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Salvage Therapy for Prostate Cancer: Which is Best? Brachytherapy versus Open and Robotic Prostatectomy

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Abstract

No standard salvage therapy exists. The objective of salvage therapy is oncological control with minimum toxicity. Advances in functional imaging, including multi parametric prostate MRI and abdominopelvic lymphangio-MRI, have paved the way for salvage therapy in localised recurrence. To date there are no randomized clinical trials comparing HDR-BT with radical prostatectomy.

Methods: We conduct as retrospective review over 20 years comparing outcomes of salvage brachytherapy compared to open and robotic radical prostatectomy, searching Embase and Medline.

Results: Whilst robotic radical prostatectomy is a clear winner, there is also a role for salvage brachytherapy.

Conclusions: The role of salvage therapies such as brachytherapy need to be further explored.

Keywords: Salvage brachytherapy; Oncological; Functional outcomes; Salvage robotic prostatectomy; Salvage open prostatectomy

Introduction

At least one third of patients who receive external beam radiation will have biochemical recurrence (BCR) with 9 and 7% having local and distant failure, respectively [1,2]. Approximately 20%–30% of men with clinically localized prostate cancer treated with radiation therapy will develop evidence of biochemical recurrence (BCR) [3]. The vast majority of men with BCR after radiation therapy are managed with observation of androgen deprivation therapy (ADT). Only 10% of men are curatively treated using salvage local therapy [3].

Methods

We conduct as retrospective review over 20 years comparing outcomes of salvage brachytherapy (SBRACH) compared to open (SORP) and robotic radical prostatectomy (SRARP), searching embase and medline. Search terms used include salvage therapy and brachytherapy or prostatectomy (open or robotic).

Results

The goal of SRARP is to cure radiation-recurrent prostate cancer and cancer-specific survival. This approaches 80% at 10 years [3]. In a recently published multicentre review of outcomes after SRARP, men with a pre-SRARP PSA of 4 ng/ml and post-radiation biopsy Gleason score 7 were considered a favorable risk group with 70% having long-term freedom from BCR [3]. SRARP is technically demanding. While outcomes have improved with better patient selection and greater surgical experience, the incidence of both bladder neck contracture (30%) and incontinence (50%) remain high; there is some suggestion that these complications may be reduced with minimally invasive RP, but further data are needed to confirm this observation [3].The improvements in surgical experience and the technical advances, including robotic surgery, have ameliorated surgical performances for salvage radical prostatectomy (SRP) over the last decade [4,5]. Erectile dysfunction and urinary incontinence were 32%and 100% [4]. Even with the limits of the retrospective studies, recent series of SRARP suggest its superiority over other salvage treatment modalities such as cryotherapy, HIFU [4]. The 5-year biochemical free probability rates after SRARP ranged between 28% and 71% [4]. Early diagnosis of this and aggressive treatment could produce better and more durable results than the other salvage approaches [6]. There is also no data available on pelvic lymph nodes dissection available for SRP. The Vattikuti Urology Institute published their series of 11 men who underwent SRRLP of which the biochemical free progression was 63% at a median follow-up of 20.5 months [7]. In the largest SRARP series, 67% of men had biochemical free progression at a median follow-up of 18 months [8]. Interestingly, of the patients who developed BCR after surgery, 67% had positive surgical margins and 33% had preoperative PSA >10 ng/ml [8]. Clearly, salvage robotic radical prostatectomy (SRARP) has better outcomes, than open robotic prostatectomy. This is especially relating to continence side effects. Previously, this could be as high as 50%. However, with the advent of DaVinci surgical systems, this is significantly reduced. This allows the patient good oncological outcomes, whilst receiving a minimally invasive operation. The other difficulty, in general with open surgery, was the inability to do nerve sparing as with the robotic prostatectomy. This results in far higher rates of erectile dysfunction with robotic prostatectomy. Additionally, the positive margin rate is slightly lower with the robotic system with straightforward dissection of lymph nodes. Additionally, the complication rate for this procedure has far reduced with a robotic system. This has impacted on overall patient care, resulting in prostatectomies even being done as daycase surgery [9]. Whole gland salvage treatments such as radical prostatectomy and brachytherapy for recurrent prostate cancer after primary irradiation show severe toxicity rates [10]. Previously, high failure rates have been observed [11].

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Salvage radical prostatectomy is a technically challenging procedure. This is associated with a high complication rates for rectal injury, urinary leak anastomotic stricture and incontinence [12]. What cause the issues are extra-prostatic fibrosis, distorted anatomy and non-anatomical tissue-planes. Additionally, robotic-assisted salvage radical prostatectomy (SRARP) is not widely performed [13]. Focal therapy, such as salvage brachytherapy (SBrach) is alternative to salvage radical prostatectomy for locally recurrent prostate cancer after primary radiation therapy [14]. If patients can be selected properly, focal therapy could enable tumor eradication without the morbidity associated with salvage radical prostatectomy (14). We review the oncological and functional outcomes of SRARP to SBRACH. SRARP accounts for only 2.9% of expected RT local failures. SRARP patients undergoing surgery have more high risk disease. As part of this, patient expectations are key. Patients should be counselled regarding side effects, anastomotic leakage on cystogram, and prolonged catheterization times [15]. Additionally the time to potency and continence in SRARP undergoing partial and no nerve sparing was significantly delayed [15]. Perioperative complications of SRARP include urinary incontinence rates of 40% to 50% and rectal injury rates of 10% to 15%. However, in the hands of an experienced surgeon, these figures will be significantly improved. Long-term disease-free survival rates of 30% to 40% can be expected [16]. The proportion of patients returning to potency and continence was also lower; however this tends to be more high risk disease. As a result patients showing high-risk disease characteristics should be informed adequately about the low chances of success [17]. Treatment results could be improved if salvage therapy is considered very early in the disease process. SRARP is technically possible and with limited perioperative morbidity [18]. This curative therapy may be underutilized in biochemical recurrence [19]. In select patients derived from a population-based cohort, SRARP resulted in effective local cancer control with acceptable perioperative outcomes [20]. However, there are factors that highlight how successful SRARP maybe. Interestingly, this cohort demonstrated PSA level >20 ng/ml is associated with positive margins and prolonged length of stay after SRARP. Clinical stage T2 or greater disease is also associated with prolonged length of stay, whereas surgery at an experienced facility reduced this risk. Salvage radical prostatectomy (SRARP) is a potentially curative operation performed for recurrent prostate cancer [20]. Salvage radical prostatectomy is a technically challenging procedure that is associated with high complication rates for rectal injury, urinary leak anastomotic stricture and incontinence [21]. There can be extensive extra-prostatic fibrosis leading to distorted anatomy and difficulty with tissue-planes a difficult dissection. Robotic-assisted salvage radical prostatectomy is not widely performed but has specific advantages to the traditional open procedure. This allows for excellent visualization of tissue planes rather than feel, reduced bleeding and a more secure anastomosis [21]. Additionally robotic extended pelvic lymph node dissection is safe and can improve the accuracy of surgical staging. Salvage radical prostatectomy is a safe and effective alternative for the treatment of locally recurrent prostate cancer. In comparison to SRARP, few patients were considered for local salvage therapy after radiation failure, and only 2% received it [22]. There is also a possible underutilization of SBRACH after radiotherapy and indicate a need for more collaboration between tertiary care centres. SBRACH has a low rate of genitourinary side effects and no late gastrointestinal side effects [23]. The treatment efficacy in the first 3 years demonstrated good outcomes [23]. Prostate cancer recurrence is often bilateral and involves multiple zones. Additionally, it can be high grade, bulky and close to the urethra [24]. This suggests salvage focal therapy after radiation failure will be difficult [24]. Yet results demonstrate HDR-BT have good oncological outcomes [25]. However, when comparing both groups SBRACH to SRARP, 5-year BCR-free rates are superior in patients treated with SRARP [25]. Salvage brachytherapy for biopsy-proven local recurrence of prostate cancer is a technically feasible alternative for lower risk disease [26]. Improved biochemical relapse free survival occurs for lower Gleason score and pre-salvage PSA [27]. SBRACH is an effective salvage technique and can be considered in well selected patients allowing for dose escalation to- the nodular recurrence.This data confirmed the feasibility and safety of SBRACH when performed by experienced centers [28]. The disease control rates and complications of treatment compare very favorably with those reported using other modalities [29].

Conclusions

This overview shows clinical practice of prostate cancer salvage therapy. Failure and toxicity rates are observed, regardless of salvage technique. Whilst salvage brachytherapy is appropriate for low risk cases, and gives low toxicity, SRARP is better for high risk disease with better oncological outcomes. Patients should be selected with great care before offering these salvage treatment strategies.

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