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Whole-gland Ablation of Localized Prostate Cancer with High-intensity Focused Ultrasound: Oncologic Outcomes and Morbidity in 1002 Patients

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Abstract

Background: High-intensity focused ultrasound (HIFU) is a nonsurgical therapy for selected patients with localized prostate cancer (PCa).
Objective: The long-term oncologic and morbidity outcomes of primary HIFU therapy for localized PCa were evaluated in a prospective, single-arm, single-institution cohort study.
Design, setting, and participants: Participants were patients treated with HIFU for localized PCa from 1997 to 2009. Excluded were patients with local recurrence following radiotherapy. A second HIFU session was systematically performed in patients with biopsy-proven local recurrence.
Intervention: Whole-gland prostate ablation with transrectal HIFU.
Outcome measurements and statistical analysis: Incontinence was assessed using the Ingelman-Sundberg score, and potency was assessed using the five-item version of the International Index of Erectile Function (IIEF-5) scores. Primary outcomes were survival rates (biochemical-free, cancer-specific, metastasis-free, and overall survival). Secondary outcomes were morbidity rates. Median follow-up was 6.4 yr (range: 0.2–13.9). The Kaplan-Meier method was used to determine survival estimates, and multivariate analysis was used to determine predictive factors of biochemical progression.
Results and limitations: A total of 1002 patients were included. The median nadir prostate-specific antigen (PSA) was 0.14 ng/ml, with 63% of patients reaching a nadir PSA $\leq$0.3 ng/ml. Sixty percent of patients received one HIFU session, 38% received two sessions, and 2% received three sessions. The 8-yr biochemical-free survival rates (Phoenix definition) were 76%, 63%, and 57% for low-, intermediate-, and high-risk patients, respectively ($p < 0.001$). At 10 yr, the PCa-specific survival rate and metastasis-free survival rate (MFSR) were 97% and 94%, respectively. Salvage therapies included external-beam radiation therapy (EBRT) (13.8%), EBRT plus androgen-deprivation therapy (ADT) (9.7%), and ADT alone (12.1%). Severe incontinence and bladder outlet obstruction decreased with refinement in the technology, from 6.4% and 34.9% to 3.1% and 5.9%, respectively. Limitations included the fact that the study was a single-arm study without a comparison group, technological improvements, changes in surgical protocol during the study, and the use of ADT to downsize the prostate in 39% of patients.
Conclusions: HIFU is a potentially effective treatment of localized PCa, with a low PCa-specific mortality rate and a high MFSR at 10 yr as well as acceptable morbidity.

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1. Introduction

The objective of prostate cancer (PCa) treatment is the achievement of optimal cancer-specific survival rates with the lowest possible morbidity. High-intensity focused ultrasound (HIFU) is a nonsurgical treatment that uses nonionizing energy to induce irreversible damage to the malignant lesion through coagulation necrosis. Transrectal delivery of ultrasound under real-time monitoring forms the basis of HIFU. The thermal and cavitational effects can be repeated with subsequent treatment administration, and salvage external-beam radiation therapy (EBRT) is a therapeutic option in cases of local relapse following HIFU [1]. Since 1993, HIFU has been evaluated in our department as a minimally invasive option for the treatment of localized PCa in nonsurgical candidates [2]. Long-term oncologic results for HIFU are sparse in the literature, and HIFU is still considered investigational in the European Association of Urology guidelines [3,4]. The goals of the current study were to report the cancer control and morbidity outcomes for all patients treated with HIFU as primary therapy between January 1997 and December 2009 as well as to analyze factors that potentially influence treatment outcome.

2. Materials and methods

Following institutional review board approval, data from all treated patients were prospectively obtained and entered into a secure database (IRB: EB/MR92027/C, 200–032B, 2003–001B). Inclusion criteria were localized PCa, prostate-specific antigen (PSA) <30 ng/ml, clinical stage T1M0–T2M0, and no previous radical therapy for PCa. None of the patients were candidates for surgery because of age, comorbidity, or patient refusal. All patients were offered the treatment options of HIFU in a research protocol, EBRT, or active surveillance. Baseline and post-HIFU PSA measures were obtained for all patients.

2.1. Treatment protocol

All patients were treated with Ablatherm HIFU devices (EDAP-TMS, Vaulx-en-Velin, France), including prototype devices (1997–1999), Ablatherm Maxis (1999–2000), and Ablatherm Integrated Imaging (since 2005). Starting in 2000, transurethral resection of the prostate (TURP) was performed immediately prior to the HIFU session, under the same anesthesia, in patients with prostate volume <30 ml. In patients with prostate volume >30 ml, two strategies were used: androgen-deprivation therapy (ADT) before 2005 and TURP performed 6 wk prior to HIFU beginning in 2006. Pre-HIFU TURP avoids the adverse effects induced by hormonal therapy and dramatically reduces catheter time and rate of urinary tract infection [5]. The most recent treatment parameters for initial HIFU therapy involved a 3-MHz nominal frequency, 6-s treatment pulse, and 4-s shot interval. Five operators performed the procedures.

2.2. Follow-up

Before June 2007, all patients underwent post-HIFU biopsy at 6 mo regardless of PSA level. After June 2007, post-HIFU biopsy was performed only in patients with a nadir PSA >0.3 ng/ml, according to the Ganzer et al. publication [6]. Based on the small post-HIFU prostate volume, a minimum of six biopsy cores were obtained. Additional follow-up biopsies were performed in cases of biochemical failure (American Society for Therapeutic Radiology and Oncology/Phoenix definition). In cases of positive biopsy without evidence of metastasis, a second HIFU treatment was offered. Before 2005, some patients continuing to show positive biopsy who had little morbidity after the second session received a third HIFU session. Analysis of the initial repeat HIFU outcomes, including the elevated risk of rectourethral fistula, led to the introduction of specific parameters for HIFU retreatment in 2007.

2.3. Salvage treatment

Salvage therapy was performed after the last HIFU session in the event of biopsy-proven local recurrence and/or biochemical failure. ADT was used in patients without biopsy-proven local recurrence or with poor general health status, and salvage radiation therapy (SRT) alone or in combination with ADT was performed in patients with demonstrated local recurrence and long life expectancy.

2.4. Survival and morbidity evaluation

For disease-free rates, *biochemical failure* was defined using the Phoenix definition (nadir +2 ng/ml). All PCa-specific deaths were verified, and hormone-refractory metastatic PCa was documented by rising PSA level despite the use of second-line ADT and chemotherapy. Additional treatment–free survival was calculated by the initiation of salvage treatment as the date of failure. Palliative treatment–free survival was calculated by the initiation of definitive ADT. Incontinence was assessed using the Ingelman-Sundberg score [7], and potency was assessed using the five-item version of the International Index of Erectile Function (IIEF-5) scores between 12 and 24 mo after HIFU. All adverse effects, such as bladder outlet obstruction (BOO) (obstruction of the outflow of urine from necrotic debris or urethral stricture), were prospectively recorded. Only patients with complete data have been included in the final analysis (multivariate analysis, survival curves).

A statistical analysis was performed with SPSS v.20 (IBM Corp., Armonk, NY, USA). Survival curves were based on the Kaplan-Meier method, and the log-rank test was used for univariate comparisons. Actuarial survival rates were based on life table methods. For multivariable analysis, the Cox proportional hazards regression model was used.

3. Results

A total of 1002 patients met inclusion criteria. Patient demographics and baseline characteristics are summarized in Table 1. Median follow-up was 6.4 yr (0.2–13.9). HIFU was delivered by prototype model in 63 patients, Ablatherm Maxis in 652 patients, and Ablatherm Integrated Imaging in 287 patients. A total of 392 patients received pre-HIFU ADT for a median duration of 4.3 mo (range: 1–56) (n = 278 [71.0%] for ≤6 mo; n = 114 [29.0%] for >6 mo). ADT was stopped after HIFU in all recipients. As only 63 patients (6.3%) did not received pre-HIFU TURP, the effect of TURP on the oncologic results was not evaluable. The median number of HIFU sessions was one (range: one to three), with 596 patients (60%) receiving one session, 383 patients (38%) receiving two sessions, and 23 patients (2%) receiving three sessions. On average, 488 ± 122 shots were delivered, corresponding to a median treated volume of 30 ml (range: 3–60), which was 130% of the actual prostate volume size because of overlap in treatment zones.

Post-HIFU biopsies after the final HIFU treatment were available for 774 patients (77%). Results were negative in 485 patients (63%) and positive in 289 patients (37%).

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Table 1 – Baseline characteristics of 1002 patients according to the three different high-intensity focused ultrasound devices

	Overall, *n* = 1002	Before 2000, *n* = 63	2000–2004, *n* = 652	2005–2009, *n* = 287	*p* value
Age, yr, median (range)	71 (48–87)	73 (56–87)	71 (48–85)	72 (52–84)	<0.001
PSA, ng/ml, median (range)	7.7 (0.0–30.0)	8.0 (0.0–26.3)	8.2 (0.0–30.0)	6.4 (0.0–30.0)	<0.001
Prostate volume, ml, median (range)	23.0 (5–78)	23.0 (8–62)	22.0 (5–78)	24.5 (6–48)	<0.001
Previous ADT, no. (%)					
No	610 (60.9)	55 (87.3)	362 (55.5)	193 (67.2)	
Yes	392 (39.1)	8 (12.7)	290 (44.5)	94 (32.8)	<0.001
Total, no.	1002	63	652	287	
Pre-HIFU Gleason score, no. (%)					
≤6	555 (55.4)	35 (55.6)	356 (54.6)	164 (57.1)	
7	348 (34.7)	10 (15.9)	235 (36.0)	103 (35.9)	
≥8	84 (8.4)	16 (25.4)	55 (8.4)	13 (4.5)	<0.001
Undefined	15 (1.5)	2 (3.2)	6 (0.9)	7 (2.4)	
Total, no.	1002	63	652	287	
Pre-HIFU PSA, no. (%)					
≤4	148 (14.8)	13 (20.6)	73 (11.2)	62 (21.6)	
4–10	569 (56.8)	24 (38.1)	373 (57.2)	172 (59.9)	
≥10	285 (28.4)	26 (41.3)	206 (31.6)	53 (18.5)	<0.001
Total, no.	1002	63	652	287	
Stage, no. (%)					
T1	518 (51.7)	31 (49.2)	328 (50.3)	159 (55.4)	
T2	449 (44.8)	29 (46.0)	303 (46.5)	117 (40.8)	
T3	28 (2.8)	3 (4.8)	20 (3.1)	5 (1.7)	0.014
Undefined	7 (0.7)	0 (0.0)	1 (0.2)	2 (2.1)	
Total, no.	1002	63	652	287	
D'Amico risk group, no. (%)					
Low	357 (35.6)	15 (23.8)	215 (33.0)	127 (44.3)	
Intermediate	452 (45.1)	23 (36.5)	308 (47.2)	121 (42.2)	
High	174 (17.4)	25 (39.7)	121 (18.6)	28 (9.8)	<0.001
Undefined	19 (1.9)	0 (0.0)	8 (1.2)	11 (3.8)	
Total, no.	1002	63	652	287	

PSA = prostate-specific antigen; ADT = androgen-deprivation therapy; HIFU = high-intensity focused ultrasound.

3.1. Biochemical survival

Nadir PSA was reached ≤6 mo after HIFU in all patients, at a median of 7.9 wk (range: 1–52) with a median nadir PSA of 0.14 ng/ml (range: 0–12.7). In all, 631 patients (63%) attained a nadir PSA ≤0.3 ng/ml, and 567 patients (56.6%) attained a nadir PSA ≤0.2 ng/ml. Table 2 compares the number of HIFU sessions and the nadir PSA values achieved with the different HIFU devices. Biochemical recurrence (Phoenix definition) was observed in 205 patients (21.2%). The 5- and 8-yr biochemical-free survival rates (BFSRs) for low-, intermediate-, and high-risk patients were 86–76%, 78–63%, and 68–57%, respectively ($p < 0.001$) (Fig. 1). The overall 10 yr BFSR was 60%. The 8-yr BFSRs in patients with and without previous ADT were 70% and 66%, respectively ($p = 0.992$). The 5-yr BFSR progressively increased over time: 66% in patients treated before 2000, 80% in patients treated from 2000 to 2004, and 83% in patients treated from 2005 onward ($p = 0.010$).

3.2. Survival rates

Eighty-nine patients (8.9%) died during follow-up from unrelated causes, 13 patients (1.3%) died from PCa, and metastatic PCa was detected in 40 patients (4.0%). The 10-yr overall survival rate and PCa-specific survival rate (PCSSR) was 80% and 97%, respectively (Fig. 2). PCSSR was 99% for low-risk patients, 98% for intermediate-risk patients, and 92% for high-risk patients (Fig. 3). The 10-yr PCa metastasis–free survival rate (MFSR) was 94% (Fig. 2) and was 99%, 95%, and 86% for low-, intermediate-, and high-risk patients, respectively.

3.3. Predictive factors

In multivariable analysis (Table 3), clinical stage, PSA, pre-HIFU Gleason score, and number of HIFU sessions were

Table 2 – Number of high-intensity focused ultrasound (HIFU) sessions and prostate-specific antigen nadir after HIFU, according to the three different HIFU devices

	Before 2000, *n* = 63	2000–2004, *n* = 652	2005–2009, *n* = 287	*p* value
No. of HIFU sessions, no. (%)				
1	25 (39.7)	350 (53.7)	221 (77.0)	
2	28 (44.4)	289 (44.3)	66 (23.0)	<0.001
≥3	10 (15.9)	13 (2.0)	0 (0)	
Total, no.	63	652	287	
PSA nadir, ng/ml, no. (%)				
≤0.3	31 (49.2)	416 (63.8)	184 (64.1)	
0.3–1	14 (22.2)	120 (18.4)	56 (19.5)	0.232
>1	18 (28.6)	111 (17.0)	45 (15.7)	
Not determined	0 (0.0)	5 (0.8)	2 (0.7)	
Total, no.	63	652	287	

HIFU = high-intensity focused ultrasound; PSA = prostate-specific antigen.

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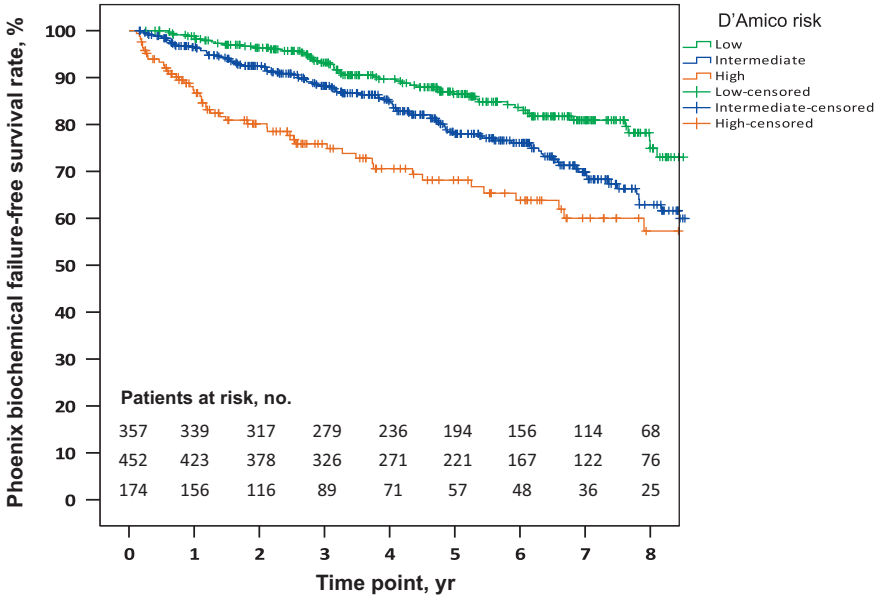

Fig. 1 – Influence of pre–high-intensity focused ultrasound (HIFU) risk group on biochemical-free survival rates (Phoenix criteria) following HIFU therapy.

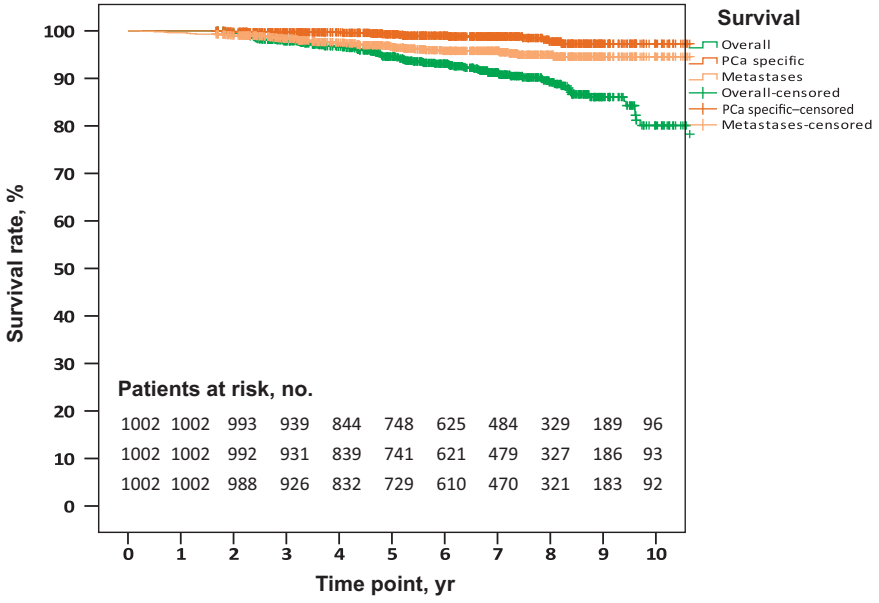

Fig. 2 – Overall, prostate cancer (PCa)–specific, and metastasis-free survival rates following high-intensity focused ultrasound (HIFU) treatment.

significantly associated with biochemical failure. The operator volume was not tested as a covariate in the multivariate analysis, because it has never been significant in previous studies. Nadir PSA was a significant predictive factor for biochemical failure. The 5- and 10-yr BFSRs were 88% and 75% with a nadir PSA ≤0.3 ng/ml, 72% and 32% with a nadir PSA 0.31–1.0 ng/ml, and 50% and 23% with a nadir PSA >1.0 ng/ml, respectively ($p < 0.001$). Predictive factors for HIFU retreatment included PSA >4 ng/ml, prostate volume >25 ml, more than three of six positive biopsies, and the year of treatment (corresponding to device generation).

3.4. *Salvage treatment*

A total of 371 patients (37.1%) presenting with a rising PSA (Phoenix definition), with or without biopsy-proven recurrence, received salvage therapy, which included SRT alone (13.9%), SRT plus ADT and/or chemotherapy (10.7%), ADT alone (12.1%), and ADT plus chemotherapy (0.4%). The median time between the last HIFU session and SRT was 17 mo (range: 2–103), with a median dose of 72 Gy (range: 65–78). The 5- and 8-yr additional treatment–free survival rates for low-, intermediate-, and high-risk patients were 81% and 68%, 66% and 53%, and 47% and 38%, respectively

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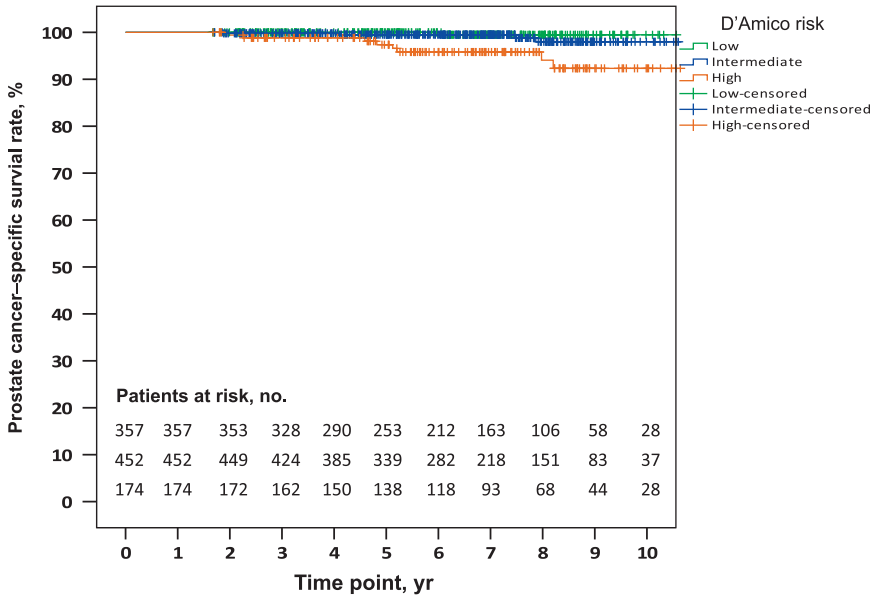

Fig. 3 – Influence of pre–high-intensity focused ultrasound (HIFU) risk group on prostate cancer–specific survival in patients treated following HIFU.

Table 3 – Prognostic factors of biochemical failure (Phoenix definition) in patients treated with high-intensity focused ultrasound: result of univariate and Cox analysis

Prognostic factors	Univariate *p* value	Univariate risk ratio	Univariate 95% CI	Multivariate *p* value	Multivariate risk ratio	Multivariate 95% CI
Age	0.018	1.03	1.01–1.06	0.641	1.01	0.98–1.03
Previous ADT	0.992	1.000	0.75–1.33	0.504	0.91	0.68–1.21
Stage						
T1	–	–	–	–	–	–
T2	0.022	1.39	1.05–1.84	0.057	1.32	0.99–1.77
T3	0.052	2.15	0.99–4.64	0.403	1.41	0.63–3.12
Gleason score						
≤6	–	–	–	–	–	–
7	0.014	1.46	1.08–1.97	0.050	1.36	1.00–1.84
≥8	<0.001	2.30	1.49–3.54	0.024	1.71	1.08–2.72
PSA, ng/ml						
≤4	–	–	–	–	–	–
4–10	0.008	2.13	1.21–3.73	0.007	2.17	1.24–3.82
>10	<0.001	4.94	2.81–8.68	<0.001	4.81	2.70–8.57
Prostate volume, ml						
≤25	–	–	–	–	–	–
>25	0.216	1.19	0.90–1.57	0.577	1.09	0.81–1.45
Positive biopsies						
≤2 of 6	–	–	–	–	–	–
3–4 of 6	0.285	1.21	0.85–1.72	0.438	1.16	0.80–1.67
≥5 of 6	0.778	0.96	0.96–1.32	0.703	1.07	0.75–1.55
No. of HIFU sessions						
1	–	–	–	–	–	–
≥2	0.005	0.66	0.50–0.88	0.001	0.60	0.45–0.81
HIFU technology						
Before 2005	–	–	–	–	–	–
After 2005	0.781	0.95	0.66–0.95	0.771	1.07	0.70–1.62

CI = confidence interval; PSA = prostate-specific antigen; HIFU = high-intensity focused ultrasound; ADT = androgen-deprivation therapy.

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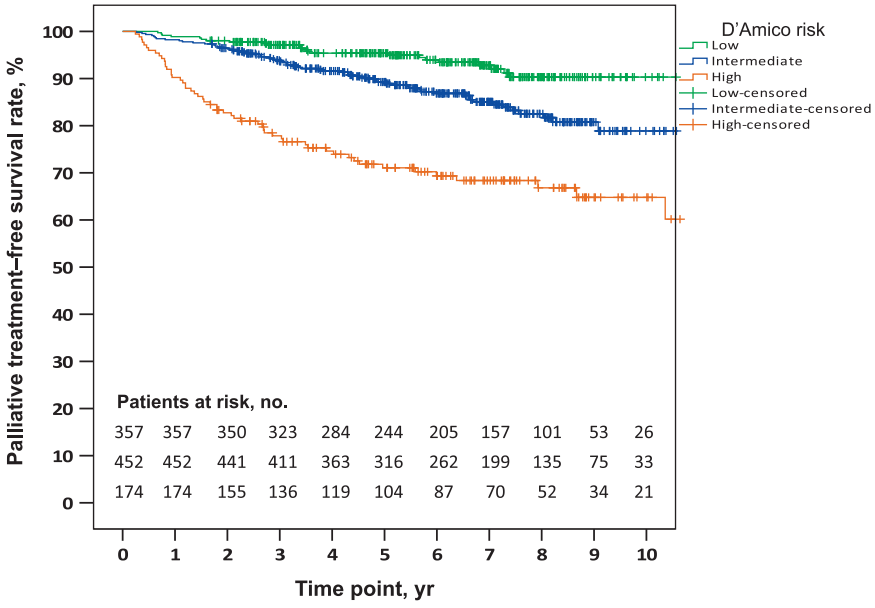

Fig. 4 – Influence of pre–high-intensity focused ultrasound (HIFU) risk group on palliative treatment–free survival following HIFU.

($p < 0.001$). No additional treatment was needed in 631 patients (63%). The median nadir PSA value after SRT was 0.09 ng/ml. Estimated with the Bolla et al. criteria [8], the 6-yr BFSR was 83% for the population receiving SRT and was 97%, 89%, and 63% for low-, intermediate-, and high-risk patients, respectively ($p = 0.003$). At 8 yr, the rates of patients requiring palliative ADT were 10%, 18%, and 34% of patients in the low-, intermediate-, and high-risk groups, respectively ($p < 0.001$) (Fig. 4).

3.5. *Morbidity*

Morbidity rates are summarized in Table 4. Baseline incontinence rates included grade 1 in 0.7% of patients and grades 2/3 in 0% of patients. Technological improvements in the HIFU device resulted in decreasing rates of grade 2/3 incontinence (from 6.4% to 3.1%, $p = 0.088$) and BOO (from 34.9% to 5.9%, $p = 0.032$). Incontinence was managed conservatively with physiotherapy (94.5%), artificial urinary sphincters (3.4%), and suburethral slings (2.1%). Bladder neck/urethral strictures were resolved with cold knife incision or TURP. Three patients required a definitive urethral stent for severe recurrent strictures, two of which occurred following SRT. Potency was evaluated in 187 patients treated after 2005 with the latest generation of device. The median IIEF-5 score decreased from 17 (range: 5–25) to 5 (range: 1–22) ($p < 0.001$). Potency was preserved (IIEF $\geq$17) in the 42.3% of patients with a baseline IIEF score $\geq$17 (<70 yr: 55.6%; $\geq$70 yr: 25.6%; $p < 0.001$) without pharmacologic aid.

Rectourethral fistula occurred in four patients (0.4%) following repeat HIFU treatment. Of those patients, three had severe comorbidity (one patient each with renal failure

Table 4 – Overall morbility and morbidity with technological improvements

	Overall, n = 1002	Ablatherm technology			
		Before 2000, n = 63	2000–2004, n = 652	2005–2009, n = 287	p value
Early complications, no. (%)					
Urinary incontinence					
Stress 1	187 (18.7)	15 (23.8)	130 (19.9)	42 (14.6)	0.088
Stress 2 or 3	50 (5.0)	4 (6.4)	37 (5.7)	9 (3.1)	0.226
Urinary tract infection	39 (3.9)	11 (17.5)	19 (2.9)	9 (3.1)	<0.001
Acute urinary retention	76 (7.6)	7 (11.1)	52 (8.0)	17 (5.9)	0.303
Bladder outlet obstruction	166 (16.6)	29 (46.0)	103 (15.8)	34 (11.8)	<0.001
Hematuria/sloughing	55 (5.5)	0 (0.0)	37 (5.7)	18 (6.3)	0.133
Late complications, no. (%)					
Stenosis	90 (9.0)	22 (34.9)	51 (7.8)	17 (5.9)	<0.001
Fistula	4 (0.4)	0 (0.0)	2 (0.3)	2 (0.7)	0.597

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and hemodialysis, acquired immunodeficiency syndrome (AIDS), and previous radiation therapy for bladder transitional urothelial carcinoma). Different treatments were applied: one York-Mason procedure, two colostomies alone (one anuric patient under hemodialysis and one patient with bladder cancer), and one gracilis muscle interposition. No de novo fecal incontinence was observed.

4. Discussion

The cancer control effectiveness of any treatment approach for PCa is influenced by three factors: efficacy as primary therapy, early detection of relapse, and feasibility and efficacy of curative salvage options.

The BFSR with HIFU seems promising in our study and is comparable to the published rates from other HIFU series [9,10]. In the GETUG 06 randomized trial, the 5-yr BFSR was 68% in the 70-Gy arm and 76.5% in the 80-Gy arm ($p = 0.09$) [11], although direct comparison between HIFU and EBRT is possible only with prospective studies or matched-pair analyses. Similar to EBRT, the BFSR with HIFU was significantly influenced by D'Amico risk category [12]. Nadir PSA was also a significant predictive factor of HIFU outcome [6]. The prostate volume was a significant predictor for HIFU retreatment. Blana et al. found a 79% BFSR at 7 yr with total-prostate HIFU (prostate height $\leq$24 mm and treated volume $>$120% of prostate volume) [10]. No difference in BFSR was observed in relation to previous ADT exposure, and in this study (unlike EBRT), no synergistic effect between ADT and HIFU was observed. Potentially, stage migration over time might have contributed to the increase in BFSR.

Local relapse was identified in 27% of the current cohort. Positive biopsy rates following conformal EBRT have ranged from 21% to 32% [13,14], and the local recurrence rate 10 yr after radical surgery was 89% (positive margin) and 95% (negative margin) [15].

The early biochemical response following HIFU allows a more rapid identification of local relapse through magnetic resonance imaging and ultrasound imaging using a contrast agent generally located in the apex and anterior regions of the prostate [16,17]. With the application of specific retreatment parameters, repeat HIFU is usually offered to patients with biopsy-proven local recurrence who have not experienced significant morbidity from previous HIFU sessions. HIFU therapy leaves an option for salvage EBRT that is effective and well tolerated, even at the mean dose of $>$70 Gy used in our study [1].

Recent reports of radical prostatectomy (RP) found a 12-yr PCa-specific mortality (PCSM) rate of 12.5% and a 10-yr PCSM rate of 0.9%, 4%, and 8% in low-, intermediate-, and high-risk patients, respectively [18,19]. The metastatic survival rate 12 yr after RP was found to be 80.7% by Bill-Axelson et al. [18], while Zelefsky et al. found an 8-yr rate of 97% in a comparative nonrandomized study [20]. The 8-yr metastatic survival rate after EBRT ($>$81 Gy) was found to be 93% [7]. A high radiation dose level significantly reduces the 10-yr risk of metastases, with survival rates of 81% found using $\leq$80 Gy compared with 87% for doses $>$81 Gy ($p < 0.001$) [21]. The PCSM rate 15 yr after iodine 125 brachytherapy was found to be 16% [22]. The 10-yr PCSM rate was 2.8% with RP, compared with 5.8% with observation in a matched cohort study of 22 244 patients [23].

The rate of rectal injury in the current study was low (0.4%), and in contrast to EBRT and brachytherapy, HIFU does not result in late-onset gastrointestinal (GI) toxicity. The GI bleeding rates were 9.3 of 1000 patients with three-dimensional EBRT, 8.9 of 1000 patients with intensity-modulated radiation therapy, 5.3 of 1000 patients with brachytherapy, and 20.1 of 1000 patients with proton therapy [24].

We found decreasing rates of incontinence with technological improvements. Following radical robot-assisted laparoscopic prostatectomy (RALP), the objective continence rate was 80% at 24 mo, based on the University of California, Los Angeles, Prostate Cancer Index questionnaire in 380 patients [25].

The rate of BOO has decreased since the introduction of real-time monitoring. Rates of BOO found with other therapies include 1.4% with open RP and 2.6% with RALP [26]. The stricture incidence rates were 1.8%, 1.7%, and 5.2% in patients treated with brachytherapy, EBRT, and combined EBRT and brachytherapy, respectively [27].

Potency was preserved in 52.6% of younger potent patients. Following RALP, the objective potency rate at 12 mo was reported as 62% [25]. In 139 potent patients receiving EBRT (78 Gy), the incidence of new-onset erectile dysfunction at 2 yr was 38% [28]. After brachytherapy, an adequate erectile function at 5 yr was found in 61.5% of previously potent patients [29], while only 24% of patients retained full potency 24 mo after cryosurgery [30].

This prospective study of HIFU is the largest published to date with 10-yr Kaplan-Meier estimated survival rates.

We acknowledge the following limitations. The study was a single-arm study without a comparison group. In addition, technological improvements and changes in surgical protocol (TURP) may have confounded some of the outcome analyses. The study used ADT to downsize the prostate with a potential bias in survival analyses, although it was not a significant predictor of survival in the Cox analyses. The study also used the Ingelman-Sundberg score originally developed for use in women with stress urinary incontinence rather than men. Incontinence evaluation was performed between 12 and 24 mo. Morbidity data were not categorized with a standardized reporting system. Finally, differences in selection criteria, study design, use of adjuvant/salvage treatments, and definition of functional outcomes among the published results of other PCa therapy modalities make direct comparisons difficult.

5. Conclusions

HIFU is a minimally invasive therapeutic option with encouraging cancer-specific survival rates in patients with localized PCa. The 10-yr PCSMs and MFSRs were low, and the morbidity was acceptable. Salvage EBRT for post-HIFU relapse was feasible, and the rate of patients requiring palliative ADT was low.

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Author contributions: Sebastien Crouzet had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gelet, Crouzet.
Acquisition of data: Gelet, Crouzet, Mege-Lechevallier, Tonoli-Catez.
Analysis and interpretation of data: Crouzet, Gelet, Rouviere.
Drafting of the manuscript: Crouzet, Gelet.
Critical revision of the manuscript for important intellectual content: Chapelon, Rouviere, Colombel.
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