Improved Outcomes with Advancements in High Intensity Focused Ultrasound Devices for the Treatment of Localized Prostate Cancer

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Purpose: We evaluated the association between long-term clinical outcomes and morbidity with high intensity focused ultrasound.

Materials and Methods: We included patients with stage T1c-T3N0M0 prostate cancer who were treated with Sonablate® (SB) devices during 1999 to 2012 and followed for more than 2 years. Risk stratification and complication rates were compared among the treatment groups (ie SB200/500 group, SB500 version 4 group and SB500 tissue change monitor group). Primary study outcomes included overall, cancer specific and biochemical disease-free survival rates determined using Kaplan-Meier analysis (Phoenix definition). Secondary outcomes included predictors of biochemical disease-free survival using Cox models.

Results: A total of 918 patients were included in the study. Median followup in the SB200/500, SB500 version 4 and the SB500 tissue change monitor groups was 108, 83 and 47 months, respectively. The 10-year overall and cancer specific survival rates were 89.6% and 97.4%, respectively. The 5-year biochemical disease-free survival rate in the SB200/500, SB500 version 4 and SB500 tissue change monitor group was 48.3%, 62.3% and 82.0%, respectively ($p < 0.0001$). The overall negative biopsy rate was 87.3%. On multivariate analysis pretreatment prostate specific antigen, Gleason score, stage, neoadjuvant androgen deprivation therapy and high intensity focused ultrasound devices were significant predictors of biochemical disease-free survival. Urethral stricture, epididymitis, urinary incontinence and rectourethral fistula were observed in 19.7%, 6.2%, 2.3% and 0.1% of cases, respectively.

Conclusions: Long-term followup of patients with high intensity focused ultrasound demonstrated improved clinical outcomes due to technical, imaging and technological advancements.

Key Words: prostatic neoplasms, high-intensity focused ultrasound ablation, treatment outcome

Abbreviations and Acronyms

ADT = androgen deprivation therapy

BDFS = biochemical disease-free survival

HIFU = high intensity focused ultrasound

IIEF-5 = International Index of Erectile Function-5

IMRT = intensity modulated radiation therapy

PSA = prostate specific antigen

SB = Sonablate

TCM = tissue change monitor

TURP = transurethral prostate resection

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PROSTATE cancer is the most common malignancy in men and the second leading cause of cancer related death in the United States.[1] Prostate cancer treatment is dependent on disease severity and staging, patient age, Gleason score and PSA.[2] Radical prostatectomy has been regarded as the appropriate therapy for patients with long-standing organ confined prostate cancer.[3] Recently many less invasive alternative treatments have

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been developed for patients with localized prostate cancer who are not candidates for surgery. Active surveillance, brachytherapy, IMRT, cryosurgical ablation, laparoscopic radical prostatectomy and robot-assisted radical prostatectomy have all been used to treat patients with prostate cancer.[4–10]

HIFU is a noninvasive technique that induces coagulative necrosis in tumors without surgical exposure or insertion of instruments into the lesion.[11–13] Currently the Ablatherm® and Sonablate devices are commercially available to treat patients with prostate cancer.[11–16] Although the fundamental HIFU features of both systems are identical, they have several technical differences.[13] We report the first long-term outcomes to our knowledge of SB HIFU devices for the treatment of patients with localized prostate cancer.

MATERIALS AND METHODS

Devices

Many improvements have been made to the SB device to shorten the operative time and improve clinical outcomes.[13] The cycle time was reduced from 16 to 6 seconds per focus lesion. The focus volume was also enlarged from 2.0 × 2.0 × 10 mm (0.04 cc) to 3.0 × 3.0 × 12 mm (0.108 cc). SB devices incorporate additional safety features including reflectivity measurements, stacking and TCM systems.[13] The stacking system can refine the treatment plan before or during the procedure. The TCM system quantifies tissue changes based on comparisons of radio frequency ultrasound pulse echo signals at each treatment site and monitors lesion temperatures by color changes.[13]

Patients and Treatment Methods

This study was conducted from 1999 to 2012, and included 918 patients with clinical stage T1c-T3N0M0, biopsy proven, localized prostate cancer with a PSA less than 30 ng/ml, any Gleason score and neoadjuvant ADT less than 24 months before HIFU. All patients were required to have a minimal followup of 2 years after the last HIFU session. The 3 treatment groups were the SB200/500 group (408 patients treated from 1999 to 2006), SB500 version 4 group (239 patients treated from 2005 to 2009) and the SB500 TCM group (271 patients treated from 2007 to 2012). All patients were fully informed of the details of this treatment and provided written consent preoperatively. This study was approved by the local ethics committee.

Followup and Definitions

Serum PSA was assayed every 3 months during followup. A postoperative prostate biopsy was performed 6 months after HIFU. Biochemical failure was defined according to the Phoenix ASTRO (American Society for Therapeutic Radiology and Oncology) definition (PSA nadir + 2 ng/ml).[17] None of the patients received ADT or anticancer therapy before documented biochemical failure. Repeat HIFU was conducted in patients who desired repeat HIFU, and had biochemical failure and viable cancer cells without distant metastasis. HIFU related complications were defined by the Clavien classification.[18] Patients were considered to have urinary continence if they did not use any pads or used only 1 safety pad daily. Erectile dysfunction was defined as a score of 7 or less on the IIEF-5 for patients who had a pretreatment IIEF-5 score of greater than 7 with no neoadjuvant androgen deprivation therapy before HIFU.[19] Patients were identified as low, intermediate and high risk according to the 2003 risk group categories of D'Amico et al.[20]

Salvage Treatment

Salvage radical prostatectomy or radiation therapy was performed after the last HIFU session in the event of biopsy proven local recurrence and/or biochemical failure with the consent of each patient. However, all patients who were treated with salvage ADT showed no viable cancer cells or poor general health status.

Statistical Analysis

All statistical analyses were performed using the StatView® 5.0 software program. The chi-square test was used to assess the correlation among groups. A Kaplan-Meier analysis was performed to determine overall, cancer specific and biochemical disease-free survival rates. Cox proportional hazard regression models were used to evaluate the predictors of BDFS and $p < 0.05$ was considered statistically significant.

RESULTS

Patient Characteristics

Median age, PSA, Gleason score and prostate volume for the entire cohort was 68 years (range 46 to 88), 8.57 ng/ml (range 1.36 to 29.8), 7 (range 3 to 10) and 22.3 ml (range 4.6 to 68.8), respectively (table 1). Clinical stages included T1b (8), T1c (551), T2a (82), T2b (112), T2c (131) and T3 (33). All patients had a histological diagnosis of prostatic adenocarcinoma according to the Gleason grading system. The histological grade included Gleason scores of 2–6 (452), 7 (337) and 8–10 (129) in the overall cohort. The number of patients with a PSA less than 10.0, 10.01 to 20.00 and greater than 20.0 ng/ml was 562 (61.2%), 289 (31.5%) and 67 (7.3%), respectively. The number of patients in the low, intermediate and high risk categories was 235 (25.6%), 465 (44.1%) and 278 (30.3%), respectively, with no significant differences among device groups.

Neoadjuvant ADT was administered to 540 (58.8%) patients for a median of 3.0 months (range 1 to 24) before the visit to our hospital, but no significant differences were observed among the groups. Median operative time and followup for the entire cohort was 116 minutes (range 30 to 394) and 78 months (range 6 to 163), respectively. In the SB200/500, SB500 version 4 and SB500 TCM

Table 1. *Baseline patient characteristics*

	SB200/500	SB500 Version 4	SB500 TCM	Overall
Surgery yrs	1999–2006	2005–2009	2007–2012	1999–2012
Median age (IQR)	68 (50–88)	67 (46–83)	67 (48–85)	68 (46–88)
Median ng/ml PSA (IQR)	9.24 (2.8–29.8)	8.09 (2.51–29.0)	8.06 (1.36–9.2)	8.57 (1.36–29.8)
Median Gleason score (IQR)	6 (3–10)	7 (4–10)	7 (4–10)	7 (3–10)
Median cc prostate wt (IQR)	21.9 (4.6–68.8)	23.0 (8.1–60.4)	22.3 (8.0–50.1)	22.3 (4.6–68.8)
No. clinical stage (%):				
T1b	4 (1.0)	1 (0.4)	3 (1.1)	8 (0.9)
T1c	222 (54.4)	154 (64.4)	175 (64.6)	551 (60.0)
T2a	19 (4.7)	21 (8.8)	42 (15.5)	82 (8.9)
T2b	72 (17.6)	21 (8.8)	20 (7.4)	113 (12.3)
T2c	71 (17.4)	33 (13.8)	27 (10.0)	131 (14.3)
T3	20 (4.9)	9 (3.8)	4 (1.5)	33 (3.6)
No. Gleason score (%):				
2–6	247 (60.5)	110 (46.0)	95 (35.1)	452 (49.2)
7	109 (26.7)	91 (38.1)	137 (50.6)	337 (36.7)
8–10	52 (12.7)	38 (15.9)	39 (14.4)	129 (14.1)
No. ng/ml PSA (%):				
0–10.0	229 (56.1)	151 (63.2)	187 (69.0)	562 (61.2)
10.1–20.0	139 (34.1)	73 (30.5)	72 (26.6)	289 (31.5)
20.1 or Greater	40 (9.8)	15 (6.3)	12 (4.4)	67 (7.3)
No. risk group (%):				
Low	112 (27.5)	61 (25.5)	62 (22.9)	235 (25.6)
Intermediate	159 (39.0)	102 (42.7)	144 (53.1)	405 (44.1)
High	137 (33.6)	76 (31.8)	65 (24.0)	278 (30.3)
No. neoadjuvant hormonal therapy (%):	250 (61.3)	143 (59.8)	177 (54.2)	540 (58.8)
Median operative mins (IQR)	145 (30–394)	95 (32–185)	107 (37–180)	116 (30–394)
Median mos followup (IQR)	108 (6–163)	83 (6–99)	47 (15–79)	78 (6–163)

groups median operative times were 145, 95 and 107 minutes ($p < 0.0001$), respectively, and median followup periods were 108, 83 and 47 months, respectively (table 1). TURP was performed in 137 (14.9%) patients to decrease prostate volume or remove large prostatic calcifications 1 month before HIFU. Twenty (4.9%), 41 (17.2%) and 76 (28.0%) patients were included in the SB200/500, SB500 version 4 and SB500 TCM groups, respectively.

Pathological Features and Salvage Treatments after HIFU

The mean number of HIFU sessions was 1.3 ± 0.5 and the numbers of patients in the sessions are listed in table 2. Post-HIFU prostate biopsies were performed in 758 of 918 (82.6%) patients. Control biopsies were negative in 662 of 758 patients (87.3%) in the entire cohort. The negative control biopsy rate in the SB200/500, SB500 version 4 and SB500 TCM group was 296 of 367 (80.6%), 182 of 195 (93.3%) and 184 of 196 (93.9%), respectively ($p < 0.0001$, table 2).

A total of 254 (27.7%) patients received salvage treatment during followup, which included ADT (169, 18.0%), radiation therapy (75, 8.2%) and radical prostatectomy (10, 1.1%; table 2). Salvage treatment was provided for 154 (37.7%), 74 (31.0%) and 26 (9.6%) patients treated with the SB200/500, SB500 version 4 and SB500 TCM devices, respectively ($p < 0.0001$).

Overall, Cancer Specific and Biochemical Disease-Free Survival

The 10-year overall and cancer specific survival rates were 88.6% and 97.4%, respectively (fig. 1). The BDFS rates at 5 and 10 years for the entire

Table 2. *Number of HIFU sessions, negative prostate biopsy rates and salvage treatment after HIFU*

	SB200/500	SB500 Version 4	SB500 TCM	Overall
No. HIFU sessions (%):				
1	254 (62.2)	188 (78.7)	258 (95.2)	700 (76.3)
2	121 (29.7)	46 (19.2)	12 (9.4)	179 (19.5)
3	29 (7.1)	5 (2.1)	1 (0.4)	35 (3.8)
4	2 (0.5)	0	0	2 (0.2)
5	2 (0.5)	0	0	2 (0.2)
No./total No. prostate biopsy (%)	296/367 (80.6)	182/195 (93.3)*	184/196 (93.9)*	662/758 (87.3)
No. salvage treatment (%)	154 (37.7)	74 (31.0)	26 (9.6)	254 (27.7)
No. salvage therapy type (%):				
Hormonal therapy	104 (25.5)	47 (19.7)	19 (7.0)	169 (18.0)
Radiation	43 (10.5)	24 (10.0)	8 (3.0)	75 (8.2)
Radical prostatectomy	7 (1.7)	3 (1.3)	0	10 (1.1)

* $p < 0.0001$.

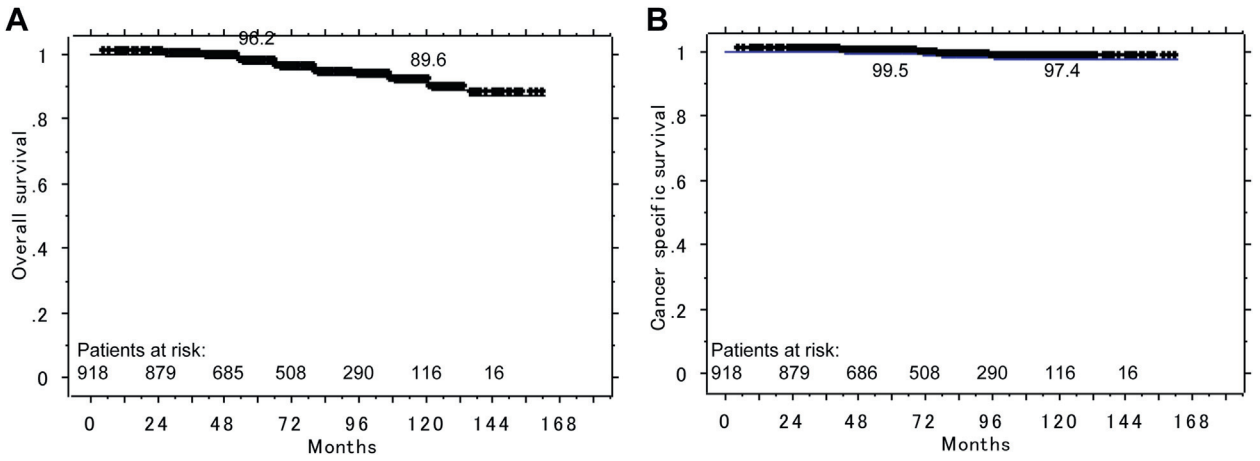

Figure 1. Overall (*A*) and cancer specific (*B*) survival rates

population were 57.1% and 48.8%, respectively (fig. 2, *A*). The 5-year BDFS rates in the SB200/500, SB500 version 4, and SB500 TCM groups were 48.3%, 62.3% and 82.0%, respectively, and the 10-year BDFS rate in the SB200/500 group was 38.4% ($p < 0.0001$; fig. 2, *B*). The 10-year BDFS rates in the low, intermediate and high risk categories for the entire population were 63.2%, 51.5% and 32.1%, respectively ($p < 0.0001$; fig. 3, *A*), whereas the 5-year BDFS rates in the low, intermediate and high risk categories in the SB500 TCM group were 95.0%, 80.9% and 71.9%, respectively ($p = 0.0134$; fig. 3, *D*).

Outcome Prognostic Factors

In the multivariate Cox regression analysis pretreatment PSA 10.1 to 20.0 ng/ml ($p = 0.0002$) and 20.1 to 30 ng/ml ($p = 0.0016$), Gleason score 8 or greater ($p = 0.0039$), stage T2cN0M0 ($p = 0.0024$), use of neoadjuvant ADT ($p < 0.0001$), and use of SB500 version 4 ($p = 0.0036$) and SB500 TCM ($p < 0.0001$) HIFU devices were significantly different (table 3).

Complications

None of the patients had perioperative mortality. The most frequent side effect was urethral stricture, which was observed in 181 of 918 (19.7%) cases during the first session and 52 of 263 (19.5%) in the repeat sessions (table 4). Patients in the first session (138 of 181, 76.2%) and those in the repeat sessions (40 of 52, 76.9%) were treated with periodical urethral dilation using metal sounds (Clavien II), while the remaining patients in the first session (43 of 181, 23.8%) and those in the repeat sessions (12 of 52, 23.1%) were treated with internal urethrotomy with or without TURP (Clavien III). The second most frequent complication was acute epididymitis,

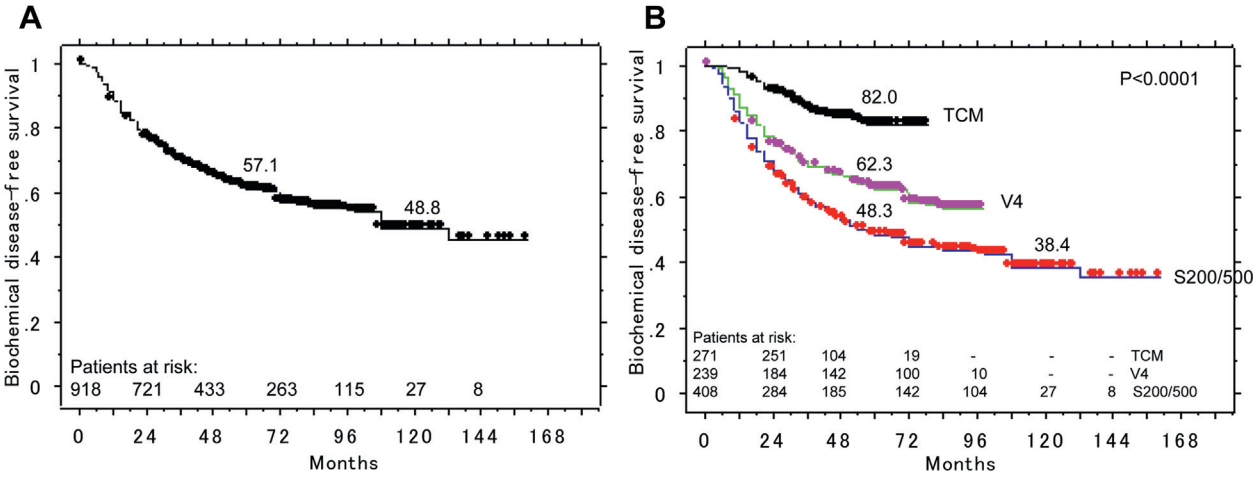

Figure 2. BDFS rates in all patients (*A*), and in SB200/500, SB500 version 4 and SB500 TCM groups (*B*)

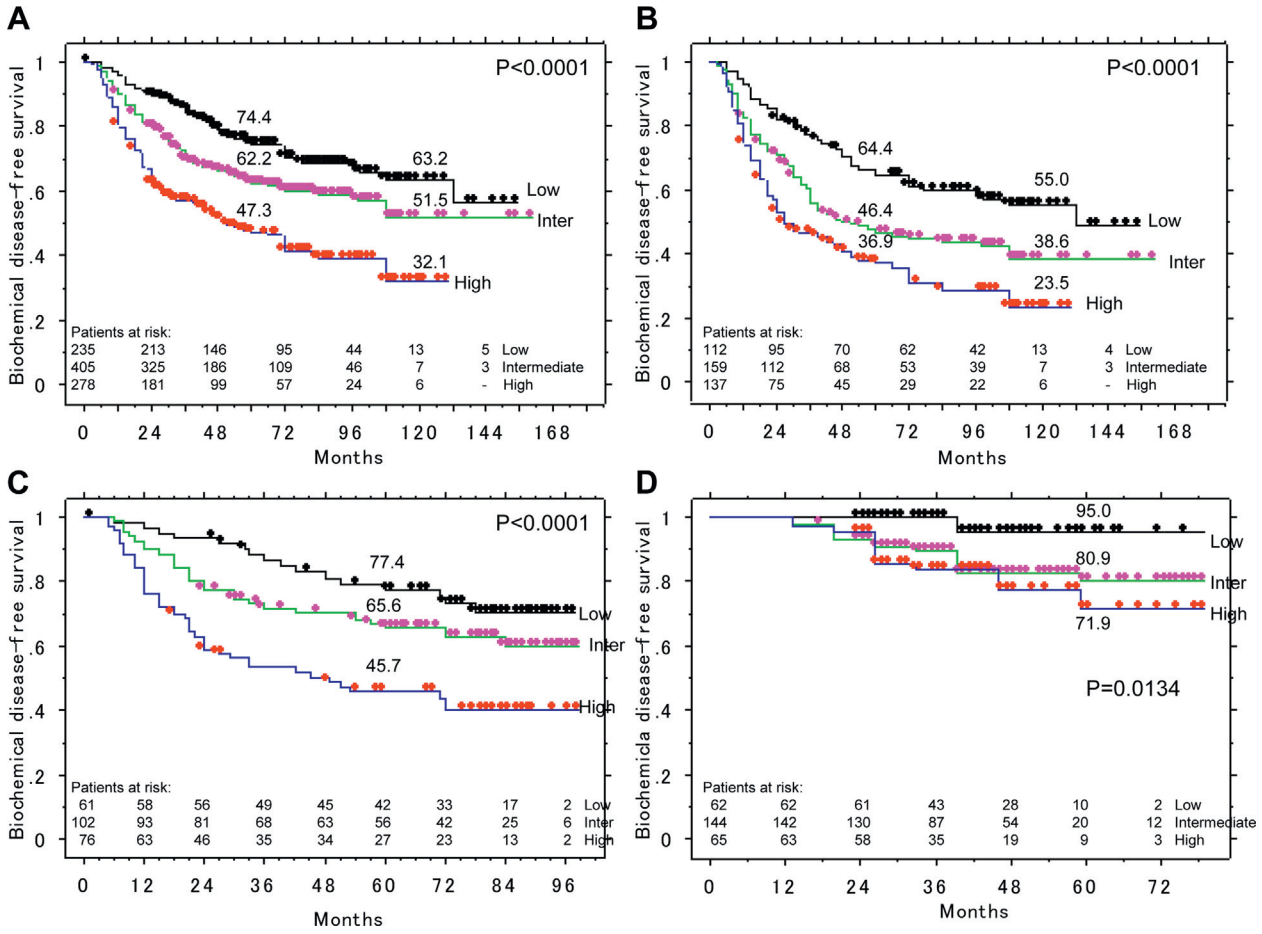

Figure 3. BDFS curves according to risk group in all patients (*A*), and in SB200/500 (*B*), SB500 version 4 (*C*) and SB500 TCM (*D*) groups

Table 3. *Prognostic factors of biochemical failure (Phoenix definition) in patients treated with HIFU*

	HR	95% CI	p Value
Age	0.992	0.976–1.008	0.3115
Prostate vol	0.992	0.979–1.006	0.2503
Pre-HIFU PSA:			
0–10.0	1	Reference	Reference
10.1–20.0	1.613	1.253–2.078	0.0002
20.1–30.0	1.937	1.284–2.921	0.0016
Pre-HIFU Gleason score:			
6 or Less	1	Reference	Reference
7	1.137	0.875–1.477	0.3370
8 or Greater	1.626	1.169–2.262	0.0039
Stage:			
T1bN0M0	1.492	0.361–6.160	0.5803
T1cN0M0	1	Reference	Reference
T2aN0M0	1.175	0.747–1.846	0.4852
T2bN0M	1.059	0.750–1.495	0.7454
T2cN0M0	1.615	1.186–2.220	0.0024
T3N0M0	1.587	0.954–2.639	0.0752
Pre-HIFU ADT:			
No	1	Reference	Reference
Yes	0.507	0.398–0.645	<0.0001
HIFU device:			
SB200/500	1	Reference	Reference
Version 4	0.683	0.528–0.883	0.0036
TCM	0.250	0.173–0.363	<0.0001

which was noted in 57 (6.2%) patients during the first session and 10 (3.8%) patients during repeat sessions. All patients were treated with antibiotics (Clavien II). Stress urinary incontinence was identified in 21 (2.3%) patients during the first session and 5 (1.9%) during repeat sessions, and all recovered within 12 months (Clavien II). There were no differences among the device groups and the number of HIFU sessions (ie first and repeat) for urethral stricture, acute epididymitis and stress urinary continence.

The incidence rate of Clavien III rectourethral fistula was significantly different in the repeat sessions for the SB200/500 (5 of 193, 2.6%; $p < 0.05$) and SB500 version 4 (2 of 56, 3.6%; $p < 0.01$) groups. In total, rectourethral fistula was observed in 1 of 918 (0.1%) and 7 of 263 (1.5%) patients during the first and repeat session(s), respectively ($p < 0.0001$). There were no cases of rectourethral fistula in the SB500 TCM group. All patients were treated with a transit colostomy and direct closure of the fistula with a transanal approach followed by colostomy reversal. Bladder neck contracture was observed in 7 (0.8%) patients after the first session

Table 4. *Overall mortality and morbidity*

	No./Total No. SB200/500 (%)	No./Total No. SB500 Version 4 (%)	No./Total No. SB500 TCM (%)	No./Total No. Overall (%)
Urethral stricture:				
First HIFU	83/408 (20.3)	42/239 (17.6)	56/271 (20.7)	181/918 (19.7)
Repeat HIFU	35/193 (19.1)	11/56 (19.6)	6/14 (42.9)	52/263 (19.5)
Epididymitis:				
First HIFU	22/408 (5.4)	16/239 (6.7)	19/271 (7.0)	57/918 (6.2)
Repeat HIFU	5/193 (2.6)	3/56 (5.4)	2/14 (14.3)	10/263 (3.8)
Urinary incontinence:				
First HIFU	4/408 (1.0)	9/239 (3.8)	8/271 (3.0)	21/918 (2.3)
Repeat HIFU	2/193 (1.0)	3/56 (5.4)	0	5/263 (1.9)
Rectourethral fistula:				
First HIFU	1/408 (0.2)	0	0	1/981 (0.1)
Repeat HIFU	5/193 (2.6)*	2/56 (3.6)†	0	7/263 (1.5)‡
Bladder neck contracture:				
First HIFU	4/408 (1.0)	1/239 (0.4)	2/271 (0.7)	7/918 (0.8)
Repeat HIFU	0	0	1/14 (7.1)*	1/263 (0.4)
Perineal edema:				
First HIFU	0	0	4/271 (1.5)	4/981 (0.4)
Repeat HIFU	1/193 (0.5)	1/56 (1.8)*	0	2/263 (0.8)
Hematospermia:				
First HIFU	1/408 (0.2)	2/239 (0.8)	1/271 (0.4)	4/918 (0.4)
Repeat HIFU	0	0	0	0
Acute pyelonephritis:				
First HIFU	0	1/239 (0.4)	2/271 (0.7)	3/918 (0.3)
Repeat HIFU	2/193 (1.0)*	0	0	2/263 (0.8)
Hemorrhoid:				
First HIFU	0	0	1/271 (0.4)	1/918 (0.1)
Repeat HIFU	0	0	0	0
Symphysitis:				
First HIFU	0	0	1/271 (0.4)	1/918 (0.1)
Repeat HIFU	0	0	0	0
Erectile dysfunction first HIFU:§				
6 Mos	19/40 (47.5)	15/35 (42.9)	43/59 (72.9)	77/134 (57.5)
1 Yr	15/36 (41.7)	8/31 (25.8)	42/61 (68.9)	65/128 (50.8)
2 Yrs	6/29 (20.7)	5/27 (18.5)	26/50 (52.0)	37/106 (34.9)

* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.0001$.
§ IIEF-5 less than 7.

and 1 (0.4%) patient after repeat sessions. All patients were treated with bladder neck incision with/without TURP (Clavien III). Perineal edema, hematospermia, acute pyelonephritis, hemorrhoid or symphysitis were noted in a few cases. Erectile dysfunction (IIEF-5 less than 8) was observed after 6 (77 of 134, 57.5%), 12 (65 of 128, 50.8%) and 24 (37 of 106, 34.9%) months after HIFU (table 4).

DISCUSSION

HIFU has emerged as an alternative therapeutic option for patients with clinically localized prostate cancer who are not suitable candidates for radical prostatectomy according to European Association of Urology guidelines.[2] Ganzer et al reported 14-year outcomes in 538 patients with localized prostate cancer.[14] The BDFS rates at 5 and 10 years were 81% and 61%, respectively. The 5-year BDFS rates for low, intermediate and high risk patients were 88%, 83% and 48%, while the 10-year BDFS rates were 71%, 63% and 32%, respectively. The salvage treatment rate was 18%. Thüroff and Chaussy conducted a 15-year study involving 704 patients.[15] The BDFS rates by risk group varied from 92% to 84% with 5-year rates and 68% to 60% with 10-year rates. At the 10-year followup salvage therapy was initiated in less than 2% of low risk patients, and 27% to 36% of intermediate and high risk patients. In addition, Crouzet et al reported on 1,002 consecutive patients treated with the Ablatherm device.[16] The 8-year BDFS rates were 76% for low risk patients, 67% for intermediate risk patients and 57% for high risk patients. Salvage therapies such as external beam radiation therapy (13.8%), external beam radiation therapy plus ADT (9.7%) and ADT alone (12.1%) were used.

In the SB treatment group we previously reported an 8-year study involving 517 consecutive patients treated with the SB200/500 and SB500 version 4 HIFU devices.[12] In this study we found a long-term clinical outcome of HIFU involving the latest SB500 TCM device. Operative time decreased from 145 minutes in the SB200/500 group to 107 minutes in the SB500 TCM group. Clinical efficacy significantly improved with the different generation of

HIFU technology. The percentage of negative prostate biopsy after HIFU increased from 80.6% in the SB200/500 group to 93.3% in the SB500 version 4 and 93.9% in the SB500 TCM group. The BDFS rates at 5 years also increased from 48.3% in the SB200/500 group to 62.3% in the SB500 version 4 group and 82.0% in the SB500 TCM group. This improvement may be due to the stack and TCM features, which can change the treatment region more accurately and allow power intensity control for maintaining appropriate temperature at each focus lesion even during treatment.[13]

Recently Vora et al reported that the BDFS rates for IMRT with a median radiation dose of 75.6 Gy at 9 years were 77.4%, 69.6% and 53.3% for low, intermediate and high risk patients.[5] In a multiinstitutional study Zelefsky et al reported that the 8-year relapse-free survival rates for brachytherapy using the Phoenix ASTRO criteria were 74% and 61% for the low and intermediate risk groups, respectively.[7] The 10-year BDFS rates in patients treated with cryotherapy were 80.6%, 74.2% and 45.5% for the low, intermediate and high risk groups, respectively.[8] Sukumar et al reported that the 8-year BDFS survival rate after robot-assisted radical prostatectomy was 81%.[10] We obtained similar clinical outcomes when we compared HIFU in the SB500 TCM group to treatment alternatives (ie IMRT, brachytherapy, cryotherapy and robot-assisted radical prostatectomy).

In this study the most frequent complication of HIFU was urethral stricture. Ganzer et al observed bladder outlet obstruction in 152 (28.3%) patients.[14] Thüroff and Chaussy also reported secondary obstructions (due to necrotic or scar tissue resulting in bladder neck or intraprostatic stenosis) in 19% to 24% of cases.[15] Crouzet et al reported a decrease in bladder outlet obstruction (from 34.9% to 5.9%) with advances in technology.[16] Combined treatments of TURP and HIFU reduced catheter time and bladder outlet obstruction rates compared to HIFU alone.[15,21]

Acute epididymitis was the second most frequent side effect after HIFU in our study. In a large series of patients treated with HIFU, rectourethral fistulas were reported in 0.23% to 0.7% of patients.[13] In our series rectourethral fistula developed in only 1 (0.1%) patient after primary HIFU but 7 of 263 (1.5%) patients had a rectourethral fistula after repeat HIFU. In fact, most fistulas occurred during the early stages of treatment. However, the incidence of rectourethral fistulas also decreased significantly with the improvement of devices and treatment procedures.

The incidence of erectile dysfunction in 2 recent HIFU series using the Ablatherm device ranged from 35% to 45%.[14–16] In the current study 34.9% of patients exhibited erectile dysfunction 24 months after HIFU therapy. In general, the radical nature of prostate cancer treatment and preservation of sexual function are controversial because postoperative erectile dysfunction depends on preservation of the neurovascular bundles that sometimes exhibit tumor invasion. Recent advances in focal therapy for prostate cancer with HIFU might reduce rates of erectile dysfunction.[22,23] Further investigations are required to confirm this important conclusion.

Limitations of this study include its single-arm nature and retrospective design. Furthermore, neoadjuvant androgen deprivation therapy performed in this study can have potential bias in the survival analysis.

CONCLUSIONS

This study involved a large consecutive series of patients treated with primary HIFU for clinically localized prostate cancer. The rate of BDFS has improved significantly in recent years due to technical improvements in the SB device. Further randomized controlled trials with other treatment modalities will clarify the benefits of this treatment.

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