periods.[17] Ultimately, our findings continue to demonstrate that with proper selection, FTLE, following neoadjuvant therapy, can result in durable low recurrence rates for incomplete responders with ypT2 cancers. These patients do not require a subsequent radical resection, but can be treated with organ preservation.

This study showed no substantial difference in cancer-related mortality during a follow-up period of over 6 years. DFS was similar, 82.7% in the FTLE group and 73.7% in the RR group ( $p = 0.494$ ). Not surprisingly the OS was higher in the RR group as the local excision group was older (57.7 vs. 69.3 years,  $p < 0.0001$ ) and frailer (44% vs. 86% with ASA  $\geq$  III,  $p < 0.0001$ ). This point is highlighted by the much higher DOC rate of 41.6% in the FTLE group vs 10.2% rate in the RR group ( $p < 0.0001$ ).

Major morbidities (CD  $\geq$  II) were significantly less frequent in the FTLE cohort than in the RR cohort, and no reoperations were required in the FTLE group. This low level of morbidity with organ preserving surgery is even more appealing when compared to the literature for TME surgery, which reports up to

34% of short-term complications and up to 46% incidence of major low-anterior resection syndrome on long-term follow-up.[2][18] Of note, we did not encounter the high rates of wound breakdown (47–61%) following local excision after chemoradiation that was reported by Perez[19] and others.[20], [21] Our wound disruption rate of 14% in the ypT2 after local excision aligns with our previously published experiences as well as similar studies.[5], [22], [23] This point we must amplify as it indicates that with proper technique FTLE can be performed safely after neoadjuvant therapy, which runs contrary to many opinions in the literature, and current surgical dogma. Additionally, organ preservation surgical strategies enable patients to avoid a permanent or even temporary stoma, which is common after chemoradiation and radical surgery.

A major strength of this experience is it corroborates the findings of others while offering a mean follow up of more than 5 years, showing durable oncologic efficacy of local excision after chemoradiotherapy for ypT2 rectal cancer. Panis' groups'[24] findings are similar to our results showing ypT2 tumors and local excision have long-term recurrence rates and survival outcomes comparable to those of patients who undergo TME, with LR rates of 5% for local excision vs 3% for TME. Peltrini et al.[5] demonstrated an improved emotional well-being in patients treated with local excision and chemoradiotherapy, offering an additional benefit to this approach. In aggregate these findings suggest local excision is a safe alternative to TME in ypT2 patients. FTLE, in properly selected patients, allows organ preservation for rectal cancer patients, while achieving acceptable long-term oncological outcomes.[5], [25]

As a multicenter randomized trial for small ypT2T3 tumors (residual tumor  $\leq 2$  cm), GRECCAR2 also showed no substantial difference between local excision and TME in 5-year LR (7% vs 7%), metastatic disease (18% vs 19%), OS (84% vs 82%), DFS (70% vs 72%), or cancer-specific mortality (7% vs 10%).[17]

The TAUTEM study results are also in keeping with our data. While theirs is a more elegant study comparing similar patients at onset, they showed no difference in oncologic outcomes with CRT-TEM with 25% of their patients having TEM as definitive therapy for ypT2 cancers.[23]

Our study has several limitations, primarily its single-center design, and its relatively small size, and the long period of time. It is important to point out that the two groups were not the same on presentation and differed by size of their tumor and post treatment nodal status, which by virtue of our selection criteria, affected their allocation to FTLE or RR.

In conclusion, this study focuses on a well-defined subset of patients to address the simple question: when a local excision following chemoradiotherapy is performed and a ypT2 cancer is found, is radical surgery indicated?

The simple answer is no, FTLE for select ypT2 cancers is adequate definitive oncologic therapy.

Contrary to strong statements in the literature, our experience and others indicate that radical surgery is neither mandated nor warranted for ypT2 rectal cancer after FTLE. LR and survival rates are excellent in the FTLE group, both when compared to radical surgery results in large trials and the radical resected

group in this study.[1], [2], [26] Most salient is the fact that these patients did not experience recurrence in the mesorectum from unresected nodal disease. This has been the theoretical argument for follow-up TME in ypT2 cancer: that cancer surviving in the muscular wall was a biological indicator of a form of cancer resistance to chemo and radiation therapy, indicating the need for nodal resection. This is not the case.

It is worth mentioning that decisions regarding candidacy for local excision must be based on the cancer after full downstaging of the cancer at an 8–10 weeks interval. This is essential to obtain the full therapeutic benefit of the tumor downstaging, setting the stage for the option of local excision. If nodal disease is present, T3 residual exists or the tumor is too large to make local excision technically feasible, then radical surgery should be performed. This experience supports the expanded role of FTLE as a definitive course of treatment that may be offered as an option for organ preservation even in low risk and young patients with incomplete response. This approach offers the possibility of a real expansion of organ preservation and sphincter preservation for rectal cancer patients.

## Declarations

## Disclosures:

John Marks, MD - Stryker: consultant, speakers bureau, Intuitive: consultant, speakers bureau, Medtronic: educational grant support, consultant, speakers' bureau, Virtual Incision: consultant, Arthrex: consultant. Henry Schoonyoung, MD – Stryker: consultant. The other authors have no disclosures. **Funding:** This study received no grant support or external funding. **Competing Interests:** The authors declare that they have no competing interests.

## Author Contribution

AM: Data acquisition, data analysis and interpretation, drafting of the original manuscript, and critical revision of the final manuscript. HS, AD, EZ, and GM: Data acquisition, data analysis and interpretation, and critical revision of the final manuscript. SK: Data analysis and interpretation, and critical revision of the final manuscript. JM: Study conception and design, data acquisition, data analysis and interpretation, drafting of the original manuscript, and critical revision of the final manuscript. All authors have read and approved the final version of the manuscript.

## Data Availability

**Data availability Statement** The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy and confidentiality considerations but are available from the

corresponding author upon reasonable request. The data are maintained in secure, controlled-access storage at Lankenau Medical Center. Sincerely, John Marks, MD. On behalf of all co-authors

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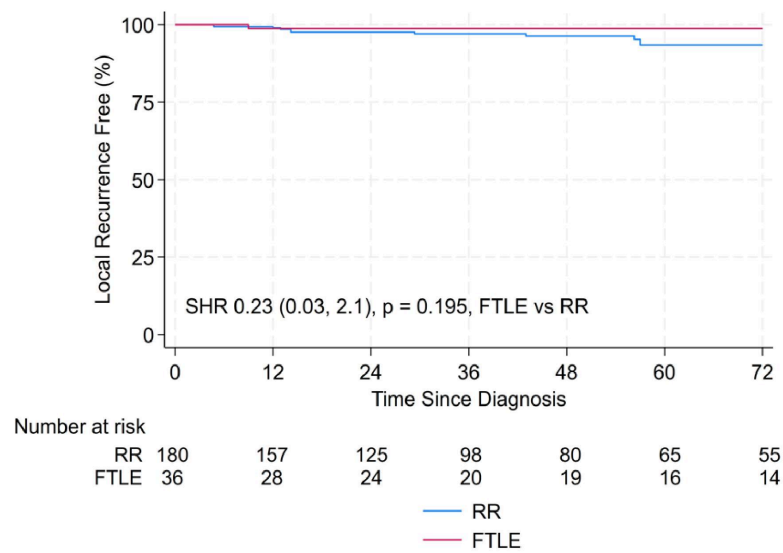
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## Figures

**Figure 1 – Entropy Balance Weighted Kaplan Meier, Local Recurrence**

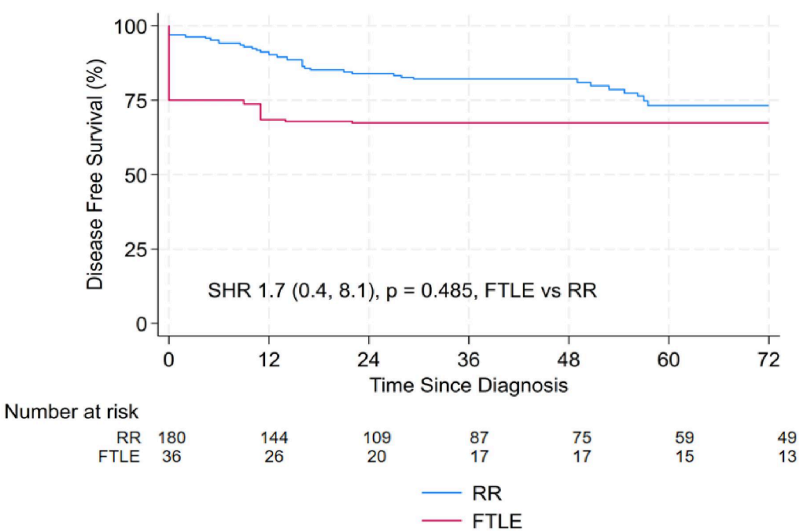


SHR – Sub-hazard Ratio  
RR – Radical Resection  
FTLE – Full Thickness Local Excision

**Figure 1**

Entropy Balance Weighted Kaplan Meier, Local Recurrence

Figure 2 – Entropy Balance Weighted Kaplan Meier, Disease Free Survival

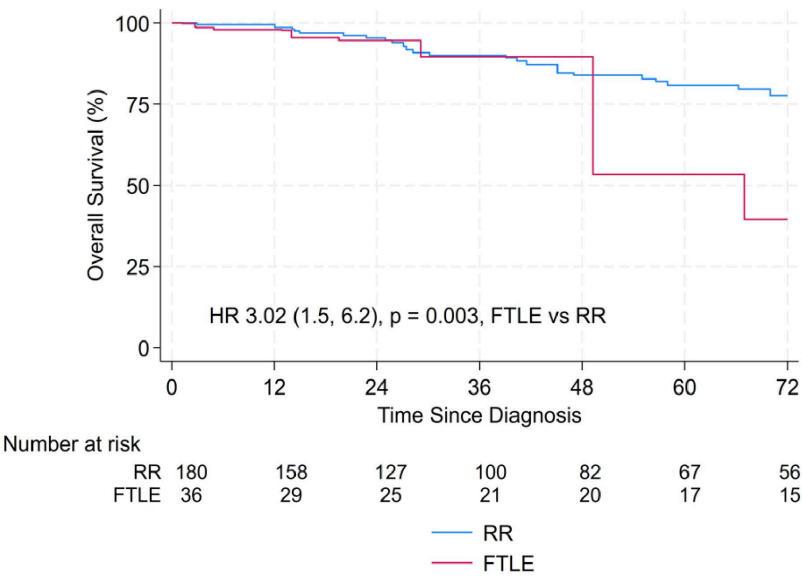


SHR – Sub-hazard Ratio  
RR – Radical Resection  
FTLE – Full Thickness Local Excision

Figure 2

Entropy Balance Weighted Kaplan Meier, Disease Free Survival

Figure 3 – Entropy Balance Weighted Kaplan Meier, Overall Survival

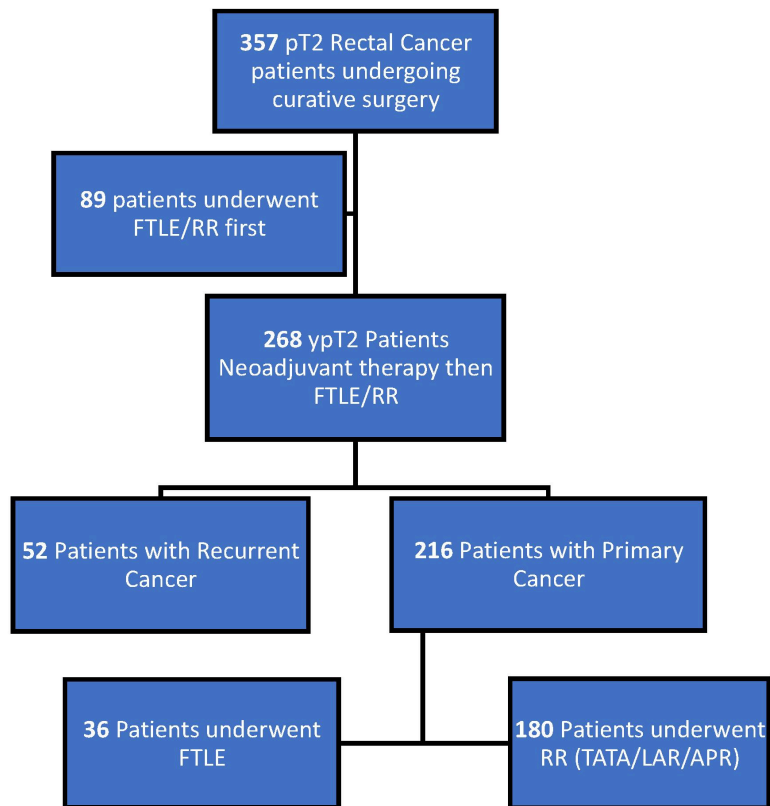


HR – Hazard Ratio  
RR – Radical Resection  
FTLE – Full Thickness Local Excision

Figure 3

Entropy Balance Weighted Kaplan Meier, Overall Survival

Figure 4: pT2 Rectal Cancer patients 04/2000-07/2024



FLTE – Full Thickness Local Excision

TATA – Aransanal Total Mesorectal Excision

LAR – Low Anterior Resection

APR – Abdominoperineal Resection

## Figure 4

pT2 Rectal Cancer patients 04/2000-07/2024

## Supplementary Files

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