Case Report

Can adjuvant pelvic radiation therapy after local excision or polypectomy for T1 and T2 rectal cancer offer an alternative option to radical surgery?

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ABSTRACT

Purpose: To determine outcomes after adjuvant pelvic local radiation therapy (RT) +/- concurrent chemotherapy for T1 and T2 rectal carcinomas treated with local excision or polypectomy.

Methods: We retrospectively identified adult patients with histologically proven T1 and T2 rectal adenocarcinoma, diagnosed incidentally at time of local excision or polypectomy between 01 January 2007 and 31 December 2019, and appropriately staged to confirm N0 M0 status. Patients were excluded if they had recurrent cancer or had received total mesorectal excision (TME): anterior resection (AR) or abdominoperineal resection (APR). Patient, tumour and treatment factors, together with disease and toxicity outcomes were collected from institutional medical records, correspondence and investigation reports. Descriptive statistical analyses were employed. The primary endpoint was loco-regional control and secondary endpoints were treatment-related toxicity, disease free survival, overall survival and rate of surgical salvage for pelvic recurrence.

Results: The median age of the 15 eligible patients was 73 (range 49–82 years). There were 9 men (60%) and 6 women (40%). The majority had T1 disease (80%) and most had received endomucosal resection (80%). All patients received 43-52Gy (EQD2) to the primary and 43-48Gy (EQD2) to the pelvis with 46.6% receiving concurrent chemotherapy (infusional 5-FU or oral capecitabine). At median follow up of 51 months, there were no local or regional recurrences. One patient experienced an isolated distant relapse at 48 months without any locoregional recurrence.

Conclusion: Our findings demonstrate good locoregional disease control with the use of adjuvant pelvic RT for T1 and T2 rectal adenocarcinoma initially treated with polypectomy or local (non-oncological) excision. These findings indicate that adjuvant pelvic RT may provide an alternative to TME surgery in patients with incidentally detected early rectal cancers.

Introduction

Total mesorectal excision (TME) is considered the gold standard to achieve local control and disease cure in rectal cancer [1,2]. However, in early T1 and T2 rectal cancer, where the risk of lymphatic spread is low, adopting this same approach may lead to overtreatment, particularly as TME carries morbidity, risks of complication and involves the formation of a temporary or permanent colostomy.

Rates of local control following local excision (LE) have been shown to be favourable in Tis, T1 sm1-2 tumours [3]. Poor prognostic factors for local recurrence include high grade, lymphovascular invasion, perineural invasion, tumour budding, depth of invasion, mucinous type, positive resection margin [4,5]. The last 10 years have seen the emergence of endoscopic resection techniques for LE for benign rectal neoplasms and early malignant lesions. Enhanced tumour visualisation and excision technique has enabled effective margin clearance and en bloc
resection which allows for more precise tumour assessment and determination of requirement of further treatment [6].

Radiation therapy (RT) with concurrent chemotherapy for radiosensitisation has demonstrated locoregional control and survival benefit in the context of locoregionally advanced rectal cancer [7], with 20% demonstrating complete pathological response (pCR) [8]. In fact, there is increasing recognition and adoption of watchful waiting with avoidance of surgery in those with clinical complete response in locoregionally advanced rectal cancer [9]. Therefore, the question of whether a minimally invasive or non-surgical approach to managing early rectal cancers is a very relevant one.

We aimed to determine locoregional and overall disease control outcomes in patients treated with adjuvant pelvic radiation therapy after LE or polypectomy for T1 and T2 rectal adenocarcinoma. We also aimed to determine the toxicity outcomes from this approach.

Method

The Lower Gastrointestinal Tumour cancer multidisciplinary service at Western Sydney Local Health District in NSW has been adopting the practice of offering the option of adjuvant pelvic RT for patients with early invasive rectal cancers who have been initially managed with LE or polypectomy. This option was offered as an alternative to radical TME surgery with either low anterior resection (LAR) or abdominoperineal polypectomy. This option was offered as an alternative to radical TME surgery with either low anterior resection (LAR) or abdominoperineal resection (APR) for those who had T2, margin positivity/very close to resection (APR) for those who had T2, margin positivity/very close to resection which allows for more precise tumour assessment and determination of requirement of further treatment [6].

The median age of the 15 eligible patients was 73 (range 48–82 years). There were 9 men (60%) and 6 women (40%). Most patients (80%) had T1 disease. The patient, disease of the patient cohort is presented in Table 1.

| Sex          | Patients n (%) |
|--------------|----------------|
| Male         | 9 (60%)        |
| Female       | 6 (40%)        |

| Age at diagnosis               | Median (range)   | % |
|-------------------------------|------------------|---|
| Age at diagnosis               | 73 (48–82)       |   |

| Radiological staging | % |
|----------------------|---|
| CT                    | 15 (100%)        |
| MRI                  | 10 (66.6%)       |
| PET                  | 2 (13.3%)        |

| T-stage | % |
|---------|---|
| T1      | 12 (80%)    |
| T2      | 3 (20%)     |

| Histopathological features | % |
|----------------------------|---|
| Margin status              |   |
| Positive                   | 5 (33.3%)   |
| Negative                   | 4 (26.6%)    |

| Depth of invasion | % |
|------------------|---|
| <1mm             | 1 (6.6%)    |
| ≥1mm             | 6 (40%)     |

| Grade | % |
|-------|---|
| Poorly differentiated | 2 (13.3%) |
| Lymphovascular invasion | 1 (6.6%) |
| Perineural invasion | 0 |
| Tumour budding | 5 (33.3%) |
| Mucinous | 2 (13.3%) |

All patients received 43–52 Gy (EQD2) to the primary and 43–48 Gy (EQD2) to the pelvic nodal regions with 11 of the 15 patients (73%) treated with 3D conformal radiation therapy (3DCRT). Patients treated more recently, had been treated with a VMAT technique.

All patients had been considered for suitability for concurrent chemotherapy but only seven patients (46.6%) received concurrent chemotherapy, with 5 patients having oral capecitabine and the other 2 patients treated with infusional 5-fluorouracil (5-FU). The remaining patients were not suitable for concurrent chemotherapy due to comorbidities and/or performance status or declined concurrent chemotherapy.

At median follow-up of 51 months (range 7–123) there were no local or pelvic nodal recurrences in the study cohort. One patient had a distant relapse at 48 months and died at 50 as a result of their metastatic disease. This patient had not had any high-risk features on their initial histopathology. They had not received concurrent chemotherapy. Six patients died of other, non-rectal cancer related causes. Of the treated cohort, the 2-year overall survival (OS) was 92% and 57% at 5 years (Fig. 1).

LE followed by adjuvant RT was well-tolerated with limited morbidity. Expected acute grade 1–2 toxicity was reported for fatigue (84.6%), proctitis (53.8%) and diarrhoea (53.8%), non-infective cystitis (46%). Only 2 patients (15%) reported grade 3 cutaneous toxicity – moist skin desquamation, which resolved by 4 weeks following treatment. All acute toxicities had resolved by 3 months with the majority resolving by 4 weeks post treatment. There were minimal reported late toxicities with 1 patient having grade 1 vaginal dryness and urge incontinence.

Discussion

Our findings suggest that LE followed by adjuvant pelvic RT is feasible, safe and yields good locoregional control in T1/T2 N0 M0 rectal adenocarcinoma, thereby avoiding definitive surgery in the form of AR or APR. There were no local recurrences at a median follow up of 51 months. To date, there are no randomised control trials comparing outcomes of LE and adjuvant RT +/- concurrent chemotherapy vs. TME.
Table 2
Patient treatment characteristics. Surgery: EMR = Endomucosal resection, TAR = Transanal resection, TEMS = Transanal endoscopic microsurgery. Radiation technique: 3DCRT = 3D conformal radiation therapy, VMAT = Volumetric arc radiation therapy. Chemotherapy: 5-FU = 5-Fluorouracil.

| Patient | T stage | Surgery | Radiation dose Gy/fr (EQD2a) | Radiation dose to primary Gy/fr (EQD2a) | Radiation dose to pelvis Gy/fr (EQD2a) | Radiation technique | Chemotherapy |
|---------|---------|---------|-------------------------------|--------------------------------------|---------------------------------------|---------------------|--------------|
| 1       | 1       | TAR     | 40/15                         | 40/15                                | 40/15                                 | 3DCRT              | –            |
| 2       | 1       | EMR     | 45/25 + 9/5                   | 54/30                                | 45/25                                 | 3DCRT              | –            |
| 3       | 1       | EMR     | 45/25 + 9/5                   | 54/30                                | 45/25                                 | 3DCRT              | –            |
| 4       | 1       | EMR     | 45/25 + 9/5                   | 54/30                                | 45/25                                 | 3DCRT              | –            |
| 5       | 1       | EMR     | 40/15                         | 40/15                                | 40/15                                 | 3DCRT              | –            |
| 6       | 1       | EMR     | 45/25 + 5.4/3                 | 50.4/28                              | 45/25                                 | 3DCRT              | –            |
| 7       | 1       | EMR     | 45/25 + 9/5                   | 54/30                                | 45/25                                 | 3DCRT              | Capcitabine  |
| 8       | 2       | TEMS    | 45/25 + 5.4/3                 | 50.4/28                              | 45/25                                 | 3DCRT              | 5-FU         |
| 9       | 2       | EMR     | 45/25 + 5.4/3                 | 50.4/28                              | 45/25                                 | 3DCRT              | Capcitabine  |
| 10      | 2       | TAR     | 45/20                         | 45/20                                | 45/20                                 | 3DCRT              | –            |
| 11      | 1       | EMR     | 54/30                         | 54/30                                | 45/30                                 | VMAT                | 5-FU         |
| 12      | 1       | EMR     | 45/25 + 5.4/3                 | 50.4/28                              | 45/25                                 | 3DCRT              | –            |
| 13      | 1       | EMR     | 45/25                         | 45/25                                | 45/25                                 | VMAT                | 5-FU         |
| 14      | 1       | EMR     | 54/30                         | 54/30                                | 50.4/30 (47.5)                        | VMAT                | 5-FU         |
| 15      | 1       | EMR     | 54/30                         | 54/30                                | 45/30                                 | VMAT                | 5-FU         |

![Fig. 1.](image-url)

Number at risk 15 14 14 12 12 10 9 9 9 8 8
in the setting of early rectal cancer. In the absence of RCTs and other high level evidence, our findings support the use of this approach in patients who may be borderline candidates for surgery or indeed those who prefer a non-surgical approach to their management.

In addition to T stage of the incidentally detected primary, where better local control has been demonstrated in pT1 vs pT2 tumours [10,11] there are multiple factors that are prognostic for locoregional recurrence after LE. These include high tumour grade, lymphovascular invasion, perineural invasion, tumour budding, deep submucosal invasion (sm3, Haggitt 4 or more than 1000 μm), mucinous type and positive resection margins [4,5,12] A recent large meta-analysis of 73 studies by Ostendorp et al. [12] has shown a local recurrence rate of 6.7% for low risk pT1 tumours treated with LE alone and no local recurrences in patients treated with adjuvant RT and concurrent chemotherapy. For high risk pT1 tumours, local recurrence rates were 13.6% vs 3.9% with LE alone vs adjuvant RT with concurrent chemotherapy [12]. For pT2 tumours, the local recurrence rates were significantly higher at 28.9% for LE 28.9% vs 14.7% following adjuvant RT with concurrent chemotherapy [12]. Despite the fact that two-thirds of our patients with pT1 disease had DCME, or more high risk factors with only 4 patients having true low-risk T1 disease, the locoregional control rate demonstrated in this study is comparable or better than the reported studies, with no (0%) local recurrences.

The rates of distant metastases in pT1 disease has been demonstrated to be low at 3.4% vs 5.0% for LE alone vs adjuvant RT with concurrent chemotherapy, with moderately higher rates 6.2% and 5.8%, respectively for pT2 disease [12]. The single patient in the current study who had a distant recurrence had pT1 disease and the histopathology of their primary tumour did not demonstrate any of the known risk factors. Whilst it is unclear as to why this patient may have recurred distantly without a locoregional recurrence, it is reassuring to note that they had remained without disease in the treated pelvis and that their distant relapse would not have been prevented had they received radical surgery. Whether this patient may have benefited from concurrent chemotherapy is uncertain. The use of concurrent radiosensitising chemotherapy was used in the most recently treated 7 patients and is consistent with the use of concurrent chemotherapy during pelvic RT in locally advanced rectal cancer. The addition of chemotherapy to the adjuvant RT setting after LE in early rectal cancer may or may not have provided additional benefit and the study sample was too small to evaluate this.

Our study cohort was older and as evidenced by the non-cancer related deaths (cause of death in 6 of 7 patients were from patient pre-treatment comorbidities), were also likely more frail. The cohort composition is likely a reflection of clinicians and patients choosing a less aggressive non-surgical treatment approach in the setting of ageing and frailty. It is important to note therefore that the LE followed by adjuvant RT +/- concurrent chemotherapy was well-tolerated with limited morbidity. Most commonly patients reported transient fatigue, with local effects of proctitis, diarrhoea and non-infective cystitis affecting 1 in 2 patients. The only reported grade 3 toxicity was moist desquamation. Toxicity rates were consistent with previous studies [13]. As this study conducted over a 13 year period of time, the majority received RT via 3DCRT technique which has been superseded by the current IMRT/VMAT techniques which offer greater conformality and better dosimetric estimation of dose received by organs at risk, namely, bladder, small bowel and skin. As such, it is expected that there would be less post-treatment skin toxicity and further improved tolerability with the employment of these techniques.

The study was a retrospective analysis at a single institution. The inherent biases of patient selection in such studies should be considered i.e. those who received the study treatment may have had multiple co-morbidities, may have been poorer surgical candidates or were desirous to avoid stoma formation. The other limitation was the heterogeneity in the dose fractionation and use of chemotherapy. This is likely reflective of the frailty of the cohort picked for this approach in the early part of this study, including the desire to limit the number of fractions employed for these patients and an evolution in practice over the time course of this study. There were also no set departmental guidelines for surveillance and follow up during the period of this study. It is therefore possible there were variations based on clinician and patient preference as well as cost of investigations: multiple progress rectal/ pelvic MRIs are currently not funded in Australia. The lack of experiential data from patients in the form of patient reported outcomes is a limitation but we hope that future prospective cohort studies with routine collection of PROs together with disease and toxicity outcomes will shed more light on the important HRQOL aspects. Nevertheless, while the results of the first randomized control trial comparing TME vs adjuvant chemoradiation that is underway in the Netherlands for high risk T1 and low risk T2 rectal cancers [14] are awaited, our experience adds to the literature on the management of patients diagnosed with early rectal cancers. Particularly those whose cancers were incidentally detected at time of LE or polypectomy for presumed non-invasive or benign lesions. Further studies to prospectively evaluate histological and molecular biomarkers that predict for recurrence and for radiation sensitivity/resistance would also be important to determine optimal management of early rectal cancers.

Conclusion

This study demonstrated good locoregional disease control with the use of adjuvant pelvic RT +/- concurrent chemotherapy for T1 and T2 rectal adenocarcinoma detected incidentally at time of LE or polypectomy. This approach was also well tolerated. These findings indicate that LE and adjuvant pelvic RT +/- chemotherapy may provide an alternative to radical surgery such as LAR or APR in these incidentally detected early rectal cancers.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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