

A prospective randomized trial to evaluate the prophylactic use of tadalafil versus tamsulosin for lower urinary tract symptoms and erectile dysfunction after low-dose-rate brachytherapy for prostate cancer: initial report

Tomonori MINAGAWA, Tomohiko OGUCHI, Hironori DAIMON, Keiichiro KOIWA, Haruaki KATO, Iwao HASHIDA, Teruyuki OGAWA, Masumi KADOYA, Osamu ISHIZUKA

Department of Urology, Shinshu University School of Medicine, Department of Urology, Nagano Municipal Hospital, Department of Radiology, Nagano Municipal Hospital, Department of Radiology, Shinshu University School of Medicine

Hypothesis / aims of study

Low-dose-rate brachytherapy (LDRB) is a well established method of treating localized prostate cancer. However, almost all patients develop some degree of lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) after LDRB. And, only alpha-blocker is a recommended drug to prevent LUTS after LDRB in the previous report. (Merrick GS, et al. Urology, 2002. Tsumura H, et al. Int J Radiat Oncol Biol Phys, 2011) On the other hand, tadalafil, phosphodiesterase-5 inhibitor, has a similar therapeutic impact to tamsulosin on LUTS among patients with benign prostatic hyperplasia. (Oelke M, et al. Eur Urol, 2012) Then, we hypothesized that tadalafil might be one of the choices for management of LUTS and ED after LDRB. The aim of this study is to evaluate the therapeutic effects of tadalafil on LUTS and ED after LDRB comparing tamsulosin.

Study design, materials and methods

Patients who were planning for LDRB were prospectively enrolled in this study. Inclusion criteria for LDRB is a male less than 80-year-old who is diagnosed as localized prostate cancer, PSA < 10.0 ng/ml, Gleason score 3+3 or 3+4. The enrolled patients were randomly divided into 2 groups: tadalafil group and tamsulosin group. HOPE eACReSS: web-based randomized program was used for division of the patients. Patients who have prostate more than 40 cm³, have prostate with mid-lobe enlargement, LUTS with medication, or previous medical history of transurethral surgery or radiation therapy for pelvic malignant disease were excluded in this study. 160 Gy was prescribed for the localized prostate cancer using permanent implantation of I¹²⁵. Each drugs (5 mg/day of tadalafil, and 0.2 mg/day of tamsulosin) were prescribed one day after the implantation of LDRB. The therapeutic effects of each drug for LUTS were evaluated on 1, 3, 6, 9, and 12 months after LDRB. The primary endpoint is international prostatic symptoms score (IPSS). QOL score, overactive bladder symptoms score (OABSS), voided volume, Qmax, residual urine volume are also evaluated. The preventing effect for ED were evaluated using international index of erectile function (IIEF5). The therapeutic effect for prostate cancer were evaluated using prostate specific antigen (PSA) value. To compare the 2 groups in each observative period, two-tailed *t*-test was used for statistical evaluation.

Results

In total, 113 patients were enrolled between January 2015 to March 2017 in this trial. As the initial report, 47 patients were analyzed. The clinical characteristics of the enrolled patients were shown in **Table 1**. There are no statistical differences of the baseline values in each parameter between tamsulosin and tadalafil groups before LDRB. And, the results of PSA value was shown in **Fig. 1**. There are no statistical differences in PSA value among the groups.

And, subjective evaluation, such as total IPSS, QOL score, OABSS, and IIEF5 were shown in **Fig. 2**. Total IPSS 3 and 9 months after LDRB are higher in the tadalafil group than the tamsulosin group.

Objective evaluation, such as voided volume, Qmax, and residual urine, were shown in **Fig. 3**. There are no statistical differences in the objective evaluation between the tamsulosin and the tadalafil groups in all of the process before and after LDRB.

	Tamsulosin (N = 25)	Tadalafil (N = 22)	
Age (years)	66.5 ± 7.3	66.0 ± 6.9	N.S.
PSA (ng/mL)	6.4 ± 2.1	5.9 ± 2.1	N.S.
Gleason score	3+3: 16 3+4: 14	11 13	
Hormone therapy (cases)	1	2	
IPSS	10.1 ± 5.2	9.8 ± 4.1	N.S.
QOL score	2.6 ± 1.4	2.7 ± 1.4	N.S.
OABSS	2.9 ± 1.9	3.5 ± 2.5	N.S.
IIEF5	11.8 ± 7.3	12.1 ± 6.6	N.S.
Voided volume (mL)	279.7 ± 142.8	294.7 ± 208.4	N.S.
Qmax (mL/sec)	17.9 ± 6.8	17.9 ± 6.5	N.S.
Residual urine (mL)	15.8 ± 15.6	20.8 ± 23.8	N.S.

Table 1 Clinical characteristics of the patients.

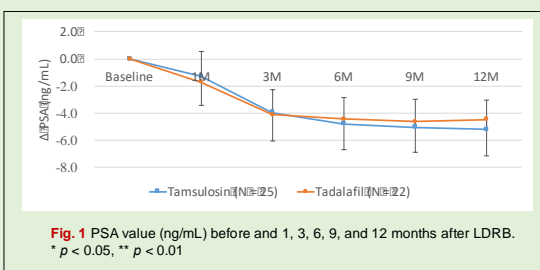


Fig. 1 PSA value (ng/mL) before and 1, 3, 6, 9, and 12 months after LDRB. * *p* < 0.05, ** *p* < 0.01

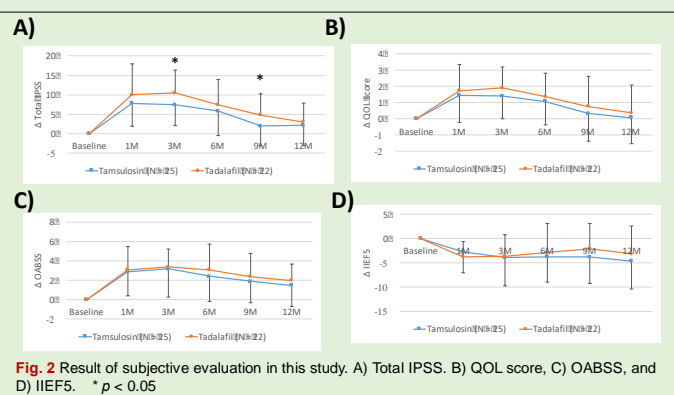


Fig. 2 Result of subjective evaluation in this study. A) Total IPSS, B) QOL score, C) OABSS, and D) IIEF5. * *p* < 0.05

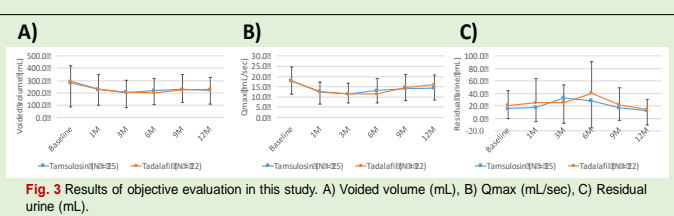


Fig. 3 Results of objective evaluation in this study. A) Voided volume (mL), B) Qmax (mL/sec), C) Residual urine (mL).

Interpretation of results

LUTS after LDRB peaked on 3 months after implantation in this study. The reductive effects of IIEF5 prolonged more than 1 year after LDRB.

In this initial report, tadalafil may have no inferior therapeutic effect to tamsulosin on LUTS in most of process after LDRB. However, there is only statistical difference on total IPSS 3 and 9 months after LDRB implantation between the tadalafil and tamsulosin groups. The course of recovery of LUTS in the tadalafil group were almost the same as the tamsulosin group. Statistical therapeutic impacts of tadalafil were not detected on erectile dysfunction after LDRB comparing tamsulosin in this analysis. However, tadalafil may have effect to reduce erectile dysfunction more than 9 months after the implantation. On the other hand, any statistical differences were not detected in all of the objective evaluation.

There are some limitations in this study such as number of patients, method to evaluate LUTS and ED. Urodynamic study was not done, and only IIEF5 was used to evaluate ED. However, the similar effects of tadalafil on LUTS and ED after LDRB were indicated in this initial analysis of this trial. Further analysis in all of process of this study should be done to conclude the difference for evaluate exact role of each drug for LUTS after LDRB.

Concluding message

In the initial analysis of this trial, prophylactic use of tamsulosin reduced total IPSS 3 and 9 months after LDRB better than tadalafil. Tadalafil may be superior to tamsulosin for management of ED after LDRB. However, to confirm the exact effect of tadalafil for LUTS and ED after LDRB, analysis with full-set of the patients should be done.