Title:

PSA kinetics to predict cancer control following focal therapy for non-metastatic prostate cancer using High Intensity Focused Ultrasound

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Abstract

Objective

To determine if PSA kinetics following focal high intensity focused ultrasound (HIFU) for the treatment of non-metastatic prostate cancer can predict treatment failure.

Materials and methods

In this analysis of our prospectively maintained HIFU (Sonablate® 500) database, 598 patients were identified who underwent a focal HIFU (Sonablate® 500) between March 2007 and November 2016. Follow-up occurred with 3-monthly clinic visits and PSA testing in the first year. Thereafter, PSA was measured 6-monthly or annually at least. Routine and for-cause mpMRI with biopsy for MRI-suspicion of recurrence. Treatment failure was defined by any secondary treatment (systemic therapy, cryotherapy, radiotherapy, prostatectomy, or further HIFU), metastasis from prostate cancer without further treatment, tumour recurrence with Gleason score >/=7 (>/=3+4) on prostate biopsy without further treatment, or prostate cancer-related mortality. We evaluated a whole series of 'nadir plus XX' thresholds (with XX varying from 0.1 to 2.0) for possible prediction of failure using sensitivity and specificity as well as Receiver Operating Characteristic (ROC) curve (statistics using R-language environment).

Results

Median age (IQR) was 65 years (60-71) and median Gleason score (range) was 7 (6-9). Eighty per cent had Gleason 3+4=7 or higher. Tumours were radiologically staged as localised T1c-T2c in 522/596 (88%) while 74/596 (12.4%) were T3a/b. Baseline median (IQR) PSA was 7.80ng/ml (5.96-10.45) in those with failure and 6.77ng/ml (2.65-9.71) in those without failure. Using radiotherapy ASTRO criteria (3 consecutive PSA rises above

nadir), sensitivity was 18.7% and specificity 68.3%; Phoenix criteria (nadir+2.0ng/ml), sensitivity was 32.5% and specificity 59.1%. When evaluating other PSA 'nadir+XX' thresholds, the highest sensitivity of 61.2% was shown for nadir+0.1ng/ml; the highest specificity was conferred by nadir+2.0ng/ml. All definitions of PSA failure incorporating 'nadir+XX' thresholds led to significant false positives with the ROC curve shifting below the 50% line.

Conclusion

We have shown that PSA kinetics following focal HIFU therapy are not predictive of failure with any 'nadir plus' definition leading to significant rates of false positives. PSA criteria should not be used to define failure after focal HIFU therapy.

Introduction

For over a decade, high-intensity focused ultrasound (HIFU) has been investigated as a treatment modality for non-metastatic prostate cancer [1], particularly in a focal therapeutic strategy whereby zones within the prostate gland involved with clinically significant prostate cancer are targeted rather than the entire prostate [2]. This seems to lead to fewer treatment-related adverse events and genitourinary functional side-effects [3] in carefully selected patients [4]. We have recently reported on medium term cancer control rates following focal HIFU within the context of a multicentre registry study [5].

There has been legitimate concern that follow-up after focal therapy is undefined with current requirements for multi-parametric MRI and biopsy [6,7,8]. Other modalities such as radiotherapy and surgery are reliant on PSA kinetics following treatment to define success or failure [9,10]. Following focal therapy, as there remains some viable prostate tissue, biochemical kinetics will be very different [11]. Nonetheless, if there was a biochemical definition that could be developed and validated for the purpose of detecting failure after focal therapy then tools such as MRI and biopsy might be targeted more appropriately. In this study, which we believe to be the first to do so, our aim was to determine if PSA kinetics following focal HIFU for the treatment of non-metastatic prostate cancer might predict treatment outcome.

Methods

The UCLH Joint Research Office granted institutional review board exemption. Our programme of health technology assessment followed the Medical Research Council (UK) guidelines for evaluating complex interventions [12]; these guidelines were recently incorporated and applied to surgical innovation within the IDEAL framework [13]. Focal

transrectal HIFU was a surgical innovation that commenced in 2006 in the UK and approved for clinical use by the UK's National Institute for Health and Clinical Excellence (NICE) under special arrangements. That is, all cases had to be prospectively and consecutively entered into an academic registry, discussed in a multidisciplinary meeting and given written information on the advantages and disadvantages of the procedure. We have previously reported on medium term outcomes following whole-gland and focal HIFU from this registry [14]. Between 1st/January/2006 and 31st/December/2015, 625 consecutive patients underwent primary focal HIFU for non-metastatic prostate cancer using the Sonablate®500 device (Sonacare Inc., USA) within 9 centres. Of these, 598 were eligible for analysis in this study as they had more than 6 months follow-up. Focal HIFU treatment was offered to patients diagnosed with non-metastatic prostate cancer with Gleason 6 through 9, stage T1c-T3bN0M0 and PSA of </=20ng/ml. Gleason 6 required a minimum of 3mm of disease. Patients were classified into low, intermediate and high-risk groups according to the D'Amico risk classification system.

Disease was localised using mpMRI, combined with targeted and systematic biopsies, or transperineal mapping biopsies. Intermediate and high-risk cases also underwent a radioisotope bone-scan and/or cross-sectional CT to rule-out distant metastases dependent on local guidelines at each hospital.

Treatments were delivered in a focal lesion ablation or quadrant or hemiablation fashion depending on the gland volume as well as tumour volume and location. Index lesion ablation alone was conducted in patients with multifocal disease provided untreated areas harboured no more than 3mm of Gleason 6 on systematic or template mapping biopsies. Up to two re-treatments with focal HIFU were offered as part of the intervention. All men were advised to undergo 3 to 6 monthly serum PSA testing. An mpMRI was routinely

performed regardless of PSA kinetics at 1 year and approximately 1-2 yearly thereafter. Two rises in PSA after the nadir level was achieved, without predefining the level of rise, was investigated with a prostate biopsy, or mpMRI followed by biopsy if the mpMRI was suspicious. We have previously reported on the high negative predictive value of mpMRI in the post-focal HIFU setting for clinically significant prostate cancer [15]. Clinically significant cancer on biopsy of untreated areas was defined as 'out-of-field' progression.

Further focal HIFU was offered when either, a) clinically significant cancer on biopsy occurred in-field or out-of-field and where the mpMRI staging indicated that the disease was still localised or, b) when the mpMRI demonstrated a clear recurrence (mpMRI Likert score 5) in-field associated with a rising PSA. Other considerations for further focal HIFU were the absence of intra-prostatic calcification or difficult disease location such as apical disease overlapping the external urinary sphincter. Patients were also routinely offered the option of radical prostatectomy or radical radiotherapy. All data was audited and quality controlled by two data managers (NM and FHJ).

Primary outcome for the validation of biochemical changes were based on a composite endpoint of failure-free survival (FFS) with failure defined as residual untreated Gleason 3+4=7 or more cancer on post-treatment biopsy, local salvage therapy (surgery or radiotherapy), systemic therapy, prostate cancer metastases or prostate cancer-specific mortality.

Statistical analysis

Variables with normal distribution are reported as mean (+/- Standard Deviation, SD) with skewed distributed variables as median (interquartile ranges, IQR). Categorical variables are reported as absolute numbers with percentages. Cases were identified and grouped

as treatment failures, or as non-treatment failures. Datasets in the failure-free group containing only one PSA value after treatment were excluded from analysis. PSA values were analysed in both groups separately. PSA nadir tests were performed for all cases along their individual PSA timeline. We conducted analyses of numerous biochemical definitions of failure by evaluating in each case, whether a known failure would have been identified at the correct date with a PSA nadir plus a cut-off between 0.1 to 2.0ng/ml. For this, all individuals had to be checked for a rising PSA over each cut-off level using the lowest PSA value as the initial nadir. We also looked at the previous ASTRO (three consecutive rises above nadir) and Phoenix criteria (nadir plus 2.0ng/ml).

These prediction test results were then accumulated and analysed according to sensitivity and specificity in two-by-two contingency (accuracy) tables, as well as in receiver operating characteristic (ROC) curves to evaluate overall performance of accuracy. Analyses were performed using the R language environment for statistical computing.

Results

Baseline HIFU demographics

In total, 598 eligible patients were identified in the national database. Median age (IQR), were 65 years (IQR 60-71) and median Gleason score (range) was 7 (80.37% were Gleason >/=3+4, range 6-9). Tumours were staged as radiologically staged as T1c-T2c in 522/596 (87.6%) and T3a/b in 74/596 (12.4%) [Table 1]. Median pre-treatment PSA was 7.8ng/ml (IQR 5.96-10.45) in the recurrence group and 6.8ng/ml (IQR 2.65-9.71) in non-treatment failure group [Table 2].

PSA values were separately and longitudinally analysed in groups for treatment and non-treatment failures [Figure 1 and 2]. In the group of treatment failures, there can be found

significantly higher median PSA values before treatment, as well as at 12, 18, 24, and 27 month after treatment (p<0.001) [Table 2].

PSA predictive models

For ASTRO criteria, the sensitivity was 18.7% and specificity 68.3%. For Phoenix criteria sensitivity was 32.5% and specificity 59.1%. Definitions incorporating PSA nadir plus a defined 'XX' PSA rise generally performed poorly with a high rate of false-positives. The highest sensitivity of 61.2% was for a nadir plus 0.1ng/ml (but corresponding specificity of 9.8%); the lowest sensitivity was 32.5% for a nadir plus 1.8ng/ml (and corresponding specificity of 56.4%). The highest specificity was 59.1% for a nadir plus 2.0ng/ml (but corresponding sensitivity of 32.6%); the lowest specificity was 9.8% for a nadir plus 0.1ng/ml [Table 3]. The highest negative predictive value was 80.3% with an associated sensitivity of 55.6% for a nadir plus 0.4ng/ml. The highest positive predictive value was 19.7% with associated specificity of 59.1% for a nadir plus 2.0ng/ml. A cumulative graph for all PSA nadir plus 'x' is demonstrated in the ROC curve [Figure 3]. No relevant changes in results were found when 71 cases with pre-focal HIFU androgen deprivation therapy were excluded [Figure 4, 5, and 6].

We also evaluated whether there were differences in these findings if we considered individual Gleason grade groups. Appendix Tables 1-3 summarises these findings for Gleason scores 3+3, 3+4, and 4+3. We found no particular biochemical kinetic definition of failure was more helpful in a particular Gleason grade group than in the entire cohort of focal HIFU.

Discussion

In summary, we have shown that PSA kinetics after focal HIFU have poor performance characteristics with a high rate of false positives. The ability of PSA kinetics to rule-out failure, as indicated by its negative predictive value was between 69.0% (using ASTRO criteria) and 80.3% (for nadir plus 0.4ng/ml).

Prior to discussing the clinical implications of our study, there are some limitations that require mentioning. First, it is a retrospective analysis of a national database. Second, there was not an underlying protocol, which defined fixed dates for MRI and prostate biopsies that may lead to a certain bias of unrecognised disease recurrence. Third, as a result of the long natural history of the disease particularly when treated, we could not use metastases or prostate cancer related mortality as the reference against which to validate biochemical parameters. We used failure free survival as we considered this a clinically meaningful composite outcome measure that reflects the recent Intermediate Clinical Endpoint in Carcinoma of the Prostate (ICECaP) consensus group's findings [16].

In localized prostate cancer focal therapy is a potential treatment with reduced morbidity because it can spare key structures such as neurovascular bundles, external sphincter, bladder neck and rectum, compared to radical treatment options [17]. Like every oncological treatment there is a need for a reliable surveillance tool to detect tumour recurrence in its early stage. Whereas PSA has a rational significance after radical surgery where the laboratory findings of a value above 0.2ng/ml demonstrates that recurrence is highly likely, its ability to define a tumour relapse after radiotherapy is reliant on an individual assessment of PSA kinetics. After radiotherapy the role of a PSA nadir individually defined as the lowest PSA value after therapy is important. A PSA above a defined cut-off of 2.0 ng/ml (for Phoenix criteria) above nadir has been the internationally accepted definition with sensitivity of 66% and specificity of 77%, a PPV of 35% and NPV

of 92% [18]. However, we have shown that PSA kinetics in the setting of treatment modalities in which the prostate gland is only treated partially, like in focal HIFU, are not predictive of treatment outcome. This has face validity considering that not only is tissue left untreated and continues to secrete PSA, there can be a significant inter-patient difference in the volume of treated prostate tissue, in the prostate volume itself, and in the extent of local tissue inflammation and subsequent benign growth with time as well as the proportion of PSA secreted by the tumour itself [19].

Nevertheless a predictive model, which allows us to accurately identify a significant tumour recurrence after focal HIFU, would be desirable. Although we have shown reasonable sensitivity for several cut-offs, the problem remains the high rate of false positives. In reality, such a low specificity would lead to further diagnostics. In general it would not only have a relevant impact on general costs due to MRI and/or prostate biopsies, but also unnecessarily raise the risk of biopsy-related complications [20].

mpMRI seems a more reliable tool of surveillance than PSA testing [15]. While intermediate risk prostate cancer usually shows relatively slow growing characteristic, a first mpMRI at the first year time stage is optimal considering that an earlier mpMRI can be difficult to interpret due to local inflammation and tissue changes post HIFU, which are often slowly resorbed. The NPV of a mpMRI at 12 months has been shown by us to be over 95% for presence of any high volume Gleason 6 or any Gleason 3+4 disease and biopsy could be considered in the setting where the mpMRI is suspicious or equivocal to detect residual or recurrent disease. The frequency of mpMRI and biopsy thereafter is uncertain but our current study demonstrates that routine mpMRI with or without biopsy may be the optimal approach rather than relying of PSA triggers for these. Validating different approaches within prospective cohorts and clinical trials will be necessary.

Conclusion

We have shown that PSA kinetics following focal HIFU therapy are not predictive of failure with any 'nadir plus' definition leading to significant rates of false positives. PSA criteria should not be used to define failure after focal HIFU therapy.

Authorship

PH, HUA, SG and NM were responsible for data collection, analysis of the data. HUA and PH were responsible for production of the first draft. PH and HUA completed the data analysis. All authors were involved in data collection, manuscript preparation/drafting and approval of the final draft. HUA had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. HUA is guarantor of the study.

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Table 1. Descriptive statistics		
Determinant	Mean/median/n	S.d./IQR/%
Age at treatment, median (IQR)	66	60-71
ADT pre treatment, N, (%)	71	11.9 %
Gleason score pre treatment, median (range)	7	6-9
3+3, N, (%)	*117*	*19.63 %*
3+4	*377*	*63.26 %*
4+3	*91*	*15.27 %*
4+4	*10*	*1.68 %*
4+5	*0*	
5+4	*1*	*0.17 %*
5+5	*0*	
T-stadium pre treatment, median, (range)	2	T1c-T3b
T1c, N, (%)	*49*	*8.15 %*
T2 (not further classified)	*250*	*41.94 %*
T2a	*61*	*10.23 %*
T2b	*58*	*9.71 %*
T2c	*104*	*17.50 %*
T3a	*68*	*11.44 %*
T3b	*6*	*1.04 %*
Treatment failures, N, (%)	209	35.07 %
Metastases from prostate cancer (not further treated), N, *(% of failures)*	2	*0.96 %*
2nd treatment, N, *(% of failures)*	162	*77.51 %*
ADT/chemotherapy, N, *(% of 2nd treatments)*	2	*1.23 %*
Cryotherapy, N, *(% of 2nd treatments)*	8	*4.94 %*
EBRT, N, *(% of 2nd treatments)*	11	*6.79 %*
RRP, N, *(% of 2nd treatments)*	19	*11.73 %*
HIFU, N, *(% of 2nd treatments)*	122	*75.31 %*
only positive biopsies post-HIFU (Gleason score min. 7, not further treated), N, *(% of failures)*	45	*21.53 %*

Abbreviations: ADT, androgen-deprivation therapy; HIFU, high-intensity focused ultrasound; IQR, interquartile range; mth, month; EBRT, external beam radiotherapy; RRP, retropubic radical prostatectomy;

Table 2. PSA development					
Determinant	Treatment failures		Non-treatment failures		p-value
	median	IQR	median	IQR	
PSA values, ng/ml					
pre-HIFU	7.80	5.96-10.45	6.77	4.65-9.71	< 0.001
at 3 mth	2.74	1.62-4.61	2.65	1.41-4.84	0.850
at 6 mth	3.00	1.70-4.91	2.61	1.21-4.60	0.070
at 9 mth	3.39	2.07-5.30	2.31	1.30-4.30	0.001
at 12 mth	3.70	2.12-6.20	2.35	1.23-4.12	< 0.001
at 15 mth	3.81	2.15-6.47	2.62	1.12-4.39	0.044
at 18 mth	3.70	2.86-7.10	2.70	1.70-4.39	< 0.001
at 21 mth	3.84	2.70-6.30	2.40	1.30-4.50	0.003
at 24 mth	5.25	3.18-7.00	2.37	1.33-3.78	< 0.001
at 27 mth	4.09	2.69-6.48	2.48	1.15-4.71	< 0.001
at 30 mth	4.25	2.58-6.90	2.21	1.27-3.78	0.017
at 33 mth	5.22	3.14-7.70	2.86	1.31-4.77	0.017
at 36 mth	4.20	2.37-6.10	2.25	1.38-4.75	0.055
at 39 mth	4.80	3.50-7.77	2.50	1.78-4.45	0.001
at 42 mth	5.54	3.05-9.30	2.65	1.64-4.49	0.042
at 45 mth	5.41	3.53-6.85	2.30	1.70-4.44	0.002
at 48 mth	5.53	3.60-7.51	2.05	1.36-3.82	0.001
at 51 mth	6.35	3.30-7.20	2.83	1.52-5.62	0.414
at 54 mth	3.64	2.54-7.18	3.30	1.55-5.28	0.935
at 57 mth	6.30	3.97-7.48	2.74	1.35-5.59	0.007
at 60 mth	6.21	4.09-9.04	2.54	1.65-5.75	0.011
at 63 mth	4.03	3.81-5.87	2.61	1.70-4.53	0.043
at 66 mth	5.11	4.02-6.88	4.97	2.19-8.52	1.000
at 69 mth	4.25	2.93-12.76	2.66	2.00-7.40	0.490
at 72 mth	4.32	3.67-7.03	2.79	1.83-7.16	0.464
at 75 mth	5.04	2.29-7.04	2.71	2.09-6.40	0.858
Nadir post-HIFU	2.36	1.38-3.77	2.04	0.99-3.60	0.090
Abbreviations: mth, month;					

| Table 3. PSA predictive models				
Test variable	Sensitivity (%)	Specificity (%)	False negative rate (%)	False positive rate (%)
ASTRO criteria	18.67 %	68.26 %	81.33 %	31.74 %
PSA nadir plus:				
0.1	61.22 %	9.84 %	38.78 %	90.16 %
0.2	58.82 %	12.90 %	41.18 %	87.10 %
0.3	58.49 %	17.21 %	41.51 %	82.79 %
0.4	55.56 %	19.88 %	44.44 %	80.12 %
0.5	46.43 %	22.40 %	53.57 %	77.60 %
0.6	45.16 %	25.57 %	54.84 %	74.43 %
0.7	43.08 %	29.46 %	56.92 %	70.54 %
0.8	42.25 %	31.72 %	57.75 %	68.28 %
0.9	42.86 %	34.47 %	57.14 %	65.53 %
1.0	43.37 %	38.15 %	56.63 %	61.85 %
1.1	43.18 %	40.09 %	56.82 %	59.91 %
1.2 (Stuttgart criteria)	39.13 %	43.08 %	60.87 %	56.92 %
1.3	38.00 %	44.97 %	62.00 %	55.03 %
1.4	37.50 %	47.63 %	62.50 %	52.37 %
1.5	37.84 %	50.46 %	62.16 %	49.54 %
1.6	35.34 %	52.67 %	64.66 %	47.33 %
1.7	33.61 %	54.67 %	66.39 %	45.33 %
1.8	32.52 %	56.37 %	67.48 %	43.63 %
1.9	32.54 %	57.72 %	67.46 %	42.28 %
2.0 (Phoenix criteria)	32.56 %	59.09 %	67.44 %	40.91 %
Abbreviations: ASTRO criteria, 3 consistent PSA raises				

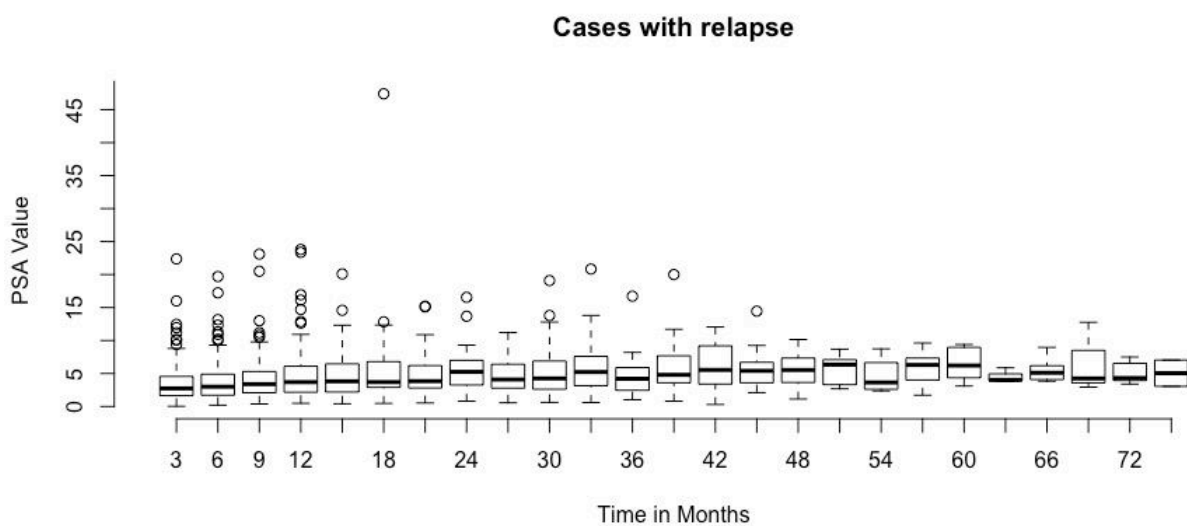Figure 1. PSA development (line graph)
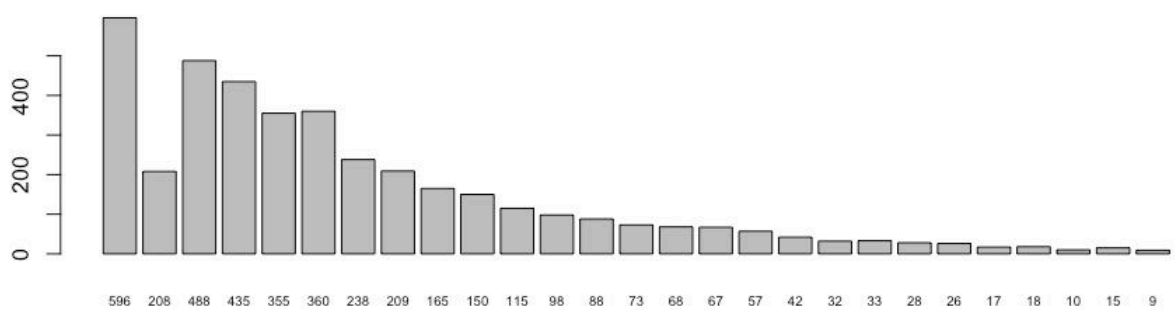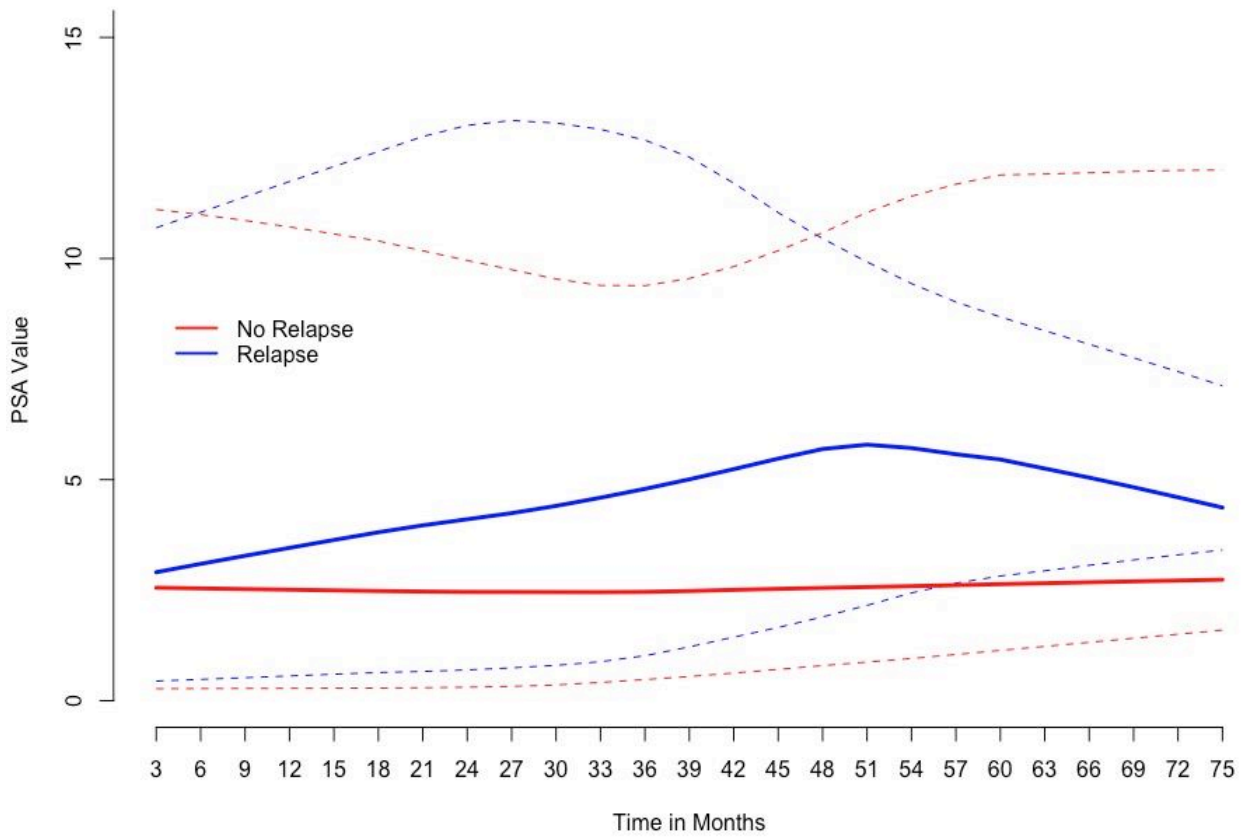
Figure 2. PSA development (Boxplots)

Cases with no relapse

Cases with relapse
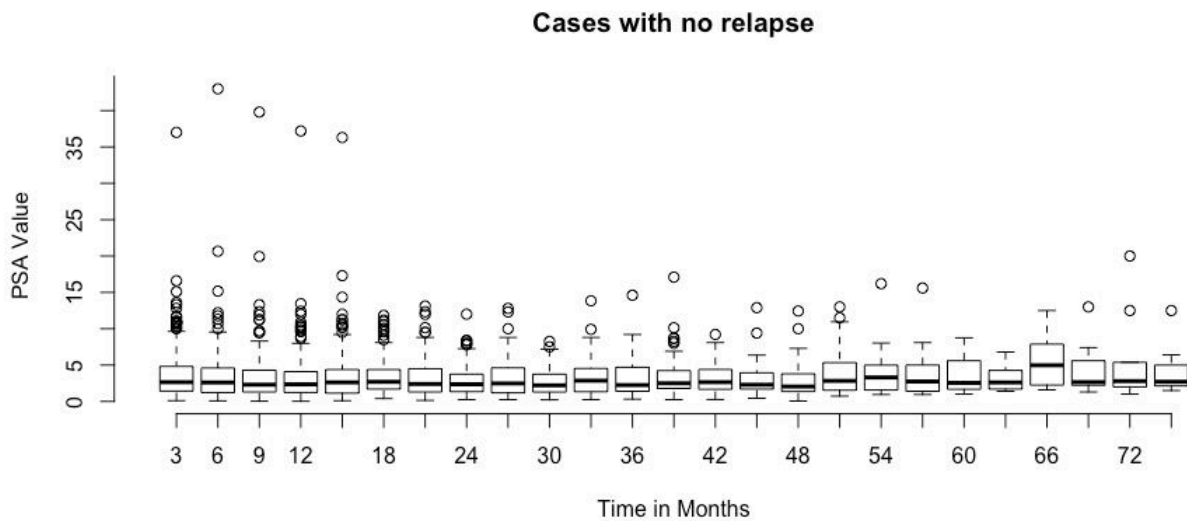
Figure 3. Receiver operative characteristic (ROC) curve

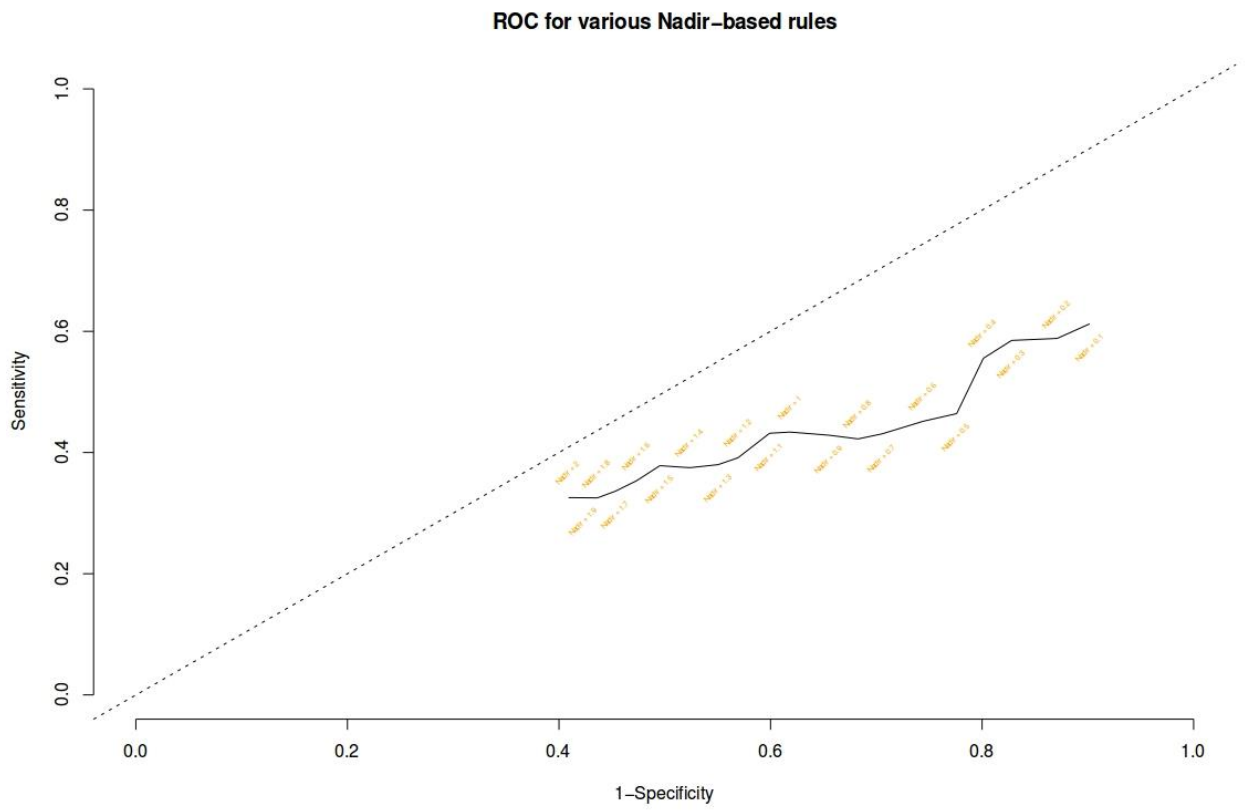ROC for various Nadir-based rules

Figure 4.PSA development: cases with pre-HIFU androgen deprivation therapy excluded (line graph)
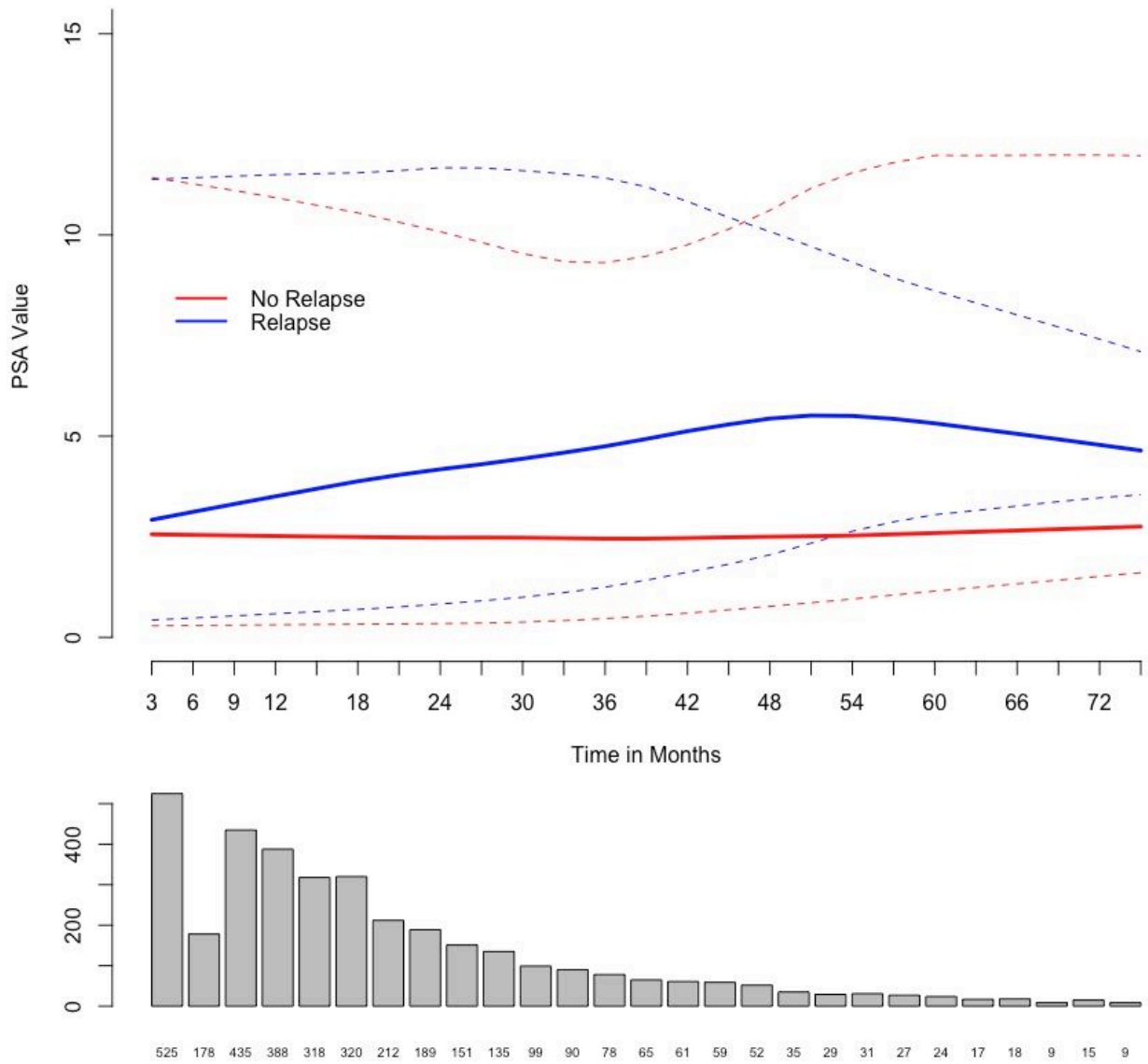
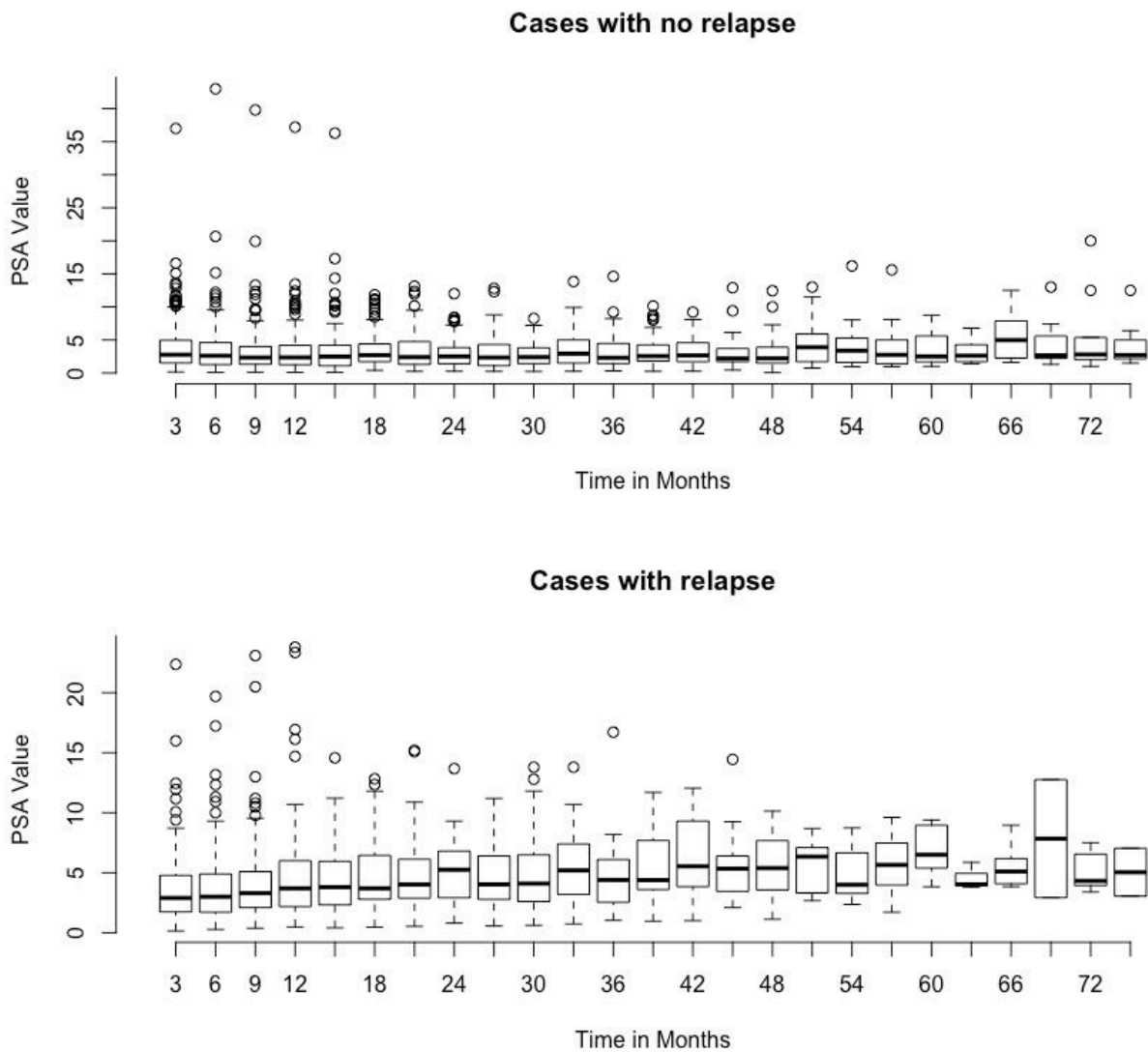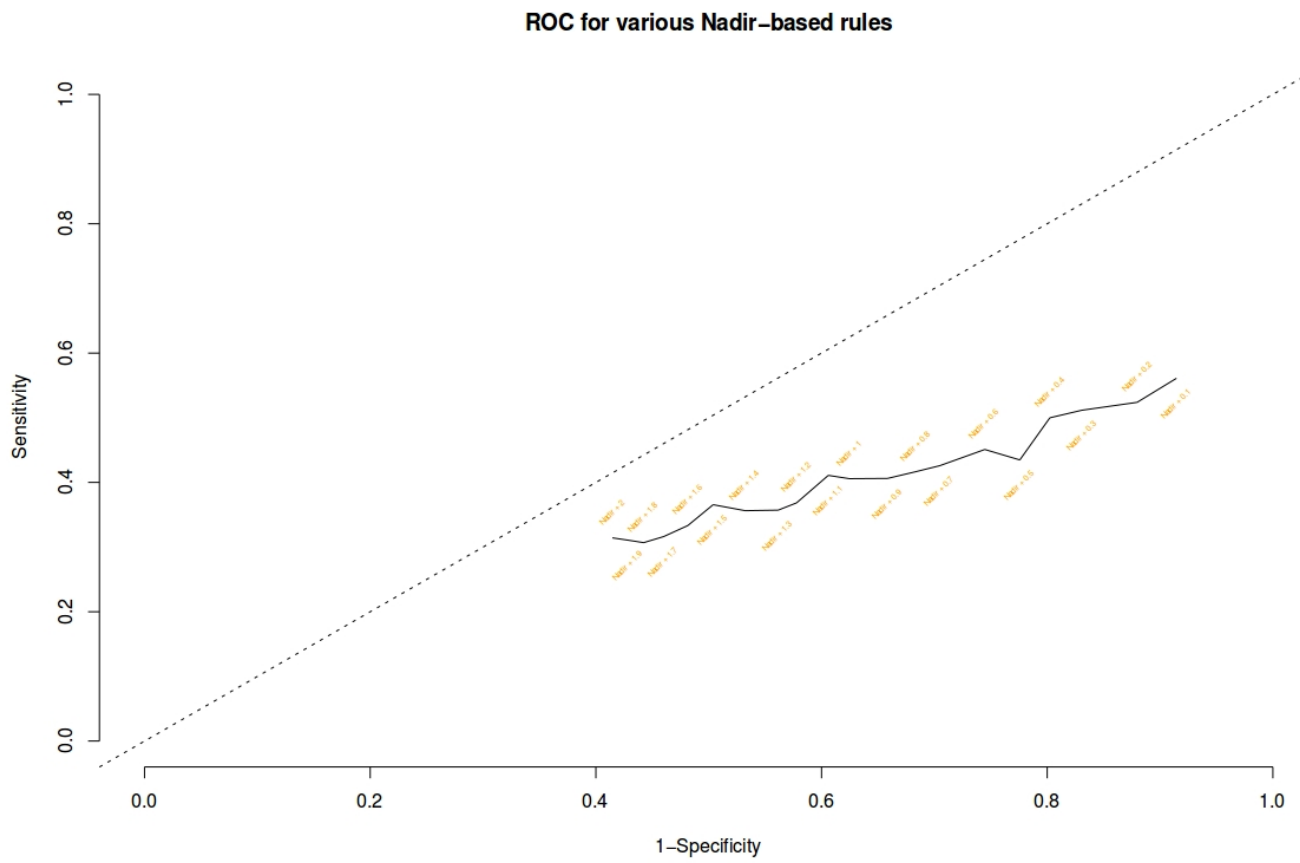Figure 5. PSA development: cases with pretherapeutic androgen deprivated therapy excluded (Boxplots)

Cases with no relapse

Cases with relapse

Figure 6. ROC curve: cases with pre-HIFU androgen deprivation therapy excluded

ROC for various Nadir-based rules

Appendix Table 1. PSA predictive models for Gleason score group 3+3				
Test variable	Sensitivity (%)	Specificity (%)	False negative rate (%)	False positive rate (%)
ASTRO criteria	12.50 %	73.42 %	87.50 %	26.58 %
PSA nadir plus:				
0.1	58.33 %	7.69 %	41.67 %	92.31 %
0.2	58.33 %	8.79 %	41.67 %	91.21 %
0.3	58.33 %	10.99 %	41.67 %	89.01 %
0.4	50.00 %	13.19 %	50.00 %	86.81 %
0.5	33.33 %	16.48 %	66.67 %	83.52 %
0.6	38.46 %	22.22 %	61.54 %	77.78 %
0.7	38.46 %	24.44 %	61.54 %	75.56 %
0.8	38.46 %	25.56 %	61.54 %	74.44 %
0.9	35.71 %	30.34 %	64.29 %	69.66 %
1.0	35.71 %	34.83 %	64.29 %	65.17 %
1.1	28.57 %	37.08 %	71.43 %	62.92 %
1.2 (Stuttgart criteria)	33.33 %	40.91 %	66.67 %	59.09 %
1.3	37.50 %	41.38 %	62.50 %	58.62 %
1.4	37.50 %	44.83 %	62.50 %	55.17 %
1.5	35.29 %	48.84 %	64.71 %	51.16 %
1.6	38.89 %	50.59 %	61.11 %	49.41 %
1.7	33.33 %	51.76 %	66.67 %	48.24 %
1.8	33.33 %	52.94 %	66.67 %	47.06 %
1.9	36.84 %	54.76 %	63.16 %	45.24 %
2.0 (Phoenix criteria)	36.84 %	57.14 %	63.16 %	42.86 %
Abbreviations: ASTRO criteria, 3 consistent PSA raises				

Appendix Table 2. PSA predictive models for Gleason score group 3+4				
Test variable	Sensitivity (%)	Specificity (%)	False negative rate (%)	False positive rate (%)
ASTRO criteria	19.15 %	67.84 %	80.85 %	32.16 %
PSA nadir plus:				
0.1	64.00 %	10.19 %	36.00 %	89.81 %
0.2	59.26 %	13.13 %	40.74 %	86.88 %
0.3	55.56 %	18.32 %	44.44 %	81.68 %
0.4	57.14 %	21.00 %	42.86 %	79.00 %
0.5	56.67 %	23.51 %	43.33 %	76.49 %
0.6	51.52 %	26.43 %	48.48 %	73.57 %
0.7	47.22 %	31.63 %	52.78 %	68.37 %
0.8	48.78 %	33.66 %	51.22 %	66.34 %
0.9	47.73 %	36.07 %	52.27 %	63.93 %
1.0	48.00 %	39.73 %	52.00 %	60.27 %
1.1	46.15 %	41.75 %	53.85 %	58.25 %
1.2 (Stuttgart criteria)	40.74 %	44.03 %	59.26 %	55.97 %
1.3	37.70 %	46.53 %	62.30 %	53.47 %
1.4	37.50 %	48.41 %	62.50 %	51.59 %
1.5	36.76 %	50.53 %	63.24 %	49.47 %
1.6	33.80 %	52.54 %	66.20 %	47.46 %
1.7	32.43 %	54.91 %	67.57 %	45.09 %
1.8	32.05 %	57.25 %	67.95 %	42.75 %
1.9	31.65 %	58.52 %	68.35 %	41.48 %
2.0 (Phoenix criteria)	31.71 %	60.00 %	68.29 %	40.00 %
Abbreviations: ASTRO criteria, 3 consistent PSA raises				

Appendix Table 3. PSA predictive models for Gleason score group 4+3				
Test variable	Sensitivity (%)	Specificity (%)	False negative rate (%)	False positive rate (%)
ASTRO criteria	17.86 %	60.78 %	82.14 %	39.22 %
PSA nadir plus:				
0.1	54.55 %	11.76 %	45.45 %	88.24 %
0.2	54.55 %	17.65 %	45.45 %	82.35 %
0.3	61.54 %	19.70 %	38.46 %	80.30 %
0.4	53.85 %	22.73 %	46.15 %	77.27 %
0.5	30.77 %	24.24 %	69.23 %	75.76 %
0.6	28.57 %	24.62 %	71.43 %	75.38 %
0.7	28.57 %	24.62 %	71.43 %	75.38 %
0.8	20.00 %	28.13 %	80.00 %	71.88 %
0.9	29.41 %	30.65 %	70.59 %	69.35 %
1.0	29.41 %	33.87 %	70.59 %	66.13 %
1.1	40.00 %	35.59 %	60.00 %	64.41 %
1.2 (Stuttgart criteria)	33.33 %	39.66 %	66.67 %	60.34 %
1.3	33.33 %	41.38 %	66.67 %	58.62 %
1.4	36.36 %	45.61 %	63.64 %	54.39 %
1.5	39.13 %	50.00 %	60.87 %	50.00 %
1.6	33.33 %	54.55 %	66.67 %	45.45 %
1.7	33.33 %	56.36 %	66.67 %	43.64 %
1.8	29.17 %	56.36 %	70.83 %	43.64 %
1.9	28.00 %	57.41 %	72.00 %	42.59 %
2.0 (Phoenix criteria)	28.00 %	57.41 %	72.00 %	42.59 %
Abbreviations: ASTRO criteria, 3 consistent PSA raises				