Outcomes of the RAFT Trial: Robotic surgery After Focal Therapy

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Abstract

Objectives: To report toxicity of treatment observed in men participating in the **R**obotic surgery **A**fter **F**ocal **T**herapy (RAFT) clinical trial.

Subjects/patients and Methods: Men were eligible for this prospective single group interventional study if they had histologically confirmed recurrent/residual prostate adenocarcinoma following primary FT. The short-form Expanded Prostate Cancer Index Composite (EPIC-26) measured prior to salvage robotic prostatectomy (S-RARP) and 3-monthly post-operatively together with Clavien-Dindo complications (I-IV). Secondary outcomes included biochemical recurrence-free survival (BCFS) following surgery and need for salvage treatment after surgery. This study is registered with ClinicalTrials.gov ***NCT03011606.***

Results: 24 men were recruited between February 2016 and September 2018. 1 patient withdrew from the trial after consenting and before S-RARP. 23 men completed 12-month post S-RARP follow-up. Median EPIC-26 urinary continence scores initially deteriorated after 3 months (82.4 versus 100) but there was no statistically significant difference from baseline at 12 months (100 versus 100, p=0.31). Median lower urinary tract symptom scores improved after 12 months compared to baseline (93.8 versus 87.5, p=0.01). At 12 months, 19/23 (83%) were pad-free and 22/23 (96%) required 0/1 pads. Median sexual function subscale scores deteriorated and remained low at 12

months (22.2 versus 58.3, p<0.001). Utilising a minimally important difference of 9 points, at 12 months after surgery 17/23 (74%) reported urinary continence to be “better” or “not different” to pre-operative baseline. The corresponding figure for sexual function (utilising a minimally important difference of 12 points) was 7/23 (30%). There was no statistically significant difference on median bowel/hormonal subscale scores. Only a single patient had a post-operative complication (Clavien-Dindo Grade I). BCFS at 12 months after surgery was 82.6% (95% confidence interval [CI]: 60.1% - 93.1%] while 4/23 (17%) received salvage radiation.

Conclusions: The RAFT clinical trial suggests toxicity of surgery after FT is low, with good urinary function outcomes, albeit sexual function deteriorated overall. Oncological outcomes at 12 months appear acceptable.

Introduction

Toxicities of traditional prostate cancer therapies including radical surgery and external beam radiation are well known. Numerous studies have demonstrated negative impact on sexual, urinary and bowel function(1,2). As a result, considerable effort has been made to reduce side-effects of these therapies. For instance, 2-dimensional planning employed in earlier radiotherapy regimens has been largely replaced by 3-dimensional conformal radiotherapy and Intensity Modulated Radiotherapy (IMRT)(3). Surgical technique has also undergone dramatic change with more patients undergoing minimal-access prostatectomy with or without assistance of robotic systems. Despite these refinements, incidence of long-term urinary incontinence and erectile dysfunction remains high following prostate radiation and surgery(1).

These issues have sparked increased interest in tissue-preserving therapies such as active surveillance and focal therapy. In an approach similar to breast cancer, there is a growing body of studies evaluating whether focusing prostate cancer treatment to part of the prostate harbouring cancer instead of treating the whole prostate gland may enable oncological success while limiting treatment toxicity. Minimally-invasive modalities such as High Intensity Focused Ultrasound (HIFU) and cryotherapy are increasingly being employed in an attempt to perform focal ablation therapy to treat clinically significant cancerous foci while preserving surrounding structures(4–6).

Early outcome data from focal therapy studies have shown that incontinence and erectile dysfunction are low. Early to medium disease control outcomes are so far encouraging but long-term data is lacking(5–7).

Despite these encouraging findings, some patients will develop recurrent disease following focal therapy (FT). Between 15 and 30% of men undergoing FT may be expected to develop recurrent prostate cancer and be eligible either to undergo a second ablation treatment or alternatively undergo whole-gland therapy, be that surgery or radiation therapy(4,5). To date, there are few data concerning safety and toxicity of surgery after FT with a recent review finding only 3 retrospective studies and highlighting the need for high-quality prospective trials.(8)

The RAFT **(R**obotic surgery **A**fter **F**ocal **T**herapy) study was set up as a prospective single group assignment interventional study designed to capture the toxicity of surgery after FT and early disease control outcomes.

Subjects/patients and Methods

Patient population

We conducted a multi-institutional prospective single group assignment interventional study on men undergoing robotic-assisted radical prostatectomy for recurrent prostate cancer following primary focal therapy over a 12-month period. Men were identified in multidisciplinary meetings or outpatient appointments and were eligible for this study if they had histologically-confirmed recurrent/residual adenocarcinoma of the prostate following primary focal prostate cancer ablation therapy. Patients were permitted to have undergone any of the following focal ablation therapies - HIFU, cryotherapy, electroporation, intraprostatic injection or photodynamic therapy. Other inclusion criteria included: absence of metastatic disease, Eastern Cooperative Oncology Group (ECOG) performance status score 0-2, Magnetic Resonance Imaging (MRI) to suggest urinary sphincter has not been incorporated in prior ablation therapy, and life expectancy ≥10 years. Recruitment occurred between February 2016 and September 2018.

Main exclusion criteria included patients with: other malignancy requiring systemic therapy, chronic autoimmune disease, coagulopathy/cirrhosis, severe obesity, inability to tolerate general anaesthesia, prior pelvic fracture and extensive tethering of the rectum caused by prior ablation therapy. Relative exclusion criteria included extensive peritoneal adhesions from prior abdominal surgery. All men were counselled appropriately and gave written informed consent.

Intervention

Recruited patients were screened for metastatic disease prior to surgery via bone scintigraphy or positron emission tomography at the clinician's discretion. Patients completed baseline functional assessment using the validated short-form Expanded Prostate Cancer Index Composite (EPIC)-26 questionnaires 6 weeks prior to salvage surgery(9,10). All robotic-assisted radical prostatectomies were performed by 2 high volume prostate cancer surgeons at 2 separate hospital sites (Guy's and University College London Hospitals, London, UK). Details of surgical technique can be found in previously published literature(11).

Regular follow-up occurred initially within 8 weeks post-operatively and then subsequently at 3, 6, 9, and 12 months from surgery. At each follow-up consultation, each patient had repeated serum Prostate Specific Antigen (PSA) measurements and completed a repeated EPIC questionnaire. The questionnaires were collected independently of clinicians by the trial nursing team and outcomes

were analysed independently of the clinicians involved by the clinical trial coordinating centre's statisticians.

The RAFT trial was closed October 2019 when the 24-patient target recruitment was met and participants had completed protocol mandated 12-month follow-up with no further analyses planned.

Outcome measures

Primary outcome measures were safety and toxicity of surgery after FT. Toxicity was quantified by comparison of bowel, urinary, hormonal and sexual function scores of pre-operative and follow-up EPIC questionnaires. The EPIC questionnaire includes questions on continence pad use and quality of erections scored from 0 (worst) to 100 (best). Erectile dysfunction was defined as a low sexual function score (<60/100). Safety was assessed by the reporting of Clavien-Dindo complications (I-IV)(12). High-risk disease was defined according to D'Amico risk classification (13). Secondary outcomes included Biochemical Recurrence-Free Survival (BCFS) following surgery and need for further salvage therapy. Biochemical recurrence was defined as post-surgical serum PSA ≥0.2 on 2 separate occasions. Further salvage therapy was defined as androgen-ablation therapy (including Bicalutamide or Goserelin) or radiation therapy after surgery.

Trial governance

RAFT was sponsored by Queen Mary University of London. The Sponsor was responsible for the overall study management (including monitoring), data management and statistical analysis. This trial was registered on ClinicalTrials.gov with **identifier NCT03011606**.

A Trial Management Group consisting of the Chief Investigator, Trial Coordinator, Project Lead and Statistician monitored all aspects of the conduct and progress of the trial, ensuring that the protocol was adhered to and that appropriate action was taken to safeguard participants and the quality of the trial itself if required.

Ethics and study conduct

This study was conducted in accordance with Good Clinical Practice (GCP), and investigators were trained according to applicable Sponsor Standard Operating Procedures (SOP). The Sponsor and the

investigators strictly adhered to the stated provisions in these guidelines. This was documented by the investigator's signature, which indicated the investigator's agreement to carry out all of its terms in accordance with the applicable regulations and law and to follow GCP.

Approval from NRES Committee London – City and East Research Ethics Committee (REC) was obtained before study start on 4th April 2014 and was documented in a letter to the investigator specifying the date on which the committee met and granted the approval. Protocol amendments were prepared by the Sponsor and were submitted to the REC and in accordance with local regulatory requirements. Approval was obtained from the REC before implementation of any changes. There were no audits during the conduct of the study.

Statistical Analysis

To compare changes from initial pre-operative assessment (primarily at 12-months follow-up), the Wilcoxon signed rank test was used to assess significance of the median change in the 5 domain summary scores of urinary continence, urinary irritative/obstructive, bowel, sexual and hormonal. The hormonal domain is presented for those patients who received hormone therapy in follow-up (with or without radiotherapy).

We utilised the methodological approach recommended by Skolarus and colleagues (14) to identify clinically relevant changes in patient reported EPIC-26 domain scores. In line with this approach, we report a clinically relevant change in bowel and hormonal symptoms as a change of 6 EPIC-26 points. For the sexual domain, the minimally important difference (MID) was 12 EPIC-26 points whereas for urinary continence the MID was 9 points and for urinary irritative/obstructive the MID was 7 points. Using the upper limits of these MIDs, clinically significant changes from initial pre-operative assessment are categorised into three groups: better, no difference, and worse. Better is defined as patients with changes greater than the aforementioned upper limits. Worse is defined as patients with changes less than the additive inverse (i.e. negative) of the upper limits. No difference is defined as all other patients, with changes between the two limits for better and worse. Kaplan-Meier technique was employed to evaluate BCFS after surgery and receipt of further salvage treatment. All analyses were performed using STATA version 16.

Results

24 men were recruited between February 25, 2016, and September 12, 2018. 1 patient did not subsequently undergo robotic prostatectomy despite consenting to the trial. 23 men completed 12 months of follow-up post S-RARP. Patient disease characteristics prior to S-RARP of the remaining 23 patients are presented in Table 1. Overall, 5/23 (22%) patients had 2 focal therapy treatments prior to S-RARP, not necessarily of the same treatment modality. 19/23 (83%) had HIFU prior to S-RARP, while 4/23 (17%) had cryotherapy, and 1/23 (4%) had electroporation. Median time from focal therapy to surgery was 2.1 years (range 0.8-9.7 years). All 23 men were continent of urine and pad-free at baseline assessment, while 12/23 (52%) patients had erectile dysfunction as defined by low sexual function scores at baseline assessment.

Median EPIC urinary continence scores initially deteriorated (3 months – 82.4 versus 100) but there was no statistically significant difference from baseline at 12 months (100 versus 100, p=0.31) (Table 2). There was an improvement in lower urinary tract symptoms, assessed by EPIC, between baseline and 12 months (93.8 versus 87.5, p=0.01) (Table 2). 10/23 (43%) patients were pad-free at initial post-operative consultation (within 8 weeks of surgery). At 12 months, 19/23 (83%) patients were pad-free, while 22/23 (96%) patients required 0/1 pads.

Utilising Skolarus definition of MID in EPIC score(14), at 12 months after surgery, 17/23 (74%) men reported their urinary continence to be “better” or “not different” to baseline, 18/19 (95%) reported their urinary obstructive symptoms to be “better” or “no different” to baseline while the corresponding figure for sexual function was 7/23 (30%) (Supplementary Table 1).

Significant deteriorations between baseline and 12 months were noted for median EPIC sexual function subscale scores (22.2 versus 58.3, p<0.001). On subset analysis, differences in median EPIC sexual function subscale scores between baseline and 12 months were smaller in men with higher sexual function scores (≥60) prior to surgery (70.2 versus 83.3, p=0.006) compared to men with lower scores (<60) prior to surgery (12.5 versus 46.6, p=0.003). Men without erectile dysfunction prior to surgery had recovering sexual function scores over the 12-month period, while men with erectile dysfunction did not show any improvement in scores over time (Table 2). Nerve-sparing was performed in 12/23 (52%) of men, 10 of which had unilateral nerve-sparing and 2 had bilateral nerve-sparing. Robotic surgery after focal therapy had no significant impact on the median EPIC bowel (p=0.31) or hormonal (p=0.12) subscale scores between baseline and 12 months.

After treatment, only a single patient had a post-operative complication (Clavien-Dindo Grade I). The patient was readmitted to hospital within 8 weeks of surgery for treatment of an acute arrhythmia

which resolved with pharmacological intervention and the patient was discharged the next day. There were no adverse events suspected to be caused by study intervention including anastomotic leaks or strictures. Peri-operative outcomes are outlined in Table 3.

Pathological analysis after surgery demonstrated 10/23 (43%) had organ confined T2 disease, while 6/23 (26%) had T3a disease and 7/23 (30%) had T3b disease. Overall, 8/23 (35%) men had a positive margin after surgery with T2, T3a and T3b positive margin rates being 2/10 (20%) , 2/6 (33%) and 4/7 (57%) respectively in each stage. Median length of a positive margin was 2.8mm (range 1-5mm) with median length of a positive margin was 1.5mm (1-2mm) for men with T2 disease and 3.2mm (range 1-5mm) for men with T3 disease. Analysing the length of positive margin demonstrated that only 4/8 (50%) men with a positive margin had a positive margin greater or equal to 3mm. For men with T2 disease, no patient had a positive margin greater or equal to 3mm. Corresponding figures for men with T3a and T3b disease were 2/2 (100%) and 2/4 (50%) respectively.

21/23 (91%) men had Gleason 7 disease on final pathological analysis (G3/4=14/23 (61%), G4/3=7/23 (30%)), while 1 patient had Gleason 8 disease and another Gleason 9 disease. 21/23 (91%) men were classified as having high risk disease on final surgical pathology according to the D'Amico risk classification.

Biochemical Recurrence-Free Survival (BCFS) at 12 months after surgery was 82.6% (95% CI: 60.1% - 93.1%) (Figure 2), while 4/23 (17%) patients received further salvage radiotherapy and androgen deprivation therapy and have not recurred since. 3/4 (75%) patients requiring salvage therapy had T2a and 1/4 (25%) had T3a disease on pre-operative biopsy. All 4 patients had Gleason 7 disease. 3/4 (75%) had T3b disease and positive margins on final histo-pathology.

Discussion

Summary

This prospective single group interventional study in men experiencing recurrent prostate cancer after focal therapy demonstrates that robotic-assisted radical prostatectomy after focal therapy is a safe therapeutic option. Standardised patient reported outcomes identified robotic surgery after focal therapy to be associated with low genitourinary toxicity in terms of continence and irritative lower urinary tract symptoms. However, median sexual function scores deteriorated, particularly in those with pre-operative poor sexual function. Furthermore, a relatively high proportion of men were identified to have high-risk disease on final surgical histo-pathology which impacted on BCFS rates.

Comparison with other studies

To our knowledge, there have been no prospective clinical trials evaluating toxicity of surgery in men with recurrent disease after focal ablation therapy. The studies that have reported outcomes of salvage surgery are often from single institutions, are often retrospective in design, lack accurate assessment of baseline function and often do not report toxicity using validated patient outcome reporting tools such as EPIC-26. In contrast, the current study patient population were mandated to complete EPIC-26 questionnaires at baseline and on a regular basis after surgery and these questionnaires were collected independently of clinicians by the trial nursing team and outcomes were analysed independently of the clinicians involved by the clinical trial coordinating centre's statisticians.

A number of centres have reported their outcomes of surgery after focal therapy. Patel and colleagues recently reported outcome of 126 men undergoing salvage prostatectomy over a 10-year period at their institution of which 32 men had undergone a form of ablation therapy(16). In their study, 77% of men who had focal ablation required 0 or 1 urinary continence pads at 12 months, similar to that reported in the current study (22/23 [96%]); however, the majority of men in their cohort had undergone whole gland ablation therapy which is likely to have a greater impact on continence recovery. Herrera-Caceres and colleagues also recently reported on their cohort of men undergoing surgery after focal ablation (17). In their study of 34 men, a similar proportion of men were continent after surgery as that reported in RAFT (31/34 [91%]). About a third of men had a positive margin at final pathological analysis (13/34 [38%]) while a similar proportion of men had non-organ confined disease (20/34 [59%]) which again impacted on BCFS, with 6/34 (18%) requiring

radiation therapy – similar to the proportion of men undergoing salvage radiation in the current study (4/23 [17%]).

Salvage radiation therapy could be considered after focal therapy, however a systematic review of salvage therapy after focal therapy found no series investigating radiotherapy after focal therapy (8). There have been a number of studies on the effect of radiotherapy after whole-gland ablation. In a series of 100 men, Riviere and colleagues reported urinary incontinence at 32% after 1 year following salvage radiotherapy after whole gland ablation (18). BCFS at 12 months was reported at 78% - similar to the current study (82.6%).

Clinical Implications

To our knowledge, this is the first prospective ethics-approved clinical trial of salvage surgery after FT. The trial was conceived to provide reliable data concerning toxicity of surgery after focal therapy as focal therapy is a treatment modality that is increasingly available. Around 1 in 4 men that undergo focal treatment will experience recurrent cancer and need to either have further focal treatment if appropriate or transition on to whole gland therapy. Understanding the cumulative toxicity of sequential treatments from initial focal treatment to downstream effects of salvage surgery afterwards is essential. Data from the RAFT study will help men in the decision-making process both before undergoing focal treatment initially, but also when considering which treatment option to choose if they experience recurrent disease after focal treatment.

The data from the current study has a number of clinical implications. First, the study clearly demonstrates urinary continence outcomes are good following surgery after focal ablation but that potency outcomes are at best moderate in men with good function initially and arguably poor in men with suboptimal sexual function before surgery.

Focal ablation is often not performed as a primary treatment in men with apical tumours due to the technical difficulty in generating a margin of ablation around the tumour. As such, virtually all men included in the current study had relative sparing of the apex of the prostate which is likely to have impacted on continence outcomes as the urethral sphincter was often not incorporated in the peri-prostatic scarring which was often seen at other locations of the prostate where ablation had been performed.

In contrast, we found surgery after focal therapy significantly impacted on potency outcomes, especially in men who had suboptimal function initially. While we always attempted to perform nerve sparing surgery where possible, incorporation of the cavernosal nerves in the ablation field, out of field contralateral tumours, or bilateral periprostatic scarring were limiting factors. All patients also had palpable tumours, with almost half being bilaterally palpable, preventing nerve sparing. It is important to contextualise the potency outcomes of the current study with contemporary potency outcomes of primary radical prostatectomy. Mulhall and colleagues have recently reported on erectile function recovery over a 10-year period at Memorial Sloan Kettering and found that of over 2000 men, only about 30% recover erectile function sufficient for intercourse and furthermore, they reported that outcomes had changed little over the last decade despite refinements in surgical technique(15). Of note, we did identify that in men with good potency at baseline, potency outcomes were improving over time (Figure 1) and it maybe that this trajectory would have continued out beyond 12 months after surgery.

Another finding of the current study is that men undergoing surgery after focal therapy were often found to have high-risk disease on final surgical histo-pathology, likely due to the selective nature of this group of men in that one ablation was not successful and usually not suitable for further ablation.

Study limitations

As this was a single group interventional study, the absence of a comparative arm with other salvage treatment strategies does not enable us to accurately compare the toxicity and oncological outcomes with other salvage options or primary RARP. The small sample size may also limit extrapolation. These patients were carefully selected for surgery and may not be representative of all patients undergoing salvage therapy after focal treatment. While short follow-up time can demonstrate functional outcomes, it does not give us an accurate picture of long-term oncological outcomes. Lastly, the two surgeons that performed the surgery in the current study are high volume surgeons and as such the results in the current study may not be generalisable. It is our opinion that salvage RARP after focal therapy should only be performed by experienced surgeons due to increased complexity, from gland asymmetry and scarring, compared to standard RARP.

Conclusions

Data from the RAFT trial demonstrates that salvage robotic-assisted radical prostatectomy for men experiencing disease recurrence after focal therapy is safe with low toxicity. Urinary continence outcomes are good and oncological outcomes are acceptable in the short-term. However, erectile function return after S-RARP is poor. S-RARP should be considered as an acceptable treatment option for recurrent/residual prostate cancer after focal therapy.

Declaration of Interests

Hashim U Ahmed reports grants and personal fees from Sonacare, BTG/Galil, and Sophiris Biocorp, outside the submitted work. Mark Emberton reports grants and personal fees from Sonacare, Sophiris Biocorp and Steba biotech, grants from Trod Medical and Immodulon, outside the submitted work. The remaining authors have nothing to disclose.

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	All Patients
	(N=23)
Age (years), median (IQR)	63 (58-69)
Ethnicity, n (%)	
White	22 (96%)
Source data not available	1 (4%)
Serum PSA (ng/mL), median (IQR)	6.8 (4.7 – 11.9)
T stage, n (%)	
T2a	7 (30%)
T2b	2 (9%)
T2c	5 (22%)
T3a	2 (9%)
T3b	3 (13%)
Not available	4 (17%)
Gleason Score, n (%)	
7 (3+4)	14 (61%)
7 (4+3)	7 (30%)
8 (3+5)	2 (9%)
Focal Therapy platform used, n (%)	
Cryotherapy	4 (17%)
HIFU	19 (83%)
Electroporation	1 (4%)

Number of Focal therapy treatments, n (%)	
1	18 (78%)
2	5 (22%)
Previous prostate surgery, n (%)	
No	23 (100%)
Previous abdominal surgery, n (%)	
Yes	5 (22%)
No	18 (78%)
ECOG, n (%)	
0 - Fully Active	19 (83%)
1 - Ambulatory, capable of light work	4 (17%)

Table 1. Summary of pre-operative characteristics. For focal therapy platform used, patients may have multiple focal therapies therefore patients may be included in multiple rows for this summary, i.e. they are not mutually exclusive. If a patient had multiple of the same focal therapy platform used (with different dates) then they will be included as one count for the specified platform. ECOG = Eastern Cooperative Oncology Group. IQR = Interquartile range. PSA = Prostate specific antigen

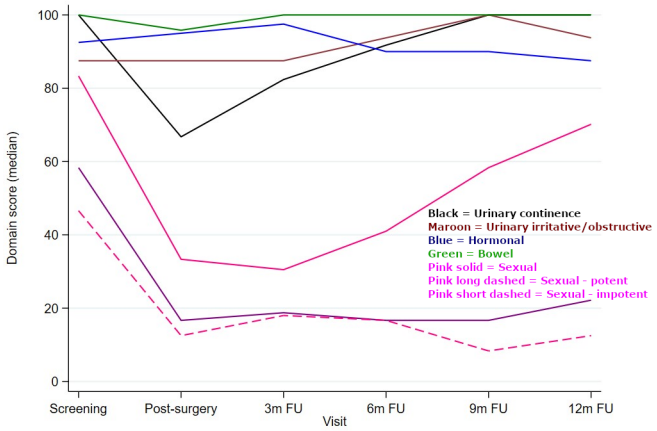
		Screening		Post-surgery		Follow-up 3 months		Follow-up 6 months		Follow-up 9 months		Follow-up 12 months		
Domain	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	P
UC	23	100 (91.8–100)	20	66.8 (55.4-88.6)	18	82.4 (52.3-91.8)	21	91.8 (79.3-100)	21	100 (79.3-100)	23	100 (85.5-100)	0.311
UO	22	87.5 (81.3-93.8)	19	87.5 (87.5-93.8)	18	87.5 (87.5-93.8)	20	93.8 (87.5-100)	19	100 (93.8-100)	20	93.8 (93.8-100)	0.010
B	20	100 (93.8-100)	20	95.8 (91.7-100)	18	100 (91.7-100)	21	100 (91.7-100)	20	100 (93.8-100)	21	100 (95.8-100)	0.313
S	22	58.3 (40.3-79.2)	20	16.7 (8.3-27.8)	18	18.8 (8.3-34.7)	20	16.7 (8.3-42.3)	19	16.7 (5.5-54.2)	23	22.2 (8.3-66.7)	<0.001
S – P	10	83.3 (75-95.8)	8	33.3 (12.5-66)	8	30.5 (8.3-59.1)	10	41 (8.3-69.5)	7	58.3 (4.2-87.5)	10	70.2 (48.7-87.5)	0.006
S - I	12	46.6 (29.2-57)	11	12.5 (8.3-26.3)	9	18 (8.3-26.3)	9	16.7 (8.3-18)	11	8.3 (5.5-32)	12	12.5 (8.3-24.3)	0.003
H	22	92.5 (85-100)	19	95 (80-100)	18	97.5 (85-100)	21	90 (85-100)	20	90 (80-100)	22	87.5 (75-100)	0.119

Table 2. Summary of EPIC-26 sub-section questionnaire scores by visit. P-values <0.05 are highlighted. B = Bowel. H = Hormonal. IQR = Interquartile range. N = Number of patients with a non-missing summary score for the specified domain at the specified visit. UC = Urinary continence. UO = Urinary irritative/obstructive. S = Sexual. S – I = Sexual: Impotent patients. S – P = Sexual: Potent patients. Post-surgery visit

occurs within 8 weeks of surgery. P-values presented are exact p-values from the Wilcoxon signed-rank test between screening and the specified post-screening visit. Potent is defined as an EPIC-26 sexual domain score at screening of ≥60 and impotent is defined as an EPIC-26 sexual domain score at screening of <60.

	All Patients
	(N=23)
Positive surgical margin, n (%)	8 (35%)
pT Stage, n (%)	
pT2	10 (43%)
pT3a	6 (26%)
pT3b	7 (30%)
Gleason score, n (%)	
7 (3+4)	14 (61%)
7 (4+3)	7 (30%)
8 (4+4)	1 (4%)
9 (4+5)	1 (4%)
Time from focal therapy to surgery (years), median (range)	2.1 (0.8 – 9.7)
Clavien-Dindo complications, n (%)	
Grade I	1 (4%)
No complications	22 (96%)

Table 3. Summary of post-operative outcomes. Time from focal therapy to surgery uses the most recent focal therapy (when comparing date of focal therapy to the date of screening visit).



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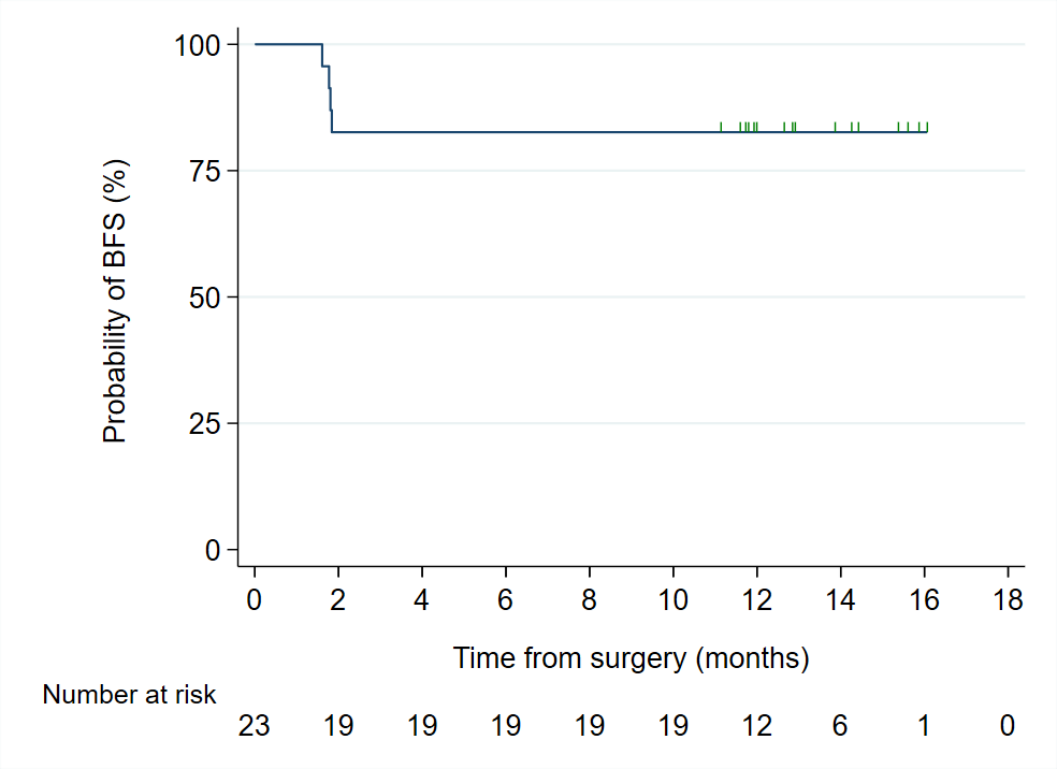

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