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Proactive rectal warming during total-gland prostate cryoablation ☆

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ABSTRACT

Purpose: Proactive rectal warming (PRW), as a modification of prostate cryoablation, was assessed in terms of rectal complications and therapeutic outcomes.

Materials and methods: A cohort of 166 patients cumulatively treated between September, 2009 and November, 2012 qualified for study, each undergoing total-gland cryoablation (TGC) for prostate cancer. The initial 100 patients accrued submitted to TGC alone. PRW was administered to the final 66 patients. Preemptive warming is achieved by inserting a cryoprobe midline through perineal skin into anterior rectal wall under ultrasound guidance. The activated probe generates warmth as the ice ball encroaches on rectum. Prospective, post-ablative grading of rectal pain was measured at weeks 1, 2, 4, 8, 12, and 24 by using the Common Terminology Criteria for Adverse Events. Recurrent prostate cancer was gauged by Phoenix criterion (nadir + 2 ng/ml). The Mann–Whitney *U* test and Chi-square test were used to compare clinical characteristics of therapeutic subsets. The Cox proportional hazard model was applied for comparison of cancer recurrence risk by group.

Results: Rectal pain (all grades) was experienced by patients treated with (62%) and without (74%) PRW. Although such pain typically resolved with time, it was milder (general lineal model, $p = 0.023$) and less prolonged (median: 0.75 vs 1.5 months; log-rank test, $p = 0.002$) in patients receiving PRW than in controls. Of note, PRW did not heighten cancer recurrence risk (hazard ratio = 1.3 [95% CI, 0.3–5.0]).

Conclusions: PRW helps to protect the rectum from freeze injury during prostate cryoablation, significantly reducing post-ablative rectal pain without compromising therapeutic outcomes.

Introduction

Treatment options for localized prostate cancer have gradually evolved over time to include radical prostatectomy, radiotherapy, cryoablation, and active surveillance/watchful waiting. Although data as yet are insufficient to endorse a particular treatment, related complications or adverse effects clearly do vary by modality selected.

Cryoablation is a minimally invasive therapy for localized prostate cancer that has proven effective in cancer control [9,14]. Still, a number of adverse effects appear postoperatively [1], some irreversible (i.e., urinary incontinence and erectile dysfunction) [10] and others resolving with passage of time. Rectal pain, also referred to as anal pain or perineal tenderness, is one such handicap with a potential to persist for months and significantly impact quality of life [2,4,11]. In particular, it may be impossible to even sit on a firm surface due to severe pain.

The underlying pathophysiology of post-ablative rectal pain is unclear, but freeze injury to rectal wall and/or adjacent soft tissues has been implicated. Rarely, an unpleasant recto-urethral fistula may develop secondarily if the vitality of anterior rectal wall is significantly weakened during cryoablation. Reported rates of rectal fistula subsequent to total-gland cryoablation (TGC) of the prostate ranged from 0.4% to 2.4% [1]. Because rectal pain and recto-urethral fistula both are linked to some extent with devitalization of rectal wall during freezing, preventing collateral injury within this region of high vulnerability is imperative. Unfortunately, past attempts to limit injury in the course of prostate cryoablation have targeted only prostatic urethra and external sphincter (via urethral warming catheters), overlooking rectal wall due to technical issues.

Abbreviations: CCED, cumulative cryoablation energy dose; PPC, posterior prostate compartment; PRW, proactive rectal warming; TGC, total-gland cryoablation; TRUS, transrectal ultrasound.

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Herein, rectal warming is introduced as an innovative means to proactively protect anterior rectal wall from cryoablative freeze injury during treatment of prostatic cancer.

Materials and methods

Patient population and enrollment criteria

Between September, 2009 and November, 2012, a total of 176 consecutive Taiwanese patients undergoing TGC for localized prostate cancer accrued as potential candidates. The study protocol was approved by the Research Ethics Committee of our hospital. Patients suffering post ablative urethral sloughing (n = 10) as a confounding issue were excluded from analysis, leaving 166 subjects. The first 100 patients treated (prior to September, 2011) were subjected to TGC of the prostate exclusively. All 66 patients remaining thereafter submitted to prostatic TGC with PRW.

Proactive rectal warming technique (Fig. 1)

The Endocare® Cryocare Surgical System (Healthtronics Inc., Austin, TX, USA) was utilized for all TGC procedures. Following placement of cryoprobes (2.4 mm V-Probe [CVA2400]) and thermocouples (16 G TempProbe [Cryo-55F]) as stipulated, an additional 2.4 mm cryoprobe was placed within anterior rectal wall to provide warmth. Under linear array transrectal ultrasound (TRUS) guidance, this probe was inserted cephalad at midline of perineal skin into anterior rectal wall, advancing some 2.5–5 cm deep at 12 o'clock position of rectal hump. Probe placement on TRUS sagittal image was held parallel to and about 0.5 cm from "serosal surface" of anterior rectal wall. Care was taken to avoid piercing rectal mucosa, thus entering rectal lumen. During the advancement of the warming probe in the anterior rectal wall, the probe tip can be tilted up away from the rectal wall and into the Denovillier's space, if the anterosuperior rectal wall becomes too thin to accommodate the probe and the Denovillier's space is wider than 0.5 cm at level of the probe tip.

Once the cryoablative ice ball began to "invade" the anterior aspect of rectum, the rectal warming probe was activated 100%, forcing helium gas against the invading ice ball and generating a cylindrical warming zone inside anterior rectal wall. The zone of protective warmth generally extended from 10 to 2 o'clock along anterior rectal wall, with a 0.5-cm radius and a temperature of 21–25 °C at the tip of the activated probe. PRW was maintained until the entire ice ball retreated from anterior rectal wall during the thawing phase. A thermocouple placed midline in Denovillier's space usually stays cold and is unaffected by PRW.

Rectal pain measurement

Evaluations of rectal pain were prospective in nature, conducted by trained study coordinators at post ablative weeks 1, 2, 4, 8, 12, and 24. The Common Terminology Criteria for Adverse Events (CTCAE, v4.02) [6] was invoked for grading purposes. In instances of persistent rectal pain, evaluations were extended past week 24 at 12-week monitoring intervals. Duration of rectal pain was determined from date of cryoablation to date of resolution, as reported by patients (i.e., ability to sit with ease on a hard surface for >60 min).

Factors predicting rectal pain

In addition to patient demographics and tumor characteristics, factors such as thickness of prostate posterior compartment (PPC) and cumulative cryoablation energy dose (CCED) delivered to PPC were recorded. Thickness of PPC was defined as the shortest distance between outer surface of midline posterior urethral wall and prostate capsule (Fig. 1). The greater the PPC value, the less chance of injury to urethra and rectum (usually in close approximation) by an ice front emanating from dual posteromedial cryoprobes. CCED delivered to PPC was defined as duration (min) of activation multiplied by the cryogenic power (%) setting of the two posteromedial probes.

Recurrence of prostatic cancer

To assess and compare therapeutic outcomes, instances of recurrent prostate cancer were gauged by Phoenix criterion (PSA ≧ nadir + 2 ng/ml). Variables included in analysis of recurrent cancers were pre-operative PSA level, Gleason sum, tumor stage, adjuvant hormonal therapy, thickness of PPC, CCED delivered to PPC, and proactive use of a rectal-warming probe.

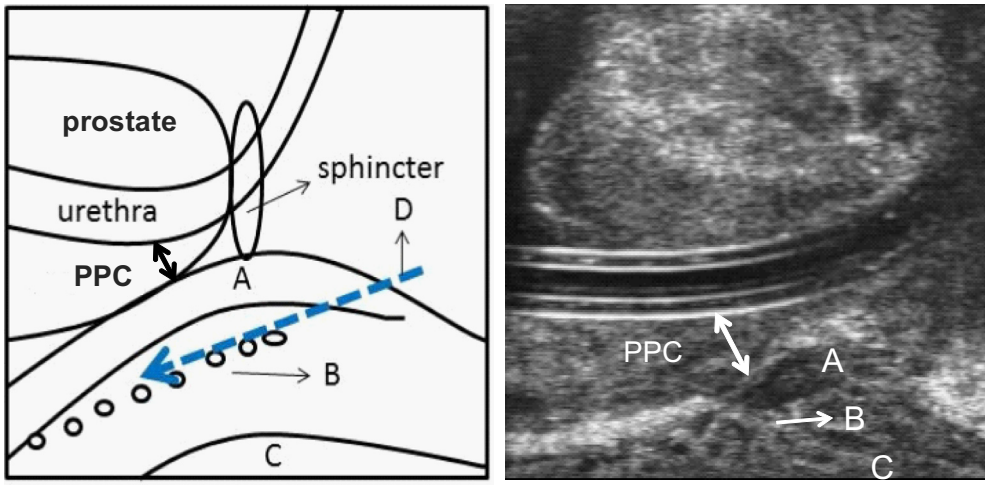

Fig. 1. The placement of rectal proactive warming probe. The proactive warming probe is inserted cephalad along the dotted line. The dotted line is parallel to the serosal surface of the anterior rectal wall and between the inner and outer muscle layers of rectal wall. A: rectal hump; B: the inner muscle layer of the rectal wall; C: rectal lumen; D: the insertion direction of proactive warming probe; PPC: prostate posterior compartment.